

ANNUAL PUBLICATIONS

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**Graduate School of
Medical and Dental Sciences
Tokyo Medical and Dental University**

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Graduate School of Medical and Dental Sciences

Medical and Dental Sciences

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Oral Pathology

Professor
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Junior Associate Professor
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Assistant Professor
Kou Kayamori

Technical Staff
Miwako Hamagaki

Graduate Students
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Akane Wada
Shoko Ishida
Maiko Tsuchiya
TEERAWONG CHANYANUCH
Akiyo Sanpei
NGUYEN PHAN THE HUY

(1) Research

- 1) Pathology and biology associated with bone
- 2) Pathological and biological studies on oral cancers, odontogenic tumors and oral premalignant lesions
- 3) Pathological and biological studies on microenvironment associated with invasion and metastasis of cancers
- 4) Clinicopathological and diagnostic histopathological studies on oral and maxillofacial lesions

(2) Education

Lectures and microscope practice in the module “Pathology” to 3rd grade students. The Pathology module comprises two sections; General pathology and Oral pathology. Main objective of General pathology is to provide students knowledge on various diseases, which is essential to work in dental, medical and biological fields. Oral pathology provides detailed knowledge on oral diseases, which is indispensable for a dentist.

(3) Clinical Services & Other Works

Our staffs and graduate students participate in diagnostic pathology practice in the Dental Hospital, where nearly 3,000 specimens are annually submitted to laboratory investigation. Our staffs and graduate students also participate in autopsy in the Medical Hospital in cooperation with the staffs and graduate students at the Faculty of Medicine.

(4) Publications

[Original Articles]

1. Yae Ohata, Maiko Tsuchiya, Hideaki Hirai, Satoshi Yamaguchi, Takumi Akashi, Kei Sakamoto, Akira Yamaguchi, Tohru Ikeda, Kou Kayamori. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. *PLoS ONE*. 2018; 13(2); e0191865
2. Minamizato, T., Koga, T., I, T., Nakatani, Y., Sumita, Y., Ikeda, T., Asahina, I.. Clinical application of autogenous partially demineralized dentin matrix prepared immediately after extraction for alveolar bone regeneration in implant dentistry: a pilot study *International Journal of Oral and Maxillofacial Surgery*. 2018.01; 47; 125-132
3. Katase, N., Nishimatsu, S. I., Yamauchi, A., Yamamura, M., Terada, K., Itadani, M., Okada, N., Hassan, N. M. M., Nagatsuka, H., Ikeda, T., Nohno, T., Fujita, S.. DKK3 overexpression increases malignant properties of head and neck squamous cell carcinoma cells *Oncology Research*. 2018.01; 26; 45-58
4. Ohata Y, Tsuchiya M, Hirai H, Yamaguchi S, Akashi T, Sakamoto K, Yamaguchi A, Ikeda T, Kayamori K. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. *PLoS ONE*. 2018.02; 13(2); e0191865
5. Yae Ohata, Kou Kayamori, Akane Yukimori, Kanako Sumikura, Toshimitsu Ohsako, Hiroyuki Harada, Kei Sakamoto, Tohru Ikeda. A lesion categorized between ghost cell odontogenic carcinoma and dentinogenic ghost cell tumor with CTNNB1 mutation. *Pathol. Int.*. 2018.05; 68(5); 307-312
6. Keiko Miura, Takumi Akashi, Noboru Ando, Shinya Ayabe, Kou Kayamori, Takeshi Namiki, Yoshinobu Eishi. Homeobox transcriptional factor engrailed homeobox 1 is expressed specifically in normal and neoplastic sweat gland cells. *Histopathology*. 2018.06; 72(7); 1199-1208
7. Komiya R, Wada T, Tsushima F, Sakamoto K, Ikeda T, Yamaguchi A, Harada H, Uo M. Quantitation and distribution of metallic elements in sequestra of medication-related osteonecrosis of jaw (MRONJ) using inductively coupled plasma atomic emission spectroscopy and synchrotron radiation X-ray fluorescence analysis. *Journal of bone and mineral metabolism*. 2018.11;
8. Sawangarun Wanlada, Mandasari Masita, Aida Junko, Morita Kei-ichi, Kayamori Kou, Ikeda Tohru, Sakamoto Kei. Loss of Notch1 predisposes oro-esophageal epithelium to tumorigenesis *EXPERIMENTAL CELL RESEARCH*. 2018.11; 372(2); 129-140
9. Shimizu R, Tanaka K, Oikawa Y, Tomioka H, Kayamori K, Ikeda T, Yoshioka T, Ebihara A, Harada H. Epithelioid cell granuloma with caseating necrosis possibly caused by periapical periodontitis: a case report. *Journal of medical case reports*. 2018.12; 12(1); 365
10. Rokutanda, S., Yamada, S., Kawasaki, G., Kawano, T., Yanamoto, S., Fujita, S., Ikeda, T., Umeda, M.. Solitary neurofibroma of the maxillary sinus: Report of a case *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*. 24(201200); 237-240

[Conference Activities & Talks]

1. NAKAZATO Keiichiro, UZAWA Narikazu, KAYAMORI Kou, TSUCHIYA Maiko, WATANABE Hiroshi, SUMINO Jun, MICHI Yasuyuki, YAMAGUCHI Satoshi. The Change of Metabolic Control Mechanism in the Development and Progress of the Tongue Carcinoma. 2018.01.25 Niigata, Japan

Bacterial Pathogenesis

Professor
SUZUKI Toshihiko
Associate Professor
ASHIDA Hiroshi
Assistant Professor
SUZUKI Shiho
Research fellow of JSPS
TSUKAZAKI Masayuki
Graduate Student
OKANO Tokuju
Graduate Student
YAMAMURA Kiyonobu
Graduate Student
LEE WANANTHAWET Anongwee (Department of Periodontology)
Graduate Student
ABASS Adiza (Department of Molecular Virology)
Graduate Student
KINOSHITA DAITOKU Ryo (University of Tokyo)
Research Co-investigator
TANAKA Mototsugu
Technical Assistant Staff
IIDA Tamako

(1) Research

Research Subjects

- 1) Molecular mechanisms of infection by pathogenic bacteria
- 2) Mechanisms of activation and regulation of inflammasomes via Nod-like receptors and caspase activation
- 3) Study of virulent genes based on comparative genomics
- 4) Relationship between persistent bacterial infection and chronic inflammatory diseases such as adipose or diabetes

(2) Lectures & Courses

Purpose of Education

The aim of our laboratory in the graduate course is to understand molecular mechanism of pathogen infection and host immune responses. Students also learn planning of research, experiments and methods for evaluating.

(3) Publications

[Original Articles]

1. Shiho Suzuki, Toshihiko Suzuki, Hitomi Mimuro, Tsunehiro Mizushima, Chihiro Sasakawa. Shigella hijacks the glomulin-cIAPs-inflammasome axis to promote inflammation. *EMBO Rep.*. 2018.01; 19(1); 89-101
2. Yuhei Maruzuru, Takeshi Ichinohe, Ryota Sato, Kensuke Miyake, Tokuju Okano, Toshihiko Suzuki, Takumi Koshiba, Naoto Koyanagi, Shumpei Tsuda, Mizuki Watanabe, Jun Arii, Akihisa Kato, Yasushi Kawaguchi. Herpes Simplex Virus 1 VP22 Inhibits AIM2-Dependent Inflammasome Activation to Enable Efficient Viral Replication. *Cell Host Microbe*. 2018.02; 23(2); 254-265.e7
3. Shiho Suzuki, Toshihiko Suzuki, Chihiro Sasakawa. IAP family members are involved in inflammasome activation in response to bacterial infection *Japanese Journal of Bacteriology*. 2018.02; 73(1); 130
4. Ayumu Saeki, Akira Hasebe, Toshihiko Suzuki, Ken-ichiro Shibata . Translocation of mycoplasmal lipopeptide FSL-1 into cytosol for the NLRP3 inflammasome activation *Japanese Journal of Bacteriology*. 2018.02; 73(1); 40
5. Ayumi Saeki, Masahiro Sugiyama, Akira Hasebe, Toshihiko Suzuki, Ken-Ichiro Shibata. Activation of NLRP3 inflammasome in macrophages by mycoplasmal lipoproteins and lipopeptides. *Mol Oral Microbiol*. 2018.04;
6. Evaluation the biological effects of Ozone Ultrafine-Bubble Water in vitro *Journal of the Japanese Society of Periodontology*. 2018.05; 60; 135
7. Yamaguchi Takayoshi, Higa Naomi, Okura Nobuhiko, Matsumoto Arina, Hermawan Idam, Yamashiro Tetsu, Suzuki Toshihiko, Toma Claudia. Characterizing interactions of *Leptospira interrogans* with proximal renal tubule epithelial cells *BMC MICROBIOLOGY*. 2018.07; 18(1); 64
8. Nakasone Noboru, Ogura Yasunori, Higa Naomi, Toma Claudia, Koizumi Yukiko, Takaesu Giichi, Suzuki Toshihiko, Yamashiro Tetsu. Effects of *Psidium guajava* leaf extract on secretion systems of gram-negative enteropathogenic bacteria *MICROBIOLOGY AND IMMUNOLOGY*. 2018.07; 62(7); 444-453
9. Okano T, Ashida H, Suzuki S, Shoji M, Nakayama K, Suzuki T. *Porphyromonas gingivalis* triggers NLRP3-mediated inflammasome activation in macrophages in a bacterial gingipains-independent manner. *European journal of immunology*. 2018.10;
10. Alafate Ayibieke, Wakana Sato, Samiratu Mahazu, Isaac Prah, John Addow-Thompson, Mitsuko Ohashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Molecular characterisation of the NDM-1-encoding plasmid p2189-NDM in an *Escherichia coli* ST410 clinical isolate from Ghana. *PLoS ONE*. 2018.12; 13(12); e0209623

[Conference Activities & Talks]

1. Shiho Suzuki. Machinery of the inflammasome regulation in response to bacterial infection.. 2018.03.06 the Institute of Medical Science, the University of Tokyo
2. Shiho Suzuki, Toshihiko Suzuki, Hitomi Mimuro, Chihiro Sasakawa. IAP family members are involved in inflammasome activation in response to bacterial infection. The 91st Annual Meeting of Japanese Society for Bacteriology 2018.03.27 Fukuoka
3. Shiho Suzuki, Toshihiko Suzuki, Hitomi Mimuro, Chihiro Sasakawa,. IAP family members are involved in inflammasome activation in response to bacterial infection. The 91st Annual Meeting of Japanese Society for Bacteriology 2018.03.27 Fukuoka convention center

Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Tatsukuni Ohno
Adjunct instructor	Hiroshi Kiyono
	Takeshi Azuma
Graduate Students(Doctor)	
	Naoto Nishii(Oral and Maxillofacial Surgery)(~Mar.)
	Xia Yulong
	Emi Furusawa(Pediatric Dentistry)
	Hiroshi Katou(Maxillofacial Surgery)(~May)
	Yang Yue
	Yoshihisa Kashima(Oral and Maxillofacial Surgery)
	Ao Xiang(Pulp Biology and Endodontics)
	Wongtim Keeratika
	Amrita Widyagarini Subagyo(Pediatric Dentistry)(Jan.~)
	Hidetake Tachinami(University of Toyama)(~Mar.)
Affiliated Researcher	
	Hidetake Tachinami(University of Toyama)(Apr.~)

(1) Research

Research Subjects

- 1) Mechanisms of immune responses in oral diseases
- 2) Studies on lymphocyte functional molecules
- 3) Immunotherapy by molecular targeting

(2) Lectures & Courses

Purpose of Education

Main objective of Molecular Immunology in the graduate course is to understand and study how the immune system works for biological defense. Students also learn immunopathology and immunophysiology of systemic and organ-specific immune diseases and how the immune diseases control and regulate.

(3) Publications

[Original Articles]

1. Ohno T, Zhang C, Kondo Y, Kang S, Furusawa E, Tsuchiya K, Miyazaki Y, Azuma M. The immune checkpoint molecule VISTA regulates allergen-specific Th2-mediated immune responses. Int Immune. 2018.02; 30(1); 3-11

2. Nishii N, Tachinami H, Kondo Y, Xia Y, Kashima Y, Ohno T, Nagai S, Li L, Lau W, Harada H, Azuma M. Systemic administration of a TLR7 agonist attenuates regulatory T cells by dendritic cell modification and overcomes resistance to PD-L1 blockade therapy. *Oncotarget*. 2018.03; 9(17); 13301-13312
3. Azuma T, Sato Y, Ohno T, Azuma M, Kume H.. Serum soluble B7-H4 is a prognostic marker for patients with non –metastatic clear cell renal cell carcinoma. *Plos One*. 2018.07; 13(7); e01997119
4. Arae K, Morita H, Unno H, Motomura K, Toyama S, Okada N, Ohno T, Tamari M, Orimo K, Mishima Y, Suto H, Okumura K, Sudo K, Miyazawa H, Taguchi H, Saito H, Matsumoto K, Nakae S. Chitin promotes antigen-specific Th2 cell-mediated murine asthma through induction of IL-33-mediated IL-1 β production by DCs. *Sci Rep*. 2018.08; 8(1); 11721

Advanced Biomaterials

Professor UO Motohiro
 Assistant Professor WADA Takahiro
 Graduate Student CHAIAMORNSUP Patcharanun
 Graduate Student Kang Donghoon (Pulp Biology and Endodontics)
 Graduate Student KOMIYA Ruri (Oral and Maxillofacial Surgery)
 Graduate Student KOYAMA Akihiro (Orthodontic Science)
 Graduate Student KINJO Rio (Sports Medicine and Dentistry)
 Graduate Student Saleh Sherif Adel Abdelfattah (Pulp Biology and Endodontics)

(1) Research

1. Analysis of Dental and biomedical materials and biological tissue using the synchrotron radiation.
 Research is aimed to apply the new analysis method using synchrotron radiation for the estimation of various properties of the dental and biomedical materials.
2. Development of the functional dental and biomedical materials using glass and ceramics.
 Research is aimed to develop and evaluate the new glass and ceramics based materials as the dental and biomedical materials, e.g. composite resins, glass ionomer cements, dental porcelains and zirconia ceramics.

(2) Education

1. Lecture of unit “Biomaterials and Dental Materials”
 A series of lectures on the “science on biomaterials”, “properties of dental and biomedical materials”, “application of dental materials” will be taught through the lecture and practice.
2. Lecture of unit “Advanced Biomaterials” (graduate school)
 Evaluation methods of various dental and biomedical materials will be taught.

(3) Publications

[Original Articles]

1. Lai Wei-Jen, Midorikawa Yoshiyuki, Kanno Zuisei, Takemura Hiroshi, Suga Kazuhiro, Soga Kohei, Ono Takashi, Uo Motohiro. A new orthodontic force system for moment control utilizing the flexibility of common wires: Evaluation of the effect of contractile force and hook length Journal of the Formosan Medical Association. 2018.01; 117(1); 71-79
2. Wakisaka Y, Uehara H, Yuan Q, Kido D, Wada T, Uemura Y, Kamei Y, Kuroda S, Ohira A, Takakusagi S, Asakura K. Extracting the surface states of Pt films under electrochemical environments using total reflection fluorescence X-ray absorption fine structure spectroscopy Photon Factory Activity Report 2017. 2018.04; 35;
3. Yuki Wakisaka, Daiki Kido, Hiromitsu Uehara, Qiuyi Yuan, Satoru Takakusagi, Yohei Uemura, Toshihiko Yokoyama, Takahiro Wada, Motohiro Uo, Tomohiro Sakata, Oki Sekizawa, Tomoya Uruga, Yasuhiro

- Iwasawa, Kiyotaka Asakura. A Demonstration of Pt L3-Edge EXAFS Free from Au L3-Edge Using Log-Spiral Bent Crystal Laue Analyzers Catalysts. 2018.05; 8(5); 204
4. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takahashi, Motohiro Uo. Improvement of the Shock Absorption Ability of a Face Guard by Incorporating a Glass-Fiber-Reinforced Thermoplastic and Buffering Space BioMed Research International. 2018.05; 2018; 1-8
5. Sai Kham Lyann, Tomohiro Takagaki, Toru Nikaido, Motohiro Uo, Masaomi Ikeda, Alireza Sadr, Junji Tagami. Effect of Different Surface Treatments on the Tensile Bond Strength to Lithium Disilicate Glass Ceramics. J Adhes Dent. 2018.05; 20(3); 261-268
6. Yoshida Yuriko, Churei Hiroshi, Takeuchi Yasuo, Wada Takahiro, Uo Motohiro, Izumi Yuichi, Ueno Toshiaki. Novel antibacterial mouthguard material manufactured using silver-nanoparticle-embedded ethylene-vinyl acetate copolymer masterbatch DENTAL MATERIALS JOURNAL. 2018.06; 37(3); 437-444
7. Takahashi A, Takagaki T, Wada T, Uo M, Nikaido T, Tagami J. The effect of different cleaning agents on saliva contamination for bonding performance of zirconia ceramics. Dental materials journal. 2018.07; 37(5); 734-739
8. Ayako Nakamoto, Masaomi Ikeda, Noriko Hiraishi, Toru Nikaido, Motohiro Uo, Junji Tagami. Effect of fluoride mouthrinse on adhesion to bovine root dentin. Dent Mater J. 2018.07;
9. Yuan Q, Wakisaka Y, Uemura Y, Wada T, Ariga-Miwa H, Takakusagi S, Asakura K, Brankovic SR. Reaction Stoichiometry and Mechanism of Pt Deposition via Surface Limited Redox Replacement of Copper UPD Layer on Au(111) The Journal of Physical Chemistry C. 2018.07; 122(29); 16664-16673
10. Wakisaka Y, Kido D, Uehara H, Yuan Q, Feiten FE, Mukai S, Takakusagi S, Uemura Y, Yokoyama T, Wada T, Uo M, Sekizawa O, Uruga T, Iwasawa Y, Asakura K. Development of Surface Fluorescence X-ray Absorption Fine Structure Spectroscopy using a Laue-Type Monochromator. Chemical record (New York, N.Y.). 2018.08;
11. Alquarni Dhaifallah Abdullah G, Masatoshi Nakajima, Keiichi Hosaka, Kurumi Ide, Daiki Nagano, Takahiro Wada, Masaomi Ikeda, Teerapong Mamane, Ornnicha Thanatvarakorn, Prasansuttiorn Taweesak, Richard Foxton, Junji Tagami. The repair bond strength to resin matrix in cured resin composites with different degrees of conversion after water aging. Dental Materials Journal. 2018.08;
12. Shimizu H, Inokoshi M, Takagaki T, Uo M, Minakuchi S. Bonding Efficacy of 4-META/MMA-TBB Resin to Surface-treated Highly Translucent Dental Zirconia. J Adhes Dent. 2018.09; 20(5); 453-459
13. Atomura Junji, Inoue Go, Nikaido Toru, Yamanaka Keisuke, Uo Motohiro, Tagami Junji. Influence of FCP-COMPLEX on bond strength and the adhesive: artificial caries-affected dentin interface Dental Materials Journal. 2018.10; 37(5); 775-782
14. Komiya R, Wada T, Tsushima F, Sakamoto K, Ikeda T, Yamaguchi A, Harada H, Uo M. Quantitation and distribution of metallic elements in sequestra of medication-related osteonecrosis of jaw (MRONJ) using inductively coupled plasma atomic emission spectroscopy and synchrotron radiation X-ray fluorescence analysis. Journal of bone and mineral metabolism. 2018.11;
15. Donghoon Kang, Takahiro Wada, Motohiro Uo, Takashi Okiji. Influence of bentonite addition on the handling and physical properties of tricalcium silicate cement Asian Pacific Journal of Dentistry. 2018.12; 18(2); 37-44

[Conference Activities & Talks]

1. Wakisaka Yuki, Kido Daiki, Uehara Hiromitsu, Yuan Qiuyi, Felix E. Feiten, Mukai Shingo, Takakusagi Satoru, Uemura Yohei, Yokoyama Toshihiko, Wada Takahiro, Uo Motohiro, Sekizawa Oki, Uruga Tomoya, Iwasawa Yasuhiro, Asakura Kiyotaka. Application of fluorescence XAFS using a BCLA to model fuel cell catalysts. Symposium on Nanomaterials for Environmental Purification and Energy Conversion (SNEPEC) 2018.02.20 Sapporo, Japan
2. Chaiaornsup P, Uo M, Yamamoto Y, Yasue T, Iwasaki N, Takahashi H. Effect of build direction and exposure time on edge reproducibility of prism specimens using DLP. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.14 Osaka, Japan

3. Wada Takahiro, Churei Hiroshi, Ueno Toshiaki, Uo Motohiro. Application of a carbon-fiber reinforced thermoplastic to face guard. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
4. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Yoshida Yuriko, Tanabe Gen, Uo Motohiro, Takahashi Hidekazu, Ueno Toshiaki. The behavior of pressure sensor with a built-in mouth guard material. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
5. Wada Takahiro, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Ueno Toshiaki, Uo Motohiro. Shock absorption analysis of face guards made of carbon fiber reinforced thermoplastics using high-speed camera. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
6. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The evaluation of a force sensor for the development of the mouth guard type wearable sensor. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
7. Churei H, Wada T, Abe K, Sasaki Y, Kondo T, Takeuchi K, Miura H, Uo M, Takahashi H, Ueno T. Influence of the setting area of buffering space and impact properties on the effect of application on glass fiber reinforced materials toward high functionality of mouth guard. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
8. Akifumi Takahashi, Tomohiro Takagaki, Toru Nikaido, Takahiro Wada, Motohiro Uo, Junji Tagami. Effect of different cleaning agents for saliva contaminated zirconia ceramics. IADR/PER GENERAL SESSION 2018.07.25
9. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Basic Properties of Novel S-PRG Contained Cement for Root Caries. 96th General Session and Exhibition of the IADR 2018.07.26 London
10. Kashaboina Upendar, Sirisit Natee, Ariga-Miwa Hiroko, Takakusagi Satoru, Asakura Kiyotaka, Wada Takahiro, Nishikawa Yuta, Kuriyama Fumiya, Dipu Arnoldus Lambertus, Inokuchi Shoji, Yamanaka Ichiro, Ogiwara Hitoshi. Methane Activation by In/SiO₂ catalyst: Structure Elucidation using Operando QXAFS technique. TOCAT8 (The 8th Tokyo Conference on Advanced Catalytic Science and Technology) 2018.08.05 PACIFICO Yokohama, Yokohama, Japan
11. Kashaboina Upendar, Sirisit Natee, Ariga-Miwa Hiroko, Takakusagi Satoru, Asakura Kiyotaka, Wada Takahiro, Nishikawa Yuta, Kuriyama Fumiya, Dipu Arnoldus Lambertus, Inokuchi Shoji, Yamanaka Ichiro, Ogiwara Hitoshi. In situ quick X-ray absorption fine structure (QXAFS) study of In/SiO₂ catalyst under thermal dehydrogenation of methane. JXAFS16 2018.09.04 Sapporo, Japan
12. Tomoya Konishi, Masaru Kamano, Nobutomo Uehara, Takeshi Fujihara, Takanori Kozai, Weiwei Xu, Shun Kamada, Motohiro Uo, Takahiro Wada. Photoluminescence and Structure of Copper and Tin-doped Glasses. ICG Annual Meeting 2018 2018.09.23 PACIFICO Yokohama, Yokohama, Japan
13. Takahiro Wada, Hiroshi Churei, Gen Tanabe, Rio Kinjo, Yasuhito Takashima, Toshiaki Ueno, Fumiyoshi Minami, Motohiro Uo. Shock absorption analysis of face guards made of carbon fiber-reinforced thermoplastics using high-speed camera and digital image correlation. 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25
14. Rio Kinjo, Takahiro Wada, Hiroshi Churei, Hidekazu Takahashi, Toshiaki Ueno, Motohiro Uo. Evaluating the use of a force sensor for the development of a mouth guard-type wearable sensor. 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
15. Yasuhito Takashima, Takahiro Wada, Motohiro Uo, Fumiyoshi Minami. Dynamic numerical analysis of impact response for implant materials. 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25
16. Chaiamornsups P, Iwasaki N, Yasue T, Wada T, Uo M, Takahashi H. Effects of glycerin immersion during post-curing process on mechanical property of polymers fabricated using digital light process. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo Garden Place Hotel

17. Donghoon Kang, Takahiro Wada, Motohiro Uo, Takashi Okiji. Rheological and physical properties of phyllosilicate clay added tricalcium silicate. IFEA (International Federation of Endodontic Association) 2018.10.04 Seoul, Korea
18. Shimizubata M, Inokoshi M, Hatano K, Wada T, Takahashi R, Uo M, Minakuchi S. Acid buffering capacity of a novel S-PRG filler containing glass ionomer cement. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Sapporo
19. Hatano K, Inokoshi M, Uo M, Wada T, Takahashi R, Minakuchi S. Acid buffering capacity of a novel S-PRG filler containing denture adhesive. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Sapporo

Oral Radiation Oncology

Professor	Masahiko MIURA
Assistant Professor	Atsushi KAIDA
Clinical Fellow	Shota SHIMIZU (～ March)
	Ryo NAKTANI (April ～)
Graduate Students	Nisha GOWRI MANILA
	Sirimanas JIARANUCHART (～ Sept.)
	Hisao HONMA
	Hitomi NOJIMA
	Hiroaki SHIMONO (April)
	Esther NG FENG YING (Oct ～)
Adjunct Instructor	Tatuaki GOTO (March)

(1) Outline

Main objective of this branch is to provide opportunities to study radiation oncology for oral cancer and translational research for radiosensitization of oral cancer.

(2) Research

- 1) Visualization of tumor radioresponse by molecular imaging
- 2) Mechanism of DNA damage response
- 3) Radioresistant signal transduction pathways
- 4) Radiotherapy for oral cancer

(3) Education

Oral Radiation Oncology is a branch of radiation oncology dealing with basic radiobiology, translational research, and radiotherapy for oral cancer. Main objective of this branch in the graduate course is to provide opportunities to study biological strategies for radiosensitization, development of radiosensitizers, molecular mechanism of tumor radioresistance, the state of the art technology of radiotherapy, and basis of individualized radiotherapy depending on each student' s research projects.

(4) Lectures & Courses

The educational policy is to cultivate researchers to be able to extract problems and to work out solutions to them.

(5) Clinical Services & Other Works

Oral Radiation Oncology clinic provides radiotherapeutic treatment for head and neck cancer patients, especially brachytherapy for oral cancer, in cooperation with Diagnostic and Therapeutic Radiology clinic in the Medical

Hospital.

(6) Clinical Performances

We are performing brachytherapy for oral cancer, which is now the only treatment modality without surgical excision, as a center institution in Japan.

(7) Publications

[Original Articles]

1. Tatsushi Ruike, Yoshihiro Kanai, Kazuki Iwabata, Yuki Matsumoto, Hiroshi Murata, Masahiro Ishima, Keisuke Ohta, Masahiko Oshige, Shinji Katsura, Koji Kuramochi, Shinji Kamisuki, Hiroeki Sahara, Masahiko Miura, Fumio Sugawara, Kengo Sakaguchi. Distribuiton and metabolism of ¹⁴C Sulfoquinovosylacetylpropanediol (¹⁴C-SQAP) after a single intravenous administration in tumor-bearing mice. *Xenobiotica*. 2018.03; 1-45
2. Sirimanas Jiaranuchart, Atsushi Kaida, Yusuke Onozato, Hiroyuki Harada, Masahiko Miura. DNA damage response following X-irradiation in oral cancer cell lines HSC3 and HSC4. *Arch. Oral Biol.* 2018.06; 90; 1-8
3. Nisha Gowri Manila, Atsushi Kaida, Ken-Ichi Nakahama, Masahiko Miura. Insulin-like growth factor I receptor regulates the radiation-induced G2/M checkpoint in HeLa cells. *Biochem. Biophys. Res. Commun.* 2018.08; 503(4); 2977-1983
4. Yoichi Takakusagi, Sarwat Naz, Kaori Takakusagi, Masahiro Ishima, Hiroshi Murata, Keisuke Ohta, Masahiko Miura, Fumio Sugawara, Kengo Sakaguchi, Shun Kishimoto, Jeeva P Munasinghe, James B Mitchell, Murali C Krishna. A Multimodal Molecular Imaging Study Evaluates Pharmacological Alteration of the Tumor Microenvironment to Improve Radiation Response. *Cancer Res.* 2018.12; 78(24); 6828-6837

[Misc]

1. Masahiko Miura. Low-dose rate brachytherapy for oral cancer *Journal of Japanese Society of Oral Oncology*. 2018.09; 30(3); 123-127
2. Masahiko Miura, Atsushi Kaida. Visualization of redistribution kinetics following irradiation and its clinical significance *Radiation Biology Research Communication*. 2018.12; 53(4); 265-279

[Conference Activities & Talks]

1. Masahiko Miura. Hypoxia: a potential target in radiotherapy for H&N cancer and its perspective. *ESTRO meets ASIA* 2018.12.07 Singapore

[Awards & Honors]

1. Robomech Journal, The Japan Society of Mechanical Engineers, 2018.06

Oral and Maxillofacial Surgery

Professor Hiroyuki HARADA

Associate Professor Eriko MARUKAWA

Junior Associate Professor Yasuyuki MICHII, Fumihiko TSUSHIMA

Assistant Professor Hiroaki SHIMAMOTO, Hirofumi TOMIOKA,

Hideaki HIRAI, Kae TANAKA, Takeshi KUROSHIMA

Specially Appointed Assistant Professor

Yumi MOCHIZUKI, Takuma KUGIMOTO, Yukinobu TAKAHASHI

Graduate Student

Shuhei FUKUDA, Ruri KOMIYA, Yoshihisa KASHIMA, Hitomi NOJIMA, Misaki YOKOKAWA,

Naoya KINOSHITA, Yuuki TAKAGAWA, Aoi KANEKO, Shintaro SAKAKITANI,

Yoshimitsu SATO, Misako TANAKA, Hiroaki SHIMONO, Kaho Takada, Shohei YANAGISAWA,

Takuya KOMIYAMA, Cuong TRAN MINH, Shunya HAYASHI, Yuta IKAMI, Junko TAKEI,

Phung TRAN XUAN

(1) Outline

Purpose of Education

The program is designed for acquiring the broad knowledge and basic skills of oral and maxillofacial surgery, mainly concerning the diagnostic procedure, treatment technique and the perioperative patient care. Also throughout the professional education, we promote the system in which each graduate student can select his or her special field in the full scope of oral and maxillofacial surgery in the future.

Research Subjects

- 1) Development of multidisciplinary treatment of oral cancer.
- 2) Clinical study on sentinel node navigation surgery for oral cancer.
- 3) Study on molecular markers for lymph node metastasis of oral cancer.
- 4) Clinical and experimental studies on bone regeneration using β -TCP and/or platelet rich plasma.
- 5) Development of multidisciplinary treatment of oral mucosal diseases.

Clinical Services

The Oral and Maxillofacial Surgery Clinic examines yearly more than 6,200 new patients with various diseases arising in oral and maxillofacial regions. The clinic has diplomat of the Japanese Society of Oral and Maxillofacial Surgeons and accepts many referrals from dentists and medical doctors. We provide a full range of services including extractions, removal of wisdom teeth and management of facial trauma, oral mucosal disease, temporomandibular joint disease, and benign and malignant tumors. The special outpatient clinics are organized by the specialists to offer the best service, especially for patients with malignant tumor, oral mucosal disease and temporomandibular joint disease which need high degree of specialty and long term follow up. We also prepare some groups for inpatients with an emphasis on specialties, to provide the recent and advanced treatment.

(2) Publications

[Original Articles]

1. Yae Ohata, Maiko Tsuchiya, Hideaki Hirai, Satoshi Yamaguchi, Takumi Akashi, Kei Sakamoto, Akira Yamaguchi, Tohru Ikeda, Kou Kayamori. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. PLoS ONE. 2018; 13(2); e0191865
2. Tatsuzawa Anna, Yamamoto Kouhei, Ohata Yae, Ohyama Yoshio, Mochizuki Yumi, Komatsu Hiroyoshi, Kitagawa Masanobu. Clinicopathologic and gene mutation analysis of oral diffuse large B-cell lymphoma CANCER SCIENCE. 2018.01; 109; 684
3. Kuroshima T, Wada M, Sato T, Takano M, and Makino S. G-CSF producing oral carcinoma with diffuse uptake of FDG in the bone marrow: A case report Oncology Letters. 2018.01; 15(1); 1241-1245
4. Nishii N, Tachinami H, Kondo Y, Xia Y, Kashima Y, Ohno T, Nagai S, Li L, Lau W, Harada H, Azuma M. Systemic administration of a TLR7 agonist attenuates regulatory T cells by dend+E11:AB11ritic cell modification and overcomes resistance to PD-L1 blockade therapy Oncotarget. 2018.01; 9; 13301-13312
5. Jehung JP, Kitamura T, Yanagawa-Matsuda A, Kuroshima T, Towfik A, Yasuda M, Sano H, Kitagawa Y, Minowa K, Shindoh M, Higashino F. Adenovirus infection induces HuR relocalization to facilitate virus replication. Biochemical and biophysical research communications. 2018.01; 495(2); 1795-1800
6. Kuroshima Takeshi, Wada Mayumi, Sato Takehiko, Takano Masashi, Makino Shujiroh. G-CSF producing oral carcinoma with diffuse uptake of FDG in the bone marrow: A case report ONCOLOGY LETTERS. 2018.01; 15(1); 1241-1245
7. Ohata Y, Tsuchiya M, Hirai H, Yamaguchi S, Akashi T, Sakamoto K, Yamaguchi A, Ikeda T, Kayamori K. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma PLoS One. 2018.02; e0191865
8. Sato M, Harada H, Nagata C, Suzuki K. A case of Ectomesenchymal Chondromyxoid Tumor on the tongue Journal of Oral and Maxillofacial Surgery, Medicine. 2018.03; 30(2); 134-137
9. Itai S, Ohishi T, Kaneko MK, Yamada S, Abe S, Nakamura T, Yanaka M, Chang YW, Ohba S, Nishioka Y, Kawada M, Harada H, Kato Y. Anti-podocalyxin antibody exerts antitumor effects via antibody-dependent cellular cytotoxicity in mouse xenograft models of oral squamous cell carcinoma. Oncotarget. 2018.04;
10. 大畑 八重, 土谷 麻衣子, 平井 秀明, 山口 聡, 明石 巧, 山口 朗, 池田 通, 栢森 高. 癌微小環境における線維芽細胞由来の白血病阻止因子 (LIF) は口腔癌の浸潤に関与する (Fibroblast-derived leukemia inhibitory factor mediates invasion of oral squamous cell carcinoma) 日本病理学会会誌. 2018.04; 107(1); 460
11. Yae Ohata, Kou Kayamori, Akane Yukimori, Kanako Sumikura, Toshimitsu Ohsako, Hiroyuki Harada, Kei Sakamoto, Tohru Ikeda. A lesion categorized between ghost cell odontogenic carcinoma and dentinogenic ghost cell tumor with CTNNB1 mutation. Pathol. Int.. 2018.05; 68(5); 307-312
12. Kaneko MK, Yamada S, Itai S, Chang YW, Nakamura T, Yanaka M, Harada H, Suzuki H, Kato Y. Elucidation of The TMab-6 Monoclonal Antibody Epitope Against Telomerase Reverse Transcriptase. Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2018.05;
13. Furusawa Y, Yamada Y, Itai S, Nakamura T, Fukui M, Harada H, Kaneko MK, Kato Y. Elucidation of critical epitope mapping of anti-rat podoplanin monoclonal antibody PMab-2 Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2018.05;
14. Miyazaki H, Ohshiro T, Romeo U, Noguchi T, Maruoka Y, Gaimari G, Tomov G, Wada Y, Tanaka K, Ohshiro T, Asamura S. Retrospective Study on Laser Treatment of Oral Vascular Lesions Using the "Leopard Technique": The Multiple Spot Irradiation Technique with a Single-Pulsed Wave Photomed Laser Surgery. 2018.05; 36(6); 320-325
15. Sirimanas Jiaranuchart, Atsushi Kaida, Yusuke Onozato, Hiroyuki Harada, Masahiko Miura. DNA damage response following X-irradiation in oral cancer cell lines HSC3 and HSC4. Arch. Oral Biol.. 2018.06; 90; 1-8

16. Yamada S, Kaneko MK, Itai S, Chang YW, Nakamura T, Yanaka M, Ogasawara S, Murata T, Uchida H, Tahara H, Harada H, Kato Y. Epitope Mapping of Monoclonal Antibody PMab-48 against Dog Podoplanin. *Monoclonal Antibodies in Immunodiagnosis and Immunotherapy*. 2018.06;
17. Yamaga E, Toriihara A, Nakamura S, Asai S, Fujioka T, Yoshimura R, Michi Y, Harada H, Tateishi U. Clinical usefulness of 2-deoxy-2-[¹⁸F] fluoro-D-glucose-positron emission tomography/computed tomography for assessing early oral squamous cell carcinoma (cT1-2N0M0) *Japanese Journal of Clinical Oncology*. 2018.07; 48(7); 633-639
18. Okuyama K, Yamashiro M, Kaida A, Kawamata A, Mizutani M, Michi Y, Uzawa N, Yano T, Tohyama R, Yamaguchi S. Does a Vascularized Fibula Free Bone Grafted Immediately After Hemimandibulectomy in a Child Grow or Relapse During Adolescence? *The Journal of craniofacial surgery*. 2018.07; 29(5);
19. Michikawa C, Izumo T, Sumino J, Morita T, Ohyama Y, Michi Y, Uzawa N. Small size of metastatic lymph nodes with extracapsular spread greatly impacts treatment outcomes in oral squamous cell carcinoma patients *International Journal of Oral and Maxillofacial Surgery*. 2018.07; 47(7); 830-835
20. Shimada Y, Kawasaki Y, Tayama M, Kindaichi J, Maruoka Y. A case of central odontogenic fibroma of the mandible in a nevoid basal cell carcinoma syndrome patient *Oral Science International*. 2018.07; 15(2); 61-67
21. Matsui T, Okada T, Kawada K, Okuda m, Ogo T, Nakajima Y, Kume Y, Ryotokuji T, Hoshino A, Tokairin Y, Michi Y, Harada H, Nakajima Y, Kawano T. Detection of second primary malignancies of the esophagus and hypopharynx in oral squamous cell carcinoma patients *Laryngoscope Investigative Otolaryngology*. 2018.08; 3(4); 263-267
22. Habiba U, Kuroshima T, Yanagawa-Matsuda A, Kitamura T, Chowdhury A, Jehung JP, Hossain E, Sano H, Kitagawa Y, Shindoh M, Higashino F. HuR translocation to the cytoplasm of cancer cells in actin-independent manner. *Experimental cell research*. 2018.08; 369(2); 218-225
23. Yamada I, Yoshino N, Hikishima K, Sakamoto J, Yokokawa M, Oikawa Y, Harada H, Kurabayashi T, Saida Y, Tateishi U, Yukimori A, Izumo T, Asahina S. Oral carcinoma: clinical evaluation using diffusion kurtosis imaging and its correlation with histopathologic findings. *Magn Reson Imaging*. 2018.09; 51; 69-78
24. Kaneko MK, Yamada S, Itai S, Furusawa S, Nakamura T, Yanaka M, Handa S, Hisamatsu K, Nakamura Y, Fukui M, Harada H, Kato Y. Epitope mapping of an anti-alpha thalassemia/mental retardation syndrome Xlinked monoclonal antibody AMab-6 *Biochem Biophys Rep*. 2018.09;
25. Itai S, Yamada S, Kaneko MK, Sano M, Nakamura T, Yanaka M, Handa S, Hisamatsu K, Nakamura Y, Furusawa Y, Fukui M, Ohishi T, Kawada M, Harada H, Kato Y. Podocalyxin is crucial for the growth of oral squamous cell carcinoma cell line HSC-2 *Biochem Biophys Rep*. 2018.09;
26. Ngamsom S, Nakamura S, Kabasawa Y, Harada H, Tohyama R, Kurabayashi T. Imaging findings of intraosseous traumatic neuroma of the mandible *Oral radiology*. 2018.09; 34(3); 257-261
27. Kurohara K, Michi Y, Yukimori A, Yamaguchi S. The glomus tumor resorbed bone and teeth in the mandible: a case report *Head and Face Medicine*. 2018.09; 14(18);
28. Mochizuki Yumi, Harada Hiroyuki, Yokokawa Misaki, Kinoshita Naoya, Kubota Kazumasa, Okado Tomokazu, Fukayama Haruhisa. Oral and maxillofacial surgery in patients undergoing dialysis for advanced renal disease: report of five cases *BMC ORAL HEALTH*. 2018.10; 18(1); 166
29. 島本 裕彰, 福田 修平, 及川 悠, 大迫 利光, 釘本 琢磨, 黒嶋 雄志, 平井 秀明, 望月 裕美, 田中 香衣, 富岡 寛文, 原田 浩之. 口腔扁平上皮癌 cN0 症例の頸部転移についての検討 *日本癌治療学会学術集会抄録集*. 2018.10; 56 回; P2-5
30. Takahashi Y, Tanaka K, Hirai H, Marukawa E, Izumo T, Harada H. Appropriate surgical margin for odontogenic myxoma: a review of 12 cases. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2018.11; 126(5); 404-408
31. Furusawa Y, Yamada S, Itai S, Sano M, Nakamura T, Yanaka M, Handa S, Mizuno T, Maeda K, Fukui M, Harada H, Kaneko MK, Kato Y. Establishment of Monoclonal Antibody PMab-202 against Horse Podoplanin *Monoclonal Antibodies in Immunodiagnosis and Immunotherapy*. 2018.11;

32. Yamada S, Itai S, Furusawa Y, Sano M, Nakamura T, Yanaka M, Handa S, Hisamatsu K, Nakamura Y, Fukui M, Harada H, Mizuno T, Sakai Y, Ogasawara S, Murata T, Uchida H, Tahara H, Kaneko MK, Kato Y. Detection of tiger podoplanin using the anti-cat podoplanin monoclonal antibody PMab-52 Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2018.11;
33. Takahashi Yukinobu, Tanaka Kae, Hirai Hideaki, Marukawa Eriko, Izumo Toshiyuki, Harada Hiroyuki. Appropriate surgical margin for odontogenic myxoma: a review of 12 cases ORAL SURGERY ORAL MEDICINE ORAL PATHOLOGY ORAL RADIOLOGY. 2018.11; 126(5); 404-408
34. Tomioka H, Mochizuki Y, Ohsako T, Hirai H, Shimamoto H, Harada H. Buccinator and Mandibular Node Metastases in Oral Squamous Cell Carcinoma. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2018.12;
35. Shimizu R, Tanaka K, Oikawa Y, Tomioka H, Kayamori K, Ikeda T, Yoshioka T, Ebihara A, Harada H. Epithelioid cell granuloma with caseating necrosis possibly caused by periapical periodontitis: a case report. Journal of medical case reports. 2018.12; 12(1); 365

[Conference Activities & Talks]

1. Yukinobu TAKAHASHI, Eriko MARUKAWA, Hiroyuki HARADA. The use of a new porous hydroxyapatite-collagen composite in a ridge preservation. 2018 AO Annual Meeting 2018.02.28 Los Angeles(USA)
2. Shunsuke ITAI, Mika K. KANEKO, Shinji YAMADA, Yukinari KATO. A core fucose-deficient anti-podocalyxin antibody exhibits anti-tumor activity via augmented antibody-dependent cellular cytotoxicity in oral squamous cell carcinoma. America association for cancer research(2018) 2018.04.18 Chicago(USA)
3. Naoto NISHII, Hidetake TACHINAMI, Yuta KONDO, Yulong XIA, Yoshihisa KASHIMA, Tatsukuni OHNO, Shigenori NAGAI, Lixin LI, Walter LAU, Hiroyuki HARADA and Miyuki AZUMA. Systemic administration of a TLR7 agonist attenuates regulatory T cells by dendritic cell modification and overcomes resistance to PD-L1 blockade therapy. 15th International symposium on dendritic cells 2018.06.09 Aachen (Germany)
4. Kaifeng LUO, Yutaka MARUOKA, Rie KINOSHITA, Teru OKITSU, Libo WU, Nobuyuki TAKAMA, Beomjoon KIM. Study on the use of dissolvable microneedles in the treatment of stomatitis. The International Symposium on Precision Engineering and Sustainable Manufacturing (PRESM 2018) 2018.07.03 札幌
5. Namiaki TAKAHARA, Atsushi KIMURA, Yusuke HIGUCHI, Yuji KABASAWA, Tetsuya YODA, Hiroyuki HARADA. Evaluation Of Postoperative Mandibular Stability After Bimaxillary Surgery For Mandibular Setback And The Clockwise Rotation Of The Proximal Segment. 24th Congress of the European Association for Cranio Maxillo Facial Surgery 2018.09.18 Munich(Germany)
6. Yuki TAKAGAWA, Yasuyuki GEN, Tomoki MURAMATSU, Hiroyuki HARADA, Johji INAZAWA. Exploring novel tumor suppressive microRNAs in OSCC. 第 77 回日本癌学会学術総会 2018.09.27 大阪
7. Shimada Y, Kawasaki Y, Hagiwara S, Nakamura F, Maruoka Y. Importance of eliminating potential dental focal infection before hematopoietic stem cell transplantation: A retrospective cohort study in Japan. The 14th Biennial Congress of the European Association of Oral Medicine (EAOM) in conjunction with the World Workshop VII on Oral Medicine 2018.09.27 Gothenburg(Sweden)
8. Shunsuke ITAI, Tomokazu OHISHI, Mika K. KANEKO, Shinji YAMADA, Shinji ABE, Yasuhiko NISHIOKA, Hiroyuki HARADA, Yukinari KATO. Antitumor activity by ADCC against oral squamous cell carcinomas by anti-podocalyxin antibody. 第 77 回日本癌学会学術総会 2018.09.27 大阪
9. Hiroaki SHIMAMOTO, Shuhei FUKUDA, Yu OIKAWA, Toshimitsu OSAKO, Takuma KUGIMOTO, Takeshi KUROSHIMA, Hideaki HIRAI, Yumi MOCHIZUKI, Kae TANAKA, Hirofumi TOMIOKA, Hiroyuki HARADA. Clinical analysis of lymph node metastasis of patients with cN0 oral squamous cell carcinoma. 第 56 回日本癌治療学会 2018.10.18 横浜
10. Eriko MARUKAWA, Narumi OSHIBE, Hiroyuki HARADA, Yoshihiro SASAKI, Kazunari AKIYOSHI. Osteoinduction Using β -TCP and Nanogel-Crosslinking Hydrogel as a Novel Scaffold for BMP-2. The 12th International BMP Conference 2018.10.24 東京

11. Hideaki Hirai, Hirofumi Tomioka, Yumi Mochizuki, Takeshi Kuroshima, Fumihiko Tsushima, Hiroaki Shimamoto, Hiroyuki Harada. Clinical Course of Oral Squamous Cell Carcinoma in Patients on Immunosuppressant and Glucocorticoid Therapy. 13th Asian Congress on oral and maxillofacial surgery 2018.11
12. Takeshi KUROSHIMA, Hiroaki SHIMAMOTO, Hirofumi TOMIOKA, Hideaki HIRAI, Yumi Mochizuki, Kae TANAKA and Hiroyuki HARADA. Clinicopathological analysis for N0 tongue squamous cell carcinoma with occult cervical lymph node metastasis. 13th Asian Congress on oral and maxillofacial surgery 2018.11
13. Hideaki HIRAI, Hirofumi TOMIOKA, Yumi MOCHIZUKI, Takeshi KUROSHIMA, Fumihiko TSUSHIMA, Hiroaki SHIMAMOTO, Hiroyuki HARADA. Clinical Course of Oral Squamous Cell Carcinoma in Patients on Immunosuppressant and Glucocorticoid Therapy. 13th Asian Congress on oral and maxillofacial surgery 2018.11.08 台北
14. Takeshi KUROSHIMA, Hiroaki SHIMAMOTO, Hirofumi TOMIOKA, Hideaki HIRAI, Yumi Mochizuki, Kae TANAKA and Hiroyuki HARADA. Clinicopathological analysis for N0 tongue squamous cell carcinoma with occult cervical lymph node metastasis. 13th Asian Congress on oral and maxillofacial surgery 2018.11.08 台北
15. Mari SHIBATA, Yasuyuki MICHI, Hiroyuki HARADA, Tetsuya YODA. Clinical histopathological study on tongue cancer accompanying revisions of the 8th edition of the AJCC/ UICC staging manuals. 13th Asian Congress on oral and maxillofacial surgery 2018.11.08 台北
16. Eri SHIBATA, Kei-ichi MORITA, Yasuyuki MICHI, Tetsuya YODA. A case of Mammary Analogue Secretory Carcinoma in Salivary Duct of Parotid Gland. 13th Asian Congress on oral and maxillofacial surgery 2018.11.08 台北
17. Hideaki Hirai, Hirofumi Tomioka, Yumi Mochizuki, Takeshi Kuroshima, Fumihiko Tsushima, Hiroaki Shimamoto, Hiroyuki Harada. Clinical Course of Oral Squamous Cell Carcinoma in Patients on Immunosuppressant and Glucocorticoid Therapy. Asian Congress on Oral & Maxillofacial Surgery(ACOMS) 2018.11.08 台北
18. Takeshi Kuroshima, Hiroaki Shimamoto, Hirofumi Tomioka, Hideaki Hirai, Yumi Mochizuki, Kae Tanaka, Hiroyuki Harada. Clinicopathological analysis for N0 tongue squamous cell carcinoma with occult cervical lymph node metastasis. Asian Congress on Oral & Maxillofacial Surgery(ACOMS) 2018.11.08 台北
19. Kaifeng LUO, Yutaka MARUOKA, Rie KINOSHITA, Teru OKITSU, Libo WU, Nobuyuki TAKAMA, Beomjoon KIM. Modeling of stomatitis in rats and novel treatment using microneedles-based patch. IEEE CPMT Symposium Japan 2018 (ICSJ 2018) 2018.11.19 京都

Oral and Maxillofacial Radiology

Professor: Tohru KURABAYASHI

Associate Professor: Hiroshi WATANABE

Junior Associate Professor: Naoto OHBAYASHI, Norio YOSHINO

Assistant Professor: Akemi TETSUMURA, Shin NAKAMURA, Ami KURIBAYASHI, Junichiro SAKAMOTO

Research Staff: Li LIU

Hospital Staff: Yoshikazu NOMURA, Mamiko FUJIKURA

Graduate Student: Hiroko ISHII, Noriko SUZUKI, Chutamas DEEPHO, Tran Thi Xuan LAN, Sakurako ASAI,

Wamasing PEERAPONG, Miharuru TAGUCHI, Yumi TSUCHIDA

Secretary: Izumi MOTOHASHI

(1) Research

- 1) Diagnosis of maxillofacial diseases by CT, MRI and PET imaging
- 2) Advantages of cone-beam CT for clinical dentistry
- 3) Development of high resolution MRI technology.
- 4) Novel MRI techniques for TMJ disorders.
- 5) Factors determining radioresistance of oral and maxillofacial cancers.

(2) Lectures & Courses

Oral and maxillofacial radiology is a branch of dental science which deals with the effective application of radiation energy to the diagnosis and treatment of oral and maxillofacial diseases. Main objective of oral and maxillofacial radiology in the graduate course is to provide students opportunity to study advanced imaging modalities including digital imaging, cone-beam CT, multi-detector row CT and MRI, and also to study image processing and image analysis technology. Students are also taught on basic radiation oncology and its related laboratory technology depending on their research project.

(3) Clinical Services & Other Works

Oral and maxillofacial radiology clinic provides a full spectrum of imaging examinations and diagnosis, including CT and MRI. Non-invasive, interventional radiology for patients with salivary gland stone is also performed in the clinic.

(4) Publications

[Original Articles]

1. Ozawa E, Honda EI, Parakonthun KN, Ohmori H, Shimazaki K, Kurabayashi T, Ono T. Influence of orthodontic appliance-derived artifacts on 3-T MRI movies. *Prog Orthod.* 2018; 19(1); 7
2. Ding X, Suzuki S, Shiga M, Ohbayashi N, Kurabayashi T, Moriyama K. Evaluation of tongue volume and oral cavity capacity using cone-beam computed tomography. *Odontology.* 2018; 106; 266-273

3. Ekprachayakoon I, Miyamoto JJ, Inoue-Arai MS, Honda EI, Takada JI, Kurabayashi T, Moriyama K. New application of dynamic magnetic resonance imaging for the assessment of deglutitive tongue movement. *Prog Orthod.* 2018; 19(1); 45
4. Otonari-Yamamoto M, Nakajima K, Sakamoto J, Imoto K, Watanabe M, Kotaki S, Kuroda M, Matsuzaka K, Shibahara T, D Curtin H, K Goto T. Atypical MRI and Histopathological Findings in Dermoid Cyst. *The Bulletin of Tokyo Dental College.* 2018; 59(3); 207-212
5. Deepho C, Watanabe H, Sakamoto J, Kurabayashi T. Mandible canal visibility using a plain volumetric interpolated breath-hold examination sequence in MRI. *Dentomaxillofacial Radiology.* 2018.01; 47(1); 20170245
6. Watanabe H, Nomura Y, Kuribayashi A, Kurabayashi T. Spatial resolution measurements using Radia diagnostic software with SEDENTEXCT Image Quality phantom in cone beam CT for dental use. *Dentomaxillofacial Radiology.* 2018.03; 47(3); 20170307
7. Yamada I, Hikishima K, Yoshino N, Sakamoto J, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using q-space imaging; correlation with histopathologic findings. *J Magn Reson Imaging.* 2018.03; 48(4); 1059-1068
8. Fujikura M, Nishikawa K, Araki K. Magnetic Resonance Imaging Signal Intensities of the Temporomandibular Joint Articular Disc and Cortical Bone: Are These Measurements Valid for the Diagnosis of Temporomandibular Joint Disease? *The Showa University Journal of Medical Sciences.* 2018.04; 29(4); 415-423
9. Yamaga E, Toriihara A, Nakamura S, Asai S, Fujioka T, Yoshimura R, Michi Y, Harada H, Tateishi U. Clinical usefulness of 2-deoxy-2-[¹⁸F] fluoro-Dglucose- positron emission tomography/computed tomography for assessing early oral squamous cell carcinoma (cT1-2N0M0) *Japanese Journal of Clinical Oncology.* 2018.07; 48(7); 633-639
10. Ishii H, Tetsumura A, Nomura Y, Nakamura S, Akiyama M, Kurabayashi T. Diagnostic ability of limited volume cone beam computed tomography with small voxel size in identifying the superior and inferior walls of the mandibular canal *International Journal of Implant Dentistry.* 2018.07; 4(1); 18
11. Ngamsom S, Nakamura S, Kabasawa Y, Harada H, Tohyama R, Kurabayashi T. Imaging findings of intraosseous traumatic neuroma of the mandible *Oral Radiology.* 2018.08; 34; 257-261
12. Yamada I, Yoshino N, Hikishima K, Sakamoto J, Yokokawa M, Oikawa Y, Harada H, Kurabayashi T, Saida Y, Tateishi U, Yukimori A, Izumo T, Asahina S. Oral carcinoma: clinical evaluation using diffusion kurtosis imaging and its correlation with histopathologic findings. *Magn Reson Imaging.* 2018.09; 51;; 69-78
13. Wamasing P, Deepho C, Watanabe H, Hayashi Y, Sakamoto J, Kurabayashi T. Imaging the bifid mandibular canal using high resolution MRI *Dentomaxillofacial Radiology.* 2018.10; 47; 20180305
14. Ichiro Yamada, Junichiro Sakamoto, Daisuke Kobayashi, Naoyuki Miyasaka, Kimio Wakana, Noriko Oshima, Akira Wakabayashi, Yukihiisa Saida, Ukihide Tateishi, Yoshinobu Eishi. Diffusion kurtosis imaging of endometrial carcinoma: Correlation with histopathological findings. *Magn Reson Imaging.* 2018.12;
15. Hoshi R, Tetsumura A, Yamaguchi S. Preoperative imaging findings as predictors of postoperative inferior alveolar nerve injury following mandibular cyst surgery. *Journal of Oral Science.* 2018.12; 60(4); 618-625

[Books etc]

1. Cone beam computed tomography in Endodontics.. 142, 2018.01

[Conference Activities & Talks]

1. Kurabayashi T. CT and MRI of odontogenic tumors and cysts. Lecture in the Master of Science Program in Dentistry of Mahidol University, 2018.02.12 Bangkok, Thailand
2. Kurabayashi T. Special lecture: Imaging characteristics of odontogenic tumors and cysts. The 30th Research Day of Faculty of Dentistry, Chulalongkorn University, 2018.02.14 Bangkok

3. Chie Watanabe, Junichiro Wada, Koji Mizutani, Hiroshi Watanabe, Noriyuki Wakabayashi. Chronological changes in supporting alveolar bone by RPD placement. IADR 86th General Session & Exhibition 2018.07.24 London
4. Kurabayashi T, Suzuki N, Kuribayashi A. Comparison of diagnostic accuracy between MRI and MDCT in detecting mandibular invasion of squamous cell carcinoma in the oral cavity. 12th Asian Congress of Oral & Maxillofacial Radiology & 5th International Green Health Conference, 2018.09.08 Mumbai, India

[Awards & Honors]

1. Robomech Journal, The Japan Society of Mechanical Engineers, 2018.06

Anesthesiology and Clinical Physiology

Professor

Haruhisa Fukayama

Associate Professor

Ryo Wakita

Junior Associate Professor

Keiko Abe (～Sep) ,

Tomoka Matsumura (Feb～)

Assistant Professors

Tomoyuki Miyamoto,

Tomoka Matsumura (～Jan)

Yukiko Baba (Apr～)

Hospital Staffs

Kotomi Uchinuma (Apr～)

Hidetaka Murata(Apr～)

Tunataka Abo

Takutoshi Inoue(Apr～)

Kouichirou Ozawa (Apr～)

Sayaka Asano (Apr～)

Graduate Students

Chihiro Suzuki,

Kaeko Araki,

Takaya Itou,

Yuu Satou,

Keiko Abe (Apr～)

Research Students

Keita Niimi(Apr～),

Moegi Toyomaki(Apr～),

Advanced Clinical Training

Feng Yu Pin (～Jun)

Secretary

Natsu Sato

(1) Outline

For safety and comfortable dentistry for both patients and dentists, educations, researches and clinical practices are performed in the department. Education includes basics and practices of local and general anesthesia, sedation, monitoring (monitored anesthesia care, MAC) in addition to cardio-pulmonary resuscitation, or, basic life support during dental treatment. Our researches are consisted of basic and clinical trials for the purposes. Many cases give us many chances to keep the patients safe and comfortable during local and general anesthesia. Local groups, such as dental associations, are welcomed to promote safe and comfortable dental treatments.

(2) Research

- 1) Non-invasive drug delivery system
- 2) New methods for local anesthesia in dentistry
- 3) Neuropathic pain in oral and maxillofacial regions
- 4) Diffuse noxious inhibitory control or controlled pain modulation
- 5) Sedation for dentistry

(3) Education

Anesthesia and anesthesiology for dentistry, which are not only local anesthesia but also general anesthesia are given to the both under and post graduate students. Lectures and trainings are consisted of local and general anesthesia, sedation and cardio-pulmonary-resuscitation (CPR), or, basic life support (BLS). For local anesthesia, the students learn mechanism of local anesthesia, local anesthetics, techniques and local and systemic complications due to local anesthesia. Physiology, biochemistry and pharmacology are also provided for general anesthesia which includes possible mechanism of general anesthesia, anesthetics, muscle relaxants and what are used for general anesthesia. They also acquire the techniques of topical, infiltration and conduction anesthesia, nitrous oxide inhalation sedation and basic life support.

(4) Lectures & Courses

Anesthesia and anesthesiology for dentistry, which are not only local anesthesia but also general anesthesia are given to the both under and post graduate students. Lectures and trainings are consisted of local and general anesthesia, sedation and cardio-pulmonary-resuscitation (CPR), or, basic life support (BLS). For local anesthesia, the students learn mechanism of local anesthesia, local anesthetics, techniques and local and systemic complications due to local anesthesia. Physiology, biochemistry and pharmacology are also provided for general anesthesia which includes possible mechanism of general anesthesia, anesthetics, muscle relaxants and what are used for general anesthesia. They also acquire the techniques of topical, infiltration and conduction anesthesia, nitrous oxide inhalation sedation and basic life support.

(5) Clinical Services & Other Works

Safe medical and perioperative managements are given to the patients of our ambulatory anesthesia service which has more than 2,000 cases per year and the central operation rooms which has 750 cases per year. Some difficult cases are referred to our hospital because of many clinical experiences.

Several cases that need emergency care are also supported by our department. ER members are sometimes called in the medical hospital.

Local groups like dental associations often ask us to hold some lectures, trainings, workshops for safe dental treatment. These proposals are welcomed by our staffs. When intravenous sedation cases are introduced, some responsible staff is sent to their own clinic.

(6) Clinical Performances

Any patient is welcomed, especially patients of oral surgery and implant operation who need special care using general anesthesia and sedation.

Referred patients from open practitioners are also accepted for safe and comfortable dental treatment.

(7) Publications

[Original Articles]

1. Matsumura T, Suzuki C, Kubota K, Minakuchi S, Fukayama H. Difficult Nasal Intubation Using Airway Scope® for a Child With Large Tumor. *Anesthesia Progress*. 2018; 65(4); 251-254
2. 中島淳, 大嶋瑛, 深山治久, 木下樹. フェロー四徴症を有する Cornelia de Lange 症候群患者の全身麻酔管理 日本歯科麻酔学会雑誌. 2018; 46(1); 14-15

3. Yamamoto T, Fujii-Abe K, Fukayama H, Kawahara H. The effect of adding midazolam to propofol intravenous sedation to suppress gag reflex during dental treatment Anesthesia Progress. 2018; 65; 76-81
4. Mochizuki Y, Harada H, Yokokawa M, Kubota K, Okado T, Fukayama H. Oral and maxillofacial surgery in patients undergoing dialysis of advanced renal disease: report of five cases BMC Oral Health. 2018; 18(166); 101-104
5. Tomoka Matsumura, DDS, PhD,* Chihiro Suzuki, DDS,* Kazumasa Kubota, DDS, PhD, † Shunsuke Minakuchi, DDS, PhD, † and Haruhisa Fukayama, DDS, PhD. Difficult Nasal Intubation Using Airway Scope® for a Child With Large Tumor Anesthesia Progress. 2018; 65(4);
6. A Case of Unexpected Intubation Difficulty during General Anesthesia in a Patient with a Previous Partial Thyroidectomy 2018.04; 46(2); 65-67
7. Wakita R, Fukayama H. Methemoglobinemia should be suspected when oxygen saturation apparently decreases after prilocaine infiltration during intravenous sedation. Clinical case reports. 2018.06; 6(6); 1077-1081

[Conference Activities & Talks]

1. Haruhisa Fukayama. 37th Myanmar Dental Conference. Tips for Local Anesthesia for Dentistry 2018.01.20 ヤンゴン, ミャンマー
2. Ryo Wakita. The effort to reduce the stimulus during local anesthesia - A new device for effective local anesthesia -. 8th Mandalay Dental Conference 2018.07.15 Mandalay
3. Haruhisa Fukayama. 9th Mandalay Dental Conference 2018. Sedation for persons with disabilities (special needs patients) 2018.07.15 マンダレー, ミャンマー
4. Wakita Ryo. Local Anesthesia Update: Strategies for Safe and Effective Outcomes Electrical Devices for Effective Local Anesthesia(和訳中). 日本歯科麻酔学会雑誌 2018.09.01
5. Hiromi Funayama, Takaaki Munemasa, Ryo Wakita, Haruhisa Fukayama, Yasuo Endo, Yoshinobu Asada.. Iontophoretic administration of bisphosphonates: a trial for establishing a method to prevent their side effects and to retain their potent anti-bone resorptive effects. 11th Biennial Conference of the Pediatric Dentistry Association of Asia (PDAA) 2018.09.15 Beijings

Orofacial Pain Management

Professor	Masahiko SHIMADA
Junior Associate Professor	Akira NISHIYAMA
Assistant Professor	Yoko YAMAZAKI
Hospital Staff	Hiroko KIMURA, Hiroko IMURA, Hiroyuki ISHIYAMA, Maya SAKAMOTO, Yuusuke HARADA, Keisuke MIYAZONO
Graduate Student	Akitoshi HOSODA, Ngan Nguyen, Liang Shanshan, KAY THWE YE MIN SOE, Masako TOBE, Ryoko KURISU

(1) Outline

Main research subjects of orofacial pain management is to establish the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders , in particular, is to elucidate the mechanism of pain, neuropathic pain, temporomandibular disorders.

(2) Research

Main research subjects of orofacial pain management is to establish the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders , in particular, is to elucidate the mechanism of pain, neuropathic pain, temporomandibular disorders.

- 1)New Treatment methods for neuropathic pain
- 2)Analyses of abnormal orofacila pain
- 3)Study on Biological Response to Dental Interventions
- 4)Analyses and new treatment of dysgeusia
- 5)Development of multidimensional evaluation system for etiological factors of TMD
- 6)Influence of patients' psychosomatic factors for TMD
- 7)Sleep bruxism: its etiology, influence and treatment
- 8)Effectiveness of physiological therapy for TMD
- 9)Mechanisms of occlusal discomfort

(3) Education

Purpose of education for students and residents in this course is to provide an opportunity to learn basic knowledge on diagnostic and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders in the orofacial area. In special course for graduate students, main objective of orofacial pain management is to learn the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders in the orofacial area, in particular, mechanism of pain, neuropathic pain, temporomandibular disorders, and we instruct statistical techniques especially with the multi variate analysis by using clinical data acquired from patients with temporomandibular disorders (TMD).

(4) Clinical Services & Other Works

Orofacial Pain Clinic is concerned with the the pain, abnormal sensation, sensory paralysis, abnormal movement, and motor paralysis in the orofacial area and management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the ptheripheral nerves including acupuncture and psychotherapies. Temporomandibular joint clinic provides diagnosis and treatment for diseases and disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

(5) Clinical Performances

Orofacial Pain Clinic is concerned with the the pain, abnormal sensation, sensory paralysis, abnormal movement, and motor paralysis in the orofacial area and management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the ptheripheral nerves including acupuncture and psychotherapies. Temporomandibular joint clinic provides diagnosis and treatment for diseases and disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

(6) Publications**[Original Articles]**

1. Nakayama R, Nishiyama A, Shimada M. Bruxism-Related Signs and Periodontal Disease: A Preliminary Study. The open dentistry journal. 2018; 12; 400-405
2. Rena Nakayama, Akira Nishiyama, Masahiko Shimada. Bruxism-Related Signs and Periodontal Disease: A Preliminary Study The Open Dentistry Journal. 2018.05; 12; 400-405
3. Nguyen Gia Kieu Ngan, Akira Nishiyama, Masahiko Shimada. Inducing temporomandibular anterior disc displacement experimentally? A model on rats J. Jpn Soc T.M.J.. 2018.07; 30(Suppl.); 121
4. S. Liang, A. Nishiyama, M. Shimada. Changes in Sensory Thresholds of the Pulp and Periodontal Ligaments after Standardized Tooth Clenching Int J Dent Oral Health . 2018.11; 4(5); 1-7

[Conference Activities & Talks]

1. Masahiko Shimada. The combination of western medicine and oriental medicine in the treatment of orofacial pain in Japan. THE 40th DENTAL SCIENTIFIC CONFERENCE 2018.04.02 Ho Chi Minh, Viet Nam
2. Akira Nishiyama. Prospects for treatment and research related to TMD. Association of International Dental Relationships 2nd Culture an 2018.06.23
3. NGUYEN G.K.Ngan, Akira NISHIYAMA , Masahiko SHIMADA . Inducing Temporomandibular Anterior Disc Displacement Experimentally – A model on Rats. The 31st Annual Meeting of The Japanese Society for Temporomandibular Joint 2018.07.08 Kokura
4. Chiaki Matsubara, Junichi Furuya, Rena Nakayama, Michiyo Obana, Shunsuke Minakuchi. Collaborative transdisciplinary team approach for oral health care of acute stroke patients. Japan-Korea joint symposium The 24th Dysphagia Rehabilitation Society in Japan 2018.09.07 仙台
5. Q. Nguyen Ho, Y. Yamazaki, M. Shimada. Does grey matter really change in classical trigeminal neuralgia?. The 32nd IADR-SEA, The 29th South East Asia Association for Dental Education (SEAADE) 2018.09.14 Da Nang, Viet Nam

Pediatric Dentistry

Associate Professor
Michiyo MIYASHIN

Junior Associate Professor
Satoko Kakino (Apr. ∼)

Assistant Professor
Yoshiaki HASHIMOTO, Mizuho MOTEGI (∼ Mar.),
Satoko KAKINO (∼ Mar.), Tomoki UEHARA, Kanae WADA (Oct. ∼)

Clinical Professor
Keiichi TAKEI (∼ Mar.)

Adjunct Lecturer
Keiichi TAKEI (Apr. ∼)
Mitsuko INOUE, Hitoyata SHIMOKAWA (∼ Mar.), Yoshiaki ONO (Apr. ∼), Masayo ONO,
Hiroaki NAGAI (∼ Mar.), Nobutaka ISOGAWA (∼ Mar.), Asuri jayawarudeina,
Yuko MATSUMURA (Apr. ∼), Ryu MATSUBARA (Apr. ∼), Makiko TAKASHI, Naoko UEHARA,
Natsumi TSUCHIHASHI

Hospital assistant professor
Kanae WADA (Apr. ∼ Sep.), Atsushi OISHI (Apr. ∼)

Hospital staff
Atsushi OISHI (∼ Mar.), Kanae WADA (∼ Mar.), Taki KEKIYA,
Kuniomi NAKAMURA (∼ Mar.), Kenichi MIURA (Apr. ∼), Ayano INOUE,
Yuko SEKI (Apr. ∼), Yui SEKIDO (∼ Mar.), Emi Kanai (Dec. ∼)

Graduate Student
Erika KUBOTA, IJBARA Manhal M.A. (∼ Sep.),
ZUMULAITI Shaokelati (∼ Sep.), WIT Yee Wint, Emi FURUSAWA,
Shigeki NAGAHIRO, Rika KODAMA, Manami TAKENOSHITA,
Amrita Widyagarini Subagyo, Cho LI (Apr. ∼)

Research Student
Chika IHARA (∼ Mar.), Yuko SEKI (∼ Mar.), Yui SEKIDO (∼ Mar.),
Emi KANAI (Apr. ∼ Nov.), Kaori KONUMA (Apr. ∼),
Haruka NAITO (Apr. ∼)

fellowship
GANBOLD Khongorzul

Enrolled dentist
Tomoko KAWAMURA, Gaku SHIMADA, Kaori KOHI

(1) Outline

The Department of Pediatric Dentistry was founded in 1955, as the first in Japan. Pediatric dentistry is a subject of clinical dentistry that deal with education and research of not only developmental oral health sciences but also prevention and treatment methods of the diseases which disturb oro-facial growth and development of children.

(2) Research

Research Subjects

- 1) Physiological and biological studies on the stomatognathic function of children
- 2) Studies on the development and developmental disturbance of the teeth
- 3) Studies on the growth and development of the maxillofacial cranium and the dentition
- 4) Development of new Endodontics and Traumatology for deciduous and immature permanent teeth
- 5) Basic research on clinical pediatric dentistry

(3) Education

Lecture subjects

Pediatric dentistry, Oral pediatrics

(4) Lectures & Courses

The main objective of pediatric dentistry in this graduate course is to provide students an opportunity to study the theory and the method for the guidance of the oro-facial growth and development and for the diagnosis, prevention and treatment of diseases and malfunctions which disturb the oro-facial growth and development during the period of childhood.

Oral pediatrics is a subject of clinical dentistry that deal with education and research of not only maintenance and promotion of the oral health for growing children but also prevention and treatment methods of diseases and malfunctions which disturb oral health of growing children. The main objective of oral pediatrics in this graduate course is to provide students an opportunity to understand that a child is a living body with mental, physical, and physiological characteristics which are different from those of adults and to study the pathogenesis, prevention, and treatment of the particular oral diseases in childhood. Students are also taught the theory and the method of ongoing health care that is necessary for maintaining and promoting oral health from infant to adult. In addition, they are taught the clinical significance and importance of the behavioral management of child patients and the necessity and importance of understanding and cooperation of the parents to it.

(5) Clinical Services & Other Works

The pediatric dentistry clinic in the department of oro-facial development and function provides the comprehensive dental treatment for a child while growing.

(6) Clinical Performances

The examination, diagnosis, and treatment of the oral diseases and the oral abnormalities are performed in the clinic. In addition, health guidance, preventive measures, and the long-term oral health management by the periodical checking system are carried out, in order to keep and promote oral health from infant to adult.

(7) Publications**[Original Articles]**

1. Ohno T, Zhang C, Kondo Y, Kang S, Furusawa E, Tsuchiya K, Miyazaki Y, Azuma M. The immune checkpoint molecule VISTA regulates allergen-specific Th2-mediated immune responses. *Int Immune.* 2018.02; 30(1); 3-11

2. Manhal Ijbara, Kanae Wada, Makoto J. Tabata, Junichiro Wada, Go Inoue, Michiyo Miyashin. Enamel Microcracks Induced by Simulated Occlusal Wear in Mature, Immature and Deciduous Teeth. *BioMed Research International* . 2018.04; 2018(5658393); 1-9
3. Takuya Koyama, Satoko Kakino, Yuji Matsuura . A Feasibility Study of Photoacoustic Detection of Hidden Dental Caries Using a Fiber-Based Imaging System *Applied Sciences*. 2018.04; 8(4); 621-1-10
4. Furusawa E., Ohno T., Miyashin M., Azuma M.. Topical application of B7-DC/PD-L2 siRNA inhibits contact hypersensitivity *EUROPEAN JOURNAL OF IMMUNOLOGY*. 2018.05; 48; 52-53
5. Atsushi Oishi, Hitoyata Shimokawa, Eri Sakaniwa, Masayoshi Takahashi, Michiyo Miyashin, Shinichi Arakawa. Oxygen and air nanobubbles in water inhibit proliferation of dental follicle stem cells in vitro *Journal of Dental Health Oral Disorders & Therapy*. 2018.11; 9(6); 460-462

[Misc]

1. Emi Furusawa, Miyuki Azuma. Immune regulation in the oral cavity Oral disease and chronic inflammation. 2018.10; 7(3); 10-14

[Conference Activities & Talks]

1. Koyama T, Kakino S, Matsuura Y. Photoacoustic imaging of hidden dental caries by using a bundle of hollow optical fibers. *SPIE Conference on Optical Fibers and Sensors for Medical Diagnostics and Treatment Applications XVIII* 2018.01.28 San Francisco
2. Taki Sekiya, Kumiko Sugimoto, Tetsumasa Nakano, Michiyo Miyashin. Objective monitoring of psychological states of children during dental treatment.. *American Academy of Pediatric Dentistry - Annual Session* 2018 2018.05.24 Honolulu
3. Sekiya T, Sugimoto K, Nakano T, Miyashin M. Objective monitoring of psychological states of children during dental treatment. 2018.05.25 Honolulu
4. Emi Furusawa, Tatsukuni Ohno, Michiyo Miyashin, Miyuki Azuma. Topical application of B7-DC/D-L2 siRNA inhibits contact hypersensitivity . *15th International Symposium on Dendritic Cells* 2018.06.10 Aachen, Germany
5. Furusawa E, Ohno T, Miyashin M, Azuma M. Topical application of B7-DC/PD-L2 siRNA inhibits contact hypersensitivity. *15th International Symposium on Dendritic Cells* 2018.06.10 Aachen, Germany
6. Yukihiro Tamura, Pornpoj Fuangtharntip, Tomoki Uehara, Yuki Arai, Michiyo Miyashin, Noriyuki Wakabayashi, Kazuhiro Aoki. Expression of metallothionein in inflammatory cytokine treated rat dental pulp cells. *The 8th International Congress of ASIAN Society of Toxicology* 2018.06.17 Thailand
7. Thaw Dar Oo, Kusano M, Kakino S, Ikeda H, Okiji T. Coldness changes transmitted-light plethysmography values in young adult human teeth. *The 66th Annual Meeting of Japanese Association for Dental Research* 2018.11.18 Sapporo

[Works]

1. Michiyo Miyashin : Natural root canal model of children, Educational Materials, 2013.04 - Now

Orthodontic Science

Professor	Takashi ONO
Associate Professor	
Junior Associate Professor	Yoshiro MATSUMOTO, Zusei KANNO, Jun HOSOMICHI
Assistant Professor	Kazuo SHIMAZAKI, Ippei WATARI, Ikuo YONEMITSU Yuji ISHIDA (Apr-), Takayoshi ISHIDA
Project Assistant Professor	Risa USUMI
Dental Resident	Yuji ISHIDA (-Mar), Chiho KATO (-Mar), Hidemasa OKIHARA Yuhei IKEDA (-Mar), Syunsuke UESUGI (-Mar) Shuji OISHI (Apr-), Soma KITA (Apr-), Tomonari MATSUMURA (Apr-) Yasunori ABE (Apr-), Yuki KASAHARA (Apr-)
Graduate Students	Jin-Gyu AN (-Sep), Takuya OGAWA (-Mar), Iku SHIBATA Eri SAITO, Kayo KIMURA (-Mar), Yuta NAKAI, Kenzo WATAKABE Erusu NIN, Huan TANG, Roody BEAUBOEUF (-Sep) Edward CHO, Masamu INOUE, Erika OZAWA Moe SATO, Kasumi HATANO, Keiko FUKINO Shin-Sheng Yang, Lu ZAHO, Thi Kim Uyen DONG Yuta UCHIKAWA, Akihiro KOYAMA, Sun-min KIM Thura AUNG PHYO, Ryo KIMURA, Shahriar Mohd SHAMS, Haixin HONG Kochakorn LEKVIJITTADA (-May), Anindya Kamaratih GUNARSO, Kai LI (Apr-) Sasin SRITARA (Apr-), Hideyuki ISHIDORI (Apr-), Seiko ISHIHARA (Apr-) Aiko TAKADA (Apr-), Yoshiyuki HAMADA (Apr-) Akiyo FUJITA (Apr-), Narubhorn ONGPRAKOBKUL (Jun-) Wirongrong WONGKITIKAMJORN (Jun-), Ahmad F J M SH ALSULAILI (Oct-)
Graduate School Research Students	Hiroko OMORI (-Oct), Shuji OISHI (-Mar), Soma KITA (-Mar) Yoichiro KUMA (-Mar), Tomomi SAKAGUCHI (-Mar) Hiroyuki YAMAGUCHI (-Mar), Mio MAKIGUCHI (-Mar) Tomonari MATSUMURA (-Mar), Junpei SUZUKI (-Mar) Kyohei YAMADA (-Mar), Misako KOKETSU Takahiro SHIMAMINE, Katsuhiko SUZUKI Mirei HAGIWARA (-Mar), Chiho SATOKAWA (-Mar) Asuka MANABE, Shuntaro SAWAZAKI (-Mar) Masako KAWADA, Shuko ARAI, Kai LI (-Mar) Ahmad F J M SH ALSULAILI (Oct-) Yixin LOU (Oct-), Ruixin LI (Nov-)
Visiting Scholar	Nguyen Tuan KHANG (Apr-Jul)

(1) Outline

Orthodontic Science is one of the dental sciences which propose to control the craniofacial growth and development in equilibrium with the whole body, and also deals with the prevention and/or treatment of malocclusion and related disorders, by which the alteration of maxillofacial function with aging could be kept to the most suitable condition.

(2) Research

Research Subjects

- 1) Biomechanical study of occlusion
- 2) Studies on biological response and functional adaptation followed by orthodontic and occlusal stimulation
- 3) Clinical application of autotransplantation in orthodontic treatment
- 4) Studies on interrelation between malocclusion and temporomandibular joint
- 5) Studies on occlusion and age-related changes in cranio-maxillofacial morphology and function
- 6) Studies on interrelation between cranio-maxillofacial complex and whole body
- 7) Development of mechanics and materials for orthodontic treatment
- 8) Pathophysiological studies on sleep and breathing disorders
- 9) Studies on interrelation between breathing and body function

(3) Education

Subjects of Education:

Orthodontic Science, Pathophysiology for Malocclusion, Biology for Functional Adaptation

(4) Lectures & Courses

Orthodontic Science

- 1) To explain the unhealthy physiological condition of malocclusion and deepen the scientific basis for orthodontic treatment.
- 2) To understand the biological reaction and adaptation of occlusal tissues to mechanical stresses such as occlusal force or orthodontic force, and also the changes with aging.
- 3) To explain the art for controlling the morphologic and functional problems of occlusion in orthodontic treatment, from the view points of biomaterials and biomechanics.
- 4) To enlighten the social dentistry for the needs and demands of orthodontic treatment.

Pathophysiology for Malocclusion

To understand the alteration of occlusal function and morphology with aging, and to explain the pathological condition of malocclusion from the viewpoint of physiology, biomechanics, biology and sociology.

Biology for Functional Adaptation

To understand the procedure of biological reaction and adaptation of occlusal system to the orthodontic stimuli, including the influence of aging, and to provide the control of the surroundings of the occlusal system.

(5) Clinical Services & Other Works

Clinical Services

In the field of practical orthodontic, with the development of materials and treatment techniques, we have taken initiatives in two big turning points at all time. Namely, one is the Direct Bonding System which has made it possible to attach brackets directly to the teeth surface without orthodontic metal bands. Another is the development of Super-Elastic Ti-Ni Alloy Wire, and following Improved Super-Elastic Ti-Ni Alloy Wire. With these new wires, we have provided an epoch-making orthodontic technique, where teeth could be moved more efficiently and safely with light continuous forces, and in consequences, the limits for teeth movement are expanded and the treatment outcomes are also improved. On the other hand, in order to determine the scientific basis for the needs of orthodontic treatment, we are engaging in the study of pathophysiology of malocclusion, and these research results are getting feedback to the orthodontic practices as soon as possible to stimulate the development of new treatment protocols.

Students in the graduate course not only pursue their scientific researches but also being educated in accordance with our curriculum for the post-graduated clinical program. In this program, we aim to bring up the leading persons of next generation who have highly specialized knowledge and skills of orthodontics as well as prominent minds of clinical researches.

(6) Clinical Performances

Highlights of Clinical Services

- 1) Orthodontic treatments by using Improved Super-Elastic Ti-Ni Alloy Wire
- 2) Comprehensive Orthodontic Treatments

With the cooperation of related field, we provide comprehensive treatments for those patients with cleft lips and palates and other congenital anomalies, jaw deformities, maxillofacial functional disorders, periodontal diseases, impacted teeth, autotransplantation combined cases, and usages of implant anchorages.

(7) Publications

[Original Articles]

1. Shimizu Y, Khan M, Kato G, Aoki K, Ono T. Occlusal disharmony-induced stress causes osteopenia of the lumbar vertebrae and long bones in mice. *Scientific Reports*. 2018.01; 8(1); 173
2. Hatano K, Ishida Y, Yamaguchi H, Hosomichi J, Suzuki J, Usumi-Fujita R, Shimizu Y, Shibutani N, Kaneko S, Ono T. The chemokine receptor type 4 antagonist, AMD3100, interrupts experimental tooth movement in rats. *Archives of Oral Biology*. 2018.02; 86; 35-39
3. Ozawa E, Honda EI, Parakonthun KN, Ohmori H, Shimazaki K, Kurabayashi T, Ono T. Influence of orthodontic appliance-derived artifacts on 3-T MRI movies. *Progress in Orthodontics*. 2018.02; 19(1); 7
4. Suzuki J, Shimazaki K, Koike S, Ono T. Gastric emptying rate before and after orthodontic treatment examined with the [¹³C] breath test: A pilot study. *American Journal of Orthodontics and Dentofacial Orthopedics* . 2018.03; 153(3); 347-354
5. Kimura-Ueda K, Shimazaki K, Sugimoto K, Ono T. Influence of habitual mouth breathing on taste sensation. *Orthodontic Waves*. 2018.03; 77(1); 24-30
6. Kanaguchi Arita A, Yonemitsu I, Ikeda Y, Miyazaki M, Ono T. Low-intensity pulsed ultrasound stimulation for mandibular condyle osteoarthritis lesions in rats. *Oral Diseases*. 2018.05; 24; 600-610
7. Ogawa T, Okihara H, Kokai S, Abe Y, Karin Harumi UK, Makiguchi M, Kato C, Yabushita T, Michikawa M, Ono T.. Nasal obstruction during adolescence induces memory/learning impairments associated with BDNF/TrkB signaling pathway hypofunction and high corticosterone levels. *Journal of Neuroscience Research*. 2018.06; 96(6); 1056-1065
8. Usumi-Fujita R, Nakakuki K, Fujita K, Kosugi M, Yonemitsu I, Fukuyama E, Ono T. Collaborative treatment for a case of condylar hyperplastic facial asymmetry. *The Angle Orthodontist*. 2018.07; 88(4); 503-517
9. Watakabe K, Yonemitsu I, Ikeda Y, Tang H, Ono T. Unilateral nasal obstruction induces morphological changes of the mandibular condyle in growing rats. *Orthodontic Waves*. 2018.09; 77(3); 157-168
10. Matsumoto Y, Sringkarnboriboon S, Ono T. Effects of continuous force application for extrusive tipping movement on periapical root resorption in the rat mandibular first molar. *The Korean Journal of Orthodontics*. 2018.09; 48(5); 339-345
11. Sato M, Asano T, Hosomichi J, Ono T, Nakata T. Optogenetic manipulation of intracellular calcium by BACCS promotes differentiation of MC3T3-E1 cells. *Biochemical and biophysical research communications*. 2018.10; 506(3); 716-722
12. Ishida T, Manabe A, Yang SS, Yoon HS, Kanda E, Ono T. Patterns of adenoid and tonsil growth in Japanese children and adolescents: A longitudinal study. *Scientific Reports*. 2018.11; 8(1); 17088
13. Hosomichi J, Shibutani N, Yamaguchi H, Hatano K, Kuma Y, Suzuki T, Kaneko S, Ono T. Localization of leucine-rich repeat-containing G-protein-coupled receptor 5- and Ki67-positive periodontal cells expressing runt-related transcription factor 2 during tooth movement. *Orthodontic Waves*. 2018.12; 77(4); 197-208

[Conference Activities & Talks]

1. Hong H, Hosomichi J, Maeda H, Kochakorn L, Oishi S, Kuma Y, Yamaguchi H, Ishida Y, Suzuki J, Yoshida K, Ono T. The impact of a β 2-adrenergic antagonist, butoxamine on mandibular growth retardation caused by intermittent hypoxia in growing rats. 5th Tokyo Medical University Memorial Hall Poster Conference 2018.02.22 Tokyo, Japan
2. Lekvijittada K, Hosomichi J, Maeda H, Hong H, Changsiripun C, Kuma Y, Oishi S, Yamaguchi H, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Suzuki JI, Yoshida KI, Ono T. Influences of intermittent hypoxia on condylar growth: A study in infant rats. 5th Tokyo Medical University Memorial Hall Poster Conference 2018.02.22 Tokyo, Japan
3. Hosomichi J, Maeda H, Kuma Y, Oishi S, Yoshida KI, Ono T. Differential effects of intermittent hypoxia on phenotypic and metabolic features of airway muscles in weaning- and adolescent-aged rats. 5th Tokyo Medical University Memorial Hall Poster Conference 2018.02.22 Tokyo, Japan
4. Hong H, Hosomichi J, Maeda H, Kochakorn L, Oishi S, Kuma Y, Yamaguchi H, Ishida Y, Suzuki J, Yoshida K, Ono T. The impact of a β 2-adrenergic antagonist, butoxamine on mandibular growth retardation caused by intermittent hypoxia in growing rats. The 11th Asian Pacific Orthodontic Conference 2018.03.05 Boracay, Republic of the Philippines
5. Lekvijittada K, Hosomichi J, Maeda H, Hong H, Changsiripun C, Kuma Y, Oishi S, Suzuki J, Yoshida K, Ono T. Influence of intermittent hypoxia on condylar growth : A study in infant rats. The 11th Asian Pacific Orthodontic Conference 2018.03.25 Boracay, Republic of the Philippines
6. Uchikawa Y, Hosomichi J, Suzuki J, Yamaguchi H, Ishida Y, Hatano K, Usumi-Fujita R, Shimizu Y, Kaneko S, Uesugi S, Ono T. Differential growth response of craniofacial and limb bones to hypertension with sympathetic hyperactivity in rats. 96th General Session and Exhibition of the International Association for Dental Research (IADR) 2018.07.27 London, UK
7. Hong H, Hosomichi J, Maeda M, Lekvijittada K, Oishi S, Kuma Y, Yamaguchi H, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Suzuki JI, Yoshida KI, Ono T. Different effects of intermittent hypoxia on mandibular growth in the juvenile and adolescent rats. Wuhan University PhD seminar 2018.08.20 Wuhan, China
8. Hashimoto T, Low S, Fujita K, Usumi-Fujita R, Yanagihara H, Takahashi C, Sugimoto M, Sugiura Y. TongueInput: Input Method by Tongue Gestures Using Optical Sensors Embedded in Mouthpiece. The SICE Annual Conference 2018 2018.09.11 Nara, Japan
9. Fukino K. Anatomical significance of the spatial distribution of the palatopharyngeus with regard to velopharyngeal closure. International Symposium of Clinical and Applied Anatomy 2018.09.15 Moscow, Russia
10. Aung Phyo T, Kato C, Abe Y, Ogawa T, Makiguchi M, Okihara H, Kokai S, Ono T. Effect of decreased occlusal loading on cortically induced rhythmic jaw movements in growing rats. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.29 Yokohama, Japan
11. Watari I, Mizumachi-Kubono M, Hsu JC, Podyma-Inoue KA, Narukawa M, Misaka T, Watabe T, Ono T. Unilateral nasal obstruction alters sweet taste preference and sweet taste receptor in circumvallate papillae. The 52nd Annual Meeting of the Japanese Association for the Study of Taste and Smell 2018.10.29 Saitama, Japan
12. Yang W, Yonemitsu I, Guo X, Ikeda Y, Watari I, Ono T. Lateral-functional-shift of rat mandible: The interaction of PRG4 with IHH and TGF- β 1 in condyle. The 77th Annual Meeting of the Japan Orthodontic Society 2018.11.01 Yokohama, Japan
13. Sato M, Asano T, Hosomichi J, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Nataka T, Ono T. Elucidation of the molecular mechanism of osteoblast differentiation and its control using optogenetics. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.11.01 Yokomaha, Japan
14. Hong H, Hosomichi J, Maeda H, Lekvijittada K, Oishi S, Kuma Y, Yamaguchi H, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Suzuki J, Yoshida K, Ono T. β 2-adrenergic antagonist butoxamine reduces the mandibular growth retardation caused by intermittent hypoxia in adolescent rats. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.11.01 Yokomaha, Japan

15. Suzuki H, Furuya J, Matsubara C, Kagihuku Y, Ono T, Akazawa C, Asada T, Minakuchi S. Approaches of investigating oral function in Mild Cognitive Impairment (MCI) patients. The 6th Tri-University Consortium 2018.11.30 Tokyo, Japan

[Awards & Honors]

1. Hong H, Hosomichi J, Maeda H, Kochakorn L, Oishi S, Kuma Y, Yamaguchi H, Ishida Y, Suzuki J, Yoshida K, Ono T. The 11th Asian Pacific Orthodontic Conference Best Presentation Award (1st Prize), Asian Pacific Orthodontic Society, 2018.03
2. Ono T. 2018 IADR/AADR William J. Gies Awards, International Association for Dental Research (IADR), 2018.07
3. Hosomichi J. Certificate of Recognition for Orthodontic Waves Reviewer, Japanese Orthodontic Society, 2018.10
4. Yang W, Yonemitsu I, Guo X, Ikeda I, Watari I, Ono T. The 77th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, 2018.11
5. Aoyagi M, Oshima M, Kita S, Shimazaki K, Omura S, Ono T. The 77th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2018.11
6. Sato M, Asano T, Hosomichi J, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Nataka T, Ono T. The 77th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2018.11
7. Hong H, Hosomichi J, Maeda H, Lekvijittada K, Oishi S, Kuma Y, Yamaguchi H, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Suzuki J, Yoshida K, Ono T. The 77th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2018.11
8. Inoue M, Ono T, Nakajima T, Ono T. The 77th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2018.11

Cariology and Operative Dentistry

Professor: Junji Tagami

Associate Professor: Masayuki Otsuki

Junior Associate Professor: Toru Nikaido, Masatoshi Nakajima

Assistant Professor: Takako Yoshikawa, Yasushi Shimada(January), Go Inoue,

Keiichi Hosaka, Tomohiro Takagaki, Rena Takahashi, Naoko Mastui(April)

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Takaaki Sato(September), Kento Sato(June) ,Yukinori Kano(April),

Juri Hayashi(April September), Takashi Hatayama(April September),

Nami Takashino(April September), Yusuke Kuno(September),

Shigeki Uchinuma(September), Akifumi Takahashi(October), Shin Rozan(October), Yuka Tsuda(November)

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JSPS Research Fellowship Noriko Hiraishi

Technical Assistant: Yuan Zhou(June)

Staff Assistant: Shiori Ogi, Takako Nakagawa

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Chihiro Matsuura (~ March) , Yukinori Kano (~ March) , Yuki Naruse (~ March) ,

Juri Hayashi (~ March) , Miho Sugiura (~ March) , Yuta Sumitani (~ March) ,

Atsuko Tagami (~ March) , Keiki Nakamura (~ March) , Yukari Noda (~ March) ,

Takashi Hatayama (~ March) , Yuka Tsuda (~ March) , Yuan Zhou (~ March) ,Nami Takashino (~ March) ,

Ayaka Kusanagi Sato (~ March) , Keita Taguchi (~ March) ,Jorge Espigares(September),

Mari Okada, Junji Atomura, Akifumi Takahashi, Ayako Nakamoto, Tomoko Tabata,

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Satomi Matsunaga, Shin Rozan, HESHAM HASSAN OSMAN MOHAMMED,

Yukiko Tanno, AHMED MOHAMED ABDELRAHMAN ABDOU,

MAHMOUD MOHAMED SAYED AHMED, SOE YU PAING, SWE ZIN AUNG,

QUTAIBA Y A A ALSANDI, SAN SAN MAY PHYO AUNG,

ALMASABI WALEED ABDULQADER M,

WIJETUNGA CHAMARI LASINDRA , ERICK LUZ MADRIGAL (April),

Motoi Takahashi(April), Sakiko Tsuchiya(April), Kim Seunggun(April),

Kyoko Ishikawa(April), Toyoaki Kobayashi(April), Miyuki Shimizu(April),

Mayu Hasegawa(April), Shun Kobayashi(April), Nanako Ueda(April),

Misa Kashiwa(April), Saki Uchiyama(April), Yosuke Minato(April),

Yuta Baba(April), LEILA NASIRY KHANLAR (April),

VICHEVA MARTINA GEORGIEVA(April), Citra Kusumasari (October),

Min Khant Ko Ko(October), Pa Pa Kay Khine (October)

Research Student: Shinji Ogura, Mineo Kijima,

VICHEVA MARTINA GEORGIEVA (March), ERICK LUZ MADRIGAL(March),

Nooruldeen Ali Saeed (April)

(1) Outline

TMDU possesses the longest history as a national dental university in Japan. We have contributed to the progress of science and education through presenting a number of world leading graduates in the field of den-

tistry. Many of their achievements are now recognized as global standards in the field of dental research and clinical practice.

At Cariology and Operative Dentistry, we believe that the ultimate goal of the oral health care programs is to provide well-being of the patients. In order to achieve this goal, besides the clinical training that we offer to the licensed graduate students, high-caliber research projects are being carried out aimed at developing, enhancing and evaluation of the materials and techniques in dentistry; particularly for adhesives, caries prevention, diagnosis and treatment, and oral health maintenance.

Cariology and Operative Dentistry is a home to the late professor Takao Fusayama, who developed the “Caries Detector” for removal of the caries, and promoted “Total-etch technique” and other restorative techniques using adhesive resin composite for the minimally invasive caries treatment.

Our group, consisting of members of the faculty, staff and graduate students, is among the international leaders in the ongoing dental research. I would hereby like to extend an invitation to those fellows and prospect graduate students interested in perusing high-level research and gaining an insight into modern concepts to join our diverse international team of scientists.

(2) Research

1) Evaluation of dentin bonding systems

Adhesion of bonding materials to enamel, dentin and cementum of tooth are evaluated using methods such as the microshear and the microtensile bond strength tests. Factors affecting adhesion such as the region and caries state of tooth substrate, light-curing irradiation, release of fluoride from material, tooth preparation methods, root canal treatment of the tooth, etc. have been investigated. We have also focused on the difference between various adhesives system in terms of their composition, performance and bonding durability.

2) Super Enamel and Super Dentin

Using various electron microscopy techniques, we have demonstrated that resistance of enamel and dentin to acid attack could be increased in an acid-base resistant zone which was formed following the application of some self-etching dental adhesives. We proposed that the diffusion of such acidic monomers beyond the classic hybrid layer (interfacial zone) and their ion-exchange interactions with the available hydroxyapatite could result in formation of stable organic-inorganic complexes, and that the structures should be termed “super tooth”, which includes the reinforced enamel and dentin.

3) Development of OCT for establishing its clinical application

Optical coherent tomography (OCT) is a noninvasive, cross-sectional imaging system that can visualize the internal structures nondestructively and without exposure to X-ray or ionizing radiation. Our research has aimed to further develop OCT and introduce a dental OCT system that can be used to diagnose dental defects and diseases such as tooth cracking and caries.

4) Non-destructive test of adhesive restorations

We are working to establish a method for non-destructive detection of gap and secondary caries beneath composite restorations using optical coherence tomography (OCT).

5) Evaluation of polymerization behavior of light-cured resin composites

Aim to establish clinical techniques to compensate polymerization shrinkage stress of resin composite, we evaluated effect of adhesives, resin composite composition, light curing methods and cavity configuration factor (C-factor) on polymerization shrinkage stress using micro-focus X-ray computed tomography (micro-CT) and 3D visualization method.

6) Resin coating technique

Resin coating using a bonding agent and flowable composite benefits the adaptation of indirect restorations to dentin surface which is a key interface within a restoration. We have proposed that this resin coating technique should be technique of choice for placement of indirect restorations.

7) Research on optical properties of the dental structure

As a part of the OCT development project, we work on characterization of the basic optical properties such as attenuation coefficient and refractive index of dentin and enamel, and their changes following demineralization and remineralization.

8) Research on direct core build up materials

Adhesive performance to the root canal dentin by resin core build up systems has been evaluated. These materials can be used in combination with fiber posts.

9) Study on dental erosion

Erosive loss of enamel due to consumption of acidic beverages and some drugs has been evaluated using 3D focus-variation microscopy as well as profilometry.

10) Caries risk assessment

We have investigated caries risk based on the measurement of saliva buffering capacity in samples collected from patients. We have also probed the association between the pH of lesion surface and caries activity.

11) Adhesion of cariogenic bacteria to dentin surface

We have developed a model to experimentally evaluate factors affecting the ability of cariogenic bacteria such as *S.mutans* to attach to the tooth surface in the initial phase of biofilm formation.

12) Biocompatibility of resin-based dental adhesives

Immunohistochemical studies have been performed to evaluate the effects of various adhesive materials on dental pulp tissue.

13) The potential of fluoride- and/or Calcium containing materials on caries prevention

Inhibitory effects of CPP-ACP paste and fluoride on the enamel and dentin demineralization have been evaluated by the micro-focus X-ray computed tomography (micro-CT) non-destructively. We have also established a standard methodology for assessment of lesion parameters such as depth and mineral loss for micro-CT.

14) Evaluation of caries removal methods

We have evaluated the effect of caries removal method by the conventional rotary cutting instruments in comparison with new caries removal methods such as chemical removal agents, laser irradiation and abrasion on the adhesion performance and restoration success.

15) Development and evaluation of aesthetic dental materials

We have worked on optical properties and color match of the composite resins, in addition to clinical applications of tooth whitening materials .

16) Clinical research

We have created a protocol to evaluate the long-term and short-term performance of restorative materials in the patients who were admitted to the operative dentistry clinics at TMDU Dental Hospital.

(3) Education

Cariology and Operative Dentistry section offers a four-year graduate program. First-year graduate students attend lectures and seminars given in the graduate school and are expected to gain an understanding of the fundamentals about methodology and the knowledge necessary for their research. The contents of the classes given in our section include topics related to cariology and operative dentistry: caries diagnosis, biocompatibility, caries treatment and restoration, prevention and control, dental materials, new instruments and equipment. In keeping with the internationally orientated philosophy of this section, lectures are conducted in English and are open to all foreign students. First-year graduate students also undergo clinical training the procedures of modern adhesive restorations. Laboratory work, which commences in the first year, is performed under the supervision of our faculty staff. During the four-year program, several papers are required to be presented in domestic and / or international conferences and submitted to journals. The minimum requirements are completing the prescribed courses, a supervised research project and a dissertation for the degree published in a top international journal.

(4) Lectures & Courses

The ultimate goal of the oral health care programs is to provide well-being of the patients. In order to achieve this goal, besides the clinical training that we offer to the licensed graduate students, high-caliber research projects are being carried out aimed at developing, enhancing and evaluation of the materials and techniques in dentistry; particularly for adhesives, caries prevention, diagnosis and treatment, and oral health maintenance.

(5) Clinical Services & Other Works

Full-time faculty see patients in Operative Dentistry and Endodontics, and provide restoration of teeth with fillings for dental cavities, trauma and tooth wear, and root canal treatments. The faculty members supervise both pre-and postdoctoral students in the clinic.

(6) Clinical Performances

Our Operative Dentistry clinic provide restoration of teeth with fillings for dental cavities, trauma and tooth wear under Minimal intervention concept. The clinical services are based on accumulated scientific researches.

(7) Publications**[Original Articles]**

1. Sato T, Takagaki T, Ikeda M, Nikaido T, Burrow MF, Tagami J. Effects of Selective Phosphoric Acid Etching on Enamel Using "No-wait" Self-etching Adhesives. *The journal of adhesive dentistry*. 2018; 20(5); 407-415
2. Yusuke Kakiuchi, Tomohiro Takagaki, Masaomi Ikeda, Takaaki Sato, Naoko Matsui, Toru Nikaido, Michael F Burrow, Junji Tagami. Evaluation of MDP and NaF in Two-step Self-etch Adhesives on Enamel Microshear Bond Strength and Morphology of the Adhesive-Enamel Interface. *J Adhes Dent*. 2018; 20(6); 527-534
3. Ali Alghamdi, Takagaki Tomohiro, Nikaido Toru, Abdou Ahmed, Tagami Junji. Influence of Ambient Air and Different Surface Treatments on the Bonding Performance of a CAD/CAM Composite Block *JOURNAL OF ADHESIVE DENTISTRY*. 2018; 20(4); 317-324
4. Takako Yoshikawa, Alireza Sadr, Junji Tagami. μ CT-3D visualization analysis of resin composite polymerization and dye penetration test of composite adaptation *Dental Materials Journal*. 2018.01; 37(1); 71-77
5. Thwe Zin Ei, Yasushi Shimada, Syozi Nakashima, Maria Jacinta Rosario H Romero, Yasunori Sumi, Junji Tagami. Comparison of resin-based and glass ionomer sealants with regard to fluoride-release and anti-demineralization efficacy on adjacent unsealed enamel. *Dent Mater J*. 2018.01; 37(1); 104-112
6. Takuya Nakata, Yuichi Kitasako, Alireza Sadr, Syozi Nakashima, Junji Tagami. Effect of a calcium phosphate and fluoride paste on prevention of enamel demineralization. *Dent Mater J*. 2018.01; 37(1); 65-70
7. Takako Yoshikawa, Alireza Sadr, Junji Tagami. μ CT-3D visualization analysis of resin composite polymerization and dye penetration test of composite adaptation *Dental Materials Journal*. 2018.01; 37(1); 71-77
8. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Yoshihara K, Nagaoka N, Zhang F, Vleugels J, Van Meerbeek B, Minakuchi S. Crystallographic and morphological analysis of sandblasted highly translucent dental zirconia. *Dent Mater*. 2018.03; 34(3); 508-518
9. Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Suppasorn Thittaweerat, Richard M Foxton, Shizuko Ichinose, Junji Tagami, Keiichi Hosaka, Masatoshi Nakajima. Smear layer-deproteinizing improves bonding of one-step self-etch adhesives to dentin. *Dent Mater*. 2018.03; 34(3); 434-441
10. Junji Tagami. pH mapping on tooth surfaces for quantitative caries diagnosis using micro Ir/IrOx pH sensor *Analytical Chemistry*. 2018.03;
11. Chindanai Ratanaporncharoen, Miyuki Tabata, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami, Yuji Miyahara. pH Mapping on Tooth Surfaces for Quantitative Caries Diagnosis Using Micro Ir/IrOx pH Sensor. *Anal. Chem.*. 2018.03; 90(7); 4925-4931
12. Jorge Espigares, Juri Hayashi, Yasushi Shimada, Junji Tagami, Alireza Sadr. Enamel margins resealing by low-viscosity resin infiltration. *Dent Mater J*. 2018.03; 37(2); 350-357
13. Kakizaki S, Aoki A, Tsubokawa M, Lin T, Mizutani K, Geena K, Alireza S, Oda S, Sumi Y, Izumi Y. Observation and determination of periodontal tissue profile using optical coherence tomography. *Journal of Periodontal Research*. 2018.04; 53(2); 188-199
14. Yukinori Kano, Masatoshi Nakajima, Asami Aida, Naoko Seki, Richard M Foxton, Junji Tagami. Influence of enamel prism orientations on color shifting at the border of resin composite restorations. *Dent Mater J*. 2018.04; 37(2); 341-349

15. Manhal Ijbara, Kanae Wada, Makoto J Tabata, Junichiro Wada, Go Inoue, Michiyo Miyashin. Enamel Microcracks Induced by Simulated Occlusal Wear in Mature, Immature, and Deciduous Teeth. *Biomed Res Int.* 2018.04; 2018; 9
16. Mahmoud Sayed, Naoko Matsui, Noriko Hiraishi, Toru Nikaido, Michael F Burrow, Junji Tagami. Effect of Glutathione Bio-Molecule on Tooth Discoloration Associated with Silver Diammine Fluoride. *Int J Mol Sci.* 2018.04; 19(5);
17. N Hiraishi, S Kobayashi, H Yurimoto, J Tagami. Ca doped remineralization study on dentin by isotope microscopy. *Dent Mater.* 2018.04; 34(4); e57-e62
18. Irene Shuping Zhao, Sherry Shiqian Gao, Noriko Hiraishi, Michael Francis Burrow, Duangporn Duangthip, May Lei Mei, Edward Chin-Man Lo, Chun-Hung Chu. Mechanisms of silver diamine fluoride on arresting caries: a literature review. *Int Dent J.* 2018.04; 68(2); 67-76
19. Sai Kham Lyann, Tomohiro Takagaki, Toru Nikaido, Motohiro Uo, Masaomi Ikeda, Alireza Sadr, Junji Tagami. Effect of Different Surface Treatments on the Tensile Bond Strength to Lithium Disilicate Glass Ceramics. *J Adhes Dent.* 2018.05; 20(3); 261-268
20. Minh Nguyet Luong, Yasushi Shimada, Alireza Sadr, Masahiro Yoshiyama, Yasunori Sumi, Junji Tagami. Cross-sectional imaging of tooth bonding interface after thermal stresses and mechanical fracture. *Dent Mater J.* 2018.05;
21. Daisuke Araoka, Keiichi Hosaka, Masatoshi Nakajima, Richard Foxton, Ornnicha Thanatvarakorn, Taweesak Prasansuttiporn, Ayaka Chiba, Kento Sato, Masahiro Takahashi, Masayuki Otsuki, Junji Tagami. The strategies used for curing universal adhesives affect the micro-bond strength of resin cement used to lute indirect resin composites to human dentin. *Dent Mater J.* 2018.06; 37(3); 506-514
22. Takashi Hatayama, Ayaka Chiba, Kimisuke Kainose, Masatoshi Nakajima, Keiichi Hosaka, Noriyuki Wakabayashi, Richard M Foxton, Junji Tagami. Stress distribution in tooth resin core build-ups with different post-end positions in alveolar bone level under two kinds of load directions. *Dent Mater J.* 2018.06; 37(3); 474-483
23. Junji Atomura, Go Inoue, Toru Nikaido, Keisuke Yamanaka, Motohiro Uo, Junji Tagami. Influence of FCP-COMPLEX on bond strength and the adhesive-artificial cariesaffected dentin interface. *Dent Mater J.* 2018.06; 37(5); 775-782
24. Yuan Zhou, Yasushi Shimada, Khairul Matin, Alireza Sadr, Masahiro Yoshiyama, Yasunori Sumi, Junji Tagami. Assessment of root caries under wet and dry conditions using swept-source optical coherence tomography (SS-OCT). *Dent Mater J.* 2018.06;
25. Yuichi Kitasako, Alireza Sadr, Yasushi Shimada, Masaomi Ikeda, Yasunori Sumi, Junji Tagami. Remineralization capacity of carious and non-carious white spot lesions: clinical evaluation using ICDAS and SS-OCT. *Clin Oral Investig.* 2018.06;
26. Daisuke Araoka, Keiichi Hosaka, Masatoshi Nakajima, Richard Foxton, Ornnicha Thanatvarakorn, Taweesak Prasansuttiporn, Ayaka Chiba, Kento Sato, Masahiro Takahashi, Masayuki Otsuki, Junji Tagami. The strategies used for curing universal adhesives affect the micro-bond strength of resin cement used to lute indirect resin composites to human dentin. *Dent Mater J.* 2018.06; 37(3); 506-514
27. Araoka Daisuke, Hosaka Keiichi, Nakajima Masatoshi, Foxton Richard, Thanatvarakorn Ornnicha, Prasansuttiporn Taweesak, Chiba Ayaka, Sato Kento, Takahashi Masahiro, Otsuki Masayuki, Tagami Junji. ユニバーサル接着剤の重合手法は、間接修復用コンポジットレジンを用いたヒト象牙質への接着に用いるレジンの微小接着強さに影響する (The strategies used for curing universal adhesives affect the micro-bond strength of resin cement used to lute indirect resin composites to human dentin) *Dental Materials Journal.* 2018.06; 37(3); 506-514
28. Hatayama Takashi, Chiba Ayaka, Kainose Kimisuke, Nakajima Masatoshi, Hosaka Keiichi, Wakabayashi Noriyuki, Foxton Richard M., Tagami Junji. 歯槽骨の水準を基準としてポスト先端の深さを様々に変えたレジンコア支台築造を行った歯に、2通りの方向で荷重を付した時に歯内に発生する応力分布 (Stress distribution in tooth resin core build-ups with different post-end positions in alveolar bone level under two kinds of load directions) *Dental Materials Journal.* 2018.06; 37(3); 474-483

29. Keita Taguchi, Keiichi Hosaka, Masaomi Ikeda, Ryuzo Kishikawa, Richard Foxton, Masatoshi Nakajima, Junji Tagami. The effect of warm air-blowing on the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *J Prosthodont Res.* 2018.07; 62(3); 330-336
30. Yuki Nakazawa, Shoichi Suzuki, Go Inoue, Toru Nikaido, Junji Tagami, Keiji Moriyama. Influence of orthodontic self-etch adhesive on acid resistance of surface enamel. *Dent Mater J.* 2018.07; 37(4); 568-574
31. Takahashi A, Takagaki T, Wada T, Uo M, Nikaido T, Tagami J. The effect of different cleaning agents on saliva contamination for bonding performance of zirconia ceramics. *Dental materials journal.* 2018.07; 37(5); 734-739
32. Yuta Sumitani, Hidenori Hamba, Keiki Nakamura, Alireza Sadr, Toru Nikaido, Junji Tagami. Micro-CT assessment of comparative radiopacity of adhesive/composite materials in a cylindrical cavity. *Dent Mater J.* 2018.07; 37(4); 634-641
33. Khine W Zan, Keiki Nakamura, Hidenori Hamba, Alireza Sadr, Toru Nikaido, Junji Tagami. Micro-computed tomography assessment of root dentin around fluoride-releasing restorations after demineralization/remineralization. *Eur. J. Oral Sci..* 2018.07;
34. Ayako Nakamoto, Masaomi Ikeda, Noriko Hiraishi, Toru Nikaido, Motohiro Uo, Junji Tagami. Effect of fluoride mouthrinse on adhesion to bovine root dentin. *Dent Mater J.* 2018.07;
35. Yuki Naruse, Tomohiro Takagaki, Naoko Matsui, Takaaki Sato, Masaomi Ikeda, Toru Nikaido, Junji Tagami. Effect of alumina-blasting pressure on adhesion of CAD/CAM resin block to dentin. *Dent Mater J.* 2018.07;
36. Kou Fujita Nakajima, Toru Nikaido, Michael Francis Burrow, Taro Iwasaki, Yasuhiro Tanimoto, Satoshi Hirayama, Norihiro Nishiyama. Effect of the demineralisation efficacy of MDP utilized on the bonding performance of MDP-based all-in-one adhesives. *J Dent.* 2018.07;
37. Kou Fujita Nakajima, Toru Nikaido, Akishi Arita, Satoshi Hirayama, Norihiro Nishiyama. Demineralization capacity of commercial 10-methacryloyloxydecyl dihydrogen phosphate-based all-in-one adhesive. *Dent Mater.* 2018.07;
38. Chihiro Matsuura, Yasushi Shimada, Alireza Sadr, Yasunori Sumi, Junji Tagami. Three-dimensional diagnosis of dentin caries beneath composite restorations using swept-source optical coherence tomography. *Dent Mater J.* 2018.07; 37(4); 642-649
39. Keita Taguchi, Keiichi Hosaka, Masaomi Ikeda, Ryuzo Kishikawa, Richard Foxton, Masatoshi Nakajima, Junji Tagami. The effect of warm air-blowing on the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *J Prosthodont Res.* 2018.07; 62(3); 330-336
40. Naruse Y, Takagaki T, Matsui N, Sato T, Ikeda M, Nikaido T, Tagami J.. Effect of alumina-blasting pressure on adhesion of CAD/CAM resin block to dentin. *Dent Mater J..* 2018.07;
41. Alquarni Dhaifallah Abdullah G, Masatoshi Nakajima, Keiichi Hosaka, Kurumi Ide, Daiki Nagano, Takahiro Wada, Masaomi Ikeda, Teerapong Mamane, Ornnicha Thanatvarakorn, Prasansuttiorn Taweesak, Richard Foxton, Junji Tagami. The repair bond strength to resin matrix in cured resin composites with different degrees of conversion after water aging. *Dental Materials Journal.* 2018.08;
42. K Y Kyaw, M Otsuki, M S Segarra, N Hiraishi, J Tagami. Effect of Calcium-phosphate Desensitizers on Staining Susceptibility of Acid-eroded Enamel. *Oper Dent.* 2018.08;
43. Bruna Marin Fronza, Patricia Makishi, Alireza Sadr, Yasushi Shimada, Yasunori Sumi, Junji Tagami, Marcelo Giannini. Evaluation of bulk-fill systems: microtensile bond strength and non-destructive imaging of marginal adaptation. *Braz Oral Res.* 2018.08; 32; e80
44. Junichi Shinagawa, Go Inoue, Toru Nikaido, Masaomi Ikeda, Michael F Burrow, Junji Tagami. Early bond strengths of 4-META/MMA-TBB resin cements to CAD/CAM resin composite. *Dent Mater J.* 2018.08;
45. Kyaw KY, Otsuki M, Segarra MS, Tagami J. Effect of sodium fluoride pretreatment on the efficacy of an in-office bleaching agent: An in vitro study. *Clinical and experimental dental research.* 2018.08; 4(4); 113-118

46. Francine Kerber Vieira Makwitz, Celso Afonso Klein Junior, Eduardo Galia Reston, Rubem Beraldo dos Santos, Fernando Freitas Portella, Keiichi Hosaka. Storage Temperature Influences the Carbamide Peroxide Concentration of at Home Bleaching Agents Biomedical Journal of Scientific and Technical Research. 2018.09;
47. Seki Naoko, Kanazawa Manabu, Komagamine Yuriko, Mizutani Koji, Hosaka Keiichi, Komada Wataru, Moross Janelle, Kuroda Shinji, Sunaga Masayo, Kawaguchi Yoko, Morio Ikuko, Kinoshita Atsuhiko. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School Journal of Medical and Dental Sciences. 2018.09; 65(3); 123-130
48. Nagano D, Nakajima M, Takahashi M, Ikeda M, Hosaka K, Sato K, Prasansuttiorn T, Foxton RM, Tagami J. Effect of Water Aging of Adherent Composite on Repair Bond Strength of Nanofilled Composites. The journal of adhesive dentistry. 2018.10; 1-9
49. Atomura Junji, Inoue Go, Nikaido Toru, Yamanaka Keisuke, Uo Motohiro, Tagami Junji. Influence of FCP-COMPLEX on bond strength and the adhesive: artificial caries-affected dentin interface Dental Materials Journal. 2018.10; 37(5); 775-782
50. Mahmoud Sayed, Naoko Matsui, Noriko Hiraishi, Go Inoue, Toru Nikaido, Michael F Burrow, Junji Tagami. Evaluation of discoloration of sound/demineralized root dentin with silver diamine fluoride: In-vitro study. Dent Mater J. 2018.11;
51. Lin WT, Thwin KM, Zaitse T, Kitasako Y, Tagami J, Kawaguchi Y. Erosive tooth wear and its related risk factors among Myanmar residents in Japan Asian Pacific Journal of Dentistry. 2018.11; 18; 21-28
52. Uchinuma S, Shimada Y, Matin K, Hosaka K, Yoshiyama M, Sumi Y, Tagami J. Effects of UVB and UVC irradiation on cariogenic bacteria in vitro. Lasers in medical science. 2018.11;
53. Alqarni D, Nakajima M, Hosaka K, Ide K, Nagano D, Wada T, Ikeda M, Mamanee T, Thanatvarakorn O, Prasansuttiorn T, Foxton R, Tagami J. The repair bond strength to resin matrix in cured resin composites after water aging. Dental materials journal. 2018.11;
54. Luong MN, Otsuki M, Shimada Y, Ei TZ, Sumi Y, Tagami J. Effect of lights with various wavelengths on bleaching by 30% hydrogen peroxide. Lasers in medical science. 2018.11;
55. Alaa Turkistani, Sofiqul Islam, Yasushi Shimada, Junji Tagami, Alireza Sadr. Dental cements: Bioactivity, bond strength and demineralization progression around restorations. Am J Dent. 2018.11; 31(Sp Is B); 24B-31B
56. Rutthanu N Wongsorachai, Ornnicha Thanatvarakorn, Taweesak Prasansuttiorn, Sumana Jittidecharaks, Keiichi Hosaka, Richard M Foxton, Masatoshi Nakajima. Effect of Polymerization Accelerator on Bond Strength to Eugenol-Contaminated Dentin. J Adhes Dent. 2018.12; 20(6); 541-547

[Books etc]

1. Durability of Dual-cured Adhesives to Enamel and Deep Dentin. LAP LAMBERT Academic Publishing, 2018.05 (ISBN : 978-613-9-83569-0)

[Misc]

1. Toru Nikaido, Junji Tagami, Hirofumi Yatani, Chikahiro Ohkubo, Tomotaro Nihei, Hiroyasu Koizumi, Toshio Maseki, Yuichiro Nishiyama, Tomoyoshi Takigawa, Yuji Tsubota. Concept and clinical application of the resin-coating technique for indirect restorations. Dent Mater J. 2018.03; 37(2); 192-196
2. Junji Tagami. Tooth wear: its pathology and treatment guidelines 2018.06; 71(3);
3. Keiichi Hosaka, Taweesak Prasansuttiorn, Ornnicha Thanatvarakorn, Sitthikorn Kunawarote, Masahiro Takahashi, Richard M Foxton, Junji Tagami, Masatoshi Nakajima. Smear layer-deproteinization: Improving the adhesion of self-etch adhesive systems to caries-affected dentin. Current Oral Health Reports. 2018.09; 5(3); 169-177

[Conference Activities & Talks]

1. Junji Tagami. Practical Training-Minimal Invasive Caries Treatment-. Asia Adhesive Restration and Periodontal Advanced Course 2018 2018.03.08 TMDU
2. Junji Tagami. Lectures and trial bond strength test. Asia Adhesive Restration and Periodontal Advanced Course 2018 2018.03.10 Tokyo medical and Dental University
3. Junji Tagami. ESTHETIC RESTORATION WITH AUTO-COLOR MATCHING COMPOSITE RESIN AND AUTO-CURE LIGHTLESS ADHESIVE. The 40th Asia Pacific Dental Congress & 109th PDA Annual Convention 2018.05.06
4. Junji Tagami. How to Maximize the Bonding Performance of Adhesive Materials in Clinical Situations Inovation in Diagnosis and Monitoring for Caries,Toothwear ,Crack andRestoration Defects. Mahidol University Dental School 50th Anniversary Lecture 2018.05.12
5. Aoki A, Takeuchi Y, Akizuki T, Mizutani K, Katagiri S, Ikeda Y, Maekawa S, Watanabe K, Matsuura T, Ohtsu A, Kakizaki S, Komazaki R, Mikami R, Hideshima M, Nikaidou T, Araki K, Izumi Y. Current Status of Clinical Practice of Periodontal Therapy by Predoctoral Dental Students at Tokyo Medical and Dental University (TMDU). The 61th Spring Meeting of The Japanese Society of Periodontology 2018.06.01 Keio plaza hotel, Tokyo
6. Prof.Shu-Fen Chuang. Investigations in polymerization shrinkage of resin composites. 2018.06.13 Lecture Room 5F,Building7
7. Ahmed Abdou, Rena Takahashi, Toru Nikaido, Junji Tagami. The influence of resin coating technique and temporalization on dentin bond strength of resin cement with CAD/CAM resin block. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Kanagawa. Japan
8. Misa Kashiwa, Juri Hayashi, Yasushi Shimada, Alireza Sadr, Masahiro Yoshiyama Masahiro, Yasunori Sumi ,Junji Tagami. Effect of C-factor on Sealing Performance of Direct Resin Composite Restoration. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
9. Inokoshi M, Shimizubata M, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Minakuchi S. Sandblasting increases the flexural strength of highly translucent zirconia. 96th General Session and Exhibition of the IADR 2018.07.25 London
10. Keiichi Hosaka, Juri Hayashi, Daisuke Araoka, Masatoshi Nakajima, Richard Foxton, Masaomi Ikeda, Wurihan, Yo Shibata, Takashi Miyazaki, Junji Tagami. Eight-year Durability of Resin-dentin Interfaces of a 1-SEA. IADR/PER General Session 2018.07.25 London, England
11. Yasushi Shimada, Keiichi Hosaka, Kazuyuki Araki, Alireza Sadr, Takashi Miyazaki, Yasunori Sumi, Junji Tagami, Masahiro Yoshiyama. 3D Diagnosis of Proximal Caries Using Swept-source Optical Coherence Tomography. IADR/PER General Session 2018.07.25 London, England
12. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Basic Properties of Novel S-PRG Contained Cement for Root Caries. 96th General Session and Exhibition of the IADR 2018.07.26 London
13. Masatoshi Nakajima, Kano Yukinori, Asami Aida, Ayaka Chiba, Keiichi Hosaka, Naoko Seki, Richard Foxton, Taweesak Pransansuttiporn, Ornnicha Thanatvarakorn, Junji Tagami. Color adaptation at enamel-composite borders with different incidnet-light directions. 96th IADR/PER General Session 2018.07.26 London, UK
14. T. Yoshikawa, A. Sadr. J. Tagami. Dye Penetration Test and Micro-CT Observation of Resin Composite/Cavity-Wall Adaptation. 96th, IADR 2018.07.26 London
15. Noriko Hiraishi, Fumiaki Hayashi, Masayuki Otsuki, Junji Tagami. Noriko Hiraishi, Fumiaki Hayashi, Masayuki Otsuki, Junji Tagami. Effect of Fluoride on Dentin Remineralization Using 1H-31P Heteronuclear-correlation NMR. 96th General Session & Exhibition of the IADR/AADR 2018.07.26 LDN, UK
16. Shimizu H, Inokoshi M, Takagaki T, Minakuchi S. Discoloration of Highly Translucent Zirconia and Composite Resin. 96th General Session and Exhibition of the IADR 2018 2018.07.27 London

17. Akifumi Takahashi, Tomohiro Takagaki, Toru Nikaido, Takahiro Wada, Motohiro Uo, Junji Tagami. Effect of different cleaning agents for saliva contaminated zirconia ceramics. The 96th General Session & Exhibition of the IADR 2018.07.27 London
18. Amr Saad, Toru Nikaido, Ahmed Abdou, Junji Tagami. Assessment of a Zinc-Containing Desensitizer for Prevention of Dentin Demineralization. 2018 IADR/PER General Session 2018.07.27 London, England
19. Tweesak Pransansuttiporn, Rutthanun Wongsorachai, Ornnicha Thanatavarakorn, Sumana Jittidecharaks, Junji Tagami, Masatoshi Nakajima.. Effect of polymerization accelerator on bond strength tp eugenol-contaminated dentin. 96th IADR/PER General Session 2018.07.28 London. UK
20. Ornnicha Thanatavarakorn, Tweesak Pransansuttiporn, Junji Tagami, Masatoshi Nakajima. Reducing agent effect on bonding durability to NaOCl-deproteinized caries-affected dentin.. 96th IADR/PER General Session 2018.07.28 London, UK
21. Seki N, Hosaka K, Komada W, Kanazawa M, Mizutani K, Komagamine Y, Moross J, Morio I. International student forum 2018 -International students' life in Japan-. International Student Forum 2018 by Japanese Dental Science Federation 2018.08.02 Tokyo
22. Junji Tagami. How the bonding was developed, and what's the next?. 35th IADR Brazilian Division Annual Meeting 2018.09.02 Expo D.Pedro
23. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. 32nd IADR-SEA & 29th SEAAD 2018.09.11 Da Nang, Vietnam
24. Seki N, Hosaka K, Moross J, Sunaga M, Morio I, Kinoshita A. Evaluating an Online Course on Clinical Expertise with Computer-assisted Simulation Materials. The 29th SEAAD Annual Scientific Meeting 2018.09.11 Da Nang, Vietnam
25. Shin ROZAN, Rena TAKAHASHI, Yutaro ODA, Toru NIKAIDO, Junji TAGAMI. The effect of the thickness of resin-coating layer and CAD/CAM block on dentin bond strength. The 29th General Scientific Meeting of Japan Academy of Esthetic Dentistry 2018.09.29 Saitama, Japan
26. Shimizubata M, Inokoshi M, Hatano K, Wada T, Takahashi R, Uo M, Minakuchi S. Acid buffering capacity of a novel S-PRG filler containing glass ionomer cement. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Sapporo
27. Hatano K, Inokoshi M, Uo M, Wada T, Takahashi R, Minakuchi S. Acid buffering capacity of a novel S-PRG filler containing denture adhesive. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Sapporo
28. Keiichi Hosaka. Is Our Direct Composite Restoration Perfect?. International Symposium on Adhesive Dentistry in Okayama 2018.10.08 Okayama University, Okayama, Tokyo
29. UEDA Nanako, TAKAGAKI Tomohiro, SATO Takaaki, Matsui Naoko, IKEDA Masaomi, NIKAIDO Toru, TAGAMI Junji. Effect of different surface treatment agents on the micro-shear bond strength to lithium disilicate ceramics. The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.01
30. Citra Kusumasari, Masatoshi Nakajima, Junji Tagami. Effect of chemomechanical caries removal agent on sealing performance of self-etch adhesive.. The 149th meeting of the Japanese Society of Conservative Dentistry 2018.11.01
31. Soe Yu Paing, Keiichi Hosaka, Masatoshi Nakajima, Junji Tagami. Effect of smear layerdeproteinizing with HOCl solution on micro-shear bond strengths of glass-ionomer cements to dentin. The 149th meeting of the Japanese Society of Conservative Dentistry 2018.11.01
32. Motoi Takahashi, Naoko Matsui, Khairul Matin, Miyuki Shimizu, Noriko Hiraishi, Toru Nikaido, Junji Tagami . Evaluation of biofilm formation on root dentin after application of silver diamine fluoride. The 149th Meeting of The Japanese Society of Conservative Dentistry 2018.11.01 Kyoto
33. VICHEVA Martina, SATO Takaaki, TAKAGAKI Tomohiro, BABA Yuuta, IKEDA Masaomi, NIKAIDO Toru, TAGAMI Junji . Effect of Repair Systems on Dentin Bonding Performance . The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.02

34. Saki Uchiyama, Rena Takahashi, Shin Rozan, Toru Nikaido, Junji Tagami. Effect of resin coating, temporary cement and length of time to cementation on dentin bond strength of CAD/CAM inlay restorations. The 37th Annual Meeting of Japan Society for Adhesive Dentistry 2018.11.10 Nigata, Japan
35. Inokoshi M, Shimizu H, Takagaki T, Minakuchi S. Influence of various surface treatments on fracture strength of zirconia-veneering ceramic interface. The 37th Annual Meeting of Japan Society for Adhesive Dentistry 2018.11.11 Niigata
36. Almasabi W, Abdou A, Hosaka K, Nakajima M, Tagami J. Effect of thermal stress of optical properties of flowable composites. The 37th meeting of the Japan Society of Adhesive Dentistry 2018.11.11
37. Keika Hoshi, Masatoshi Adachi, Hidemichi Yuasa, Rena Takahashi, Yoshihiro Toyoshima, Toru Naito, Eishu Nango, Rina Nango. Evidence for Decrease in Mortality Rates Following Oral Cancer Screening Intervention in an Asymptomatic Japanese Population: A Systematic Review. The 13th International Conference of the Asian Academy of Preventive Dentistry 2018.11.22 Khon Kaen, Thailand
38. Junji Tagami. Keys to obtain maximum performance of recent adhesives and composites in clinical situation. The 22nd Turkish Society of Restorative Dentistry International Scientific congress 2018.11.30
39. Keiichi Hosaka. The Power of Direct Composite Restorations. The Legacy Lives On - 40 Years of Dental Innovations (KAI Dental Symposium 2018) 2018.12.08 Phoenix, Arizona, US

[Works]

1. μ TBS jig, Other, 2009 - Now

Fixed Prosthodontics

Professor
Hiroyuki MIURA

Associate Professor
Kenichi YOSHIDA

Junior Associate Professor
Daizo OKADA
Wataru KOMADA

Assistant Professor
Chiharu SHIN
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Michiko NODA
Kunihiko MIZUSAWA
Shinya OISHI
Yasuyuki KOWAKA
Ruri TSUKAHARA
Tomoyuki MIHARA
Ko YANAKA
Syu YOSHIMATSU

(1) Research

- 1)Occlusion and Mastication.(mandibular position, mandibular movement, articulator, masticatory efficiency)
- 2)Influence of mechanical stress caused by occlusal contact on stomatognathic system. (Tooth displacement, distortion of alveolar bone, occlusal contact, proximal contact etc.)
- 3)Relationship of main occluding area and occlusal contact
- 4)Research on post and core(materials, stress analysis etc.)
- 5)Clinical application of latest technology and development of new materials (CAD/CAM, Zirconia, optical impression etc.)
- 6)Influence of occlusal contact for an important prosthesis on the periodontal tissues of the antagonist.
- 7)Application of laser welding in crown and bridge restorations.
- 8)Influence of dental materials for periodontal tissues and biological body.
- 9)Functional analysis of abnormal stomatognathic function

(2) Lectures & Courses

The major subjects of the studies are occlusion of Cr-Br prostheses (fixed restoration such as crown and fixed partial denture), analysis of mandibular movement, influence of crown and periodontal tissue and its systemic affect, accuracy of manufacturing processes of crown (i.e. casting, soldering, luting and adjustment of occlusion), functional analysis of stomatognathic system and development of apatite ceramic implant. The research themes are investigated with measurement systems of mandibular movement, measuring instruments of tooth micro-displacement, electromyography, measurement apparatus of dimensional accuracy, EPMA (electron probe microanalyzer) for analyzing very small amount of dental alloy and histopathological methods. Clinical training and general lecture on prosthodontics are prepared for the graduate students in the first year. After the second year they will have special training for their research methods and experiments will be performed according to the research plan. In the last year the students will write the paper for thesis under the direction of the professor.

(3) Clinical Services & Other Works

- 1) Clinic for prosthodontics (Prosthodontics practice clinic)

This clinic is organized by clinical teams, and 4 to 8 dentists compose 1 team working in cooperation between teams. Here offers a complete range of restorative, rehabilitative, and esthetic dentistry, treatment types include since simple one teeth to complete oral rehabilitation using the latest technologies.

- 2) Clinic for dental allergy (Dental allergy clinic)

This clinic provides allergy tests test for dental alloys and dental materials on potential patients before dental treatment, besides, patients with skin and/or oral diseases histories induced by previous dental restorations. The causal allergen/s is/are identified by patch tests or if some metal restoration is allergy set on, is analyze by Electron Probe Micro Analyzer (EPMA), removing out only restoration such content allergens.

(4) Publications

[Original Articles]

1. Kazuhisa Fujita, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Hiroyuki Miura, Akiko Nagai. Regulation of periodontal ligament-derived cells by type III collagen-coated hydroxyapatite. *Biomed Mater Eng.* 2018.01; 29(1); 15-27
2. Kubo Mariko, Komada Wataru, Otake Shiho, Inagaki Tasuku, Omori Satoshi, Miura Hiroyuki. 漏斗状根管を有する歯牙をコンポジットレジンのポストとコアを用いて修復したときの破折強さに、ガラス繊維のポストやリボンが及ぼす影響 (The effect of glass fiber posts and ribbons on the fracture strength of teeth with flared root canals restored using composite resin post and cores) *Journal of Prosthodontic Research.* 2018.01; 62(1); 97-103
3. Hirotaka Nishiyama, Shinpei Tanakla, Reina Nemoto, Hiroyuki Miura, Kazuyoshi Baba. Zirconia-Reinforced Framework for Maxillary Complete Dentures *The International Journal of Prosthodontics.* 2018.02; 31(2); 114-116
4. Uraba Ayana, Nemoto Reina, Nozaki Kosuke, Inagaki Tasuku, Omori Satoshi, Miura Hiroyuki. Biomechanical behavior of adhesive cement layer and periodontal tissues on the restored teeth with zirconia RBFDPs using three-kinds of framework design: 3D FEA study(和訳中) *Journal of Prosthodontic Research.* 2018.04; 62(2); 227-233
5. Seki N, Kanazawa M, Komagamine Y, Mizutani K, Hosaka K, Komada W, Moross J, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School. *Journal of Medical and Dental Sciences.* 2018.09; 65; 123-130
6. Ayaka Shirasaki, Satoshi Omori, Chiharu Shin, Mina Takita, Reina Nemoto, Hiroyuki Miura. Influence of occlusal and axial tooth reduction on fracture load and fracture mode of polyetheretherketone molar restorations after mechanical cycling *Asian Pacific Journal of Dentistry.* 2018.12; 18(2); 29-36

[Books etc]

1. Hiroyuki Miura. *Crown and Bridge Technique.* 2018.03 (ISBN : 978-4-263-45816-7)
2. Hiroyuki Miura. *Today's Therapy in Otorhinolaryngology-Head & Neck Surgery.* 2018.05 (ISBN : 978-4-260-03452-4)

[Conference Activities & Talks]

1. Kubo Mariko, Komada Wataru, Otake Shiho, Inagaki Tasuku, Omori Satoshi, Miura Hiroyuki. 漏斗状根管を有する歯牙をコンポジットレジンのポストとコアを用いて修復したときの破折強さに、ガラス繊維のポストやリボンが及ぼす影響 (The effect of glass fiber posts and ribbons on the fracture strength of teeth with flared root canals restored using composite resin post and cores). *Journal of Prosthodontic Research* 2018.01.01
2. Ayaka Shirasaki, Satoshi Omori, Chiharu Shin, Mina Takita, Hiroyuki Miura . The influence of thickness of PEEK crowns on the fracture load after cyclic loading. *Annual Scientific Meeting of Japan Prosthodontic Society Kansai Branch* 2018.01.20 Kyoto, Japan
3. Takita M, Omori S, Shin C, Shirasaki A, Miura H. Effect of framework design on fracture strength of resin veneered PEEK crowns . *Annual Scientific Meeting of Japan Prosthodontic Society Kansai branch* 2018.01.20 Kyoto, Japan
4. Seki Naoko, Kanazawa Manabu, Komagamine Yuriko, Moross Janelle, Mizutani Koji, Hosaka Keiichi, Komada Wataru, Kuroda Shinji, Sunaga Masayo, Kawaguchi Yoko, Morio Ikuko, Kinoshita Atsuhiko. TMDU の大学院における臨床専門知識習得のための国際的歯学教育コースの評価 (Assessment of International dental education course for clinical expertise at TMDU graduate school). *口腔病学会雑誌* 2018.03.01
5. Okada D, Shin C, Ogura R, Komada W, Miura H. The Investigation of the Stress Distribution in the Abutment Teeth for Connected Crowns in Function. *The 127th Scientific Meeting of Japan Prosthodontic Society* 2018.06.16 Okayama, Japan

6. Matsumura M, Matsumura M, Kitazaki H, Baba S, Nokiba K, Fukumoto I, Okamoto H, Matsui H, Shibaguchi K, Yoshida K, Miura H. A case report of Pustulosis Palmaris et Plantaris improved by elimination of intraoral metal with a diagnosis based on Patch testing. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.16 Okayama
7. S OTAKE, K HAYASHI, K NOZAKI, W KOMADA, K YOSHIDA, H MIURA. Bond strengths of cements to a newly developed pressable ceramics. 2018.07.27
8. Kosuke Nozaki, Kazuhisa Fujita, Naohiro Horiuchi, Kimihiro Yamashita, Kazuaki Hashimoto, Hiroyuki Miura, Akiko Nagai. Calcium deficiency regulates surface charges of β -tricalcium phosphate. 96th General Session and Exhibition of the IADR 2018.07.28
9. Seki N, Hosaka K, Komada W, Kanazawa M, Mizutani K, Komagamine Y, Moross J, Morio I. International student forum 2018 -International students' life in Japan-. International Student Forum 2018 by Japanese Dental Science Federation 2018.08.02 Tokyo
10. Seki Naoko, Kanazawa Manabu, Komagamine Yuriko, Mizutani Koji, Hosaka Keiichi, Komada Wataru, Moross Janelle, Kuroda Shinji, Sunaga Masayo, Kawaguchi Yoko, Morio Ikuko, Kinoshita Atsuhiko. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School(和訳中). Journal of Medical and Dental Sciences 2018.09.01
11. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. 32nd IADR-SEA & 29th SEAAD 2018.09.11 Da Nang, Vietnam
12. Kenichiro Hayashi, Kosuke Nozaki, Zhenquan Tan, Naohiro Horiuchi, Kimihiro Yamashita, Hiroyuki Miura, Keiji Itaka and Satoshi Ohara. Antibacterial property of titania nanosheet synthesized by organic ligand-assisted hydrothermal reaction. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25
13. Matsumura M, Nozaki K, Yamashita K, Matsumura M, Miura H. Optimization of surface roughness of composite resin block by controlling milling condition. 2018.10.07 Hokkaido
14. Wataru Komada. A case report of prosthodontic rehabilitation of a patient with severely worn dentition for occlusal function and esthetics.. 2018.11.11
15. K. Sugano, W. Komada, D. Okada and H. Miura. The fracture strength of PEEK (Poly Ether Ether Ketone) posts and composite resin cores in the case of flared root canals. The 66th Annual Meeting of Japanese Association for Dental Research 2018.11.17 Sapporo, Hokkaido
16. Mina Takita, Shiho Otake, Ayaka Shirasaki, Rie Fujita, Hiroyuki Miura. Bond strengths of cements to a new indirect resin composite.

Pulp Biology and Endodontics

Professor:

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Mitsuhiro SUNAKAWA

Junior Associate Professor:

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Yuki KASAHARA, Shunsuke KIMURA, Masashi KURAMOTO, Bin GU, Akira KOUNO,
Yasuhiro HOSHIHARA, Keiichiro MAKI, Shinya YAMAUCHI, Thaw Dar Oo, Phyo Pyai Sone,
Su Yee Myo Zaw, Pyae Hein Htun, Taro NAKATSUKASA, Hiroki MURANO, Yadanar Su Phyo,
Xu AO, Aung Nyein Pyae Sone, Htoo Shwe Sin Thein, Sherif Adel Abd El-Fattah SALEH,
Zar Chi Thein Zaw, Yamato OKADA (April~), Shion ORIKASA (April~),
Dumrogvute KUNLANUN (April~), Myint Thu (October~), KIEU Quoc Thoai (October~)

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Tamae HASEGAWA, Aseel Sabah Mahdi ALCHAWOOSH (April~),
Nanami NIKAIDO (October~), Radnaased ALTANZUL (April~September),
Peifeng HAN (October~)

(1) Outline

The Department of Pulp Biology and Endodontics provides research, education and patient care on the prevention, diagnosis and treatment of dental pulp and periapical diseases. In order to preserve and well maintain the function of the teeth in the oral cavity, it is important to understand the structural and functional features of the dental pulp and protect this tissue carefully from noxious stimuli. However, pulp diseases, if left untreated, may progress to develop pulp necrosis and apical periodontitis, where meticulous treatment is required to eliminate infection from the complex root canal system. The goal of endodontics is to achieve long term maintenance of tooth function by the prevention and treatment of pulpal and periapical diseases.

(2) Research

1. Biology of dentin/pulp complex and dental pulp tissue regeneration
 - Establishment of an experimental model of rat dental pulp tissue engineering using mesenchymal stem cells
 - Analysis of macrophage populations in rat engineered dental pulp tissue
 - Immunohistochemical and gene expression analysis of stem-cell-associated markers in rat dental pulp
 - Effect of cell culture condition on the osteogenic differentiation of human dental pulp-derived mesenchymal stem cells
 - Expression and function of transient receptor potential channels in dental pulp cells
2. Mechanisms of dental pulp inflammation
 - microRNA regulation of inflammatory responses in dental pulp
 - Role of hypoxia inducible factor 1 α in dental pulp inflammation
3. Root canal irrigation
 - Evaluation of efficacy- and safety-related properties of laser-activated root canal irrigation
 - EDTA irrigation-induced cellular adhesion and differentiation on NaOCl-treated denatured dentin
4. Evaluation of newly developed endodontic sealers and pulp capping materials
 - Anti-inflammatory effects of mineral trioxide aggregate
 - Cytotoxicity of an experimental sealer containing surface reaction type pre-reacted glassionomer (S-PRG) to osteoblastic cells
 - Evaluation of strontium ranerate as a direct pulp capping material
 - Development of new tricalcium silicate-based endodontic materials
5. Nickel-titanium rotary root canal instrumentation
 - Evaluation of mechanical and metallurgical properties of newly developed NiTi rotary instruments
 - Comparison of hand and NiTi rotary root canal shaping performed by undergraduate students
 - Comparison of the mechanical property of differently-tapered NiTi rotary instruments
 - Comparative stress analysis of NiTi rotary instrumentation with different rotational modes
 - Effect of different speeds of up-and-down motion on shaping ability of nickel-titanium rotary instruments
6. Endodontic diagnosis
 - Detection of periapical bone defects and vertical root fracture with cone beam computed tomography
 - Application of optical coherence tomography in endodontic diagnosis
 - Diagnosis of dental pulp vitality using transmitted-light plethysmography
7. Dental pulp injury-induced gene expression in the central nervous system
 - Alteration of pain-associated gene expression in the thalamus following dental pulp stimulation in rats

(3) Education

The educational aim of the Department of Pulp Biology and Endodontics is to cultivate students so that they can obtain knowledge and skills required for leading scientists, researchers or practitioners of endodontics. Since recent progress of pulp biology and endodontics is remarkable, the students are educated to acquire the newest knowledge on modern endodontology and its related subjects, such as neuroscience, microbiology, molecular biology, immunology and biomaterial sciences, and are trained to master the newest technology of endodontics. All the students are asked to add new findings to the field of endodontics based on their own original research.

(4) Clinical Services & Other Works

The Department of Pulp Biology and Endodontics is in charge of the Clinic of Operative Dentistry and Endodontics in our Dental Hospital, together with the Department of Cariology & Operative Dentistry, and offers the global standard of care in the treatment of pulpal and periapical diseases to our patients. We provide clinical care in the full spectrum of endodontics including;

- Vital pulp therapy,

- Nonsurgical root canal therapy,
- Root canal retreatment,
- Endodontic microsurgery,
- Internal tooth bleaching, and
- Post-endodontic restoration.

(5) Clinical Performances

The latest development of endodontics is remarkable as seen in root canal instrumentation with super-elastic Ni-Ti rotary files, diagnosis with cone beam computed tomography, and microendodontics by using a surgical operating microscope. In particular, microendodontics has dramatically changed conventional “blind” endodontics into more predictable endodontics since it allows us to obtain accurate diagnostic information and provide precise procedures under an illuminated and magnified view. Also, we seek to provide evidence-based endodontic treatment based on our laboratory and clinical research.

(6) Publications

[Original Articles]

1. Ohkura M, Ohkura N, Yoshida N, Yoshida K, Ida-Yonemochi H, Ohshima H, Saito I, Okiji T. Orthodontic force application upregulated pain-associated prostaglandin-I2/PGI2-receptor/TRPV1 pathway-related gene expression in rat molars. *Odontology*. 2018.01; 106(1); 2-10
2. Sueyama Y, Kaneko T, Ito T, Okiji T. Effect of lipopolysaccharide stimulation on stem cell-associated marker-expressing cells *International Endodontic Journal*. 2018.02; 51(Suppl 2); e107-e114
3. Hashimoto K, Kawashima N, Ichinose S, Nara K, Sonoko Noda S, Takashi Okiji T. EDTA treatment for NaOCl-treated dentin recovers disturbed attachment and induces differentiation of mouse dental papillae cells *Journal of Endodontics*. 2018.02; 44(2); 256-262
4. Nishijo M, Ebihara A, Tokita D, Doi H, Hanawa T, Okiji T. Evaluation of selected mechanical properties of NiTi rotary glide path files manufactured from controlled memory wires *Dental Materials Journal*. 2018.04; 37(4); 549-554
5. Bakhit A, Kawashima N, Hashimoto K, Noda S, Nara K, Kuramoto M, Tazawa K, Okiji T. Strontium ranelate promotes odonto-/osteogenic differentiation/mineralization of dental papillae cells in vitro and mineralized tissue formation of the dental pulp in vivo. *Scientific Reports*. 2018.06;
6. Hanada T, Hashimoto M, Ikegami M, Uraba S, Okiji T, Yoshinari N, et al.. Reasons for the extraction of permanent teeth in Kami-ina area, Nagano Prefecture, Japan *Japanese Journal of Conservative Dentistry*. 2018.06; 61(3); 163-170
7. Fukumori Y, Nishijyo M, Tokita D, Miyara K, Ebihara A, Okiji T. Comparative analysis of mechanical properties of differently tapered nickel-titanium endodontic rotary instruments *Dental Materials Journal*. 2018.07; 37(4); 667-674
8. Rashed B, Iino Y, Komatsu K, Nishijo M, Hanada T, Ebihara A, Sunakawa M, Sumi Y, Okiji T. Evaluation of root canal anatomy of maxillary premolars using swept-source optical coherence tomography in comparison with dental operating microscope and cone beam computed tomography *Photomedicine and Laser Surgery*. 2018.08; 36(9); 487-492
9. Kaneko T, Gu B, Sone PP, Zaw SYM, Murano H, Zaw ZCT, Okiji T. Dental pulp tissue engineering using mesenchymal stem cells: A review with a protocol *Stem Cell Reviews and Reports*. 2018.09; 14(5); 668-676
10. Kang D, Wada T, Uo M, Okiji T. Influence of bentonite addition on handling and physical properties of tricalcium silicate cement *Asian Pacific Journal of Dentistry*. 2018.12; 18(2); 37-44

[Books etc]

1. Cone Beam Computed Tomography in Endodontics. 2018.01 (ISBN : 978-4-7812-0598-4)
2. Cone Beam Computed Tomography in Endodontics. QUINTESSENCE PUBLISHING, 2018.01 (ISBN : 978-4-7812-0598-4)
3. Okiji T. Non-surgical root canal treatment, Case 5. Komabayashi T, ed.. Clinical Cases in Endodontics. Wiley Blackwell, 2018.03 (ISBN : 9781119147046)
4. Edt) Kitamura H,A) Kaneko T,Okiji T. Revolution of Endodontics. 2018.04 (ISBN : 978-4-263-44522-8)

[Misc]

1. Murano H, Watanabe S, Okiji T. Capping carious exposures in adults: a randomized controlled trial investigating mineral trioxide aggregate versus calcium hydroxide 2018.06; 37(6); 202-204
2. Iino Y, Ebihara A, Sunakawa M, Okiji T. Application of optical coherence tomography in endodontics. The Journal of Japan Society for Laser Surgery and Medicine. 2018.08; 39(1); 50-58
3. Okiji T. Future Strategy of Conservative Dentistry in the Super Aging Society Japanese Journal of Conservative Dentistry. 2018.10; 61(5); 264-269
4. Okiji T. Preparing Future Strategies for Dentistry in the Super-aging Society Japanese Journal of Conservative Dentistry. 2018.10; 61(5); 251
5. Kasahara Y, Watanabe S, Okiji T . Clinical outcome of non-surgical root canal treatment using a single-cone technique with Endosequence bioceramic sealer:A retrospective analysis the Quintessence. 2018.11; 11(37); 204-206
6. Watanabe S, Kouno A, Hongo T, Yao K, Okiji T. A Review of LLLT in Dentistry :Current Evidence from Systematic Reviews and Randomized Clinical Trials 2018.12; 29(1); 10-25

[Conference Activities & Talks]

1. Okiji T. Defense, repair and regeneration of the dentin/pulp complex: a biological basis for vital pulp therapy. 2018.03.18 Tokyo
2. Sone PP,Kaneko T,Zaw SYM,Sueyama Y,Gu B,Murano H,Zaw ZCT,Okiji T. Regeneration of PGP9.5- and CGRP-positive nerve fibers in a rat experimental Model of coronal pulp tissue engineering with mesenchymal stem cells-. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
3. Gu B, Kaneko T, Zaw SYM ,Sone PP, Murano H, Sueyama Y, Okiji T. Kinetic analysis of M1 and M2 macrophages in the regenerative process of rat engineered coronal pulp tissue. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
4. Murano H, Kaneko T, Sunakawa M, Sone PP, Zaw SYM, Gu B, Okiji T. Experimental pulp inflammation-induced modulation of pain-associated gene expression in rat thalamus: A microarray analysis. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
5. Kouno A, Watanabe S, Hongo T, Yao K, Ide A, Satake K, Okiji T. Vaporized cavitation bubbles during root canal irrigation activated by Er:YAG laser: Effect of tip diameter and laser energy. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
6. Pyae Hein Htun, Maki K, Kimura S, Nishijo M, Tokita D, Ebihara A, Okiji T. Comparison of hand and rotary instrumentation during glide path preparation with regard to apical force, torque and root canal dentin removal. The 148th Meeting of the Japanese Society of Coservative Dentistry 2018.06.14 Yokohama
7. Yadanar Su Phyo, Kawashima N, Bakhit A, Kuramoto M, Hashimoto K, Okiji T. In vitro evaluation of the cytotoxicity of three methacrylate-based resin sealers. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama

8. Okiji T. Conservative dentistry in the super aging society: current status and future strategies. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.15 Yokohama
9. Kaneko T. Establishment of rat experimental dental pulp tissue engineering model . The 39th Annual Scientific Meeting of Japan Endodontic Association 2018.07.07 Fukuoka
10. Zaw SYM,Kaneko T,Sueyama Y,Okiji T. Effect of NF- κ B decoy ODN treatment on VEGF/VEGFR2 expression in experimentally-induced periapical lesions in rat molars. The 39th Annual Scientific Meeting of Japan Endodontic Association 2018.07.07 Fukuoka
11. Sone PP,Kaneko T,Zaw SYM,Sueyama Y,Zaw ZCT,OKiji T. Expression of substance P in a rat experimental model of coronal pulp tissue engineering with mesenchymal stem cells. The 39th Annual Scientific Meeting of Japan Endodontic Association 2018.07.07 Fukuoka
12. Kimura S, Tokita D, Maki K, Nishijo M, Nakatsukasa T Ebihara A, Okiji T. Evaluation of phase transformation behavior and cyclic fatigue characteristics of HyFlex EDM NiTi rotary instruments. The 39 th Annual Scientific Meeting of Japan Endodontic Association 2018.07.07 Fukuoka
13. Ksahara Y, Komatsu K, Iino Y, Ebihara A, Okiji T. Relationship of vertical root fracture and position of sinus tracts in teeth treated with endodontic microsurgery . The 39th Annual Scientific Meeting of Japan Endodontic Association 2018.07.07 hukuoka
14. Maki K, Tokita D, Nakatsukasa T, Kimura S, Nishijo M, Ebihara A, Okiji T. Shaping ability and stress generation of Reciproc Blue nickel titanium instruments. The 38th Annual Scientific Meeting of Japanese Endodontic Association 2018.07.07 Fukuoka
15. Tazawa K, Kawashima N, Ikeda H, Okiji T. LYVE-1 expressing cells co-express CD163 in rat normal dental pulp tissue. The 39th Annual Scientific Meeting of Japan Endodontic Association 2018.07.07 Hukuoka
16. Noda S, Kawashima N, Hashimoto K, Nara K, Kuramoto M, Tazawa K, Okiji T. *In Vivo* Mineralization and *In Vitro* Differentiation of Dense-Cultured DPSCs. 96th General Session & Exhibition of the IADR 2018.07.25 London, England
17. Kawashima N, Kuramoto K, Bakhit A, Hashimoto K, Okiji T. Osteoblast differentiation induced by a prototype S-PRG filler-containing endodontic sealer. IADR/AADR/CADR General Session & Exhibition 2018.07.25 London, England
18. Hama Y, Minakuchi S, Sasaki K, Maeda T, Hamura A, Ichinohe T, Okiji T. The Dental Education Consortium to promote healthy longevity -Fourth report- Towards the final year. Annual Meeting of the 37th Japanese Dental Education Association 2018.07.27 Koriyama
19. Ebihara A, Kawamura J, Tokita J, Tsuruta J, Kinoshita A, Okiji T. Improvement of flipped teaching in preclinical practice of endodontics. 37th annual meeting of Japanese Dental Education Association 2018.07.28 Koriyama
20. Kawamura J, Tokita D, Ebihara A, Okiji T. Introduction of dental operating microscope into pre-clinical practice of endodontics. 37th annual meeting of Japanese Dental Education Association 2018.07.28 Koriyama
21. Maki K, Ebihara A, Kimura S, Nishijo M, Tokita D, Okiji T. Effect of up-and-down speeds on canal centering ability and stress generation of NiTi rotary instruments. IFEA 11th World Endodontic Congress 2018 2018.10.04 Seoul, Korea
22. Murano H, Kaneko T, Sunakawa M, Zaw SYM, Sone PP, Okiji T. Screening of a representative gene related to thalamic neuronal activation following dental pulp inflammation in rats. the IFEA 11th World Endodontic Congress 2018.10.04 Seoul, Korea
23. Kang D, Wada T, Uo M, Okiji T. Rheological and physical properies of phyllosilicate clay added tricalcium silicate. IFEA 11th World Endodontic Congress 2018 2018.10.04 Seoul, Korea
24. Kouno A, Watanabe S, Hongo T, Yao K, Satake K, Okiji T. Generation of apical pressure and intracanal vaporized cavitation bubbles during root canal irrigation activated by Er:YAG laser: Effect of tip diameter and configuration. The 30th Annual Scientific Meeting of Japanese Society for Laser Dentistry 2018.10.21 Tokyo

25. Yamaguchi H, Ebihara A, Otsuki M, Takamori K, Matsumi H, Yashima A, Nakajima A, Nagai S, Shimizu N, Miyazaki H, Yoshida K, Watanabe H. History of social insurance introduction of new laser dental technologies. The 30 th Annual Meeting of Japanese Society for Laser Dentistry 2018.10.21
26. Kuramoto M, Kawashima N, Nara K, Fujii M, Noda S, Hashimoto K, Tazawa K, Okiji T. MTA negatively regulates inflammatory mediator-synthesis from human dental pulp cells. The 149rd Meeting of the Japanese Society of Conservative Dentistry 2018.11.01 Kyoto
27. Tazawa K, Kawashima N, Kuramoto M, Nara K, Noda S, Fujii M, Hashimoto K, Okiji T. Expression of TRPA1 is induced by NO/P38MAPK signals in LPS-stimulated human dental pulp cells. The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.01 Kyoto
28. Kouno A, Watanabe S, Hongo T, Yao K, Satake K, Okiji T. Generation of apical pressure and intracanal vaporized cavitation bubbles during root canal irrigation activated by Er:YAG laser: Effect of laser energy. The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.01 Kyoto
29. Nakatsukasa T, Tokita D, Maki K, Kimura S, Nishijo M, Ebihara A, Okiji T. Mechanical properties of a newly developed heat-treated NiTi rotary instrument. The 149rd Meeting of the Japanese Society of Conservative Dentistry 2018.11.01 Kyoto
30. Aung S, Watanabe S, Kouno A, Hongo T, Yao K, Satake K, Okiji T. Cleaning the apical area beyond the ledge using Er:YAG laser-activated irrigation: A particle image velocimetry analysis. The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.01 kyoto
31. Nara K, Kawashima N, Noda S, Fujii M, Hashimoto K, Okiji T. Kinetics of microRNA21 expression in the human dental pulp cells and its mechanisms to regulate inflammatory mediator synthesis. 2018.11.02
32. Thaw Dar Oo, Kusano M, Kakino S, Ikeda H, Okiji T. Coldness changes transmitted-light plenthysmography values in young adult human teeth. The 66th Annual Meeting of Japanese Association for Dental Research 2018.11.18 Sapporo

[Awards & Honors]

1. Excellence Presentation Award (Akira Kouno), The 30th Annual Scientific Meeting of Japanese Society for Laser Dentistry, 2018.10

Removable Partial Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Kenji Fueki

Junior associate professor - Takeshi Ueno

Assistant professors

- Ichiro Minami, Juro Wadachi, Eiko Kohno,
Junnichiro Wada, Natsuko Murakami, Atsushi Takaichi

Hospital staff

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Kensuke Takakusaki, Yasuo Nakajima, Gen Nabeshima,
Hironari Hayama, Masahiro Hirasawa, Chie Watanabe

Graduate students

- Yurika Ishioka, Keigo Isoshima, Keiichiro Uchikura,
Hirofumi Uchida, Wang Zuo, Hisami Okawara, Taihei Kasai,
Kittikundecha Nuttaphon, K Zin Myint Oo, Hiroki Saito,
Kazuki Sakamoto, SAN WIN THANT, Yuka Shichiri, Erina Seki,
Tenhaku Tan, Gu Zheng, Zhao Qian, Tomiharu Nagayama,
Gen Nabeshima, Yoko Hayashi, Hao Jialin, Daiki Hikita,
Shiro Hibi, Hein Linn Htat, Hitomi Matsuno,
Toshiki Yamazaki, Hla Htoot Wai Cho, Yu Huaxin

(1) Outline

The Department of Removable Partial Prosthodontics specializes in removable partial denture treatment, which is one of the major disciplines of clinical dentistry. The department has taken the baton from the First Department of Prosthodontics and the Department of Masticatory Function Rehabilitation.

Our objectives are to enhance the art and science of removable prosthodontics for the management of various oral conditions associated with tooth loss, from a single missing tooth to a single remaining tooth, in the maxillary and/or mandibular arch.

(2) Research

1. Function and Physiology in Partial Denture Wearers
2. Optimization of Partial Denture Design based on Stress Analysis
3. Development and Applications of New Prosthodontic Biomaterials
4. Biology of Oral Tissues in Denture Wearers
5. Epidemiology and Education for Removable Partial Prosthodontics

(3) Education

School of Dentistry

Year 1

Introduction to Dentistry

Year 3

Tooth Carving

Introduction to Clinical Dentistry

Observation and assistance at clinic term I and II

Basic Occlusal Reconstruction

Introduction to Research article writing and Patent acquisition

Year 4

Research Project

Removable Partial Prosthodontics

Advanced knowledge and skill with occlusion

Experience learning of dental practice

Years 5 and 6

Case study

Dental Practice and Clinical Practicum for Comprehensive Patient Care (Clinical Internship)

School of Oral Health Care Sciences, School of Oral Health Care Sciences

Year 2 Prosthodontics

Years 3 and 4 Practice for Dental Hygiene Care

School of Oral Health Care Sciences, Course for Oral Health Engineering

Year 2 Removable Prosthodontics Technology

(4) Lectures & Courses

The Department of Removable Partial Prosthodontics offers a variety of educational courses pertaining to the specialized clinical management of tooth loss, primarily for undergraduate students at the School of Dentistry. The courses include lectures, tutorials, hands-on sessions, clinical simulations, and clinical internship instructions.

The ability to perform clinical operations on patients with tooth loss, including the skills required for medical interviews, oral examinations, diagnosis, decision making, impression making, bite registration, denture design and technology, and denture delivery and maintenance, is essential for clinical dental professionals. The objectives of our courses are to provide learning and training in contemporary removable prosthodontics and enhance the knowledge and skills of students to help them develop and flourish in their future career as dental and oral health professionals.

(5) Clinical Services & Other Works

All faculty members of the Department of Removable Partial Prosthodontics are assigned to treat patients at the Prosthodontics department in the Dental Hospital of the Tokyo Medical and Dental University. While the rate of tooth retention has increased in comparison with previously reported rates, the number of patients in need of a removable partial denture has increased. Our specialists primarily work on advanced cases that are referred from other departments and outside the hospital. The departmental mission also includes the development and application of new prosthodontic materials, their clinical trial, and the spread of novel and inventive knowledge to the community.

(6) Clinical Performances

The department specializes in removable partial prosthodontics and aims to restore missing teeth and associated oral tissues; improve physiological functions such as occlusion, mastication, swallowing, and speech; maintain normal oral sensation; and restore the original appearance of individual patients.

Treatment modalities, materials, and denture design are all based on the case history and chief complaint of the patients. The ultimate goal is to improve the oral health-related quality of life of patients.

(7) Publications

[Original Articles]

1. Teisuke Akimoto, Takeshi Ueno, Yusuke Tsutsumi, Hisashi Doi, Takao Hanawa, Noriyuki Wakabayashi. Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions. *J. Biomed. Mater. Res. Part B Appl. Biomater.*. 2018.01; 106(1); 73-79
2. Hideaki Inagawa, Natsuki Suzuki, Kazuhiro Aoki, Noriyuki Wakabayashi. Potential for estimation of Young's modulus based on computed tomography numbers in bone: A validation study using a nano-indentation test on murine maxilla *Dental, Oral and Craniofacial Research*. 2018.01; 4(4); 1-7
3. Manhal Ijbara, Kanae Wada, Makoto J. Tabata, Junichiro Wada, Go Inoue, Michiyo Miyashin. Enamel Microcracks Induced by Simulated Occlusal Wear in Mature, Immature and Deciduous Teeth. *BioMed Research International* . 2018.04; 2018(5658393); 1-9
4. Nakamura K, Minami I, Wada J, Ikawa Y, Wakabayashi N. Head position affects the direction of occlusal force during tapping movement. *Journal of Oral Rehabilitation*. 2018.05; 45(5); 363-370
5. Yuka Kajima, Atsushi Takaichi, Nuttaphon Kittikundecha, Takayuki Nakamoto, Takahiro Kimura, Naoyuki Nomura, Akira Kawasaki, Takao Hanawa, Hidekazu Takahashi, Noriyuki Wakabayashi. Effect of heat-treatment temperature on microstructures and mechanical properties of Co-Cr-Mo alloys fabricated by selective laser melting. *Materials Science and Engineering: A*. 2018.05; 726(30); 21-31
6. Takashi Hatayama, Ayaka Chiba, Kimisuke Kainose, Masatoshi Nakajima, Keiichi Hosaka, Noriyuki Wakabayashi, Richard M Foxton, Junji Tagami. Stress distribution in tooth resin core build-ups with different post-end positions in alveolar bone level under two kinds of load directions. *Dent Mater J*. 2018.06; 37(3); 474-483
7. Kensuke Takakusaki, Kenji Fueki, Chiaki Tsutsumi, Yusuke Tsutsumi, Naohiko Iwasaki, Takao Hanawa, Hidekazu Takahashi, Kazuo Takakuda, Noriyuki Wakabayashi. Effect of incorporation of surface pre-reacted glass ionomer filler in tissue conditioner on the inhibition of *Candida albicans* adhesion. *Dent Mater J*. 2018.06; 37(3); 453-459
8. Hironari Hayama, Kenji Fueki, Juro Wadachi, Noriyuki Wakabayashi. Trueness and precision of digital impressions obtained using an intraoral scanner with different head size in the partially edentulous mandible. *J Prosthodont Res*. 2018.07; 62(3); 347-352
9. G Nabeshima, K Fueki, Y Inamochi, N Wakabayashi. Effect of dietary counselling with prosthetic restoration on fruit and vegetable intake in partially dentate patients: A prospective study. *J Oral Rehabil*. 2018.08; 45(8); 618-626
10. Wada J, Hideshima M, Inukai S, Katsuki A, Matsuura H, Wakabayashi N.. Influence of Oral Morphology on Speech Production in Subjects Wearing Maxillary Removable Partial Dentures with Major Connectors. *Folia Phoniatrica et Logopaedica*. 2018.08; 70; 138-148
11. Minami I, Wirianski A, Harakawa R, Wakabayashi N, Murray GM. The three-axial gyroscope sensor detects the turning point between opening and closing phases of chewing. *Clinical and experimental dental research*. 2018.12; 4(6); 249-254

[Books etc]

1. Wakabayashi N, Murakami N, Takaichi A. Handbook of Mechanics of Materials. Chapter 37: Current Applications of Finite Element Methods in Dentistry. Springer Nature Pte Ltd, , 2018.01 (ISBN : 978-981-10-6855-3)

[Misc]

1. Fueki K, Inamochi Y. Clinical evidence for Shortened Dental Arch Concept The journal of the Tokyo Dental Association. 2018.09; 66(9); 405-412

[Conference Activities & Talks]

1. HIGUCHI Tomoya, MATSUURA Hiroshi, WADA Junichiro, HIDESHIMA Masayuki. Automatic estimation of the intonation using phonetic segments for the utterances of Japanese learners. The Spring Annual Meeting of Acousitcal Society of Japan in 2018 2018.03.15 Saitama
2. Junichiro Wada, Masayuki Hideshima, Hiroshi Matsuura. Dental treatment and speech impairment in partially edentulous elderly patients - Treatment approach with speech recognition -. 11th Annual Meeting of Aging Society Design Association 2018.03.16 Tokyo
3. Kajima Y, Takaichi A, Kittikundecha N, Nomura N, Takahashi H, Hanawa T, Wakabayashi N and Kawasaki A. Investigation of the effective heat treatment condition for controlling the anisotropy of selective laser melted Co-Cr alloy.. The Japan Institute of metals and materials 2018 Spring Annual Meeting 2018.03.20 Chiba
4. Kittikundecha Nuttaphon, Kajima Yuka, Takaichi Atsushi, Nakamoto Takayuki, Doi Hisashi Tsutsumi Yusuke, Nomura Naoyuki, Kawasaki Akira, Takahashi Hidekazu, Hanawa Takao, Wakabayashi Noriyuki . Effect of heat treatment on the microstructure and fatigue strength of the Co-Cr-Mo alloy prepared by selective laser melting. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka
5. E Kohno, H Kumagai, K Fueki, N Wakabayashi. A structural equation modeling examining relationship between mucosal pain and oral health-related quality of life in patients with removable partial dentures. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.15 Okayama
6. Kenji Fueki. Clinical decision-making for prosthetic treatment of SDA in view of oral health-related quality of life. The 127 Annual Meeting of Japan Prosthodontic Society 2018.06.16 Okayama
7. Sanda M, Fueki K, Kusumoto Y, Mukawa K, Hara M, Yokoyama S, Matsumoto T, Higuchi D, Baba K. Comparison of immediate and conventional loading protocol regarding marginal bone loss around implants supporting mandibular overdentures : A systematic review and meta-analysis. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.16 Okayama
8. Nagayama T, Wada J, Murakami N, Watanabe C, Mizutani K, Takakusaki K, Uchida H, Wakabayashi N. Influence of removable partial denture designs on stabilizing effects for mobile teeth: a basic study. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.17 Okayama
9. Yukihiko Tamura, Pornpoj Fuangtharntip, Tomoki Uehara, Yuki Arai, Michiyo Miyashin, Noriyuki Wakabayashi, Kazuhiro Aoki. Expression of metallothionein in inflammatory cytokine treated rat dental pulp cells. The 8th International Congress of ASIAN Society of Toxicology 2018.06.17 Thailand
10. T. Yamazaki, N. Murakami, S. Suzuki, M. Yatabe, H. Takahashi, N. Wakabayashi.. Influence of block-out area on retentive force of non-metal clasp denture. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.17 Okayama
11. Kajima Y, Takaichi A, Takahashi H, Wakabayashi N. Evaluation of effectiveness of heat treatment on Co-Cr-Mo alloy fabricated by selective laser melting. The 127th annual meeting of the Japan Prosthodontic society 2018.06.17
12. Yuka Inamochi, Kenji Fueki, Eiko Kohno, Masaru Yatabe, Noriyuki Wakabayashi . Cost-effectiveness Analysis of Prosthetic Treatment with Non-metal Clasp Dentures. 2018.06.17 Okayama
13. Chie Watanabe, Junichiro Wada, Koji Mizutani, Hiroshi Watanabe, Noriyuki Wakabayashi. Chronological changes in supporting alveolar bone by RPD placement. IADR 96th General Session & Exhibition 2018.07.24 London, England
14. Keigo Isoshima, Takeshi Ueno, Yuki Arai, Hiroki Saito, Tianbo Tan, Peng Chen, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi.. Increased extracellular proteins adsorption on electropositive titanium surfaces. The 96th general session & exhibition of the IADR 2018.07.27 London

15. C. Tsutsumi-Arai, M. Hirasawa, K. Takakusaki, Y. Arai, K. Fueki, K. Satomura, N. Wakabayashi. Reduction in *C. albicans* adhesion by SBMAm co-polymer coating on PMMA.. International Association for Dental Research 96th General session 2018.07.27 London, England
16. N. Murakami, T. Yamazaki, S. Suzuki, M. Yatabe, H. Takahashi, N. Wakabayashi. Influence of block-out on retention of thermoplastic non-metal resin clasps. 96th General Session & Exhibition of the IADR IADR/PAN European regional congress 2018.07.28 London, England
17. N. Wakabayashi, H. Inagawa, N. Suzuki, K. Aoki, T. Yamazaki, C. Watanabe, N. Murakami.. Validity of Young's Modulus Estimated Based on Computed Tomography. 96th General Session & Exhibition of the IADR 2018.07.28 London, England
18. Tan Tianbo, Takeshi Ueno, Yuki Arai, Keigo Isoshima¹, Hiroki Saito, Yusuke Tsutsumi, Hisashi Doi, Takao Hanawa, Noriyuki Wakabayashi. Surface characterization and bioactivity of Ti-Zr alloy with compositional change. The 96th general session & exhibition of the IADR 2018.07.28 London
19. Kajima Y, Takaichi A, Kittikundecha N, Nomura N, Hanawa T, Wakabayashi N, Kawasaki A. Investigation of heat treatment condition for CoCrMo alloy fabricated by selective laser melting. Annual meeting of the Japanese Society for Biomaterials Tohoku Block 2018.08.24 Miyagi
20. Kittikundecha N, Kajima Y, Takaichi A, Doi H, Nomura N, Hanawa T, Wakabayashi N, Kawasaki A. Effect of heat treatment temperature on microstructures and fatigue strength of Co-Cr-Mo alloy clasps prepared by selective laser melting. Annual meeting of the Japanese Society for Biomaterials Tohoku Block 2018.08.24 Miyagi
21. HIGUCHI Tomoya, MATSUURA Hiroshi, WADA Junichiro, HIDEISHIMA Masayuki. Estimation of the accent and intonation of utterances using phonetic segments and deep learning. The Autumn Annual Meeting of Acoustical Society of Japan in 2018 2018.09.13 Ohita
22. Kajima Y, Takaichi A, Kittikundecha N, Ashida M, Nomura N, Hanawa T, Wakabayashi N, Kawasaki A. Investigation of heat treatment condition for anisotropic control in laser laminate fabrication method. The Japan Institute of metals and materials 2018 Autumn Annual Meeting 2018.09.20 Miyagi
23. Kittikundecha N, Kajima Y, Takaichi A, Nakamoto T, Doi H, Tsutsumi Y, Nomura N, Kawasaki A, Takahashi H, Hanawa T, Wakabayashi N. Relationship between microstructures and fatigue strengths in selective laser melted CoCrMo alloy subjected to heat treatment. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Hokkaido
24. Wakabayashi N. New Design Concept and Material Selection in Removable Partial Prosthodontics on Symposium "Current Topics of Prosthodontic Treatment using Partial Dentures". The 66th Annual Meeting of Japanese Association for Dental Research 2018.11.17 Hokkaido University, Sapporo, Japan
25. Seki E, Takaichi A, Kajima Y, Wakabayashi N. Effect of heat treatment on the microstructure and fatigue strength of CoCrMo alloys fabricated by selective laser melting. The 22nd Scientific Meeting of Japan Prosthodontic Society Tokyo branch 2018.11.24 Tokyo
26. Takaichi A, Kajima Y, Doi H, Hanawa T, Wakabayashi N.. Effect of Preheating Treatments on Interfacial Reaction between Dental Porcelain and Low Magnetic Susceptibility Zr-14Nb Alloy.. AVS Pacific Rim Symposium on Surfaces, Coatings and Interfaces (PacSurf 2018) 2018.12.04
27. Kajima Y, Takaichi A, Oishi T, Kittikundecha N, Tsutsumi Y, Nomura N, Hanawa T, Wakabayashi N, Kawasaki A.. Surface Characteristics and Corrosion Behavior of CoCrMo Alloys Fabricated by Selective Laser Melting after Various Heat Treatments. . AVS Pacific Rim Symposium on Surfaces, Coatings and Interfaces (PacSurf 2018) 2018.12.04

Oral Implantology and Regenerative Dental Medicine

Professor Shohei KASUGAI
Associate Professor Makoto SHIOTA
Senior Lecturer Noriko TACHIKAWA, Sinji KURODA
Assistant Professor Hidemi NAKATA, Kazuhiro KON, Masahiro SHIMOGISHI
Clinical Fellow Maiko YAMAMOTO, You-Kyoung KIM, Munemitsu MIYASAKA
Seiji OHARA, Maki SHIBASAKI, Reo IKUMI

(1) Outline

Prosthetic treatment with dental implants (dental implant treatment) is very effective. We are conducting researches and educations of clinical procedures, materials and tissue regeneration related to dental implant treatment. In addition, we are treating patients with dental implants in the university dental hospital.

(2) Research

We conducted the following studies: Development of bone substitute stimulating bone formation, development of implant surface stimulating bone formation and preventing infection, stimulation of bone formation with dissociated soft tissue, development of resorbable DBG membrane and effects of liposomal chondronate on osteoblastic differentiation.

(3) Education

We gave lectures about basic knowledge necessary for implant treatment to dental students. Dental students also practiced treatment planning using computer soft wear and real patient data. In dental implant clinic, dental students also learned every step of dental implant treatment: Examinations, implant placement surgery and bone augmentation, prosthetic treatment and maintenance. We also gave lectures about advanced knowledge of dental implant treatment and regenerative medicine to post-graduate students.

(4) Lectures & Courses

Acquire basic knowledge and an attitude of thinking continuously.

(5) Clinical Services & Other Works

In dental implant clinic we treated patients, who missed teeth, with dental implants recovering aesthetics and functions. We further observed and followed these patients after the treatments (Maintenance Procedure).

(6) Clinical Performances

In dental implant clinic in TMDU, the number of clinical cases of dental implant treatments is the most in 29 dental schools in Japan. Difficult cases of dental implant treatments in other hospitals and clinics and problem

cases, which have been treated by other dentists, are increasing. We can handle most of these difficult and problem cases.

(7) Publications

[Original Articles]

1. Hao J, Chou J, Kuroda S, Otsuka M, Kasugai S, Lang NP. Injectable simvastatin gel for minimally invasive periosteal distraction: In vitro and in vivo studies in rat. *Clinical Oral Implants Research*. 2018.02; 29(2); 227-234
2. Okada E, Nakata H, Yamamoto M, Kasugai S, Kuroda S. Indirect osteoblast differentiation by liposomal clodronate. *Journal of Cellular and Molecular Medicine*. 2018.02; 22(2); 1127-1137
3. Ding Lin, Zhang Peng, Wang Xin, Hao Jia, Aoki Kazuhiro, Kuroda Shinji, Kasugai Shohei. ハイドロキシアパタイト表面をドキシサイクリンで処理したときに骨付加への作用 マウス上顎における組織形態計測研究 (Effect of doxycycline-treated hydroxyapatite surface on bone apposition: A histomorphometric study in murine maxillae) *Dental Materials Journal*. 2018.02; 37(1); 130-138
4. 柴崎 真樹, 渡辺 孝康, 春日井 昇平, 中川 一路. 異なる地域に発生した猩紅熱の流行より採取された emm12 型 A 群連鎖球菌株における遺伝子変異の分布 (Distribution of Single Nucleotide Polymorphisms in Protein-coding Regions of emm12 Group A Streptococcus from Two Scarlet Fever Outbreaks) *口腔病学会雑誌*. 2018.03; 85(1); 1-8
5. Manabu Kanazawa, Mariko Tanoue, Anna Miyayasu, Shin Takeshita, Daisuke Sato, Mari Asami, Thuy Vo Lam, Khaing Myat Thu, Ken Oda, Yuriko Komagamine, Shunsuke Minakuchi, Jocelyne Feine. The patient general satisfaction of mandibular single-implant overdentures and conventional complete dentures: Study protocol for a randomized crossover trial. *Medicine (Baltimore)*. 2018.05; 97(20); e10721
6. Seki N, Kanazawa M, Komagamine Y, Mizutani K, Hosaka K, Komada W, Moross J, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School. *Journal of Medical and Dental Sciences*. 2018.09; 65; 123-130
7. Shinji Kuroda, Hidemi Nakata, Shohei Kasugai. The use of implant-supported fixed bridge in a case of severe pharyngeal reflex: Implant-supported fixed prosthesis during a short period *口腔病学会雑誌*. 2018.11; 85(3);
8. Lia Kartika Wulansari, Boosana Kaboosaya, Masud Khan, Mariko Takahashi, Hidemi Nakata, Shinji Kuroda, Kazuhiro Aoki, Shohei Kasugai. Beneficial effects of fasting regimens on periodontal tissues in experimental periodontitis mice model *Journal of International Dental and Medical Research*. 2018.11; 11(2); 362-369
9. 黒田 真司, 中田 秀美, 春日井 昇平. 嘔吐反射の強い患者に対して固定性ブリッジによるインプラント補綴を行った症例報告 固定性インプラント補綴装置の短期間使用例 (The Use of Implant-supported Fixed Bridge in a Case of Severe Pharyngeal Reflex: Implant-supported Fixed Prosthesis during a Short Period) *口腔病学会雑誌*. 2018.11; 85(3); 77-82
10. Komagamine Y, Kanazawa M, Sato D, Minakuchi S. A preliminary comparison of masticatory performances between immediately loaded and conventionally loaded mandibular two-implant overdentures with magnetic attachments. *Clinical implant dentistry and related research*. 2018.12; 21(1); 130-137
11. Zhang P, Ding L, Kasugai S. Effect of doxycycline doped bone substitute on vertical bone augmentation on rat calvaria. *Dental materials journal*. 2018.12;
12. Ikumi Reo, Miyahara Takayuki, Akino Norio, Tachikawa Noriko, Kasugai Shohei. Guided bone regeneration using a hydrophilic membrane made of unsintered hydroxyapatite and poly(L-lactic acid) in a rat bone-defect model *DENTAL MATERIALS JOURNAL*. 2018.12; 37(6); 912-918
13. Ikumi Reo, Miyahara Takayuki, Akino Norio, Tachikawa Noriko, Kasugai Shohei. Guided bone regeneration using a hydrophilic membrane made of unsintered hydroxyapatite and poly(L-lactic acid) in a rat bone-defect model(和訳中) *Dental Materials Journal*. 2018.12; 37(6); 912-918

14. Kudoh K, Fukuda N, Kasugai S, Tachikawa N, Koyano K, Matsushita Y, Ogino Y, Ishikawa K, Miyamoto Y. Maxillary Sinus Floor Augmentation Using Low-Crystalline Carbonate Apatite Granules With Simultaneous Implant Installation: First-in-Human Clinical Trial. *Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons*. 2018.12;
15. Kazuhiro Kon, Makoto Shiota, Maho Ozeki, Shohei Kasugai. The effect of graft bone particle size on bone augmentation in a rabbit cranial vertical augmentation model: a microcomputed tomography study. *Int J Oral Maxillofac Implants*. 29(2); 402-406

[Misc]

1. Madi M, Htet M, Zakaria O, Alagl A, Kasugai S.. Re-osseointegration of Dental Implants After Periimplantitis Treatments: A Systematic Review. *Implant Dentistry*. 2018.02; 27(1); 101-110

[Conference Activities & Talks]

1. Kasugai S. Seven keys for long term good prognosis in dental implant treatment. 38th Myanmar Dental Association Congress 2018.01.18 Melia Hotel, Yangon, Myanmar
2. Kasugai S. One implant system with long term stability for broad range of clinical cases. 4th Thai-German International Congress: Implant Dentistry 2018.01.18 The Empress Convention Center, Empress Hotel, Chaing Mai, Thailand
3. Kasugai S. Bone substitutes in dentistry. The 3rd Meeting of Orthopedic Injury and Artificial Bone Study Group 2018.01.27 Shinagawa Season Terrace, Tokyo
4. Hasegawa Y, Motoyama S, Matsubara A, Ooba Y, Kuroda S, Tachikawa N, Shiota M, Kasugai S. Technical procedure for repairing implant-upper structure in two times.. The 37th Kanto Kohshinetsu Section Meeting of Japanese Association of Oral Implantology 2018.02.11 Tsurumi University
5. Iwaki Maiko, Kanazawa Manabu, Sato Daisuke, Miyayasu Anna, Kasugai Shohei, Araki Kouji, Minakuchi Shunsuke. Masticatory Functions with Immediate Loading of Two-implant Mandibular Overdentures: 5-year prospective study.. Academy of Osseointegration Annual Meeting 2018 2018.03.01 Los Angeles, CA, USA
6. Wataru Kozuma, Kazuhiro Kon, Sawako Kawakami, A.BO BO THIKE, Masahiro Shimogishi, Makoto Shiota, Shohei Kasugai. Effect of Hydroxyapatite Fiber Material with Magnesium on Bone Regeneration: in vivo and in vitro study. 2018.03.01 Los Angeles
7. ThihaTin Kyaw, Miyahara Takayuki, HidemiNakata, Shinji Kuroda, ShoheiKasugai. Cleaning Methods of Contaminated Metal Surface. The Annual Meeting of the Academy of Osseointegration 2018.03.02 Los Angeles, CA, USA
8. Asami Mari,Kanazawa Manabu,Miyayasu Anna,Shimada Ryo,Negoro Masatoshi,Sato Daisuke,Kasugai Shohei, Minakuchi Shunsuke. Survival and marginal bone loss of single-implant overdentures -A 12-month follow-up-. The 127th Scientific Meeting of Japan Prosthodontic Society 2018.06.16 Okayama
9. Thuy Vo Lam, Manabu Kanazawa, Khaing Myat Thu, Mari Asami, Anna Miyayasu, Shimada Ryo, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi. Are One-Implant Overdentures Superior to Complete Dentures in Masticatory Function?. IADR 2018 General Session in London 2018.07.26 London
10. K. M. Thu, M. Kanazawa, T. Vo Lam, M. Asami, A. Miyayasu, S. Ryo, D. Sato, S. Kasugai, S. Minakuchi. Durability of Locator and Optimal Retention for Single Implant Overdenture. 2018 IADR/PER General Session 2018.07.27 ExCel Convention center, London, UK
11. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. 32nd IADR-SEA & 29th SEAAGE 2018.09.11 Da Nang, Vietnam
12. Asami M, Kanazawa M, Vo T, Thu K, Miyayasu A, Shimada R, Sato D, Kasugai S, Minakuchi S. Marginal bone loss and stability of single implant overdentures. 32nd IADR-SEA & 29th SEAAGE, Vietnam 2018.09.13 Ariyana Convention Center, Da Nang, Vietnam
13. Effect of Hydroxyapatite Fiber Material with Magnesium on Bone Regeneration. 2018.09.16

14. Sawako Kawakami, Makoto Shiota, Kazuhiro Kon, Wataru Kozuma, Hajime Iijima, Shohei Kasugai. Application of dissociated soft tissue using rat palatal mucosa on osteogenesis. European Association for Osseointegration 2018.10.14 Vienna, Austria
15. Negoro Masatoshi, Kanazawa Manabu, Shimada Ryo, Miyayasu Anna, Sato Daisuke, Kusumoto Yuriko, Abe Yuka, Baba Kazumi, Minakuchi Syunsuke. Patient report outcomes of IARPD with magnetic attachments. 2018.11.03 Niigata

[Awards & Honors]

1. AO Best Poster award for 2018 (Maiko Iwaki), Academy of Osseointegration Annual Meeting 2018, 2018.03

Plastic and Reconstructive Surgery

Professor(Chairman):Mori Hiroki

Professor:Tanaka Kentaro

Assistant Professor (Hospital Staff):Uemura Noriko

Project Assistant Professor (Hospital Staff) :Inoue Makiko

Graduate Student:Homma Tsutomu,Usami Satoshi,Suesada Nobuko,Hamanaga Mayuko,Imai Kazuya

(1) Research

Plastic and Reconstructive Surgery :
MORI Hiroki

1. Pre and post operative breast or facial contour evaluation using 3D camera
2. Sensory recovery in the nipple-sparing or skin-sparing mastectomy
3. Development of classification and algorithm in blepharoptosis and blepharospasm surgery
4. Elucidation of the role of TRP channel and the midline in the interaction between keratinocyte and peripheral nervous system
5. Blood circulation study of the surgical flap using indocyanine green angiography and multi slice CT

Functional Reconstruction :
TANAKA Kentaro

1. Development of functional and aesthetic reconstruction following cancer ablation in head and neck
2. Does the improvement of capillary patency rate contribute to the preservation of transferred fatty tissue volume ?
3. Evaluation of blood supply to various flaps using ICG fluorescence angiography
4. Development of ambulatory functional reconstruction for refractory ulcer especially in CLI patients
5. Development of functional and aesthetic reconstruction for facial paralysis

(2) Education

Plastic surgery is a specialized branch of surgery concerned with the repair of deformities and the correction of functional deficits. The specialty of plastic surgery covers a wide range of procedures, and unlike other medical specialties which concentrate on one particular area of the body, plastic surgeons are involved in the reconstruction and remodeling of nearly all external body structures.

(3) Clinical Performances

We cover the whole field of plastic surgery. In particular, we deal with the following field; congenital anomaly (cleft lip and palate, microtia blepharoptosis or polydactyly etc), LASERs, cutaneous malignant tumor, skin ulcer, breast reconstruction, head and neck reconstruction, facial palsy, axillary osmidrosis.

(4) Publications

[Original Articles]

1. Mori H,Uemura N,Koga H,Okazaki M. Objective assessment of reconstructed breast hardness using a durometer. *Breast Cancer*. 2018.01; 25(1); 81-85
2. Ishii Y,Yano T,Ito O. Use of the facial dismasking flap approach for surgical treatment of a multifocal craniofacial abscess. *Arch Plast Surg*. 2018.05; 45(3); 271-274
3. Usami S, Inami K, Hirase Y. Coverage of the dorsal surface of a digit based on a pedicled free-style perforator flap concept. *J Plast Reconstr Aesthet Surg*. 2018.06; 71(6); 863-869
4. Usami S, Kawahara S, Kuno H, Takamure H, Inami K. A retrospective study of closed extension block pinning for mallet fractures: Analysis of predictors of postoperative range of motion. *J Plast Reconstr Aesthet Surg*. 2018.06; 71(6); 876-882
5. Higashino T, Okazaki M, Mori H, Yamaguchi K, Akita K. Microanatomy of Sensory Nerves in the Upper Eyelid: A Cadaveric Anatomical Study. *Plastic and reconstructive surgery*. 2018.08; 142(2); 345-353
6. Tanaka K,Yano T,Homma T,Tsunoda A,Aoyagi M,Kishimoto S,Okazaki M. A new method for selecting auricle positions in skull base reconstruction for temporal bone cancer. *Laryngoscope*. 2018.11; 128(11); 2605-2610
7. Nomura F,Ariizumi Y,Kiyokawa Y,Tasaki A,Tateishi Y,Koide N,Kawabe H,Sugawara T,Tanaka K,Asakage T. Pigmented villonodular synovitis occurring in the temporomandibular joint. *Auris Nasus Larynx*. 2018.11;

[Conference Activities & Talks]

1. Usami S,Inami K. Free posterior interosseous artery perforator flap for fingertip resurfacing . FESSH2018 2018.06.13 Copenhagen,Denmark
2. Usami S,Inami K,Hirase Y. Digital soft tissue reconstruction based on a pedicled free-style perforator flap concept. KSSH Annual Internation Meeting 2018 2018.11.02 Seoul,Korea

Head and Neck Surgery

Professor: Takahiro Asagkage

Junior associate professor: Yosuke Ariizumi, Kazuchika Ohno

Assistant professor: Akihisa Tasaki, Yusuke Kiyokawa, Fuminori Nomura

Senior Resident: Hiroaki Kawabe, Nobuaki Koide, Ryuhei Okada

Student: Hirofumi Fukushima, Takao Tokumaru, Masaharu Kishikawa

(1) Outline

Our department is responsible for clinical management, education and research in the field of head and neck surgery. Clinically, the Department of Head and Neck Surgery manages the tumor of extensive area of head and neck, except brain, eye and vertebra. Surgical and medical treatment of the head and neck tumors are mainly employed in our department.

(2) Research

Surgical approaches to the skull base and deep area of the face.

Surgical anatomy of the skull base.

Establishment of the standard neck dissection.

Treatment of pediatric head and neck tumors.

Chemoradiotherapy for head and neck cancers.

Clinical application of navigation system and 3D entity model surgery for skull base surgery.

Diagnosis and treatment for superficial squamous cell carcinoma of head and neck region.

Human papilloma virus infection and head and neck cancer.

Polymorphisms in alcohol metabolism genes and Head and Neck Cancers.

(3) Education

Education: Undergraduate Course

In the classes at the 3th grade of medical school, head and neck oncology are systematically lectured. Clinical practice is experienced at the 4th to 6th grade in the out-patient clinic, the ward, and operating theater.

Education :Graduate Course

Education and researches at the graduate school are focused on (1)surgery of the head and neck tumor, (2)clinical management of the patients with head and neck tumor, and (3)clinical anatomy of head and neck region.

(4) Publications

[Original Articles]

1. Kenro Kawada, Taro Sugimoto, Ryuhei Okada, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuuichiro Kume, Andres Mora, Tairo Ryotokuji, Takuta Okada, Akihiro Hoshino, Yutaka Tokairin, Yausaki

- Nakajima, Yusuke, Kiyokawa, Fuminori, Nomura, Yosuke, Ariizumi, Shohei, Tomii, Takashi, Ito, Takahiro, Asakage, Yusuke, Kinugasa, Tatsuyuki, Kawano. A case of simultaneous triple primary cancers of the hypopharynx, esophagus and stomach which were dissected by endoscopic laryngo-pharyngeal surgery combined with endoscopic submucosal dissection. *Open Journal of Gastroenterology*. 2018.03; 8(3); 94-102
2. Kiyokawa Yusuke, Ariizumi Yousuke, Nomura Fuminori, Tasaki Akihisa, Okada Ryuhei, Tsunoda Atsunobu, Kishimoto Seiji, Asakage Takahiro. 線維性骨異形成症に生じた側頭部の骨肉腫の1症例 (A Case of Osteosarcoma of the Temporal Region Arising in Fibrous Dysplasia) 耳鼻咽喉科臨床 補冊. 2018.03; (補冊 152); 96-97
 3. Takuya Okada, Kenro Kawada, Taro Sugimoto, Takashi Ito, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuichiro Kume, Tairo Ryotokuji, Akihiro Hoshino, Yutaka Tokairin & Yasuaki Nakajima. Asymptomatic marginal zone lymphoma of mucosa-associated lymphoid tissue in the hypopharynx, detected with esophagogastroduodenoscopy. *Acta Oto-Laryngologica Case Reports*. 2018.05; 3(1); 19-23
 4. Kubota A, Nakatani E, Tsukahara K, Hasegawa Y, Takemura H, Terada T, Taguchi T, Nagahara K, Nakatani H, Yoshino K, Higashi Y, Iwase S, Beppu T 他. Adjuvant chemotherapy with S-1 after curative chemoradiotherapy in patients with locoregionally advanced squamous cell carcinoma of the head and neck: Reanalysis of the ACTS-HNC study. *PLoS One*. 2018.06; 8 (13(6));
 5. 岸川 正大, 井上 純, 濱本 英利, 小林 勝則, 藤原 恭子, 朝蔭 孝宏, 稲澤 譲治. 皮膚癌に対する miR-634 軟膏の塗布による抗腫瘍効果 日本癌学会総会記事. 2018.09; 77 回; 1476
 6. 朝蔭孝宏. 鼻副鼻腔癌に対する特殊なアプローチ法. *JOHNS*. 2018.09; 34(9); 1357-1361
 7. Nomura F, Ariizumi Y, Kiyokawa Y, Tasaki A, Tateishi Y, Koide N, Kawabe H, Sugawara T, Tanaka K, Asakage T. Pigmented villonodular synovitis occurring in the temporomandibular joint. *Auris Nasus Larynx*. 2018.11;
 8. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol*. 35(3); 402-404

[Books etc]

1. Hiroyuki Miura. Today's Therapy in Otorhinolaryngology-Head & Neck Surgery. 2018.05 (ISBN : 978-4-260-03452-4)

[Misc]

1. 朝蔭孝宏. D's Mind 医の道をつなぐ D-to-D. 2018.01; (30); 4-9

[Conference Activities & Talks]

1. 別府武. Facial nerve management for parotid cancer; how to make decision whether it should be preserved or sacrificed and how to seek it in difficult case. 第41回顔面神経学会 2018.06.09 山形
2. 別府武. 座長：一般口演. 埼玉頭頸部癌免疫療法セミナー 2018.09.19 川越
3. 岸川正大, 井上純, 朝蔭孝宏, 稲澤譲治, 他. Therapeutic potential of the topical treatment of miR-634 ointment for skin cancer. 第77回日本癌学会学術総会 2018.09.28 大阪
4. 朝守智明, 得丸貴夫, 山田雅人, 杉山智宣, 谷美有紀, 金子昌行, 別府武. 当院における lenvatinib の潮受け意見-治療効果と有害事象について. 第130回日耳埼玉県地方部会学術講演会 2018.10.14 埼玉県

Radiation Therapeutics and Oncology

Professor Ryoichi Yoshimura

Lecturers Kazuma Toda

Research Associates Keiko Nakagawa, Mio Kojima

Hospital Staff members Ryoko Suzuki (~May.), Kazuma Sasamura (Apr.~)

Resident Daigoro Matsubara (Apr.~)

(1) Outline

At the Department of Radiation Therapeutics and Oncology, clinical services, research, and education related to radiotherapy for all cancers are undertaken.

(2) Research

Mainly clinical research related to radiotherapy is performed.

(3) Education

Lectures are given to medical students or graduate students, and clinical clerkship is organized.

After the students enter our department, comprehensive training is provided at both our department and the Department of Diagnostic Radiology and Nuclear Medicine for 3 years, since the certified radiologist exam is common.

Our department holds a radiation oncology seminar for students and residents with the Department of Radiation Oncology of Juntendo University and Showa University.

Lectures for medical students or graduate students, and clinical clerkship are performed.

(4) Lectures & Courses

Our department teaches students and residents about cancer therapy from the radiation oncologist's perspective. Every student/resident of this department aims to be a certified radiation oncologist.

(5) Clinical Services & Other Works

All the staff members are engaged in performing external beam radiation therapy or high-dose-rate or low-dose-rate brachytherapy in the hospital.

A total of 695 patients, including 181 head and neck cancer patients, 160 urological cancer patients, 63 breast cancer patients, 77 lung cancer patients, and 44 esophageal cancer patients, were treated at our hospital in 2017.

(6) Clinical Performances

Our department specializes in low-dose-rate brachytherapy for oral cancer patients.

(7) Publications

[Original Articles]

1. Hajime Tanaka, Soichiro Yoshida, Fumitaka Koga, Kazuma Toda, Ryoichi Yoshimura, Yutaka Nakajima, Emiko Sugawara, Takumi Akashi, Yuma Waseda, Masaharu Inoue, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Impact of Immunohistochemistry-Based Subtypes in Muscle-Invasive Bladder Cancer on Response to Chemoradiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.*. 2018.06;
2. Tanaka H, Yoshida S, Koga F, Toda K, Yoshimura R, Nakajima Y, Sugawara E, Akashi T, Waseda Y, Inoue M, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Impact of Immunohistochemistry-Based Subtypes in Muscle-Invasive Bladder Cancer on Response to Chemoradiation Therapy. *International Journal of Radiation Oncology, Biology, Physics*. 2018.06; 18;
3. Yamaga Emi, Toriihara Akira, Nakamura Shin, Asai Sakurako, Fujioka Tomoyuki, Yoshimura Ryoichi, Michi Yasuyuki, Harada Hiroyuki, Tateishi Ukihide. Clinical usefulness of 2-deoxy-2-[¹⁸F] fluoro-D-glucose-positron emission tomography/computed tomography for assessing early oral squamous cell carcinoma(cT1-2NOMO) *Japanese Journal of Clinical Oncology*. 2018.07; 48(7); 633-639
4. Yoshida Soichiro, Takahara Taro, Ishii Chikako, Nakagawa Keiko, Toda Kazuma, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Yoshimura Ryoichi, Kihara Kazunori, Fujii Yasuhisa. Loco-regional radiotherapy targeting for oligo-progressive CRPC on the diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) *INTERNATIONAL JOURNAL OF UROLOGY*. 2018.10; 25; 358
5. Kuwabara H, Toriihara A, Yuasa-Nakagawa K, Toda K, Tateishi U, Yoshimura R.. Prognostic value of metabolic tumor burden calculated using dual-time-point ¹⁸F-fluorodeoxyglucose positron emission tomography/CT in patients with oropharyngeal or hypopharyngeal cancer. *Head and Neck*. 2018.12; 41;

[Books etc]

1. Ryoichi Yoshimura. *Brachytherapy*. Springer, 2018.08 (ISBN : 978-981-13-01489-7)

[Conference Activities & Talks]

1. Ryoichi Yoshimura. Low-dose-rate Brachytherapy for Prostate Cancer and Oral Cancer. The 1st International Academic Conference of 3D printing Technology & Brachytherapy 2018.09.08 北京

[Awards & Honors]

1. Robomech Journal, The Japan Society of Mechanical Engineers, 2018.06

Maxillofacial Anatomy

Professor Shunichi SHIBATA
Assistant Professor Shun-ichi SHIKANO
Graduate Student Masato Takahashi
Graduate Student Maki Hasegawa
Graduate Student Angamma Randilini
Lecturer Rei Sato
Lecturer Kumiko Sugimoto
Postdoctoral fellow Chiho Kadota

(1) Outline

Maxillofacial anatomy section is engaged in lecture and practical course of gross anatomy and dental anatomy in undergraduate school. In graduate school, this section is engaged in morphological studies of hard tissues such as tooth, bone and cartilage.

(2) Research

Research Subjects

- 1) Structural features of mandibular condylar cartilage.
- 2) Mechanism of epithelial attachment of junctional epithelium in human gingiva.
- 3) Comparative histology and embryology of teeth.
- 4) Observation on the structural features of oral mucous
- 5) Anatomical names of the structures of human skeletal system.
- 6) Hyaluronan synthesis in tooth germ.
- 7) Studies on regeneration of jaw bone.
- 8) Structural features of dental pulp and extracellular matrix

(3) Education

In Undergraduate school

Lecture for 2nd degree students: Human structure I, II, Dental anatomy, Neuroanatomy,

Practical course for 2nd degree students: Gross Anatomy, Neuroanatomy, Dental Anatomy

Lecture and practical course for 5th degree students: Clinical craniofacial anatomy

In Graduate school

Lecture, seminar and practical course to understand the function of various oral organs in a morphological viewpoint, and to evaluate various vital phenomenon encountered in medical practice.

(4) Lectures & Courses

The main purpose of education in undergraduate school is to understand human structure and function from the viewpoints of gross anatomy. In line with this purpose, we execute lectures of systematic anatomy (osteology, myology, neurology, angiology, splanchnology) and topographic anatomy (craniofacial anatomy). To

understand three-dimensional structures of human body, we execute practical course of human gross anatomy after completing lectures. In the practical course, we make an effort to make students understand ethics as dental students to be bright future dentist.

The main purpose of education in graduate school is to understand various vital phenomenon, which we encounter in research fields of basic and clinical sciences, from the viewpoints of morphology. In lectures, we teach various techniques to investigate structural features from the standpoints of light and electron microscopy, organ and tissue culture, and molecular biology.

(5) Publications

[Original Articles]

1. Kim JH, Park C, Yang X, Murakami G, Abe H, Shibata S. Pacinian corpuscles in the human fetal finger and thumb: A study using 3D reconstruction and immunohistochemistry *Anatomical Record*. 2018.01; 301(1); 154-165
2. Fukuoka H, Sato R, Moriyama K, Shibata S. Effect of β -D-xyloside on developing mouse mandibular condylar cartilage in organ culture *Anatomy & Physiology: Current Research*. 2018.02; 8(1); 290
3. Cho KH, Jang HS, Abe H, Yamamoto M, Murakami G, Shibata S. Fetal development of fasciae around the arm and thigh muscles: a study using late stage fetuses *Anatomical Record*. 2018.07; 301(7); 1235-1243
4. Ida-Yonemochi H, Morita W, Sugiura N, Kawakami R, Morioka Y, Takeuchi Y, Sato T, Shibata S, Watanabe H, Imamura T, Igarashi M, Ohshima H, Takeuchi. Craniofacial abnormality with skeletal dysplasia in mice lacking chondroitin sulfate Nacetylgalactosaminyltransferase-1 *Scientific Reports*. 2018.11; 8(17134);

[Conference Activities & Talks]

1. Shunichi Shibata. Development of gonial bone with reference to reduction of Meckel's cartilage in mice. フロンティアミーティング in 新潟 2018 2018.02.10 Niigata University, Niigata, Japan
2. Hikita R, Higashihori N, Kadota C, Akiyama S, Takahashi Y, Ito Y, Moriyama K. Effects of tongue-jaw bone relationship on respiratory function during sleep after orthognathic surgery in patients with mandibular prognathism: Comparison between one-jaw and two-jaw surgery. The 11th Asian Pacific Orthodontic Conference(APOC 2018) 2018.03.05 Boracay, Phillipines
3. Shibata S, Takahashi M, Fujikawa K. Relationship between Gonial bone and reducing Meckel's cartilage in mice. 96th General session and Exhibition of IADR 2018.07.27 ExCel London London
4. Shibata S. Structural features of developing mandibular condylar cartilage. The 6th Tri-University Consortium 2018.11.30 Tokyo

[Awards & Honors]

1. The 11th Asian Pacific Orthodontic Conference(APOC 2018) Posterboard Presentation 2nd Place Research(Hikita R, Higashihori N, Kadota C, Akiyama S, Takahashi Y, Ito Y, Moriyama K), The Asian Pacific Orthodontic Society, 2018.03

Cognitive Neurobiology

Assistant Professor: Narumi Katsuyama
Assistant Professor: Nobuo Usui
Staff Assistant: Takako Kishida
Research Student: Yuri Kim
Adjunct Lecturer:
Hisayuki Ojima
Akiko Yamashita
Rui Watanabe
Eriko Kikuchi(Tachi)
Yoko Kono

(1) Outline

The neuronal mechanisms underlying higher brain function, such as judgement, decision making, and language, are largely unknown. Our goal is to elucidate the neuronal mechanisms by using various techniques in neuroscience including functional MRI, psychophysical experiments, and animal experiments.

(2) Research

1. Neural Mechanisms of control of motor behavior.

Research is aimed at understanding the brain mechanisms of execution and control of the motion and behavior of animals and human.

2. Neuronal mechanisms for perception and cognition.

Research is aimed at understanding the brain mechanisms of perception and cognition of objects through vision and tactile senses of animals and human.

(3) Education

1. Lectures of unit "Functions of Nervous Systems I (Introduction to Neurophysiology, Motor Functions)"

Basic knowledge of neurophysiology will be lectured as an introduction together with the motor functions.

2. Lectures of unit "Functions of Nervous Systems II (Perception, Emotion, Instinct, Sleep, Higher functions)".

A series of lectures will be taught on functions of the sensation, perception, and motion as well as the neural mechanisms of higher brain functions.

3. Lectures of unit "Homeostatic Functions for Life Support".

Lectures will be taught on the structure of the autonomic nervous system and its regulatory mechanisms in the circulation, respiration, digestion/absorption, humor/body temperature, metabolism, excretion, and internal secretion/reproduction.

4. Unit of "Practice of Physiology"

The purpose of the practice is to learn about the physiological mechanisms underlying the normal functions of human body through experiments. The goal is to master the basic experimental procedures, and to experience how to capture and analyze the data in order to draw conclusions.

(4) Lectures & Courses

Students are expected to be voluntarily involved in research activity. Brain is an extremely complicated organ in terms of its morphology and functions. Learning of textbook knowledge is mandatory and is followed by capturing up-to-date scientific information through reading published articles. Once the overview of the field in which graduates/undergraduate students are interested in is completed, they will start to be engaged in on-going research topics under the tutelage of laboratory staff. Through this process, students are encouraged to associate their own research interests with the on-going research topics and will learn practically how data can be captured, rearranged and analyzed through real experiments.

(5) Publications

[Original Articles]

1. Ikeda A, Miyamoto JJ, Usui N, Taira M, Moriyama K. Chewing Stimulation Reduces Appetite Ratings and Attentional Bias toward Visual Food Stimuli in Healthy-Weight Individuals. *Frontiers in Psychology*. 2018.02; 9;
2. Juri Fujiwara, Nobuo Usui, Satoshi Eifuku, Toshio Iijima, Masato Taira, Ken-Ichiro Tsutsui, Philippe N Tobler. Ventrolateral Prefrontal Cortex Updates Chosen Value According to Choice Set Size. *J Cogn Neurosci*. 2018.03; 30(3); 307-318
3. Yoko Kono, Ayako Kubota, Masato Taira, Narumi Katsuyama, Kumiko Sugimoto. Effects of oral stimulation with capsaicin on salivary secretion and neural activities in the autonomic system and the brain. *Journal of Dental Sciences*. 2018.06; 13(2); 116-123
4. Narumi Katsuyama, Eriko Kikuchi-Tachi, Nobuo Usui, Hideyuki Yoshizawa, Aya Saito, Masato Taira. Effect of Visual Information on Active Touch During Mirror Visual Feedback. *Front Hum Neurosci*. 2018.10; 12; article424

[Conference Activities & Talks]

1. Rui Watanabe, Narumi Katsuyama, Nobuo Usui, Masato Taira. The effects of pseudoexperience on the understanding of hemiplegic movements: A Functional Magnetic Resonance Imaging study using physical therapists as subjects. SANS(Social & Affective Neuroscience Society) 2018 2018.05.04 New York
2. Kikuchi Eriko, Ojima Hisayuki, Akiko Yamashita, Narumi Katsuyama, Masato Taira. Properties of jaw movements induced by stimulation of cortical masticatory area in guinea pigs. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.22 Kobe
3. Yuri Kim, Nobuo Usui, Atsushi Miyazaki, Tomoki Haji, Kenji Matsumoto, Katsuki Nakamura, Masato Taira, Narumi Katsuyama. Cortical mechanisms underlying solidness perception under influence of visual information revealed by multivoxel pattern-based fMRI. The 41st Annual meeting of the Japan neuroscience society 2018.07.27 Kobe
4. Akiko Kamada, Nobuo Usui, Daisuke Yoshino. The influence of Go/No-go judgement on the mere exposure effect. The 82nd Annual Convention of the Japanese Psychological Association 2018.09.27 Sendai
5. Yoko Kono, Ayako Kubota, Narumi Katsuyama, Nobuo Usui, Naomi Yoshida, Kumiko Sugimoto. Associations of preference to pungent taste with personality traits and physiological responses to pungent stimulation. The 52nd Annual Meeting of the Japanese Association for the Study of Taste and Smell 2018.10.29 Saitama
6. Rui Watanabe, Narumi Katsuyama, Nobuo Usui, Masato Taira. The effects of experience of treatments for hemiplegia on the understanding of hemiplegic movements: A Functional Magnetic Resonance Imaging study. The 23rd Congress of Japanese Society of Physical Therapy Fundamentals 2018.12.15 Kyoto

Molecular Craniofacial Embryology

Staffs and Students

Professor

Sachiko ISEKI

Associate Professor

Masa-Aki IKEDA

Tenure Track Assistant Professor

Masaki TAKECHI

Part-time lecturers

Shumpei YAMADA

Youichirou NINOMIYA

Toshiko FURUTERA

Shigeru Okuhara

Graduate Students

Erika KUBOTA

RAJENDRAN Arun kumar

Takahiko YAMADA

Shohei YANAGISAWA

VU HOANG Tri

Manami TAKENOSHITA

Rika TAKEUCHI

NAMANGKALAKUL Worachat

Research students

Yukiko HOSHINO

(1) Research

- 1) Molecular mechanisms of mammalian craniofacial development
- 2) Application of developmental mechanisms to regenerative medicine
- 3) Identification of tissue stem cells in craniofacial region and molecular mechanism of the mechanism of their stemness
- 4) Regulation of gene expression in cell growth and differentiation
- 5) Modulating endochondral ossification of mesenchymal stem cells for bone regeneration

(2) Publications

[Original Articles]

1. Charoenlarp, P, Rajendrana, AK, Fujihara, R, Kojima T, Nakahama K, Sasaki, Y, Akiyoshi K, Takechi M, Iseki S. The improvement of calvarial bone healing by durable nanogel-crosslinked materials Journal of Biomaterials Science, Polymer Edition. 2018.08;
2. Mya, N., Furutera, T., Okuhara, S., Kume, T., Takechi, M., Iseki, S. Transcription factor Foxc1 is involved in anterior part of cranial base formation. Congenit Anom (Kyoto). 2018.09; 58(5); 158-166

[Conference Activities & Talks]

1. Takechi M. Evolution and Development of the mammalian middle ear. Helsinki university Institute of biotechnology seminar 2018.02.09 Helsinki, Finland

2. Takechi M, Furutera T, Kitazawa T, Rijli F, Kurihara H, Kuratani S, Iseki S.. Differing contributions of the first and second pharyngeal arches to tympanic membrane formation in the mouse and chick. Gordon Research Conference, Craniofacial Morphogenesis and Tissue Regeneration 2018.02.11 Il Ciocco, Italy
3. Altan Z, Şahin Y, Yassin AR, Ikeda MA, Saadat K ASM. The Interaction between LncRNA MEG3 and its Target, miR-203, in Bladder Cancer. International Eurasian Conference on Biological and Chemical Sciences 2018.04.26 Ankara, Turkey
4. Yokoyama N, Takechi M, Iseki S. Expression and functional analysis of type X collagen during osteogenesis in amniotes. Joint Annual Meeting of JSDB 51st and JSCB 70th 2018.06.08 Tower Hall Funabori
5. Hoang, TV, Takechi, M, Shimizu, M, Kitazawa, T, Higashiyama, H, Kurihara, H, Iseki, S. Dlx5-Augmentation in Neural Crest Cells Induced Calvarial Ectopic Cartilage. International Association for Dental Research, Southeast Asian division 2018.09.11 Da nang, Vietnam
6. Arman K, Saadat K ASM, Altan Z, Sahin Y, Ikeda MA, Igci M. Opposite roles of lncRNA ERICD and ARID3A in DNA damage-induced apoptosis. 5th World Congress on Epigenetics and Chromosome 2018.11.15

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Yasuki Ishizaki, Masao Saito

Research Student : Hong Ding Liu
: Syun Nishihara
: Hiroki Kuwahara
:Syuhei Fukuda
:Hirohito Miki

(1) Outline

In our Lab, we study the role of cell-communication in bone remodeling, cancer and vascular calcification using various techniques, for example, cell culture, molecular biology and mutant mice.

(2) Research

Research Subjects

- 1, Cell-cell communication and cell functions
- 2, Bone remodeling and cell communications
- 3, Cancer and cell communications
- 4, Mechanism of vascular calcification

(3) Education

For undergraduate students. We have some class in biological chemistry for the second grader.

For graduate students. These students can choose the one of themes in our lab. They have to attend meetings and seminars in our Lab.

(4) Lectures & Courses

Undergraduate students should understand basic biochemistry and physiology under healthy/diseased conditions.

Graduate students are expected to solve the problems by themselves. However, appropriate suggestions will be given by at least three supervisors whenever you want.

(5) Publications

[Original Articles]

1. Nisha Gowri Manila, Atsushi Kaida, Ken-Ichi Nakahama, Masahiko Miura. Insulin-like growth factor I receptor regulates the radiation-induced G2/M checkpoint in HeLa cells. *Biochem. Biophys. Res. Commun.*. 2018.08; 503(4); 2977-1983
2. Charoenlarp, P, Rajendrana, AK, Fujihara, R, Kojima T, Nakahama K, Sasaki, Y, Akiyoshi K, Takechi M, Iseki S. The improvement of calvarial bone healing by durable nanogel-crosslinked materials *Journal of Biomaterials Science, Polymer Edition*. 2018.08;
3. Fukuda S, Akiyama M, Harada H, Nakahama KI. Effect of gap junction-mediated intercellular communication on TGF- β induced epithelial-to-mesenchymal transition. *Biochemical and biophysical research communications*. 2018.12;

[Conference Activities & Talks]

1. Yuki Kasahara, Masako Akiyama, Jun Hosomichi, Takashi Ono, Ken-ichi Nakahama. Mineralization of osteoblasts is controlled by the expression of Dscr1.v2. The 4th Annual Meeting of Japanese Society of Osteoimmunology 2018.06.24 Okinawa
2. Role of GPR68 in osteoclasts. 2018.11.29 Yokohama
3. Effect of intercellular communication via gap junction on epithelial-mesenchymal transition by TGF- β .. 2018.11.30 Yokohama

Maxillofacial Surgery

Professor: Tetsuya Yoda

Junior Associate Professor: Keiiti MORITA

Assistant Professor: Hiroyuki YOSHITAKE, Kouichi NAKAKUKI, (June) Yasuyuki Michi,
(April)Namiaki TAKAHARA, Nobuyoshi TOMOMATSU

Special Assistant Professor: Ryouzuke NAGAOKA

Hospital Staff: Machiko KOSUGI

(April) Chie AKATSU, Yasuhiro KURASAWA, Eri TSUCHIDA, Takayuki YAMADA,
Reiko HOSHI, Syun NISHIHARA, Erina TONOUCHI, Akiyo NORIME, Koutarou WACHI

Graduate Student: Eri SONE, Narumi OSIBE, Keiichiro NAKAZATO,
Hiroshi KATO, Takahiko YAMADA, Yusun KIMU,
Katuya HYODO, Daisuke YAMAMOTO, Eri SIBATA,
Hiroki MASUDA

Student: Tizuko KOMURO, Takahiro KIKUTI, Sinya KOUSAKA,
Souiti ROKUSIMA

Emeritus Professor: Teruo AMAGASA

Clinical professor: Masashi YAMASHIRO

Part-time Lecturer: Kazuki HASEGAWA, Hiroyuki WAKE,
Fumiaki SATO, Junichi ISHII, Eizi FUZII,
Akiko KOBAYASHI, Yutaka SATO, Yasushi NIINAKA,
Takao WATANABE, Testuo SUZUKI, Masayuki YAMANE,
Takashi MISHIMAGI, Kazuto KUROHARA,
Katuya AIKOU, Yosio OOHARA, Shigehiro ABE,
Itaru SONODA, Chieko MICHIKAWA

(1) Research

Research Subjects

- 1) Head and Neck Surgery: Innovation of management patients with benign and malignant tumors and cysts in oral and facial region.
- 2) Reconstructive Surgery: Developing method of correcting jaw, facial bone and facial soft tissue trouble left as the result of removal of disease or previous trauma.
- 3) Correction of Birth Defects: Improving surgically correction of birth defects of the face and skull, including cleft lip and palate.
- 4) Dentofacial Deformities and Orthognathic Surgery: Development of new surgical techniques to improving reconstruct and realign the upper and lower jaws.
- 5) Temporomandibular Joint Disorders: Renewing skills in the diagnosis and treatment due to temporomandibular joint problem.
- 6) Oral Mucosa Disease: Creation new method with light and color for diagnosis of oral mucosa disease, including leukoplakia and cancer.

(2) Lectures & Courses

Oral and maxillofacial surgery is a surgical specialty involving the diagnosis, surgical treatment and management of defects and injuries related to the function and aesthetics of the face and jaws. In order to practice the full scope of the specialty, oral and maxillofacial surgeons are required education in dentistry, medicine and surgery for regional requirement.

(3) Clinical Performances

Clinical Services

- 1) Diagnosis, removing and reconstruction of jaw, oral or facial tumor or cyst.
- 2) Diagnosis and treatment of cleft lip and palate.
- 3) Treatment of jaw aligned with orthognathic surgery.
- 4) Therapy of temporomandibular disorder with or without temporomandibular joint surgery.
- 5) Diagnosis and treatment of oral mucosa disease.
- 6) Treatment of inflammation in the region jaw and facial trauma.
- 7) Extraction tooth including wisdom tooth.

(4) Publications

[Original Articles]

1. Tomoki Kanemaru, Yoshio Ohyama, Kazuhiro Aoki, Atsushi Tamura, Nobuhiko Yui, Satoshi Yamaguchi, Yoshiyuki Mochida. Modulation of Matrix Mineralization by von Willebrand Factor C Domain Containing 2 in Vivo and in Vitro J Oral Tissue Engin . 2018; 15(3); 131-142
2. Yoshitake H. Development of the new instrument for measurement of mouth opening and mandibular movement. Journal of Oral and Maxillofacial Surgery, Medicine and Pathology.. 2018; 30; 488-491
3. Yoshitake H. Development and clinical application of a new mouth-opening exercise device that induces a protrusive sliding movement of the mandibular condyle and increases the hinge mobility of the temporomandibular joint Journal of Oral and Maxillofacial Surgery, Medicine and Pathology.. 2018; 31; 131-134
4. Takasuke Inada, Atsushi Tamura, Masahiko Terauchi, Satoshi Yamaguchi, Nobuhiko Yui. A silencing-mediated enhancement of osteogenic differentiation by supramolecular ternary siRNA polyplexes comprising bioleavable cationic polyrotaxanes and anionic fusogenic peptides. Biomaterials Science. 2018.02; 6(2); 440-450
5. Ohata Y, Tsuchiya M, Hirai H, Yamaguchi S, Akashi T, Sakamoto K, Yamaguchi A, Ikeda T, Kayamori K. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. PLoS ONE. 2018.02; 13(2); e0191865
6. Hayashi N, Sato T, Fukushima Y, Takano A, Sakamoto I, Yoda T. A two-year follow-up of surgical and non-surgical treatments in patients with masticatory muscle tendon-aponeurosis hyperplasia International Journal of Oral and Maxillofacial Surgery. 2018.02; 47(2); 199-204
7. Kanai Y, Nishihara H, Miyagi Y, Tsuruyama T, Taguchi K, Katoh H, Takeuchi T, Gotoh M, Kuramoto J, Arai E, Ojima H, Shibuya A, Yoshida T, Akahane T, Kasajima R, Morita K, Inazawa J, Sasaki T, Fukayama M, Oda Y. The Japanese Society of Pathology Guidelines on the handling of pathological tissue samples for genomic research: Standard operating procedures based on empirical analyses Pathology International. 2018.02; 68(2); 63-90
8. Shibata M, Yoshitake H, Terauchi M, Akane Yukimori A, Yamaguchi S. Submandibular triangle cavernous hemangioma: Case report and review of literature Journal of Oral and Maxillofacial Surgery, Medicine and Pathology. 2018.03; 30; 353-358
9. Tonouchi E, Gen Y, Muramatsu T, Hiramoto H, Tanimoto K, Inoue J, Inazawa J. miR-3140 suppresses tumor cell growth by targeting BRD4 via its coding sequence and downregulates the BRD4-NUT fusion oncoprotein. Scientific reports. 2018.03; 8(1); 4482

10. Sano Y, Kogashiwa Y, Araki R, Enoki Y, Ikeda T, Yoda T, Nakahira M, Sugawara M. Correlation of Inflammatory Markers, Survival, and COX2 Expression in Oral Cancer and Implications for Prognosis Otolaryngology-Head and Neck surgery. 2018.04; 158(4); 667-676
11. Hayashi N, Sato T, Kokabu S, Usui M, Yumoto M, Ikami E, Sakamoto Y, Nifuji A, Hayata T, Noda M, Yoda T. Possible association of oestrogen and Cryba4 with masticatory muscle tendon-aponeurosis hyperplasia. Oral diseases. 2018.04;
12. Masahiko Terauchi, Atsushi Tamura, Satoshi Yamaguchi, Nobuhiko Yui. Enhanced cellular uptake and osteogenic differentiation efficiency of melatonin by inclusion complexation with 2-hydroxypropyl β -cyclodextrin. International Journal of Pharmaceutics. 2018.05; 547(1-2); 53-60
13. Usumi-Fujita R, Nakakuki K, Fujita K, Kosugi M, Yonemitsu I, Fukuyama E, Ono T. Collaborative treatment for a case of condylar hyperplastic facial asymmetry. The Angle orthodontist. 2018.07; 88(4); 503-517
14. Okuyama K, Yamashiro M, Kaida A, Kawamata A, Mizutani M, Michi Y, Uzawa N, Yano T, Tohyama R, Yamaguchi S. Does a Vascularized Fibula Free Bone Grafted Immediately After Hemimandibulectomy in a Child Grow or Relapse During Adolescence? The Journal of craniofacial surgery. 2018.07; 29(5);
15. Michikawa C, Izumo T, Sumino J, Morita T, Ohyama Y, Michi Y, Uzawa N. Small size of metastatic lymph nodes with extracapsular spread greatly impacts treatment outcomes in oral squamous cell carcinoma patients International Journal of Oral and Maxillofacial Surgery. 2018.07; 47(7); 830-835
16. Sato T, Okubo M, Hayashi N, Yumoto M, Fukushima Y, Yoda T. Osteonecrosis of the jaw with pancytopenia in a patient receiving methotrexate for rheumatoid arthritis without antiresorptive or antiangiogenic agents: Report of a case Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2018.09; 30(5); 418-421
17. Kurohara K, Michi Y, Yukimori A, Yamaguchi S. The glomus tumor resorbed bone and teeth in the mandible: a case report Head and Face Medicine. 2018.09; 14(18);
18. Kim Y, Hayashi M, Ono T, Yoda T, Takayanagi H, Nakashima T. Suppression of hematopoietic cell kinase ameliorates the bone destruction associated with inflammation. Modern rheumatology. 2018.11; 1-17
19. Sawangarun Wanlada, Mandasari Masita, Aida Junko, Morita Kei-ichi, Kayamori Kou, Ikeda Tohru, Sakamoto Kei. Loss of Notch1 predisposes oro-esophageal epithelium to tumorigenesis EXPERIMENTAL CELL RESEARCH. 2018.11; 372(2); 129-140
20. Tomomatsu N, Kurohara K, Nakakuki K, Yoshitake H, Kanemaru T, Yamaguchi S, Yoda T. Influence of the anatomical form of the posterior maxilla on the reliability of superior maxillary repositioning by Le Fort I osteotomy. International Journal of Oral and Maxillofacial Surgery. 2018.11;
21. Kitamura T, Sato T, Ikami E, Fukushima Y, Yoda T. A case of a patient who is diagnosed with mild acquired hemophilia A after tooth extraction died of acute subdural hematoma due to head injury Case Rep Dent. 2018.12;
22. Kurohara K, Tomomatsu N, Nakakuki K, Sakuma T, Arai N, Yoda T. Treatment of refractory non-union after maxillary osteotomy: A case report. Journal of stomatology, oral and maxillofacial surgery. 2018.12;
23. Hoshi R, Tetsumura A, Yamaguchi S. Preoperative imaging findings as predictors of postoperative inferior alveolar nerve injury following mandibular cyst surgery. Journal of Oral Science. 2018.12; 60(4); 618-625

[Misc]

1. Kato T, Morita H, Tsuzuki T, Yamaguchi M, Ohta H, Tanoue D, Nakakuki K. Emerging role of dental professionals in collaboration with medical personnel in disaster relief following the 2016 Kumamoto earthquakes: implications for the expanding scope of dental practice. International dental journal. 2018.06;

[Conference Activities & Talks]

1. NAKAZATO Keiichiro, UZAWA Narikazu, KAYAMORI Kou, TSUCHIYA Maiko, WATANABE Hiroshi, SUMINO Jun, MICHl Yasuyuki, YAMAGUCHI Satoshi. The Change of Metabolic Control Mechanism in the Development and Progress of the Tongue Carcinoma. 2018.01.25 Niigata, Japan
2. Ogasawara T, Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama K. Shape optimization of subperiosteal devices using finite element analysis. The 11th Asian Pacific Orthodontic Conference(APOC 2018) Residents' Forum 2018.03.04 Boracay, Phillipines
3. Baba Y, Ogawa T, Uezono M, Mibu M, Sumita Y, Mishimagi T, Sato Y, Morita K, Moriyama K. Changes of pharyngeal morphology and speech function after maxillary distraction in two cases of CLP. The 42nd Annual Meeting of Japanese Cleft Palate Association 2018.05.24 Osaka
4. Hiroyuki YOSHITAKE. Diagnosis and treatment of Synovialchondromatosis of Temporomandibular Joint (TMJ). 2018.07.07
5. Hiroyuki YOSHITAKE. Clinical application of the Yasec Mouth-opening Exercise Device. 2018.07.07
6. Takahara N, Kimura A, Higuchi Y, Kabasawa Y, Yoda T. Evaluation of postoperative mandibular stability after bimaxillary surgery for mandibular prognathism depending on the amount of mandibular setback and the clockwise rotation of the proximal segment. 24th Congress of the European Association for Cranio Maxillo Facial Surgery 2018.09
7. Hyodo K, Arisaka Y, Yamaguchi S, Yui N. Design of sulfonated polyrotaxane surfaces to activate vascular endothelial cells. 5th TERMIS World Congress 2018.09.05
8. Yoshitake H. Clinical application of the New Temporomandibular Joint (TMJ) Rehabilitation device.. 24th Congress of the European Association for Cranio Maxillo-Facial Surgery. 2018.09.18
9. Shibata E, Morita K, Kayamori K, Maruiwa M, Michi Y, Sato Y, Takeuchi K, Ikeda T, Harada H, Yoda T. A case of mammary analogue secretory carcinoma in salivary duct of parotid gland. 13th Asian Congress on Oral and Maxillofacial Surgery (ACOMS) 2018.11
10. Namiaki Takahara, Atsushi Kimura, Yusuke Higuchi, Yuji Kabasawa, Tetsuya Yoda. Accuracy of maxillary repositioning using vertical positionig devices in Le Fort I osteotomy. 2018.11.03
11. Eri SHIBATA, Kei-ichi MORITA, Yasuyuki MICHl, Tetsuya YODA. A case of Mammary Analogue Secretory Carcinoma in Salivary Duct of Parotid Gland. 13th Asian Congress on oral and maxillofacial surgery 2018.11.08 台北
12. Katsuya Hyodo,Yoshinori Arisaka,Satoshi Yamaguchi,Tetsuya Yoda,Nobuhiko Yui. Induction of vascular network in vitro on polyrotaxane surfaces with vascular endothelial growth factors. 13th Asian Congress on Oral and Maxillofacial Surgery 2018.11.10

Maxillofacial Orthognathics

Professor

Keiji MORIYAMA

Associate Professor

Shoichi SUZUKI

Junior Associate Professor

Takuya OGAWA

Assistant Professor

Michiko TSUJI, Norihisa HIGASHIHORI,

Jun MIYAMOTO, Yukiho KOBAYASHI,

Tsutomu MATSUMOTO

Research Assistant Professor

Chiho KADOTA, Yuko YASUDA, Masayoshi UEZONO

Clinical Fellow

Kenji OGURA, Naoki KOUDA, Ayumi SHOJI

Graduate Student

Taizo HIRATSUKA, Aung Bhone Myat,
Hiroyuki KAMIMOTO, Kyoko HIRABAYASHI,
Kenta FUNAHASHI, Hideyuki YOSHIZAWA,
Wu Yu Yun, Kaori IWANAMI, Soonhwa KANG,
Hidekazu MATSUMOTO, Takayuki MIYAZAKI,
Teramoto Iida Airy, Nay Myo Min Swe, Phyo Thiha,
Nanase IGARASHI, Yumi INAGAKI, Masaki INOUE,
Yoshiya KAISAKA, Yuki NIKI, Thili HLA Myint,
Badrakhkhuu Nomin Dulguun, Sakurako KANO,
Yuki SAGAWA, Sumika NAKAJIMA, Lin Tun Oo,
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Miyu ARAKI, Takeshi OGASAWARA, Rie KINOSHITA,
Ruriko NAKAMURA, Syuhei AKIYAMA, Megumi ARIMURA,
Asuka TAMURA, Cheng Shih-Wei Eric, Yuri BABA,
Kenjiro MATSUMURA, Yukiko KINOSHITA,
Chisato TOMINAGA, Daichi HAYAKA, Atsuhiko INOUE,
Riho YOKOUCHI, Akitsu IKEDA, Sahori MATSUNO,
Misato HANDA

Part-time Lecturer

Tatsuo KAWAMOTO, Naoto SUDA, Takafumi SUSAMI,
Tamiko TERASHIMA, Yoshiyuki KATO,
Yasuo ISHIWATA, Yoshiyuki BABA,
Toshimoto TENGAN, Masahiko YOKOZEKI,
Shigetoshi HIYAMA, Shigeki TAKAHASHI,
Maristela Sayuri ARAI, Hiroki FUKUOKA,
Junichi TAKADA, Rina HIKITA, Yosuke ITO,
Lisa R.Amir

(1) Research

- 1) Basic and clinical studies of cleft lip and/or palate and other congenital craniofacial conditions
- 2) Morphological and physiological studies of facial deformity
- 3) Physiological study about control mechanism of stomatognathic function
- 4) Functional MRI study in the craniofacial region
- 5) Clarify the factors of malocclusion with epidemiological technique

(2) Education

The goal of the program of Maxillofacial Orthognathics is to provide information related to craniofacial growth and development, and stomatognathic function in order to develop basic knowledge and skills for the treatment of the patients with a wide variety of malocclusion. It also provides valuable information of diagnosis and treatment planning for orthodontic and orthognathic therapies of the patients with jaw deformities and congenital craniofacial anomalies.

Comprehensive care by a team of specialists including maxillofacial surgeons, orthodontists, speech therapists etc. is needed for the treatment of the patients with cleft lip and palate and other craniofacial anomalies. The Graduate Program provides the clinical education of orthodontics as a part of the multi-disciplinary approach for such patients.

(3) Clinical Performances

In the Clinic, we treat a large number of patients presenting a variety of malocclusions to be assigned to group practice in order to gain valuable experience in diagnosis, treatment planning, orthodontic therapy, and patient management. Especially for patients born with cleft lip and/or palate and who need craniofacial and orthognathic surgery, we have clinical meetings and conferences for the comprehensive care through a team approach with maxillofacial surgeons, maxillofacial prosthodontists and speech therapists. We also provide supportive counseling to families who have members with congenital anomalies before the treatment.

(4) Publications

[Original Articles]

1. Lin W, Izu Y, Smriti A, Kawasaki M, Pawaputanon C, Böttcher RT, Costell M, Moriyama K, Noda M, Ezura Y. Profilin1 is expressed in osteocytes and regulates cell shape and migration. *Journal of Cellular Physiology*. 2018.01; 233(1); 259-268
2. Ikeda A, Miyamoto JJ, Usui N, Taira M, Moriyama K. Chewing Stimulation Reduces Appetite Ratings and Attentional Bias toward Visual Food Stimuli in Healthy-Weight Individuals *Frontiers in Psychology*. 2018.02; 9; Article99
3. Takada J, Miyamoto JJ, Sato C, Dei A, Moriyama K. Comparison of EMG activity and blood flow during graded exertion in the orbicularis oris muscle of adult subjects with and without lip incompetence: a cross-sectional survey. *European Journal of Orthodontics*. 2018.05; 40(3); 304-311
4. Ding X, Suzuki S, Shiga M, Ohbayashi N, Kurabayashi T, Moriyama K. Evaluation of tongue volume and oral cavity capacity using cone-beam computed tomography. *Odontology*. 2018.07; 106(3); 266-273
5. Nakazawa Y, Suzuki S, Go Inoue G, Nikaido T, Tagami J, Moriyama K. Influence of orthodontic self-etch adhesive on acid resistance of surface enamel. *Dental Materials Journal*. 2018.07; 37(4); 568-574
6. Higashihori N, Takada J, Katayanagi M, Takahashi Y, Moriyama K. Frequency of missing teeth and reduction of mesiodistal tooth width in Japanese patients with tooth agenesis *Progress in Orthodontics*. 2018.08; 19(1); 30
7. Yoshida M, Honda E, Ozawa E, Inoue-Arai SM, Ohmori H, Moriyama K, Ono T, Kurabayashi T, Yoshihara H, Nunthayanon Parakonthun K. Principles of the magnetic resonance imaging movie method for articulatory movement. *Oral Radiology*. 2018.09;
8. Takahashi Y, Higashihori N, Yasuda Y, Takada J, Moriyama K. Examination of craniofacial morphology in Japanese patients with congenitally missing teeth: a cross-sectional study *Progress in Orthodontics*. 2018.10; 19(1); 38

9. Matsuno S, Tsuji M, Hikita R, Matsumoto T, Baba Y, Moriyama K. Clinical study of dentocraniofacial characteristics in patients with Williams syndrome. *Congenit Anom (Kyoto)*. 2018.10;
10. Katsuyama N, Kikuchi-Tachi E, Usui N, Yoshizawa H, Saito A, Taira M. Effect of Visual Information on Active Touch During Mirror Visual Feedback. *Frontiers in Human Neuroscience*. 2018.10; 12; article424
11. Ekprachayakoon I, Miyamoto JJ, Inoue-Arai MS, Honda EI, Takada JJ, Kurabayashi T, Moriyama K. New application of dynamic magnetic resonance imaging for the assessment of deglutitive tongue movement. *Progress in Orthodontics*. 2018.11; 19(1); 45
12. Yamaji K, Morita J, Watanabe T, Gunjigake K, Nakatomi M, Shiga M, Ono K, Moriyama K, Kawamoto T. Maldevelopment of the submandibular gland in a mouse model of apert syndrome. *Developmental Dynamics*. 2018.11; 247(11); 1175-1185
13. Myat AB, Ogawa T, Kadota-Watanabe C, Moriyama K. Nuclear import of transcriptional corepressor BCOR occurs through interaction with karyopherin α expressed in human periodontal ligament. *Biochemical and Biophysical Research Communications*. 2018.12; 507(1-4); 67-73

[Conference Activities & Talks]

1. Ogasawara T, Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama K. Shape optimization of subperiosteal devices using finite element analysis. The 11th Asian Pacific Orthodontic Conference(APOC 2018) Residents' Forum 2018.03.04 Boracay, Phillipines
2. Koda N, Ogawa T, Moriyama K. A case of Angle Class II malocclusion with dental crowding in a growing patient. The 11th Asian Pacific Orthodontic Conference(APOC 2018) Residents' Forum 2018.03.04 Boracay, Phillipines
3. Higashihori N, Moriyama K. Long-term management of occlusion after surgical-orthodontic treatment for jaw deformity patient with schizophrenia: a case report. The 11th Asian Pacific Orthodontic Conference(APOC 2018) 2018.03.05 Boracay, Phillipines
4. Yasuda Y, Fujiwara T, Ogawa T, Araki M, Sato M, Yamagata Z, Moriyama K. Association between malocclusion and temporomandibular disorders in 12–15-year-old Japanese adolescents : A population-based study. The 11th Asian Pacific Orthodontic Conference(APOC 2018) 2018.03.05 Boracay, Phillipines
5. Hikita R, Higashihori N, Kadota C, Akiyama S, Takahashi Y, Ito Y, Moriyama K. Effects of tongue-jaw bone relationship on respiratory function during sleep after orthognathic surgery in patients with mandibular prognathism: Comparison between one-jaw and two-jaw surgery. The 11th Asian Pacific Orthodontic Conference(APOC 2018) 2018.03.05 Boracay, Phillipines
6. Ogura K, Kobayashi Y, Hikita R, Shoji A, Tsuji M, Moriyama K. Analysis of palatal morphology of craniosynostosis patients: Comparison between Apert syndrome and Crouzon syndrome . The 11th Asian Pacific Orthodontic Conference(APOC 2018) 2018.03.05 Boracay, Phillipines
7. Ogawa T, Wu YY, Moriyama K. Long-term management of a patient with arthrogryposis multiplex congenita with cleft palate. The 42nd Annual Meeting of Japanese Cleft Palate Association 2018.05.24 Osaka
8. Baba Y, Ogawa T, Uezono M, Mibu M, Sumita Y, Mishimagi T, Sato Y, Morita K, Moriyama K. Changes of pharyngeal morphology and speech function after maxillary distraction in two cases of CLP. The 42nd Annual Meeting of Japanese Cleft Palate Association 2018.05.24 Osaka
9. Funahashi K, Ogawa T, Muramoto K, Moriyama K. Metatranscriptomic analysis of the oral microbiota in cleft lip and palate patients. The 42nd Annual Meeting of Japanese Cleft Palate Association 2018.05.24 Osaka
10. Moriyama K. Long-term changes after maxillary distraction osteogenesis in patient with cleft lip and/or palate. Korean Cleft Lip and Palate Association Meeting 2018.06.09 Seoul, Korea
11. Takada J, Miyamoto JJ, Sato C, Dei A, Moriyama K. Electromyographic Activity And Blood Flow During Graded Exertion In The Orbicularis Oris Muscle Of Adult Subjects With And Without Lip Incompetence. 94th European Orthodontic Society Congress 2018.06.17 Edinburgh, Scotland

12. Kikuchi M, Uchikoshi T, Iwanami-Kadowaki K, Uezono M, Moriyama K, Sato T, Aizawa M, Shirosaki Y, Oshima S, Honda M, Ozeki K. Hydroxyapatite/Collagen Bone-Like Nanocomposite: Novel Applications. Finland-Japan Workshop: The next generation medical engineering in biomaterials 2018.06.17 Oulu, Finland
13. Moriyama K. Plan-Do-Check-Act (PDCA) of the Joint Degree Program between Tokyo Medical and Dental University in Japan and Chulalongkorn University in Thailand. The international dental education & research conference 2018.06.22 Seoul, Korea
14. Kamimoto H, Kobayashi Y, Moriyama K. Relaxin Accelerates Rat Mid-palatal Suture Expansion and Subsequent Bone Formation. 96th General Session & Exhibition of International Association for Dental Research 2018.07.25 London, England
15. Shoji-Matsunaga A, Ono T, Nakashima T, Moriyama K. Osteocyte-derived RANKL is a Key Regulator of Orthodontic Tooth Movement. 96th General Session & Exhibition of International Association for Dental Research 2018.07.25 London, England
16. Moriyama K. Dental Equilibrium Revisited - Soft Tissue Considerations in Treatment of Dentofacial Deformity. The 6th Annual Meeting of Mongolian Association of Orthodontists 2018.09.01 Ulaanbaatar, Mongolia
17. Moriyama K. Keys to Conducting Cutting-edge Research. The 3rd International Conference on Global Health (ICGH) 2018.09.14 Bali, Indonesia
18. Moriyama K. Dental Education and Clinical Practice in our Super Aging Society. The 3rd International Conference on Global Health (ICGH) 2018.09.15
19. Moriyama K. Long-term interdisciplinary care for patients with craniofacial anomalies. 2018 International Orthodontic Conference and the 17th Annual Meeting of Chinese Orthodontic Society 2018.09.18 Changchun, China
20. Kamimoto H, Kobayashi Y, Moriyama K. Relaxin Accelerates Rat Midpalatal Suture Expansion and Subsequent Bone Formation. ASBMR 2018 Annual Meeting 2018.09.28 Montreal, Canada
21. Shoji A, Tsuji M, Kinoshita Y, Ogura K, Kobayashi Y, Suzuki S, Moriyama K. Myofunctional therapy in orthodontic patients with congenital anomalies with orofacial myofunctional disorders. The 63th Annual Meeting of the Japan Society of Human Genetics 2018.10.10 Kanagawa
22. Hirabayashi K, Uehara D T, Abe H, Atsushi Ishii A, Moriyama K, Hirose S, Inazawa J. Copy number variations in children with early-onset epileptic encephalopathy. The 63th Annual Meeting of the Japan Society of Human Genetics 2018.10.10 Kanagawa
23. Iwanami-Kadowaki K, Uchikoshi T, Uezono M, Kikuchi M, Moriyama K. Novel EPD Coating of Hap/Col Realizes Strong Adhesion to Substrate Metal. The 30th anniversary edition of the Symposium and Annual Meeting of the International Society for Ceramics in Medicine (Bioceramics 30) 2018.10.26 Nagoya, Aichi
24. Moriyama K. Current status and future perspectives of The Japanese orthodontic Society. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 kanagawa
25. Myat AB, Ogawa T, Kadota-Watanabe C, Moriyama K. Nuclear-cytoplasmic transportation of BCOR through interaction with KPNA5. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
26. Kamimoto H, Kobayashi Y, Moriyama K. Relaxin target-oriented by magnetic controlled liposome accelerates rat midpalatal suture expansion and subsequent bone formation. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
27. Shoji A, Tsuji M, Kinoshita Y, Ogura k, Kobayashi Y, Miura Y, Kasai M, Suzuki S, Moriyama K. Clinical study of myofunctional therapy in orthodontic patients with Down syndrome. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
28. Yoshizawa H, Miyamoto J, Hanakawa T, Honda M, Moriyama K. Cortical function of masticatory motor control system in incisal biting and molar biting. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa

29. Araki M, Yasuda Y, Ogawa T, Kang S, Yamagata Z, Fujiwara T, Moriyama K. Association between malocclusion and oral health-related quality of life in Japanese adolescents. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
30. Koda N, Higashihori N, Matsumura K, Arimura M, Akiyama S, Uezono M, Suzuki S, Moriyama K. Clinicostatistical investigation on patients treated with orthodontic anchor screw at TMDU over the past decade. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
31. Akiyama S, Araki M, Yasuda Y, Higashihori N, Tsuji M, Ogawa T, Moriyama K. A survey of orthodontic patients in our department for latest 10 years. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
32. Teramoto A, Matsumoto T, Kadota-Watanabe C, Higashihori N, Suzuki S, Obayashi N, Kurabayashi T, Moriyama K. Changes of tongue volume and oral cavity capacity after orthodontic surgery in facial deformity patients. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
33. Funahashi K, Watanabe T, Shiba T, Muramoto K, Ogawa T, Moriyama K. Study on bacterial networks on the oral microbiota in cleft lip and palate patients. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
34. Niki Y, Higashihori N, Uezono M, Igarashi N, Inagaki Y, Inoue M, Kaisaka Y, Badrakhkhuu N, Kobayashi Y, Tsuji M, Moriyama K. Maxillofacial morphology of oculo-auriculo-vertebral spectrum patients classified according to severity of temporomandibular dysplasia. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
35. Tominaga C, Matsumoto T, Tsuji M, Moriyama K. Characteristics of craniofacial morphology of cleidocranial dysplasia patients during and after growing stage. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
36. Nakamura R, Kobayashi Y, Kamimoto H, Hikita R, Higashihori N, Takahara N, Kabasawa Y, Moriyama K. A case of mandibular prognathism with constricted maxillary arch treated by SARME and two-jaw surgery. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
37. Ogasawara T, Matsumoto T, Miyazaki T, Baba Y, Ito Y, Kabasawa Y, Moriyama K. A case of surgical orthodontic treatment for skeletal Class II malocclusion with sleep disordered breathing. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
38. Hikita R, Tsuji M, Ogura K, Moriyama K. An orthodontic treatment case of Marfan syndrome with severe crowding and constricted dental arch. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
39. Wu YY, Kadota-Watanabe C, Ogawa T, Moriyama K. Combination of estrogen deficiency and excessive mechanical stress exacerbates TMJ-OA in mice. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.10.30 Kanagawa
40. Moriyama K. Early Treatment of Class II Malocclusion - Lessons Learned from our Clinical Experience. 2018 Taiwan International Orthodontic Forum 2018.12.07 Taipei, Taiwan

[Awards & Honors]

1. The 11th Asian Pacific Orthodontic Conference(APOC 2018) Posterboard Presentation 3rd Place Research(Ogura K, Kobayashi Y, Hikita R, Shoji A, Tsuji M, Moriyama K), The Asian Pacific Orthodontic Society, 2018.03
2. The 11th Asian Pacific Orthodontic Conference(APOC 2018) Posterboard Presentation 2nd Place Research(Hikita R, Higashihori N, Kadota C, Akiyama S, Takahashi Y, Ito Y, Moriyama K), The Asian Pacific Orthodontic Society, 2018.03

Maxillofacial Prosthetics

2018 April

Junior Associate Professor
SUMITA Yuka

Assistant Professor
HATTORI Mariko
OTOMARU Takafumi

Contract Assistant Professor
HARAGUCHI Mihoko
MURASE Mai

Clinical Staff
WATANABE Mao

Graduate Student
KAMIYANAGI Ayuko
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YEERKEN Yesiboli
AWUTI Shater
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LIU Rongguang
TANI Hiroko

Part-time Special Student
GAO Yuan
WANG Yujia

Part-time Lecturer (Faculty of Dentistry)
SATO Iwao
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ELBASHTI Mahmoud Ellarousi
HATANO Noriko
KANAZAKI Ayako

Part-time Lecturer (Graduated School)
OZAWA Shogo
KADOTA Chiaki
INOHARA Ken
KOSAKA Moe

Speech-Language-Hearing Therapist
MIBU Michiko

(1) Outline

Department of Maxillofacial Prosthetic is the special unit of the prosthodontic and/or prosthetic treatment for patients with defects in oral and/or maxillofacial regions. The main objective of this course is to provide students with opportunity to gain sound understanding of the restoration of functional and esthetic disorders of oral and/or maxillofacial areas that are caused by congenital developmental or acquired diseases by means of the high-advanced dental and medical cares.

(2) Research

Our department is the special unit for the prosthodontic treatment for patients with congenital or acquired defects in head and neck regions. The main goal of the research is to establish a novel theory and feedback it to the clinic to improve the quality of life of each patient. In this respect, we are focusing on several projects.

Diagnosis of functional impairment in patients with a maxillofacial defect

Treatments for functional rehabilitation of patients with a maxillofacial defect

Masticatory evaluation in patients with a maxillofacial defect

Speech evaluation in patients with a maxillofacial defect

Development of new materials for facial prosthesis

(3) Publications**[Original Articles]**

1. Kamiyanagi A, Sumita YI, Ino S, Chikai M, Nakane A, Tohara H, Minakuchi S, Seki Y, Endo H, Taniguchi H. Evaluation of swallowing ability using swallowing sounds in maxillectomy patients. *Journal of Oral Rehabilitation*. 2018.02; 45(2); 126-131
2. Sumita YI, Hattori M, Murase M, Elbashti ME, Taniguchi H. Digitised evaluation of speech intelligibility using vowels in maxillectomy patients. *Journal of Oral Rehabilitation*. 2018.03; 45(3); 216-221
3. Yeerken Y, Otomaru T, Said M, Li N, Sumita YI, Taniguchi H. Prosthetic treatment of a unilateral left cleft lip and palate with an oronasal fistula: A case report. *Open Journal of Clinical and Medical Case Reports*. 2018.03; 4(6); 1394
4. Hattori M, Sumita YI, Elbashti ME, Kurtz KS, Taniguchi H.. Effect of experimental palatal prosthesis on voice onset time *Journal of Prosthodontics*. 2018.03; 27(3); 223-226
5. Said M, Otomaru T, Kanazaki A, Fujita H, Taniguchi H. Prosthodontic treatment of a patient with gnathodiaphyseal dysplasia: 30-year follow-up. *International Journal of Prosthodontics*. 2018.04; 31(2); 138-141
6. Li N, Otomaru T, Said M, Yeerken Y, Fujita H, Taniguchi H. Prosthodontic management of a bilateral total maxillary defect patient with chemoradiotherapy - related progressive osteonecrosis. A case report. *Open Journal of Clinical and Medical Case Reports*. 2018.04; 4(8); 1405
7. Kamarudin KH, Hattori M, Sumita YI, Taniguchi H. A chairside technique to add customized anterior acrylic resin teeth to a surgical obturator. *Journal of Prosthetic Dentistry*. 2018.05; 119(5); 852-854
8. Aswehlle A, Hattori M, Elbashti ME, Sumita YI, Taniguchi H. Geometric evaluation of the effect of prosthetic rehabilitation on facial asymmetry in patients with unilateral maxillectomy. *International Journal of Prosthodontics*. 2018.05; 31(3); 228-235
9. Li N, Otomaru T, Said M, Kanazaki A, Yeerken Y, Taniguchi H. Factors associated with sleep quality in maxillectomy patients. *International Journal of Prosthodontics*. 2018.05; 31(3); 223-225
10. Yeerken Y, Otomaru T, Said M, Oki M, Taniguchi H. Non-contact eye surface impression and fabrication of radiotherapy prosthesis for eyelid tumor with CAD/CAM technique. *Materials Today Communications*. 2018.06; 15; 322-324

11. Elbashti ME, Sumita YI, Aswehlee A, Haraguchi M, Otomaru T, Hattori M, Taniguchi H. Preschool and school phases of post-maxillectomy prosthetic rehabilitation in a child: A clinical report. *Journal of Prosthodontics*. 2018.06; 27(5); 482-487
12. Elbashti ME, Aswehlee A, Sumita YI, Hattori M, Taniguchi H. The role of portable documentation format in three-dimensional interactive visualization in maxillofacial prosthetics. *International Journal of Prosthodontics*. 2018.07; 31(4); 399-400
13. Yanagi A, Sumita YI, Hattori M, Kamiyanagi A, Otomaru T, Kanazaki A, Haraguchi M, Murase M, Hatano N, Taniguchi H. Clinical survey over the past 35 years at the Clinic for Maxillofacial Prosthetics Tokyo Medical and Dental University. *Journal of Prosthodontic Research*. 2018.07; 62(3); 309-312
14. Aswehlee AM, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Feasibility and Accuracy of Noncontact Three-Dimensional Digitizers for Geometric Facial Defects: An In Vitro Comparison. *International Journal of Prosthodontics*. 2018.11; 31(6); 601-606
15. Elbashti ME, Sumita YI, Hattori M, Aswehlee A, Taniguchi H. Digitized speech characteristics in patients with maxillectomy defects *Journal of Prosthodontics*. 2018.12; accepted;
16. Awuti S, Sumita YI, Kelimu S, Hattori M, Taniguchi H. One-day refabrication technique for a lip plumper in a patient with cleft lip and palate: A clinical report. *Open Journal of Clinical and Medical Case Reports*. 2018.12; 4(23); 1495

[Conference Activities & Talks]

1. Matunari J, Abe T, Saitou T, Sakuma S, Abe T, Udagawa H, Otomaru T, Satou H. Low invasive technique of Sinus lift using new type reamer. *Japanese Society of Oral Implantology 35th Kyushu Branch Scientific Meeting 2018.01.27 Fukuoka(Japan)*
2. Murase M, Sumita YI, Taniguchi H. A case of left cleft lip and palate patient treated with removable prostheses. *The 42nd Annual Meeting of Japanese Cleft Palate Association 2018.05.24 Osaka (Japan)*
3. Baba Y, Ogawa T, Uezono M, Mibu M, Sumita YI, Mishimagi T, Satou Y, Morita K, Moriyama K. Changes of pharyngeal morphology and speech function after maxillary distraction in two cases of CLP. *The 42nd Annual Meeting of Japanese Cleft Palate Association 2018.05.24 Osaka (Japan)*
4. Haraguchi M, Yoshimura R, Harada H, Shimamoto H, Michi Y, Sumita YI, Taniguchi H. Prosthetic rehabilitations for 2 patients with maxillary defect caused by radiation osteomyelitis. *The 42nd Annual Meeting of Japan Society for Head and Neck Cancer 2018.06.14 Tokyo(Japan)*
5. Otomaru T. Newly emerging issues and solutions for implant treatment in super-aged society. *The 127th annual meeting of the Japan Prosthodontic Society 2018.06.16 Okayama (Japan)*
6. Otomaru T, Yeerken K, Kamiyanagi A, Taniguchi H. Maxillofacial prosthetic treatment for soft palate defect due to the resection of pleomorphic adenoma: A case report. *The 35th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2018.06.29 Tokushima (Japan)*
7. Matsumoto Y, Sakaguchi Y, Haraguchi M, Otomaru T, Sumita YI, Adachi T, Taniguchi H. Oral hygiene management by dental hygienists for a patient with burns, blindness, and bilateral forearm amputation after car accident. *The 35th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2018.06.29 Tokushima (Japan)*
8. Hattori M, Elbashti ME, Kelimu S, Sumita YI, Taniguchi H. Impressions using an intraoral scanner for mandibular defects: An in vitro comparative study. *The 35th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2018.06.29 Tokushima (Japan)*
9. Haraguchi M, Harada H, Mukohyama H, Sumita YI, Michi Y, Kanazaki A, Taniguchi H. Prosthetic rehabilitation for the patients undergone maxillectomy or mandibulectomy due to oral tumor in young age. *The 35th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2018.06.30 Tokushima (Japan)*
10. Awuti S, Elbashti ME, Kelim S, Aswehlee AM, Hattori M, Sumita YI. Digitized evaluation of prosthetic effect on facial appearance and asymmetry of reconstructed segmental mandibulectomy patients. *15th Meeting International Society for Maxillofacial Rehabilitation 2018.07.26 Melbourne (Australia)*

11. Elbashti ME, Sumita Y, Kelimu S, Aswehlee A, Hattori M, Taniguchi H. Application of digital technologies in maxillofacial prosthetic literature: A 10-year observation of prosthodontic journals. 15th Meeting International Society for Maxillofacial Rehabilitation 2018.07.26 Melbourne (Australia)
12. Sumita YI. Speech rehab Forum: Talk to.. Talk with me. 11th Biennial Congress of Asian Academy of Prosthodontics and 8Th Scientific Conference & AGM of Malaysian Association for Prosthodontics 2018.09.20 Kuala Lumpur (Malaysia)
13. Zhang M, Hattori M, Kelimu S, Elbashti ME, Liu R, Sumita YI, Taniguchi H. Observation of the teeth position in cleft lip and palate patients using three-dimensional assessment. 11th Biennial Congress of Asian Academy of Prosthodontics and 8Th Scientific Conference & AGM of Malaysian Association for Prosthodontics 2018.09.21 Kuala Lumpur (Malaysia)
14. Fujita H, Otomaru T, Takahashi H, Iwasaki N., Sumita YI. Effect of Direct Retainer Types of Dent-Maxillary Prosthesis in Maxillectomy Patients: An In Vitro Study. 11th Biennial Congress of Asian Academy of Prosthodontics and 8Th Scientific Conference & AGM of Malaysian Association for Prosthodontics 2018.09.21 Kuala Lumpur (Malaysia)
15. Kamiyanagi A, Sumita YI. Investigation of Swallowing Ability Using the Eating Assessment Tool 10 (EAT-10) in Maxillectomy Patients. 11th Biennial Congress of Asian Academy of Prosthodontics and 8Th Scientific Conference & AGM of Malaysian Association for Prosthodontics 2018.09.21 Kuala Lumpur (Malaysia)
16. Tani H, Hattori H, Sumita YI. The 28 Years Observation of a Maxillectomy Patient: A Case Report. 11th Biennial Congress of Asian Academy of Prosthodontics and 8Th Scientific Conference & AGM of Malaysian Association for Prosthodontics 2018.09.21 Kuala Lumpur (Malaysia)
17. Sumita YI. Current Maxillofacial Prosthetics Treatment and Research in TMDU. 11th Biennial Congress of Asian Academy of Prosthodontics and 8Th Scientific Conference & AGM of Malaysian Association for Prosthodontics 2018.09.21 Kuala Lumpur (Malaysia)

Cell Biology

Professor : Takao Nakata
Junior Associate Professor : Tomohiro Ishii
Assistant Professor : Toshifumi Asano
Assistant Professor : Hironori Inaba
Technical Staff : Satoko Nakamura

(1) Outline

We started a new laboratory from April 2009. We are interested in the cellular responses to spatio-temporal activation of signaling molecules. For this purpose, we took synthetic approaches combined with optogenetics. We introduce the photo switches into cells, and analyze signaling systems quantitatively. Research will be conducted by using molecular biology, molecular genetics, cell biology, theoretical biology, and live-imaging techniques.

(2) Research

We are studying cell signaling using optogenetics. We made photo-switch of various signaling proteins and introduced them into cells. Parts of the cells were stimulated by blue lasers. The photo-switches are activated locally within the cells and we observe the cell phenotypes by time-lapse microscope using these techniques. We can understand molecular mechanisms of cell signaling in spatio-temporal fashion and also can manipulate cellular conditions using these switches.

(3) Education

We teach histology and cell biology to 2nd year medical students. The courses are composed of sets of lecture and laboratory study of tissues and organs. Our goal in undergraduate course is to provide students with fundamental knowledge and skill to analyze microscopic samples of normal human body.

In new curriculum, lecture provide students information on fine structure and hints or laboratory work. This helps the students to sketch the tissue in their laboratory work. The aim of our lecture is to provide fundamental knowledge of human tissues and organ to understand clinical lectures. In laboratory work we adopt classical sketch of tissues because we believe it shows the ability of students to search the representative area and extract essential structure. Evaluation depends on paper test, sketch and laboratory test.

In cell biology course we start a little bit advanced lectures such as cell death and cell cycle because we avoid to teach the same contents that they have learned in the past year biology course. We also provide more stimulative lectures in later half of the course such as autophagy, zebrafish genetics and mathematical model.

(4) Publications

[Original Articles]

1. Hironori Inaba, Daishi Yamakawa, Yasuko Tomono, Atsushi Enomoto, Shinji Mii, Kousuke Kasahara, Hidemasa Goto, Masaki Inagaki. Regulation of keratin 5/14 intermediate filaments by CDK1, Aurora-B, and Rho-kinase. Biochemical and Biophysical Research Communications. 2018.04; 498(3); 544-550

2. Sachiko Akiyoshi, Tomohiro Ishii, Zhaodai Bai, Peter Mombaerts. Subpopulations of vomeronasal sensory neurons with coordinated coexpression of type 2 vomeronasal receptor genes are differentially dependent on Vmn2r1. *The European Journal of Neuroscience*. 2018.04; 47(7); 887-900
3. Toshifumi Asano, Hiroyuki Igarashi, Toru Ishizuka, Hiromu Yawo. Organelle Optogenetics: Direct Manipulation of Intracellular Ca^{2+} Dynamics by Light *Frontiers in Neuroscience*. 2018.08; 12; 561
4. Moe Sato, Toshifumi Asano, Jun Hosomichi, Takashi Ono, Takao Nakata. Optogenetic manipulation of intracellular calcium by BACCS promotes differentiation of MC3T3-E1 cells *Biochemical and Biophysical Research Communications*. 2018.10; 506(3); 716-722

[Books etc]

1. Hidemasa Goto, Hironori Inaba, Masaki Inagaki. *Encyclopedia of Signaling Molecule* 2nd edition. Springer, 2018.01 (ISBN : 978-3-319-67199-4)

[Misc]

1. Tomohiro Ishii. Development and application of Ca^{2+} optogenetic tool *Brain Science Review* 2018. 2018.03; 31-50

[Conference Activities & Talks]

1. Yuka Aoki, Toshifumi Asano, Nakata Takao. Study of activity-dependent formation of neuromuscular junction. The 123rd Annual Meeting of the Japanese Association of Anatomists 2018.03.28 Nippon Medical School
2. Takao Nakata. Optogenetics of Signaling Proteins in Neurons. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.27 Kobe Convention Center
3. Sato M, Asano T, Hosomichi J, Ishida Y, Usumi-Fujita R, Shimizu Y, Kaneko S, Nataka T, Ono T. Elucidation of the molecular mechanism of osteoblast differentiation and its control using optogenetics. The 77th Annual Meeting of the Japanese Orthodontic Society 2018.11.01 Yokomaha, Japan

Medical Biochemistry

Professor Yutaka Hata

Assistant Professor Hiroaki Iwasa

Assistant Professor Kyoko Arimoto-Matsuzaki

Assistant Professor Junichi Maruyama

Other two staffs

(1) Research

- 1) The biological and chemical approach to study the Hippo pathway that controls cell proliferation, cell differentiation, and cell death.
- 2) Versatile roles of the tumor suppressor RASSF proteins
- 3) Discovery and development of chemical compounds that suppress cancer stemness and metastasis
- 4) Discovery and development of chemical compounds that facilitate myogenesis and prevent muscle atrophy
- 5) Development of mouse models mimicking human progeria syndromes
- 6) Study of health life span in *Caenorhabditis elegans*

(2) Education

1 : Undergraduate course

We organized the course of Biochemistry for the undergraduate students.

2 : Master course

We organized the course of Biochemistry for the master students.

3 : Others

We gave a lecture about metabolism of cancer cells.

We gave a lecture entitled "How is the life of human maintained?" for the students of Tokyo University of Foreign Studies.

(3) Lectures & Courses

1) Undergraduate

We organize the course, "Medical Biochemistry". The students are requested through these courses to obtain a comprehensive integrated knowledge of human biochemistry, which is important to understand how health is maintained and which molecular and biochemical events cause human diseases and underlie the rational treatments.

2) Graduate and others

We are studying the signaling pathway that regulates cell proliferation, cell differentiation, cell polarity, and cell death. This pathway is well conserved from fly to human. The mutations of the components lead to oncogenesis and organ malformation. Several recent studies suggest that this pathway is implicated in inflammation and cell differentiation such as adipogenesis, osteogenesis, and keratinocyte differentiation. The pathway plays an important role in various human diseases and could be a new therapeutic target. We give lectures about

our current studies to graduate students and others, and provide graduate students with the opportunity to participate in them.

(4) Publications

[Original Articles]

1. Matsuzaki Kyoko, Hata Yutaka. Chemical compounds that suppress stress granule formation enhance the cancer drug sensitivity of HeLa cells. *CANCER SCIENCE*. 2018.01; 109; 1001
2. Junichi Maruyama, Kazutoshi Inami, Fumiyoshi Michishita, Xinliang Jiang, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Norio Miyamura, Jun Hirayama, Hiroshi Nishina, Daichi Nogawa, Kouhei Yamamoto, Yutaka Hata. Novel YAP1 Activator, Identified by Transcription-Based Functional Screen, Limits Multiple Myeloma Growth. *Mol. Cancer Res.*. 2018.02; 16(2); 197-211
3. Hara Hironori, Takeda Norifumi, Saito Tatsuo, Fujiwara Takayuki, Maemura Sonoko, Hata Yutaka, Uchiyama Masanobu, Komuro Issei. Discovery of a Small Molecule to Increase Cardiomyocytes and Protect the Heart after Ischemic Injury(和訳中) 日本循環器学会学術集会抄録集. 2018.03; 82 回; YIA-B
4. Hossain S, Iwasa H, Sarkar A, Maruyama J, Arimoto-Matsuzaki K, Hata Y. The RASSF6 tumor suppressor protein regulates apoptosis and the cell cycle < i> via< /i> Retinoblastoma protein. *Molecular and cellular biology*. 2018.06;
5. Iwasa H, Sarkar A, Shimizu T, Sawada T, Hossain S, Xu X, Maruyama J, Arimoto-Matsuzaki K, Withanage K, Nakagawa K, Kurihara H, Kuroyanagi H, Hata Y. UNC119 is a binding partner of tumor suppressor Ras-association domain family 6 and induces apoptosis and cell cycle arrest by MDM2 and p53. *Cancer science*. 2018.06;
6. Li Qiaojing, Yoshimura Hideaki, Komiya Maki, Tajiri Ken, Uesugi Motonari, Hata Yutaka, Ozawa Takeaki. A robust split-luciferase-based cell fusion screening for discovering myogenesis-promoting molecules ANALYST. 2018.07; 143(14); 3472-3480
7. Shikshya Timalisina, Kyoko Arimoto-Matsuzaki, Masami Kitamura, Xiaoyin Xu, Qiu Wenzhe, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Yutaka Hata. Chemical compounds that suppress hypoxia-induced stress granule formation enhance cancer drug sensitivity of human cervical cancer HeLa cells. *J. Biochem.*. 2018.07;
8. Hara H, Takeda N, Kondo M, Kubota M, Saito T, Maruyama J, Fujiwara T, Maemura S, Ito M, Naito AT, Harada M, Toko H, Nomura S, Kumagai H, Ikeda Y, Ueno H, Takimoto E, Akazawa H, Morita H, Aburatani H, Hata Y, Uchiyama M, Komuro I. Discovery of a Small Molecule to Increase Cardiomyocytes and Protect the Heart After Ischemic Injury. *JACC. Basic to translational science*. 2018.10; 3(5); 639-653
9. Hata Yutaka. Hippo Pathway in Cancer, towards the Realization of Hippo-Targeted Therapy *CANCERS*. 2018.10; 10(10);
10. Timalisina Shikshya, Arimoto-Matsuzaki Kyoko, Kitamura Masami, Xu Xiaoyin, Wenzhe Qiu, Ishigami-Yuasa Mari, Kagechika Hiroyuki, Hata Yutaka. Chemical compounds that suppress hypoxia-induced stress granule formation enhance cancer drug sensitivity of human cervical cancer HeLa cells(和訳中) *The Journal of Biochemistry*. 2018.11; 164(5); 381-391
11. Lu Y, Maruyama J, Kuwata K, Fukuda H, Iwasa H, Arimoto-Matsuzaki K, Sugimura H, Hata Y. Doublecortin-like kinase 1 compromises DNA repair and induces chromosomal instability. *Biochemistry and biophysics reports*. 2018.12; 16; 130-137

[Books etc]

1. Iwasa H, Shimizu T, Hata Y.. *Encyclopedia of Signaling Molecules RASSF6*. Springer, (ISBN : 978-1-4419-0460-7)
2. Xu X, Kodaka M, Iwasa H, Hata Y. *Encyclopedia of Signaling Molecules MAGI2/S-SCAM*. Springer,
3. Kodaka M, Xu X, Yang X, Maruyama J, Hata Y. *SPringer Protocol Application of split-GFP reassembly assay to the study of the in vitro myogenesis and myofusion..* Springer,

[Misc]

1. Hiroaki Iwasa, Shakhawoat Hossain, Yutaka Hata. Tumor suppressor C-RASSF proteins. Cell. Mol. Life Sci.. 2018.01;
2. Yutaka Hata, Takeru Sawada. Hippo tumor suppressor pathway Journal of Molecular Targeted Therapy for Cancer. 14(4); 10-16

Joint Surgery and Sports Medicine

Hideyuki Koga
Hiroki Katagiri, Kazumasa Miyatake

Department of Cartilage Regeneration
Kunikazu Tsuji
Yusuke Nakagawa

Kei Inomata, Hiroko Ueki, Mai Katakura, Takashi Hoshino
Masaki Amemiya, Naoko Araya, Hiroaki Onuma, JaeSung An,
Kazumasa Kawata, Masaaki Isono, Aritoshi Yoshihara, Tang Guo,
Zhu Ling

Miyoko Ojima
Miho Okada, Masayo Tsukamoto

(1) Research

1. Development and establishment of isolation and expansion of mesenchymal stem cells
2. Research of biological characteristics of mesenchymal stem cells
3. Development and improvement of treatment method of articular cartilage defect with mesenchymal stem cells
4. Development of treatment strategy to joint structure injuries with mesenchymal stem cells
5. Development of artificial cartilage and bone
6. Development of novel agents related to bone and cartilage metabolism
7. Genetical approach to bone and cartilage metabolism
8. Clarifying mechanism and control of post-injury and postoperative inflammation with tissue fibrosis
9. Clarifying mechanism of joint pain with novel treatment strategy
10. Genetic approach to secondary hip osteoarthritis
11. Novel treatment strategy for cufftear

(2) Lectures & Courses

We are working with the Orthopaedic and Spinal Surgery as a Department of Orthopaedic Surgery of University Hospital. The doctors start to have education of orthopedic surgery as a member of the department from the staffs of the department of Orthopaedic Surgery according to the orthopaedic education and training program after completing the two-year fundamental education and training program as a junior resident. They experience a lot of traumatic patients and deepen their basic orthopaedic skills for two-year junior orthopaedic training in one of the branch hospitals every year. They expand their skills and obtain orthopaedic specialty educations in the advanced two-year education and training program. After completing a six-year educational program of the orthopaedic surgery, they are recommended to apply to the orthopedic specialist form the Japanese Orthopaedic Association. They usually apply to enter the graduate school program after 4 or 5 years of clinical experience. We encourage not only orthopedic doctors but doctors of other specialty, veterinarian doctors and physical therapists, etc to work with us.

(3) Clinical Services & Other Works

Treatment for sports injuries

Prevention, conservative treatment and rehabilitation for sports injuries

Anatomic double-bundle anterior cruciate ligament (ACL) reconstruction for ACL injuries

Surgical treatment for knee multiple ligament injuries

Surgical treatment for meniscal injuries to restore meniscal function

Regenerative medicine for unrepairable meniscus and cartilage injuries

Treatment for osteoarthritis (OA)

Conservative approaches to early OA

Joint-sparing surgeries such as osteotomies for moderate OA

Total arthroplasties for severe OA

Clinical researches and clinical results for above-mentioned approaches have been presented at both domestic and international congresses, as well as reported in Japanese and English articles.

(4) Clinical Performances

Sports injuries

We have been performing double-bundle ACL reconstruction since 1994 as a pioneer, and reported good clinical outcomes regarding knee stability, ratio of return to sports and patients' satisfaction. As for meniscal surgeries, we have been trying to repair as much as possible to restore meniscal function. In addition, we have developed a novel surgical procedure to restore meniscal function for patients with post-meniscectomy and discoid meniscus. We have also analyzed mechanisms and preventive methods for ACL injuries, and first in the world clarified a detailed ACL injury mechanism. Based on the findings, various approaches to ACL injury prevention and rehabilitation after ACL reconstruction is being conducted.

Arthroplasties

We have developed a new total knee system called Actiyas, named after the combination of active and healed ("iyas" in Japanese), which is specifically designed for Japanese. In order to develop this, we analyzed Japanese bone morphology, and this system is designed for more functional and "active" motion without knee pain, and eventually patients to be "healed". Ceramic is used for the femoral implant, by which we can expect lesser implant wear, resulting in better long-term results. We perform simultaneous bilateral arthroplasties for Bilateral OA patients, helping them earlier return to daily life.

Regenerative medicine for cartilage and meniscus injuries using synovial stem cells

Based on numerous basic researches performed in our laboratory, we started stem cell therapy for cartilage injuries using synovial stem cells since April 2008. In this therapy, we take synovium from patients at day surgery, culture synovial stem cells at the cell processing center in our university, and transplant them arthroscopically. The safety and effectiveness had been already confirmed. In addition, we also started a clinical trial of synovial stem cell transplantation for unrepairable meniscal tear since August 2014.

(5) Publications

[Original Articles]

1. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep.* 2018.01; 8(1); 1288
2. Hideyuki Koga, Atsuo Nakamae, Yosuke Shima, Roald Bahr, Tron Krosshaug. Hip and Ankle Kinematics in Noncontact Anterior Cruciate Ligament Injury Situations: Video Analysis Using Model-Based Image Matching. *Am J Sports Med.* 2018.02; 46(2); 333-340

3. L F Mendes, Hiroki Katagiri, W L Tam, Y C Chai, L Geris, S J Roberts, F P Luyten. Advancing osteochondral tissue engineering: bone morphogenetic protein, transforming growth factor, and fibroblast growth factor signaling drive ordered differentiation of periosteal cells resulting in stable cartilage and bone formation in vivo. *Stem Cell Res Ther.* 2018.02; 9(1); 42
4. Guangwen Jin, Alkebaier Aobulikasimu, Jinying Piao, Zulipiya Aibibula, Daisuke Koga, Shingo Sato, Hiroki Ochi, Kunikazu Tsuji, Tetsuo Nakabayashi, Toshio Miyata, Atsushi Okawa, Yoshinori Aso. A small-molecule PAI-1 inhibitor prevents bone loss by stimulating bone formation in a murine estrogen deficiency-induced osteoporosis model *FEBS Open Bio.* 2018.02; 8(4); 523-532
5. Yuji Kohno, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Koji Otabe, Hideyuki Koga, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Ichiro Sekiya. Comparison of mesenchymal stem cells obtained by suspended culture of synovium from patients with rheumatoid arthritis and osteoarthritis. *BMC Musculoskelet Disord.* 2018.03; 19(1); 78
6. Ken Watanabe, Koji Otabe, Norio Shimizu, Keiichirou Komori, Mitsuru Mizuno, Hisako Katano, Hideyuki Koga, Ichiro Sekiya. High-sensitivity virus and mycoplasma screening test reveals high prevalence of parvovirus B19 infection in human synovial tissues and bone marrow. *Stem Cell Res Ther.* 2018.03; 9(1); 80
7. Kanehiro Hiyama, Yusuke Nakagawa, Toshiyuki Ohara, Takeshi Muneta, Toshifumi Watanabe, Masafumi Horie, Koji Otabe, Hiroki Katagiri, Kenta Katagiri, Mai Katakura, Takashi Hoshino, Hiroko Ueki, Kei Inomata, Naoko Araya, Ichiro Sekiya, Hideyuki Koga. Anterior cruciate ligament injuries result in a larger functional deficit in fighting sport athletes: comparison of functional status among different sport types. *Journal of ISAKOS.* 2018.03; (3); 128-133
8. Takao Minami, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Takeshi Muneta. Posteriorly inserted anterior cruciate ligament in knees with discoid lateral meniscus corresponding to bony morphological characteristics of femoral lateral condyle. *J Orthop Sci.* 2018.03; 23(2); 350-355
9. Sasaki S., Koga H., Krosshaug T., Kaneko S., Fukubayashi T.. Kinematic analysis of pressing situations in female collegiate football games: New insight into anterior cruciate ligament injury causation *SCANDINAVIAN JOURNAL OF MEDICINE & SCIENCE IN SPORTS.* 2018.03; 28(3); 1263-1271
10. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Shizuka Fujii, Koji Otabe, Keiichiro Komori, Nobutake Ozeki, Hideyuki Koga, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Specific markers and properties of synovial mesenchymal stem cells in the surface, stromal, and perivascular regions. *Stem Cell Research & Therapy.* 2018.05; 9(1); 123
11. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Nobutake Ozeki, Koji Otabe, Keiichiro Komori, Shizuka Fujii, Shizuko Ichinose, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Petaloid recombinant peptide enhances in vitro cartilage formation by synovial mesenchymal stem cells. *Journal of Orthopaedic Research.* 2018.05;
12. Takada R, Jinno T, Miyatake K, Yamauchi Y, Koga D, Yagishita K, Okawa A. Longitudinal morphological change of acetabular subchondral bone cyst after total hip arthroplasty in developmental dysplasia of the hip *Eur J Orthop Surg traumatol.* 2018.05; 28(4); 621-625
13. Hisayo Nasu, Akimoto Nimura, Sara Sugiura, Hitomi Fujishiro, Hideyuki Koga, Keiichi Akita. An anatomic study on the attachment of the joint capsule to the tibia in the lateral side of the knee. *Surg Radiol Anat.* 2018.05; 40(5); 499-506
14. Mari Uomizu, Takeshi Muneta, Miyoko Ojima, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. PDGF-induced proliferation and differentiation of synovial mesenchymal stem cells is mediated by the PI3K-PKB/Akt pathway. *J Med Dent Sci.* 2018.06; 65(2); 73-82
15. Mindae Kim, Watanabe Toshifumi, Muneta Takeshi, Ohara Toshiyuki, Sekiya Ichiro, Koga Hideyuki. Coronal Instability after Total Knee Arthroplasty using Bi-Surface type 3: An Averaged 10 Year Follow-up Study *Journal of Medical and Dental Sciences .* 2018.06; 65(2); 51-58
16. Kaori Nakamura, Kunikazu Tsuji, Mitsuru Mizuno, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Initial cell plating density affects properties of human primary synovial mesenchymal stem cells. *J. Orthop. Res..* 2018.07;

17. Hisako Katano, Hideyuki Koga, Nobutake Ozeki, Koji Otabe, Mitsuru Mizuno, Makoto Tomita, Takeshi Muneta, Ichiro Sekiya. Trends in isolated meniscus repair and meniscectomy in Japan, 2011-2016 PLoS ONE. 2018.07; 23(4); 676-681
18. Takashi Hoshino, Kunikazu Tsuji, Hiroaki Onuma, Mio Udo, Hiroko Ueki, Masako Akiyama, Kahaer Abula, Hiroki Katagiri, Kazumasa Miyatake, Toshihumi Watanabe, Ichiro Sekiya, Hideyuki Koga, Takeshi Muneta. Persistent synovial inflammation plays important roles in persistent pain development in the rat knee before cartilage degradation reaches the subchondral bone. BMC Musculoskelet Disord. 2018.08; 19(1); 291
19. Akari Sasaki, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Manabu Mochizuki, Ichiro Sekiya. Canine mesenchymal stem cells from synovium have a higher chondrogenic potential than those from infrapatellar fat pad, adipose tissue, and bone marrow. PLoS ONE. 2018.08; 13(8); e0202922
20. Takada Ryohei, Jinno Tetsuya, Miyatake Kazumasa, Hirao Masanobu, Kimura Akimasa, Koga Daisuke, Yagishita Kazuyoshi, Okawa Atsushi. Direct anterior versus anterolateral approach in one-stage supine total hip arthroplasty. Focused on nerve injury: A prospective, randomized, controlled trial J Orthop Sci. 2018.09; 23(5); 783-787
21. Dean Wang, Hongbo Tan, Amir H Lebaschi, Yusuke Nakagawa, Susumu Wada, Patrick E Donnelly, Liang Ying, Xiang-Hua Deng, Scott A Rodeo. Kartogenin Enhances Collagen Organization and Mechanical Strength of the Repaired Enthesis in a Murine Model of Rotator Cuff Repair. Arthroscopy. 2018.09; 34(9); 2579-2587
22. Guang-Ting Cong, Amir H Lebaschi, Christopher L Camp, Camila B Carballo, Yusuke Nakagawa, Susumu Wada, Xiang-Hua Deng, Scott A Rodeo. Evaluating the role of subacromial impingement in rotator cuff tendinopathy: Development and analysis of a novel murine model. J. Orthop. Res.. 2018.10; 36(10); 2780-2788
23. Shoichi Hasegawa, Masafumi Horie, Hiroki Katagiri, Kunikazu Tsuji, Takeshi Muneta, Hideyuki Koga. Bilateral Hypoplasia of Both Medial and Lateral Menisci Partially Fused With the Cartilage Surface of the Tibial Plateau Orthopedics. 2018.11; 41(6); e884-e887
24. Hiroaki Onuma, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Shigenori Kawabata, Atsushi Okawa. Clinical and radiologic outcomes of bone grafted and non-bone grafted double-door laminoplasty, the modified Kirita-Miyazaki method, for treatment of cervical spondylotic myelopathy: Five-year follow-up. J Orthop Sci. 2018.11; 23(6); 923-928
25. Hiroko Ueki, Yusuke Nakagawa, Toshiyuki Ohara, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Kenta Katagiri, Kanehiro Hiyama, Mai Katakura, Takashi Hoshino, Kei Inomata, Naoko Araya, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Risk factors for residual pivot shift after anterior cruciate ligament reconstruction: data from the MAKS group Knee Surgery, Sports Traumatology, Arthroscopy . 2018.12; 26(12); 3724-3730

[Misc]

1. Hideyuki Koga, Stefano Zaffagnini, Alan M Getgood, Takeshi Muneta. ACL graft selection: state of the art. Journal of ISAKOS. 2018.01; (3); 177-184

[Conference Activities & Talks]

1. Hideyuki Koga. ACL Injury Mechanisms / Restoration of Meniscus Function. Hospital for Special Surgery Orthopaedic Soft Tissue Research Meeting 2018.01.10 New York, USA
2. Hideyuki Koga. In order to restore knee function - ACL and meniscus -. University of Pittsburgh Sports Meeting 2018.01.11 Pittsburgh, USA
3. Hideyuki Koga. In order to restore knee function - ACL and meniscus -. Taos Orthopaedic Institute Meeting 2018.01.14 Taos, USA
4. Hideyuki Koga, Mai Katakura, Stefano Zaffagnini, Takeshi Muneta. Contribution of Meniscus Repair to Pivot Shift during ACL Reconstruction: Objective Evaluation Using Triaxial Accelerometer . ACL Study Group Meeting 2018.01.28 Queenstown, New Zealand

5. Mai Katakura, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Kenta Katagiri, Hiroko Ueki, Takeshi Muneta. Effect of ACL Reconstruction and Meniscus Repair on Anterolateral Rotational Instability of the ACL Injured Knee: Quantitative Assessment of the Pivot Shift Phenomenon Using Triaxial Accelerometer. Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
6. Toshifumi Watanabe, Akino Aoki, Kenji Hoshi, Kazuyoshi Gamada, Takeshi Muneta, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kenta Katagiri, Ichiro Sekiya, Hideyuki Koga. Evaluation of Anterior Tibial Post Impingement in Posterior-Stabilized Total Knee Prosthesis during Stair Climbing. Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
7. Masaki Amemiya, Kunikazu Tsuji, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Evaluation of articular cartilage repair ability using synovial fluid derived mesenchymal stem cells. Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
8. Etsuko Matsumura, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. IL1b enhances proliferation of synovial mesenchymal stem cells independent from its cell surface receptor, CD121a. Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
9. Takashi Hoshino, Kunikazu Tsuji, Hiroaki Onuma, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Evaluation Of Pain Behavioral And Joint Change Of Rat Arthritis Model Induced By Low And High Dose Monoiodoacetic Acid. Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
10. Kei Inomata, Kunikazu Tsuji, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Inflammatory cell dynamics and pain behavior during acute inflammation in rat knee joint. Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
11. Hiroko Ueki, Hiroki Katagiri, Kunikazu Tsuji, Kazumasa Miyatake, Takashi Hoshino, Hiroaki Onuma, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga, Takeshi Muneta. Intra-articular Injection of Synovial Mesenchymal Stem Cells in the Anterior Cruciate Ligament Transection Model in Rats :Evaluation of Cell-number Difference on Prevention of Cartilage Damage and Lower Limb Pain . Orthopaedic Research Society 2018 Annual Meeting 2018.03.10 New Orleans, USA
12. Hiroaki Onuma, Kunikazu Tsuji, Takashi Hoshino, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Leg pain behavior correlates fibrosis and angiogenesis of the infrapatellar fat pad induced by monoiodoacetic acid. OARSI 2018 World Congress on Osteoarthritis 2018.04.26 Liverpool, United Kingdom
13. Miyoko Ojima, Kanehiro Hiyama, Kazumasa Miyatake, Hiroki Katagiri, Takeshi Muneta, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. Acute inflammatory response is prerequisite to initiate proper healing process during meniscal regeneration in mice. OARSI 2018 World Congress on Osteoarthritis 2018.04.26 Liverpool, UK
14. Masaki Amemiya, Kunikazu Tsuji, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Characteristics and usefulness of synovial fluid-derived stem cells compared with synovium-derived stem cells. OARSI 2018 World Congress on Osteoarthritis 2018.04.26 Liverpool, United Kingdom
15. Takashi Hoshino, Kunikazu Tsuji, Hiroaki Onuma, Hiroki Katagiri, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Chronic synovial Inflammation Play Important Roles To Establish Residual Pain In Monoiodoacetic Acid Induced Arthritis Rat Model. OARSI 2018 World Congress on Osteoarthritis 2018.04.26 Liverpool, United Kingdom
16. Mai Katakura, Hideyuki Koga, Stefano Zaffagnini, Takeshi Muneta. Meniscus Repair Reduces Anterolateral Rotational Instability of the ACL Injured Knee: Quantitative Assessment of the Pivot Shift Phenomenon Using Triaxial Accelerometer. 2018th ESSKA 2018.05.09 Glasgow, UK
17. Hiroko Ueki, Hideyuki Koga, Yusuke Nakagawa, Toshiyuki Ohara, Mai Katakura, Ichiro Sekiya, Takeshi Muneta, TMDU MAKS Study Group. Risk Factors for Residual Pivot Shift after ACL Reconstruction: Data from a multicenter cohort study. 2018th ESSKA 2018.05.09 Glasgow, UK
18. Takashi Hoshino, Hideyuki Koga, Yusuke Nakagawa, Toshiyuki Ohara, Hiroko Ueki, Mai Katakura, Takeshi Muneta. Two-year clinical outcomes after double-bundle anterior cruciate ligament reconstructions among different procedures for meniscus -TMDU MAKS study. 2018th ESSKA 2018.05.09 Glasgow, UK

19. Toshifumi Watanabe, Akino Aoki, Kenji Hoshi, Kazuyoshi Gamada, Takeshi Muneta, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Ichiro Sekiya, Hideyuki Koga. Anterior tibial post impingement in posterior-stabilized prosthesis during stair climbing. Annual Meeting of JOA 2018.05.24 Kobe, Japan
20. Hideyuki Koga, Mai Katakura, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta. How to eliminate residual instability in ACLR - Rotational instability and Meniscus -. 10th JOSKAS 2018.06.14 Fukuoka, Japan
21. Hideyuki Koga, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta. Meniscus repair up to date -Treatment strategy for meniscus extrusion-. 10th JOSKAS 2018.06.14 Fukuoka, Japan
22. Hideyuki Koga. Restoring knee joint function by preserving meniscus function. 10th JOSKAS 2018.06.14 Fukuoka, Japan
23. Toshifumi Watanabe, Takeshi Muneta, Ichiro Sekiya, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Kenta Katagiri, Hideyuki Koga . ACTIYAS: Implant design, surgical tips, and clinical outcomes. 10th JOSKAS 2018.06.14 Fukuoka, Japan
24. Yusuke Nakagawa, Amir H. Lebaschi, Susumu Wada Xiang-Hua Deng, Scott A. Rodeo . Duration of Postoperative Immobilization Affects MMP Activity at the Healing Graft-Bone Interface: Evaluation in a Mouse ACL Reconstruction Model. 10th JOSKAS 2018.06.14 Fukuoka, Japan
25. Hideyuki Koga. Treatment strategy for meniscus extrusion to preserve meniscal function. 62th Korean Orthopaedic Association Annual Meeting 2018.10.18 Seoul, Korea
26. Kunikazu Tsuji, Miyoko Ojima, Koji Otabe, Masafumi Horie, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Factor A, a TGFb/BMP family molecule, surges in the acute inflammatory phase after joint injury and promotes meniscus regeneration in a rat anterior half of medial meniscus resection model. 12th International BMP Conference 2018.10.24 Tokyo
27. Hideyuki Koga. Centralization of medial meniscus (live surgery). 11th Murup Hospital Live Surgery 2018.11.24 Busan, Korea

[Awards & Honors]

1. 2018 ORS/OREF Travel Award in Orthopaedic Research Translation(Katakura Mai) , Orthopaedic Research Society, 2018.03
2. Orthopaedic Research Socieity Annual Meeting 2018. New Investigator Recognition Awards [NIRA] (Nakagawa Yusuke), Orthopaedic Research Socieity, 2018.05

Biostructural Science

Associate Professor: Makoto TABATA
 Technician: Makoto SUGIURA
 Secretary: Tomoko YAMAMOTO
 Graduate Student: Takafumi NAKANO
 Eri USHIMURA
 Momoko SAKAGUCHI

(1) Outline

Section of biostructural science is the inheritor of the laboratory of Oral Anatomy II, then we focus understanding of the mechanism of tooth development, tooth cell differentiations, and tooth evolution using methods of histology, cell biology, and molecular biology. We also teach three courses of histology for the second grade of dental student, and attend to the preparation works of gross anatomy.

(2) Research

The study of the mechanisms of dental formation and their evolution is the central focus of our research. Followings are rough description of current research subjects in our laboratory.

- 1)Research of Tooth Germ Developmen
- 2)Research of Ameloblast Differentiation & Function
- 3)Research of Fish Scales & Teeth
- 4)Space Experiments using Fish
- 5)Comparative Morphology of the Tooth

(3) Lectures & Courses

We are inheritor of the laboratory of Oral Anatomy II, then we involved in the education of histology, embryology, and oral histology.

In the first place, anatomy and histology is the study to learn the structure, the name, and the function of "HUMAN BODY". Then the subject histology is not able to separate from subject anatomy, relate to physiology, pathology, and embryology and further become to be the fundamentals of clinical subjects. So we carry out of our subjects, with an awareness of the relationships between histology and other subjects.

On the curriculum of the 2nd grade of dental students, lectures of histology contains practical histology using tissue sections and microscopy. This skills work is a good opportunity to know the variation and the finesse of the human body in histology.

(4) Publications

[Original Articles]

1. Manhal Ijbara, Kanae Wada, Makoto J. Tabata, Junichiro Wada, Go Inoue, Michiyo Miyashin. Enamel Microcracks Induced by Simulated Occlusal Wear in Mature, Immature and Deciduous Teeth. BioMed Research International . 2018.04; 2018(5658393); 1-9
2. Shunsuke F, Tatsuya A, Shu H, Takanori M, Ammar SA, Munehiro O, Yasuhiko T, Makoto M, Makoto J T, Makoto S-N, Yuichi I. Comparison between different isoelectric points of biodegradable gelatin sponges incorporating β -tricalcium phosphate and recombinant human fibroblast growth factor-2 for ridge augmentation: A preclinical study of saddle-type defects in dogs. J. Periodont. Res. 2018.11;

[Conference Activities & Talks]

1. Hiroshi Takase, Makoto Sugiura-Nakazato, Kaori Yamaguchi. Universal design of a diamond knife for ultra-thin sectioning.. The 61st Symposium of The Japanese Society of Microscopy 2018.11.01 TOYAMA INTERNATIONAL CONFERENCE CENTER

Pharmacology

Staffs and Students

Assistant Professor Yukihiro TAMURA
Technologist Mariko TAKAHASHI

Researchers

Tomoki UEHARA (Pediatric Dentistry)
Yuki ARAI (Removable Prosthodontics)
Hideaki INAGAWA (Removable Prosthodontics)
Noriko HIRAISHI (Cariology and Operative Dentistry)
Graduate Students

Kenya YONEDA (Regenerative Dental Medicine)
Lia Kartika Wulansari (Regenerative Dental Medicine)
Eri SONE (Maxillofacial Surgery)
Hisami OKAWARA (Removable Prosthodontics)
Michiko OZAWA
Shigeki NAGAHIRO (Pediatric Dentistry)
Keo Preksa (Orthodontic Science)

Lecturers

Yoshihiro WAKI
Etsuko TAKAHASHI
Kenichi NAGANO
Eiichi MURASE
Hiroyuki SETO
Toshimi SATO
Genki KATO
Kiichi NONAKA
KHAN Md Abudulla Al Masud

(1) Research

Research subjects

- 1) Pharmacological analyses of formation and resorption on bones and teeth
- 2) Identification of a new therapeutic target for hard tissue-related diseases
- 3) Translational research for hard tissue regeneration
- 4) Analyses of drug side effects appeared at oral tissues

(2) Lectures & Courses

Purpose of Education

Pharmacology is situated between the basic and clinical sciences and is important for dental students. There is a growing demand on the dental clinicians to know huge knowledge of drugs and how to use them for patients.

For these purpose, the first lecture is aimed to teach the scientific aspects of pharmacology and how drugs act on the various organ system. The second lecture deals with drugs of medical and dental fields and the last with drugs of special importance of dentistry. Dental students learn the principle of pharmacology through laboratory practice. Following these learning, they must acquire an adequate background for drug use in general practice.

(3) Publications

[Original Articles]

1. M Urata , S Kokabu, T Matsubara, G Sugiyama,C Nakatomi, H Takeuchi, S Hirata - Tsuchiya, K Aoki, Y Tamura , Y Moriyama , Y Ayukawa, M Matsuda, M Zhang, K Koyano, C Kitamura, E Jim. A peptide that blocks the interaction of NF - κ B p65 subunit with Smad4 enhances BMP2 - induced osteogenesis Journal of Cellular Physiology. 2018.04; 233(9); 7356-7366
2. Lia Kartika Wulansari, Boosana Kaboosaya, Masud Khan, Mariko Takahashi, Hidemi Nakata, Shinji Kuroda, KazuhiroAoki, ShoheiKasugai. Beneficial effects of fasting regimens on periodontal tissues in experimental periodontitis mice model Journal of International Dental and Medical Research. 2018.05; 11(2); 362-369
3. X Cui, T Murakami, Y Tamura, K Aoki, Y Hoshino, Y Miura. Bacterial Inhibition and Osteoblast Adhesion on Ti Alloy Surfaces Modified by Poly(PEGMA-r-Phosmer) Coating ACS Applied Materials & Interfaces. 2018.06; 10(28); 23674-23681

[Conference Activities & Talks]

1. Y. Arai, K.Aoki, Y.Tamura, H. Nagahiro, H. Ogawara, T.Uehara, M.Miyashi, N.Wakabayashi. Evaluation of alveolar bone formation using RANKL binding peptide in excess occlusion model mouse. Japanese Society for Bone Morphometry 2018.06.21 Osaka
2. E. Sone, K. Masud, D.Noshiro, Y.Ikebuchi, M.Honma, Y.Tamura, Y.Sugamori, Y.Suzuki, N.Udagawa, K.Aoki. Investigation of bone formation promotion mechanism by RANKL binding peptide. Japanese Society for Bone Morphometry 2018.06.21 Osaka
3. E Sone, D Noshiro, Y Ikebuchi, M Khan, Y Sugamori, Y Tamura, T Yoda, M Honma, K Aoki.. A stimulatory mechanism of RANKL-Binding peptide on osteoblast differentiation.. 32nd IADR-SEA & 29th SEAADE 2018.09.11 Da Nang, Vietnam

Connective Tissue Regeneration

Associate Professor Tamayuki SHINOMURA

(1) Outline

Our group is interested in the restoration of damaged connective tissue. In general, connective tissue is characterized by the presence of abundant extracellular matrix, and its function is highly dependent on the properties of extracellular matrix. Therefore, to restore connective tissue normal, it is essential for us to understand the behavior of extracellular matrix molecules. So, we pursue research on the molecular mechanisms underlying the formation and maintenance of extracellular matrix in connective tissues.

(2) Research

Currently, we are engaged in the following research subject.

1. Study on the mechanisms that regulate the expression of type II collagen and aggrecan in chondrocytes.
2. Study on transcription factors necessary for the maintenance of chondrogenic phenotype.
3. Study on the molecular dynamics of extracellular matrix in connective tissues.

(3) Education

We give a lecture on molecular biology in general and laboratory exercise for undergraduate students. Also, in our graduate course, we offer lectures on the synthesis and formation of extracellular matrix focusing on cartilage tissue.

(4) Lectures & Courses

We provide education based on the belief that an integrated and organized connection of various knowledge is important to understand life phenomena.

(5) Publications

[Original Articles]

1. [Connective Tissue Regeneration : SHINOMURA Tamayuki] Hamada S, Nishida Y, Zhuo L, Shinomura T, Ikuta K, Arai E, Koike H, Kimata K, Ushida T, Ishiguro N. Suppression of hyaluronan synthesis attenuates the tumorigenicity of low-grade chondrosarcoma Journal of Orthopaedic Research. 2018.06; 36(6); 1573-1580
2. [Connective Tissue Regeneration : SHINOMURA Tamayuki] Miyazaki Y, Horie A, Tani H, Ueda M, Okunomiya A, Suginami K, Kondoh E, Baba T, Konishi I, Shinomura T, Sato Y. Versican V1 in human endometrial epithelial cells promotes BeWo spheroid adhesion in vitro. Reproduction (Cambridge, England). 2018.10;

[Conference Activities & Talks]

1. [Connective Tissue Regeneration : SHINOMURA Tamayuki] Giang thi hien Nham, Zhang Xiang, Tamayuki Shinomura. Histone modifications differently regulate the activity of type II collagen enhancers. 第31回日本軟骨代謝学会 2018.03.02 ウィンクあいち (愛知県名古屋市)
2. [Connective Tissue Regeneration : SHINOMURA Tamayuki] Koike H, Nishida Y, Shinomura T, Hamada S, Ishiguro N. Effects of KIAA1199, a novel hyaluronidase, over expression on tumorigenicity of low grade chondrosarcoma. 第31回日本軟骨代謝学会 2018.03.02
3. [Connective Tissue Regeneration : SHINOMURA Tamayuki] Tamayuki Shinomura. Transcriptional regulation in cartilage. 2018.11.10
4. [Connective Tissue Regeneration : SHINOMURA Tamayuki] Zhang Xiang, Nham Thi Hien Giang, Tamayuki Shinomura. Identification of an enhancer-specific transcription factor regulating type II collagen gene expression. The 6th Tri-University Consortium on Oral Science and Education 2018.11.30 Tokyo, Japan

Biochemistry

Professor Testuro Watabe

Associate Professor Miki Yokoyama

Junior Associate Professor Yasuhiro Kumei, Yasuhiro Yoshimatsu

Assistant Professor Katarzyna Anna Podyma-Inoue

Technical staff Megumi Naito, Kazue Terasawa

Part-time Lecturer Akira Asari

Graduate student Kazuki Takahashi, Akihiko Inagawa, Takumi Matsuda, Nagoya Takahashi, Shiori Kimuro, Rina Takayama

(1) Outline

Since cancer is the leading cause of death in Japan, we need to develop novel strategies to cure it. Tumor consists of not only cancer cells but also the non-cancerous cells including fibroblasts, immune cells and cells that comprise the blood and lymphatic vessels. We aim to elucidate the mechanisms how cancer cells become malignant by the various cytokines in cancer microenvironment in order to develop novel therapeutic strategies targeting multiple components of cancer microenvironment.

(2) Research

(1) Understanding the molecular mechanisms underlying endothelial-mesenchymal transition (EndMT)

Endothelial cells undergo differentiation into mesenchymal cells during not only various physiological processes including heart valve formation but also pathological processes including cancer progression, heart failure and diabetes. However, the molecular mechanisms that regulate such endothelial-mesenchymal transition (EndMT) remain to be elucidated. We aim to study the molecular mechanisms underlying EndMT in order to identify novel targets and attempt to develop therapeutic strategies for EndMT-related diseases.

(2) Elucidation of the molecular mechanisms underlying tumor angio- and lymphangiogenesis

Tumor angiogenesis and lymphangiogenesis are key features of tumor progression and metastasis. While multiple signaling pathways have been implicated in the formation of blood and lymphatic vessels, the molecular mechanisms underlying these processes have not yet fully elucidated. Recent findings revealed that members of the transforming growth factor- β (TGF- β) family play pivotal roles on in angiogenesis and lymphangiogenesis, and that abnormalities in TGF- β family signaling lead to development of certain vascular disorders, including hereditary hemorrhagic telangiectasia (HHT), pulmonary arterial hypertension, Marfan syndrome and Loeys-Dietz syndrome. We attempt to elucidate the molecular mechanisms how TGF- β family signals regulate angiogenesis and lymphangiogenesis in tumor microenvironment.

(3) Understanding the molecular mechanisms underlying metastasis of cancer cells

Epithelial-mesenchymal transition (EMT) plays important roles in various physiological and pathological processes, and is regulated by signaling pathways mediated by cytokines including TGF- β . Using various types of in vitro cultured oral carcinoma cells and in vivo systems, we aim to identify the molecules involved in the acquisition of invasive properties of cancer cells, in order to develop novel therapeutic strategies.

(4) Elucidation of the role of LAMP-1/2 proteins in the lysosomal intracellular degradation system

Lysosomes are intracellular organelles, containing various hydrolytic enzymes, essential for maintaining cell

homeostasis such as acquisition of energy and nutrients, biological defense, removal of unnecessary substances. In recent years it has also been found that lysosomes sense the state of energy acquisition of cells and decide whether the cells proliferate or gain nutrition. Lysosomal dysfunction clinically results in progressive and severe effects, especially notable in the nervous system, bone, connective tissue.

Lysosome-associated membrane protein-1/2 is the abundant membrane - spanning glycoprotein present in lysosomal membranes. Most of the proteins of LAMP-1 and LAMP-2 are present on the luminal side of lysosomes, both of which are composed of two homologous domains. However, LAMP-2 deficient mice exhibit a more severe phenotype than LAMP-1 deficient mice and Danone disease develops in humans due to abnormalities of LAMP-2. Accumulation of autophagosome-like vesicles was observed in myocytes of Danone disease, suggesting that LAMP-2 is associated with autophagy. Since LAMP-1 and LAMP-2 are considered to be similar proteins, the reason why they are functionally different remained mystery. We first discovered that the mode of multimerization is different between LAMP-1 and LAMP-2. We reported the crystal structure analysis of the domains of LAMP-1 and LAMP-2 and based on the findings we analyzed the mode of multimerization at the atomic level by site-specific crosslinking reaction utilizing introduction of non-natural amino acid. Then we are generating LAMP-1/2 with mutation in multimerization. We would like to answer the questions "How lysosomes fuse with autophagosomes?", "What is lysosomal identity? (the mechanism by which lysosomes are reformed from autolysosomes after fusion of lysosomes with autophagosomes)?".

(5) Heparan sulfate proteoglycan-dependent cellular logistics

Heparan sulfate proteoglycans (HSPGs) are one of the basic constituents of plasma membranes and have ability to interact with a number of the extracellular ligands. HSPGs have been suggested to mediate the trafficking of various macromolecules from the cell surface. Growth factors, cytokines, lipoproteins, cell penetrating peptides, polycation-nucleic acid complexes, along with exosomes, and pathogens enter cells through HSPG-dependent endocytosis. HSPGs-dependent endocytic events have been involved in tumor progression, stressing the importance of the identification of HSPG species participating in a formation of various endocytic complexes. We have characterized the intracellular trafficking complexes formed in the presence of HSPGs in a rat C6 glioma cell line model. Successful isolation of HSPG-positive transport vesicles followed by detailed proteomic analysis allowed us the identification of over eighty proteins related to vesicular transport; i.e. endocytosis or recycling. Part of HSPGs in glioma cells found to be internalized through clathrin-dependent endocytosis and underwent recycling. Further characterization of HSPG-rich vesicular compartments will help us understand the nature of HSPG-ligand interactions and to design the tools for targeted delivery of ligands into the cells.

(6) Posture, behavior, and motion sickness of common marmosets in low gravities.

In planetary development projects such as manned Mars exploration that will take longer than 3 years, long-term biological adaptation to weightlessness and partial-gravity environments is a critical issue. Since rodents of short lifespan (rats and mice) cannot survive in such a long-term flight, other animals of longer lifespan must be used alternatively so as to conduct appropriate studies on posture and exploration as well as voice communication and social behaviors of animals that have some relevance to long-term manned spaceflight. Common marmoset belonging to the same anthropoid with humans has a lifespan of 15 years is characterized by unique social behavior resembling humans with abundant squealing. In parabolic flight experiment carried out, we first examined the adaptation and social behavior of common marmoset under such conditions as Moon and Mars simulation or weightlessness. We have gained new knowledge on the response and behavior of primates in partial gravities.

(3) Education

For the second-year undergraduate students, we are in charge of the unit, "Molecular aspect of cell biology" and "Laboratory course" under the module of "Molecular basis of biology". The contents of "Molecular aspect of cell biology (lecture)" includes, topics related to the structure and function of membranes, transport across membranes, organization and function of intracellular organelles, intracellular trafficking, cytoskeleton, extracellular matrix, signal transduction, cell cycle and cell death.

For the graduate students, in order to demonstrate various research examples, we lectured on the structure and function of proteoglycans and the structure and role of extracellular matrix.

(4) Lectures & Courses

For the undergraduate students, our aim is to provide the students with the basic knowledge in biochemistry to help them to understand cellular function based on the structure and function of biomolecules. For the graduate students, we encourage them to acquire an ability and research skill to study the cellular responses at molecular levels.

(5) Publications**[Original Articles]**

1. Kazuki Takahashi, Katarzyna A. Podyma-Inoue, Chihiro Takao, Yasuhiro Yoshimatsu Y, Tomoki Muramatsu, Johji Inazawa and Tetsuro Watabe. Regulatory role of transforming growth factor- β signals in the migration and tumor formation of HOC313-LM cells, an oral squamous cell carcinoma Journal Stomatological Society, Jpn. 2018.07; 85(2); 52-61
2. Y Kumei, R Shimokawa, M Kimoto, Y Kawauchi, H Shimokawa, K Makita, K Ohya, K Toda. Gravity stress elevates the nociceptive threshold level with immunohistochemical changes in the rat brain. Acta Astronaut. 49(3-10); 381-390

[Misc]

1. Jin-Ichi Inokuchi, Takashi Ode, Miki Hara-Yokoyama. Pharmacological Modulation of Glycosphingolipid Metabolism. Methods Mol. Biol.. 2018; 1804; 401-410
2. Katarzyna A. Inoue and Tetsuro Watabe. Vessels and exosomes Inflammation and Immunity. 2018.06; 26(4); 280-285

[Conference Activities & Talks]

1. Tetsuro Watabe. Elucidation of the molecular mechanisms underlying pathogenesis of diseases caused by the failure of dynamic maintenance of homeostasis in vascular system. The 10th sakigake 2018.01.19 miyazaki
2. Katarzyna A. Inoue. Roles of TGF- β signal in the progression of oral squamous cell carcinoma. TMDU Joint Symposium of Immunology and Pathological Biochemistry Units 2018.03.08 Tokyo
3. Tetsuro Watabe. TGF- β signals induce endothelial-to-mesenchymal transition of lymphatic endothelial cells by decreasing PROX1 expression. Lymphatics Gordon Research Conference 2018.03.11 Lucca(Barga), IT
4. Tetsuro Watabe. Roles of signaling and transcriptional networks during the formation and maintenance of lymphatic vessels. 138th Annual Meeting of the Pharmaceutical Society of Japan 2018.03.26 Kanazawa
5. Tetsuro Watabe. TGF- β family signals in the formation and maintenance of vascular systems.. International Vascular Biology Meeting 2018 2018.06.03 Helsinki,Finland
6. Tetsuro Watabe. Roles of signaling and transcriptional networks during the maintenance of lymphatic vessels. The 42nd Annual Meeting of the Japanese Society of Lymphology 2018.06.22 Hirosaki
7. Tetsuro Watabe. Roles of TGF- β family signals during the formation and maintenance of vascular systems.. Kitasato Research Forum 2018 2018.07.09 Tokyo
8. Tetsuro Watabe. Roles of signaling networks during progression of melanoma.. Kofe Stem Cell Conference 2018 2018.08.02 Kofu
9. Kazue Terasawa, Seisuke Kusano, Shigeyuki Yokoyama, Tetsuro Watabe, Miki Yokoyama. LAMP-1 and LAMP-2 with tandem b-prism domains assemble via distinct modes. The 37th Annual Meetings of Japanese Society of Carbohydrate Research 2018.08.29 Sendai
10. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced metastasis. 2018.09.29

11. Kazuki Takahashi, Katarzyna A. Inoue, Yasuhiro Yoshimatsu, Atsushi Kaida, Masahiko Miura, Tetsuro Watabe. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced migration. The 77th Annual Meeting of Japanese Cancer Association 2018.09.29 Osaka, Japan
12. Tetsuro Watabe. BMP family signals in the formation and maintenance of vascular systems.. 12th International BMP Conference 2018.10.27 Tokyo, Japan
13. Tetsuro Watabe. TGF- β family signals in the formation and maintenance of lymphatic systems.. The 41st Annual Meeting of the Molecular Biology Society of Japan 2018.11.28 Yokohama, Japan
14. Yasuhiro Yoshimatsu. Transcription factors and signaling pathways that control lymphatic vessel formation and lymphatic endothelial identity. 2018.11.28
15. Tetsuro Watabe. Roles of Signaling and Transcriptional Networks during Maintenance of Vascular Systems. Cardiovascular and Metabolic Week 2018 2018.12.07 Tokyo

Cell Signaling

Professor(Principal Investigator)Tomoki NAKASHIMA
 Assistant Professor Mikihiro HAYASHI
 Assistant Professor Takehito ONO

(1) Research

Research Subjects

- 1)Regulation of bone remodeling by bone cells
- 2)Identification of bone-derived systemic regulatory factors (osteokines)
- 3)Mechanism of sensing and adapting to mechanical stress
- 4)Functional analysis of genes by gene manipulations and gene-disrupted mice
- 5)Development of clinical application by experimental animal disease models

(2) Education

Purpose of Education

Organized signal networks in the body are crucial for the higher physiological functions and the tissue organization. To understand the regulation of signal events, we take on cell signaling course including the molecular mechanism of both the “intra” cellular and the “inter” cellular signal transduction. Especially, the course will be focused on the molecular networks of signal transduction in osteoclasts, osteoblasts and osteocytes which is a new integrated field of osteonetwork (systemic network between bone and other systems). Besides, to promote the practical and clinical understanding, the course will deal with the molecular mechanism of osteoporosis and inflammatory bone destructed diseases, such as periodontal disease and rheumatoid arthritis, in parallel with the basic molecular biology.

(3) Publications

[Original Articles]

1. Masayuki Tsukasaki, Noriko Komatsu, Kazuki Nagashima, Takeshi Nitta, Warunee Pluemsakunthai, Chisa Shukunami, Yoichiro Iwakura, Tomoki Nakashima, Kazuo Okamoto, Hiroshi Takayanagi. Host defense against oral microbiota by bone-damaging T cells. *Nat Commun.* 2018.02; 9(1); 701
2. Sasaki F, Koga T, Ohba M, Saeki K, Okuno T, Ishikawa K, Nakama T, Nakao S, Yoshida S, Ishibashi T, Ahmadieh H, Kanavi MR, Hafezi-Moghadam A, Penninger JM, Sonoda KH, Yokomizo T. Leukotriene B4 promotes neovascularization and macrophage recruitment in murine wet-type AMD models. *JCI insight.* 2018.09; 3(18);
3. Kim Y, Hayashi M, Ono T, Yoda T, Takayanagi H, Nakashima T. Suppression of hematopoietic cell kinase ameliorates the bone destruction associated with inflammation. *Modern rheumatology.* 2018.11; 1-17

4. Maia Inoue, Kazuo Okamoto, Asuka Terashima, Takeshi Nitta, Ryunosuke Muro, Takako Negishi-Koga, Toshio Kitamura, Tomoki Nakashima, Hiroshi Takayanagi. Arginine methylation controls the strength of γ c-family cytokine signaling in T cell maintenance. Nat. Immunol.. 2018.11; 19(11); 1265-1276

[Misc]

1. Takehito Ono, Tomoki Nakashima. Recent advances in osteoclast biology Histochem. Cell Biol.. 2018.02;
2. Takehito Ono. Why and how do teeth come off? –New insights into the tooth loss during periodontitis– Dental, Oral and Craniofacial Research. 2018.04; 4(4); 1-2

[Conference Activities & Talks]

1. Tomoki Nakashima. Bone homeostasis and mechanomedicine. 第 95 回 日本生理学会 2018.03.29 高松
2. Takehito Ono. Inflammatory regulation of mesenchymal cells in bone regeneration . The 16th Stem Cell Research Symposium 2018.06.01 Kyushu University
3. 小野岳人、傳田良亮、権藤理夢、河崎万鈴、木下佑理、中島友紀. ケミカルライブラリーを用いた新規スクリーニング法による運動器疾患の治療薬探索. 第 4 回日本骨免疫学会 2018.06.24 沖縄
4. Ayumi Shoji-Matsunaga, Takehito Ono, Keiji Moriyama, Tomoki Nakashima. Osteocyte-derived RANKL Is A Key Regulator of Orthodontic Tooth Movement. International Association for Dental Research 2018.07.20

Periodontology

From January.2018

【Professor】 Yuichi Izumi(～ Mar)

【Associate Professor】 Akira Aoki

【Junior Associate Professor】 Yasuo Takeuchi, Tatsuya Akizuki

【Assistant Professor】 Koji Mizutani, Sayaka Katagiri, Yuichi Ikeda

【Specially appointed Assistant Professor】 Yuuka Tsumanuma, Takanori Matsuura, Takahiko Shiba, Shogo Maekawa,

【Clinical Fellow】 Takahiro Ikawa(～ Mar), Hiroki Sato(～ Mar), Masahiro Noda(～ Mar), Kosei Yano(～ Mar), Takeaki Sudo, Toru Takagi(Apr ～), Risako Tanimoto(Apr ～), Wataru Ono(Apr ～)

【Graduate Students】 Anri Ohtsu(～ Mar), mmr Shujaa Addin(～ Mar), Chantida Pawauputanon Na Mahasarakham(～ Mar), Eri Ikeda(～ Mar), Sayuri Udagawa(～ Mar), Sho Kakizaki(～ Mar), Daisuke Kido(～ Mar), Rina Komazaki(～ Mar), Sophannary Kong(～ Mar) ,

Shinta Suzuki, Nay Aung, Thatawee Khemwong, Yujin Ohsugi, Naoki Sasaki, Kohei Takeda, Yosuke Tuchiya, Shunsuke Fukuba, Anongwee Leewananthawet, Prima Buranasin, Munehiro Okada, Chihiro Kano, Yuji Kato, Rie Kawamura, Keitetsu Kure,

Yutaro Kitanaka, Kohei Nohara, Kazuki Watanabe, Keiji Komatsu, Ryo Satou(Apr ～), Daiki Tanaka(Apr ～), Takashi Nemoto(Apr ～),

Hiromi Kawakami(Apr ～), Hiromi Kominato(Apr ～), Natsumi Saito(Apr ～)

【Adult graduate student】

Kaori Fujiwara, Masaki Tsubokawa, Naho Suzuki, Akiko Kobayashi, Miho Ogawa

【Graduate Research Student】

Hideyuki Takamatsu, Yukako Kusunoki, Shogo Takeuchi,

Akihito Nakazato(～ Mar), Takashi Furuichi(～ Mar), Taiki Mise(～ Mar),

Takae Shimoda, Ryo Hirai, Yuto Mukaiyama, Naoaki Yoshida,

Yoshiyuki Iwabuchi, Aya Suzuki, Keiji Komatsu, Shotaro Mori,

Takeshi Iida(Apr ～), Tomoaki Kariya(Apr ～), Ryo Mikami(Apr ～),

Ayako Kawada(Apr ～), Mai Kitamura(Apr ～)

【Clinical Professor】 Hiroaki Kobayashi

【Registered dentist】 : 40

【Assistant Administrative Staff】 Tomomi Anai, Kyoto Sogabe

(1) Outline

Periodontology is a branch of dental sciences which deals with the research, prevention and treatment of periodontal diseases. Periodontal disease is a general disease name which occurred in the periodontal tissue: gingiva, periodontium, cementum and alveolar bone. At present, it is indicated mainly an acute or chronic inflammatory diseases. The mission of our department was to educate etiology of periodontal diseases, host response, oral bacteria, periodontal medicine, regenerative therapy and so on profoundly, and to find a solution through discussion research outcomes as to periodontal destructive process and to develop a novel periodontal treatment modalities.

(2) Research

- 1) Inflammatory and immunological factors in periodontal diseases
- 2) Periodontopathic bacteria and their pathogenicity
- 3) Influence of periodontal disease on general health
- 4) Analyses of growth factors and bio materials in periodontal regeneration
- 5) Clinical applications of laser in periodontics

(3) Lectures & Courses

Periodontology is a branch of dental science which deals with supporting structures of teeth, diseases and conditions affect them. Main objectives of periodontology in the graduate course is to provide students basic knowledge of etiology of periodontal diseases, its treatment modality and prognosis, and also to study advanced regenerative therapy.

(4) Clinical Performances

Periodontal clinic provides diagnosis, treatment and prevention of periodontal disease. Periodontal surgery and regenerative therapy are also performed in the clinic.

(5) Publications

[Original Articles]

1. Buranasin P, Mizutani K, Iwasaki K, Pawaputanon Na Mahasarakham C, Kido D, Takeda K, Izumi Y. High glucose-induced oxidative stress impairs proliferation and migration of human gingival fibroblasts. *PloS one*. 2018; 13(8); e0201855
2. Takeda K, Mizutani K, Matsuura T, Kido D, Mikami R, Noda M, Buranasin P, Sasaki Y, Izumi Y. Periodontal regenerative effect of enamel matrix derivative in diabetes. *PloS one*. 2018; 13(11); e0207201
3. Udagawa S, Katagiri S, Maekawa S, Takeuchi Y, Komazaki R, Ohtsu A, Sasaki N, Shiba T, Watanabe K, Ishihara K, Sato N, Miyasaka N, Izumi Y. Effect of *Porphyromonas gingivalis* infection in the placenta and umbilical cord in pregnant mice with low birth weight. *Acta Odontologica Scandinavica*. 2018.01; 1-9
4. Aoyama N, Suzuki JI, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, Shiheido Y, Sato H, Minabe M, Izumi Y, Isobe M. Associations among tooth loss, systemic inflammation and antibody titers to periodontal pathogens in Japanese patients with cardiovascular disease. *Journal of Periodontal Research*. 2018.02; 53(1); 117-122
5. Hirata J, Hirota T, Ozeki T, Kanai M, Sudo T, Tanaka T, Hizawa N, Nakagawa H, Sato S, Mushiroda T, Saeki H, Tamari M, Okada Y. Variants at HLA-A, HLA-C, and HLA-DQB1 confer risk of psoriasis vulgaris in Japanese. *Journal of Investigative Dermatology*. 2018.03; 138(3); 542-548
6. Komazaki R, Katagiri S, Takahashi H, Maekawa S, Shiba T, Takeuchi Y, Kitajima Y, Ohtsu A, Udagawa S, Sasaki N, Watanabe K, Sato N, Miyasaka N, Eguchi Y, Anzai K, Izumi Y. Author Correction: Periodontal pathogenic bacteria, *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. *Scientific reports*. 2018.03; 8(1); 4620
7. Kakizaki S, Aoki A, Tsubokawa M, Lin T, Mizutani K, Geena K, Alireza S, Oda S, Sumi Y, Izumi Y. Observation and determination of periodontal tissue profile using optical coherence tomography. *Journal of Periodontal Research*. 2018.04; 53(2); 188-199
8. Taniguchi Y, Sawada K, Aoki A, Miyazawa M, Yamada A, Nakahara K, Izumi Y. Novel Prosthesis Technique for Fabricating a CAD/CAM Implant Superstructure Frame Using a 3D Printer. *EC Dental Science*. 2018.04; 17(5); 459-468
9. Ikeda E, Ikeda Y, Wang Y, Fine N, Sheikh Z, Viniegra A, Barzilay O, Ganss B, Tenenbaum H, Glogauer M. Resveratrol derivative-rich melinjo seed extract induces healing in a murine model of established periodontitis. *Journal of Periodontology*. 2018.05; 89(5); 586-595

10. Tsubokawa M, Aoki A, Kakizaki S, Taniguchi Y, Ejiri K, Mizutani K, Koshy G, Akizuki T, Oda S, Sumi Y, Izumi Y. In vitro and clinical evaluation of optical coherence tomography for the detection of subgingival calculus and root cementum. *Journal of oral science*. 2018.05; 60(3); 418-427
11. Chigasaki O, Takeuchi Y, Aoki A, Sasaki Y, Mizutani K, Aoyama N, Ikeda Y, Gokyu M, Umeda M, Ishikawa I, Izumi Y. A cross-sectional study on the periodontal status and prevalence of red complex periodontal pathogens in a Japanese population. *Journal of oral science*. 2018.06; 60(2); 293-303
12. Yoshida Y, Churei H, Takeuchi Y, Wada T, Uo M, Izumi Y, Ueno T. Novel antibacterial mouthguard material manufactured using silver-nanoparticle-embedded ethylene-vinyl acetate copolymer masterbatch. *Dental Materials Journal*. 2018.06; 37(3); 437-444
13. Takagi T, Aoki A, Ichinose S, Taniguchi Y, Tachikawa N, Shinoki T, Meinzer W, Sculean A, Izumi Y. Effective removal of calcified deposits on microstructured titanium fixture surfaces of dental implants with erbium lasers. *Journal of Periodontology*. 2018.06; 89(6); 680-690
14. Khemwong T, Kobayashi H, Ikeda Y, Sudo T, Kano C, Matsuura T, Izumi Y. *Eubacterium Saphenum* as a Novel Bacterial Biomarker for Periodontitis Screening. *The journal of the stomatological society*. 2018.07; 85(2); 62-67
15. Shujaa Addin A, Akizuki T, Matsuura T, Hoshi S, Ikawa T, Maruyama K, Ono W, Fukuba S, Izumi Y. Histological healing after nonsurgical periodontal treatment with enamel matrix derivatives in canine experimental periodontitis. *Odontology*. 2018.07; 106(3); 289-296
16. Lee BS, Shih KS, Lai CH, Takeuchi Y, Chen YW. Surface property alterations and osteoblast attachment to contaminated titanium surfaces after different surface treatments: An in vitro study. *Clinical implant dentistry and related research*. 2018.08; 20(4); 583-591
17. Washio K, Tsutsumi Y, Tsumanuma Y, Yano K, Srithanyarat Supreda S, Takagi R, Ichinose S, Meinzer W, Yamato M, Okano T, Hanawa T, Ishikawa I. In Vivo Periodontium Formation Around Titanium Implants Using Periodontal Ligament Cell Sheet. *Tissue Engineering Part A*. 2018.08; 24(15-16); 1273-1282
18. Morozumi T, Yashima A, Gomi K, Ujiie Y, Izumi Y, Akizuki T, Mizutani K, Takamatsu H, Minabe M, Miyauchi S, Yoshino T, Tanaka M, Tanaka Y, Hokari T, Yoshie H. Increased systemic levels of inflammatory mediators following one-stage full-mouth scaling and root planing. *Journal of Periodontal Research*. 2018.08; 53(4); 536-544
19. Saida H, Fukuba S, Miron R, Shirakata Y. Efficacy of flapless intentional replantation with enamel matrix derivative in the treatment of hopeless teeth associated with endodontic-periodontal lesions: A 2-year prospective case series. *Quintessence International*. 2018.09; 49(9); 699-707
20. Seki N, Kanazawa M, Komagamine Y, Mizutani K, Hosaka K, Komada W, Moross J, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School. *Journal of Medical and Dental Sciences*. 2018.09; 65(3); 123-130
21. Sasaki N, Katagiri S, Komazaki R, Watanabe K, Maekawa S, Shiba T, Udagawa S, Takeuchi Y, Ohtsu A, Kohda T, Tohara H, Miyasaka N, Hirota T, Tamari M, Izumi Y. Endotoxemia by *Porphyromonas gingivalis* Injection Aggravates Non-alcoholic Fatty Liver Disease, Disrupts Glucose/Lipid Metabolism, and Alters Gut Microbiota in Mice. *Frontiers in Microbiology*. 2018.10; 9; 2470
22. Yumoto M, Saito N, Lin T, Kawamura R, Aoki A, Izumi Y, Wada S. High-energy, nanosecond pulsed Cr: CdSe laser with a 2.25-3.08 μ m tuning range for laser biomaterial processing. *Biomedical Optics Express*. 2018.11; 9(11); 5645-5653
23. Fukuba S, Akizuki T, Hoshi S, Matsuura T, Shujaa Addin A, Okada M, Tabata Y, Matsui M, Tabata JM, Sugiura-Nakazato M, Izumi Y. Comparison between different isoelectric points of biodegradable gelatin sponges incorporating β -tricalcium phosphate and recombinant human fibroblast growth factor-2 for ridge augmentation: A preclinical study of saddle-type defects in dogs. *Journal of Periodontal Research*. 2018.11; Epub ahead of print
24. Ikeda Y, Neshatian M, Holcroft J, Ganss B. The enamel protein ODAM promotes mineralization in a collagen matrix. *Connective Tissue Research*. 2018.12; 59(sup1); 62-66

25. Iwata T, Yamato M, Washio K, Yoshida T, Tsumanuma Y, Yamada A, Onizuka S, Izumi Y, Ando T, Okano T, Ishikawa I. Periodontal regeneration with autologous periodontal ligament-derived cells sheets - A safety and efficacy study in ten patients. *Regenerative Therapy*. 2018.12; 9; 38-44

[Books etc]

1. Roncati M, Izumi Y, Aoki A. Nonsurgical periodontal therapy. Quintessence Publishing, 2018.03 (ISBN : 978-4-7812-0609-7)
2. Jr.,Paul A. Levi, Robert J. Rudy, Y.Natalie Jeong, Daniel K. Coleman, Izumi Y, Kinoshita A, Nagasawa T, Aoki A. Non-surgical Control of Periodontal Diseases. Ishiyaku Publishing, 2018.06
3. Ikawa T, Akizuki T, Izumi Y. Hand manual of oral & maxillofacial surgery '18. Quintessence publishing, 2018.07

[Misc]

1. Takeuchi Y, Aoki A, Hiratsuka K, Chanthoeun C, Ichinose A, Uekubo A, Izumi Y. Application of antimicrobial photodynamic therapy in dental treatments The Journal of Japan Society for Laser Surgery and Medicine. 2018.04; 38(4); 457-470
2. Pavlic V, Brkic Z, Marin S, Cicmil S, Gojkovic-Vukelic M, Aoki A. Gingival melanin depigmentation by Er:YAG laser: a literature review. *Journal of Cosmetic and Laser Therapy*. 2018.04; 20(2); 85-90
3. Tsubokawa M, Aoki A, Kakizaki S, Mizutani K, Sumi Y, Izumi Y. Application of OCT for Periodontal Treatment. 2018.04; 39(1); 37-48
4. Washio K, Ishikawa I, Yano K, Iwasaki K, Tsumanuma Y. Innovative Potential of Periodontal Ligament Cell Sheet Engineering in Functional Implant Therapy. *Innovation in Tissue Engineering & Regenerative Medicine*. 2018.10; 1(2); 1-4

[Conference Activities & Talks]

1. Ohtsu A. Periodontal pathogenic bacteria, *Porphyromonas gingivalis*, affect gut microbiota in streptozotocin-induced diabetic mice. NTU-TMDU Periodontology Joint Symposium 2018.01.27 National Taiwan University, Taiwan
2. Takeuchi Y. Long-term success of implant treatment -a microbiological view-. The 37th Meeting of Japanese Society of oral Implantology 2018.02.11 Yokohama
3. Aoki A. Application of Er:YAG laser in periodontal pocket therapy. 6th Annual Meeting of Yokohama-Tsurumi Society for Periodontal Disease Research 2018.03.11 Tsurumi University Hall, Tsurumi
4. Aoki A. Current Status of Er:YAG Laser in Periodontal and Peri-implant Therapy. Cycle of Laser lectures 2018.04.07 Krakow, Poland
5. Aoki A. Current Status of Er:YAG Laser in Periodontal and Peri-implant Therapy. Special lectures regarding laser therapy in periodontics and dental surgery 2018.04.09 Wroclaw, Poland
6. Kong S, Aoki A, Iwasaki K, Mizutani K, Katagiri S, Suda T, Ichinose S, Ogita M, Pavlic V, Izumi Y. Photo-thermal Effect of Er:YAG Laser Irradiation on the Proliferation of Human Gingival Fibroblasts. The 25th Annual Meeting of the Academy of Laser Dentistry 2018.04.27 Orlando, Florida
7. Hirai R, Ikawa T, Kano C, Yoshida N, Ikeda Y, Mizutani K, Izumi Y. Clinical evaluation of plaque removal efficacy using High density filling toothbrush. The 61st Spring Meeting of the Japanese Society of Periodontology 2018.06.01 Tokyo
8. Aoki A, Takeuchi Y, Akizuki T, Mizutani K, Katagiri S, Ikeda Y, Maekawa S, Watanabe K, Matsuura T, Ohtsu A, Kakizaki S, Komazaki R, Mikami R, Hideshima M, Nikaidou T, Araki K, Izumi Y. Current Status of Clinical Practice of Periodontal Therapy by Predoctoral Dental Students at Tokyo Medical and Dental University (TMDU). The 61th Spring Meeting of The Japanese Society of Periodontology 2018.06.01 Keio plaza hotel, Tokyo

9. Buranasin P, Mizutani K, Iwasaki K, Pawaputanon C, Izumi Y. The effect of high glucose on primary human gingival fibroblasts. The 61st Spring Meeting of the Japanese Society of Periodontology 2018.06.01 Tokyo
10. Ogawa M, Katagiri S, Takeuchi Y, Tatsuro K, Ikawa T, Takayuki S, Arai Y, Kazama R, Wakabayashi N, Izumi Y. Measurement of palatal mucosal thickness using Cone-Beam Computed Tomography (CBCT). The 61 st Spling Meeting of the Japanese Society of Periodontology 2018.06.01 Tokyo
11. Leewananthatwet A, Arakawa S, Okano T, Kinoshita R, Ashida H, Izumi Y, Suzuki T. Evaluation the biological effects of Ozone Ultrafine Bubble Water in vitro. The 61st Spring Meeting of the Japanese Society of Periodontology 2018.06.01 Tokyo
12. Benhamou V, Aoki A. Lasers for the Management of Periodontal & Peri-Implant Diseases. 2018 Ramfjord symposium in University of Michigan 2018.06.14 University of Michigan, MI
13. Iwabuchi Y, Ikawa T, Suzuki A, Kano C, Sudo T, Ikeda Y, Mizutani K, Izumi Y. Clinical evaluation of plaque removal efficacy using T-shape toothbrush. The 148th Meeting of The Japanese Society of Conservative Dentistry 2018.06.15 Kyoto
14. Aoki A. What 's New in Dental Laser Therapy ?- Er:YAG Laser in Periodontics and Peri-implant Therapy. 2018 Ramfjord symposium in University of Michigan 2018.06.15 University of Michigan, MI
15. Nagayama T, Wada J, Murakami N, Watanabe C, Mizutani K, Takakusaki K, Uchida H, Wakabayashi N. Influence of removable partial denture designs on stabilizing effects for mobile teeth: a basic study. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.17 Okayama
16. Sasaki N, Katagiri S, Komazaki R, Watanabe K, Maekawa S, Shiba T, Takeuchi Y, Ohtsu A, Udagawa S, Izumi Y. Sonicated Porphyromonas gingivalis affect non-alcoholic fatty liver disease via glucose metabolism. Europerio 9 2018.06.20 Amsterdam, Netherlands
17. Shiba T, Takagi T, Koyanagi T, Taniguchi Y, Shogo M, Sawada K, Katagiri S, Takeuchi Y, Aoki A, Izumi Y. The clinical application of the novel diagnosis and treatment flowchart for peri-implantitis: Part 1 clinical application to mild case. EuroPerio9 2018.06.20 Amsterdam, Netherlands
18. Koyanagi T, Taniguchi Y, Takagi T, Shiba T, Sawada K, Takeuchi Y, Aoki Y, Izumi Y. The clinical application of a novel diagnosis and treatment flowchart for peri-implantitis: Part 2 - application to moderate cases . EuroPerio9 2018.06.20 Amsterdam, Netherlands
19. Taniguchi Y, Koyanagi T, Sawada K, Shiba T, Takagi T, Aoki A, Takeuchi Y, Yamada A, Izumi Y. The clinical application of the novel diagnosis and treatment flowchart for peri-implantitis: Part 3 clinical application on severe case. EuroPerio9 2018.06.20 Amsterdam, Netherlands
20. Aoki A. Periodontal laser therapy. EuroPerio9 2018.06.20 RAI, Amsterdam, Netherlands
21. Grzech-Le'sniak K, Matys J, Dominiak M, Sculean A, Aoki A. Clinical Outcomes of Nonsurgical Periodontal Treatment by Means of Er:YAG alone, Er:YAG + SRP and Er:YAG + Nd:YAG+ SRP: A Controlled Randomized Clinical Study. EuroPerio9 2018.06.20 RAI, Amsterdam, Netherlands
22. Sasaki N, Katagiri S, Komazaki R, Watanabe K, Maekawa S, Shiba T, Udagawa S, Takeuchi Y, Ohtsu A, Izumi Y. Sonicated Porphyromonas gingivalis affect non-alcoholic fatty liver disease via glucose metabolism. EuroPerio9 2018.06.20 Amsterdam Netherlands
23. Fukuba S, Akizuki T, Matsuura T, Hoshi S, Addin AS, Okada M, Izumi Y. Effects of combined use of recombinant human Fibroblast growth factor-2 and β -Tricalcium phosphate on ridge preservation in dehiscence bone defects after tooth extraction: A split-mouth study in dogs. Europerio9 2018.06.21 Amsterdam, Netherlands
24. Khemwong T, Kobayashi H, Sudo T, Kano C, Matsuura T, Ikeda Y, Izumi Y. Fretibacterium oral taxon 360 is salivary biomarker for periodontitis. Europerio9 2018.06.23 Amsterdam, Netherlands
25. Buranasin P, Mizutani K, Iwasaki K, Mahasarakham C, Izumi Y. High glucose impaired the proliferation and migration of human gingival fibroblasts. EuroPerio9 2018.06.23 Amsterdam, Netherlands

26. Tsubokawa M, Aoki A, Kakizaki S, Mizutani K, Sumi Y, Izumi Y. Application of optical coherence tomography in periodontal therapy: in vitro and clinical evaluation of dental calculus and cementum detection.. Japan Laser Therapy Association 2018.06.24 Tokyo
27. Watanabe C, Wada J, Mizutani K, Watanabe H, Wakabayashi N. Chronological changes in supporting alveolar bone by RPD placement. IADR 86th General Session & Exhibition 2018.07.24 London
28. Seki N, Hosaka K, Komada W, Kanazawa M, Mizutani K, Komagamine Y, Moross J, Morio I. International student forum 2018 -International students' life in Japan-. International Student Forum 2018 by Japanese Dental Science Federation 2018.08.02 Tokyo
29. Noritake K, Tsuruta J, Mizutani K, Kondo K, Arakawa S, Araki K. Study on educational effect measurement of the IPW program in practical clinical training.. The 50th Annual Meeting of the Japan Society for Medical Education 2018.08.04 Tokyo
30. Iwata T, Onizuka S, Park S, Tsumanuma Y, Nakai K, Izumi Y, Ando T. The establishment of safety and efficacy evaluation for allogeneic periodontal ligament derived multipotent mesenchymal stromal cell sheet with next-generation sequencer. TERMIS World Congress 2018 2018.09.07 Kyoto
31. Torii D, Kobayashi T, Horie T, Tsutsui TW. Tenomodulin expression in Scleraxis-knockout immortalized human periodontal ligament cells. The 60th Annual Meeting of Japanese Association for Oral Biology 2018.09.07 Fukuoka
32. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. 32nd IADR-SEA & 29th SEAAD 2018.09.11 Da Nang, Vietnam
33. Furusawa T, Ohshima M, Yamaguchi Y, Takayama S, Shiba T, Noda M, Aoki A, Sakuma A. Evaluation of clinical usefulness of newly developed periodontal jaw model > using food-derived ingredients. The Japanese Society of Mechanical Engineers annual meeting of 2018 2018.09.11 Kansai University, Osaka
34. Kawamura R, Aoki A, Mizutani K, Lin T, Mimata A, Saito N, Meinzer W, Izumi Y. In vitro evaluation of gingival ablation with various laser systems. The 32nd IADR-SEA Division Annual Scientific Meeting 2018.09.13 Ariyana Danang Exhibition & Convention Centre, Da Nang, Vietnam
35. Kano C, Kobayashi H, Nozaki K, Tsumanuma Y, Sudo T, Khemwong T, Izumi Y. The effective scaling strokes for root planing. The 32nd IADR-SEA Division Annual Scientific Meeting 2018.09.14 Da Nang, Vietnam
36. Kano C, Mizutani K, Ikawa T, Sudo T, Kobayashi H, Izumi Y. The effect of electric-powered ionic tooth-brushing on plaque removal – randomized clinical trial –. Europerio9 2018.09.20 Amsterdam, Netherlands
37. Aoki A. Er:YAG laser-assisted comprehensive periodontal pocket therapy (Er-LCPT). 16th World Laser Congress 2018.10.01 Aachenl, Germany
38. Ohsugi Y, Aoki A, Mizutani K, Katagiri S, Komaki M, Noda M, Takagi T, Kakizaki S, Meinzer W, Izumi Y. Comparison of Er:YAG laser ablation vs. Bur drilling in rat calvarial bone healing. The 16th congress of the World Federation for lasers Dentistry (WFLD) 2018.10.02 Aachen, Germany
39. Aung N, Aoki A, Takeuchi Y, Hiratsuka K, Katagiri S, Kong S, Ammar Shujaa Addin, Meinzer W, Sumi Y, Izumi Y. The effects of different UV LED wavelengths on periodontopathic bacteria. The 16th congress of the World Federation for lasers Dentistry (WFLD) 2018.10.02 Aachen, Germany
40. Ohsugi Y, Mizutani K, Katgiri S, Noda M, Takagi T, Kakizaki S, Kitanaka Y, Lin T, Aoki A. Evaluation of bone healing following Er:YAG laser ablation in rat compared with bur drilling. The 30th annual meeting of Japanese society for laser dentistry 2018.10.21 The Nippon dental university school of life dentistry at Tokyo, Tokyo
41. Aoki A. Healing and regeneration of periodontal tissue and laser. The 30th annual meeting Janapese society for laser dentistry 2018.10.21 The Nippon dental university school of life dentistry at Tokyo, Tokyo
42. Nay A, Takeuchi Y, Hiratsuka K, Katagiri S, Aoki A. UV LED effects on Periodontopathic bacteria. The 30th Annual meeting of Japanese Society for Laser Dentistry 2018.10.21 Fujimi hole, Nippon Dental University Hospital, Tokyo

43. Fukuba S, Akizuki T, Matsuura T, Ono W, Okada M, Nohara K, Mori S, Sato R, Hoshi S, Addin AS, Izumi Y. The effect of recombinant human fibroblast growth factor-2 on bone grafts for periodontal regeneration.. The 61st Spring Meeting of the Japanese Society of Periodontology 2018.10.26 Osaka
44. Nohara K, Matsuura T, Akizuki T, Addin A S, Fukuba S, Okada M, Mori S, Sato R, Izumi Y. Effects of experimental periodontitis on regenerated periodontal tissue by bone grafts. The 61st Autumn Meeting of Japanese Society of Periodontology 2018.10.26 Osaka
45. Kakizaki S, Aoki A, Ohsugi Y, Mizutani K, Tsubokawa M, Kawamura R, Izumi Y. Application of dental endoscope for non-surgical periodontal pocket therapy. The 61th Autumn Meeting of the Japanese Society of Periodontology 2018.10.27 Osaka
46. Maekawa S, Suzuki S, Aoki A, Katagiri S, Ikeda Y, Ejiri K, Kong S, Nagata M, Yamaguchi Y, Ohshima M, Izumi Y. A new screening system for periodontitis using Hepatocyte growth factor. 104th Annual Meeting of American Academy of Periodontology 2018.10.29 Vancouver
47. Harada Y, Sunaga M, Takeuchi Y, Aoki A, Maekawa S, Izumi Y, Kinoshita A.. Effectiveness of Improved Dental Model for Training of Pocket Probing.. The 104th Annual Meeting of American Academy of Periodontology 2018.10.29 Vancouver, Canada
48. Ohsugi Y, Aoki A, Mizutani K, Katagiri S, Komaki M, Noda M, Takagi T, Kitanaka Y, Izumi Y. Evaluation of new bone formation and gene expression following bone ablation with Er:YAG laser. The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.02 Miyako Messe, Kyoto
49. Shiba T, Takeuchi Y, Katagiri S, Komatsu K, Koyanagi T, Nemoto T, Aoki A. Omics analyses reveal microbial etiology and development of polymicrobial oral disease. The Stomatological Society 2018.12.01 Tokyo

[Awards & Honors]

1. (Kong S) Eugene Seidner Student Scholarship 2nd prize , ALD, Academy of Laser Dentistry, 2018.04
2. (Aoki A) H30 Peer review achievement Award, Japan Society for Laser Surgery and Medicine, 2018.11

Global Health Promotion

Professor: Takeo Fujiwara, MD, MPH, PhD

Junior Associate Professor: Masashi Kizuki, MD, MPH, PhD

Assistant Professor: Ayako Morita, PhD

Specially Appointed Assistant Professor (Institute of Education); Nobutoshi Nawa, MD, MPH, PhD

Project Assistant Professor: Aya Isumi, PhD; Satomi Doi, PhD

Research Fellow of Japan Society for the Promotion of Science: Yukako Tani, PhD; Yusuke Matsuyama, PhD

(1) Outline

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases. Participants will: understand broad risk factors from individual factors (e.g., genetic factor) and environmental factors, especially social determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

(2) Research

The main focus of the department is as follows:

1. Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
2. Life-course epidemiology (impact of child poverty and adverse childhood experiences on health) and international comparison study
3. Prevention on child abuse and neglect
4. Mental health (antenatal and postnatal mental health, mental health after a disaster, and child mental health)
5. Nutritional epidemiology (childhood nutrition from prenatal to early school-years and the food environment)
6. Environmental health (the physical environment and climate change)
7. Occupational health (harassment and work-place social capital)

(3) Lectures & Courses

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases. Participants will: understand broad risk factors from individual factors (e.g., genetic factor) and environmental factors, especially social determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

The participants will be able to: 1. explain the risk of disease.

2. verbalize own research question and develop a hypothesis to test it.

3. develop research field or access secondary data to test the hypothesis.
4. explain an epidemiologic study design.
5. calculate a sample size.
6. analyse basic model (multivariate analysis, logistic analysis, etc) and conduct advnced analysis (multilevel analysis, propensity score moathcing, multiple imputation, etc)
7. justify the research question logically, in scientific writing in English.
8. develop an intervention (policy or program) and design a study protocol to assess its effectiveness.

(4) Publications

[Original Articles]

1. Aida J, Cable N, Zaninotto P, Tsuboya T, Tsakos G, Matsuyama Y, Ito K, Osaka K, Kondo K, Marmot MG, Watt RG. Social and Behavioural Determinants of the Difference in Survival among Older Adults in Japan and England. *Gerontology*. 2018; 64(3); 266-277
2. Satomi Doi, Masaya Ito, Yoshitake Takebayashi, Kumiyako Muramatsu, Masaru Horikoshi. Factorial validity and invariance of the Patient Health Questionnaire (PHQ)-9 among clinical and non-clinical populations. *Plos One*. 2018; 13(7); e0199235
3. Mari Kawamura, Tomoya Irie, Kengo Yokomitsu, Satomi Doi. Development of "The Nijmegen Motivation List 2 Japanese Version" Which Measures Patient Motivation for Treatment in Cognitive-Behavior Therapy Japanese journal of clinical psychology. 2018; 18(5); 593-603
4. Asuka Tsutsui, Kengo Yokomitsu, Satomi Doi, Yuji Sakano. Examination of psychological factors related to the maintenance of binge eating Behavioral science research. 2018; 57; 1-10
5. Airi Amemiya, Takeo Fujiwara, Hiroshi Murayama, Yukako Tani, Katsunori Kondo. Adverse childhood experiences and higher-level functional limitations among older Japanese people: results from the JAGES study. *JOURNALS OF GERONTOLOGY SERIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES*. 2018.01; 73(2); 261-266
6. Shobugawa Yugo, Fujiwara Takeo, Tashiro Atsushi, Saito Reiko, Kondo Katsunori. Social participation and risk of influenza infection in older adults: a cross-sectional study. *BMJ OPEN*. 2018.01; 8(1); e016876
7. Yanagi N, Hata A, Kondo K, Fujiwara T. Association between childhood socioeconomic status and fruit and vegetable intake among older Japanese: The JAGES 2010 study. *Preventive medicine*. 2018.01; 106; 130-136
8. Nawa N, Ishida H, Sugino H, Katsuragi S, Baden H, Takahashi K, Narita J, Kogaki S, Ozono K. Analysis of public discourse on heart transplantation in Japan using social network service data. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*. 2018.01; 18(1); 232-237
9. Doi, S., Fujiwara, T., Ochi, M., Isumi, A., & Kato, T.. Association of sleep habits with behavior problems and resilience of 6- to 7-year-old children: Results from the A-CHILD study *Sleep Medicine*. 2018.02; 45; 62-68
10. Nawa N. Loop-Mediated Isothermal Amplification test for the diagnosis of pertussis in Japan. *Vaccine*. 2018.02; 36(6); 771
11. Matsuyama Y, Tsuboya T, Bessho SI, Aida J, Osaka K. Copayment Exemption Policy and Healthcare Utilization after the Great East Japan Earthquake. *The Tohoku journal of experimental medicine*. 2018.02; 244(2); 163-173
12. Maho Haseda, Naoki Kondo, Toyo Ashida, Yukako Tani, Daisuke Takagi, Katsunori Kondo. Community Social Capital, Built Environment, and Income-Based Inequality in Depressive Symptoms Among Older People in Japan: An Ecological Study From the JAGES Project. *J Epidemiol*. 2018.03; 28(3); 108-116
13. Yuri Sasaki, Jun Aida, Taishi Tsuji, Yasuhiro Miyaguni, Yukako Tani, Shihoko Koyama, Yusuke Matsuyama, Yukihiro Sato, Toru Tsuboya, Yuiko Nagamine, Yoshihito Kameda, Tami Saito, Kazuhiro Kaki-moto, Katsunori Kondo, Ichiro Kawachi. Does Type of Residential Housing Matter for Depressive Symptoms in the Aftermath of a Disaster? Insights From the Great East Japan Earthquake and Tsunami. *Am. J. Epidemiol.*. 2018.03; 187(3); 455-464

14. Takada S, Kameoka S, Okuyama M, Fujiwara T, Yagi J, Iwadare Y, Honma H, Mashiko H, Nagao K, Fujibayashi T, Asano Y, Yamamoto S, Osawa T, Kato H. Feasibility and psychometric properties of the UCLA PTSD reaction index for DSM-5 in Japanese youth: A multi-site study. *Asian journal of psychiatry*. 2018.03; 33; 93-98
15. Matsuyama Y, Aida J, Tsuboya T, Koyama S, Sato Y, Hozawa A, Osaka K. Social Inequalities in Second-hand Smoke Among Japanese Non-smokers: A Cross-Sectional Study. *Journal of epidemiology*. 2018.03; 28(3); 133-139
16. Sato Y, Aida J, Tsuboya T, Shirai K, Koyama S, Matsuyama Y, Kondo K, Osaka K. Generalized and particularized trust for health between urban and rural residents in Japan: A cohort study from the JAGES project. *Social science & medicine (1982)*. 2018.04; 202; 43-53
17. Doi Satomi, Fujiwara Takeo, Ochi Manami, Isumi Aya, Kato Tsuguhiko. Association of sleep habits with behavior problems and resilience of 6-to 7-year-old children: results from the A-CHILD study SLEEP MEDICINE. 2018.05; 45; 62-68
18. Tani Yukako, Fujiwara Takeo, Ochi Manami, Isumi Aya, Kato Tsuguhiko. Does Eating Vegetables at Start of Meal Prevent Childhood Overweight in Japan? A-CHILD Study. *Frontiers in Pediatrics*. 2018.05; 6; 134
19. Ogawa Kohei, Morisaki Naho, Kobayashi Minatsu, Jwa Seung Chik, Tani Yukako, Sago Haruhiko, Horikawa Reiko, Fujiwara Takeo. Maternal vegetable intake in early pregnancy and wheeze in offspring at the age of 2 years. *EUROPEAN JOURNAL OF CLINICAL NUTRITION*. 2018.05; 72(5); 761-771
20. Kachi Yuko, Fujiwara Takeo, Yamaoka Yui, Kato Tsuguhiko. Parental Socioeconomic Status and Weight Faltering in Infants in Japan. *Frontiers in Pediatrics*. 2018.05; 6; 127
21. Doi S, Fujiwara T, Isumi A, Ochi M, Kato T. Relationship Between Leaving Children at Home Alone and Their Mental Health: Results From the A-CHILD Study in Japan. *Frontiers in psychiatry*. 2018.05; 9(192);
22. Igarashi A, Aida J, Sairenchi T, Tsuboya T, Sugiyama K, Koyama S, Matsuyama Y, Sato Y, Osaka K, Ota H. Does cigarette smoking increase traffic accident death during 20 years follow-up in Japan?: The Ibaraki Prefectural Health Study. *Journal of epidemiology*. 2018.05;
23. Masashi Kizuki, Manami Ochi, Aya Isumi, Tsuguhiko Kato, Takeo Fujiwara. Parental Time of Returning Home From Work and Child Mental Health Among First-Year Primary School Students in Japan: Result From A-CHILD Study. *Frontiers in Pediatrics*. 2018.07; 6; 179
24. Murayama Hiroshi, Fujiwara Takeo, Tani Yukako, Amemiya Airi, Matsuyama Yusuke, Nagamine Yuiko, Kondo Katsunori. Long-term Impact of Childhood Disadvantage on Late-Life Functional Decline Among Older Japanese: Results From the JAGES Prospective Cohort Study. *JOURNALS OF GERONTOLOGY SERIES A-BIOLOGICAL SCIENCES AND MEDICAL SCIENCES*. 2018.07; 73(7); 973-979
25. Kaori Honjo, Yukako Tani, Masashige Saito, Yuri Sasaki, Katsunori Kondo, Ichiro Kawachi, Naoki Kondo. Living Alone or With Others and Depressive Symptoms, and Effect Modification by Residential Social Cohesion Among Older Adults in Japan: The JAGES Longitudinal Study. *J Epidemiol*. 2018.07; 28(7); 315-322
26. Ogawa Kohei, Morisaki Naho, Sago Haruhiko, Fujiwara Takeo, Horikawa Reiko. Association between women's perceived ideal gestational weight gain during pregnancy and pregnancy outcomes. *Scientific Reports*. 2018.08; 8(1); 11574
27. Kizuki Masashi, Fujiwara Takeo. Adult Attachment Patterns Modify the Association Between Social Support and Psychological Distress. *Frontiers in Public Health*. 2018.09; 6; 249
28. Isumi A, Fujiwara T, Nawa N, Ochi M, Kato T. Mediating effects of parental psychological distress and individual-level social capital on the association between child poverty and maltreatment in Japan. *Child abuse & neglect*. 2018.09; 83; 142-150
29. Hikichi H, Aida J, Matsuyama Y, Tsuboya T, Kondo K, Kawachi I. Community-level social capital and cognitive decline after a natural disaster: A natural experiment from the 2011 Great East Japan Earthquake and Tsunami. *Social science & medicine (1982)*. 2018.09;

30. Satomi Doi, Masaya Ito, Yoshitake Takebayashi, Kumiyako Muramatsu, Masaru Horikoshi. Factorial validity and invariance of the 7-item Generalized Anxiety Disorder Scale (GAD-7) among populations with and without self-reported psychiatric diagnostic status *Front Psychol.* 2018.09; 9; 1741
31. Barr RG, Barr M, Rajabali F, Humphreys C, Pike I, Brant R, Hlady J, Colbourne M, Fujiwara T, Singhal A. Eight-year outcome of implementation of abusive head trauma prevention. *Child abuse & neglect.* 2018.10; 84; 106-114
32. Matsuyama Y, Fujiwara T, Ochi M, Isumi A, Kato T. Self-control and dental caries among elementary school children in Japan. *Community dentistry and oral epidemiology.* 2018.10; 46(5); 465-471
33. Takahashi Y, Fujiwara T, Nakayama T, Kawachi I. Subjective social status and trajectories of self-rated health status: a comparative analysis of Japan and the United States. *Journal of public health (Oxford, England).* 2018.10; 40(4); 713-720
34. Tani Y, Suzuki N, Fujiwara T, Hanazato M, Kondo N, Miyaguni Y, Kondo K. Neighborhood food environment and mortality among older Japanese adults: results from the JAGES cohort study. *International Journal of Behavioral Nutrition and Physical Activity.* 2018.10; 15(1); 101
35. Kusama T, Aida J, Sugiyama K, Matsuyama Y, Koyama S, Sato Y, Yamamoto T, Igarashi A, Tsuboya T, Osaka K. Does the type of temporary housing make a difference in social participation and health for evacuees of the Great East Japan Earthquake and Tsunami?: A Cross-sectional Study. *Journal of epidemiology.* 2018.10;
36. Nawa N, Isumi A, Fujiwara T. Community-level social capital, parental psychological distress, and child physical abuse: a multilevel mediation analysis. *Social psychiatry and psychiatric epidemiology.* 2018.11; 53(11); 1221-1229
37. Ando E, Morisaki N, Asakura K, Sasaki S, Fujiwara T, Horikawa R. Serum 25-hydroxyvitamin D levels showed strong seasonality but lacked association with vitamin D intake in 3-year-old Japanese children. *British Journal of Nutrition.* 2018.11; 120(9); 1034-1044
38. Yuiko Nagamine, Naoki Kondo, Kenichi Yokobayashi, Asami Ota, Yasuhiro Miyaguni, Yuri Sasaki, Yukako Tani, Katsunori Kondo. Socioeconomic Disparity in the Prevalence of Objectively Evaluated Diabetes Among Older Japanese Adults: JAGES Cross-Sectional Data in 2010. *J Epidemiol.* 2018.11;
39. Koyama S, Aida J, Cable N, Tsuboya T, Matsuyama Y, Sato Y, Yamamoto T, Kondo K, Osaka K. Sleep duration and remaining teeth among older people. *Sleep medicine.* 2018.12; 52; 18-22

[Misc]

1. Iso Hiroyasu, Matsuo Keitaro, Katanoda Kota, Fujiwara Takeo. New Policy of the Journal of Epidemiology Regarding the Relationship With the Tobacco Industry. *Journal of Epidemiology.* 2018.01; 28(1); 1-2
2. Hashimoto Hideki, Fujiwara Takeo. 日本の小児と青年の健康に関する展望における貧困問題 (Poverty in the perspective of child and adolescent health in Japan). *日本小児科学会雑誌.* 2018.02; 122(2); 164
3. Ichikawa Kayoko, Fujiwara Takeo, Kawachi Ichiro. Prenatal Alcohol Exposure and Child Psychosocial Behavior: A Sibling Fixed-Effects Analysis. *FRONTIERS IN PSYCHIATRY.* 2018.11; 9; 570

[Conference Activities & Talks]

1. Amemiya A, Fujiwara T, Murayama H, Tani Y, Kondo K. Adverse Childhood Experiences and Higher-Level Functional Limitations Among Older Japanese People: Results From the JAGES Study.. *The journals of gerontology. Series A, Biological sciences and medical sciences* 2018.01.16
2. 森田彩子、葛西真理、千田佳子、加藤ゆり子、内柴佑基、高田純子、山本真澄、熊居慶一、中村馨、目黒謙一、青沼孝徳、藤原武男. 日本語版 Quick Mild Cognitive Instrument の構成概念妥当性の検討. 2018.02.01
3. Matsuyama Yusuke, Tsuboya Toru, Bessho Shun-ichiro, Aida Jun, Osaka Ken. 東日本大震災後の患者自己負担の免除政策および医療制度の利用 (Copayment Exemption Policy and Healthcare Utilization after the Great East Japan Earthquake). *The Tohoku Journal of Experimental Medicine* 2018.02.01

4. Doi, S., Fujiwara, T., & Isumi, A. Development of Domestic Violence during Pregnancy Scale (DVPS). 2018.02.03
5. Matsuyama Yusuke, Aida Jun, Tsuboya Toru, Koyama Shihoko, Sato Yukihiro, Hozawa Atsushi, Osaka Ken. 日本人非喫煙者における間接喫煙の社会格差 横断研究 (Social Inequalities in Secondhand Smoke Among Japanese Non-smokers: A Cross-Sectional Study). Journal of Epidemiology 2018.04.01
6. Takeo Fujiwara, Satomi Doi, Aya Isumi. Prediction of intimate partner violence using administrative data on pregnancy. European Congress of Epidemiology 2018.06.04
7. Takeo Fujiwara. school social capital and child mental health. 10th ISSC Conference 2018.06.15 Hvar Croatia
8. Kusama T, Aida J, Tani Y, Shinozaki T, Tsuboya T, Sugiyama K, Koyama S, Igarashi A, Yamamoto T, Yamamoto T, Kondo K, Osaka K. . Does fewer remaining teeth causes weight loss by restricting food intake? . IADR/PER General Session & Exhibition 2018 2018.07
9. Aya Isumi, Takeo Fujiwara, Junko Yagi, Hiroaki Homma, Hirobumi Mashiko, Keizo Nagao, Makiko Okuyama. Causation between child behavior problems and physical abuse in the area affected by the Great East Japan Earthquake and Tsunami. European Congress of Epidemiology 2018 2018.07.05 Lyon, France
10. Ayako Morita, Takeo Fujiwara. Risk for late-life depression associated with childhood suicidal ideation. European Congress of Epidemiology 2018 2018.07.06 Leon, France
11. Takeo Fujiwara. PREDICTION OF INTIMATE PARTNER VIOLENCE USING ADMINISTRATIVE DATA ON PREGNANCY. European Congress of Epidemiology 2018 2018.07.06 LYON FRANCE
12. Takeo Fujiwara. ASSOCIATION BETWEEN CHILDHOOD SUICIDAL IDEATION AND GERIATRIC DEPRESSION: A LIFE-COURSE APPROACH. European Congress of Epidemiology 2018 2018.07.06 LYON FRANCE
13. Takeo Fujiwara. CHILDHOOD POVERTY, PARENTING, AND CARIES: A MEDIATION ANALYSIS. European Congress of Epidemiology 2018 2018.07.06 LYON FRANCE
14. Doi. S, Fujiwara, T., Ochi. M., Isumi. A., Kato. T. Relationships between sleep habits and mental health among Japanese 6 to 7-year-old children: Results from the A-CHILD study. The 21st International Epidemiological Association World Congress of Epidemiology 2018.08.20 Saitama, Japan
15. Nawa N, Isumi A, Fujiwara T. Neighborhood social capital, parental depression, and physical abuse toward children: multilevel mediation analyses. International Society for Prevention of Child Abuse and Neglect (ISPCAN) International Congress on Child Abuse and Neglect 2018.09
16. Sasaki Yuri, Aida Jun, Tsuji Taishi, Miyaguni Yasuhiro, Tani Yukako, Koyama Shihoko, Matsuyama Yusuke, Sato Yukihiro, Kakimoto Kazuhiro, Kondo Katsunori. 被災地域において年配の生存者の隣人との連帯性の変化はうつ症状の発症率と関連しているのか? 長期間のデータの分析 (Does the change of neighborhood tie of older survivors in a disaster area associate with the incidence of depressive symptoms? A longitudinal data analysis). 国際保健医療 2018.09.01
17. Satomi Doi, Takeo Fujiwara. Association between adverse childhood experiences and thoughts of self-harm among postpartum women. ISPCAN XXII International Congress on Child Abuse and Neglect 2018.09.02
18. Takeo Fujiwara, Aya Isumi, Satomi Doi. Development of supporting system for pregnant women using digital devise during home-visit by public health nurse to prevent child maltreatment. 2018.09.02
19. Aya Isumi, Takeo Fujiwara, Hirotaka Kato, Taishi Tsuji, Daisuke Takagi, Naoki Kondo, Katsunori Kondo. Additional medical costs of Japanese older people with childhood maltreatment history: A life-course approach. the ISPCAN XXII International Congress on Child Abuse and Neglect 2018.09.04 Prague, Czech Republic

Environmental Parasitology

Professor : Shiroh IWANAGA
 Lecturer : Takashi KUMAGAI
 Assistant Professor : Naoaki SINZAWA, Sora Enya
 PhD Course Students :
 Kofi Dadzie KWOFIE (D4)
 Michael Amoa-BOSOMPEM (D3)
 Sho ARIMOTO (D3)
 Daniel Addo-GYAN(D2)
 Rie KUBOTA (D1)
 Master Course Students:
 Tsubasa NISHI (M2)
 Taishi HIRAYAMA(M2)
 Takeshi SEKINE(M1)

(1) Outline

Parasitic infectious diseases including Malaria and some neglected tropical diseases have been still prevalent over the world and the countermeasures against them are urgent issues in the global public health. The scientific research plays an important role in not only understanding the biology of the parasites, but also in developing the effective vaccines and new drugs.

Our laboratory carries molecular biological studies out on malaria and schistosome parasites. In particular, we are interested in transcriptional and epigenetic regulation of gene expression in malaria parasites, *P. falciparum*, and the communication between schistosome parasites using the extracellular vesicles including small RNAs. We are also interested in the drug resistance of malaria parasites and are thus attempt to identify the drug resistance gene by *Plasmodium* artificial chromosome, which is developed by us. In addition, we performed the epidemiological studies about *Opisthorchis* and *Schistosomiasis* to develop the new diagnostic tools.

(2) Research

The following studies have been carried out in our laboratory with molecular genetic, cell biological, and biochemical techniques:

- (1) Elucidation of molecular mechanism of transcriptional regulation of Malaria parasite, *P. falciparum*. (the functional analysis of AP2 transcriptional factors)
- (2) Identification of drug resistance genes of Malaria parasite using the artificial chromosome technology.
- (3) Investigation of cell-cell communication of schistosome parasites with extracellular vehicle containing small RNA.
- (4) Host immune response during parasite infection: Th2 response to helminth infection.
- (5) Epidemiological survey of *Opisthorchis* infection and *Schistosomiasis* in SE Asian areas using new diagnostic tools based on LAMP method.

(3) Education

Main objective of the parasitology course for undergraduate students is to provide them the basic knowledge of pathogenicity, treatment and diagnosis of parasitic diseases. We also lecture about the global action against parasitic diseases and basic biology of parasites. In the parasitology course for graduate students, they carry out the advanced molecular biology study about the parasites, in particular malaria and *Schistosoma* parasites, using genetic engineering, cellular biological, genome editing technologies. Furthermore, they have to join the weekly seminar, which are “seminar for the selected papers” and “the study session about the advanced molecular biology”.

(4) Lectures & Courses

Lecture and practices of basic and clinical parasitology are given. Further more, Field practice is important for future career. It is important to have field experiences where each student find matters and problems to be clarified. Together with those, final goal is to develop human resources with enough knowledge and experiences.

(5) Clinical Services & Other Works

Clinical services for the diagnosis of parasitic infections are our routine activities. Furthermore, epidemiological surveillance and disease control activities in the endemic fields are intended to enhance health and welfare of residents.

(6) Publications**[Original Articles]**

1. Keisuke Ishigaki, Naoaki Shinzawa, Sayaka Nishikawa, Koichiro Suzuki, Aya Fukui-Miyazaki, Yasuhiko Horiguchi. Ectopic Expression of O Antigen in *Bordetella pertussis* by a Novel Genomic Integration System. *mSphere*. 2018.01; 3(1);
2. Vicky L Hunt, Akina Hino, Akemi Yoshida, Taisei Kikuchi. Comparative transcriptomics gives insights into the evolution of parasitism in *Strongyloides* nematodes at the genus, subclade and species level. *Sci Rep*. 2018.03; 8(1); 5192
3. Tongchai Payungwong, Naoaki Shinzawa, Akina Hino, Tubasa Nishi, Yuho Murata, Masao Yuda, Shiroh Iwanaga. CRISPR/Cas9 system in *Plasmodium falciparum* using the centromere plasmid. *Parasitology International*. 2018.06; 67(5); 605-608
4. Blay Emmanuel Awusah, Kumagai Takashi, Yamabe Masafumi, Hino Akina, Shimogawara Rieko, Kim Hye-Sook, Sato Akira, Ichimura Koichiro, Ayi Irene, Iwanaga Shiroh, Ohta Nobuo. Insights into the mode of action of 1,2,6,7-tetraoxaspiro [7.11] nonadecane (N-89) against adult *Schistosoma mansoni* worms *PARASITOLOGY INTERNATIONAL*. 2018.08; 67(4); 403-412
5. Aya Fukui-Miyazaki, Hirono Toshima, Yukihiro Hiramatsu, Keisuke Okada, Keiji Nakamura, Keisuke Ishigaki, Naoaki Shinzawa, Hiroyuki Abe, Yasuhiko Horiguchi. The Eukaryotic Host Factor 14-3-3 Inactivates Adenylate Cyclase Toxins of *Bordetella bronchiseptica* and *B. parapertussis*, but Not *B. pertussis*. *MBio*. 2018.08; 9(4);
6. Alafate Ayibieke, Wakana Sato, Samiratu Mahazu, Isaac Prah, John Addow-Thompson, Mitsuko Ohashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Molecular characterisation of the NDM-1-encoding plasmid p2189-NDM in an *Escherichia coli* ST410 clinical isolate from Ghana. *PLoS ONE*. 2018.12; 13(12); e0209623

[Conference Activities & Talks]

1. The evaluations of risk-map using the infected snail with *Schistosoma mekongi* by LAMP assay. 2018.03.18
2. Naoaki Shinzawa, Fumiya Hiyoshi, Akina Hino, Masao Yuda, Shiroh Iwanaga. Highly improved gene targeting by homology directed repair in malaria parasites with constitutive Cas9 expression. 2018.03.18

3. Shiroh Iwanaga. Transcriptional Regulation of Plasmodium parasites: Functional Analysis of AP2 Transcription Factors. 2018.05
4. Shiroh Iwanaga. Evolution of ticks; Involvement of horizontal gene transfer. 70th, Annual meeting of Japanese Medical Entomology. 2018.05.12
5. Shiroh Iwanaga, Masao Yuda. Transcriptional regulation mechanism of Plasmodium parasites.. ICOPA 2018 2018.08
6. Takashi Kumagai et al.. The functional analysis of female-biased mirnas, mir-Bantam, in the extracellular vesicles of Schistosoma japonicum using the Tough-decoy miRNA blocking system.. 14th International Congress of Parasitology. 2018.08.20 Daegu, Korea
7. Takashi Kumagai et al.. Risk-mapping using LAMP method targeting Schistosoma mekongi infections in Lao PDR.. Forum Cheju-20. 2018.08.22 Daegu, Korea
8. Shiroh Iwanaga. Transcriptional Regulation of Plasmodium parasites: Functional Analysis of AP2 Transcription Factors.. 2018.09
9. Takashi Kumagai et al.. THE DEVELOPMENT OF A RISK MAP FOR SCHISTOSOMIASIS MEKONGI BY COMBINING LAMP DIAGNOSIS WITH THE SATELLITE DATA IN CHAMPASAK PROVINCE, LAOS. 12th National Health Research Forum 2018.10.17 Vientiane, Laos
10. Shiroh Iwanaga. The J-GRID project between NMIMR and TMDU. 2018.11

Forensic Medicine

Professor
Koichi UEMURA

Associate Professor
Toshihiko AKI

Junior Associate Professor
Kana UNUMA

Assistant Professor
Takeshi FUNAKOSHI

Specially Appointed Assistant Professor
Kanao NORITAKE
Naho HIRAYAMA

Graduate Student
Ryo WATANABE
Midori NAGAI
Rina KASEDA
Tomomi SANO
Renho TAKAHASHI
Mako FURUKAWA

(1) Research

Research Subjects

- 1) Toxicology
- 2) Alcohol medicine
- 3) Forensic pathology

(2) Education

Purpose of education

Forensic medicine provides fundamental human rights, public safety and nation's welfare to make a fair judgment on the items on the law which requires the medical knowledge. Education of forensic medicine is included forensic medicine in a narrow sense and medical law. Purpose of education in forensic medicine is to provide students opportunity to study the essential knowledge of the relationship between medical and society (include law, ethics, suit and administration). Students are also taught a blood type and an alcohol medicine in a practical training.

(3) Clinical Services & Other Works

Practical services

Forensic Medicine provides the expert opinion on a living body and a corpse to clarify causes of wound and death, mainly entrusted by a public prosecutor or the police, thereby, contributing fair trial in a court.

(4) Publications

[Original Articles]

1. Kana Unuma, Toshihiko Aki, Suguru Nagano, Ryo Watanabe, Koichi Uemura. The down-regulation of cardiac contractile proteins underlies myocardial depression during sepsis and is mitigated by carbon monoxide. *Biochem. Biophys. Res. Commun.* 2018.01; 495(2); 1668-1674
2. Naho Hirayama, Toshihiko Aki, Takeshi Funakoshi, Kanako Noritake, Kana Unuma, Koichi Uemura. Necrosis in human neuronal cells exposed to paraquat. *J Toxicol Sci.* 2018.03; 43(3); 193-202
3. Toshihiko Aki, Kana Unuma, Kanako Noritake, Hatsumi Kurahashi, Takeshi Funakoshi, Koichi Uemura. Interaction of carbon monoxide-releasing ruthenium carbonyl CORM-3 with plasma fibronectin. *Toxicol In Vitro.* 2018.03; 50; 201-209

[Books etc]

1. Toshihiko Aki, Kanako Noritake, Kana Unuma, and Koichi Uemura. “Autophagy in health and disease”, “Stem Cell Biology and Regenerative Medicine” book series. Humana press, Springer-Nature, 2018 (ISBN : 978-3-319-98145-1)
2. Toshihiko Aki, Kanako Noritake, Takeshi Funakoshi, Koichi Uemura.. *Comprehensive Toxicology* 3rd ed Volume 1. Elsevier UK, 2018 (ISBN : 9780081006016)

[Conference Activities & Talks]

1. Hajime Utsuno, Toru Kageyama, Keiichi Uchida, Namiko Ishii, Saki Minegishi, Koichi Sakurada, Koichi Uemura. Morphological sex differences of mid facial proportion in Japanese population. *IALM 2018* 2018.06.06 Fukuoka, Japan
2. Ryo Watanabe, Midori Nagai, Tomomi Sano, Renho Takahashi, Mako Furukawa, Koichi Uemura. A Case Report of Death from invasive Myocoses. *IALM 2018* 2018.06.06
3. Naho Hirayama, Toshihiko Aki, Koichi Uemura. Paraquat-induced cell death pathway, mmitochondrial stress and autophagy in human neuronal cell line SH-SY5Y.. *IALM 2018* 2018.06.06
4. Rina Kaseda, Toshihiko Aki, Koichi Uemura. SH-SY5Y human neuroblastoma cell death by methamphetamine involves downregulation of cell cycle regulators. *IALM 2018* 2018.06.08
5. Kana Unuma, Toshihiko Aki, Ryo Watanabe, Koichi Uemura. Down-regulation of cardiac contractile protein is involved in cardiac dysfunction during sepsis and is mitigated by carbon monoxide. *IALM 2018* 2018.06.08
6. Kanako Noritake, Toshihiko Aki, Koichi Uemura. Involvement of microRNA in ethanol-induced cardiotoxicity. *ISBRA 2018* 2018.09.12 Kyoto

Health Care Management and Planning

Professor Kazuo KAWAHARA

Assistant Professor Makiko SUGAWA

Graduate Student

Masakazu KIKUCHI

Daisuke KUMAZAWA

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Ritsuki NEGISHI

Katsunori OHYAMA

Toshio OHKA

Kiyoyuki TOMITA

Takeshi MATSUI

Hisayuki HASEGAWA

Haruka HANADA

Jian CHEN

(1) Outline

By analyzing the Japanese healthcare policies and system and by reviewing their interaction with society, the structural characteristics and issues can be clarified. To resolve or find better ways to handle these issues, we conduct research into public health and welfare, and its related disciplinary areas. With the cooperation of active policy makers and personnel from the healthcare departments, the research results can be applied to the present healthcare policies and system. Through this education on collecting data, clarifying issues, analyzing the situation, and evaluating options, students taking this course are expected to grow in their ability to make healthcare policies.

(2) Research

In the academic areas mentioned above, we conduct research under the following topic areas:

1) The significance of public healthcare planning, its challenges, and influences on the healthcare system
We conduct research on issues related to new healthcare policies including planning, analysis, issue resolution, and making positive changes to the healthcare plan. This research area includes the Japanese emergency medical service and the impartial evaluation of the travel distance of aid agents and the time required for them to reach their destination.

2) Structural choices concerning national blood services
In Japan, we experienced HIV infection from tainted blood products. There were various causes for this event, and improvements are required in all processes: collecting blood, screening blood, manufacturing blood products, and following-up on the usage of these products. By analyzing background information related to the adverse events and their causes, we can propose the most appropriate policies related to blood services, thus

ensuring safety, and securing a stable supply. To achieve a stable supply of blood products, we also conduct epidemiological studies to review guidelines on collecting blood.

3) Structural analyses of healthcare system in the community

By reviewing and analyzing activities related to disease prevention and health promotion conducted by local healthcare centers, we research the role of the local healthcare system and its effectiveness and efficiency.

4) Systemizing and evaluating public health policies

We review the processes of creating public health policies and systems, address the association with the creating processes and stakeholders such as political parties and lobby groups, evaluate their policies, and then suggest improvements to these policies and systems.

5) The role of healthcare communication to fill in gaps between medical providers and patients, and to share the uncertainties related to medicine and healthcare

6) The influence of healthcare communication on patient and medial safety

7) Reviewing communication tools and skills, and their systematic introduction into the healthcare system in order to realize patient participation and proactive involvement in treatment processes

(3) Education

Through the MMA course, we provide education on the characteristics and issues of Japanese medical policy. In addition, the Graduate School of Policy Science provides lectures on analysis of the current state of the Japanese medical environment and solutions for medical problems. The dates and times of the lectures are as follows.

1)Lecture and Conference 18:00-19:30 Monday

2)Special Lecture as occasion demands 19 : 30-21 : 00 Monday

3)Seminar as occasion demands (Presentation and Conference) 21:00-22:30 Monday

(4) Lectures & Courses

Students are expected to learn how to analyze health and welfare policies adopted domestically and overseas using objective indicators as well as the ability to theoretically and systematically discuss what they think would be the optimal solution.

(5) Publications

[Original Articles]

1. Chiharu Kano, Minoko Takanashi, Asami Suzuki, Kazuo Kawahara, Koichi Chiba, Hideo Nakanishi, Junki Takamatsu, Akiko Kitai, Koki Takahashi. Estimate of future blood demand in Japan and the number of blood donations required ISBT Science Series. 2018;
2. Yoko KOMURA, Takamichi KOGURE, Kazuo KAWAHARA, Hiroo YOKOZEKI. Economic assessment of actual prescription of drugs for treatment of atopic dermatitis: Differences between dermatology and pediatrics in large-scale receipt data The Journal of DERMATOLOGY. 2018.02; 45; 165-174
3. Woonkwan Hyun, Kazuo Kawahara, Miyuki Yokota, Sotaro Miyoshi, Kazunori Nakajima, Koji Matsuzaki, Makiko Sugawa . The Possibility of Increasing the Current Maximum Volume of Platelet Apheresis Donation Journal of Medical and Dental Sciences. 2018.06; 65(2); 89-98

Molecular Epidemiology

Professor: Masaaki MURAMATSU
Associate Professor : Noriko SATO
Assistant Professor : Chihiro Imai

Adjunct Instructor : Tomio Arai

Graduate Student: Fujitani, Tay Zar Kyaw, Tadaaki Katsuta, Shilpa Pavethynath, Maidina Abudushataer,
Ake Ko Ko Minn, Zong Yuan, Yui Tsubota, Naomi Hichiwa, Jin Xin
Research Student: Arisa Nakata, Tong Daike

(1) Outline

Many common chronic diseases are multifactorial in that they are caused by multiple genetic and environmental factors. By applying the technology and information of human genome to epidemiological studies, we aim to clarify the role of genetic polymorphisms, epigenetic changes, as well as their interaction with environmental factors, which may contribute to the development of these diseases.

(2) Research

Our research subjects are as follows.

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
4. The role of epigenetic regulation and fetal programming in common diseases.
5. Application of personal genome to preemptive & preventive medicine.

(3) Education

Masaaki Muramatsu: Holistic Study of Disease Prevention I
Masaaki Muramatsu: Environmental/Social Health
Masaaki Muramatsu: Negotiation and Debate in English
Noriko Sato, Masaaki Muramatsu: Bioscience I
Noriko Sato: Molecular and Cellular Biology
Noriko Sato: Molecular and Cellular Biology

(4) Lectures & Courses

We focus on common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis which are caused by multiple genetic and environmental factors, and aim to decipher these factors as well as

their interactions by applying the technology and information of human genome to epidemiology. Our goal is not only to identify disease genes and polymorphisms but also to elucidate gene-environment interactions that contribute to the onset and progression of the diseases. Epigenetic changes in common diseases are also in our scope. A new project has been started to study methods for educating genome-based health literacy by employing information generated from personal genome sequences.

(5) Publications

[Original Articles]

1. Sayuri Udagawa, Sayaka Katagiri, Shogo Maekawa, Yasuo Takeuchi, Rina Komazaki, Anri Ohtsu, Naoki Sasaki, Takahiko Shiba, Kazuki Watanabe, Kazuyuki Ishihara, Noriko Sato, Naoyuki Miyasaka, Yuichi Izumi. Effect of *Porphyromonas gingivalis* infection in the placenta and umbilical cord in pregnant mice with low birth weight. *Acta Odontol. Scand.*. 2018.01; 1-9
2. Matsuda Yoko, Tanaka Masashi, Sawabe Motoji, Mori Seijiro, Muramatsu Masaaki, Mieno Makiko Naka, Furukawa Toru, Arai Tomio. Relationship between pancreatic intraepithelial neoplasias, pancreatic ductal adenocarcinomas, and single nucleotide polymorphisms in autopsied elderly patients *GENES CHROMOSOMES & CANCER*. 2018.01; 57(1); 12-18
3. Hayashi M, Watanabe A, Muramatsu M, Yamashita N. Effectiveness of personal genomic testing for disease-prevention behavior when combined with careful consultation with a physician: a preliminary study. *BMC research notes*. 2018.04; 11(1); 223

[Misc]

1. Noriko Sato. The Advent of a New Era for Understanding DOHaD: A New Perspective of the Link between Genome/Epigenome and Age-Related Chronic Disease 2018.09; 55(9); 613-620

[Conference Activities & Talks]

1. Noriko Sato. Perinatal Immunomethylomics towards DOHaD. 17 th Surugadai International Symposium & Joint Usage/Research Program of Medical Research Institute International Symposium 2018.11.19 Tokyo

Research Development

Faculty Staff
Professor
Kozo TAKASE

Graduate Students
Doctor course
Akemi HIRABAYASHI
Akira MIURA
Yasumasa OOSHIRO
Hideki TERUYA
Masakazu HARAMO
Rinshuu SHIMABUKURO
Kazushige ENDOH

Master course (Master of Medical Administration)
Tomoyasu ASANO
Koichi ASAMI
Hironori OKABAYASHI
Koji KAWADA
Tsutomu HIROTA
Sae MORI

(1) Outline

Department of Research Development was established in 2000.
This department has been managing the course of Master of Medical Administration.

(2) Research

- 1) Introduction of Clinical Pathway in hospital
- 2) Medical law suit and professional information
- 3) Quality management of medical law suit
- 4) Organizational logic for hospital
- 5) Health care policy and rational
- 6) Management of medical information and privacy
- 7) Hospitality in medicine
- 8) Clinical guideline and medical quality
- 9) Patient satisfaction and patient experience
- 10) Development of medical engineering apparatus

(3) Education

- 1) Hospital Information Management
- 2) Medical Informatics, statistics
- 3) TQM in medicine
- 4) Biological bias and data management
- 5) Medical Law and Ethics
- 6) Medical induction course for Judges and Prosecutors (collaborated with the Supreme Court and Department of Justice)
- 7) Health Promotion Policy program (General Medicine, Risk Management in Medicine) with Hitotsubashi University

(4) Lectures & Courses

Study on development of medical system and hospital management

Goals/outline:

The goals supposed in the lecture are mastering the technique of implementation of research development and acquiring the ability of management of projects.

(5) Clinical Services & Other Works

Kozo TAKASE

Committee member of Legal Training for Judicial Apprentice, Japanese Supreme Court

Committee member of Tokyo District Court

Chief Editorial Board of Japanese Society for Clinical Pathway

(6) Publications**[Misc]**

1. Hiromasa Sakaguchi, Ko Arai, Kozo Takase. A Preliminary Investigation on Management Education for Hospital Staff: Focusing on Accounting Education in Hospital Group Organization Journal of Japanese Association for Health Care Administrators. 2018.02; 11(1); 17-23

Health Policy and Informatics

Professor: Kiyohide FUSHIMI

Graduate Student: Asako TUKASAKI, Kyoko SHINODA,
Ayako MATSUO, Yuya MIZUNO, Tetu OHNUMA, Akira HOMMA,
Eishi UECHI, Tomomitsu ICHIKAWA, Mariko KODAN,
Norihiko INOUE, Kyoko HIRANO, Mihoko OTA, Ken KAWASAKI,
Natsuko KANAZAWA, Shunsuke EDAKUBO, Yoshiteru YANO,
Senri WATANABE, Risa SUZUKI, Akihito UDA, Yuka SATO,
Takuaki Tani, Sayomi Tsukada, Kyunghee Lee
Graduate Research Student: Masahiro INOUE

(1) Research

- 1) Functional differentiation and coordination of healthcare facilities
- 2) Development and application of patient case mix system for Japanese healthcare settings
- 3) Application of information technology to standardization of health care and sharing of health care information.

(2) Education

Health policy informatics is a branch of health policy science which deals with the application of information technology to health policy research. Main objective of health policy informatics in the graduate course is to acquire ability to independently design, manage and accomplish researches in health policy and health informatics fields.

(3) Publications

[Original Articles]

1. Kikuchi H, Kanda E, Mori T, Sato H, Iimori S, Nomura N, Naito S, Sohara E, Okado T, Uchida S, Fushimi K, Rai T. Short-term prognosis of emergently hospitalized dialysis-independent chronic kidney disease patients: A nationwide retrospective cohort study in Japan. *PloS one*. 2018; 13(11); e0208258
2. Hiroyuki Toi, Keita Kinoshita, Satoshi Hirai, Hiroki Takai, Keiji Hara, Nobuhisa Matsushita, Shunji Matsubara, Makoto Otani, Keiji Muramatsu, Shinya Matsuda, Kiyohide Fushimi, Masaaki Uno. Present epidemiology of chronic subdural hematoma in Japan: analysis of 63,358 cases recorded in a national administrative database. *J. Neurosurg.* 2018.01; 128(1); 222-228
3. Yusuke Okubo, Nobuaki Michihata, Naho Morisaki, Mayumi Hangai, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Recent trends in practice patterns and comparisons between immunoglobulin and corticosteroid in pediatric immune thrombocytopenia. *Int. J. Hematol.* 2018.01; 107(1); 75-82

4. Keiji Muramatsu, Yoshihisa Fujino, Tatsuhiko Kubo, Makoto Otani, Kiyohide Fushimi, Shinya Matsuda. Efficacy of Antimicrobial Catheters for Prevention of Catheter-Associated Urinary Tract Infection in Acute Cerebral Infarction. *J Epidemiol.* 2018.01; 28(1); 54-58
5. Yoshifumi Mizobuchi, Makoto Ohtani, Junichiro Satomi, Kiyohide Fushimi, Shinya Matsuda, Shinji Nagahiro. The Current Status of Microvascular Decompression for the Treatment of Trigeminal Neuralgia in Japan: An Analysis of 1619 Patients Using the Japanese Diagnosis Procedure Combination Database. *Neurol. Med. Chir. (Tokyo).* 2018.01; 58(1); 10-16
6. Seiko Mizuno, Susumu Kunisawa, Noriko Sasaki, Kiyohide Fushimi, Yuichi Imanaka. Effects of night-time and weekend admissions on in-hospital mortality in acute myocardial infarction patients in Japan. *PLoS ONE.* 2018.01; 13(1); e0191460
7. Keishi Oda, Kazuhiro Yatera, Yoshihisa Fujino, Takashi Kido, Tetsuya Hanaka, Konomi Sennari, Kiyohide Fushimi, Shinya Matsuda, Hiroshi Mukae. Respiratory comorbidities and risk of mortality in hospitalized patients with idiopathic pulmonary fibrosis. *Respir Investig.* 2018.01; 56(1); 64-71
8. Tomoki Wada, Hideo Yasunaga, Kent Doi, Hiroki Matsui, Kiyohide Fushimi, Yoichi Kitsuta, Susumu Nakajima. Impact of hospital volume on mortality in patients with severe torso injury. *J. Surg. Res.* 2018.02; 222; 1-9
9. Yusuke Okubo, Nobuaki Michihata, Kazuhiro Uda, Naho Morisaki, Isao Miyairi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Dose-response relationship between weight status and clinical outcomes in pediatric influenza-related respiratory infections. *Pediatr. Pulmonol.* 2018.02; 53(2); 218-223
10. Yasuko Abe, Kentaro Shimokado, Kiyohide Fushimi. Donepezil is associated with decreased in-hospital mortality as a result of pneumonia among older patients with dementia: A retrospective cohort study. *Geriatr Gerontol Int.* 2018.02; 18(2); 269-275
11. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi, Hideo Yasunaga. Clinical characteristics of patients with Takotsubo syndrome diagnosed without coronary artery evaluation: A retrospective nationwide study. *J Cardiol.* 2018.03; 71(3); 268-276
12. Chie Koizumi, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. In-Hospital Mortality for Hepatic Portal Venous Gas: Analysis of 1590 Patients Using a Japanese National Inpatient Database. *World J Surg.* 2018.03; 42(3); 816-822
13. Asuka Tsuchiya, Hideo Yasunaga, Yusuke Tsutsumi, Hiroki Matsui, Kiyohide Fushimi. Mortality and Morbidity After Hartmann's Procedure Versus Primary Anastomosis Without a Diverting Stoma for Colorectal Perforation: A Nationwide Observational Study. *World J Surg.* 2018.03; 42(3); 866-875
14. Yusuke Okubo, Nobuaki Michihata, Naho Morisaki, Kazuhiro Uda, Isao Miyairi, Yuichi Ogawa, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Recent trends in practice patterns and impact of corticosteroid use on pediatric Mycoplasma pneumoniae-related respiratory infections. *Respir Investig.* 2018.03; 56(2); 158-165
15. Tetsu Ohnuma, Daisuke Shinjo, Alan M Brookhart, Kiyohide Fushimi. Predictors associated with unplanned hospital readmission of medical and surgical intensive care unit survivors within 30 days of discharge. *J Intensive Care.* 2018.03; 6; 14
16. Yusuke Sawada, Yusuke Sasabuchi, Yasuo Nakahara, Hiroki Matsui, Kiyohide Fushimi, Nobuhiko Haga, Hideo Yasunaga. Early Rehabilitation and In-Hospital Mortality in Intensive Care Patients With Community-Acquired Pneumonia. *Am. J. Crit. Care.* 2018.03; 27(2); 97-103
17. Shintaro Mandai, Hidehiko Sato, Soichiro Iimori, Shotaro Naito, Takayasu Mori, Daiei Takahashi, Moko Zeniya, Naohiro Nomura, Eisei Sohara, Tomokazu Okado, Shinichi Uchida, Kiyohide Fushimi, Tatemitsu Rai. Dialysis Case Volume Associated With In-Hospital Mortality in Maintenance Dialysis Patients. *Kidney International Reports.* 2018.03; 3(2); 356-363
18. Hiraku Funakoshi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Variation in Patient Backgrounds, Practice Patterns, and Outcomes of High-Risk Pulmonary Embolism in Japan. *Int Heart J.* 2018.03; 59(2); 367-371

19. Tomoki Wada, Hideo Yasunaga, Hayato Yamana, Hiroki Matsui, Kiyohide Fushimi, Naoto Morimura. Development and validation of an ICD-10-based disability predictive index for patients admitted to hospitals with trauma. *Injury*. 2018.03; 49(3); 556-563
20. Hiroko Okinaga, Hideo Yasunaga, Kiyoshi Hasegawa, Kiyohide Fushimi, Norihiro Kokudo. Short-Term Outcomes following Hepatectomy in Elderly Patients with Hepatocellular Carcinoma: An Analysis of 10,805 Septuagenarians and 2,381 Octo- and Nonagenarians in Japan. *Liver Cancer*. 2018.03; 7(1); 55-64
21. Mikio Nakajima, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Clinical features and outcomes of tetanus: Analysis using a National Inpatient Database in Japan. *J Crit Care*. 2018.04; 44; 388-391
22. Yusuke Okubo, Naho Morisaki, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Dose-dependent relationships between weight status and clinical outcomes among infants hospitalized with respiratory syncytial virus infections. *Pediatr. Pulmonol*. 2018.04; 53(4); 461-466
23. Eishi Uechi, Masato Okada, Kiyohide Fushimi. Effect of plasma exchange on in-hospital mortality in patients with pulmonary hemorrhage secondary to antineutrophil cytoplasmic antibody-associated vasculitis: A propensity-matched analysis using a nationwide administrative database. *PLoS ONE*. 2018.04; 13(4); e0196009
24. Yuki Taniguchi, Takeshi Oichi, Junichi Ohya, Hirotaka Chikuda, Yasushi Oshima, Yoshitaka Matsubayashi, Hiroki Matsui, Kiyohide Fushimi, Sakae Tanaka, Hideo Yasunaga. In-hospital mortality and morbidity of pediatric scoliosis surgery in Japan: Analysis using a national inpatient database. *Medicine (Baltimore)*. 2018.04; 97(14); e0277
25. Manabu Kawata, Yusuke Sasabuchi, Shuji Taketomi, Hiroshi Inui, Hiroki Matsui, Kiyohide Fushimi, Hirotaka Chikuda, Hideo Yasunaga, Sakae Tanaka. Annual trends in arthroscopic meniscus surgery: Analysis of a national database in Japan. *PLoS ONE*. 2018.04; 13(4); e0194854
26. H Abe, M Sumitani, K Uchida, T Ikeda, H Matsui, K Fushimi, H Yasunaga, Y Yamada. Association between mode of anaesthesia and severe maternal morbidity during admission for scheduled Caesarean delivery: a nationwide population-based study in Japan, 2010-2013. *Br J Anaesth*. 2018.04; 120(4); 779-789
27. Yusuke Sasabuchi, Hiroki Matsui, Alan Kowarai Lefor, Taisuke Jo, Nobuaki Michihata, Kiyohide Fushimi, Hideo Yasunaga. Japanese Herbal Kampo Hochu-Ekki-To or Juzen-Taiho-To after Surgery for Hip Fracture Does Not Reduce Infectious Complications. *Evid Based Complement Alternat Med*. 2018.04; 2018(8620198); 6
28. Nobuo Sakata, Yasuyuki Okumura, Kiyohide Fushimi, Miharuru Nakanishi, Asao Ogawa. Dementia and Risk of 30-Day Readmission in Older Adults After Discharge from Acute Care Hospitals. *J Am Geriatr Soc*. 2018.05; 66(5); 871-878
29. Takeshi Umegaki, Susumu Kunisawa, Yasufumi Nakajima, Takahiko Kamibayashi, Kiyohide Fushimi, Yuichi Imanaka. Comparison of In-hospital Outcomes Between Transcatheter and Surgical Aortic Valve Replacement in Patients with Aortic Valve Stenosis: A Retrospective Cohort Study Using Administrative Data. *J. Cardiothorac. Vasc. Anesth*. 2018.06; 32(3); 1281-1288
30. Hiroji Shinkawa, Hideo Yasunaga, Kiyoshi Hasegawa, Hiroki Matsui, Kiyohide Fushimi, Nobuaki Michihata, Norihiro Kokudo. Mortality and morbidity after hepatic resection in patients undergoing hemodialysis: analysis of a national inpatient database in Japan. *Surgery*. 2018.06; 163(6); 1234-1237
31. Kazuhiro Uda, Yusuke Okubo, Kensuke Shoji, Isao Miyairi, Naho Morisaki, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Trends of neuraminidase inhibitors use in children with influenza related respiratory infections. *Pediatr. Pulmonol*. 2018.06; 53(6); 802-808
32. Akira Endo, Atsushi Shiraishi, Kiyohide Fushimi, Kiyoshi Murata, Yasuhiro Otomo. Comparative effectiveness of elemental formula in the early enteral nutrition management of acute pancreatitis: a retrospective cohort study. *Ann Intensive Care*. 2018.06; 8(1); 69
33. Akihisa Mitani, Taisuke Jo, Hideo Yasunaga, Yukiyo Sakamoto, Wakae Hasegawa, Hirokazu Urushiyama, Yasuhiro Yamauchi, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Venous thromboembolic events in patients with lung cancer treated with cisplatin-based versus carboplatin/nedaplatin-based chemotherapy. *Anticancer Drugs*. 2018.07; 29(6); 560-564

34. Yusuke Okubo, Nobuaki Michihata, Naho Morisaki, Robert P Sundel, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Association Between Dose of Glucocorticoids and Coronary Artery Lesions in Kawasaki Disease. *Arthritis Care Res (Hoboken)*. 2018.07; 70(7); 1052-1057
35. Hayato Yamana, Mariko Kodan, Sachiko Ono, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Tomoaki Imamura, Hideo Yasunaga. Hospital quality reporting and improvement in quality of care for patients with acute myocardial infarction. *BMC Health Serv Res*. 2018.07; 18(1); 523
36. Sayaka Suzuki, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Mizuo Ando, Tatsuya Yamasoba. Postoperative mechanical bowel obstruction after pharyngolaryngectomy for hypopharyngeal cancer: Retrospective analysis using a Japanese inpatient database. *Head Neck*. 2018.07; 40(7); 1548-1554
37. A Endo, A Shiraishi, K Fushimi, K Murata, Y Otomo. Outcomes of patients receiving a massive transfusion for major trauma. *Br J Surg*. 2018.07;
38. Toba M, Moriwaki M, Oshima N, Aiso Y, Shima M, Nukui Y, Obayashi S, Fushimi K. Prevention of surgical site infection via antibiotic administration according to guidelines after gynecological surgery. *The journal of obstetrics and gynaecology research*. 2018.07;
39. Fumino Tadokoro, Kojiro Morita, Nobuaki Michihata, Kiyohide Fushimi, Hideo Yasunaga. Association between sugammadex and anaphylaxis in pediatric patients: A nested case-control study using a national inpatient database. *Paediatr Anaesth*. 2018.07; 28(7); 654-659
40. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Akira Kohyama, Kiyohide Fushimi, Hideo Yasunaga. Clinical features and peripartum outcomes in pregnant women with cardiac disease: a nationwide retrospective cohort study in Japan. *Heart Vessels*. 2018.08; 33(8); 918-930
41. Hirokazu Urushiyama, Taisuke Jo, Hideo Yasunaga, Nobuaki Michihata, Hayato Yamana, Hiroki Matsui, Wakae Hasegawa, Yoshihisa Hiraishi, Akihisa Mitani, Kiyohide Fushimi, Takahide Nagase, Yasuhiro Yamauchi. Effect of Hangeshashin-To (Japanese Herbal Medicine Tj-14) on Tolerability of Irinotecan: Propensity Score and Instrumental Variable Analyses. *J Clin Med*. 2018.08; 7(9);
42. Hiroyuki Ohbe, Taisuke Jo, Hayato Yamana, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Early enteral nutrition for cardiogenic or obstructive shock requiring venoarterial extracorporeal membrane oxygenation: a nationwide inpatient database study. *Intensive Care Med*. 2018.08; 44(8); 1258-1265
43. Akira Endo, Atsushi Shiraishi, Kiyohide Fushimi, Kiyoshi Murata, Yasuhiro Otomo. Impact of continuous regional arterial infusion in the treatment of acute necrotizing pancreatitis: analysis of a national administrative database. *J. Gastroenterol.*. 2018.09; 53(9); 1098-1106
44. Kazuhiko Nakaharai, Kojiro Morita, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Early prophylactic antibiotics for severe acute pancreatitis: A population-based cohort study using a nationwide database in Japan. *J. Infect. Chemother*. 2018.09; 24(9); 753-758
45. Hiroyuki Ohbe, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Cholinergic Crisis Caused by Cholinesterase Inhibitors: a Retrospective Nationwide Database Study. *J Med Toxicol*. 2018.09; 14(3); 237-241
46. Taisuke Jo, Hideo Yasunaga, Nobuaki Michihata, Yusuke Sasabuchi, Wakae Hasegawa, Hideyuki Takeshima, Yukiyo Sakamoto, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase, Yasuhiro Yamauchi. Influence of Parkinsonism on outcomes of elderly pneumonia patients. *Parkinsonism Relat. Disord*. 2018.09; 54; 25-29
47. Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Effect of cyclosporine A on mortality after acute exacerbation of idiopathic pulmonary fibrosis. *J Thorac Dis*. 2018.09; 10(9); 5275-5282
48. Naoyoshi Nagata, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Kazuhiro Watanabe, Junichi Akiyama, Naomi Uemura, Ryota Niikura. Therapeutic endoscopy-related GI bleeding and thromboembolic events in patients using warfarin or direct oral anticoagulants: results from a large nationwide database analysis. *Gut*. 2018.10; 67(10); 1805-1812
49. Yuko Sato, Mitsunori Miyashita, Kazuki Sato, Kenji Fujimori, Koichi Benjamin Ishikawa, Hiromasa Horiguchi, Kiyohide Fushimi, Chikashi Ishioka. End-of-life care for cancer patients in Japanese acute care hospitals: A nationwide retrospective administrative database survey. *Jpn. J. Clin. Oncol*. 2018.10; 48(10); 877-883

50. Yusuke Sasabuchi, Hiroki Matsui, Alan Kawai Lefor, Kiyohide Fushimi, Hideo Yasunaga. Timing of surgery for hip fractures in the elderly: A retrospective cohort study. *Injury*. 2018.10; 49(10); 1848-1854
51. Hirokazu Urushiyama, Taisuke Jo, Hideo Yasunaga, Nobuaki Michihata, Hiroki Matsui, Wakae Hasegawa, Hideyuki Takeshima, Yukiyo Sakamoto, Yoshihisa Hiraishi, Akihisa Mitani, Kiyohide Fushimi, Takahide Nagase, Yasuhiro Yamauchi. Oral fluorouracil vs vinorelbine plus cisplatin as adjuvant chemotherapy for stage II-III non-small cell lung cancer: Propensity score-matched and instrumental variable analyses. *Cancer Med*. 2018.10; 7(10); 4863-4869
52. Takeshi Oichi, Yasushi Oshima, Hirotaka Chikuda, Junichi Ohya, Hiroki Matsui, Kiyohide Fushimi, Sakae Tanaka, Hideo Yasunaga. In-hospital complication rate following microendoscopic versus open lumbar laminectomy: a propensity score-matched analysis. *Spine J*. 2018.10; 18(10); 1815-1821
53. Yoshitaka Kinoshita, Toru Sugihara, Hideo Yasunaga, Hiroki Matsui, Akira Ishikawa, Tetsuya Fujimura, Hiroshi Fukuhara, Yoshitaka Ishibashi, Kiyohide Fushimi, Yukio Homma. Hospital-Volume Effects on Perioperative Outcomes in Peritoneal Dialysis Catheter Implantation: Analysis of 2,505 Cases. *Perit Dial Int*. 2018.11; 38(6); 419-423
54. Sayaka Suzuki, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Tatsuya Yamasoba. Trend in otolaryngological surgeries in an era of super-aging: Descriptive statistics using a Japanese inpatient database. *Auris Nasus Larynx*. 2018.12; 45(6); 1239-1244
55. Michimasa Fujiogi, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Jun Fujishiro. Postoperative Small Bowel Obstruction Following Laparoscopic or Open Fundoplication in Children: A Retrospective Analysis Using a Nationwide Database. *World J Surg*. 2018.12; 42(12); 4112-4117
56. Asuka Tsuchiya, Hayato Yamana, Takuya Kawahara, Yusuke Tsutsumi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Tracheostomy and mortality in patients with severe burns: A nationwide observational study. *Burns*. 2018.12; 44(8); 1954-1961
57. Manabu Kawata, Yusuke Sasabuchi, Shuji Taketomi, Hiroshi Inui, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Sakae Tanaka. Atopic dermatitis is a novel demographic risk factor for surgical site infection after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2018.12; 26(12); 3699-3705
58. Taisuke Jo, Nobuaki Michihata, Hayato Yamana, Yusuke Sasabuchi, Hiroki Matsui, Hirokazu Urushiyama, Akihisa Mitani, Yasuhiro Yamauchi, Kiyohide Fushimi, Takahide Nagase, Hideo Yasunaga. Reduction in exacerbation of COPD in patients of advanced age using the Japanese Kampo medicine Dai-kenchu-to: a retrospective cohort study. *Int J Chron Obstruct Pulmon Dis*. 2018.12; 14; 129-139
59. Takeshi Aoyama, Susumu Kunisawa, Kiyohide Fushimi, Teiji Sawa, Yuichi Imanaka. Comparison of surgical and conservative treatment outcomes for type a aortic dissection in elderly patients. *J Cardiothorac Surg*. 2018.12; 13(1); 129

[Conference Activities & Talks]

1. Moriwaki, M., Toba, M., Obayashi, S., Fushimi, K. Risk Analysis of the Incidence of Fractures in Hospitalized Patients Aged 75 Years and Older. International Forum on QUALITY & SAFETY in HEALTH-CARE. 2018.09.10 Melbourne, Australia
2. Shinjo, D., Matsumoto, K., Terashima, K., Takimoto, T., Noguchi, T., Fushimi, K. Brain tumor resection surgery in pediatric patients; retrospective epidemiological study using Japanese Administrative database. ISPOR Europe 2018. 2018.11.10 Barcelona, Spain

Life Sciences and Bioethics

Masayuki Yoshida
Yusuke Ebana
Hiroko Kohbata
Mizuko Osaka
Eiichiro Kanda

(1) Outline

Department of Life Sciences and Bioethics (Bioethics Research Center) offers classes and seminars regarding bioethics, research ethics, and clinical ethics in Graduate School of Medical and Dental Sciences, Graduate School of Health Care Sciences, and School of Medicine. Our lecture includes fundamental bioethics and research ethics so that students can absorb the current concept of the bioethics and research ethics. We try to include clinical materials such as cases of genetic counseling, where ethics-based approach is critically important.

Apart from class for juniors, we give bioethics seminars for hospital staff and faculties based on the research ethics guideline revised 2008, in which attendance of bioethics lecture is mandatory for any person who conducts medical research.

We dynamically participated in extra-campus activities; such as the ethical committee members of the National Institute of Health etc.

(2) Publications

[Original Articles]

1. 鶴 裕美, 大坂 瑞子, 吉田 雅幸. 高脂肪食誘発性の血管の炎症における補体系 D 因子の潜在的役割 (Potential Role of Complement Factor D in High-fat Diet-induced Vascular Inflammation) 日本循環器学会学術集会抄録集. 2018.03; 82 回; PJ035-2
2. Tani M, Kamata Y, Deushi M, Osaka M, Yoshida M.. 7-Ketocholesterol enhances leukocyte adhesion to endothelial cells via p38MAPK pathway. PLoS One. 2018.06; 13(7); e0200499
3. Tani M, Kamata Y, Deushi M, Osaka M, Yoshida M. 7-Ketocholesterol enhances leukocyte adhesion to endothelial cells via p38MAPK pathway PloS one. 2018.06;
4. Yoshida Masayuki, Osaka Mizuko. POTENTIAL ROLE OF NEUTROPHIL-MEDIATED VASCULAR INFLAMMATION AND NET FORMATION IN ATHEROSCLEROSIS ATHEROSCLEROSIS SUPPLEMENTS. 2018.06; 32; 107

[Misc]

1. Yusuke Ebana. Establishment of Certified Research Ethics Committee Professionals in Japan Journal of New Remedies & Clinics. 2018.10; 67(10); 1251-1253

[Conference Activities & Talks]

1. Osaka M, Deushi M, Yoshida M. Citrullinated neutrophil plays a key role in high fat diet-induced atherosclerotic plaque formation in LDL receptor null mice. 1st JCS Council Forum on Basic Cardio-Vascular Research 2018.01.06 Shinagwa, Japan
2. Osaka M, Yoshida M. High fat diet-triggered neutrophil activation initiates leukocyte adhesion to murine artery in vivo.. 23rd Annual Scientific meeting of ISCP 2018 2018.05.26 Kyoto, Japan
3. Tani M, Kamata Y, Deushi M, Osaka M, Yoshida M. 7-ketocholesterol Induces Leukocyte Interaction to Endothelial Cells thorough p38MAPK-dependent pathway. The 23rd Annual Scientific Meeting of International Society of Cardiovascular Pharmacotherapy 2018.05.26
4. Osaka M, Deushi M, Yoshida M. Neutrophil extracellular traps (NETs) triggers atherosclerotic lesion development in high fat diet fed mice. . The 20th International Vascular Biology Meeting 2018 2018.06.03 Helsinki, Finland
5. Mizuko Osaka. Involvement of neutrophil extracellular trap (NET) for formation of atherosclerotic lesion. Japan Atheroscleorir Society 2018.07.12
6. Hiromi Tsuru, Mizuko Osaka, Masayuki Yoshida. High-fat diet promote complement factor in liver. 2018.07.12
7. Syed Masudur Rahman Dewan, Mizuko Osaka, Masayuki Yoshida. Complement component C5a induces qualitative change on neutrophil-endothelial interaction under physiological flow condition. 第16回日韓血管生物合同シンポジウム 2018.09.14
8. The role of the department of medical genetics in precision cancer medicine. 2018.10
9. Yusuke Ebana. Genetics of atrial fibrillation in Japanese Population. The 11th Asia Pacific Heart Rhythm Society Scientific Session 2018.10.15 Taipei, Taiwan
10. Mizuko Osaka. Curcial role of neutrophil-citrullination on high-fat diet-induced vasuclar inflammation. The 41st Annual Meeting of the Molecular Biology Society of Japan 2018.11.12
11. Hiromi Tsuru, Mizuko Osaka, Masayuki Yoshida. The effect of complement factor D (FD) on the development of non-alcoholic fatty liver disease (NAFLD). Cardiovascular and Metabolic Week 2018 2018.12.07

[Awards & Honors]

1. Ueda Award, Japanese College of Cardiology, 2018.09

[Others]

1. Grant-in-Aid for Young Scientists (B) JSPS KAKENHI (16K19048)
S-nitrosylation, a novel posttranslational protein modification, mediated glycolipid metabolism disorder and chronic inflammation. 2016-2017
2. Takeda Science Foundation for Medical Research
The missing link between the metabolic syndrome pathogenesis and chronic inflammation. 2016-2018
3. Grant-in-Aid for Exploratory Research JSPS KAKENHI (16K15120)
Elucidation of a role of de-nitrosylation in septic myocardial injury and development for therapeutic drugs. PI: Toshihiro Tanioka. Role on Project: Co- Investigator 2016-2017

Forensic Dentistry

Professor Koichi SAKURADA
 Assistant Professor Hajime UTSUNO
 Assistant Professor Namiko ISHII
 Graduate Student Saki MINEGISHI
 Graduate Student Jun OHTA
 Graduate Student Chihiro TANAKA

(1) Outline

Forensic dentistry plays an important role in society through the use identification of victims after major accidents or disasters using dental findings, as well as the identification of cadavers or persons from biological samples in relation to crime. In particular, the establishment of two laws related to cause of death investigation in June 2012 further promoted research, identification, and education related to individual identification. The primary function of our laboratory is the identification of individuals from hard tissues such as teeth and bones, soft tissues, body fluids, or facial images, using the latest molecular biological and imaging techniques.

(2) Research

1. Individual identification
 - Identification based on dental findings
 - Identification using hard tissues such as teeth and bones, soft tissues, and body fluids
 - Identification based on facial reconstruction and image analysis
2. Child abuse and neglect
3. Dental accidents and lawsuits
4. Problems associated with the dental care system
5. Forensic toxicology

(3) Education

We teach dental students a relation between death investigation systems and dentists and make them understand that society expects them as dentists to perform individual identification based on dental findings. Also, students are likely to have opportunities to assist the regional administrative and police activities in the future. To protect the rights of the deceased individuals and improve public health, dental students need to acquire basic knowledge about forensic medical sciences including postmortem changes and cause of death identification. To foster independent researchers, we teach graduate students the latest research directions in forensic dentistry and how to plan their own research project. In addition, students learn practical individual identification methods and their importance through forensic autopsy.

(4) Lectures & Courses

We believe that students learn more effectively in an environment where they can simultaneously conduct practical work and research.

(5) Clinical Services & Other Works

Forensic autopsy for the identification of cadavers and other related activities. Individual identification following accidents or disasters. Participation in disaster prevention and individual identification training programs held by various communities.

(6) Publications

[Original Articles]

1. Jun Ohta, Atsunori Tanaka. Elimination of contaminating amplified short tandem repeat products by autoclaving and ultraviolet irradiation. *Med Sci Law*. 2018.01; 58(1); 25-31
2. Tomoko Akutsu, Ken Watanabe, Ayari Takamura, Koichi Sakurada. Evaluation of skin- or sweat-characteristic mRNAs for inferring the human origin of touched contact traces. *Leg Med (Tokyo)*. 2018.05; 33; 36-41
3. Hajime Utsuno, Toru Kageyama, Keiichi Uchida, Namiko Ishii, Saki Minegishi, Koichi Uemura, Koichi Sakurada. Establishment of a prediction method for the mid-facial region of unknown human Mongoloid skeletal remains. *Forensic Sci. Int.*. 2018.05; 288; 297-303
4. Hisako Saitoh, Hiroshi Ikegaya, Koichi Sakurada, Hiroyuki Inoue, Sayaka Nagasawa, Ayaka Sakuma, Namiko Ishii, Go Inokuchi, Fumiko Chiba, Suguru Torimitsu, Hirotaro Iwase. Usefulness of human herpes simplex virus type 1 genotyping for tracing the geographical origins of unidentified cadavers. *Future Virology*. 2018.06; 13(6); 391-398
5. Chiba Fumiko, Makino Yohsuke, Torimitsu Suguru, Motomura Ayumi, Inokuchi Go, Ishii Namiko, Hoshio Yumi, Abe Hiroko, Yamaguchi Rutsuko, Sakuma Ayaka, Nagasawa Sayaka, Saito Hisako, Yajima Daisuke, Fukui Yuta, Iwase Hirotaro. Stature estimation based on femoral measurements in the modern Japanese population: a cadaveric study using multidetector computed tomography *International Journal of Legal Medicine*. 2018.09; 132(5); 1485-1491

[Books etc]

1. Koichi Sakurada. Q&A Identification method when giant disasters. *Dental Diamond*, 2018.06
2. Hiroshi Ikegaya, Koichi Sakurada. *The New Textbook for Forensic Death Investigations and Autopsies*. Kinpodo, 2018.11 (ISBN : 978-4-7653-1759-7)

[Conference Activities & Talks]

1. Koichi Sakurada. Current status of personal identification. The 2nd Study Meeting of the System on the Cause of Death Investigation and Personal Identification 2018.04.08 The university of Tokyo
2. Ohta J, Noda N, Sakurada K.. Efficacy of mtDNA-based individualization and bacterial DNA-based saliva identification of degraded forensic samples.. The 24th Congress of the International Academy of Legal Medicine 2018.06.05 Fukuoka International Congress Center
3. Sayaka nagasawa, Hisako Saitoh, Shiori Kasahara, Namiko Ishii, Fumiko Chiba, Hirotaro Iwase. Relationship between KCNQ1 (LQT1) and KCNH2 (LQT2) gene mutations and sudden death during illegal drug use. 2018.06.06 Fukuoka
4. Hisako Saitoh, Toru Moriya, Mirei Takeyama, Ayaka Sakuma, Hiroko Abe, Sayaka Nagasawa, Namiko Ishii, Saki Minegishi, Koichi Sakurada, Hirotaro Iwase, Fuyuki Tokanai. Date of birth estimation via radiocarbons using teeth: analysis of corpse conditions in Japanese cadavers. 24th Congress of the International Academy of Legal Medicine 2018.06.06 Fukuoka
5. Hajime Utsuno, Toru kageyama, Keiichi Uchida, Namiko Ishii, Saki Minegishi, Koichi Sakurada. Morphological sex differences of mid facial proportion in Japanese population. 24th Congress of the International Academy of Legal Medicine 2018.06.06 Fukuoka

6. Saki Minegishi, Namiko Ishii, Hajime Utsuno, Kanako Noritake, Takeshi Funakoshi, Koichi Uemura, Ayaka Sakuma, Hisako Saitoh, Susumu Ohtani, Koichi Sakurada. . Preparation of dentin standard samples for age estimation based on increased aspartic acid racemization rate with overheating. The 102nd Congress of the Japanese Society of Legal Medicine 2018.06.07 Fukuoka
7. Namiko Ishii, Hisako Saitoh, Hajime Utsuno, Saki Minegishi, Koichi Sakurada.. Improvement of the age estimation method using dentin aspartic acid racemization: Study of aspartic acid extraction technique. . 24th Congress of the International Academy of Legal Medicine 2018.06.08
8. Koichi Sakurada. The Role of Forensic Odontology in Personal Identification. The 86th Meeting of Matsumoto Dental University (General Assembly) 2018.06.30 Shiojiri City
9. Chiro Tanaka, Hajime Utsuno, Yosuke Makino, Namiko Ishii, Saki Minegishi, Jyun Ohta, Ayaka Sakuma, Hisako Saitoh, Hirotaro Iwase, Koichi Sakurada. Study on adult face soft tissue thickness in Japanese using the postmortem CT image. 87th Kanto District Meeting of the Japanese Society of Legal Medicine 2018.10.06
10. Jun Ohta, Nao Noda, Tadao Tateno, Chihiro Tanaka, Saki Minegishi, Namiko Isii, Hajime Utsuno, Koichi Sakurada. Origin estimation of saliva attaching to forensic samples using localization of the bacterial flora of the mouth (the first report). 12th Annual Meeting of Japanese Society of Forensic Dental Science 2018.10.20 Chiba City

[Social Contribution]

1. Personal identification using dental findings and others (75cases) , 2018.01.01 - 2018.12.31
2. 2017 Individual Identification training program (Second, Tokyo metropolitan) (Koichi Sakurada), Tokyo Dental Association, Japan Dental Association Building, 2018.02.14
3. 2nd IT & Integrated management Lecture in H29 Fiscal Year(Koichi Sakurada), Setagaya Dental Association, Setagaya Dental Association Building, 2018.03.14
4. General Conference Academic Lecture of Tokyo Medical and Dental University Giyukai in H30 Fiscal Year(Koichi Sakurada), Tokyo Medical and Dental University Giyukai, Tokyo Medical and Dental University, 2018.03.17
5. The social role of forensic dentistry (Koichi Sakurada), Graduate School of Dental Medicine, Hokkaido University, The 3rd FD Lecture meeting of Graduate School of Dental Medicine, Hokkaido University in 2018, Hokkaido University, 2018.06.20
6. Role of the identification by the dentist(Koichi Sakurada), Tokyo Metropolitan, PT meeting of inspection, postmortem examination and identification training, Hamacho Memorial, 2018.07.24
7. 2018 Joint Disaster Prevention Drill of Tokyo Metropolitan, Chuo-ku, and Minato-ku, Chuo-ku Sports Center, 2018.09.02
8. Narrowing down unidentified cadavers(Koichi Sakurada), Gunma Prefectural Police Medical Association, 2018.09.22
9. DNA typing (Koichi Sakurada), 2018.11.14
10. 2018 Personal Identification training program (First, Tokyo metropolitan) (Koichi Sakurada) , Tokyo Dental Association, Japan Dental Association, 2018.11.19

Health Care Economics

Koichi Kawabuchi
Isao Igarashi

(1) Outline

The role of health care extends to improving such aspects of life as dietary habit and relationship with others, and is deeply connected to quality of life. Looking back, however, discussion on healthcare has too often originated from political dynamics and interests of parties involved, and not from the voices of general public. This is due partially to the lack of quality data available among the people. The reality of healthcare and what it brings to the society are not necessarily always clear to the general public. In terms of dental care especially, it is hard to say that enough evidences have been established and widely recognized among people to the extent that matches to its importance in providing quality life. Thus, we apply economics in conducting interdisciplinary review of healthcare along with other related fields, and pursue how the healthcare system should be for the people.

(2) Research

Research activities involve conducting analysis on phenomena and observations in health care from the viewpoint of macro as well as micro economics.

Main focuses are:

- 1) Cross-sectional research on healthcare, dental care, nursing care, long-term care, and pharmaceuticals from the viewpoint of economics
- 2) Proposals on policy making in efficient delivery of healthcare, nursing care, and long-term care
- 3) Borderless and mutual development of various specialties such as dental care, healthcare, economics, management and accounting.

(3) Education

Understanding the methods of research on phenomena and observations in health care field through economics point of view. As we have many part-time students with jobs as well as foreign students, the lecture will be centered around such topics as the approach to a research theme in economics and other social sciences (especially empirical studies), how to proceed with the research, and paper writing. Specifically, we will provide outline of healthcare economics by a weekly lecture for Ph. D. candidates as well as once a year lecture for the master course. Some of them adapt more interactive style of problem solving with input from visiting lecturers. Emphasis is placed on methods of quantitative analysis, learning both theoretical and empirical approaches to phenomena and observations in health care field through economics point of view. Lectures for undergraduate education will be focused on the outline of healthcare economics in dental care, with specific themes as 1) Economical analysis of dental healthcare, 2) Expenditure on dental care, 3) Reimbursement, and 4) Quality assessment of dental care.

(4) Lectures & Courses

Faced with recent changes in healthcare and long-term care, core hospitals and other healthcare related institutions in communities with responsibility of supporting front-line healthcare long for personnel competent in healthcare management. Call for such personnel is strong among research organizations and public offices as well, looking for those who are proficient in qualitative and quantitative analysis. Therefore, we aim to train students to be capable in making immediate contribution to the healthcare and welfare field, and to educate future "academic doctors" who can voice their messages in policy making.

(5) Clinical Services & Other Works

Igarashi, Assistant Professor in our department, practices three times a week in the clinic for Oral Diagnosis and General Dentistry of the Dental Hospital. Findings from our research activities are shared to the public through papers, reports, lectures and symposiums in both academic and less academic settings. Comments on healthcare reform, for instance, have been televised on and printed in various media.

(6) Publications**[Original Articles]**

1. G.M. Rabiul Islam, Isao Igarashi, Koichi Kawabuchi. Inequality and Mother's Age as Determinants of Breastfeeding Continuation in Bangladesh. *Tohoku J. Exp. Med.*. 2018.09; 246(1); 15-25

[Conference Activities & Talks]

1. Kyaw Htin, Isao Igarashi, Koichi Kawabuchi. Research on betel quid chewing behavior among adults in Bago region, Myanmar. The 6th Tri-University Consortium 2018.11.30 Tokyo

Dental Education Development

Professor: Ikuko MORIO
Assistant: Professor Naoko SEKI
Graduate Student: Chinatsu MATSUKAWA
Graduate Student: Akira TAKINAGA
Graduate Student: NGUYEN THI THANH TAM
Graduate Student: Mio NAITO
Graduate Student: Ai OSATO

(1) Research

- 1) Research on curriculum for health care professional education
- 2) Comparative study of domestic and international dental education
- 3) Research and development of educational methods in health care professional education
- 4) Research and development of English education programs in health care professional education

(2) Education

Main educational goal of this section as part of graduate school is to help students in health care sciences learn the basics of medical/dental curriculum: educational objectives, strategies and evaluation. This section is currently involved in the undergraduate dental education as the coordinators of multiple modules: the students' research project, courses for global communication, and the electives including various English courses and courses for international exchange for dental students.

(3) Clinical Services & Other Works

[Coordination for Seminar, Symposium, Workshop or other events]

1. Essential Expertise for Clinical Dentistry Online -Aesthetic Dentistry 1-, Tokyo, Japan (TMDU). March 14-24.
2. Essential Expertise for Clinical Dentistry 4 (Seminar/Hands-on), Tokyo, Japan (TMDU). August 21-31.
3. International Faculty Development Course 2018 : Essential Expertise for Clinical Dentistry for Dental Professionals (Seminar/Hands-on), Tokyo, Japan. November 27-December 6.
4. Top 6 Summit for Global Dental Education, Tokyo, Japan. November 29.
5. International Dental Program 2018, Tokyo, Japan. October 9-16.

(4) Publications

[Original Articles]

1. Yukinori Kano, Masatoshi Nakajima, Asami Aida, Naoko Seki, Richard M Foxton, Junji Tagami. Influence of enamel prism orientations on color shifting at the border of resin composite restorations. Dent Mater J. 2018.04; 37(2); 341-349
2. Takehara S, Wright FAC, Yoko Kawaguchi, Yuji Ishida, Ikuko Morio, and Junji Tagami. The Impact of Outbound Exchange Programs on Japanese Dental Students 2018.06; 65(2); 99-105

3. Nguyen TTT, Seki N, Morio I. Stress predictors in two Asian dental schools with an integrated curriculum and traditional curriculum. *European Journal of Dental Education*. 2018.08; 22(3); e594-e601
4. Seki N, Kanazawa M, Komagamine Y, Mizutani K, Hosaka K, Komada W, Moross J, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School. *Journal of Medical and Dental Sciences*. 2018.09; 65; 123-130
5. Matsukawa C, Sasaki Y, Seki N, Morio I. Survey of Professional Training Colleges' Curricula for Dental Hygienist Programs in Japan. *Journal of Medical and Dental Sciences*. 2018.12; 65(4); 131-138

[Books etc]

1. Naoko SEKI, Masayo SUNAGA, Yuji FUKUI, Janell MOROSS, Hiromi OTSUKA, Yukiko TAKATSUNA, Atsuhiko KINOSHITA. TMDU Clinical Training Series for ESL Dental Hygienists. University of Tokyo Press, 2018.06

[Conference Activities & Talks]

1. Seki N, Hosaka K, Komada W, Kanazawa M, Mizutani K, Komagamine Y, Moross J, Morio I. International student forum 2018 -International students' life in Japan-. International Student Forum 2018 by Japanese Dental Science Federation 2018.08.02 Tokyo
2. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. 32nd IADR-SEA & 29th SEAADE 2018.09.11 Da Nang, Vietnam
3. Seki N, Hosaka K, Moross J, Sunaga M, Morio I, Kinoshita A. Evaluating an Online Course on Clinical Expertise with Computer-assisted Simulation Materials. The 29th SEAADE Annual Scientific Meeting 2018.09.11 Da Nang, Vietnam
4. Morio I. Recent development in Japanese dental education. The Annual Scientific Meeting of the ADS-ROC 2018.10.20 Kaohsiung, Taiwan ROC
5. Seki N, Moross J, Sunaga M, Osato A, Morio I, Kinoshita A. Development and evaluation of English simulation educational materials for dental emergency response -English proficiency required in dental practice-. 83rd Annual Meeting of the Stomatological Society 2018.11.30 Tokyo

Oral Health Promotion

Professor	Yoko Kawaguchi
Associate Professor	Masayuki Ueno (till September)
Assistant Professor	Takashi Zaitso
Assistant Professor	Akiko Oshiro
Office administrator	Yuko Onishi (from April)
Registered Resident	Hiromi Nishiyama
Graduate Student	Yuka Shizuma (till March)
	Kaung Myat Thwin (till September)
	Toshiya Kanazawa
	Takashi Tanemura
	Jin Aoki
	Zar Chi Kyaw Myint
	Nguyen Thi Nhat Vy
	Tomoya Saito (from April)
	Srinarupat Jarassri(from October)
	Chou Jan(from October)

(1) Research

Research Subjects

Research topics are innovative, academic and international research in the field of dental public health and preventive dentistry to proceed with oral health promotion that contributes to human health. The current main research themes are:

1. Epidemiology and prevention of dental disease
2. Relationship between oral health and general health
3. Diagnosis and treatment system construction of oral malodor
4. Oral health care system
5. International oral health
6. Tele-dental system
7. Oral health promotion

(2) Lectures & Courses

1) Graduate School Education, Oral Health Promotion

The educational purpose is to foster professionals in dental public health and preventive dentistry who can think oral health problems as related issues with living environment, life style, health policy and social condition, and can conduct innovative, academic and international research on oral health for maintaining and improving oral health.

2) Undergraduate School Education

The department is in charge of module units of “Introduction to dentistry” , “Environment and society II” and “Comprehensive problem exercise” for the third year dental students, and module units of “Basis for dentistry” , “Prevention and health management I” , “Prevention and health management II” and “Dentistry

and nutrition" for the fourth year dental students. The department is also in charge of "Experiential research exercise" for the fourth year dental students, and "Comprehensive clinical practice phase I & II" for the fifth and sixth year dental students, in cooperation with other departments.

(3) Clinical Services & Other Works

Clinical Services

"Fresh breath clinic" in Dental hospital, Tokyo Medical and Dental University is a special clinic for diagnosis, treatment and prevention of oral malodor. About half of oral malodor patients are referred from other departments in the dental hospital or outside dental clinics. Other patients visit the clinic by finding the information of the clinic from mass media such as the internet, newspapers and television.

For oral malodor examination, gas chromatography and gas sensor instrument are used to measure the concentration of volatile sulfur compounds (VSCs) along with the organoleptic test. Oral malodor is treated based on diagnosis by precise measurement and oral examination, besides psychological aspects of the patient are paid attention. Treatment of oral malodor needs continuous periodontal disease management and oral care in cooperation with oral care department in the dental hospital and patient's family dentist.

(4) Publications

[Original Articles]

1. Yuka Shizuma, Takashi Zaitzu, Masayuki Ueno, Mari Ohnuki, Yoko Kawaguchi. Relationship between self-assessment and clinical evaluation of dental plaque and gingival condition in Japanese adolescents. *Int J Dent Hyg.* 2018.02; 16(1); 144-150
2. Yen Hoang Thi Nguyen, Masayuki Ueno, Takashi Zaitzu, Toai Nguyen, Yoko Kawaguchi. Early childhood caries and risk factors in Vietnam *Journal of Clinical Pediatric Dentistry.* 2018.05; 42(3); 173-181
3. Masayuki Ueno, Taichi Shimazu, Norie Sawada, Shoichiro Tsugane, Yoko Kawaguchi. Validity of self-reported tooth counts and masticatory status study of a Japanese adult population *Journal of Oral Rehabilitation.* 2018.05; 45(5); 393-398
4. Masayuki Ueno, Mari Ohnuki, Takashi Zaitzu, Sachiko Takehara, Sayaka Furukawa, Yoko Kawaguchi. Prevalence of halitosis and risk factors in Japanese school children *Pediatrics International.* 2018.06; 60(6); 588-592
5. Takehara S, Wright FAC, Yoko Kawaguchi, Yuji Ishida, Ikuko Morio, and Junji Tagami. The Impact of Outbound Exchange Programs on Japanese Dental Students 2018.06; 65(2); 99-105
6. Kaung Myat Thwin, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Effects of oral health education in Myanmar preschool children and guardians *Journal of Investigative and Clinical Dentistry.* 2018.09; 9(3); e12346
7. Seki N, Kanazawa M, Komagamine Y, Mizutani K, Hosaka K, Komada W, Moross J, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School. *Journal of Medical and Dental Sciences.* 2018.09; 65; 123-130
8. Takashi Zaitzu, Mari Ohnuki, Chiyoko Hakuta and Yoko Kawaguchi. Association between Masticatory Performance and Exercise Capacity of Adolescents *J Oral Hyg Health.* 2018.09; 6(3);
9. Wa Than Lin, Kaung Myat Thwin, Takashi Zaitzu, Yuichi Kitasako, Junji Tagami, Yoko Kawaguchi. Erosive tooth wear and its related risk factors among Myanmar residents in Japan *Asian Pacific Journal of Dentistry.* 2018.11; 18; 21-28
10. Toshiya Kanazawa, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Masticatory performance measured with a chewing gum containing spherical resinous microparticles *International Journal of Clinical Preventive Dentistry.* 2018.12; 14(4); 256-263

[Books etc]

1. Editors: Mariño, Rodrigo, Morgan, Michael V., Walmsley, A. Damien . Career Paths in Oral Health. Springer International Publishing, 2018.09

[Misc]

1. 川口陽子. 気になる口臭の話 8020 会誌. 2018.02; 17; 38-44
2. Takashi Zaitzu, Tomoya Saito, Yoko Kawaguchi. The Oral Healthcare System in Japan. Healthcare (Basel). 2018.07; 6(3);
3. Ei Ei Aung,Khin Maung,Takashi Zaitzu and Yoko Kawaguchi. An Overview of Oral Health Situation and Challenges in Myanmar Asian Journal of Research in Medicine and Medical Science. 2018.10; 1(1); 1-10

[Conference Activities & Talks]

1. Kaung Myat Thwin, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Antibacterial and caries arresting effects of silver diamine fluoride in Myanmar preschool children. The 38th Myanmar Dental Conference 2018.01.18 Melia Hotel, Yangon, Myanmar
2. Yoko Kawaguchi. School-based Oral Health Education and Promotion Programs in Japan. The 38th Myanmar Dental Conference 2018.01.18 Melia Hotel, Yangon, Myanmar
3. Yoko Kawaguchi. Strategies and approaches for tackling Early Childhood Caries (ECC). The36th Myanmar Dental Conference 2018.01.26
4. Zar Chi Kyaw Myint, Kaung Myat Thwin, Takashi Zaitzu, Akiko Oshiro, Masayuki Ueno, Yoko Kawaguchi. Oral health status and oral health behaviors among school children in Myanmar. 第 67 回日本口腔衛生学会・総会 2018.05.19 札幌市、北海道
5. Kaung Myat Thwin, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Effects of oral health education in Myanmar preschool children and guardians. 第 67 回日本口腔衛生学会・総会 2018.05.20 札幌市、北海道
6. Rezende LO, Borges LS, de Campos PS, Kagiya K, Baba O, Picinato M, Takehara S, Kumei Y, Zeredo JLL. Cineradiographic study of the development of mastication in the common marmoset. 第 41 回日本神経科学大会 2018.07.26 神戸
7. Yoko Kawaguchi,Tomoya Saito,Takashi Zaitzu,Masayuki Ueno. Oral Health Related Concern and Awareness Among Adolescents in Japan. 96th General session & exhibition of the IADR 2018.07.27 London, England
8. Tomoya Saito, Takashi Zaitzu, Masayuki Ueno, Yoko Kawaguchi. Oral Malodor and Occupational Parameters in Japanese Workers. 96th General session & exhibition of the IADR 2018.07.28 London, England
9. Yoko Kawaguchi. Special lecture “Oral health programs for the elderly in Japan” . ベトナム・フエ大学 歯学部学生対象講演 2018.09.10
10. Yoko Kawaguchi. Special lecture “Emergency oral health systems in times of disaster” . ベトナム・フエ大学 歯学部学生対象講演 2018.09.10
11. Yoko Kawaguchi,DDS,PhD. The 8020 campaign and future perspectives for elder oral health in Japan, Symposium “Appropriate Dental Care for Older Population” . 32nd IADR-SEA & 29thSEAIDE VIETNAM2018 2018.09.14 Ho Chi Minh City,Viet Nam
12. Yen H.Nguyen,Masayuki Ueno,Takashi Zaitzu,Toai Nguyen, Yoko Kawaguchi. Arresting Effect of Silver Diamine Fluoride on Early Childhood Caries. 32nd IADR-SEA & 29th SEAIDE VIETNAM2018 2018.09.14 Ho Chi Minh City,Viet Nam

Sports Medicine and Dentistry

[Associate Professor] Toshiaki Ueno
 [Assistant Professor] Hiroshi Churei
 [Clinical fellow] Kairi Hayashi
 [Graduate Student] Nana Shiota, Gen Tanabe, Chiho Shibata, Phyu Sin Tun, Rio Kinjo, Nanami Ito, Thet Khaing Aung, Yuumi Takahashi
 [Research Student] Aki Kanasaki, Kaito Togawa
 [Part-time Instructor] Goshi Kondo, Yukio Sasaki, Ryo Sato, Takuto Yamanaka, Sachiko Fujino, Yuriko Yoshida, Takefumi Negoro, Kazushi Watanabe
 [Part-time Resident] Takaaki Fukuda, Chie Ichihara
 [Research fellow] Ruman Uddin Chowdhury

(1) Outline

Sport medicine/dentistry is a branch of clinical medical and dental sciences which deals with the clinical management of oral health of athletes and sports-active people, the safety measures of sports-related traumatic injuries and disorders, and medical and dental supports to improve athletic performance.

(2) Research

- 1) Oral health promotion of athletes and sports-active people
 - (1) Field survey of oral health conditions in athletes and sports-active people
 - (2) Changes of oral environment associated with physical and sporting activities
 - (3) Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
 - (1) Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
 - (2) Development and innovation of sports mouthguard
 - (3) Development and innovation of sports faceguard
 - (4) Development and innovation of scuba diving mouthpiece
- 3) Correlations between occlusion and general motor functions
 - (1) Biomechanical assessment of motor performance associated with occlusion
 - (2) Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
 - (1) Effect of occlusion on static posture
 - (2) Influence of occlusion on dynamic posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

(3) Education

academic classes for sports medicine/dentistry in undergraduate and graduate courses in undergraduate and graduate courses are listed as follows;

- 1) D1: Shigaku-Gaietu
- 2) D3: Sogo-Kadai-Ensyu

- 3)D3:Rinsyo-Taiken-Jissyu
- 4)D4:Kenkyu-Taiken-Jissyu
- 5)D5:Hatten-Shika-Rinsyo/Sports Dentistry
- 6)D5-D6:Hokatsu Rinsyo-Jissyu Phase I to II
- 7)OH2:Kiso-Kagaku-Jissyu
- 8)OH3:Seijin-Koukuhoken-Eiseigaku
- 9)OH3-OH4:Koukuhoken-Eisei-Jissyu
- 10)OE4:Sports dental engineering
- 11)Master course:Kankyo-Syakai-Ishigaku
- 12)PhD course: Tokuron, Ensyu and Kenkyu-Jissyu of Sports Medicine and Dentitry
- 13)Clinical training course:Sports Dentistry

(4) Lectures & Courses

Main objectives of academic education programs of sports medicine/dentistry in from undergraduate to graduate courses is to provide the students to study the oral health conditions in athletes and sports-active people, the changes of oral environment associated with physical and sporting activities, the possible correlations between occlusion and general motor functions and body posture, the novel techniques of sports mouthguard and faceguard, the relations between mastication and occlusion and brain functions, and so on. Students are also taught to advanced knowledge on sports medicine/dentistry and up-to-date techniques to fabricate custom mouthguard and faceguard.

(5) Clinical Services & Other Works

Sports dentistry clinic in Dental Hospital of Tokyo Medical and Dental University offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and faceguard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art. Sports dentistry clinic is positioned as a dental branch of Clinical Center for Sports Medicine and Dentistry under TMDU Sports Science Organization. In addition, Our clinic maintains close cooperation with Japan Institute of Sports Science/National Training Center under Japan Sport Council.

(6) Clinical Performances

< Certified specialists>

Toshiaki Ueno (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by Japanese Academy of Sports Dentistry, 3.Mouthguard technical instructor certified by JASD, 4.Dental specialist certified by Japanese Academy of Maxillofacial Prosthetics, 5.Dental Material Senior Advisor certified by Japanese Society of Dental Materials and Devices), 4.Dental specialist certified by Japanese Academy of Dental Traumatology, 7.JPSA Sports Dentist certified by Japanese Para-Sports Association

Hiroshi Churei (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3. MG technical instructor certified by JASD)

Kairi Hayashi (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Sachiko Fujino (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3.MG technical instructor certified by JASD)

Yuriko Yoshida (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Gen Tanabe (1.MG technical instructor certified by JASD)

Aki Kanasaki(1. Sports dental hygienist certified by JASD)

Nanami Ito(1. Sports dental hygienist certified by JASD)

(7) Publications

[Original Articles]

1. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takahashi, Motohiro Uo. Improvement of the Shock Absorption Ability of a Face Guard by Incorporating

- a Glass-Fiber-Reinforced Thermoplastic and Buffering Space BioMed Research International. 2018.05; 2018; 1-8
2. Yoshida Yuriko, Churei Hiroshi, Takeuchi Yasuo, Wada Takahiro, Uo Motohiro, Izumi Yuichi, Ueno Toshiaki. Novel antibacterial mouthguard material manufactured using silver-nanoparticle-embedded ethylene-vinyl acetate copolymer masterbatch DENTAL MATERIALS JOURNAL. 2018.06; 37(3); 437-444
3. Tanabe-Ikegawa M, Takahashi T, Churei H, Mitsuyama A, Ueno T. Interactive effect of rehydration with diluted sports drink and water gargling on salivary flow, pH, and buffering capacity during ergometer exercise in young adult volunteers Journal of Oral Science. 2018.06; 60(2); 269-277
4. Tanabe-Ikegawa M, Hayashi K, Churei H, Takahashi T, Shimoyama K, Yagishita K, Ueno T. Interactive effect of toothbrush abrasion and enamel erosion caused by a sports drink: An in vitro analysis Int J Sports Dent. 2018.11; 11(1); 16-24

[Conference Activities & Talks]

1. Wada Takahiro, Churei Hiroshi, Ueno Toshiaki, Uo Motohiro. Application of a carbon-fiber reinforced thermoplastic to face guard. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
2. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Yoshida Yuriko, Tanabe Gen, Uo Motohiro, Takahashi Hidekazu, Ueno Toshiaki. The behavior of pressure sensor with a built-in mouth guard material. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
3. Wada Takahiro, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Ueno Toshiaki, Uo Motohiro. Shock absorption analysis of face guards made of carbon fiber reinforced thermoplastics using high-speed camera. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
4. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The evaluation of a force sensor for the development of the mouth guard type wearable sensor. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
5. Aung W, Shwe H, Tun PS, Aung TK, Tanabe G, Kinjo R, Takahashi Y, Hayashi K, Yoshiada Y, Yano A, Churei H, Ueno T. Effectiveness of mouthguard for Myanmar Lethwei player and coach. 9th Mandalay Dental Conference 2018.07.14 Mandalay, Myanmar
6. Kinjo R, Wada T, Churei H, Takahashi H, Ueno T, Uo M. Evaluating the use of a force sensor for the development of a mouth guard-type wearable sensor. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo Garden Place Hotel

Educational System in Dentistry

Professor Kouji ARAKI

Associate Professor Jun TSURUTA

Junior Associate Professor(non-full time) Kouji IIDA

Hiroki KATAOKA

Graduate Student Moriyuki KATOH (~2018.2) Kazuki TAKAHASHI (~2018.3) Akitaka HATTORI

Kanako TODA

Secretary Satomi ITOH

(1) Outline

Main object of educational system in dentistry in the graduate course is to provide opportunity to study evaluation method for dental education curriculum, inspection method of the validity and reliability of the evaluation system for dental education, evaluation system compared between international and Japanese education level in undergraduate or after the graduation periods, and dental clinical skills improvement by the virtual reality simulation system.

(2) Research

- 1) The development of evaluation method for dental education curriculum
- 2) The development of inspection method of the validity and reliability of the evaluation system for dental education
- 3) The development of evaluation system compared between international and Japanese education level in undergraduate or after the graduation periods
- 4) The development of the program for dental clinical skills improvement by the virtual reality simulation system

(3) Education

The education to the postgraduate students performs a lecture, practice, and Lab.

The education to the undergraduate students performs of a lecture and practice of all human general oral diagnoses.

(4) Lectures & Courses

The aim of the lecture is to understand the purpose and method about the evaluation of dental education system. In addition, it is to understand the level and inspection method of international dental education. The aim of the practice is to understand a method of data analysis provided by the evaluation system for the dental education, In addition, it is to understand the comparison with the international education level.

The aim of the Lab is to manage the teaching materials developed for simulation education and is to understand the inspection method of the evaluation for new education system.

(5) Clinical Services & Other Works

In the Clinic of Oral Diagnosis and General Dentistry, University Hospital, we performs manner and oral diagnosis education, for a student during clinical training.

(6) Publications**[Original Articles]**

1. Yasuyuki Kimura, Ken-ichi Tonami, Jun Tsuruta, Kouji Araki. Rise of blood pressure value in young patients at first visit at a dental university hospital in Japan Journal of Dental Sciences. 2018.11; 14(1); 93-98

[Conference Activities & Talks]

1. UMEMORI Sachi, Aida J, Tonami K, Tabuchi T, Araki K, Mataka S, Kondo K. Does the secondhand smoking associate with tooth loss? : JAGES cross sectional study. The 28th Annual Scientific Meeting of the Japan Epidemiological Association 2018.02.02 Fukushima
2. Iwaki Maiko, Kanazawa Manabu, Sato Daisuke, Miyayasu Anna, Kasugai Shohei, Araki Kouji, Minakuchi Shunsuke. Masticatory Functions with Immediate Loading of Two-implant Mandibular Overdentures: 5-year prospective study.. Academy of Osseointegration Annual Meeting 2018 2018.03.01 Los Angeles, CA, USA
3. Aoki A, Takeuchi Y, Akizuki T, Mizutani K, Katagiri S, Ikeda Y, Maekawa S, Watanabe K, Matsuura T, Ohtsu A, Kakizaki S, Komazaki R, Mikami R, Hideshima M, Nikaidou T, Araki K, Izumi Y. Current Status of Clinical Practice of Periodontal Therapy by Predoctoral Dental Students at Tokyo Medical and Dental University (TMDU). The 61th Spring Meeting of The Japanese Society of Periodontology 2018.06.01 Keio plaza hotel, Tokyo
4. KANAKO NORITAKE, SHIGERU ODA, KOUJI ARAKI. Effects of a rhFGF impregnated gelatin hydrogel GBR membrane containing β -tricalcium phosphate on bone neogenesis in rat calvaria.. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
5. Maruyama Kiich, Oda Shigeru, Araki Kouji. Alveolar bone regeneration in vertical bone defect by Regroth®: A Case Report.. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.15 Yokohama
6. Kanako Toda, Jun Tsuruta. The condition status of Inter professional work related to Dental Hygienists by literature survey. The academic conference of Japanese Society of Dental Practice Administration 2018.07.22 Nigata
7. NORITAKE Kanako, TSURUTA Jun, ARAKI Kouji. . A report of the trial of observation experience for dental students at palliative care ward. The 37th General and Scientific Meeting of the Japanese Dental Education Association 2018.07.28 Kouriyama
8. TSURUTA Jun, NORITAKE Kanako, ARAKI Kouji. . A report of the trial of observation experience for medical students at dental student clinic. The 37th General and Scientific Meeting of the Japanese Dental Education Association 2018.07.28 Kouriyama
9. UMEMORI Sachi, Tonami K, Nitta H, Araki K,. The Analysis of Introduction of Behavioral Science class in Faculty of Dentistry. The 50th Annual Meeting of the Japan Society by Medical Education 2018.08.04 Tokyo
10. Kanako NORITAKE, Jun TSURUTA, Koji MIZUTANI, Keiko KONDO, Shinichi ARAKAWA, Kouji ARAKI. Study on educational effect measurement of the IPW program in practical clinical training.. The 50th Annual Meeting of the Japan Society for Medical Education 2018.08.04 Tokyo
11. Yasuyuki Kimura, Ken-ichi Tonami, Jun Tsuruta, Kouji Araki. Effect of psychological and social factors on hypertension in dental clinics. 2018.09.02 Yotsuya, Tokyo

12. Jun Tsuruta, Kanako Noritake, Kouji Araki.. PRELIMINARY STUDY FOR A NEW OBSERVATION PROGRAM FOR MEDICAL STUDENTS AT THE DENTAL STUDENT' S CLINIC.. 32nd IADR-SEA and 29th SEAAGE 2018.09.11 Viet Nam
13. Kanako Noritake, Jun Tsuruta, Tomoe Miyoshi, Maiko Iwaki, Yuko Mitsuma, Hiroshi Nitta, and Kouji Araki. Development a new IPE program for dental and medical students in clinical practicum. 2018.12.01 Tokyo

[Awards & Honors]

1. AO Best Poster award for 2018 (Maiko Iwaki), Academy of Osseointegration Annual Meeting 2018, 2018.03

[Social Contribution]

1. The Journal of Dental Education,peer reviewer, 2015.08.01 - Now
2. European Journal of Dental Education,peer reviewer, 2017.09.01 - Now

Educational Media Development

Professor KINOSHITA Atsuhiko
 Assistant Professor SUNAGA Masayo
 Graduate Student MIYOSHI Tomoe(~March)
 Graduate Student HOBOKoki(~March)
 Graduate Student CAO Ridan
 Graduate Student AKIYAMA Kyoko
 Graduate Student HARADA Yusuke
 Graduate Student TAKENOUCHI Akane
 Graduate Student TAKATSUNA Yukiko(~March)

(1) Research

1) Development of computer-assisted clinical simulation system for medical and dental practice training.

In our university, we executed the Establishment of Computer-Assisted Education System on Clinical Simulation for Medical and Dental Practice Training project, which was adopted as part of the Support Program for Distinctive University Education in 2005, and developed the computer simulation materials on clinical education by utilizing digital clinical data from our Medical and Dental hospitals. We have expanded our study into a new project, 'Progress of Computer-Assisted Simulation for Medical and Dental Practice Training. Computer-Assisted Simulation Promoting Clinical Inference, Decision-making, Problem Solving and Cooperation Abilities of Health Professionals', which was subsequently selected to be part of the Program for Promoting the University Education Reform in 2009 by the Ministry of Education, Culture, Sports, Science and Technology. After utilizing the simulation materials for our students, we will evaluate and analyze their educational efficacy. Furthermore, we will develop a computer-assisted clinical simulation system for the entire university.

2) Development of new education system using information and communication technologies for medical and dental students.

At our university, we executed the Integration of Information and Communication Technologies into Clinical Training project, which was adopted as part of the Support Program for the Contemporary Educational Needs in 2007. The aim of this program is to integrate traditional educational methods with advanced information and communication technologies in order to allow clinical training, practical training and lectures to be effectively interlinked. By expanding digital content and employing an automatic visual recording system, we are planning to establish a digital archive of treatments and surgeries, demonstrations of dental techniques, lectures and student training. We will then launch an on-demand distribution system in order to incorporate this content into clinical education, which the students will be able to use for their self-evaluation and learning.

3) Development and utilization of an educational media for medical and dental students.

- Development and Study of Dental Model and Kit for Practical Training:

Dental and dental hygiene students must acquire skills for measuring periodontal pockets and must learn to identify the base of the pocket. However, few dental models are commercially available, and students cannot measure deep periodontal pockets by practicing on one another. Thus, we developed a new dental model with which the students can practice the probing of deep periodontal pockets, and plan to evaluate its effectiveness in training and evaluation of examiners.

- Development of Composing and Screening System for Original 3D Movies from Operator's Viewpoint:

If students can experience and recognize three-dimensional space from the operator's (instructor's) viewpoint during their practice sessions and lectures, it would have educational benefits. Thus, we plan to develop a

Composing and Screening System for Original 3D Movies from an Operator's Viewpoint. Furthermore, we will improve the quality of distance learning and remotely operated instruction using the superimposing method.

- Development of Dental Handpiece System with CCD camera:

We plan to develop a system equipped with a CCD camera, mirror and reverse image units in order to allow students in the lecture room to observe dental treatment sites in real-time, thereby giving them a sense of being at a clinic.

(2) Education

We will assist graduate students in understanding new educational systems and media utilizing information-communication technologies, such as the computer-assisted education system, the e-learning system and the live broadcasting lecture system. We will also assist these students in mastering how to create related educational media and apply it to medical, dental, nursing and dental hygiene education, as well as interprofessional cooperation.

First-year students at the School of Dentistry, and first and second-year students at the School of Oral Health Care Sciences will learn to process media information and create media content, as well as how to search the Internet for information that is necessary for their study and research activities. They will also learn how to make use of various databases.

Fourth-year students at the School of Dentistry will acquire the practical knowledge, communication skills and attitude to build good relationships with patients by gaining clinical experience at an early stage. This practice consists of two units; clinical experience in the teaching clinic and the computer-assisted simulation practice. This experience will enhance the students' abilities, enabling them to be effective clinicians.

(3) Publications

[Original Articles]

1. Ridan Cao, Masayo Sunaga, Tomoe Miyoshi, Atsuhiko Kinoshita. Development and Evaluation of a Study Level Announcement System in e-Learning J. Med. Dent. Sci.. 2018.09; 65(3); 113-122
2. Naoko Seki, Manabu Kanazawa, Yuriko Komagamine, Koji Mizutani, Keiichi Hosaka, Wataru Komada, Janelle Moross, Shinji Kuroda, Masayo Sunaga, Yoko Kawaguchi, Ikuko Morio, Atsuhiko Kinoshita. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School J. Med. Dent. Sci.. 2018.09; 65(3); 123-130

[Conference Activities & Talks]

1. Naoko Seki, Keiichi Hosaka, Janelle Moross, Masayo Sunaga, Ikuko Morio, Atsuhiko Kinoshita. Evaluating an Online Course on Clinical Expertise with Computer-assisted Simulation Materials . The 29th Annual Scientific Meeting South East Asia Association For Dental Education (SEAADE), 11-14 September 2018.09.11 Da Nang, Vietnam
2. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. The 29th Annual Scientific Meeting South East Asia Association For Dental Education (SEAADE), 11-14 September 2018.09.11 Da Nang, Vietnam
3. Yusuke Harada, Masayo Sunaga, Yasuo Takeuchi, Akira Aoki, Shogo Maekawa, Yuichi Izumi, Atsuhiko Kinoshita. Effectiveness of Improved Dental Model for Training of Pocket Probing. The 104th Annual Meeting American Academy of Periodontology, Abstracts of JACP/JSP Poster Session, p16, 27-30 October 2018.10.29 Vancouver, Canada
4. Atsuhiko Kinoshita, Masayo Sunaga. Dental Education with ICT. - Introduction of TMDU SimPrac - IT Simulation 1, Educational Session. International Faculty Development Course(IFDC) 2018 2018.11.28 Tokyo Medical and Dental University (TMDU), Bunkyo-ku, Tokyo

5. Atsuhiko Kinoshita, Masayo Sunaga. Dental Education with ICT experience. - Introduction of TMDU SimPrac -. The 3rd Top 6 Summit of Global Dental Education 2018.11.29 Tokyo Medical and Dental University (TMDU), Bunkyo-ku, Tokyo
6. Atsuhiko Kinoshita, Masayo Sunaga. IT Simulation Workshop. The 3rd Top 6 Summit of Global Dental Education 2018.11.29 Tokyo Medical and Dental University (TMDU), Bunkyo-ku, Tokyo
7. Seki N, Moross J, Sunaga M, Osato A, Morio I, Kinoshita A. Development and evaluation of English simulation educational materials for dental emergency response -English proficiency required in dental practice-. 83rd Annual Meeting of the Stomatological Society, J.Stomatol.Soc.,Jpn, Program and Abstract Book, p27, Oct.30th- Dec.1st 2018.11.30 Tokyo
8. Atsuhiko Kinoshita, Masayo Sunaga. Dental Education with ICT. Hands-on. IT Simulation 2, Educational Session. International Faculty Development Course(IFDC) 2018 2018.11.30 Tokyo Medical and Dental University (TMDU), Bunkyo-ku, Tokyo
9. Kanako Noritake, Jun Tsuruta, Tomoe Miyoshi, Maiko Iwaki, Yuko Mitsuma, Hiroshi Nitta, and Kouji Araki. Development a new IPE program for dental and medical students in clinical practicum. 2018.12.01 Tokyo

Insured Medical Care Management

Professor Masumi AI
J Associate Professor Junichiro ISHIOKA
Graduate Student Hiroshi KAWAMURA
Graduate Student Marie Nakamura

(1) Outline

Our department supports an appropriate practice on insured medical care and billing for medical service fees at the TMDU medical hospital.

We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

(2) Research

1) Development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

2) Studies on management and supports for billing for medical service fees at insurance medical institutions.

3) Studies on affairs of medical insurance system and provision of medical services.

In addition, the staff has been engaged in clinical studies and epidemiological studies on lipid metabolism, diabetes mellitus, atherosclerosis, laboratory medicine, and urology.

(3) Education

The staff has been in charge for education of social health insurance system and rules for insured medical treatment at the TMDU medical hospital (May 2016 and February 2017).

A doctor course student is in his second year.

(4) Lectures & Courses

*Providing practical supports for an appropriate insured medical care in the clinical fields.

Providing individual support for an appropriate billing for medical service fees at the medical hospital.

We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

(5) Clinical Services & Other Works

The staff has been in charge for assisting appropriate medical fee claims, and also providing clinical service on diabetes, dyslipidemia, atherosclerosis, geriatrics, and Urology.

(6) Clinical Performances

As a managing section of the medical hospital, we collaborate all kinds of hospital workers practically and efficiently to provide an appropriate insured medical care.

(7) Publications

[Original Articles]

1. Sho Uehara, Soichiro Yoshida, Hiroshi Tanaka, Yosuke Yasuda, Hajime Tanaka, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii. Prediction of Intraoperative Urinary Collecting System Entry in Patients with Peripheral Renal Tumors Undergoing Partial Nephrectomy: Usefulness of Tumor-Centered Multiplanar Reconstruction. *Urol. Int.*. 2018.01; 100(1); 85-91
2. Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Clinical outcomes of patients with histologic variants of urothelial carcinoma treated with tetra-modality bladder-sparing protocol incorporating consolidative partial cystectomy. *JOURNAL OF CLINICAL ONCOLOGY*. 2018.02; 36(6);
3. Nobuhisa Morimoto, Chikako Kasuga, Airi Tanaka, Keiko Kamachi, Masumi Ai, Kevin Y Urayama, Akira Tanaka. Association between dietary fibre:carbohydrate intake ratio and insulin resistance in Japanese adults without type 2 diabetes. *Br. J. Nutr.*. 2018.03; 119(6); 620-628
4. Hiromasa Goto, Tomoya Mita, Yoshio Fujitani, Shimpei Fujimoto, Kiyohito Takahashi, Hiroaki Satoh, Takahisa Hirose, Toru Hiyoshi, Masumi Ai, Yosuke Okada, Hideki Nishimura, Hisamoto Kuroda, Toshiki Matsubara, Masahiko Goshō, Hitoshi Ishii, Hirotaka Watada. Effects of linagliptin versus voglibose on treatment-related quality of life in patients with type 2 diabetes: sub-analysis of the L-STEP study. *Endocr. J.*. 2018.04;
5. Yosuke Yasuda, Kazutaka Saito, Takahiko Soma, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazunori Kihara, Yasuhisa Fujii . PD07-05 THE OUTCOME OF GASLESS LAPAROSCOPIC SINGLE-PORT CLAMPLESS SUTURELESS PARTIAL NEPHRECTOMY USING THREE-DIMENSIONAL HEAD-MOUNTED DISPLAY 2018.04;
6. shugo yajima, Soichiro Yoshida, Taro Takahara Minato Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii . MP08-03 ABSENCE OF INCHWORM SIGN ON DWI: A PREDICTIVE MARKER FOR PROGRESSION IN PT1 BLADDER CANCER the journal of UROLOGY. 2018.04;
7. Takahiko Soma, Junichiro Ishioka, Hajime Tanaka, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. MP36-08 A CONVOLUTIONAL NEURAL NETWORKS ALGORITHM FOR DIFFERENTIAL DIAGNOSIS OF FAT-POOR ANGIOMYOLIPOMA AND RENAL CELL CARCINOMA IN ENHANCED CT AND T2-WEIGHTED MAGNETIC RESONANCE IMAGING the journal of UROLOGY. 2018.04;
8. Yoh Matsuoka, Junichiro Ishioka, Hiroshi Tanaka, Tomo Kimura, Yuma Waseda, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, and others. MP20-09 MRI-BASED RISK ASSESSMENT FOR POSTOPERATIVE BIOCHEMICAL RECURRENCE USING THE PROSTATE IMAGING REPORTING AND DATA SYSTEM (PI-RADS) SCORES AND CAPSULAR CONTACT LENGTH 2018.04;
9. Minato Yokoyama, Naoko Kawamura, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Junichiro Ishioka, Yoh Matsuoka, and others. MP42-05 ACUTE KIDNEY INJURY AND INTERMEDIATE-TERM RENAL FUNCTION AFTER CLAMPLESS PARTIAL NEPHRECTOMY the journal of UROLOGY. 2018.04;
10. Yosuke Yasuda, Kazutaka Saito, Takahiko Soma, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, and others. PD07-05 THE OUTCOME OF GASLESS LAPAROSCOPIC SINGLE-PORT CLAMPLESS SUTURELESS PARTIAL NEPHRECTOMY USING THREE-DIMENSIONAL HEAD-MOUNTED DISPLAY the journal of UROLOGY. 2018.04;

11. Junichiro Ishioka, Yoh Matsuoka, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Kazutaka Saito, and others. MP20-10 DEEP LEARNING WITH A CONVOLUTIONAL NEURAL NETWORK ALGORITHM FOR FULLY AUTOMATED DETECTION OF PROSTATE CANCER USING PRE-BIOPSY MRI the journal of UROLOGY. 2018.04;
12. Toshiki Kijima, Thomas Prince, Katsuo Mori, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, and others. MP64-14 TARGETING HEAT SHOCK FACTOR 1 SENSITIZES CASTRATION-RESISTANT PROSTATE CANCER CELLS TO HSP90 INHIBITION IN PART BY DESTABILIZING ANDROGEN RECEPTOR SPLICE VARIANTS the journal of UROLOGY. 2018.04;
13. Yosuke Yasuda, Kazutaka Saito, Takahiko Soma, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, and others. PD07-05 THE OUTCOME OF GASLESS LAPAROSCOPIC SINGLE-PORT CLAMPLESS SUTURELESS PARTIAL NEPHRECTOMY USING THREE-DIMENSIONAL HEAD-MOUNTED DISPLAY the journal of UROLOGY. 2018.04;
14. Yoh Matsuoka, Junichiro Ishioka, Hiroshi Tanaka, Tomo Kimura, Yuma Waseda, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, and others. MP20-09 MRI-BASED RISK ASSESSMENT FOR POSTOPERATIVE BIOCHEMICAL RECURRENCE USING THE PROSTATE IMAGING REPORTING AND DATA SYSTEM (PI-RADS) SCORES AND CAPSULAR CONTACT LENGTH the journal of UROLOGY. 2018.04;
15. Matsuoka Yoh, Tanaka Hiroshi, Kimura Tomo, Waseda Yuma, Uehara Sho, Yasuda Yosuke, Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Clinical significance of MRI-targeted biopsy for the risk stratification of oncological outcome after radical prostatectomy(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; AOP-070
16. Uehara Sho, Yoshida Soichiro, Matsuoka Yoh, Yasuda Yosuke, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Head-mounted display assisted MRI-US elastic fusion prostate biopsy system(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; AVP-06
17. Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Novel therapy targeting androgen receptor splice variants by inhibiting heat shock factor 1(HSF1) for the treatment of castration-resistant prostate cancer(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; AOP-065
18. Junichiro Ishioka, Yoh Matsuoka, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Kazutaka Saito, Kazunori Kihara, Noboru Numao, Tomo Kimura, Kosei Kudo, Itsuo Kumazawa, Yasuhisa Fujii. Computer-aided diagnosis of prostate cancer on magnetic resonance imaging using a convolutional neural network algorithm. BJU Int.. 2018.05;
19. Shingo Moriyama, Soichiro Yoshida, Hajime Tanaka, Hiroshi Tanaka, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Intensity ratio curve analysis of small renal masses on T2-weighted magnetic resonance imaging: Differentiation of fat-poor angiomyolipoma from renal cell carcinoma. Int. J. Urol.. 2018.06; 25(6); 554-560
20. Hajime Tanaka, Soichiro Yoshida, Fumitaka Koga, Kazuma Toda, Ryoichi Yoshimura, Yutaka Nakajima, Emiko Sugawara, Takumi Akashi, Yuma Waseda, Masaharu Inoue, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Impact of Immunohistochemistry-Based Subtypes in Muscle-Invasive Bladder Cancer on Response to Chemoradiotherapy. Int. J. Radiat. Oncol. Biol. Phys.. 2018.06;
21. Takahiko Soma, Junichiro Ishioka, Hajime Tanaka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii. Potential for computer-aided diagnosis using a convolutional neural network algorithm to diagnose fat-poor angiomyolipoma in enhanced computed tomography and T2-weighted magnetic resonance imaging. Int. J. Urol.. 2018.08;
22. Kawamura N, Saito K, Inoue M, Ito M, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Kihara K, Fujii Y. Adherent Perinephric Fat in Asian Patients: Predictors and Impact on Perioperative Outcomes of Partial Nephrectomy. Urologia internationalis. 2018.10; 1-6
23. Waseda Y, Saito K, Ishikawa Y, Kawano K, Yokoyama M, Ishioka J, Matsuoka Y, Morimoto S, Kihara K, Fujii Y. Predictive ability of renal cortex enhancement in dynamic computed tomography for residual renal function after nephroureterectomy: Comparison with ^{99m}Tc -diethylenetriaminopentacetic acid renography and validation study. International journal of urology : official journal of the Japanese Urological Association. 2018.10;

24. Yoshida Soichiro, Takahara Taro, Ishii Chikako, Nakagawa Keiko, Toda Kazuma, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Yoshimura Ryoichi, Kihara Kazunori, Fujii Yasuhisa. Loco-regional radiotherapy targeting for oligo-progressive CRPC on the diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) INTERNATIONAL JOURNAL OF UROLOGY. 2018.10; 25; 358
25. Hisamitsu Ishihara, Motonobu Anai, Hiroaki Seino, Toru Kitazawa, Hiroshi Ohashi, Masumi Ai, Masahiro Inoue, Midori Fujishiro, Takeshi Inazawa, Hisamoto Kuroda, Masayo Yamada. Rationale and Design of the STOP-OB Study for Evaluating the Effects of Tofogliflozin and Glimepiride on Fat Deposition in Type 2 Diabetes Patients Treated with Metformin/DPP-4 Inhibitor Dual Therapy. Diabetes Ther. 2018.10; 9(5); 2117-2125
26. Araki S, Kijima T, Waseda Y, Komai Y, Nakanishi Y, Uehara S, Yasuda Y, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Nakano Y, Yoshimoto T, Uchida T, Fujii Y. Incidence and predictive factors of hypoglycemia after pheochromocytoma resection. International journal of urology : official journal of the Japanese Urological Association. 2018.11;
27. Soma Takahiko, Ishioka Junichiro, Tanaka Hajime, Matsuoka Yoh, Saito Kazutaka, Fujii Yasuhisa. 造影 CT と T2 強調 MRI による脂肪に乏しい血管筋脂肪腫の診断を目的とした畳み込みニューラルネットワークアルゴリズムを用いたコンピュータ補助診断の可能性 (Potential for computer-aided diagnosis using a convolutional neural network algorithm to diagnose fat-poor angiomyolipoma in enhanced computed tomography and T2-weighted magnetic resonance imaging) International Journal of Urology. 2018.11; 25(11); 978-979

[Conference Activities & Talks]

1. Ishioka J, Matsuoka Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Matsuoka Y, Saito K, Kihara K, Kimura T, Kudo K, Kumazawa I, Fujii Y. Computer-aided diagnosis with a convolutional neural network algorithm for fully automated detection of prostate cancer using pre-biopsy MRI. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.16 Denmark
2. Soma T, Ihioka J, Tanaka H, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Matsuoka Y, Saito K, Kihara K, Fujii Y. Computer-aided differential diagnosis of fat-poor angiomyolipoma using a deep neural networks algorithm in enhanced CT and T2-weighted magnetic resonance imaging. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.17 Denmark
3. Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Favorable locoregional control in patients with histologic variants of urothelial carcinoma treated with tetra-modality bladder-sparing protocol incorporating consolidative partial cystectomy with lymph node dissection. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.18 Denmark
4. Yoshida S., Takahara T., Ishii C., Arita Y., Kijima T., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Kihara K., Fujii Y. 935 METastasis Reporting And Data System for Prostate cancer (MET-RADS-P) score of whole-body DWI as a prognostic biomarker for castration-resistant prostate cancer. The 33th Annual Congress of the European Association of Urology 2018.03.19 Copenhagen, Denmark
5. Yajima S, Yoshida S, Takahara T, Arita Y, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Absence of inchworm sign on DWI as a predictive marker for progression in pT1 bladder cancer. The 18th annual meeting of the European Association of Urology 2018.03.19 Copenhagen, Denmark
6. Yajima S, Yoshida S, Arita Y, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Absence of inchworm sign on DWI as a predictive marker for progression in pT1 bladder cancer. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
7. Soma T, Yoshida S, Tanaka H, Uehara S, Yasuda Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . The usefulness of diffusion-weighted MRI in the differential diagnosis of urachal disorders. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark

8. Kaneko K, Yoshida S, Takahara T, Sakamoto T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . Diffusion-weighted MRI as an imaging biomarker for histological grade of bladder cancer: Semi-automatic segmentation analysis. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
9. Kaneko K, Yoshida S, Takahara T, Sakamoto T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Diffusion-weighted MRI as an imaging biomarker for histological grade of bladder cancer: Semi-automatic segmentation analysis. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
10. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Characteristics of global Gleason grading for MRI-targeted biopsy in comparison with systematic biopsy and prostatectomy grades.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
11. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Clinical significance of MRI-targeted biopsy in prediction of adverse pathological and oncological outcome after radical prostatectomy.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
12. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Clinical significance of MRI-targeted biopsy in prediction of adverse pathological and oncological outcome after radical prostatectomy.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
13. Yoshida S, Takahara T, Ishii C, Arita Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . METastasis reporting and data system for prostate cancer score of whole-body DWI as a prognostic biomarker for castration-resistant prostate cancer. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
14. Uehara S, Matsuoka Y, Tanaka H, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Do the Prostate Imaging Reporting and Data System scores reflect oncological outcome? Potential usefulness of scoring criteria-based assessment. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
15. Uehara S, Yoshida S, Tanaka H, Yasuda Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . Prediction of intraoperative urinary collecting system entry in patients with peripheral renal tumors undergoing partial nephrectomy: Usefulness of tumor-centered multiplanar reconstruction.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
16. Uehara S, Yoshida S, Matsuoka Y, Yasuda Y, Kijima T, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y. . Head-mounted display assisted magnetic resonance/ultrasound fusion prostate biopsy system.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
17. Waseda Y, Yoshida S, Takahara T, Arita Y, Sakamoto T, Yajima S, Uehara S, Yasuda Y, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Feasibility of perfusion MRI to predict renal function after nephroureterectomy in upper tract urothelial carcinoma patients.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
18. Waseda Y, Yoshida S, Takahara T, Arita Y, Sakamoto T, Yajima S, Uehara S, Yasuda Y, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Feasibility of perfusion MRI to predict renal function after nephroureterectomy in upper tract urothelial carcinoma patients. The 33th European Association of Urology annual congress 2018.03.26 Copenhagen, Denmark
19. Yajima Shugo, Yoshida Soichiro, Tanaka Hiroshi, Tanaka Hajime, Inoue Masaharu, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. pT1 膀胱癌の進行に関する拡散強調 MRI 上の inchworm sign 欠如の予測的意義 (Predictive significance of absence of inchworm sign on diffusion-weighted MRI for progression of the pT1 bladder cancer). 日本泌尿器科学会総会 2018.04.01

20. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y. Clinical significance of MRI-targeted biopsy for the risk stratification of oncological outcome after radical prostatectomy. 第 106 回日本泌尿器科学会総会 2018.04.19 京都
21. Matsuoka Y, Ishioka J, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Saito K, Kihara K, Fujii Y. MRI-based risk assessment for postoperative biochemical recurrence using the Prostate Imaging Reporting and Data System (PI-RADS) scores and capsular contact length. The 114th annual meeting of the American Urological Association 2018.05.18 San Francisco
22. 1 Yasuda Y, Saito K, Soma T, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Kihara K, Fujii Y. The outcome of gasless laparoscopic single-port clampless sutureless partial nephrectomy using three-dimensional head-mounted display. The outcome of gasless laparoscopic single-port clampless sutureless partial nephrectomy using three-dimensional head-mounted display. The 112th annual meeting of the American Urological Association 2018.05.18 San Francisco, USA
23. Ishioka J, et al. DEEP LEARNING WITH A CONVOLUTIONAL NEURAL NETWORK ALGORITHM FOR FULLY AUTOMATED DETECTION OF PROSTATE CANCER USING PRE-BIOPSY MRI. AUA 2018 2018.05.18 San Francisco, USA
24. Yokoyama M, Kawamura N, Uehara S, Yasuda Y, Kijima T, Yoshida S, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Acute kidney injury and intermediate-term renal function after clampless partial nephrectomy. The 113rd annual meeting of the American Urological Association 2018.05.19 San Francisco, USA
25. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y. The role of MRI-targeted biopsy in prediction of adverse pathological and oncological outcome after radical prostatectomy. The 114th annual meeting of the American Urological Association 2018.05.20 San Francisco

[Awards & Honors]

1. The selection of the best poster, 2018.03

[Others]

1. IRB Member, Sony Corporation 2012-

Department of Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD
Junior Associate Professor: Kaoruko Seino, PhD
JSPS Research Fellow: Md. Mosiur Rahman, PhD
Research Fellow: AL-SOBAlHI Saber,RN,MPH;PhD
Graduate Student: Dasavanh Manivong, MD, MSc;
Delgermaa Doshzeveg, MPH; Iskander Isaac Maro, MD, MPH;
Hoang Thuy Linh Nguyen, MD, MPH; Ahmad Shekib Arab,MD;
Yuri Tashiro,MPharm,MPH; Deogratius Bintabara MD, MSc;
TJ Robionson Moncatar, RN, MPH;
Kathryn Lizbeth Lucena Siongco, RN, RM;
Tran Dai Tri Han, MD, MPH; Hue Man Vo, MD;
HASAN S M Mahmudul Hasan,DMD;
Shayo Festo Kasmir, MD; Alemi Sharifullah, MD;
Romnalin Thonglor, MPH;
Ayano Miyashita; Nozomi Watanabe;
Rueda Saleh Alojaimy, RN

(1) Outline

The department of Global Health Entrepreneurship seeks to elucidate physical, social, economic and cultural factors determining inequity in health. The department works closely with WHO and other international agencies to help develop guidelines of scientific evaluation and recommended practices.

(2) Research

Major Research Topics:

- 1) Transfiguration of the ecosystem and its interaction with human health
- 2) Socio-cultural factors determining health
- 3) Social entrepreneurship development through applying the Healthy Settings approach
- 4) Use of information technology to improve public health
- 5) International health workforce and trade in health services
- 6) Universal health coverage in ageing society

(3) Education

PhD programs

Our doctoral program provides a flexible curriculum that allows students to customize their research goals, methods, and activities based upon their own interests and preferences. Students on the Public Health Medicine (PHM) track of the Disease Prevention Global Leader Program (DP-GLP) attain the skills required for public health professionals with an international perspective. The program prepares them for leadership roles in public institutions. Advanced students from many countries around the world are now enrolled. All the classes are conducted in English, thus facilitating the acquisition of international communication skills.

A rich variety of educational activities have been arranged in the program. These include: individual discussion sessions with professors and other faculty members; field investigations; and seminars on various topics such as community health care, community medicine, public health policy, biostatistics, academic presentation, development of foreign language skills, and communication skills. Students work closely with faculty members on an individual basis in setting the right direction for their research and confirmation of their progress.

Master Programs

Master degree students receive systematic intensive training that leads to the acquisition of broad expertise in the field of global public health. This program is open to students who have majored in any field.

(4) Lectures & Courses

The objective of our postgraduate education is to provide professional qualifications to high-caliber people who exhibit leadership in the advancement of public health and promotion of health on an international scale. The department helps students attain the knowledge, skills, attitude, and experiences that are necessary for competent health specialists and social entrepreneurs in healthcare.

By completion of the doctoral course, the participants are expected to be able to:

- Assess health and well being the populations in local, national, and international settings,
- Assess evidence to show effectiveness of health interventions, programs and strategies,
- Think strategically to develop local, national, and international policies,
- Manage projects to successful completion
- Demonstrate leadership in local, national, or international public health programs
- Communicate properly when listening, presenting, writing, and negotiating
- Pursue a full-cycle of an academic, public health research project
- Facilitate learning of staff, students, and colleagues, and
- Practice and respect professional ethics in a socio-culturally diverse environment.

(5) Publications

[Original Articles]

1. Deogratius Bintabara, Bonaventura C T Mpondo. Preparedness of lower-level health facilities and the associated factors for the outpatient primary care of hypertension: Evidence from Tanzanian national survey. PLoS ONE. 2018.02; 13(2); e0192942
2. Hao D Cheng, Sebastian K Grimm, Morgan Sa Gilman, Luc Christian Gwom, Devin Sok, Christopher Sundling, Gina Donofrio, Gunilla B Karlsson Hedestam, Mattia Bonsignori, Barton F Haynes, Timothy P Lahey, Isaac Maro, C Fordham von Reyn, Mirosław K Gorny, Susan Zolla-Pazner, Bruce D Walker, Galit Alter, Dennis R Burton, Merlin L Robb, Shelly J Krebs, Michael S Seaman, Chris Bailey-Kellogg, Margaret E Ackerman. Fine epitope signature of antibody neutralization breadth at the HIV-1 envelope CD4-binding site. JCI Insight. 2018.03; 3(5);
3. Isaac I. Maro; Keiko Nakamura; Kaoruko Seino; Kisali Pallangyo; Patricia Munseri; Mecky Matee; Charles Fordham von Reyn. Social activity patterns drive high rates of latent tuberculosis infection among adolescents in urban Tanzania Journal of Tuberculosis Research . 2018.03; 6(1); 81-95
4. Maro II, Nakamura K, Seino K, Pallangyo K, Munseri P, Matee M, von Reyn CF. Social activity patterns drive high rates of latent tuberculosis infection among adolescents in urban Tanzania. Journal of Tuberculosis Research. 2018.03; 6(1); 81-95
5. Shafiqullah H, Morita A, Nakamura K, Seino K . The family planning conundrum in Afghanistan Health Promotion International. 2018.04; 33(2); 311-317
6. Syed Emdadul Hauque Kayako Sakisaka Mosiur Rahman . Examining the relationship between socioeconomic status and the double burden of maternal over-and child under nutrition in Bangladesh Eur J Clin Nutr.. 2018.04;

7. MosiurRahman, Syed Emdadu lHaque, Md. Sarwar Zahan, Md. Jahirul Islam, Md. Mosfequr Rahman, Md. AsaduzzamanM.Sc., Md.fNuruzzamanHaque, Ahmed Zohirul Islam, Md. Durul Huda, Md.Golam Mostofa . Maternal high-risk fertility behavior and association with chronic undernutrition among children under age 5 y in India, Bangladesh, and Nepal: Do poor children have a higher risk? *Nutrition*. 2018.05;
8. Terada T, Nakamura K, Seino K, Kizuki M, Inase N. Cost of shifting from healthcare to long-term care in later life across major diseases: analysis of end-of-life care during the last 24 months of life. *Journal of rural medicine* . 2018.05;
9. Terada Tomoko, Nakamura Keiko, Seino Kaoruko, Kizuki Masashi, Inase Naohiko. Cost of shifting from healthcare to long-term care in later life across major diseases: analysis of end-of-life care during the last 24 months of life(和訳中) *Journal of Rural Medicine*. 2018.05; 13(1); 40-47
10. Bintabara D, Nakamura K, Seino K. Improving access to health care for women in Tanzania by addressing socioeconomic determinants and health insurance: a population-based cross-sectional survey. *BMJ Open*. 2018.08; 8; e023013
11. Shayo Festo, Nakamura Keiko, Seino Kaoruko, Nguyen Hoang Thuy Linh, Tashiro Yuri, Miyashita Ayano, Watanabe Nozomi. Albuminuria among African COPD patients(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 275
12. WATANABE Nozomi, NGUYEN Hoang Thuy Linh, MARO Isaac, NAKAMURA Keiko, SEINO Kaoruko, VO Van Thang. Assessment of physical activity among Vietnamese children using accelerometer(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 598
13. NGUYEN HOANG THUY LINH, NAKAMURA KEIKO, SEINO KAORUKO, WATANABE NOZOMI, MIYASHITA AYANO, Vo Van Thang. Associations between bullying the self-harming among Vietnamese schoolchildren(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 598
14. Bintabara Deogratiuss, Nakamura Keiko, Seino Kaoruko, Tashiro Yuri, Miyashita Ayano, Watanabe Nozomi. Facility readiness in primary care for non-communicable diseases in Tanzania(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 599
15. Arab Ahmad Shekib, Nakamura Keiko, Seino Kaoruko, Nguyen Hoang Thuy, Bintabara Deogratiuss Felician, Tashiro Yuri, Mohammad Omar Mashal, Shafiqullar Hemat. Food insecurity, knowledge of NCD and its risk factors among educators in Kabul(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 599
16. Miyashita Ayano, AL-SOBAlHI Saber, NAKAMURA Keiko, SEINO Kaoruko, HIRAKI Aya. Geographical and Demographic patterns of notified TB cases in Phnom Penh city(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 595
17. Maro Isaac, Nakamura Keiko, Seino Kaoruko, von Reyn Fordham, Tashiro Yuri, Miyashita Ayano, Watanabe Nozomi. Latent tuberculosis infection among adolescents in urban Tanzania(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 596
18. Tashiro Yuri, Nakamura Keiko, Chiba Mitsuyuki, Ishii Hiroshi, Seino Kaoruko, Ochi Shiro, Maro Isaac, Bintabara Deogratiuss. Lifestyle behaviour and relating factors among Health Promoting School children(和訳中) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 597
19. Keiko Nakamura, Lorenzo Fely Marilyn, Vo Van Thang, Canila Carmelita, MONCATAR TJ, Siongco Kathryn, Dai Tri Han Tran, Vo Thi Hue Man, Tashiro Yuri, Sugimura Masaki, Seino Kaoruko, Takano Takehito. 保健医療人材の国際的流動性のための多国間協力の研究 (第 1 報)(International Collaboration for Health Workforce Mobilization across Borders(1) Research framework for workforce development aimed at providing quality health and social care services for older adults in ASEAN countries) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 593
20. MONCATAR TJ, Nakamura Keiko, Siongco Kathryn, Tran Dai Tri Han, Vo Thi Hue Man, Canila Carmelita, Lorenzo Fely Marilyn, Vo Van Thang, Sugimura Masaki, Seino Kaoruko, Takano Takehito. 保健医療人材の国際的流動性のための多国間協力の研究 (第 2 報)(International Collaboration for Health Workforce Mobilization across Borders(2) Analysis of Utilization of Health Facilities among Elderly in the Philippines) *日本公衆衛生学会総会抄録集*. 2018.10; 77 回; 593

21. Siongco Kathryn Lizbeth L., Nakamura Keiko, Moncatar TJ, Dai Tri Han Tran, Vo Thi Hue Man, Canila Carmelita, Lorenzo Fely Marilyn E., Vo Van Thang, Sugimura Masaki, Seino Kaoruko, Takano Takehito. 保健医療人材の国際的流動性のための多国間協力の研究 (第 3 報)(International Collaboration for Health Workforce Mobilization across Borders(3) Association of NCD, Health Insurance and Health Facility Use among Filipino Elderly) 日本公衆衛生学会総会抄録集. 2018.10; 77 回; 594
22. Dai Tri Han Tran, Nakamura Keiko, Vo Thi Hue Man, Moncatar TJ, Siongco Kathryn Lizbeth L, Vo Van Thang, Canila Carmelita, Lorenzo Fely Marilyn E., Masaki Sugimura, Seino Kaoruko, Takano Takehito. 保健医療人材の国際的流動性のための多国間協力の研究 (第 4 報)(International Collaboration for Health Workforce Mobilization across Borders(4) Work status and financial security of the elderly in Vietnam) 日本公衆衛生学会総会抄録集. 2018.10; 77 回; 594
23. Vo Thi Hue Man, Nakamura Keiko, Dai Tri Han Tran, Moncatar TJ, Siongco Kathryn Lizbeth Lucen, Vo Van Thang, Canila Carmelita, Lorenzo Fely Marilyn E., Sugimura Masaki, Seino Kaoruko, Takano Takehito. 保健医療人材の国際的流動性のための多国間協力の研究 (第 5 報)(International Collaboration for Health Workforce Mobilization across Borders(5) Health patterns of Vietnamese elderly: review of the Vietnam Ageing Survey) 日本公衆衛生学会総会抄録集. 2018.10; 77 回; 594
24. Dashzeveg D, Nakamura K, Seino K, Al-Sobaihi S, Palam E.. Changes in the configuration and patterns of physical activity among Mongolian adults, 2005-2013. *Journal of Rural Medicine*. 2018.11; 13(2); 151-159
25. Manivong D, Rahman M, Nakamura K, Seino K.. Assessing the link between endorsing attitudes justifying partner abuse and reproductive health care utilization among women in Lao PDR. *Journal of Rural Medicine*. 2018.11; 13(2); 124-133
26. Manivong Dasavanh, Rahman Mosiur, Nakamura Keiko, Seino Kaoruko. Assessing the link between endorsing attitudes justifying partner abuse and reproductive health care utilization among women in Lao PDR(和訳中) *Journal of Rural Medicine*. 2018.11; 13(2); 124-133
27. Manivong D, Rahman M, Nakamura K, Seino K. Assessing the link between endorsing attitudes justifying partner abuse and reproductive health care utilization among women in Lao PDR. *Journal of rural medicine : JRM*. 2018.11; 13(2); 124-133
28. Dashzeveg Delgermaa, Nakamura Keiko, Seino Kaoruko, Al-Sobaihi Saber, Palam Enkhtuya. Changes in the configuration and patterns of physical activity among Mongolian adults, 2005-2013(和訳中) *Journal of Rural Medicine*. 2018.11; 13(2); 151-159
29. Dashzeveg D, Nakamura K, Seino K, Al-Sobaihi S, Palam E. Changes in the configuration and patterns of physical activity among Mongolian adults, 2005-2013. *Journal of rural medicine : JRM*. 2018.11; 13(2); 151-159

[Conference Activities & Talks]

1. Nakamura K, Seino K, Canila C, Lorenzo M, Thang V.. Workforce development aimed at providing quality health and social care services for older adults in ASEAN countries through inter-professional training towards acceleration of universal health coverage.. 2018.03.13
2. Canila C, Nakamura K, Seino K, Lorenzo M, Thang V.. Workforce development aimed at providing quality health and social care services for older adults in ASEAN countries through inter-professional training towards acceleration of universal health coverage. . Meeting on Universal Health Coverage (UHC) and Impact of Population Ageing 2018.03.26 Yokohama
3. Nakamura K. Healthy Cities and SDGs. 2018.05.16
4. Nakamura K. Translate Active Ageing Concept in Community to Improve the Livings of Older Persons. 2018.07.09
5. Nakamura K. Promoting partnerships for healthy cities between local governments and private sector. 2018.09.07

Rehabilitation Medicine

Professor	Atsushi Okawa(May-)
Associate Professor	Tetsuya JINNO(-Jun.)
Assistant Professor	Tomoko SAKAI
Assistant Professor	Dai UKEGAWA
Graduate Student	Chisato HOSHINO
	Kazuko KATSUKI
	Shunsuke OHJI
	Ryo ONUMA
	Yuji TAKAHASHI
	Kenji HIROHATA

(1) Research

Research Subjects

- 1) Rehabilitation for total joint arthroplasty
- 2) Motion and gait analysis of healthy and disabled subjects
- 3) Biomechanical research for prevention of sports injury
- 4) Patient safety in rehabilitation medicine
- 5) Osteoporosis of children (individuals) with severe motor and intellectual disabilities

(2) Lectures & Courses

Purpose of Education:

Rehabilitation medicine consists of physical, occupational and speech therapy. Main theme of rehabilitation medicine in graduate course is to study 3-dimensional motion analysis in activities of daily living and molecular biological analysis of disuse atrophy.

(3) Publications

[Original Articles]

1. Development of the Japanese Version of the Lumbar Stiffness Disability Index Following Lumbar Spinal Surgery 2018;
2. Yuko Uesugi, Takashi Sakai, Taisuke Seki, Shinya Hayashi, Junichi Nakamura, Yutaka Inaba, Daisuke Takahashi, Kan Sasaki, Goro Motomura, Naohiko Mashima, Tamon Kabata, Akihiro Sudo, Tetsuya Jinno, Wataru Ando, Satoshi Nagoya, Kengo Yamamoto, Satoshi Nakasone, Hiroshi Ito, Takuaki Yamamoto, Nobuhiko Sugano. Quality of life of patients with osteonecrosis of the femoral head: a multicentre study. Int Orthop. 2018; 42(7); 1517-1525

3. Ikeda T, Jinno T, Masuda T, Aizawa J, Ninomiya K, Suzuki K, Hirakawa K. Effect of exercise therapy combined with branched-chain amino acid supplementation on muscle strengthening in persons with osteoarthritis Hong Kong Physiother J. 2018; 38(1); 1-9
4. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Limb-dominance and gender differences in the ground reaction force during single-leg lateral jump-landings. Journal of Physical Therapy Science. 2018.03; 30(3); 387-392
5. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Yuki Yamauchi, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Longitudinal morphological change of acetabular subchondral bone cyst after total hip arthroplasty in developmental dysplasia of the hip. Eur J Orthop Surg Traumatol. 2018.05; 28(4); 621-625
6. N Taniguchi, T Jinno, R Takada, D Koga, T Ando, A Okawa, H Haro. Do screws and screw holes affect osteolysis in cementless cups using highly crosslinked polyethylene? A 7 to 10-year follow-up case-control study. Orthop Traumatol Surg Res. 2018.05; 104(3); 307-315
7. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Akimasa Kimura, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Direct anterior versus anterolateral approach in one-stage supine total hip arthroplasty. Focused on nerve injury: A prospective, randomized, controlled trial. J Orthop Sci. 2018.09; 23(5); 783-787
8. Ushio S, Hoshino Y, Kawabata S, Adachi Y, Sekihara K, Sumiya S, Ukegawa D, Sakaki K, Watanabe T, Hasegawa Y, Okawa A. Visualization of the electrical activity of the cauda equina using a magnetospinography system in healthy subjects. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology. 2018.11; 130(1); 1-11
9. Suzuki M, Koyama S, Kimura Y, Ishiyama D, Otobe Y, Nishio N, Ichikawa T, Kunieda Y, Ohji S, Ito D, Yamada M. Relationship between characteristics of skeletal muscle and oral function in community-dwelling older women. Archives of gerontology and geriatrics. 2018.11; 79; 171-175

[Books etc]

1. Jinno T, Watanabe T, Yagishita K. What' s new in orthopedics: Asian perspective - hip?. Courtney PM, ed. Recent Advances in Orthopedics -2. Jaypee Brothers Medical Publishers, 2018.04
2. Watanabe T, Jinno T, Yagishita K. What' s new in orthopedics: Asian perspective - knee?. Courtney PM, ed. Recent Advances in Orthopedics -2. Jaypee Brothers Medical Publishers, 2018.04

[Conference Activities & Talks]

1. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Kazuyoshi Yagishita, Atsushi Okawa. Comparison between direct anterior and anterolateral approach in one-stage total hip arthroplasty: A prospective, randomized, controlled trial.. American Academy of Orthopaedic Surgeons 2018.03.06 New Orleans (USA)
2. Gaku Koyano, Seiichiro Hasegawa, Tetsuya Jinno, Ryohei Takada, Atsushi Okawa. Comparison of Perioperative Features of the Anterolateral and the Direct Anterior Approaches in Supine Total Hip Arthroplasty in Relation to Morphology of the Pelvis. Orthopaedic Research Society 2018.03.10 New Orleans (USA)
3. Akira Takahashi, Tetsuya Jinno, Kazumasa Miyatake, Ryohei Takada, Masanobu Hirao, Atsushi Okawa. Association Between Intraoperative Injury And Postoperative Change In TFL After Total Hip Arthroplasty Using Direct Anterior Approach. 19th EFORT Congress 2018.05.30 Barcelona (Spain)
4. Sho Mitomo, Kenji Hirohata, Kaori Teraguchi, Mari Takase, Kaito Nemoto, Yuya Oota, Masakazu Kida. Relationship between Muscle Strength in Different Positions and Forward Jump Ability after ACL Reconstruction. Australian Orthopaedic Association (AOA) Continuing Orthopaedic Education Conference (COE) and the 2018 Asia-Pacific Knee, Arthroscopy and Sports Medicine 2018.05.31 Sidney
5. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlation Between Kinesiophobia and Vastus Medialis Activation Prior to Landing During Single-Leg Jump Landing in Athletes After Anterior Cruciate Ligament Reconstruction.. AOA & APKASS Combined Meeting 2018.05.31 Sidney

Gerodontology and Oral Rehabilitation

Professor

MINAKUCHI Shunsuke

Associate Professor

TOHARA Haruka

Junior Associate Professor

SEKITA Toshiaki, KOBAYASHI Ken-ichi, KUBOTA Kazumasa

Assistant Professor

AKIBA Norihisa, INOKOSHI Masanao, KANAZAWA Manabu, KOMAGAMINE Yuriko, MOTOMURA Kazuo, NAKAGAWA Kazuharu, NAKANE Ayako, SATO Yusuke, OKUBO Mai,

Project Assistant Professor

HAMA Yohei

Dental Resident

ARAKIDA Toshio, INOUE Minoru, UEDA Kaori, OOWADA Gaku, KAMOUCHI Go, SUZUKI Hiroyuki, SOEDA Hitomi, BABA Yuya, Hara Takeshi, MIYAYASU Anna, YAMAGUCHI Kohei, YOSHIZAKI Taro, YOSHIMI Kanako

Graduate Student

AMAGAI Noriko, SATO Eriko, MATSUDA Yuhei, MATSUBARA Mariko, YAMAZAKI Yasuhiro, ASAMI Mari, KYOSAKA Yuka, SHIMIZU Haruki, MIURA Akemi, KAIDILIYA Yalikun, ANDO Mariko, VO Lam Thuy, KHAING Myat Thu, KAGIFUKU Yuko, KUROSAWA Yukiko, SHIMADA Ryo, SHIMIZUBATA Makoto, DOUKE Midori, YOSHIDA Saori, YOSHINAKA ShinSOEDA Yumika, CHANTARAMANEE Ariya, TUN Min Bo. NEGORO Masatoshi, HASEGAWA Syouhei, HADA Tamaki, HATANO Keita, HARA Yoshiko, Awutsadaporn Katheng, Thaw Di Cho Too, ISHII Miki, UEHARA Yoko, OTAKE Ryosuke, ONUMA Hiraku, OKUMURA Takuma, OBANA Michiyo, SAI TUN NAING, SHIROBE Maki, TAKAGI Daisuke, TAKANO Satoru, NOMOTO Akiko, MATSUBARA Chiaki, YAMAMOTO Mao

Student

ARAMAKI Oto, IMADA Ryoko, ONO Airi, OGAWA Takahiko, OKANO Sakiko, ODANI Tomoko, OBARA Mana, KAWAI Yosuke, KAWAKATSU Miri, KONISHI Emi, JOKO Natsuka, TAMURA Atsuko, NAKATOMI Hana, NAMIKI Chizuru, NISHIMIYA Yui, HAYASHI, Ayano, MIYAHARA Kotomi, YAGUCHI Shiho

Staff

TERADA Mito, FUKUSHIMA Rie

(1) Research

- 1) Medical management of Elderly Patients During Dental Treatment
- 2) New Examination Method for Dry Mouth
- 3) Oral Stereognosis Ability in the Elderly

- 4) Threshold of Mucous Membrane under Denture Base in Elderly Oral Mucosa Patients
- 5) State of the art Lasers in Zirconia Prosthetic Processing and Pain-free Treatment
- 6) Denture Mobility
- 7) Deglutition in Elderly Patients Requiring Nursing Care
- 8) Eating and Swallowing Rehabilitation in Post-Oral Tumor Surgery Patients
- 9) Dysphagia of Medullary Infarction Patients
- 10) Dental Approaches to Dysphagia
- 11) Screening Methods of Silent Aspiration
- 12) Swallowing Dynamics and Brain Activity
- 13) Stress analyses of implant overdenture
- 14) Factorial analysis of complete denture prosthesis
- 15) Resilient denture lining material
- 16) CAD/CAM system for fabricating complete dentures
- 17) Evaluations of masticatory performance using color-changeable chewing gum
- 18) Development of novel restorative materials for root caries
- 19) Development of novel aesthetic, strong and ageing resistant highly translucent zirconia
- 20) Ultrastructural analysis of zirconia-veneering ceramic interface

(2) Education

Given the increased health needs of an aging society, we aim to integrate diverse clinical specialties related to geriatric dental practice and to educate individuals of fundamental studies in each field. We emphasize a comprehensive approach to patient interactions by examining daily life functionality rather than focusing only on their diseases.

With regard to dysphagia, which can lead to aspiration pneumonia, we provide comprehensive education on causes, diagnostic methods, and rehabilitation options from a dentistry point of view. Since we regard rehabilitation as the medicine of daily living, we emphasize that dysphagia rehabilitation should be considered a method to ameliorate disability rather than diseases by introducing practical approaches in addition to factual knowledge.

(3) Clinical Performances

We manage the prosthodontic, special care and dysphagia rehabilitation departments.

(4) Publications

[Original Articles]

1. Mariko Matsubara, Haruka Tohara, Koji Hara, Hiromichi Shinozaki, Yasuhiro Yamazaki, Chiaki Susa, Ayako Nakane, Yoko Wakasugi, Shunsuke Minakuchi. High-speed jaw-opening exercise in training suprahypoid fast-twitch muscle fibers Clinical Interventions in Aging. 2018.01; 13; 125-131
2. Anna Miyayasu, Manabu Kanazawa, Ayami Jo, Yusuke Sato, Shunsuke Minakuchi. Cost-effectiveness analysis of two impression methods for the fabrication of mandibular complete dentures. J Dent. 2018.01; 68; 98-103
3. Yusuke Sato. A case report of occlusal reconstruction using overdenture and cross-arch bridge Annals of Japan Prosthodontic Society. 2018.01; 10(1); 71-74
4. Taniguchi H, Aoyagi Y, Matsuo K, Nakagawa K, Saitoh E. Development of an esophageal stimulation method to elicit swallowing reflex in humans. Journal of Oral Rehabilitation. 2018.01; 45; 211-215
5. Tagashira I., Tohara H., Wakasugi Y., Hara K., Nakane A., Yamazaki Y., Matsubara M., Minakuchi S. A new evaluation of masticatory ability in patients with dysphagia: The Saku-Saku Test. Archives of Gerontology and Geriatrics. 2018.01; 74; 106-111

6. Thammajaruk P, Inokoshi M, Chong S, Guazzato M. Bonding of composite cements to zirconia: A systematic review and meta-analysis of in vitro studies. *J Mech Behav Biomed Mater.* 2018.02; 80; 258-268
7. Kamiyanagi A, Sumita YI, Ino S, Chikai M, Nakane A, Tohara H, Minakuchi S, Seki Y, Endo H, Taniguchi H. Evaluation of swallowing ability using swallowing sounds in maxillectomy patients. *Journal of Oral Rehabilitation.* 2018.02; 45(2); 126-131
8. Suzuki H, Kanazawa M. Responses to the letter titled "No clinically significant effect of new complete denture fabrication and simple dietary advice on nutrient intake and masticatory function of edentulous older people." *Clinical nutrition (Edinburgh, Scotland).* 2018.02; 37(1); 408-409
9. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Yoshihara K, Nagaoka N, Zhang F, Vleugels J, Van Meerbeek B, Minakuchi S. Crystallographic and morphological analysis of sandblasted highly translucent dental zirconia. *Dent Mater.* 2018.03; 34(3); 508-518
10. Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Shunsuke Minakuchi. Digital impression and jaw relation record for the fabrication of CAD/CAM custom tray. *J Prosthodont Res.* 2018.03; 62(4); 509-513
11. Kohei Yamaguchi, Haruka Tohara , Koji Hara, Ayako Nakane, Eriko Kajisa, Kanako Yoshimi, Shunsuke Minakuchi. Relationship of aging, skeletal muscle mass, and tooth loss with masseter muscle thickness *BMC Geriatrics.* 2018.03; 18(1)(67);
12. Kajisa E., Tohara H., Nakane A., Wakasugi Y., Hara K., Yamaguchi K., Yoshimi K., Minakuchi S.. The relationship between jaw-opening force and the cross-sectional area of the suprahyoid muscles in healthy elderly *Jouranal of Oral Rehabilitation.* 2018.03; 45(3); 222-227
13. Pongprueksa P, De Munck J, Inokoshi M, Van Meerbeek B. Polymerization efficiency affects interfacial fracture toughness of adhesives. *Dent Mater.* 2018.04; 34(4); 684-692
14. Yamaga Eijiro, Sato Yusuke, Minakuchi Shunsuke. A structural equation model to test a conceptual framework of oral health in Japanese edentulous patients with an item weighting method using factor score weights: a cross-sectional study. *BMC Oral Health.* 2018.04; 18(1); 71
15. Manabu Kanazawa, Mariko Tanoue, Anna Miyayasu, Shin Takeshita, Daisuke Sato, Mari Asami, Thuy Vo Lam, Khaing Myat Thu, Ken Oda, Yuriko Komagamine, Shunsuke Minakuchi, Jocelyne Feine. The patient general satisfaction of mandibular single-implant overdentures and conventional complete dentures: Study protocol for a randomized crossover trial. *Medicine (Baltimore).* 2018.05; 97(20); e10721
16. Hara Koji, Tohara Haruka, Kobayashi Kenichiro, Yamaguchi Kohei, Yoshimi Kanako, Nakane Ayako, Minakuchi Shunsuke. Age-related declines in the swallowing muscle strength of men and women aged 20-89 years: A cross-sectional study on tongue pressure and jaw-opening force in 980 subjects *Archives of Gerontology and Geriatrics.* 2018.05; 78; 64-70
17. Shunsuke Minakuchi, Kazuhiro Tsuga, Kazunori Ikebe, Takayuki Ueda, Fumiyo Tamura, Kan Nagao, Junichi Furuya, Koichiro Matsuo, Ken Yamamoto, Manabu Kanazawa, Yutaka Watanabe, Hirohiko Hirano, Takeshi Kikutani, Kaoru Sakurai. Oral hypofunction in the older population: Position paper of the Japanese Society of Gerodontology in 2016. *Gerodontology.* 2018.06; 35(4); 317-324
18. Yamaga Eijiro, Sato Yusuke, Minakuchi Shunsuke. An intervention study to test Locker's conceptual framework of oral health in edentulous elders. *Gerodontology.* 2018.06; 35(3); 260-267
19. Kenichiro Ozaki, Satoshi Teranaka, Takeshi Okada, Shunsuke Minakuchi. Rehabilitation Dental Practice of Inpatients in a Community Hospital. *Gerodontology.* 2018.06; 33(1); 17-24
20. Toshio Arakida, Manabu Kanazawa, Maiko Iwaki, Tetsuya Suzuki, Shunsuke Minakuchi. Evaluating the influence of ambient light on scanning trueness, precision, and time of intra oral scanner. *J Prosthodont Res.* 2018.07; 62(3); 324-329
21. Kanako Yoshimi, Koji Hara, Haruka Tohara, Ayako Nakane, Kazuharu Nakagawa, Kohei Yamaguchi, Yukiko Kurosawa, Saori Yoshida, Chantaramanee Ariya, Shunsuke Minakuchi. Relationship between swallowing muscles and trunk muscle mass in healthy elderly individuals: A cross-sectional study. *Archives of Gerontology and Geriatrics.* 2018.07; 79; 21-26

22. Baba Y, Sato Y, Owada G, Minakuchi S. Effectiveness of a combination denture-cleaning method versus a mechanical method: comparison of denture cleanliness, patient satisfaction, and oral health-related quality of life. *Journal of Prosthodontic Research*. 2018.07; 62(3); 353-358
23. Kazumasa Kubota, Tomoyuki Miyamoto, Takutoshi Inoue and Haruhisa Fukayama. Alternating current iontophoresis for control of postoperative pain. *Anesthesia Progress*. 2018.08; (65); 106-110
24. Shimizu H, Inokoshi M, Takagaki T, Uo M, Minakuchi S. Bonding Efficacy of 4-META/MMA-TBB Resin to Surface-treated Highly Translucent Dental Zirconia. *J Adhes Dent*. 2018.09; 20(5); 453-459
25. Seki N, Kanazawa M, Komagamine Y, Mizutani K, Hosaka K, Komada W, Moross J, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School. *Journal of Medical and Dental Sciences*. 2018.09; 65; 123-130
26. Masahiro Nakazawa, Hiroki Mori, Jun Handa, Terushige Sato Takehumi Kozima, Shiro Ook), Yohei Hama, Haruka Tohara. Simple Training for Maintaining and Improving Chewing Ability Japanese journal of gerodontology. 2018.09; 33(2); 63-69
27. Seki Naoko, Kanazawa Manabu, Komagamine Yuriko, Mizutani Koji, Hosaka Keiichi, Komada Wataru, Moross Janelle, Kuroda Shinji, Sunaga Masayo, Kawaguchi Yoko, Morio Ikuko, Kinoshita Atsuhiro. International Dental Education Course for Clinical Expertise at Tokyo Medical and Dental University Graduate School *Journal of Medical and Dental Sciences*. 2018.09; 65(3); 123-130
28. Manabu Kanazawa, Hiroyuki Suzuki, Yuriko Komagamine, Maiko Iwaki, Noriko Amagai, Shunsuke Minakuchi. Combined effects of new complete denture fabrication and simplified dietary advice on nutrient intake in edentulous elderly patients for 6 months. *Clin Oral Investig*. 2018.10;
29. Yalikun K, Kanazawa M, Tanoue M, Minakuchi S. In vitro variation measurement of mandibular denture displacement resistance involving 1 to 3 implants. *The Journal of prosthetic dentistry*. 2018.10; 121(3); 492-497
30. Komagamine Y, Kanazawa M, Yamada A, Minakuchi S. . Association between tongue and lip motor functions and mixing ability in complete denture wearers. *Aging Clinical and Experimental Research*. 2018.11;
31. Komagamine Y, Kanazawa M, Sato D, Minakuchi S. A preliminary comparison of masticatory performances between immediately loaded and conventionally loaded mandibular two-implant overdentures with magnetic attachments. *Clinical implant dentistry and related research*. 2018.12; 21(1); 130-137
32. Kenichiro Ozaki, Mikoto Baba, Shunsuke Minakuchi et al. Impact of Oral Hygiene Management through a Multidisciplinary Approach on Patients with Acute Stroke: Building a Pneumonia-Prevention System by Dentistry. *the Japanese Society of Dysphagia Rehabilitation*. 2018.12; 22(3); 225-236

[Conference Activities & Talks]

1. Iwaki Maiko, Kanazawa Manabu, Sato Daisuke, Miyayasu Anna, Kasugai Shohei, Araki Kouji, Minakuchi Shunsuke. Masticatory Functions with Immediate Loading of Two-implant Mandibular Overdentures: 5-year prospective study.. *Academy of Osseointegration Annual Meeting 2018* 2018.03.01 Los Angeles, CA, USA
2. Koji Hara, Haruka Tohara. The strength of masticatory muscle affects tongue pressure. *Dysphagia Research Society* 2018.03.15 Baltimore
3. Yukiko K, Haruka T, Ayako N, Koji H, Yasuhiro Y, Chizuru N, Yoko W, Shunsuke M. The relationship between neck circumference and swallowing function in the elderly with dysphagia. *Dysphagia Research Society* 2018.03.15 Baltimore
4. Kohei Yamaguchi, Haruka Tohara, Ayako Nakane, Kanako Yoshimi, Shunsuke Minakuchi. Potential factors that influence the echo intensity of masseter muscle . 2018 DRS Annual meeting 2018.03.16 Baltimore

5. Kyosaka Y, Inokoshi M, Owatari T, Inoue M, Minakuchi S. Influence of Adrenaline and Felypressin on Blood Pressure and Heart Rate of the Medically Compromised Elderly. The 27th Annual Meeting of Japanese Society of Dentistry for Medically Compromised Patients 2018.03.23 Tokyo
6. Yumika Soeda, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Shunsuke Minakuchi. The new method of manufacturing CAD/CAM complete denture applying the customized disk. The 9th Scientific Meeting of the Japan Academy of Digital Dentistry 2018.04.14 Morioka
7. Arakida T, Kanazawa M, Iwaki M, Soeda Y, Hada T, Suzuki T, Minakuchi S . The effect of artificial landmark to the precision of digital impression for edentulous jaw . 2018.04.14
8. Zhang F, Van Meerbeek B, Inokoshi M, Vleugels J, Reveron H, Chevalier J. Zirconia ceramics for dental restorations: trade-off between strength, stability and translucency. 9th International Workshop on Interfaces, New Frontiers in Biomaterials 2018.04.18 Santiago de Compostela, Spain
9. Nasiry Khanlar L, Takagaki T, Inokoshi M, Ikeda M, Nikaido T, Tagami J. The Effect of Carboxyl-based Monomers on Resin Bonding to Zirconia Ceramics. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
10. Yumika Soeda, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Shunsuke Minakuchi. The new method of manufacturing CAD/CAM complete denture applying the customized disk. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.15 Okayama
11. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Kazuhiro Shimoyama, Shunsuke Minakuchi. The effect of new complete denture fabrication combined with simplified dietary advice on nutrient intake of edentulous patients: 6-month progress report.. The 127th Scientific Meeting of Japan Prosthodontic Society 2018.06.16 Okayama
12. Asami Mari,Kanazawa Manabu,Miyayasu Anna,Shimada Ryo,Negoro Masatoshi,Sato Daisuke,Kasugai Shohei, Minakuchi Shunsuke. Survival and marginal bone loss of single-implant overdentures -A 12-month follow-up-. The 127th Scientific Meeting of Japan Prosthodontic Society 2018.06.16 Okayama
13. Arakida T, Kanazawa M, Iwaki M, Soeda Y, Hada T, Suzuki T, Minakuchi S . The effect of artificial landmark to the precision of digital impression to edentulous jaw . 2018.06.16
14. Yumika Soeda, Kazumasa Kubota, Natsuka Joko, Shunsuke Minakuchi, Kazuhiro Shimoyama. A case of a patient with bone necrosis in the mandible after administration of denosumab for prostate cancer. The 29th Annual Meeting of the Japanese Society of Gerodontology 2018.06.22 Shinagawa
15. Kaori Ueda,Kazumasa Kubota,Masanao Inokoshi,Shunsuke Minakuchi. A case of tooth extraction and prosthetic treatment for a Glucocorticoid-induced Osteoporosis patient.. The 29th Annual Meeting of Japanese Society of Gerodontology 2018.06.22 Shinagawa
16. Anri Higashinakagawa, Toshiaki Sekita, Akiko Nomoto, Eriko Tsugawa, Seiko Kaneko, Syunsuke Minakuchi. A case report of immediate repair with replacing artificial teeth. The 29th Annual Meeting of Japanese Society of Gerodontology 2018.06.22 shinagawa
17. Toshiaki Sekita, Anri Higashinakagawa, Syuhei Takeuchi, Syunsuke Minakuchi. Estimation of breathing rate using a laser ranging sensor. The 29th Annual Meeting of Japanese Society of Gerodontology 2018.06.22 shinagawa
18. Mana Obara , Kazumasa Kubota, Shunsuke Minakuchi . Oral health management of a patient after the operation of valvular disease and cardiac arrest. Japanese society of Gerodontology 2018.06.22 Shinagawa
19. Yosuke Kawai, Kazumasa Kubota, Shunsuke Minakuchi. Management of a patient with supraventricular tachycardia identified during medical examination for dental treatment. Japanese Society of Gerodontology 2018.06.22 Shinagawa
20. Misato Kawakatsu, Kazumasa Kubota, Itoe Tagashira, Kaori Ueda, Shunsuke Minakuchi. Cases of patients with premature ventricular constriction during dental treatment. Japanese Society of Gerodontology 2018.06.22 Shinagawa
21. Mana Obara, Kazumasa Kubota, Shunsuke Minakuchi. Oral health management of a patient after the operation of valvular disease and cardiac arrest. 2018.06.22

22. Suzuki H, Kanazawa M, Komagamine Y, Iwaki M, Amagai N, Minakuchi S. The effect of prosthesis and dietary intervention for edentulous persons. IADR GORG Symposium with the European College of Gerodontology (ECG) and the Japanese Society of Gerodontology (JSG) 2018.07.24 London
23. Kyosaka Y, Owatari T, Inokoshi M, Inoue M, Minakuchi S. Effects of Adrenaline and Felypressin on Medically Compromised Elderly. IADR GORG Symposium with the European College of Gerodontology (ECG) and the Japanese Society of Gerodontology (JSG) 2018.07.24 London
24. KANAZAWA M. Does oral rehabilitation improve masticatory performance, food intake and QoL in super aged society?. IADR GORG Symposium with the European College of Gerodontology (ECG) and the Japanese Society of Gerodontology (JSG) 2018.07.24 London, UK
25. Inokoshi M, Shimizubata M, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Minakuchi S. Sandblasting increases the flexural strength of highly translucent zirconia. 96th General Session and Exhibition of the IADR 2018.07.25 London
26. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Basic Properties of Novel S-PRG Contained Cement for Root Caries. 96th General Session and Exhibition of the IADR 2018.07.26 London
27. Thuy Vo Lam, Manabu Kanazawa, Khaing Myat Thu, Mari Asami, Anna Miyayasu, Shimada Ryo, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi. Are One-Implant Overdentures Superior to Complete Dentures in Masticatory Function?. IADR 2018 General Session in London 2018.07.26 London
28. Hama Y, Minakuchi S, Sasaki K, Maeda T, Hamura A, Ichinohe T, Okiji T. The Dental Education Consortium to promote healthy longevity -Fourth report- Towards the final year. Annual Meeting of the 37th Japanese Dental Education Association 2018.07.27 Koriyama
29. K. M. Thu, M. Kanazawa, T. Vo Lam, M. Asami, A. Miyayasu, S. Ryo, D. Sato, S. Kasugai, S. Minakuchi. Durability of Locator and Optimal Retention for Single Implant Overdenture. 2018 IADR/PER General Session 2018.07.27 ExCel Convention center, London, UK
30. Shimizu H, Inokoshi M, Takagaki T, Minakuchi S. Discoloration of Highly Translucent Zirconia and Composite Resin. 96th General Session and Exhibition of the IADR 2018 2018.07.27 London
31. Yuriko Komagamine, Manabu Kanazawa, Maiko Iwaki, Hiroyuki Suzuki, Noriko Amagai. The Effect of New Complete Denture and Simple Dietary Advice . 96th General Session & Exhibition of the IADR 2018.07.28 London
32. Seki N, Hosaka K, Komada W, Kanazawa M, Mizutani K, Komagamine Y, Moross J, Morio I. International student forum 2018 -International students' life in Japan-. International Student Forum 2018 by Japanese Dental Science Federation 2018.08.02 Tokyo
33. KANAZAWA M. The Current Stream of Implant Overdentures. The 3rd International Symposium in Geriatric Dentistry CU-TMDU Joint Symposium 2018.09.06 Bangkok
34. Chiaki Matsubara, Junichi Furuya, Rena Nakayama, Michiyo Obana, Shunsuke Minakuchi. Collaborative transdisciplinary team approach for oral health care of acute stroke patients. Japan-Korea joint symposium The 24th Dysphagia Rehabilitation Society in Japan 2018.09.07 Sendai
35. Inokoshi M. Special Care Dentistry for Elderly and Root Caries. CU-TMDU Joint Symposium: The 3rd International Symposium in Geriatric Dentistry 2018.09.07 Bangkok
36. Yuriko Komagamine. Masticatory Performance in Elders — How to Evaluate. CU-TMDU Joint Symposium The 3rd International Symposium in Geriatric Dentistry: Application from Research to Clinic for the Elders 2018.09.07 Bangkok
37. Komagamine Y, Kanazawa M, Seki N, Mizutani K, Hosaka K, Komada W, Janelle Moross, Kuroda S, Morio I, Kinoshita A. Effort Toward International Dental Education By Tokyo Medical And Dental University. 32nd IADR-SEA & 29th SEAADE 2018.09.11 Da Nang, Vietnam
38. Thu K, Kanazawa M, Vo T, Asami M, Miyayasu A, Shimada R, Sato D, Kasugai S, Minakuchi S. Retention and Patient Satisfaction of Locator in Single Implant-Overdenture. 32nd IADR-SEA & 29th SEAADE, Vietnam 2018.09.13 Ariyana Convention Center, Da Nang, Vietnam

39. Asami M, Kanazawa M, Vo T, Thu K, Miyayasu A, Shimada R, Sato D, Kasugai S, Minakuchi S. Marginal bone loss and stability of single implant overdentures. 32nd IADR-SEA & 29th SEAADE, Vietnam 2018.09.13 Ariyana Convention Center, Da Nang, Vietnam
40. Thuy Vo Lam, Manabu Kanazawa, Khaing Myat Thu, Mari Asami, Anna Miyayasu, Ryo Shimada, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi. Masticatory function of single implant overdentures: 1-year results. 32nd IADR-SEA & 29th SEAADE, Vietnam 2018.09.13 Ariyana Convention Center, Da Nang, Vietnam
41. Yuriko Komagamine. Evaluation for Masticatory Performance and Nutrition. Lecture in University of Dental Medicine, Mandalay 2018.10.02 Mandalay
42. Inokoshi M, Nozaki K, Shimizu H, Minakuchi S. Influence of yttria content on translucency and flexural strength of highly translucent dental zirconia. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.06 Sapporo
43. Shimizubata M, Inokoshi M, Hatano K, Wada T, Takahashi R, Uo M, Minakuchi S. Acid buffering capacity of a novel S-PRG filler containing glass ionomer cement. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Sapporo
44. Hatano K, Inokoshi M, Uo M, Wada T, Takahashi R, Minakuchi S. Acid buffering capacity of a novel S-PRG filler containing denture adhesive. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Sapporo
45. Negoro Masatoshi, Kanazawa Manabu, Shimada Ryo, Miyayasu Anna, Sato Daisuke, Kusumoto Yuriko, Abe Yuka, Baba Kazumi, Minakuchi Syunsuke. Patient report outcomes of IARPD with magnetic attachments. 2018.11.03 Niigata
46. Kenichiro Ozaki. Medical and dental collaboration. 2018.11.10
47. Inokoshi M, Shimizu H, Takagaki T, Minakuchi S. Influence of various surface treatments on fracture strength of zirconia-veneering ceramic interface. The 37th Annual Meeting of Japan Society for Adhesive Dentistry 2018.11.11 Niigata
48. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yuuko Kagihuku, Takashi Ono, Chihiro Akazawa, Takashi Asada, Shunsuke Minakuchi. Approaches of investigating oral function in Mild Cognitive Impairment (MCI) patients. The 6th Tri-University Consortium 2018.11.30 Tokyo
49. Kanazawa M, Minakuchi S. Simultaneous broadcasting lecture: Impression with border molding for mandibular complete dentures. International Faculty Development Course 2018 2018.11.30 Tokyo
50. Kanazawa M, Komagamine Y. Oral Hypofunction. International Faculty Development Course 2018 2018.12.03 Tokyo
51. KANAZAWA M. The Current Stream of Implant Overdentures. International Faculty Development Course 2018 2018.12.06 Tokyo

[Awards & Honors]

1. AO Best Poster award for 2018 (Maiko Iwaki), Academy of Osseointegration Annual Meeting 2018, 2018.03
2. Pre-Prosthetic Regenerative Science (PPRS) Award (Vo Lam Thuy), IADR General Session, London, 2018.07

[Others]

1. Inokoshi M. Japanese Dental Science Federation, 2018.03
Literature review of restorative materials for root caries

[Social Contribution]

1. Inokoshi M. responsible person of the international program with the Chulalongkorn University, 2017.07.01 - Now

Laboratory Medicine

Professor Shuji TOHDA

Assistant Professor Mai ITOH

Graduate Students Mika OHTAKA, Erika SHIRATORI, Yuki KODA, Tatsuya SAITO, Salwa MOHAMMAD

(1) Outline

Laboratory medicine is a field of research to develop analytical methods of pathophysiology of various diseases, new diagnostic tests, and diagnosis-supporting system using laboratory tests.

(2) Research

Our research subjects are as follows:

- 1) Cellular and molecular mechanism of abnormal growth of acute leukemia cells and drug-sensitivity tests for molecularly targeted therapy
- 2) Molecular diagnostic tests for cancer and detection of minimal residual cancer cells
- 3) Mechanism of abnormal growth of lymphoma cells
- 4) Molecular diagnostic tests for infectious diseases

(3) Education

To graduates students, we provide opportunity to study and develop novel diagnostic tests using cellular and molecular biological technique in our laboratories.

To undergraduate students, we give a lecture and practical training on laboratory medicine.

(4) Lectures & Courses

Main objective of Laboratory Medicine in the graduate course is to provide students opportunity to study analysis of pathophysiology, development of new diagnostic tests, and establishment of diagnosis-supporting system using laboratory tests. We focus on the analysis of pathophysiology of hematological malignancies and the development of molecular diagnostic tests for cancer and infectious diseases.

(5) Clinical Services & Other Works

We are performing laboratory tests for hematology, clinical chemistry, immunology, and microbiology in cooperation with doctors and technologists of clinical laboratory in University hospital. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

(6) Clinical Performances

We are developing new diagnostic methods collaborating with various clinical departments. We are also supporting them in their diagnostic procedure.

(7) Publications

[Original Articles]

1. Koda Y, Itoh M, Tohda S. Effects of MERTK inhibitors UNC569 and UNC1062 on the growth of acute myeloid leukaemia cells. *Anticancer Res.* 2018.01; 38(1); 199-204
2. Yuna Horiuchi, Shao-Jui Lai, Azusa Yamazaki, Ayaka Nakamura, Ryunosuke Ohkawa, Kouji Yano, Takahiro Kameda, Shigeo Okubo, Shitsuko Shimano, Michio Hagihara, Shuji Tohda, Minoru Tozuka. Validation and application of a novel cholesterol efflux assay using immobilized liposomes as a substitute for cultured cells. *Biosci. Rep..* 2018.04; 38(2);
3. Shinji Ogihara, Ryoichi Saito, Etsuko Sawabe, Takahiro Kozakai, Mari Shima, Yoshibumi Aiso, Toshihide Fujie, Yoko Nukui, Ryuji Koike, Michio Hagihara, Shuji Tohda. Molecular typing of methicillin-resistant *Staphylococcus aureus*: Comparison of PCR-based open reading frame typing, multilocus sequence typing, and *Staphylococcus* protein A gene typing. *J. Infect. Chemother..* 2018.04; 24(4); 312-314
4. Horiuchi Yuna, Lai Shao-Jui, Yamazaki Azusa, Nakamura Ayaka, Ohkawa Ryunosuke, Yano Kouji, Kameda Takahiro, Okubo Shigeo, Shimano Shitsuko, Hagihara Michio, Tohda Shuji, Tozuka Minoru. VALIDATION AND APPLICATION OF A NOVEL CHOLESTEROL EFFLUX ASSAY USING IMMOBILIZED LIPOSOMES AS A SUBSTITUTE FOR CULTURED CELLS ATHEROSCLEROSIS SUPPLEMENTS. 2018.06; 32; 59
5. Yonekura S, Itoh M, Shiratori E, Ohtaka M, Tohda S. FOXP3 knockdown inhibits the proliferation and reduces NOTCH1 expression of T cell acute lymphoblastic leukemia cells. *BMC research notes.* 2018.08; 11(1); 582
6. Wang S, Itoh M, Shiratori E, Ohtaka M, Tohda S. NOTCH activation promotes glycosyltransferase expression in human myeloid leukemia cells. *Hematology reports.* 2018.09; 10(3); 7576
7. Hamada Satomi, Hasegawa Yuki, Oono Ai, Suzuki Anna, Takahashi Naomi, Nishimura Takuro, Koyama Takatoshi, Hagihara Michio, Tohda Shuji, Furukawa Tetsushi, Hirao Kenzo, Sasano Tetsuo. Differential Assessment of Factor Xa Activity and Global Blood Coagulability Utilizing Novel Dielectric Coagulometry SCIENTIFIC REPORTS. 2018.10; 8(1); 16129
8. Okuhashi Yuki, Itoh Mai, Tohda Shuji. GLI1 and CTNNB1 Knockdown Activates NOTCH and mTOR Signalling in NB4 Myeloid Leukaemia Cells ANTICANCER RESEARCH. 2018.11; 38(11); 6329-6332

[Conference Activities & Talks]

1. Kazuaki Yamamoto, Yumi Iwasaki, Michio Hagihara, Shuji Tohda. Multiplex strip PCR test for rapid and simultaneous detection of twelve kinds of virus DNA in patients' samples. 15th congress of the Asian society of clinical pathology and laboratory medicine 2018.09.07

Intensive Care Medicine

Professor and Chairman
Hidenobu Shigemitsu (2016.9.1 -)

Professor
Hideo Takahashi(2017.4.1 -)

Associate Professor
Toyomu Ugawa (2018.11.1 -)

Junior Associate Professor
Michio Nagashima (2017.4.1 -)

Assistant Professor
Takahiro Masuda (Intensive Care Unit) (2014.4.1 -)
Kenji Wakabayashi (2015.4.1 -)
Fumi Maruyama (Intensive Care Unit) (2017.2.1 -)

Specially Appointed Assistant Professor
Nobuhiro Shiota (2017.4.1 -)
Shin Inukai (Intensive Care Unit) (2017.4.1 -)
Kensuke Hirasawa (Intensive Care Unit) (2018.4.1 -)

Fellow:
Yuka Mishima (Intensive Care Unit) (2017.4.1 -)
Sachiyo Sato (Intensive Care Unit) (2017.4.1 -)

Postgraduate students:
Mariko Senda (2014.4.1 -)
Shotaro Matsumoto (2016.4.1 -)
Nobuhiro Shiota (2017.4.1 -)
Yoichi Iki (2018.4.1 -)

Research student:
Michiko Abe (2018.4.1 -)

(1) Outline

Critical care medicine provides intensive care and treatment for critically ill patients. To treat critically ill patients, intensivists have to catch the changes of the patients' condition by monitoring and evaluation, and practice appropriate therapy. It is important that intensivists practice minute-to-minute titration therapy in cooperation with other multidisciplinary professionals.

Practice of critical care medicine includes intensive care for various types of shock, acute respiratory distress syndrome/acute lung injury, sepsis, multiple organ dysfunction syndrome, abnormal acid-base balance, electrolyte disturbance, acute kidney injury, central nervous system dysfunction, and hospital-acquired infection,

mechanical ventilation, pharmacological support, cardiopulmonary support system, blood purification, and nutrition support.

(2) Research

Our themes of research are derived from clinical questions in critically ill patients.

Clinical research:

- 1) Effective Medical Creation (EMC) project, in liaison with Yamaha Co. and world-renowned designer Hiroko Koshino.
- 2) Clinical implementation of US-style bundle in the ICU (Shigemitsu, funded by Grant-in-Aid for Scientific Research C)

Basic research:

- 1) Role of microvesicles in patients on ECMO (Shiota, funded by Grant-in-Aid for Young Scientists B)
- 2) Role of microvesicles in bronchopulmonary dysplasia (Wakabayashi, funded by Grant-in-Aid for Young Scientists B)
- 3) Role of urinary microvesicles in acute liver failure (Wakabayashi, funded by National Center of Child Health and Development)
- 4) Impact of residual neuromuscular blockade in the ICU (Nagashima, funded by Grant-in-Aid for Young Scientists B)
- 5) Effect of nutrition status in the ICU (Masuda, funded by Grant-in-Aid for Young Scientists B)

(3) Education

Undergraduate education

Lectures: Fourth-year medical students

- 1) Mechanical ventilation (Wakabayashi)

Clinical clerkship: Fifth-year and Sixth-year medical students

Critical care medicine is a branch of faculty of medicine which deals with monitoring and care of critically ill patients. Main objective of critical care medicine is to provide students opportunity to study diagnosis and treatment of critically ill patients in the intensive care unit (ICU). Students are taught on clinical practice in the ICU. Students take charge of 1-2 patients with attending physician and intensivist. Students do an oral presentation at ICU educational rounds.

Conference: Students are assigned to read recent articles of critical care medicine and make presentations by power point at the conference.

Residents: Residents in training rotate the ICU for 2-3 months. They study respiratory, circulatory, and metabolic management of critically ill patients. They learn how to use ultrasound and bronchoscope.

(4) Lectures & Courses

US-based training system has been in place at the Department of Intensive Care Medicine under the Prof Shigemitsu who was a program director of ACGME-accredited fellowship program at the University of Nevada. We regularly hold educational conferences on every Tuesday called 'academic day'.

(5) Clinical Services & Other Works

Intensivists are staying in the ICU, and take charge treatment of critically ill patients in the ICU.

Every morning, intensivists, nurses, pharmacist, nutritionist, rehabilitation staffs, infection control staffs, medical engineers, and attending physicians get together, go round, and talk about the best treatment of the patients. From March 2017, we also started a novel Rapid Response System (we named as RAS: Risk Assessment System), in collaboration with the Department of Acute Critical Care and Disaster Medicine.

(6) Clinical Performances

Our early rehabilitation program based on the multidisciplinary round was awarded a 'best team prize' in 2017, and presented at an invited seminar at the national conference of Japanese Society of Respiratory Care Medicine.

(7) Publications**[Original Articles]**

1. Mishima Y., Wakabayashi K., Shigemitsu H.. A Ten-Minute Lecture Impacted the Interpretation of Do-Not-Attempt-Resuscitation Order in Resident Physicians in Japan AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2018; 197;
2. Mitsui Y., Dea K. P. O., Uchida T., Takata M., Wakabayashi K.. Pro-Inflammatory Activity of Granulocyte-Derived Microvesicles Is Potentiated by Endotoxin Pre-Stimulation AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2018; 197;
3. Nakano T, Kuwahira I, Shigemitsu H, Nakagawa T, Nagai A, Ebihara A, Oka T, Iwazaki M. A 48-Year-Old Man With Multiple Pulmonary Nodular Opacities and Elevated KL-6 Level. Chest. 2018; 154; 77-81
4. Mishima Y., Wakabayashi K., Shigemitsu H.. A Ten-Minute Lecture Impacted the Interpretation of Do-Not-Attempt-Resuscitation Order in Resident Physicians in Japan AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2018; 197;
5. Shiota Nobuhiro, Sato Sachiyo, Wakabayashi Kenji, Tsukada Yoko, Tanaka Marie, Shigemitsu Hidenobu. MULTIDISCIPLINARY ROUNDS SHORTEN ICU LENGTH OF STAY IN A JAPANESE UNIVERSITY TERTIARY HOSPITAL CRITICAL CARE MEDICINE. 2018.01; 46(1); 35
6. Nishida Osamu, Ogura Hiroshi, Egi Moritoki, Fujishima Seitaro, Hayashi Yoshiro, Iba Toshiaki, Imaizumi Hitoshi, Inoue Shigeaki, Kakihana Yasuyuki, Kotani Joji, Kushimoto Shigeki, Masuda Yoshiki, Matsuda Naoyuki, Matsushima Asako, Nakada Taka-aki, Nakagawa Satoshi, Nunomiya Shin, Sadahiro Tomohito, Shime Nobuaki, Yatabe Tomoaki, Hara Yoshitaka, Hayashida Kei, Kondo Yutaka, Sumi Yuka, Yasuda Hideto, Aoyama Kazuyoshi, Azuhata Takeo, Doi Kent, Doi Matsuyuki, Fujimura Naoyuki, Fuke Ryota, Fukuda Tatsuma, Goto Koji, Hasegawa Ryuichi, Hashimoto Satoru, Hatakeyama Junji, Hayakawa Mineji, Hifumi Toru, Higashibeppu Naoki, Hirai Katsuki, Hirose Tomoya, Ide Kentaro, Kaizuka Yasuo, Kan'o Tomomichi, Kawasaki Tatsuya, Kuroda Hiromitsu, Matsuda Akihisa, Matsumoto Shotaro, Nagae Masaharu, Onodera Mutsuo, Ohnuma Tetsu, Oshima Kiyohiro, Saito Nobuyuki, Sakamoto So, Sakuraya Masaaki, Sasano Mikio, Sato Norio, Sawamura Atsushi, Shimizu Kentaro, Shirai Kunihiro, Takei Tetsuhiro, Takeuchi Muneyuki, Takimoto Kohei, Taniguchi Takumi, Tatsumi Hiroomi, Tsuruta Ryosuke, Yama Naoya, Yamakawa Kazuma, Yamashita Chizuru, Yamashita Kazuto, Yoshida Takeshi, Tanaka Hiroshi, Oda Shigeto. 敗血症および敗血症性ショックの診療ガイドライン 2016(J-SSCG 2016)(The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016(J-SSCG 2016)) Journal of Intensive Care. 2018.01; 6(January); 1-77
7. Nishida Osamu, Ogura Hiroshi, Egi Moritoki, Fujishima Seitaro, Hayashi Yoshiro, Iba Toshiaki, Imaizumi Hitoshi, Inoue Shigeaki, Kakihana Yasuyuki, Kotani Joji, Kushimoto Shigeki, Masuda Yoshiki, Matsuda Naoyuki, Matsushima Asako, Nakada Taka-aki, Nakagawa Satoshi, Nunomiya Shin, Sadahiro Tomohito, Shime Nobuaki, Yatabe Tomoaki, Hara Yoshitaka, Hayashida Kei, Kondo Yutaka, Sumi Yuka, Yasuda Hideto, Aoyama Kazuyoshi, Azuhata Takeo, Doi Kento, Doi Matsuyuki, Fujimura Naoyuki, Fuke Ryota, Fukuda Tatsuma, Goto Koji, Hasegawa Ryuichi, Hashimoto Satoru, Hatakeyama Junji, Hayakawa Mineji, Hifumi Toru, Higashibeppu Naoki, Hirai Katsuki, Hirose Tomoya, Ide Kentaro, Kaizuka Yasuo, Kan'o Tomomichi, Kawasaki Tatsuya, Kuroda Hiromitsu, Matsuda Akihisa, Matsumoto Shotaro, Nagae Masaharu, Onodera Mutsuo, Ohnuma Tetsu, Oshima Kiyohiro, Saito Nobuyuki, Sakamoto So, Sakuraya Masaaki, Sasano Mikio, Sato Norio, Sawamura Atsushi, Shimizu Kentaro, Shirai Kunihiro, Takei Tetsuhiro, Takeuchi Muneyuki, Takimoto Kohei, Taniguchi Takumi, Tatsumi Hiroomi, Tsuruta Ryosuke, Yama Naoya, Yamakawa Kazuma, Yamashita Chizuru, Yamashita Kazuto, Yoshida Takeshi, Tanaka Hiroshi, Oda Shigeto. 日本版敗血症・敗血症性ショック診療ガイドライン 2016(J-SSCG 2016)(The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016(J-SSCG 2016)) Acute Medicine & Surgery. 2018.01; 5(1); 3-89

8. The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016 (J-SSCG 2016). *J Intensive Care*. 2018.02; 6(7);
9. The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016 (J-SSCG 2016). *Acute Med Surg*. 2018.02; 5(1); 3-89
10. Shiota Nobuhiro, Sato Sachiyo, Wakabayashi Kenji, Tanaka Marie, Tsukada Yoko, Asada Mizuho, Shigemitsu Hidenobu. 総合回診は日本の大学附属三次医療病院における ICU 滞在日数を短縮した (Multidisciplinary rounds shorten ICU length of stay in a Japanese university tertiary hospital) *日本集中治療医学会雑誌*. 2018.02; 25(Suppl.);
11. Tsukada Yoko, Tanaka Marie, Nishi Nao, Wakabayashi Kenji, Takahashi Hideo, Shigemitsu Hidenobu. 飲料制限は高度治療室における術後早期動作開始遅延と関連している (Fluid restriction is associated with delayed postoperative early mobilization in the high care unit) *日本集中治療医学会雑誌*. 2018.02; 25(Suppl.);
12. Nishida Osamu, Ogura Hiroshi, Egi Moritoki, Fujishima Seitaro, Hayashi Yoshiro, Iba Toshiaki, Imaizumi Hitoshi, Inoue Shigeaki, Kakihana Yasuyuki, Kotani Joji, Kushimoto Shigeki, Masuda Yoshiki, Matsuda Naoyuki, Matsushima Asako, Nakada Taka-aki, Nakagawa Satoshi, Nunomiya Shin, Sadahiro Tomohito, Shime Nobuaki, Yatabe Tomoaki, Hara Yoshitaka, Hayashida Kei, Kondo Yutaka, Sumi Yuka, Yasuda Hideto, Aoyama Kazuyoshi, Azuhata Takeo, Doi Kent, Doi Matsuyuki, Fujimura Naoyuki, Fuke Ryota, Fukuda Tatsuma, Goto Koji, Hasegawa Ryuichi, Hashimoto Satoru, Hatakeyama Junji, Hayakawa Mineji, Hifumi Toru, Higashibeppu Naoki, Hirai Katsuki, Hirose Tomoya, Ide Kentaro, Kaizuka Yasuo, Kan'o Tomomichi, Kawasaki Tatsuya, Kuroda Hiromitsu, Matsuda Akihisa, Matsumoto Shotaro, Nagae Masaharu, Onodera Mutsuo, Ohnuma Tetsu, Oshima Kiyohiro, Saito Nobuyuki, Sakamoto So, Sakuraya Masaaki, Sasano Mikio, Sato Norio, Sawamura Atsushi, Shimizu Kentaro, Shirai Kunihiro, Takei Tetsuhiro, Takeuchi Muneyuki, Takimoto Kohei, Taniguchi Takumi, Tatsumi Hiroomi, Tsuruta Ryosuke, Yama Naoya, Yamakawa Kazuma, Yamashita Chizuru, Yamashita Kazuto, Yoshida Takeshi, Tanaka Hiroshi, Oda Shigeto, the Japanese Society of Intensive Care Medicine, the Japanese Association for Acute Medicine. 日本版敗血症診療ガイドライン 2016(J-SSCG2016)(The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2016(J-SSCG 2016)) *Journal of Intensive Care*. 2018.02; 6(February); 1-77
13. Tatham Kate Colette, O'Dea Kieran Patrick, Romano Rosalba, Donaldson Hannah Elizabeth, Kenji Wakabayashi, Patel Brijesh Vipin, Thakuria Louit, Simon Andre Rudiger, Sarathchandra Padmini, Marczin Nandor, Takata Masao. Intravascular donor monocytes play a central role in lung transplant ischaemia-reperfusion injury *THORAX*. 2018.04; 73(4); 350-360
14. Stefan J Schaller, Michio Nagashima, Martin Schönfelder, Tomoki Sasakawa, Fabian Schulz, Mohammed A S Khan, William R Kem, Gerhard Schneider, Jürgen Schlegel, Heidrun Lewald, Manfred Blobner, J A Jeevendra Martyn. GTS-21 attenuates loss of body mass, muscle mass, and function in rats having systemic inflammation with and without disuse atrophy. *Pflugers Arch*. 2018.07;
15. Moritoki Egi, Jun Kataoka, Takashi Ito, Osamu Nishida, Hideto Yasuda, Hiroshi Okamoto, Akira Shimoyama, Masayo Izawa, Shinsaku Matsumoto, Nana Furushima, Shigeki Yamashita, Koji Takada, Masahide Ohtsuka, Noritomo Fujisaki, Nobuaki Shime, Nobuhiro Inagaki, Yasuhiko Taira, Tomoaki Yatabe, Kenichi Nitta, Takeshi Yokoyama, Shigeki Kushimoto, Kentaro Tokunaga, Matsuyuki Doi, Takahiro Masuda, Yasuo Miki, Kenichi Matsuda, Takehiko Asaga, Keita Hazama, Hiroki Matsuyama, Masaji Nishimura, Satoshi Mizobuchi, . Oxygen management in mechanically ventilated patients: A multicenter prospective observational study. *J Crit Care*. 2018.08; 46; 1-5
16. Nakano Takayuki, Kuwahira Ichiro, Shigemitsu Hidenobu, Nakagawa Tomoki, Nagai Asuka, Ebihara Akinori, Oka Teruaki, Iwazaki Masayuki. A 48-Year-Old Man With Multiple Pulmonary Nodular Opacities and Elevated KL-6 Level *CHEST*. 2018.09; 154(3); E77-E81
17. Mishima Y, Fukaishi T, Inase N, Isogai S. Nivolumab-induced Hypophysitis, Secondary Adrenal Insufficiency and Destructive Thyroiditis in a Patient with Lung Adenocarcinoma: A Case Report. *Internal medicine (Tokyo, Japan)*. 2018.11;
18. Saito H, Tsuchiya K, Chiba S, Ogata T, Imase R, Yagi T, Mishima Y, Jinta T, Saito K, Taki R, Isogai S, Jin Y, Kawasaki T, Natsume I, Miyashita Y, Takagiwa J, Ishiwata N, Chiaki T, Kishi M, Tsukada Y, Yamasaki M, Inase N, Miyazaki Y. Treatment of asthma in smokers: A questionnaire survey in Japanese clinical practice. *Respiratory investigation*. 2018.12;

[Misc]

1. Shotaro MATSUMOTO. Characteristics of respiration in children Pickup in pediatric emergency care and intensive care 2. 2018.11;

[Conference Activities & Talks]

1. Mishima Y., Wakabayashi K., Shigemitsu H. . A Ten-Minute Lecture Impacted the Interpretation of Do-Not-Attempt-Resuscitation Order in Resident Physicians in Japan . AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 2018
2. 高橋 英夫. 院内急変対応システム～いかに導入して成果をあげるか～ 有害事象 (ATCS 症候群等) 発生時の拡大防止の対応. 医療の質・安全学会 2018
3. H. Shigemitsu. Ethic Resuscitation in Asian vs American Culture . 2018.01.27
4. Shiota Nobuhiro, Sato Sachiyo, Wakabayashi Kenji, Tanaka Marie, Tsukada Yoko, Asada Mizuho, Shigemitsu Hidenobu. 総合回診は日本の大学附属三次医療病院における ICU 滞在日数を短縮した (Multidisciplinary rounds shorten ICU length of stay in a Japanese university tertiary hospital). 日本集中治療医学会雑誌 2018.02.01
5. Tsukada Yoko, Tanaka Marie, Nishi Nao, Wakabayashi Kenji, Takahashi Hideo, Shigemitsu Hidenobu. 飲料制限は高度治療室における術後早期動作開始遅延と関連している (Fluid restriction is associated with delayed postoperative early mobilization in the high care unit). 日本集中治療医学会雑誌 2018.02.01
6. Multidisciplinary rounds shorten ICU length of stay in a Japanese university tertiary hospital. . 2018.02.22
7. Kenji Wakabayashi. Ventilator-induced lung injury - past, present, and future -. The 45th annual congress of Japanese Society of Intensive Care Medicine 2018.02.22 Chiba
8. Multidisciplinary rounds shorten ICU length of stay in a Japanese university tertiary hospital. . 2018.02.25
9. Shiota, Nobuhiro; Sato, Sachiyo; Wakabayashi, Kenji; Tsukada, Yoko; Tanaka, Marie; Shigemitsu, Hidenobu. MULTIDISCIPLINARY ROUNDS SHORTEN ICU LENGTH OF STAY IN A JAPANESE UNIVERSITY TERTIARY HOSPITAL. 2018.02.25
10. Kensuke Hirasawa, Masaki Izumo, Taro Sasaoka, Tomoyuki Umemoto, Kengo Suzuki, Tomoo Harada, Takashi Ashikaga, Kenzo Hirao, Yoshihiro J Akashi. Prognostic Significance of Cardiac Index Reserve During Exercise in Asymptomatic Patients with Aortic Stenosis.. 2018.03.25
11. Kensuke Hirasawa, Masaki Izumo, Tomoyuki Umemoto, Takashi Ashikaga, Kengo Suzuki, Tomoo Harada, Hirokuni Arai, Mitsuaki Isobe, Yasuhiro J Akashi. Tricuspid Valve Morphological Assessment of Barlow Disease using Three-Dimensional Transesophageal Echocardiography and the Impact on Residual Regurgitation after Tricuspid Annuloplasty.. 2018.03.25
12. Mitsui Y, O' Dea KP, Uchida T, Takata M, Wakabayashi K. Pro-inflammatory Activity of Granulocyte-derived Microvesicles is Potentiated by Endotoxin Pre-stimulation. American Thoracic Society Conference 2018 2018.05.22 San Diego, CA
13. Y. Mishima, K. Wakabayashi, H. Shigemitsu. A Ten-minute Lecture Impacted the Interpretation of Do-Not-Attempt-Resuscitation Order in Resident Physicians in Japan. American Thoracic Society Conference 2018 2018.05.23 San Diego, CA
14. Y. Mishima, K. Wakabayashi, H. Shigemitsu. A Ten-Minute Lecture Impacted the Interpretation of Do-Not-Attempt-Resuscitation Order in Resident Physicians in Japan. 2018.05.23
15. Kensuke Hirasawa, Masaki Izumo, Tomoyuki Umemoto, Kengo Suzuki, Yosuke Kitasaka, Keiji Oi, Tomohiro Mizuno, Tomoo Harada, Takashi Ashikaga, Takeshi Miyairi, Hirokuni Arai, Kenzo Hirao, Yoshihiro J Akashi. Geometry of tricuspid valve apparatus in patients with mitral regurgitation due to fibroelastic deficiency versus Barlow disease: A real-time three-dimensional transesophageal echocardiography study.. American Society of Echocardiography 2018.06.25
16. Shigemitsu H. The Japanese Story of AI in Healthcare. 2018.07.06

17. H. Shigemitsu. How do I handle big data. 2018.10.03

Liaison Psychiatry and Palliative Medicine

Assistant Professor Miho Miyajima
 Visiting Lecture Eisuke Matsushima, Katsuya Ota,
 Kanako Ichikura, Tetsuya Matsuda,
 Takashi Hosaka, Kouichi Fujiwara,
 Toshitaka Yamakawa,
 Clinical Psychologist Nao Nakayama, Tomoko Sugano,
 Graduate Student Noriko Ishiduka, Toshi Kuriyama,
 Hiroshi Koubou, Toshimi Takano, Rie Tani,
 Takamasa Noda, Noriko Yoshida,
 Nami Kondou, Hiroki Sakurai,
 Sumie Nemoto, Mayo Fujiwara,
 Kanako Amano, Sayaka Ozaka,
 Saori Koshimoto, Shiho Matsuoka,
 Kazuhiro Kosugi, Takafumi Watanabe,
 Mayuko Iijima, Yu Okura, Jun Kakou,
 Kensuke Komatsu, Hiroyuki Tanaka
 Research Student Okihiko Aihara, Ryuho Ibaraki.
 Technical Assistant Satoko Ogi, Wakana Takeshita,
 Hiroyuki Takano, Takuya Seki,
 Takeshi Ohno, Sinterou takiguchi,
 Office Assistant Yoriko Mizukane, Hitomi Matsuda,
 Motoaki Iimori,

(1) Outline

The purpose of the section is to help understanding characteristics of psychosocial distress in patients with physical and mental disorders from a comprehensive viewpoint. Objects are mainly physical patients accompanied with pain, anxiety, depressive mood and so on. Students study these patients' symptoms, how to diagnose, practice of treatment and methods of preventive measures.

(2) Research

- 1) Assessment of mental state in cancer and other physical patients using written questionnaire
- 2) Research on quality of life (QOL) in cancer patients and their families
- 3) Investigation cognitive function of patients with organic disorders (SLE, diabetics, and so on) undergoing a battery of psychometry tests and neuroimaging examinations
- 4) Explanation for the relationship between physical symptoms and mental states in patients with psychosomatic diseases including chronic pain and irritable bowel syndrome (IBS)
- 5) Examination for physiological phenomenon of psychiatric patients using eye mark recorder, electroencephalogram (EEG) and functional MRI (fMRI)

(3) Clinical Services & Other Works

Psychosomatic clinic provides consultation-liaison psychiatry services at the request of the treating medical or surgical staffs. Patients accompanied with insomnia, anxiety, depressive mood and delirium are treated with psychotherapy and prescription medicines.

(4) Publications

[Original Articles]

1. Yu Ohkura, Masaki Ueno, Toshiro Iizuka, Harushi Udagawa. Effectiveness of etilefrine regimen for chylothorax after esophagectomy with thoracic duct resection. *Esophagus*. 2018; 15(1); 33-38
2. Ogawa Shintaro, Koga Norie, Hattori Kotaro, Matsuo Junko, Ota Miho, Hori Hiroaki, Sasayama Daimei, Teraishi Toshiya, Ishida Ikki, Yoshida Fuyuko, Yoshida Sumiko, Noda Takamasa, Higuchi Teruhiko, Kunugi Hiroshi. Plasma amino acid profile in major depressive disorder: Analyses in two independent case-control sample sets *J. Psychiatr. Res.*. 2018.01; 96; 23-32
3. Shinsuke Hidese, Miho Ota, Junko Matsuo, Ikki Ishida, Moeko Hiraishi, Sumiko Yoshida, Takamasa Noda, Noriko Sato, Toshiya Teraishi, Kotaro Hattori, Hiroshi Kunugi. Association of obesity with cognitive function and brain structure in patients with major depressive disorder. *J Affect Disord*. 2018.01; 225; 188-194
4. Jun Kako, Tatsuya Morita, Takuhiro Yamaguchi, Asuko Sekimoto, Masamitsu Kobayashi, Hiroya Kinoshita, Asao Ogawa, Sadamoto Zenda, Yosuke Uchitomi, Hironobu Inoguchi, Eisuke Matsushima. Evaluation of the Appropriate Washout Period Following Fan Therapy for Dyspnea in Patients With Advanced Cancer: A Pilot Study. *Am J Hosp Palliat Care*. 2018.02; 35(2); 293-296
5. Kanako Ichikura, Aya Yamashita, Taro Sugimoto, Seiji Kishimoto, Eisuke Matsushima. Patterns of stress coping and depression among patients with head and neck cancer: A Japanese cross-sectional study *Psycho-Oncology*. 2018.02; 27(2); 556-562
6. Miho Ota, Takamasa Noda, Noriko Sato, Shinsuke Hidese, Toshiya Teraishi, Shiori Setoyama, Daichi Sone, Hiroshi Matsuda, Hiroshi Kunugi. The use of diffusional kurtosis imaging and neurite orientation dispersion and density imaging of the brain in major depressive disorder. *J Psychiatr Res*. 2018.03; 98; 22-29
7. Kazuho Hisamura, Eisuke Matsushima, Shouichi Tsukayama, Shinya Murakami, Yoshiharu Motoo. An exploratory study of social problems experienced by ambulatory cancer patients in Japan: Frequency and association with perceived need for help *Psycho-Oncology*. 2018.03; 27; 1704-1710
8. Iino H, Ohta K, Hara K, Miyajima M, Hara M, Matsushima E, Matsuura M. Vowel-speech versus pure-tone processing in healthy subjects. *Neuroscience research*. 2018.04;
9. Takashi Takeuchi, Kanako Ichikura, Kanako Amano, Wakana Takeshita, Kazuho Hisamura. The degree of social difficulties experienced by cancer patients and their spouses. *BMC Palliative Care*. 2018.06; 17;
10. Yu Ohkura, Junichi Shindoh, Masaki Ueno, Toshiro Iizuka, Harushi Udagawa. Comparison of Outcome of Esophagectomy Versus Nonsurgical Treatment for Resectable Esophageal Cancer with Clinical Complete Response to Neoadjuvant Therapy. *Ann. Surg. Oncol.*. 2018.08; 25(8); 2428-2433
11. Yu Ohkura, M Ueno, junichi Shindoh, T Iizuka, Harushi Udagawa. Randomized controlled trial on efficacy of oligomeric formula (HINE E-GEL®) versus polymeric formula (MEIN®) enteral nutrition after esophagectomy for esophageal cancer with gastric tube reconstruction. *Dis. Esophagus*. 2018.08;
12. Yu Ohkura, Masaki Ueno, Junichi Shindoh, Toshiro Iizuka, Hairin Ka, Harushi Udagawa. Risk Factors for Postoperative Chylothorax After Radical Subtotal Esophagectomy. *Ann. Surg. Oncol.*. 2018.09; 25(9); 2739-2746
13. Yu Ohkura. ASO Author Reflections: Esophagectomy Versus Nonsurgical Treatment for Resectable Esophageal Cancer. *Ann. Surg. Oncol.*. 2018.09;

14. Yu Ohkura. ASO Author Reflections: Postoperative Chylothorax After Radical Subtotal Esophagectomy. *Ann. Surg. Oncol.*. 2018.09;
15. Jun Kako, Tatsuya Morita, Takuhiro Yamaguchi, Masamitsu Kobayashi, Asuko Sekimoto, Hiroya Kinoshita, Asao Ogawa, Sadamoto Zenda, Yosuke Uchitomi, Hironobu Inoguchi, Eisuke Matsushima. Fan Therapy Is Effective in Relieving Dyspnea in Patients With Terminally Ill Cancer: A Parallel-Arm, Randomized Controlled Trial. *J Pain Symptom Manage.* 2018.10; 56(4); 493-500
16. Kanako Nakazawa, Takamasa Noda, Kanako Ichikura, Tomoko Okamoto, Yuji Takahashi, Takashi Yamamura, Kazuyuki Nakagome. Resilience and depression/anxiety symptoms in multiple sclerosis and neuromyelitis optica spectrum disorder. *Mult Scler Relat Disord.* 2018.10; 25; 309-315
17. Jun Kako, Masamitsu Kobayashi, Yusuke Kanno, Asao Ogawa, Tomofumi Miura, Yoshihisa Matsumoto. The Optimal Cutoff Point for Expressing Revised Edmonton Symptom Assessment System Scores as Binary Data Indicating the Presence or Absence of Symptoms. *Am J Hosp Palliat Care.* 2018.11; 35(11); 1390-1393
18. Yu Ohkura, Masaki Ueno, Toshiro Iizuka, Harushi Udagawa. Prognostic Factors and Appropriate Lymph Node Dissection in Salvage Esophagectomy for Locally Advanced T4 Esophageal Cancer. *Ann. Surg. Oncol.*. 2018.11;
19. Ayako Matsuda, Yosuke Yamada, Noriko Ishizuka, Eisuke Matsushima, Kunihiko Kobayashi, Takayoshi Ohkubo, Kazue Yamaoka. Effects of a Self-Monitoring Quality of Life Intervention for Patients with Cancer Receiving Palliative Care in Japan: Study Protocol for a Randomized Controlled Trial *Asian Pac J Cancer Prev.* 2018.11; 19(11); 3027-3032
20. Yoko Suzuki, Miho Miyajima, Katsuya Ohta, Noriko Yoshida, Takafumi Watanabe, Mayo Fujiwara, Masaki Okumura, Mitsuru Nakamura, Tetsuo Sasano, Tokuhiro Kawara, Masato Matsuura, Eisuke Matsushima. Changes in cardiac autonomic nervous system activity during a course of electroconvulsive therapy *Neuropsychopharmacology Reports.* 2018.11;
21. Koji Amano, Tatsuya Morita, Saori Koshimoto, Teruaki Uno, Hirofumi Katayama, Ryohei Tatara. Eating-related distress in advanced cancer patients with cachexia and family members: a survey in palliative and supportive care settings *Supportive Care in Cancer.* 2018.12;
22. Hiroko Iino, Katsuya Ohta, Keiko Hara, Miho Miyajima, Minoru Hara, Eisuke Matsushima, Masato Matsuura. Vowel-speech versus pure-tone processing in healthy subjects *Neuroscience Research.* 2018.12; 137; 43-48
23. Go Taniguchi, Miho Miyajima, Masako Watanabe, Yoshiko Murata, Daichi Sone, Yutaka Watanabe, Mitsutoshi Okazaki, Motonori Kobayashi-Kimura, Masaaki Kato, Teiichi Onuma. . Nonconvulsive status epilepticus in the elderly associated with newer antidepressants used at therapeutic doses: A report of three cases. *Epilepsy Behav.* (accepted).

[Conference Activities & Talks]

1. Fumiya Sakane, Koichi Fujiwara, Miho Miyajima, Yoko Suzuki, Toshitaka Yamakawa, Manabu Kano, Taketoshi Maehara. Generalized Epileptic Seizure Prediction and Mechanism Analysis by Using Heart Rate Variability. *IEEE BHI 2018* 2018.03
2. Kento Shoji, Toshitaka Yamakawa, Koichi Fujiwara, Manabu Kano, Miho Miyajima, Tadashi Sakata, Yuichi Ueda. Evaluating the Improvement Factor of R-Wave Detection Rate after Gain Readjustment. *IEEE BHI 2018* 2018.03
3. K. Komatsu, E. Kinai, M. Sakamoto, T. Taniguchi, A. Nakao, T. Sakata, I. Akiko, T. Koyama, T. Ogata, A. Inui, S. Oka, for the HIV-associated neurocognitive disorders in Japanese (J-HAND) study group. . Different association pattern of each cognitive impairment with age and time of infection in HIV-infected patients. . 22nd International AIDS Conference (AIDS 2018). 2018.07 Amsterdam, the Netherlands
4. Fumiya Sakane, Koichi Fujiwara, Miho Miyajima, Yoko Suzuki, Toshitaka Yamakawa, Manabu Kano, Taketoshi Maehara. Seizure Prediction Algorithms for Realizing Closed-Loop Treatment of Refractory Epilepsy. *EMBC2018* 2018.07.18

5. Miho Miyajima, Toshitaka Yamakawa, Koichi Fujiwara, Fumiya Sakane, Motoki Inaji, Hiromichi Osoegawa, Michiyoshi Buniu, Manabu Kano, Taketoshi Maehara. Wearable ECG Monitoring System with Garment-type Sensor for Real-time Epileptic Seizure Prediction. 2018.07.20
6. Miho Miyajima, Yoshimi Morita, Yoji Takubo, Masako Watanabe.. A Retrospective Review of Mortality Cases Neuropsychiatric Epilepsy Clinic.. 2018.10.26 Yokohama
7. Fumiya Sakane, Koichi Fujiwara, Miho Miyajima, Yoko Suzuki, Toshitaka Yamakawa, Manabu Kano, Taketoshi Maehara. Generalized Epileptic Seizure Prediction Based on Heart Rate Variability Analysis and Discussion on Its Mechanism. AES2018 2018.12
8. Koichi Fujiwara, Fumiya Sakane, Miho Miyajima, Toshitaka Yamakawa, Manabu Kano, Taketoshi Maehara. Heart Rate Variability Analysis-Based Epileptic Seizure Prediction Using Neural Network. AES2018 2018.12
9. Miho Miyajima, Toshitaka Yamakawa, Koichi Fujiwara, Yoko Suzuki, Masako Watanabe, Manabu Kano, Taketoshi Maehara. Views of Patients With Epilepsy on Wearable Seizure Prediction System Based on Heart Rate Variability. AES2018 2018.12

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata
Postgraduate student Kohta Tsuge
Research student Xue Bingyang

(1) Research

- 1) Kinetics of drug action in disease states
- 2) Therapeutic drug monitoring and clinical pharmacokinetics

(2) Education

Department of Pharmacokinetics and Pharmacodynamics is in charge of the education of pharmacokinetics and pharmacodynamics for the establishment of safe and effective drug therapy. In the graduate course, the lecture on the recent progress of the pharmacokinetic analysis will be given. Students will have the practice of pharmacokinetic analysis and animal experiments.

(3) Publications

[Original Articles]

1. Masashi Nagata, Yuri Kimura, Yasuyoshi Ishiwata, Hiromitsu Takahashi, Masato Yasuhara. Clozapine-Induced Acute Hyperglycemia Is Accompanied with Elevated Serum Concentrations of Adrenaline and Glucagon in Rats. *Biol. Pharm. Bull.*. 2018.08; 41(8); 1286-1290
2. Asada M, Nagata M, Mizuno T, Uchida T, Kurashima N, Takahashi H, Makita K, Arai H, Echizen H, Yasuhara M. Effects of cardiopulmonary bypass on the disposition of cefazolin in patients undergoing cardiothoracic surgery. *Pharmacology research & perspectives*. 2018.12; 6(6); e00440

Medical Education Research and Development

Professor Yujiro TANAKA
Junior Associate Professor Makoto TAKAHASHI
Junior Associate Professor Eriko OKADA
Junior Associate Professor Yasuhiro ITSUI
Assistant professor Fukiko KITAHATA
Graduate Student Hisashi SHIMOZONO

(1) Outline

Department of General Medicine was established in 2000, we have aimed to coordinate and support a wide range of innovations for the department of medicine and its affiliated hospitals. Accordingly, we launched the following projects to carry out our mission; 1) Designing a new postgraduate clinical training program for TMDU affiliated hospitals, 2) Forming patient support system including social casework, 3) Establishing the Center for Cell Therapy, 4) Reforming the undergraduate medical education, 5) Establishing the working group for ward management 6) Managing the medical safety committee, 7) Providing second opinion support system. Recently we have been focusing on providing systems for undergraduate and postgraduate education, such as reforming the undergraduate educational curriculum (e.g. educational cooperation with Harvard Medical School) and clinical training system. The medical training center was established for the clinical residency program. In 2006, the department of General Medicine was transformed into the Department of Medical Education Research and Development. We are working in close cooperation with Center for Extraprofessional Education which we took in part of its establishment to materialize the interprofessional education introduced due to a revision of a new curriculum in 2011.

(2) Research

* Research on continuing education in clinical EBM

Although the theory of EBM (Evidence-Based Medicine) has become common knowledge, there are many practical problems yet to be solved. Researches on teaching and assessment techniques for under- and post-graduate clinical training are ongoing.

* Research on medical education

We are developing comprehensive research projects regarding under- and post-graduate medical education, e.g. Clinical reasoning, clinical competence, medical interview, PBL system, and informed consent, are our research themes.

(3) Education

*Undergraduate Education

As a division, which is responsible for the education of students and residents, our primary goal is to foster doctors who have both a 'patient-centered perspective as a specialist' and 'up-to-date knowledge as a generalist'. To achieve our goal, we are designing and offering a continuing medical educational (CME) program for clerkship students, emphasizing the educational systems spreading among multiple departments. Since we think it is crucial to foster medical prospective with a patient-centered perspective, we introduced an early

exposure course (MIC: Medical Introductory Course) for the 1st and 2nd year medical students, as well as some medicine oriented English courses, including a special course titled "Language and Philosophy of Western Medicine" regarding some of the needs of this globalized era of medicine. Besides, we are managing a training course for simulated patients who can contribute to medical education cooperating with the International Center for Medical Education at the University of Tokyo. To improve the quality of clinical training, we are currently developing an evaluation system for tutors and trainers.

Postgraduate Education (Clinical Training)

Our department has offered postgraduate clinical training since 2004 according to the new national residency system in Japan. We have also played an important role in developing the online evaluation system for postgraduate clinical training (EPOC), which is used in 60% of education hospitals in Japan. Results of the questionnaire in Japan Residency Matching Program, 2018 showed one of the highest satisfaction rates among all national universities.

Postgraduate Education (Master's degree courses)

We have been offering master's degree courses in Medical Administration since this MMA program started in 2004, and were in charge of two courses this year, "Human resources management" and "Leadership in the medical care."

(4) Clinical Services & Other Works

We are aiming to improve initial clinical training through the recruitment of medical interns, training management, holding various workshops, such as Evening Seminars, and operation of the "Tasukigake" training system with each partner hospital. We also hold clinical training sessions for supervising physicians to learn better teaching methods, and staff training classes about medical safety, infection control and medical information throughout the year. We also devised an evaluation system for the residency training program (EPOC), which was later adopted as a national online evaluation system for postgraduate clinical training.

(5) Publications

[Original Articles]

1. Okada E, Inukai K, Aoyama H. Wait Time for Hip Fracture Surgery and Mortality. JAMA. 2018.06; 319(21); 2233

Acute Critical Care and Disaster Medicine

Professor Yasuhiro Otomo

(1) Outline

1. Purpose of Education

We, the department of acute critical care and disaster medicine, investigate following wide range of fields, such as the search for mechanisms of biological response to severe stresses, the development of strategy for multiple organ dysfunction from the view of intensive care medicine, basic and clinical research about trauma, trauma preventive medicine and disaster medicine. Our targets of research are practical and cutting edge to work not only as a medical scientist but as a researcher for government projects.

2. Research Subjects

Basic research of the mechanism of multiple organ dysfunction following hemorrhagic/septic shock

Development of strategy for multiple organ dysfunction

Basic and clinical research of multiple trauma

Trauma epidemiology and trauma preventive medicine

Disaster medicine

Clinical research of cerebrovascular disease on acute phase

3. Clinical Services

Our emergency center was authorized to hold the 21st level I center in Tokyo on April 1, 2007. We give treatments over 8000 patients annual who are under critical condition like multiple organ dysfunction, severe sepsis and septic shock, life-threatening trauma as well. We also contribute to medical services, rushing to the emergency scene by a Doctor-Car/Helicopter at times.

(2) Publications

[Original Articles]

1. Takayama W, Koguchi H, Akira E, Otomo Y. The Association between Cardiopulmonary Resuscitation in Out-of-Hospital Settings and Chest Injuries: A Retrospective Observational Study *Prehosp Disaster Med.* 2018.03; 33; 171-175
2. Endo A, Shiraishi A, Fushimi K, Murata K, Otomo Y. Impact of continuous regional arterial infusion in the treatment of acute necrotizing pancreatitis: analysis of a national administrative database *Journal of Gastroenterology.* 2018.03; 53; 1098-1106
3. Sekiya K, Mori S, Otomo Y. Coin pica-induced gastric perforation resulting from ingestion of 1,894 coins, 8 kg in total: case report and review of published works *Acute Medicine & Surgery.* 2018.04; 5; 177-180
4. Takayama W, Koguchi H, Akira E, Otomo Y. A Case of Impalement Brain Injury That Could Achieve Good Neurological Outcome by Introducing Early Sedation and Immobilization Strategy *Case Reports in Emergency Medicine.* 2018.04;

5. Takayama W, Akira E, Koguchi H, Sugimoto M, Murata K, Otomo Y. The impact of blood type O on mortality of severe trauma patients: a retrospective observational study *Crit Care*. 2018.05; 22; 100
6. Abe T, Ogura H, Shiraishi A, Kushimoto S, Saitoh D, Fujishima S, Mayumi T, Shiino Y, Nakada T, Tarui T, Hifumi T, Otomo Y, Okamoto K, Umemura Y, Kotani J, Sakamoto Y, Sasaki J, Shiraishi S, Takuma K, Tsuruta R, Hagiwara A, Yamakawa K, Masuno T, Takeyama N, Yamashita N, Ikeda H, Ueyama M, Fujimi S, Gando S. Characteristics, management, and in-hospital mortality among patients with severe sepsis in intensive care units in Japan: the FORECAST study *Crit Care*. 2018.05; 22; 322
7. Endo A, Shiraishi A, Fushimi K, Murata K, Otomo Y. Outcomes of patients receiving a massive transfusion for major trauma *British Journal of Surgery*. 2018.07; 105; 1426-1434
8. Akira Endo, Atsushi Shiraishi, Shigeki Kushimoto, Yasushiro Otomo. Verification of conventional criteria of the lethal triad and development of novel criteria as an indicator of decision making

[Conference Activities & Talks]

1. Otomo Y. International Preparedness & Response to Emergencies and Disasters Medical Response to Terrorism in Japan. 5th International Preparedness & Response to Emergencies and Disasters 2018.01.16 Tel Aviv, Israel
2. Otomo Y. The First Asia Emergency Medicine Friendship Forum on Acute Stroke and Myocardial Infarction in the Elderly Stroke in JAPAN Current situation. The First Asia Emergency Medicine Friendship Forum 2018.03.14 Bangkok, Thailand
3. Otomo Y. AED/PAD in JAPAN Current situation. SOS @ Hotel Forum 2018.03.15 Bangkok, Thailand
4. Otomo Y. Traumatic Coagulopathy: Is it All the Same? DIC or Trauma-Induced Coagulopathy? Eastern Perspective. The 4th World Trauma Congress 2018.09.27 San Diego, USA
5. Otomo Y. Traumatic Coagulopathy. The 4th World Trauma Congress 2018.09.28 San Diego, USA
6. Otomo Y. ACS Board Certified Surgeon in Japan. The 4th World Trauma Congress 2018.09.28 San Diego, USA
7. Otomo Y. Key Area of Work in H-EDRM Research and Up-to-Date Activities How to Build Strong Domestic Emergency Medical Teams Capacities - The Case of Japan. The 14th Asia Pacific Conference on Disaster Medicine (APCDM) 2018.10.16 Kobe, Hyogo
8. Otomo Y. Medical Response to Terrorism in Japan. The 14th Asia Pacific Conference on Disaster Medicine (APCDM) 2018.10.17 Kobe, Hyogo

Clinical Oncology

Professor MIYAKE Satoshi
Project Assistant Professor

SAKASHITA Hiroyuki
Graduate Student
KAWASAKI Machiko

(1) Outline

Department of Clinical Oncology was established in May 2012 to promote the field of palliative medicine and cancer chemotherapy according to “Training Program for Next Generation Specialists to Promote Cancer Therapy” . As for the education in medical school, we are involved in the course of Hematology-Oncology block and have a class of palliative medicine in the third year grade. In addition, we have a class of clinical ethics mainly focusing on the end-of-life care. As for the post-graduate education, we organized the “Training Program for Next Generation Specialists to Promote Cancer Therapy” .

(2) Research

- 1)Application of palliative care when the patient is diagnosed as cancer.
- 2)Improvement of QOL in the end-of -life care of cancer patients.
- 3)Communication skills in the team health care.
- 4)Multi-institutional research in pancreatic cancer treatment.
- 5)The role of biomarkers for newly developed anti-cancer drugs in lung cancer.

(3) Education

- 1)Hematology/Oncology
- 2)GI tract cancer
- 3)Lung cancer
- 4)Ethics
- 5)Communication

(4) Clinical Services & Other Works

Department of Clinical Oncology manages Cancer Center of the medical school hospital.
There are five divisions below.

- 1)Division of palliative medicine
- 2)Division of cancer chemotherapy
- 3)Division of cancer registry
- 4)Division of coordination of cancer treatment
- 5)Division of cancer consultation and support

(5) Publications**[Original Articles]**

1. Sato Ayako, Fujimori Maiko, Shirai Yuki, Umezawa Shino, Mori Masanori, Jinno Sayaka, Umehashi Mihoto, Miyake Satoshi, Matsuoka Yutaka, Uchitomi Yosuke. Development of a question prompt list (QPL) for promoting discussions about the cessation of anticancer treatment PSYCHO-ONCOLOGY. 2018.10; 27; 111

Dentistry for Persons with Disabilities

Associate Professor
Osamu SHINOZUKA

Junior Associate Professor (Part-time)
Minoru INADA
Goro SEKIGUCHI
Naoki HAYASHI
Yohei TAKEUCHI
Syohei TAMURA
Moriyuki NAKAMURA

Assistant Professor
Yasuka KUSUMOTO

Specially Appointed Assistant Professor
Taiji HOSHIAI

Graduate Student
Aiko HOSHIAI
Yusuke IWABUCHI

Hospital Staff
Takae AIDA
Anna KUMAKURA
Ayana NATORI

Clinical Junior Associate Professor (Part-time)
Seiji SAKURAI
Tomo SUZUKI
Yosuke KINOSHITA

(1) Research

- 1) Formation of oral biofilm
- 2) Elimination of oral biofilm of persons with disabilities
- 3) Oral health status of the medically compromised patients
- 4) Oral management of genetic syndrome

(2) Lectures & Courses

Our department was started as a graduate course of the special dentistry section on April, 1999. The sections are the dentistry for persons with disabilities and medically compromised individuals .

The main objective of this course is to provide the opportunity for students to understand the outline of the reconstruction of functional and esthetic disorders of oral and/or maxillofacial areas by means of the high-advanced dental cares for patients with special needs.

(3) Clinical Performances

The clinical purpose of our department is to treat oral problems of special patients who are unable to receive normal dental care by reason of a disability which may be physical, mental, medical, or emotional, or combination of any of these under using behavior management and systemic support.

For example,

- 1) The patients requiring behavior management are physically disabled, intellectual disability, autistic spectrum disorder, etc.
- 2) The patients requiring systemic support are internal impediment, dental phobia, etc.

(4) Publications

[Original Articles]

1. Fujii-Abe Keiko, Wakita Ryo, Kusumoto Yasuka, Shinozuka Osamu, Fukayama Haruhisa. General management using noninvasive cardiac output measurements and transthoracic echocardiography for dilated cardiomyopathy patient Journal of Japanese Society of Dentistry for Medically Compromised Patient. 2018.07; 27(2); 101-105
2. Taiji Hoshiai, Yasuka Kusumoto, Aiko Hoshiai, Yusuke Iwabuchi, Takae Aida, Anna Nosue, Ayana Hama, Osamu Shinozuka. A case Report of a Mouth Stick with Replaceable Shaft Parts for a Cerebral Palsy with Quadriplegia Journal of the Japanese Society for Disability and Oral Health. 2018.10; 39(4); 413-417

[Conference Activities & Talks]

1. A case of infective endocarditis after first visit . 2018.11.17
2. Long -term changes of adaptability of a patient with autism spectrum disorder in dental treatment. 2018.11.17
3. Dental treatment under intravenous anesthesia of mentally retarded patient with giant thyroid tumor and palatine tonsil hypertrophy. 2018.11.18
4. A case of making health-education manual in cooperation with facilities for the disabled. 2018.11.18
5. The clinical utility of tower configurational carts for sedation with auto anesthesia recording device in dental clinic. 2018.11.18
6. Dental treatment in a patient with Costello syndrome. 2018.11.18
7. A questionnaire survey on patients who do not want to refer to local institutions. 2018.11.18
8. Development of an oral biofilm-associated disease vaccine using membrane vesicles from *Streptococcus mutans*. 2018.12.12

General Dentistry

Associate Professor Shigeru ODA
Junior Associate Professor Masayuki HIDEISHIMA
Junior Associate Professor Ken-ichi TONAMI
Assistant Professor Sachi UMEMORI
Assistant Professor Kanako NORITAKE
Project Assistant Professor Shuuhei NAKAMURA
Project Assistant Professor Yuko MITSUMA
Project Assistant Professor Maiko IWAKI
Hospital Staff Yasuyuki KIMURA
Hospital Staff Shota HAYASHI
Hospital Staff Naoki ISHIHARA
Hospital Staff Daisuke KIDO
Hospital Staff Kiichi MARUYAMA

(1) Outline

Recent dentistry is sectionalized into various specialized fields of research and education. On the other hand, as a general practitioner, a dentist must possess not only integrated knowledge and skills of all the fields but also should be competent to apply such generalized knowledge and skills to individual patients. The department of General Dentistry performs researches and education for practicing such general and holistic dentistry. General dentistry related to clinical and affective education for dental students and residents. Therefore, the research theme includes dental education as well as oral diagnosis and general dentistry, cooperating with the department of Educational System in Dentistry, Behavioral Dentistry and Educational Media Development. Researches for sleep apnea syndrome have been also conducted in association with Dental Clinic for Sleep Disorders. The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry which missions in the Dental Hospital are initial diagnosis for new outpatients and general dental practice. Clinics of General Dentistry 1 and 2, where dental students and residents are trained, also relate to the department of General Dentistry.

(2) Research

Recent research themes are listed below.

1. Study for structure of health problems and treatment planning for dental patients.
2. Study for verification and improvement of oral diagnosis.
3. Study for dental education for dental students and residents.

(3) Education

The educational objective of General Dentistry is that the students/residents acquire transversal academic framework of dental knowledge and skills and competency to provide patients with personalized treatment.

(4) Lectures & Courses

1. Introduction to the Behavioral Science. (For the 2nd-year dental students)
2. Holistic Oral Diagnosis. (For the 5th-year dental students)
3. Comprehensive Clinical Training Phase I Phase II. (For the 5th and 6th-year dental students)
4. Clinical training (For the dental residents)

(5) Clinical Services & Other Works

The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry. In the clinic, dental examination and health assessment for new outpatients are conducted to decide initial treatment plan and a clinic in charge for the patients. The patients who need comprehensive dental care and who cannot cooperate students' practice also attend this clinic to receive general dental practice.

(6) Clinical Performances

In the Dental Hospital, the clinic of Oral Diagnosis and General Dentistry is the first clinic for new outpatients. That is, the clinic is responsible for constructing good relationship between patients and the hospital. Therefore, the doctors pay attention actively to psychosocial aspects of patients during examination. In diagnosing and deciding clinic for patients, initial-treatment plans are introduced to patients. In this process, doctors think treatment plans together with patients thoroughly to obtain sound informed consent. Many patients who visits the dental hospital demands high medical level of the university hospital while not a few patients needs primary care. Oral Diagnosis and General Dentistry provides such patients with general dental practice to meet various kinds of patients' needs, makes effort to improve patients' satisfaction.

(7) Publications**[Original Articles]**

1. Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Shunsuke Minakuchi. Digital impression and jaw relation record for the fabrication of CAD/CAM custom tray. *J Prosthodont Res.* 2018.03; 62(4); 509-513
2. Kakizaki S, Aoki A, Tsubokawa M, Lin T, Mizutani K, Geena K, Alireza S, Oda S, Sumi Y, Izumi Y. Observation and determination of periodontal tissue profile using optical coherence tomography *Journal of Periodontal Research.* 2018.04; 53(2); 188-199
3. W Ono, K Maruyama, M Ogiso, S Mineno, Y Izumi. Implant insertion into an augmented bone region using the canine mandible augmented by the "Casing Method" *The Anatomical Record.* 2018.04; 301(5); 892-901
4. Kuboki T, Ichikawa T, Baba K, Fujisawa M, Sato H, Aita H, Koyama S, Hideshima M, Sato Y, Wake H, Kimura-Ono A, Nagao K, Kodaira-Ueda Y, Tamaki K, Sadamori S, Tsuga K, Nishi Y, Sawase T, Koshino H, Masumi SI, Sakurai K0, Ishibashi K, Ohyama T, Akagawa Y, Hirai T, Sasaki K, Koyano K, Yatani H, Matsumura H.. A multi-centered epidemiological study evaluating the validity of the treatment difficulty indices developed by the Japan Prosthodontic Society. *J Prosthodont Res.* 2018.04; 62(2); 162-170
5. S. H. Le, K. Tonami, S. Umemori, L. T. -B. Nguyen, L. T. -Q. Ngo, S. Mataka. The potential of heart rate variability for exploring dental anxiety in mandibular third molar surgery *International Journal of Oral & Maxillofacial Surgery.* 2018.06; 47(6); 809-815
6. Toshio Arakida, Manabu Kanazawa, Maiko Iwaki, Tetsuya Suzuki, Shunsuke Minakuchi. Evaluating the influence of ambient light on scanning trueness, precision, and time of intra oral scanner. *J Prosthodont Res.* 2018.07; 62(3); 324-329
7. Addin AS, Akizuki T, Matsuura T, Hoshi S, Ikawa T, Maruyama K, Ono W, Fukuba S, Izumi Y. Histological healing after nonsurgical periodontal treatment with enamel matrix derivatives in canine experimental periodontitis *ODONTOLOGY.* 2018.07; 106(3); 289-296

8. Maruyama Kiichi, Ogiso Makoto, Mineno Seiji, Ono Wataru, Izumi Yuichi. Histological Changes in Alveolar Bone After Onlay Augmentation Using the Casing Method ANATOMICAL RECORD-ADVANCES IN INTEGRATIVE ANATOMY AND EVOLUTIONARY BIOLOGY. 2018.07; 301(7); 1148-1158
9. Wada J, Hideshima M, Inukai S, Katsuki A, Matsuura H, Wakabayashi N.. Influence of Oral Morphology on Speech Production in Subjects Wearing Maxillary Removable Partial Dentures with Major Connectors. *Folia Phoniatrica et Logopaedica*. 2018.08; 70; 138-148
10. Manabu Kanazawa, Hiroyuki Suzuki, Yuriko Komagamine, Maiko Iwaki, Noriko Amagai, Shunsuke Minakuchi. Combined effects of new complete denture fabrication and simplified dietary advice on nutrient intake in edentulous elderly patients for 6 months. *Clin Oral Investig*. 2018.10;
11. Yasuyuki Kimura, Ken-ichi Tonami, Jun Tsuruta, Kouji Araki. Rise of blood pressure value in young patients at first visit at a dental university hospital in Japan *Journal of Dental Sciences*. 2018.11; 14(1); 93-98

[Conference Activities & Talks]

1. UMEMORI Sachi, Aida J, Tonami K, Tabuchi T, Araki K, Mataka S, Kondo K. Does the secondhand smoking associate with tooth loss? : JAGES cross sectional study. The 28th Annual Scientific Meeting of the Japan Epidemiological Association 2018.02.02 Fukushima
2. Iwaki Maiko, Kanazawa Manabu, Sato Daisuke, Miyayasu Anna, Kasugai Shohei, Araki Kouji, Minakuchi Shunsuke. Masticatory Functions with Immediate Loading of Two-implant Mandibular Overdentures: 5-year prospective study.. Academy of Osseointegration Annual Meeting 2018 2018.03.01 Los Angeles, CA, USA
3. HIGUCHI Tomoya, MATSUURA Hiroshi, WADA Junichiro, HIDESHIMA Masayuki. Automatic estimation of the intonation using phonetic segments for the utterances of Japanese learners. The Spring Annual Meeting of Acoustical Society of Japan in 2018 2018.03.15 Saitama
4. Junichiro Wada, Masayuki Hideshima, Hiroshi Matsuura. Dental treatment and speech impairment in partially edentulous elderly patients - Treatment approach with speech recognition -. 11th Annual Meeting of Aging Society Design Association 2018.03.16 Tokyo
5. Yumika Soeda, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Shunsuke Minakuchi. The new method of manufacturing CAD/CAM complete denture applying the customized disk. The 9th Scientific Meeting of the Japan Academy of Digital Dentistry 2018.04.14 Morioka
6. Arakida T, Kanazawa M, Iwaki M, Soeda Y, Hada T, Suzuki T, Minakuchi S . The effect of artificial landmark to the precision of digital impression for edentulous jaw . 2018.04.14
7. Aoki A, Takeuchi Y, Akizuki T, Mizutani K, Katagiri S, Ikeda Y, Maekawa S, Watanabe K, Matsuura T, Ohtsu A, Kakizaki S, Komazaki R, Mikami R, Hideshima M, Nikaidou T, Araki K, Izumi Y. Current Status of Clinical Practice of Periodontal Therapy by Predoctoral Dental Students at Tokyo Medical and Dental University (TMDU). The 61th Spring Meeting of The Japanese Society of Periodontology 2018.06.01 Keio plaza hotel, Tokyo
8. KANAKO NORITAKE, SHIGERU ODA, KOUJI ARAKI. Effects of a rhFGF impregnated gelatin hydrogel GBR membrane containing β -tricalcium phosphate on bone neogenesis in rat calvaria.. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.14 Yokohama
9. Yumika Soeda, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Shunsuke Minakuchi. The new method of manufacturing CAD/CAM complete denture applying the customized disk. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.15 Okayama
10. Maruyama Kiich, Oda Shigeru, Araki Kouji. Alveolar bone regeneration in vertical bone defect by Regroth®: A Case Report.. The 148th Meeting of the Japanese Society of Conservative Dentistry 2018.06.15 Yokohama
11. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Kazuhiro Shimoyama, Shunsuke Minakuchi. The effect of new complete denture fabrication combined with simplified dietary advice on nutrient intake of edentulous patients: 6-month progress report.. The 127th Scientific Meeting of Japan Prosthodontic Society 2018.06.16 Okayama

12. Arakida T, Kanazawa M, Iwaki M, Soeda Y, Hada T, Suzuki T, Minakuchi S . The effect of artificial landmark to the precision of digital impression to edentulous jaw . 2018.06.16
13. Suzuki H, Kanazawa M, Komagamine Y, Iwakil M, Amagai N, Minakuchi S. The effect of prosthesis and dietary intervention for edentulous persons. IADR GORG Symposium with the European College of Gerodontology (ECG) and the Japanese Society of Gerodontology (JSG) 2018.07.24 London
14. Yuriko Komagamine, Manabu Kanazawa, Maiko Iwaki, Hiroyuki Suzuki, Noriko Amagai. The Effect of New Complete Denture and Simple Dietary Advice . 96th General Session & Exhibition of the IADR 2018.07.28 London
15. NORITAKE Kanako, TSURUTA Jun, ARAKI Kouji. . A report of the trial of observation experience for dental students at palliative care ward. The 37th General and Scientific Meeting of the Japanese Dental Education Association 2018.07.28 Kouriyama
16. TSURUTA Jun,NORITAKE Kanako, ARAKI Kouji. . A report of the trial of observation experience for medical students at dental student clinic. The 37th General and Scientific Meeting of the Japanese Dental Education Association 2018.07.28 Kouriyama
17. UMEMORISachi, TonamiK, NittaH, Araki K,. The Analysis of Introduction of Behavioral Science class in Faculty of Dentistry. The 50th Annual Meeting of the Japan Societu by Medical Education 2018.08.04 Tokyo
18. Kanako NORITAKE,Jun TSURUTA,Koji MIZUTANI,Keiko KONDO,Shinich ARAKAWA,Kouji ARAKI. Study on educational effect measurement of the IPW program in practical clinical training.. The 50th Annual Meeting of the Japan Society for Medical Education 2018.08.04 Tokyo
19. Mina Nakagawa, Kanako Noritake, Kumiko Yamaguchi, Janelle Moross, Jun Tsuruta, Kazuki Takada.. Introduction of Clinical Exchange Training for Medical and Dental Students.. AMEE 2018 2018.08.25 Basel,Switzerland
20. Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa, Kanako Noritake, Jun Tsuruta, Kazuki Takada.. How the presence of social welfare students influences multi-disciplinary decision making in IPE.. AMEE 2018 2018.08.25 Basel,Switzerland
21. Yasuyuki KImura, Ken-ichi Tonami, Jun Tsuruta,Kouji Araki. Effect of psychological and social factors on hypertension in dental clinics. 2018.09.02 Yotsuya, Tokyo
22. Jun Tsuruta, Kanako Noritake, Kouji Araki.. PRELIMINARY STUDY FOR A NEW OBSERVATION PROGRAM FOR MEDICAL STUDENTS AT THE DENTAL STUDENT' S CLINIC.. 32nd IADR-SEA and 29th SEAAD 2018.09.11 Viet Nam
23. HIGUCHI Tomoya,MATSUURA Hiroshi,WADA Junichiro, HIDESHIMA Masayuki. Estimation of the accent and intonation of utterances using phonetic segments and deep learning. The Autumn Annual Meeting of Acousitcal Society of Japan in 2018 2018.09.13 Ohita
24. Kanako Noritake, Jun Tsuruta, Tomoe Miyoshi, Maiko Iwaki, Yuko Mitsuma, Hiroshi Nitta, and Kouji Araki. Development a new IPE program for dental and medical students in clinical practicum. 2018.12.01 Tokyo

[Others]

1. Maiko Iwaki. Grant-in-Aid for Scientific Research(C) (JSPS), 2018.04
Prospective study of CAD/CAM complete denture for the Edentulous Patients. 2018-2020.

Psychosomatic Dentistry

Professor	Akira Toyofuku
Assistant Professor	Miho Takenoshita
Project Assistant Professor	Takeshi Watanabe
Hospital Staff	Takayuki Suga, Yuma Aota,
Graduate Student	Yukiko Shinohara, Lou Mikuzuki Kaoru Kawasaki, Shiori Sugawara, Tu Thi Huyen Trang Takayuki Suga, Kazuya Watanabe, Yuma Aota
Lecturer (part-time)	Haruhiko Motomura, Ayano Katagiri, Tatsuya Yoshikawa,

(1) Outline

Psychosomatic dentistry is the only one department in Japan, which research and develop new diagnosis and treatment methods for MUOS such as BMS, AO, PBS etc.

(2) Research

- 1) Study on pathophysiological mechanisms of oral psychosomatic disorders
- 2) Psychosomatic study on oro-facial medically and psychiatrically unexplained symptoms
- 3) Brain imaging of oral psychosomatic disorders
- 4) Psychopharmacological study on oral psychosomatic disorders

(3) Education

It is not uncommon to see the patients diagnosed with “Oral Psychosomatic Disorders”, so there is a growing need for proper treatment of the disorders from both sides of doctors and patients. It is, therefore, extremely important for dental students to instruct in psychosomatic dentistry. However, few Dental Universities in Japan are following this. At the same time, there’s a great deal of misunderstanding about psychosomatic dentistry, in spite of we have many years of consistent education. For example, “Your work is only hearing to complaints from patients”, “Patients with not otherwise specified mental illness is eventually referred to your clinic”, or “The mission of your clinic is to calm down your patients with unidentified dental and oral complaints”.

So, regarding undergraduate medical education, we focus on not only lessons from lectures and books but also practical experience through clinical training. We have comprehensive medical teaching for fifth and sixth-year students. Students can listen to patient’s complaints directly and deepen their understanding. Actually they can see patients with dental psychosomatic disorders, and they know that these disorders are treatable. Moreover, they can learn negative effects of wrong ideas as a psychogenic disorder, and they can understand serious distress in patients and family members.

This practice is arduous effort, but in the future, it is hoped that efforts will be made to facilitate uniformed services for patients with dental psychosomatic disorders, enhance coping skills for refractory cases, and reduce trouble with patients by the graduates of our department who mastered psychosomatic dentistry.

It is important to have identity as a dentist on practice of psychosomatic dentistry. Therefore we have advanced strengthening of human resource development. In particular, we focus on cultivation of dentists who can be readily applied their knowledge of psychosomatic medicine to clinical practice. And we are working towards establishment of ‘psychosomatic dentistry’ introduced psychotherapy.

Also regarding education for graduate student, we focus on clinical practice for development of dentists who have great skill in psychosomatic dentistry.

(4) Clinical Services & Other Works

We take charge of “Psychosomatic Dentistry clinic” in dental hospital of Tokyo Medical and Dental University. This special clinic is for patients with oral psychosomatic disorders, such as glossodynia (burning mouth syndrome), atypical facial pain, atypical odontalgia, oral dysesthesia, occlusal discomfort(dysesthesia).

Main psychosomatic treatment is psychopharmacological one with SSRIs(Selective Serotonin Reuptake Inhibitors), SNRI(Serotonin-Noradrenaline Reuptake Inhibitor), SDAs(Serotonin-Dopamine antagonists) etc. And supportive psychotherapies are applied.

Intractable cases are increasing year by year, we take care of every patient and have good clinical courses about 70% of them.

We believe there are exactly “oral psychosomatic disorders”, and dentists should be in charge of treatment. Psychosis, as a matter of course, should be taken care by psychiatrists, so we discriminate them from oral psychosomatic disorders, and properly refer to psychiatry.

On the other hand, on “functional somatic symptoms secondary to psychiatry disorders”, which are refer to us from psychiatrists, we do our best in cooperation with psychiatrists.

We have about 600 new outpatients per year, and almost of them were referred from other specialists not only in dentistry but also internal medicine, otorhinolaryngology, dermatology, psychosomatic medicine, and psychiatry. They come from the Metropolitan area, of course, Osaka, Kyushu, Hokkaido and so on. We take fine-grained care and follow up, total number of patients is up to 10,000 per year.

We have a mission to meet the demand of these patients and their families, so better treatment outcome and increasing efficiency are required, and cooperation with other medical specialists is needed.

(5) Clinical Performances

Psychosomatic dentistry clinic is very unique, specialized for patients with MUOS. We have treated a large number of patients with various oral psychosomatic problems. With our unrivalled clinical experiences for MUOS, we offer our best clinical setting for the treatments of every MUOS.

(6) Publications

[Original Articles]

1. Anna Miura, Trang T H Tu, Yukiko Shinohara, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Takayuki Suga, Takeshi Watanabe, Motoko Watanabe, Yojiro Umezaki, Tatsuya Yoshikawa, Haruhiko Motomura, Miho Takenoshita, Hidefumi Maeda, Akira Toyofuku. Psychiatric comorbidities in patients with Atypical Odontalgia. *J Psychosom Res.* 2018.01; 104; 35-40
2. Kaoru Kawasaki, Takahiko Nagamine, Takeshi Watanabe, Takayuki Suga, Trang T H Tu, Shiori Sugawara, Lou Mikuzuki, Anna Miura, Yukiko Shinohara, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toyofuku. An increase in salivary flow with amitriptyline may indicate treatment resistance in burning mouth syndrome. *Asia Pac Psychiatry.* 2018.03; e12315
3. Takeshi Watanabe, Kaoru Kawasaki, Trang T.H Tu, Takayuki Suga, Shiori Sugawara, Lou Mikuzuki, Anna Miura, Yukiko Shinohara, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toyofuku, Takahiko Nagamine. The QTc shortening with amitriptyline may indicate treatment resistance in chronic nonorganic orofacial pain *Clinical Neuropsychopharmacology and Therapeutics.* 2018.04; 9; 12-14

4. Takeshi Watanabe *Takahiko Nagamine Lou Mikuzuki Yuma Aota Takayuki Suga Trang T.H Tu Miho Takenoshita Akira Toyofuku. An increase in corrected QT interval may indicate a good clinical response to amitriptyline in female patients with burning mouth syndrome neurology and neurobiology. 2018.08; 1(1); 1-3
5. T T H Tu, A Uezato, A Toyofuku. Psychology: Psychiatric dimension to oral pain. Br Dent J. 2018.08; 225(4); 276
6. Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Shiori Sugawara, Kaoru Kawasaki, Trang Th Tu, Takeshi Watanabe, Takayuki Suga, Motoko Watanabe, Miho Takenoshita, Tatsuya Yoshikawa, Akihito Uezato, Toru Nishikawa, Ken Hoshiko, Toru Naito, Haruhiko Motomura, Akira Toyofuku. Clinical characteristics and course of oral somatic delusions: a retrospective chart review of 606 cases in 5 years. Neuropsychiatr Dis Treat. 2018.08; 14; 2057-2065
7. Takayuki Suga, Takeshi Watanabe, Yuma Aota, Takahiko Nagamine, Akira Toyofuku. Burning mouth syndrome: The challenge of an aging population. Geriatr Gerontol Int. 2018.12; 18(12); 1649-1650

[Conference Activities & Talks]

1. TRANG TU, Kaoru Kawasaki, Shiori Sugawara, Anna Miura, Miho Takenoshita, Yukiko Shinohara, Lou Mikuzuki, Takayuki Suga, Akira Toyofuku, . Treatment Outcome in Atypical Odontalgia: Determinants of Pain Relief,. The 96th General Session of the IADR 2018.07.27 London, England
2. Shiori Sugawara, Ayano Katagiri, Kinuyo Ohara, Lou Mikuzuki, Shigeru Nakamura, Kazuo Tsubota, Akira Toyofuku, Koichi Iwata:. Dry-Eye Pain by Diquafosal Sodium Administration. The 96th General Session of the IADR 2018.07.27 London, England
3. Miho Takenoshita, Yukiko Shinohara, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Tu Thi Huyen Trang, Takayuki Suga, Takeshi Watanabe, Hirofumi Matsuoka, Yoshihiro Abiko, Akira Toyofuku. Clinical study on pain catastrophizing and short-term outcomes of patients with burning mouth syndrome. 18th Congress of the ACPM(Asian College of Psychosomatic Medicine) 2018.08.25 Kyung Hee University, Seoul, Korea
4. Trang T.H. Tu, Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Takayuki Suga, Takeshi Watanabe, Yuma Aota, Tatsuya Yoshikawa, Miho Takenoshita, Akira Toyofuku. New potential pharmacotherapeutic approaches for Atypical Odontalgia. 18th Congress of the ACPM(Asian College of Psychosomatic Medicine) 2018.08.25 Kyung Hee University, Seoul, Korea
5. Takayuki Suga, Takeshi Watanabe, Tu Thi Huyen Trang, Yuma Aota, Kaoru Kawasaki, Shiori Sugawara, Lou Mikuzuki, Yukiko Shinohara, Miho Takenoshita, Akira Toyofuku. Efficacy and safety of low-dose amitriptyline for elderly patients with Burning mouth syndrome. 18th Congress of the ACPM(Asian College of Psychosomatic Medicine) 2018.08.25 Kyung Hee University, Seoul, Korea
6. Takeshi Watanabe, Takahiko Nagamine, Kaoru Kawasaki, Trang T.H. Tu, Takayuki Suga, Yuma Aota, Miho Takenoshita, Akira Toyofuk. The change in QTc intervals predicts the response to tricyclic antidepressants in patients with chronic nonorganic orofacial pain. 18th Congress of the ACPM(Asian College of Psychosomatic Medicine) 2018.08.25 Kyung Hee University, Seoul, Korea
7. Akira Toyofuku. Psychosomatic Dentistry;from brain to a new dentistry. The 32nd IADR-SEA Division Annual Scientific Meeting 2018.09.14 Da Nang city, Vietnam
8. Trang T.H Tu, Kaoru Kawasaki, Shiori Sugawara, Takeshi Watanabe, Takayuki Suga, Lou Mikuzuki, Yukiko Shinohara, Anna Miura, Miho Takenoshita, Akira Toyofuku. PAIN, DEPRESSION AND CATASTROPHIZING IN PATIENTS WITH ATYPICAL ODONTALGIA. 32th IADR-SEA (International Association for Dental Research Southeast Asian Division) 2018.09.14 Furama Resort Da Nang, Da Nang, Vietnam

Behavioral Dentistry

Associate Professor Hiroshi Nitta
Research Associate Sachi Umemori

(1) Research

- 1) Construction of educational system of behavioral dentistry for dental students
- 2) Application of behavioral science to development of dental educational curriculum
- 3) Patients' evaluation of the dental hospital and the dental educational system
- 4) Application of behavioral science to dental clinic

(2) Lectures & Courses

Topic of Behavioral Dentistry included characteristics of human behavior, especially of relationship between patients and dental staff based on the informed consent. Main objective of behavioral dentistry in the graduate course is to provide students opportunity to study application of behavioral science to deal with dental patients showing various perception and behavior in clinic.

(3) Clinical Services & Other Works

Behavioral Dentistry provides medical interview for preliminary diagnosis and general dental practice at the clinic of oral diagnosis and general dentist cooperating with General Dentistry.

(4) Publications

[Original Articles]

1. S. H. Le, K. Tonami, S. Umemori, L. T. -B. Nguyen, L. T. -Q. Ngo, S. Mataka. The potential of heart rate variability for exploring dental anxiety in mandibular third molar surgery International Journal of Oral & Maxillofacial Surgery. 2018.06; 47(6); 809-815

[Conference Activities & Talks]

1. UMEMORI Sachi, Aida J, Tonami K, Tabuchi T, Araki K, Mataka S, Kondo K. Does the secondhand smoking associate with tooth loss? : JAGES cross sectional study. The 28th Annual Scientific Meeting of the Japan Epidemiological Association 2018.02.02 Fukushima
2. UMEMORISachi, TonamiK, NittaH, Araki K,. The Analysis of Introduction of Behavioral Science class in Faculty of Dentistry. The 50th Annual Meeting of the Japan Societu by Medical Education 2018.08.04 Tokyo
3. Kanako Noritake, Jun Tsuruta, Tomoe Miyoshi, Maiko Iwaki, Yuko Mitsuma, Hiroshi Nitta, and Kouji Araki. Development a new IPE program for dental and medical students in clinical practicum. 2018.12.01 Tokyo

4. Hiroshi Nitta, Masayuki Hideshima, Toru Nikaido, Kenichi Tonami, Maiko Iwaki, Yuko Mitsuma, Shota Hayashi, Kiichi Maruyama, Kanako Noritake, Sachi Umemori and Kouji Araki. Questionnaire survey of post-graduate dental trainees who completed their general practice program of TMDU dental hospital -Comparison between under- and post- graduate clinical training-. The 83rd Annual Meeting of The Stomatological Society, Japan 2018.12.01 Tokyo

Professional Development in Health Sciences

Professor Kazuki Takada

(1) Outline

Worldwide, accelerated aging and the shift in disease burdens have created a demand for innovations in health sciences, healthcare, and the healthcare delivery system. Innovation requires not only a vast amount of knowledge and superior skills, but also critical and creative thinking skills. Innovation concerning new drugs and medical devices further requires understanding of the entire flow and process of research and development. In our department, we provide educational opportunities for learners to acquire high-level and practical knowledge of the followings: history of medical and dental education in Japan, professional education/development/certification in Japan and North American/European countries, key pedagogical theories and learning methods, process-based approach and logic models in curriculum development, and competencies and their assessment/evaluation.

(2) Research

- Needs assessment in health care and in professional development in health science fields
- Curriculum development for professionals of the future needs in health sciences

(3) Education

Undergraduate schools

Courses

- School of medicine (1st year): Medical Introductory Courses
- Schools of medicine/dentistry (2nd/3rd years): Global Communication for Health Professionals
- School of medicine (4th year): Preparation for Clinical Clerkship
- School of medicine (5th/6th years): Clinical Clerkship
- Health Sciences Leadership Program: Moral and Political Philosophy
- Health Sciences Leadership Program: Applied Critical Thinking for Health Sciences
- Health Sciences Leadership Program: Problem-solving in the Health Sciences

Graduate school

Course

- 【Master level】 Public Health Biology

(4) Clinical Services & Other Works

Medical Hospital

Kazuki TAKADA (Rheumatology)

(5) Publications**[Original Articles]**

1. Yano T, Akita K, Yamaguchi K, Sawaizumi M. A Cadaver Study to Assess the Feasibility of a Cross-Nerve Transfer of the Infraorbital Nerve for Patients With Peripheral Infraorbital Nerve Injury. *Annals of plastic surgery*. 2018.02; 80(2); 141-144
2. Nakajima Y, Tokairin Y, Nakajima Y, Kawada K, Nagai K, Yamaguchi K, Akita K, Kawano T. Anatomical study of the left superior mediastinal lymphatics for tracheal branches of left recurrent laryngeal nerve-preserving mediastinoscope-assisted surgery in esophageal cancer. *Surgery today*. 2018.03; 48(3); 333-337
3. Okada R, Muro S, Eguchi K, Yagi K, Nasu H, Yamaguchi K, Miwa K, Akita K. The extended bundle of the tensor veli palatini: Anatomic consideration of the dilating mechanism of the Eustachian tube. *Auris, nasus, larynx*. 2018.04; 45(2); 265-272
4. Asahina Y., Kaneko S., Kakinuma S., Kamiya A., Miyoshi M., Tsunoda T., Inoue E., Nitta S., Sato A., Nagata H., Kawai-Kitahata F., Murakawa M., Itsui Y., Nakagawa M., Azuma S., Watanabe M.. HBV reactivation and changes in interferon-stimulated gene expression during treatment of direct-acting antivirals for HCV: Analyses in a novel in vitro model for HBV-HCV coinfection using human induced pluripotent stem cell-derived hepatic cells *JOURNAL OF HEPATOLOGY*. 2018.04; 68; S770-S771
5. Kampan N, Tsutsumi M, Okuda I, Nasu H, Hur MS, Yamaguchi K, Akita K. The malaris muscle: its morphological significance for sustaining the intraorbital structures. *Anatomical science international*. 2018.06; 93(3); 364-371
6. Maekawa Shinya, Sato Mitsuaki, Kuratomi Natsuhiko, Inoue Taisuke, Suzuki Yuichiro, Tatsumi Akihisa, Miura Mika, Matsuda Shuya, Muraoka Masaru, Nakakuki Natsuko, Amemiya Fumitake, Takano Shinichi, Fukasawa Mitsuharu, Nakayama Yasuhiro, Yamaguchi Tatsuya, Sato Tadashi, Sakamoto Minoru, Murakawa Miyako, Nakagawa Mina, Asahina Yasuhiro, Enomoto Nobuyuki. Association between alanine aminotransferase elevation and UGT1A1*6 polymorphisms in daclatasvir and asunaprevir combination therapy for chronic hepatitis C *J. Gastroenterol*. 2018.06; 53(6); 780-786
7. Kampan Natnicha, Tsutsumi Masahiro, Okuda Itsuko, Nasu Hisayo, Hur Mi-Sun, Yamaguchi Kumiko, Akita Keiichi. Malaris muscle 眼窩内の構造を保持する仕組みの形態学的重要性 (The malaris muscle: its morphological significance for sustaining the intraorbital structures) *Anatomical Science International*. 2018.06; 93(3); 364-371
8. Yamaguchi R, Nimura A, Amaha K, Yamaguchi K, Segawa Y, Okawa A, Akita K. Anatomy of the Tarsal Canal and Sinus in Relation to the Subtalar Joint Capsule. *Foot & ankle international*. 2018.07; 1071100718788038
9. Higashino T, Okazaki M, Mori H, Yamaguchi K, Akita K. Microanatomy of Sensory Nerves in the Upper Eyelid: A Cadaveric Anatomical Study. *Plastic and reconstructive surgery*. 2018.08; 142(2); 345-353
10. Asahina Yasuhiro, Kawai-Kitahata Fukiko, Murakawa Miyako, Nitta Sayuri, Nakagawa Mina, Kakinuma Sei, Watanabe Mamoru. Gene Mutational Profile and Viral Integration in Hepatocellular Carcinoma with or without HBV/HCV Suppression *HEPATOLOGY*. 2018.10; 68; 531A
11. Nakagawa Mina, Asahina Yasuhiro, Kawai-Kitahata Fukiko, Murakawa Miyako, Nitta Sayuri, Itsui Yasuhiro, Azuma Seishin, Kakinuma Sei, Tomita Makoto, Watanabe Mamoru. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients *HEPATOLOGY*. 2018.10; 68; 398A
12. Nitta Sayuri, Kato Takanobu, Tuchiya Junichi, Sato Ayako, Tsunoda Tomoyuki, Miyoshi Masato, Inoue-Shinomiya Emi, Kawai-Kitahata Fukiko, Murakawa Miyako, Itsui Yasuhiro, Nakagawa Mina, Azuma Seishin, Kakinuma Sei, Asahina Yasuhiro. The Characteristic and the Anti-HCV Reagents Susceptibility Analysis of NS5A Resistance-Associated Substitutions (RAS) Detected after Daa Treatment Failure Patients *HEPATOLOGY*. 2018.10; 68; 600A

[Conference Activities & Talks]

1. Kitahata-kawai F, Asahina Y, Kakinuma S, Murakawa M, Nitta S, Nagata H, Kaneko S, Inoue E, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N and Watanabe M. Difference of gene mutational profile among viral- and non-viral HCC with or without prior HBV infection: Results of comprehensive deep sequencing analyses of cancer genes and HBV/A AV integration. EASL, The International Liver Congress 2018 2018.04.14 Paris (France)
2. Mina Nakagawa. Post-treatment M2BPGi level is useful for predicting the development of hepatocellular carcinoma in chronic hepatitis C patients treated with IFN-based and IFN-free therapy. Asian Pacific Association for the Study of the Liver Single Topic Conference (APASL STC) 2018.05.11
3. Kumiko Yamaguchi, Chiharu Kawakami, Mina Nakagawa, Kanako Noritake, Jun Tsuruta, Kazuki Takada. How the presence of welfare professional influences multi-discipline team decision making. ANNUAL CONFERENCE 2018, AN INTERNATIONAL ASSOCIATION FOR MEDICAL EDUCATION 2018.08.28
4. Nitta S, Kato T, Tuchiya J, Shinomiya-Inoue E, Sato A, Tsunoda T, Miyoshi M, Kitahata-Kawai F, Murakawa M, Istui Y, Azuma S, Nakagawa M, Kakinuma S, Asahina Y. The in vitro analysis of NS5A resistance-associated substitutions (RAS) observed in DAA treatment failure patients. 25th International Symposium on Hepatitis C Virus and Related Viruses 2018.10.09 Dublin (Ireland)
5. Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Nakagawa M, Kakinuma S, Watanabe M. Gene Mutational Profile and Viral Integration in Hepatocellular Carcinoma with or without HBV/HCV Suppression. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
6. Nakagawa M, Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tomita M, Watanabe M. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
7. Nitta S, Kato T, Tuchiya J, Sato A, Tsunoda T, Miyoshi M, Inoue- Shinomiya E, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The Characteristic and the Anti-HCV Reagents Susceptibility Analysis of NS5A Resistance-Associated Substitutions (RAS) Detected after Daa Treatment Failure Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)

Family Medicine

Yosuke Takemura
Toru Yamada
Masashi Beppu
Suguru Mabuchi
Yoshiro Hadano
Kazuhisa Sakai
Mari Fukuhara
Yuiko Nagamine
Shoko Yoshida
Hiroshi Koike
Masako Sugihara
Yuya Ando
Hiroki Nin

(1) Publications

[Original Articles]

1. Ie K, Murata A, Tahara M, Komiyama M, Ichikawa S, Takemura YC, Onishi H. What determines medical students' career preference for general practice residency training?: a multicenter survey in Japan. *Asia Pacific family medicine*. 2018; 17; 2
2. Nakatomi Takahiro, Ichikawa Shuhei, Wakabayashi Hideki, Takemura Yousuke C.. Children and adolescents in institutional care versus traditional families: a quality of life comparison in Japan *Health and Quality of Life Outcomes*. 2018.07; 16(1); 151
3. Noguchi Masamitsu, Oshita Shizuka, Yamazoe Naohisa, Miyazaki Mitsukazu, Takemura Yousuke C.. Important Clinical Features of Japanese Spotted Fever *American Journal of Tropical Medicine and Hygiene*. 2018.08; 99(2); 466-469
4. Saito G., Yoshimoto H., Takayashiki A., Kawaida K., Takemura Y.. The association between binge drinking prior to injury time and occurrence of alcohol-related injuries a cross-sectional study among Japanese college students *Alcoholism-Clinical and Experimental Research*. 2018.08; 42; 36A

[Misc]

1. 松岡尚則, 永塚憲治, 別府正志. 宇津木昆台の字 漢方の臨床. 2018; 65(7); 721-726

[Conference Activities & Talks]

1. 別府正志. 中西医結合による月経調節と周期療法概論. 日本東洋医学会高知県部会 2018.10.21 高知県婦人会館大ホール (高知市)
2. 大内 修司, 沼沢 祥行, 鈴木 里彩, 佐々木 真理, 阿部 庸子, 藍 真澄, 金子 英司, 竹村 洋典. インスリンデグルデクの週4回投与で良好な血糖管理を得た血液透析患者の1例. 第647回日本内科学会関東地方会 2018.12

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio

Assistant Professor: KAWAGISHI Masahiko

Assistant Professor: SAITO Kenta

Assistant Professor: SATO Keisuke

Lab Manager, Administrative Assistant: TAGUCHI Mie

(1) Research

Our lab has focused in two major directions:

(1) How are cytoplasmic proteins transported in cells, and what other intracellular elements are necessary for their quality control during transport? How are the dynamics of cytoskeletal proteins in neurons regulated and coordinated?

Neuronal cells such as neurons and glial cells are atypical and asymmetric in their morphology; both of them having long processes. They have to endure the burden of energy-consuming long-distance intracellular transport, and develop specialized cytoskeletal structures. Both intracellular transport and cytoskeletal dynamics are inseparably interrelated, and essential for the cellular homeostasis and function. One of the main interests of our laboratory is to understand how their dynamics are regulated and how these dynamics define neuronal morphologies and functions.

(2) How do inhalation anesthetics exert their effects on synaptic transmissions?

Our interests are in deciphering the long-lasting mystery of inhalation anesthetic effects on synaptic transmissions, major mechanism in mammals that insures secure and painless surgical operations. We use electrophysiological preparations as well as newly developed spectroscopic techniques to identify their principles.

(2) Education

Department of neuroanatomy and cellular neurobiology takes charge of basic neuroscience education for medical undergraduate student (Lectures and Wet labs), especially from the morphological point of view.

For graduate school students, our group offers introductory courses on both optical and electron microscopy (Lectures and Wet labs), with close relation to molecular and cellular neurobiology.

(3) Publications

[Conference Activities & Talks]

1. Sumio Terada. Toward deciphering the mystery of cytoskeletal dynamics. The 33rd Joint Annual Conference of Biomedical Science 2018.03.24 Taipei, ROC

2. Nori Nakai, Fumiya Sato, Keisuke Sato, Tomomi Tani, Sumio Terada. Development of genetically-encoded actin probes for fluorescence polarization microscopy. Joint Annual Meeting of 70th JSCB and 51st JSDB 2018.06.08 Tokyo, Japan
3. Nori Nakai, Fumiya Sato, Keisuke Sato, Tomomi Tani, Sumio Terada. Development of genetically-encoded actin probes for fluorescence polarization microscopy. . ASCB/EMBO 2018 Meeting 2018.12.10 San Diego, CA, USA

Systems Neurophysiology

Professor Izumi Sugihara
Associate Professor Yuriko Sugiuchi
Lecturer Yoshiko Izawa
Assistant Professor Mayu Takahashi
Project Researcher Yuanjun Luo
Students (doctoral) 6

(1) Outline

Department of Systems Neurophysiology, formerly Department of Physiology #1 of the medical school, is one of the basic medicine departments and take charge of research and education in the field of neurophysiology and related neurosciences.

(2) Research

Our main interest lies in clarifying the structures that underlies function of the central nervous system and then understanding their function. We are focused on the part of the central nervous system that is involved in control of eye movements. The eye movement control system is located in the cerebrum, brainstem and cerebellum, has been studied in great detail and is important clinically. The cerebellum itself is another site of focus. Dysfunction of the cerebellum causes ataxia, a movement disorder associated with impaired control of movement. We use electrophysiological, morphological and cell-biological approaches.

1) Cerebellar function

Distinct regions in the cerebellum make specific connections with different areas of the brain and are involved in the control of various movements including eye movements. For example, the neuronal circuitry that connects the lateral cerebrum, pontine nuclei, cerebellar cortex (hemisphere), cerebellar nucleus (dentate nucl.), thalamus and cerebrum is important for initiation, execution and control of movements. To understand cerebellar function, it is important to understand the organization of the cerebellum into distinct anatomical regions, to characterize the specific neuronal circuitry of these regions, and to identify how the cerebellum is organized into regions and functions by way of the input and output systems. Our systematic approach to this question includes (developmental) anatomy, molecular biology, and electrophysiology. We have expertise in neuronal labeling with marker molecules and tracers, single-axonal reconstruction, three-dimensional mapping of neuronal projection patterns.

(3) Education

We participate in Introductory Neurophysiology, Neuroscience and Physiology Lab courses for medical students (2nd year) as well as in courses for graduate students. We mainly teach the neurophysiology sections in these courses. Our goal is for students to understand normal function of nerve cells and the nervous system and, on this ground, to understand pathological states of the nervous system in disease. For this purpose, we give clinically-oriented lectures and laboratory courses linked with morphology and pharmacology.

(4) Lectures & Courses

Our lectures cover transport and electric potential of the cell membrane, excitation and synaptic transmission (Introductory Neurophysiology), sensory systems, motor systems, autonomic nervous systems, and higher brain function (Neuroscience), i.e. neurophysiology in general from the molecular, cellular through the organismic levels. To promote students' self-learning attitude, we sometimes employ an "active-learning" style. In the laboratory course, we promote student-teacher discussion in small groups. We have had three "elective research course" students.

(5) Publications

[Original Articles]

1. Yoshiko Izawa, Hisao Suzuki. Motor Action of the Frontal Eye Field on the Eyes and Neck in the Monkey. *J. Neurophysiol.* 2018.06; 119(6); 2082-2090
2. Sarpong GA, Vibulyaseck S, Luo Y, Biswas MS, Fujita H, Hirano S, Sugihara I.. Cerebellar modules in the olivo-cortico-nuclear loop demarcated by pcdh10 expression in the adult mouse. *Journal of Comparative Neurology*. 2018.07; 526(15); 2406-2427

[Misc]

1. Sugihara I. Crus I in the rodent cerebellum: its homology to crus I and II in the primate cerebellum and its anatomical uniqueness among neighboring lobules. *Cerebellum*. 2018.02; 17(1); 49-55
2. Apps R, (14 authors), Sugihara I, (3 authors), Ruigrok TJH. Cerebellar modules and their role as operational cerebellar processing units: A consensus paper. *Cerebellum*. 2018.06; 17(5); 654-682
3. Mayu Takahashi, Yoshikazu Shinoda. Brain Stem Neural Circuits of Horizontal and Vertical Saccade Systems and Their Frame of Reference Neuroscience. 2018.09; 392; 281-328

[Conference Activities & Talks]

1. Luo Y, Sugihara I.. Single axon morphology revealed distinct groups of spinocerebellar projections.. 第10回CBIR/ONSA/大学院セミナー共催若手インスパイアシンポジウム 2018年2月13日東京医科歯科大学 2018.02.13 Tokyo Medical and Dental University, Tokyo
2. Mayu Takahashi. Brainstem Neural Circuits for Horizontal and Vertical Saccadic Eye movements and their Frame of Reference. *Mathematical Modeling in Motor Neuroscience* 2018.06.07 Pavia, Italy
3. Mayu Takahashi. The Semicircular Canal Coordinate System and Its Relation to Neural Circuits for Saccades. XXXth Barany Society meeting 2018.06.11 Uppsala, Sweden
4. Mayu Takahashi. Input-output organization of the posterior vermis and fastigial nucleus for control of saccadic eye movements. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.27 Kobe
5. Yoshiko Izawa, Hisao Suzuki. Effects of microstimulation of the frontal eye field on motor actions of the eyes and neck in the monkey. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.28 Kobe
6. Mayu Takahashi. Input-output organization of posterior vermal and fastigial regions in relation to saccadic eye and head movements. The 75th FUJIHARA Seminar 2018.12.01
7. Sugihara I, Biswas MS, Sarpong GA, Luo Y. The lobular and striped organization of the cerebellar hemisphere in relation to projection patterns of afferent and efferent axons in rodents, with a special focus on crus I.. The 75th Fujihara Seminar 'cerebellum as a CNS hub' 2018.12.03 Tokyo Medical and Dental University, Tokyo
8. Yuriko Sugiuchi. Neural Substrates of Functional Synergies — Structural Basis for Muscle Synergies in the Eye-head Motor System—. The 2nd International Symposium on Embodied-Brain System Scinece (Embos2018) 2018.12.05 Osaka

Pharmacology and Neurobiology

Professor: Tsutomu TANABE
 Assistant professor: Hironao SAEGUSA
 Assistant professor: Makoto FUJIKAWA
 Assistant professor: Daisuke TANAKA

(1) Outline

Many intriguing mysteries left in the issue of brain function like (1) learning and memory, (2) cognition and behavior, (3) generation of consciousness, (4) personality and mentality. On the other hand, in the modern-day world with a complicated human relations and prolonged life span, necessity of deeper understanding and development of the means to cure the numerous neurological disorders and pain is enormously increased.

(2) Research

1. Regulation of Microglial function in Neuroinflammation/Neurodegenerative diseases
2. Regulation of Macrophage function in Inflammatory bowel disease and Rheumatoid arthritis
3. Energy metabolic imaging at single cell level of cancer stem cell/cancer cell using Bioluminescence and FRET and Imaging
4. Energy metabolic imaging at single cell level of neuron, microglia and astrocyte in the degenerative area of the mouse model of various neurodegenerative diseases
5. Neural mechanisms of pleasure and motivation in feeding
6. Molecular basis of Calcium channelopathy
7. Alteration of Neuron-Glia interaction in Neurological disorders

(3) Education

Undergraduate course: Pharmacology course provides the principle of pharmacological basis of therapeutics. Several representative therapeutic drugs in each disease will be picked up and systematic lectures -from basic pharmacology to mechanism of action, drug metabolism, clinical application and side effects- will be provided. Students are projected to acquire self-learning skills during the course and expected to be ready for handling clinical cases by pharmacological means.

We consider education through the pharmacology lab work is important. Students are given opportunity to dissect out several tissues (heart, skeletal muscle, ileum and vas deferens) from living animals by themselves and test the effect of a number of drugs including specific agonist, antagonist and non-selective drugs. Lab work course is divided into two parts. In the first part, students were given several known drugs for testing the known effect on these tissues. In the second part, students are given two unknown drugs and requested to identify the name and concentration of each drug using the tissues they prepare by themselves.

Graduate course: During the first couple of months, students are requested to acquire basic techniques of biochemistry, molecular biology, pharmacology and electrophysiology that are routinely used in our laboratory. Then students will be given a small project to do using the techniques they have learned during the initial

training. Students are also required to read relevant scientific papers and conduct seminar style lectures to other lab members monthly. After completion of the initial phase, students start their own project under the supervision of the faculties in the lab.

(4) Publications

[Original Articles]

1. Jun-Ichi Kishikawa, Yuki Inoue, Makoto Fujikawa, Kenji Nishimura, Atsuko Nakanishi, Tsutomu Tanabe, Hiromi Imamura, Ken Yokoyama. General anesthetics cause mitochondrial dysfunction and reduction of intracellular ATP levels. PLoS ONE. 2018.01; 13(1); e0190213
2. Daisuke Kondo, Hironao Saegusa, Tsutomu Tanabe. Involvement of phosphatidylinositol-3 kinase/Akt/mammalian target of rapamycin/peroxisome proliferator-activated receptor γ pathway for induction and maintenance of neuropathic pain. Biochem. Biophys. Res. Commun.. 2018.03; 499; 253-259
3. Tanaka, D.H. and Tanabe, T. . A Conjecture for Objectification of the Content of Consciousness. viXra. 2018.04; 1804.0169;
4. Tanaka, D.H. and Tanabe, T.. CHANCE: a method that enables a researcher to fully know the content of consciousness of a subject in scientific experiments. bioRxiv. 2018.12;

Molecular Neuroscience

Professor Kohichi Tanaka
Associate Professor Tomomi Aida
Assistant Professor Saeko Ishida
Assistant Professor Yuichi Hiraoka

Graduate Student (doctor course)
Zhao Zhuoyang
Takehisa Handa

Graduate Student (master course)
Kurumi Hagiwara
Bi Haining
Haruna Aikawa
Yuuta Sawada
Zhao Di

Graduate International Research Student
Cheng Zhao

Technical Staff
Satomi Ohno

(1) Outline

The final goal of our research is to understand molecular, cellular, and neuronal ensemble mechanisms underlying higher order brain functions including learning and memory. For that purpose, we combine molecular genetics, physiological and behavioral methods. The laboratory also studies the mechanism that underlies neuronal cell death and regeneration.

(2) Research

1. Functions of glutamate transporters in the brain

Glutamate is a major excitatory neurotransmitter and plays an important role in neuronal plasticity and neurotoxicity in the central nervous system. Glutamate transport proteins provide the mechanism by which synaptically released glutamate is inactivated and kept below toxic levels in the extracellular space. By now, five subtypes of high-affinity glutamate transporters have been identified in the mammalian brain. Our lab studies the physiological and pathological roles of glutamate transporter subtypes using subtype-specific knockout mice.

Recent human genetic studies have suggested that de novo mutations in GLT1 (EAAT2) cause early-onset epilepsy with multiple seizure types. Consistent with these findings, global GLT1 null mice show lethal spontaneous seizures. The consequences of GLT1 dysfunction vary between different brain regions, suggesting that the role of GLT1 dysfunction in epilepsy may also vary with brain regions. In this study, we generated region-specific GLT1 knockout mice by crossing floxed-GLT1 mice with mice that express the Cre recombinase in a particular domain of the ventricular zone. Selective deletion of GLT1 in the diencephalon, brainstem and spinal cord is

sufficient to reproduce the phenotypes of the global GLT1 null mice. By contrast, dorsal forebrain-specific GLT1 knockout mice showed nonlethal complex seizures including myoclonic jerks, hyperkinetic running, spasm and tonic-clonic convulsion via the activation of NR2A-containing NMDA receptors during a limited period from P12 to P14 and selective neuronal death in cortical layer II/III and the hippocampus. Thus, GLT1 dysfunction in the dorsal forebrain is involved in the pathogenesis of infantile epilepsy and GLT1 in the diencephalon, brainstem and spinal cord may play a critical role in preventing seizure-induced sudden death.

Among glutamate signaling components, accumulating evidence suggests that the glial glutamate transporter GLT1 plays a critical role in neuropathic pain. Here, we generated periaqueductal gray (PAG)-specific and spinal cord-specific GLT1 knockout mice. Nerve injury-induced neuropathic pain was enhanced in spinal cord-specific GLT1 knockout mice but alleviated in PAG-specific GLT1 knockout mice. In addition, ceftriaxone upregulated GLT1 expression in the spinal cord, but not the PAG, of control mice and attenuated tactile hypersensitivity in nerve-injured control mice but not in nerve-injured spinal cord-specific GLT1 knockout mice. Based on these results, the anti-neuropathic pain effect of ceftriaxone is mediated by the upregulation of GLT1 expression in the spinal cord.

2. Role of DEPDC5 in the pathogenesis of epilepsy and psychiatric disorder

Epilepsy is one of the most frequent (1%) neurological disorders characterized by spontaneous and recurrent seizures. However, pharmacoresistance occurs in 30% of the patients. Recently, a role for genetic factors in idiopathic epilepsies, with no identified structural lesion or metabolic cause, is becoming clear. DEP (Dishevelled, Egl-10 and Pleckstrin) domain containing protein 5 (DEPDC5) is a newly identified causative gene for epilepsy (Ishida et al., 2013). DEPDC5 has no transmembrane domain and no homology with known epilepsy genes encode ion channel or transmitter receptor subunits. Its role in epileptogenesis likely differs from the mechanisms known so far. In addition, some individuals also have psychiatric disorder, like autistic features and schizophrenia. This suggests that DEPDC5 is a new key to clarify the common mechanism of refractory epilepsy and psychosis.

So far, we revealed that knockout *Depdc5* in rats or mice results in embryonic lethal (Marsan and Ishida et al., 2016), and knock down it in Zebrafish leads hyperactive behavior (de Calbiac et al., 2018). We also clarified that *Depdc5* heterozygous KO mice show abnormal behaviors. We strongly promote our research to understand the pathogenesis. Research of DEPDC5 is likely to give new insight into epilepsy and psychosis research.

(3) Education

Goals/Outline:

Students should generate genetically modified animals to comprehensively understand the cognitive mechanisms at the level of molecule to behavior. Then, students should analyze cognitive deficits of mutant animals and those molecular mechanisms.

Available programs:

Participation in the ongoing research project; as needed

Training for cell biology: five times a year 13:00 – 16:00

Experiment:

1. Gene cloning and generation of targeting vector.
2. Generation of genetically modified mice
3. Behavioral analysis of the mice
4. Morphological analysis of central nervous systems.

(4) Lectures & Courses

The aim of this practice is to learn molecular biological, anatomical, electrophysiological and psychological approaches to elucidate the mechanism of cognition. Moreover, based on previous case reports of cognitive deficits, students should plan and discuss what kinds of the researches are possible and meaningful to elucidate the pathology of these diseases, leading to unveil the mechanism of cognition.

(5) Publications**[Original Articles]**

1. Kaori Sugiyama, Kohichi Tanaka. Spinal cord-specific deletion of the glutamate transporter GLT1 causes motor neuron death in mice. *Biochem. Biophys. Res. Commun.*. 2018.03; 497(2); 689-693
2. Menon R, Grund T, Zoicas I, Althammer F, Fiedler D, Biermeier V, Bosch OJ, Hiraoka Y, Nishimori K, Eliava M, Grinevich V, Neumann ID. Oxytocin Signaling in the Lateral Septum Prevents Social Fear during Lactation. *Current biology : CB*. 2018.04; 28(7); 1066-1078.e6
3. Junya Sugimoto, Moeko Tanaka, Kaori Sugiyama, Yukiko Ito, Hidenori Aizawa, Miho Soma, Tomoko Shimizu, Akira Mitani, Kohichi Tanaka. Region-specific deletions of the glutamate transporter GLT1 differentially affect seizure activity and neurodegeneration in mice. *Glia*. 2018.04; 66(4); 777-788
4. Bettina Reichenbach, Johanna Classon, Tomomi Aida, Kohichi Tanaka, Maria Genander, Christian Göritz. Glutamate transporter Slc1a3 mediates inter-niche stem cell activation during skin growth. *EMBO J.*. 2018.05; 37(9); e98280
5. Zhuoyang Zhao, Yuichi Hiraoka, Hiroshi Ogawa, Kohichi Tanaka. Region-specific deletions of the glutamate transporter GLT1 differentially affect nerve injury-induced neuropathic pain in mice. *Glia*. 2018.05;
6. Emma M Perkins, Yvonne L Clarkson, Daumante Suminaite, Alastair R Lyndon, Kohichi Tanaka, Jeffrey D Rothstein, Paul Skehel, David J A Wyllie, Mandy Jackson. Loss of cerebellar glutamate transporters EAAT4 and GLAST differentially affects the spontaneous firing pattern and survival of Purkinje cells. *Hum. Mol. Genet.*. 2018.05;
7. Hortense de Calbiac, Adriana Dabacan, Elise Marsan, Hervé Tostivint, Gabrielle Devienne, Saeko Ishida, Eric Leguern, Stéphanie Baulac, Raul C Muresan, Edor Kabashi, Sorana Ciura. Depdc5 knockdown causes mTOR-dependent motor hyperactivity in zebrafish. *Ann Clin Transl Neurol*. 2018.05; 5(5); 510-523
8. Miyasaka Y, Uno Y, Yoshimi K, Kunihiro Y, Yoshimura T, Tanaka T, Ishikubo H, Hiraoka Y, Takemoto N, Tanaka T, Ooguchi Y, Skehel P, Aida T, Takeda J, Mashimo T. CLICK: one-step generation of conditional knockout mice. *BMC genomics*. 2018.05; 19(1); 318
9. Rie Murayama, Mariko Kimura-Asami, Marina Togo-Ohno, Yumiko Yamasaki-Kato, Taeko K Naruse, Takeshi Yamamoto, Takeharu Hayashi, Tomohiko Ai, Katherine G Spoonamore, Richard J Kovacs, Matteo Vatta, Mai Iizuka, Masumi Saito, Shotaro Wani, Yuichi Hiraoka, Akinori Kimura, Hidehito Kuroyanagi. Phosphorylation of the RSRP stretch is critical for splicing regulation by RNA-Binding Motif Protein 20 (RBM20) through nuclear localization. *Sci Rep*. 2018.06; 8(1); 8970
10. Nakade S, Mochida K, Kunii A, Nakamae K, Aida T, Tanaka K, Sakamoto N, Sakuma T, Yamamoto T. Biased genome editing using the local accumulation of DSB repair molecules system. *Nature communications*. 2018.08; 9(1); 3270

[Conference Activities & Talks]

1. Ishida Saeko, Ogawa Hiroshi, Tanaka Kohichi. Glutamate-induced excitotoxicity in midbrain and cerebellum. *Experimental Animals* 2018.07.01

Neuropathology

Professor: Hitoshi Okazawa

Practical Professor: Kazuhiko Tagawa

Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone, Toshiki Uchihara

Assistant Professor: Kyota Fujita

Project Assistant Professor: Xigui Chen, Hidenori Homma, Emiko Yamanishi

Assistant Administrative Staff: Shigemi Sato, Xuemei Zhang

Secretary: Marie Tanaka

Graduate Student : Kanoh Kondo, Hikari Tanaka, Maiko Inotsume, Yuki Yoshioka

(1) Outline

The goals of our research are to elucidate molecular mechanisms of neurodegenerative disorders as well as of mental retardation, and to develop novel therapeutics for those intractable diseases. In neurodegeneration, we are now focusing on polyglutamine diseases including hereditary spinocerebellar degenerations and Huntington's disease. Knowledge from transcriptome and proteome analyses of the pathologies will lead to new types of molecular therapeutics. In reference to mental retardation, we are developing animal models and analyzing molecular pathologies of our original molecule PQBP1 whose mutations cause mental retardation with microcephaly. This line of research is also for developing new therapeutics of the common but intractable diseases.

(2) Research

Research Contents

Following studies have been intensively carried out in our laboratory.

- 1) Investigation of molecular pathologies of neurodegenerative diseases.
- 2) Studies on impairment of DNA-repair in polyglutamine diseases.
- 3) Development of new seed drugs for neurodegeneration.
- 4) Development of new seed drug for mental retardation.
- 5) Investigation of molecular functions of Oct-3/4

Below is the brief report of this year' s progress.

1. Early changes to synapse gene regulation may cause Alzheimer's disease (Tanaka H. et al., Molecular Psychiatry. 2018)

Alzheimer's disease (AD) is the most common form of dementia, involving memory loss and a reduction in cognitive abilities. Patients with AD develop multiple abnormal protein structures in their brains that are thought to destroy or damage nerve cells (neurons). One of these structures, the senile plaque, is made up of clumps of beta-amyloid (Abeta) peptide which form in the spaces between neurons.

Many advanced clinical trials in patients with AD have attempted to slow down or reverse the disease by targeting these plaques for removal. However, despite the successful decrease in Abeta aggregation, these trials mostly have failed to improve memory or cognitive function in AD patients.

Before the formation of Abeta aggregates, studies revealed changes in the phosphorylation (a chemical modification) of certain proteins, including SRRM2. This protein was thought to be involved in a form of gene

regulation known as splicing, but its exact function was unclear.

Now, we have examined levels of SRRM2 phosphorylation in a mouse model of AD, and found that they increased prior to A β aggregation. This ultimately prevented the nuclear transport of SRRM2 and led to reduced levels of PQBP1 protein, which has been linked with the neurodevelopmental and intellectual disorders. We showed that the increased phosphorylation of SRRM2 prevented it from interacting with another protein which aids protein folding. In the absence of this interaction, SRRM2 remained unfolded so was not transported to the nucleus and was degraded in the cytoplasm. We next measured levels of SRRM2 and PQBP1 protein in the cerebral cortex of early-phase AD mice and human end-stage AD patients as well as in human AD iPS cells. Both proteins were greatly reduced compared with corresponding amounts in healthy controls.

To find out what effect a reduction in PQBP1 would have in vivo, we generated knockout mice in which the PQBP1 gene was disrupted. We observed cognitive decline and changes in the morphology of their synapses, which are junctions between neurons that allow electrical and chemical communication. These changes were caused by disrupted patterns of synapse gene splicing.

A viral vector containing PQBP1 was used to recover the synapse protein expression in these mice. Not only did this restore PQBP1 expression, but it also recovered the abnormal phenotypes. These findings offer a new insight into early changes that occur during AD pathology involving splicing proteins, suggesting possibilities for gene therapies by virus vectors.

(Highlight: pathomechanism of SRRM2 phosphorylation at Sert1068)

To understand the molecular mechanism underlying the change of subcellular localization of SRRM2, proteins binding to wild-type or phosphorylation site mutants of SRRM2 were screened by analysis of co-precipitated proteins using mass spectrometry. We revealed that phosphorylated SRRM2 caused by activated ERK1/2 lost its interaction with TCP1 α (T-complex protein 1 subunit α). Next, we found that loss of interaction of TCP1 α disables nuclear transport of SRRM2, resulting the destabilization of PQBP1 (polyglutamine binding protein 1). Concurrent deficiency of SRRM2 and PQBP1 was confirmed in human AD brains. Reduction of SRRM2 and PQBP1 impaired synapses via RNA splicing of synapse genes, which were revealed by comparison of RNA sequence analysis between 5xFAD (AD model mice) and PQBP1-cKO (neuron-specific knockout) mouse cerebral cortex. Therefore, restoration of PQBP1 gene by an adeno-associated virus (AAV) vector recovered synaptic structures and cognitive function in AD model mice.

2. Ser46-phosphorylated MARCKS is a marker of neurite degeneration at the pre-aggregation stage in PD/DLB pathology

Phosphorylation of myristoylated alanine-rich C kinase substrate (MARCKS) reflects neurite degeneration at the early stage of Alzheimer's disease (AD), before extracellular A β aggregates are histologically detectable. In this study, we detected similar phosphorylation of MARCKS at Ser46 in BAC-Tg mice overexpressing human normal alpha-synuclein (alpha-Syn) in the glucocerebrosidase (GBA)-heterozygous-knockout (KO) background (human alpha-Syn-BAC-Tg/GBA-hetero-KO mice), as well as in human DLB patients. The increase in the level of pSer46-MARCKS began before alpha-synuclein aggregate formation, at a time when human alpha-Syn-BAC-Tg/GBA-hetero-KO mice exhibited no symptoms, and was sustained during aging, consistent with the pattern in human postmortem brains. Next, we investigated the upstream kinases that phosphorylate MARCKS at Ser46. MARCKS is a representative substrate of PKC, as known from its name, myristoylated alanine-rich C kinase substrate. However, our previous experiments revealed that Erk1/Erk2 (MAPK3/MAPK1) instead of PKC phosphorylates MARCKS at Ser46. In this study, we revealed abnormal increase of Erk1/2 phosphorylation and its age-dependent enhancement in cortical neuron under the PD/DLB pathology. These results strongly imply a common mechanism of pre-aggregation neurite degeneration in AD and DLB pathologies.

(3) Education

As educational tasks, we have lecture and experiment classes of neuropathology for medical/dental graduate school program and medical school program. We also have general pathology and neuropathology classes for graduate school for health sciences, and clinical anatomical and therapeutic pathology classes for research students.

(4) Lectures & Courses

We provide students with opportunities to learn practical research techniques on neuropathology, especially neurodegenerative diseases.

(5) Publications

[Original Articles]

1. Fujita K, Chen X, Homma H, Tagawa K, Amano M, Saito A, Imoto S, Akatsu H, Hashizume Y, Kaibuchi K, Miyano S, Okazawa H. Targeting Tyro3 ameliorates a model of PGRN-mutant FTLTDP via tau-mediated synaptic pathology. *Nature communications*. 2018.01; 9(1); 433
2. Kawahori K, Hashimoto K, Yuan X, Tsujimoto K, Hanzawa N, Hamaguchi M, Kase S, Fujita K, Tagawa K, Okazawa H, Nakajima Y, Shibusawa N, Yamada M, Ogawa Y. Mild Maternal Hypothyroxinemia During Pregnancy Induces Persistent DNA Hypermethylation in the Hippocampal Brain-Derived Neurotrophic Factor Gene in Mouse Offspring. *Thyroid : official journal of the American Thyroid Association*. 2018.03; 28(3); 395-406
3. Fujita K, Homma H, Kondo K, Ikuno M, Yamakado H, Tagawa K, Murayama S, Takahashi R, Okazawa H. Ser46-Phosphorylated MARCKS Is a Marker of Neurite Degeneration at the Pre-aggregation Stage in PD/DLB Pathology. *eNeuro*. 2018.07; 5(4);
4. Furotani K, Kamimura K, Yajima T, Nakayama M, Enomoto R, Tamura T, Okazawa H, Sone M. Suppression of the synaptic localization of a subset of proteins including APP partially ameliorates phenotypes of the *Drosophila* Alzheimer's disease model. *PLoS ONE*. 2018.09; 13(9); e0204048
5. Tanaka H, Kondo K, Chen X, Homma H, Tagawa K, Kerever A, Aoki S, Saito T, Saido T, Muramatsu S, Fujita K, Okazawa H. The intellectual disability gene PQBP1 rescues Alzheimer's disease pathology. *Mol psychiatry*. 2018.10; 23(10); 2090-2110

[Misc]

1. Hitoshi Okazawa. Bridging Multiple Dementias. *ACS Chem Neurosci*. 2018.04; 9(4); 636-638
2. Takuya Tamura, Hitoshi Okazawa. TRIAD(Transcriptional Repression-Induced Atypical Death) Apoptosis and Beyond :The Many Ways Cells Die. 2018.09; 2; 411-426

[Conference Activities & Talks]

1. Hitoshi Okazawa. New Molecularly Targeted Therapeutics Deduced from Unbiased Approaches. 21st US-Japan Cellular and Gene Therapy Conference 2018.03.01 FDA White Oak Campus(USA Maryland)
2. Hitoshi Okazawa. Comprehensive analyses reveal new concepts of neurodegeneration in time axis. JNS-JSN Joint Symposium 2018.07.26 Kobe Convention Center (Hyogo Kobe)
3. Kanoh Kondo, Xigui Chen, Kazumi Motoki, Hidenori Homma, Hitoshi Okazawa. In vivo imaging of intracellular organelle in neurons of Alzheimer's disease and other neurodegenerative disease model.. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.27 Kobe Convention Center (Hyogo Kobe)
4. Kyota Fujita, Ying Mao, Xigui Chen, Emiko Yamanishi, Hidenori Homma, Kazuhiko Tagawa, Hitoshi Okazawa . A novel form of necrosis, TRIAD, in Huntington's disease. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.28 Kobe Convention Center(Hyogo Kobe)
5. Kazuhiko Tagawa, Kyota Fujita Ying Mao, Shigenori Uchida, Xigui Chen, Kei Watase, Hidenori Homma, Marius Sudol, Hitoshi Okazawa. Developmental YAPdeltaC determines adult pathology in a model of spinocerebellar ataxia type 1. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.28 Kobe Convention Center (Hyogo Kobe)

6. Hikari Tanaka, Ying Mao, Takuya Tamura, Yoshie Yuki, Daisu Abe, Hidenori Homma, Kazuhiko Tagawa, Hitoshi Okazawa. The hnRNP-Htt axis regulates necrotic cell death induced by transcriptional repression through impaired RNA splicing. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.28 Kobe Convention Center (Hyogo Kobe)
7. Seika Inoue, Kanehiro Hayashi, Kyota Fujita, Kazuhiko Tagawa, Hitoshi Okazawa, Ken-ichiro Kubo, Kazunori Nakajima,. Reelin-DBNL signaling regulates neuronal migration via N-cadherin/ α -N-catenin complex in the intermediate zone and multipolar cell accumulate zone of the developing mouse cerebral neocortex. The Joint Congress of the 40th Annual Meeting of Japanese Society of Biological Psychiatry and the 61st Annual Meeting of the Japanese Society for Neurochemistry 2018.09.07 Kobe Convention Center (Hyogo Kobe)
8. Hitoshi Okazawa. Novel Hippo pathway-dependent necrosis, TRIAD and Huntington' s disease. ICN 2018 Tokyo 2018.09.24 Keio Plaza Hotel (Tokyo)
9. Hitoshi Okazawa. Comprehensive proteome analysis reveals ultra-early phase pathologies of neurodegenerative diseases. ICN 2018 Tokyo 2018.09.27 Keio Plaza Hotel (Tokyo)
10. Hitoshi Okazawa. Symptomatic and Disease Modifying Treatments for Chorea and Huntington' s Disease. MDS2018 International Congress 2018.10.07 HongKong Convention and Exhibition Centre (China Hong Kong)
11. Hitoshi Okazawa. Developmental YAPdeltaC determines adult pathology of spinocerebellar ataxia type 1. The 75th Fujihara Seminar 2018.12.03 Tokyo Medical and Dental University (Tokyo)

Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui

Specially-appointed professor;Makoto Aihara

Associate Professor;Takeshi Yoshida

Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Shintaro Horie

Assistant Professor; Tae Yokoi, Hiroyuki Takahashi, Kousei Shinohara, Yuko Iwasaki

Graduate student;Natsuko Nagaoka, Minami Uchida, keijia Cao, Yuxin Fang, Ran Du, Hisako Karube

(1) Outline

Our department was established in 1944. Prof. Jin Ohtsuka initiated research on myopia in 1946, and Emeritus Prof. Takashi Tokoro established high myopia clinic in 1974 as the world only clinic specific to pathologic myopia. To date, clinical practice as well as basic research on myopia have continuously been performed in our department. Uveitis clinic was established by Emeritus Prof. Manabu Mochizuki in 1988. Since Prof. Kyoko Ohno-Matsui was appointed to a professorship in our department, clinical practice and basic research on wide variety of fields such as glaucoma, cataract, diabetic retinopathy, vitreoretinal disorder, and macular diseases in addition to myopia and uveitis have been actively performed.

(2) Research

1. High myopia

- 1) Analysis of retinochoroidal complications in high myopia (choroidal neovascularization, myopic tractional retinopathy)
- 2) Evaluation of the molecular mechanism of choroidal angiogenesis using the cultured cells as well as experimental animals (collaboratory project with Department of Cellular Physiological Chemistry)
- 3) Gene analysis of highly myopic patients (collaborator project with Kyoto University)
- 4) Establishment of a novel therapy to prevent an axial elongation or the formation of posterior staphyloma

2. Ocular immunology and inflammation

- 1) Evaluation of the molecular mechanism of immunoregulation in intraocular inflammation
- 2) Pathogenic mechanism of intraocular inflammatory diseases
- 3) Development of novel treatments of intraocular inflammation
- 4) Molecular diagnosis of virus-infected uveitis and intraocular lymphomas.

3. Neuro-ophthalmology

- 1) Evaluation of the change of the circulation as well as the glucose metabolism in the visual cortex using positron emission tomography (PET) in various ocular disorders
- 2) Mechanism of visual pathway in normal conditions as well as in the patients with amblyopia.

4. Vitreoretinal disorder

- 1) Development of a novel treatment for vitreoretinal disorders like retinal detachment, diabetic retinopathy, and macular holes.

5. Strabismus and amblyopia clinic

- 1) Effect of the visual background on binocular vision as well as the influence of strabismus on dynamic visual

acuity.

(3) Education

Undergraduate education of ophthalmology is composed of 1) classes on histology and physiology of the eye, and on diagnosis and treatment of ocular disorders, 2) combination block in which clinical examination is trained, and the diagnostic process is actively learned through group discussion using case series, 3) pre-clerkship and clerkship in which the medical students practically learn the major ocular disorders by seeing the patients and discussing in the conference.

After the initial residency of the first two years, the residency in ophthalmology is programmed for four years according to the educational program on diploma of ophthalmology by Japanese ophthalmological society.

The graduate students are expected to be academic doctors who develop and perform highly-qualified ophthalmologists, as well as become scientists who can perform basic research focusing on their clinical interest.

(4) Lectures & Courses

Main objective of ophthalmology and visual science in the graduate course is to obtain the highly-advanced knowledge in the diagnosis and the treatment of various ocular disorders and to perform the basic research based on clinical experience.

(5) Clinical Services & Other Works

Clinical practice is organized by the general ophthalmology clinic as well as the several subspecialty clinics. When the patients visited our department, they are screened in the general clinic, and then the final decision of the diagnosis and treatment is made in cooperation with each subspecialty clinic. Subspecialty clinics include high myopia clinic, uveitis clinic, glaucoma clinic, vitreoretinal disorder clinic, diabetic retinopathy clinic, neuro-ophthalmology clinic, and medical retina clinic. Approximately, 1,300 surgeries are performed per year (e.g., cataract surgery, vitreoretinal surgery, glaucoma surgery, strabismus surgery).

(6) Publications

[Original Articles]

1. Koju Kamoi, Akihiko Okayama, Shuji Izumo, Isao Hamaguchi, Kaoru Uchimar, Arinobu Tojo, Kyoko Ohno-Matsui. Adult T-Cell Leukemia/Lymphoma-Related Ocular Manifestations: Analysis of the First Large-Scale Nationwide Survey. *Front Microbiol.* 2018; 9; 3240
2. Hiroyuki Takahashi, Hiroshi Takase, Yukiko Terada, Manabu Mochizuki, Kyoko Ohno-Matsui. Acquired myopia in Vogt-Koyanagi-Harada disease. *Int Ophthalmol.* 2018.02;
3. Jost B Jonas, Rahul A Jonas, Ohno-Matsui K, Leonard Holbach, Songhomitra Panda-Jonas. Corrugated Bruch's membrane in high myopia. *Acta Ophthalmol.* 2018.03; 96(2); e147-e151
4. Hiroshi Keino, Shintaro Horie, Sunao Sugita. Immune Privilege and Eye-Derived T-Regulatory Cells. *J Immunol Res.* 2018.05; 2018; 1679197
5. Caixia Lin, Shi-Ming Li, Ohno-Matsui K, Bing Song Wang, Yu Xin Fang, Kai Cao, Li Qin Gao, Jie Hao, Ye Zhang, Jian Wu, Ning Li Wang, . Five-year incidence and progression of myopic maculopathy in a rural Chinese adult population: the Handan Eye Study. *Ophthalmic Physiol Opt.* 2018.05; 38(3); 337-345
6. Jost B Jonas, Yuxin Fang, Pascal Weber, Ohno-Matsui K. PARAPAPILLARY GAMMA AND DELTA ZONES IN HIGH MYOPIA. *Retina (Philadelphia, Pa.).* 2018.05; 38(5); 931-938
7. Yoshikatsu Hosoda, Munemitsu Yoshikawa, Masahiro Miyake, Yasuharu Tabara, Noriaki Shimada, Wanting Zhao, Akio Oishi, Hideo Nakanishi, Masayuki Hata, Tadamichi Akagi, Sotaro Ooto, Natsuko Nagaoka, Yuxin Fang, , Kyoko Ohno-Matsui, Ching-Yu Cheng, Seang Mei Saw, Ryo Yamada, Fumihiko Matsuda, Akitaka Tsujikawa, Kenji Yamashiro. CCDC102B confers risk of low vision and blindness in high myopia. *Nat Commun.* 2018.05; 9(1); 1782

8. Masato Sakai, Hiroshi Takase, Kenichi Namba, Kazuomi Mizuuchi, Daiju Iwata, Susumu Ishida. Two cases of cytomegalovirus panuveitis in immunocompetent patients. *Am J Ophthalmol Case Rep.* 2018.06; 10; 189-191
9. Yuxin Fang, Tae Yokoi, Natsuko Nagaoka, Kosei Shinohara, Yuka Onishi, Tomoka Ishida, Takeshi Yoshida, Xian Xu, Jost B Jonas, Ohno-Matsui K. Progression of Myopic Maculopathy during 18-Year Follow-up. *Ophthalmology.* 2018.06; 125(6); 863-877
10. Hiroshi Goto, Masahiro Zako, Kenichi Namba, Noriyasu Hashida, Toshikatsu Kaburaki, Masanori Miyazaki, Koh-Hei Sonoda, Toshiaki Abe, Nobuhisa Mizuki, Koju Kamoi, Antoine P Brézín, Andrew D Dick, Glenn J Jaffe, Quan Dong Nguyen, Noritaka Inomata, Nisha V Kwatra, Anne Camez, Alexandra P Song, Martina Kron, Samir Tari, Shigeaki Ohno. Adalimumab in Active and Inactive, Non-Infectious Uveitis: Global Results from the VISUAL I and VISUAL II Trials. *Ocul. Immunol. Inflamm..* 2018.07; 1-11
11. Yan Ni Yan, Ya Xing Wang, Yan Yang, Liang Xu, Jie Xu, Qian Wang, Jing Yan Yang, Xuan Yang, Wen Jia Zhou, Ohno-Matsui K, Wen Bin Wei, Jost B Jonas. Ten-Year Progression of Myopic Maculopathy: The Beijing Eye Study 2001-2011. *Ophthalmology.* 2018.08; 125(8); 1253-1263
12. Koju Kamoi, Manabu Mochizuki, Ohno-Matsui K. Dengue fever-associated necrotizing scleritis: A case report with long-term follow-up. *Medicine (Baltimore).* 2018.08; 97(32); e11875
13. Hiroyuki Kanda, Tetsuro Oshika, Takahiro Hiraoka, Satoshi Hasebe, Ohno-Matsui K, Satoshi Ishiko, Osamu Hieda, Hidemasa Torii, Saulius R Varnas, Takashi Fujikado. Effect of spectacle lenses designed to reduce relative peripheral hyperopia on myopia progression in Japanese children: a 2-year multicenter randomized controlled trial. *Jpn. J. Ophthalmol..* 2018.08;
14. Kengo Uramoto, Noriaki Shimada, Hiroyuki Takahashi, Hideki Murai, Kosei Shinohara, Ohno-Matsui K. Suprachoroidal hemorrhage followed by swept-source optical coherence tomography: a case report. *BMC Ophthalmol.* 2018.08; 18(1); 203
15. Yee-Ling Wong, Charumathi Sabanayagam, Yang Ding, Chee-Wai Wong, Anna Chwee-Hong Yeo, Yin-Bun Cheung, Gemmy Cheung, Audrey Chia, Ohno-Matsui K, Tien-Yin Wong, Jie Jin Wang, Ching-Yu Cheng, Quan V Hoang, Ecosse Lamoureux, Seang-Mei Saw. Prevalence, Risk Factors, and Impact of Myopic Macular Degeneration on Visual Impairment and Functioning Among Adults in Singapore. *Invest. Ophthalmol. Vis. Sci..* 2018.09; 59(11); 4603-4613
16. Yee-Ling Wong, Yang Ding, Charumathi Sabanayagam, Chee-Wai Wong, Pavan Verkicharla, Ohno-Matsui K, Donald Tan, Anna Chwee-Hong Yeo, Quan V Hoang, Ecosse Lamoureux, Seang-Mei Saw. Longitudinal Changes in Disc and Retinal Lesions Among Highly Myopic Adolescents in Singapore Over a 10-Year Period. *Eye Contact Lens.* 2018.09; 44(5); 286-291
17. Jost B Jonas, Pascal Weber, Natsuko Nagaoka, Ohno-Matsui K. TEMPORAL VASCULAR ARCADE WIDTH AND ANGLE IN HIGH AXIAL MYOPIA. *Retina (Philadelphia, Pa.).* 2018.09; 38(9); 1839-1847
18. Kosei Shinohara, Noriko Tanaka, Jost B Jonas, Noriaki Shimada, Muka Moriyama, Takeshi Yoshida, Ohno-Matsui K. Ultrawide-Field OCT to Investigate Relationships between Myopic Macular Retinoschisis and Posterior Staphyloma. *Ophthalmology.* 2018.10; 125(10); 1575-1586
19. Yonese I, Takase H, Yoshimori M, Onozawa E, Tsuzura A, Miki T, Mochizuki M, Miura O, Arai A. CD79B mutations in primary vitreoretinal lymphoma: Diagnostic and prognostic potential. *European journal of haematology.* 2018.11;
20. Xian Xu, Yuxin Fang, Jost B Jonas, Ran Du, Kosei Shinohara, Noriko Tanaka, Tae Yokoi, Yuka Onishi, Kengo Uramoto, Koju Kamoi, Takeshi Yoshida, Kyoko Ohno-Matsui. RIDGE-SHAPED MACULA IN YOUNG MYOPIC PATIENTS AND ITS DIFFERENTIATION FROM TYPICAL DOME-SHAPED MACULA IN ELDERLY MYOPIC PATIENTS. *Retina (Philadelphia, Pa.).* 2018.11;
21. Nikolle W Tan, Ohno-Matsui K, Hyoungh J Koh, Yoshimi Nagai, Montse Pedros, Rita L Freitas, Wayne Macfadden, Timothy Y Lai. LONG-TERM OUTCOMES OF RANIBIZUMAB TREATMENT OF MYOPIC CHOROIDAL NEOVASCULARIZATION IN EAST-ASIAN PATIENTS FROM THE RADIANCE STUDY. *Retina (Philadelphia, Pa.).* 2018.11; 38(11); 2228-2238

22. Yuxin Fang, Ran Du, Jost B Jonas, Takashi Watanabe, Kengo Uramoto, Tae Yokoi, Yuka Onishi, Takeshi Yoshida, Koju Kamoi, Kyoko Ohno-Matsui. RIDGE-SHAPED MACULA PROGRESSING PARALLEL TO BRUCH MEMBRANE DEFECTS AND MACULAR SUPRACHOROIDAL CAVITATION. *Retina* (Philadelphia, Pa.). 2018.12;
23. Kritchai Vutipongsatorn, Natsuko Nagaoka, Tae Yokoi, Takeshi Yoshida, Koju Kamoi, Shintaro Horie, Kengo Uramoto, Akira Hirata, Laurence M Occelli, Simon M Petersen-Jones, Fabiano Montiani-Ferreira, Olivier Cases, Renata Kozyraki, Jost B Jonas, Kyoko Ohno-Matsui. CORRELATIONS BETWEEN EXPERIMENTAL MYOPIA MODELS AND HUMAN PATHOLOGIC MYOPIA. *Retina* (Philadelphia, Pa.). 2018.12;
24. Ohno-Matsui K, Makoto Suzaki, Rie Teshima, Nina Okami. Real-world data on ranibizumab for myopic choroidal neovascularization due to pathologic myopia: results from a post-marketing surveillance in Japan. *Eye (Lond)*. 2018.12; 32(12); 1871-1878

[Misc]

1. Ohno-Matsui K. Pathologic myopia. *Annals of Eyes Science*. 2018.02;
2. Ohno-Matsui K, Yasushi Ikuno, Timothy Y Y Lai, Chui Ming Gemmy Cheung. Diagnosis and treatment guideline for myopic choroidal neovascularization due to pathologic myopia. *Prog Retin Eye Res*. 2018.03; 63; 92-106
3. Ohno-Matsui K. OCT-A Findings of myopic CNV: where does myopic CNV originate?. *Retina Today*. 2018.08; 16(5); 4-6
4. Tae Yokoi, Ohno-Matsui K. Diagnosis and Treatment of Myopic Maculopathy. *Asia Pac J Ophthalmol* (Phila). 2018.10; 7(6); 415-421
5. Manabu Mochizuki, Koju Kamoi. F1000Prime Recommendation of [Gül A et al., *Ann Rheum Dis* 2012, 71(4):563-6] . F1000 Prime.

[Conference Activities & Talks]

1. Ohno-Matsui K, Shinohara K. Wide-Field OCT for Pathologic Myopia. 2018APAO 2018.02.09 Hongkong, China
2. Koju Kamoi. Ocular Involvement in Hematological Malignancies. The 33rd Asia-Pacific Academy of Ophthalmology (APAO). Symposium. 2018.02.11 Hong Kong
3. Ohno-Matsui K. The origin of myopic CNV. The 2nd annual International Swept Source OCT and Angiography Conference 2018.02.16 Paris, France
4. Ohno-Matsui K. Imaging of pathologic myopia. *RetinaChina2018* 2018.03.30 Qingdao, China
5. Mari Miyauchi, Hiroshi Takase, Miyuki Tanaka, Manabu Mochizuki, Kyoko Ohno-Matusi. A validation study in a single Japanese institute for the revised international criteria for the diagnosis of ocular sarcoidosis proposed by the 6th International Workshops on Ocular Sarcoidosis. The Association for Research in Vision and Ophthalmology Annual Meeting 2018.05.02 Honolulu, USA
6. Miyuki Tanaka, Hiroshi Takase, Mari Miyauchi, Manabu Mochizuki, Kyoko Ohno-Matusi. Diagnostic value of serum soluble interleukin-2 receptor level in Japanese patients with ocular sarcoidosis. The Association for Research in Vision and Ophthalmology Annual Meeting 2018.05.02 Honolulu, USA
7. Manabu Mochizuki, Justine R Smith, Hiroshi Takase, Toshikatsu Kaburaki, Narsing A Rao, IWOS Study Group. Revised International Criteria for the Diagnosis of Ocular Sarcoidosis. The Association for Research in Vision and Ophthalmology Annual Meeting 2018.05.02 Honolulu, USA
8. Satoko Nakano, Yasuhiro Tomaru, Hiroshi Takase, Toshiaki Kubota, Manab Mochizuki, Norio Shimizu, Sunao Sugita. Evaluation of a multiplex Strip PCR examination for infectious uveitis and endophthalmitis: A prospective multi-center study. The Association for Research in Vision and Ophthalmology Annual Meeting 2018.05.02 Honolulu, USA
9. Ohno-Matsui K. Complications of High Myopia. *WOC2018* 2018.06.16 Barcelona, Spain

10. Ohno-Matsui K, Shinohara K. Ultra wide-field OCT on pathologic myopia. WOC2018 2018.06.17
11. Ohno-Matsui K, Shinohara K. Ultra wide-field OCT of posterior staphyloma and retinoschisis in pathologic myopia. XX1st Meeting of the Club Jules Gonin 2018.07.13 CHANNEL ISLANDS (GB)
12. Hiroshi Takase. Current immunosuppressive therapies for noninfectious uveitis in Japan. The 52nd Annual Meeting of the Japanese Ocular Inflammation Society 2018.07.15 Tokyo
13. Ohno-Matsui K. Pathological changes in the optic nerve area in pathologic myopia. Allegan Glaucoma Summit 2018.09.01 Soul, Korea
14. Ohno-Matsui K. Ultra wide-field optical coherence tomography to investigate relationships between myopic macular retinoschisis and posterior staphylomas in highly myopic eyes. The retina society 2018.09.12 San Francisco, USA
15. Ohno-Matsui K. Swept-source OCT and OCT angiography of pathologic myopia. AAO (American Academy of Ophthalmology)2018 2018.10.17 Chicago, USA
16. Takahashi H, Shinohara K, Yokoi T, Yoshida T, Ohno-Matsui K. Ultra Wide-Field OCT for Scleral Ridge in Pathologic Myopia. AAO (American Academy of Ophthalmology)2018 2018.10.19 Chicago, USA
17. Ohno-Matsui K, Sadda S, Stanga P, Moussa M. Spectral domain and swept source cross-sectional, en face, and angiographic OCT:diagnosis and management of vitreoretinal and retinochoroidal disorders. AAO (American Academy of Ophthalmology)2018 2018.10.28 Chicago, USA
18. Ohno-Matsui K, Cheung G, Lai T, Hirakata A. Diagnosis and management of vitreoretinal and retinochoroidal disorders. AAO (American Academy of Ophthalmology)2018 2018.10.28 Chicago, USA
19. Grzybowski A, Ohno-Matsui K, Koffler B, Repka MX. New approaches to the prevention and treatment of myopia: Update 2018. AAO (American Academy of Ophthalmology)2018 2018.10.28 Chicago, USA
20. Fang Y, Du R, Nagaoka N, Yokoi T, Shinohara K, Xu X, Takahashi H, Onishi Y, Yoshida T, Ohno-Matsui K. Optical coherent tomography-based diagnosis criteria for myopic maculopathy. AAO (American Academy of Ophthalmology)2018 2018.10.29 Chicago, USA
21. Ohno-Matsui K. Mystery case. AAO (American Academy of Ophthalmology)2018 2018.10.30 Chicago, USA
22. Yokoi T, Ohno-Matsui K. Surgical/management of complications of high myopia. The WHO and International Agency for the Prevention of Blindness (IAPB) meeting on Myopia 2018.11.13 Singapore
23. Ohno-Matsui K. Problems with dome-shaped macula. Pathologic Myopia 2018 2018.11.16 Paris, France
24. Ohno-Matsui K. Imaging the staphylomas. Pathologic Myopia 2018 2018.11.16 Paris, France
25. Yokoi T, Ohno-Matsui K. Updates of myopic maculopathy. The Aier Optometry Development Conference 2018 2018.11.19 China
26. Koju Kamoi. HTLV-1 related ocular diseases. Alice Springs Hospital Educational Lecture 2018.11.27 Alice Springs, Australia
27. Ohno-Matsui K. Swept-source OCT imaging of pathologic myopia. Capital Retina Club 3rd Meeting 2018.11.30 Tokyo
28. Saito R, Yokoi T, Yoshida T, Nagaoka N, Shinohara K, Kaneko Y, Moriyama M, Ohno-Matsui K. Long-term change of optic disc appearance in children with pathologic myopia and its impact on visual Field. The 11th Joint Meeting of Japan-China-Korea Ophthalmologists 2018.12.02 Fukuoka
29. Hiroshi Takase. Intraocular Lymphoma. The 12th Asia-Pacific Vitreo-retina Society (APVRS) congress 2018.12.15 Seoul, Korea
30. Ohno-Matsui K. The origin of myopia . APVRS 2018 2018.12.15 Seoul, Korea
31. Ohno-Matsui K. PCV at the margin of inferior staphyloma. APVRS 2018 2018.12.15 Seoul, Korea

Otorhinolaryngology

Professor: Takeshi Tsutsumi

Associate Professor: Yoshiyuki Kawashima

Junior Associate Professor: Yasuhiro Suzuki

Assistant Professor: Taku Itou, Tarou Fujikawa, Keiji Honda

Hospital Staff: Takamori Takeda, Natsuko Kurata, Ayame Yamazaki, Midori Inoue, Saki Tsukamoto, Sotaro Oosaki, Tat

Graduate Student: Keiko Ohno, Ayane Makabe, Takamori Takeda, Ayako Maruyama, Yusuke Kiyokawa, Motomu Honjo

(1) Research

- 1) Deafness gene analysis
- 2) Neurophysiological study of hearing
- 3) Histoanatomical study of ear, nose, throat, head, and neck
- 4) Eye movement analysis in patients with dizziness
- 5) Clinical study of treatment and prognosis in patients with allergic rhinitis, acute and chronic sinusitis, and benign tumors
- 6) Treatment of tinnitus
- 7) Treatment using endoscope
- 8) Development of a new mapping procedure for cochlear implant
- 9) Bio-Marker of external ear canal carcinoma

(2) Lectures & Courses

Pre-graduate clinical education

Clinical systematic lecture covers anatomy, a general idea of diseases, their pathological conditions and treatments in the field of otorhinolaryngology. Clinical clerkship I (general diagnostic training) provides instruction in the diagnosis and testing techniques of the otorhinolaryngological field; clinical clerkship II (clinical training) provides detailed explanations of disease mechanisms, training in the performance of examinations, and clinical responsibilities involving both inpatient and outpatient care. Clinical clerkship III provides advanced training beyond the scope of clinical clerkship II. In particular, students develop an advanced understanding of otorhinolaryngological diseases by conducting outpatient procedures (including taking histories, visual inspection, and palpation), and gaining practical experience in assessment and diagnosis of patients' conditions. Furthermore, in the clinical clerkship III, students also attend a "micro-conference" on teaching. Finally, students are assigned to patients throughout their treatment, consistently dealing with the same individuals before, during, and after surgery; this allows the students to become familiar with the course of clinical care.

(3) Clinical Performances

Otorhinolaryngology clinic provides full examinations and treatment for diseases in ear, nose, throat, head, and neck, including dizziness, sudden deafness, facial palsy, infectious disease and benign as well as malignant disease in the otorhinolaryngeal area. We have performed the first implementation of bone anchored hearing aid implant in Japan and since then we have experienced many patients for this surgery. We also have performed surgery for patients with malignant disease as well as skull base lesions in collaboration with the Department of

the Head and Neck Surgery. Our outpatient clinic includes general ear, nose and throat clinic as well as allergy, sinusitis, dizziness, otitis media, tumor, deafness, and tinnitus clinic.

(4) Publications

[Original Articles]

1. Takeda Takamori, Makabe Ayane, Hirai Chiaki, Tsutsumi Takeshi. Determination of the time course of caloric nystagmus in patients with spinocerebellar degeneration using caloric step stimulus procedure. *Acta Oto-Laryngologica* . 2018.01; 138(1); 41-45
2. Taku Ito, Hiroki Watanabe, Motomu Honjo, Tomoaki Asamori. Two pediatric cases of post-traumatic facial paralysis with delayed onset *Acta Oto-Laryngologica Case Reports* . 2018.01; 3; 11-14
3. Hiroshi Nakanishi, Yoshiyuki Kawashima, Kiyoto Kurima, Julie A Muskett, H Jeffrey Kim, Carmen C Brewer, Andrew J Griffith. Gradual Symmetric Progression of DFNA34 Hearing Loss Caused by an NLRP3 Mutation and Cochlear Autoinflammation. *Otol. Neurotol.* 2018.03; 39(3); e181-e185
4. Kenro Kawada, Taro Sugimoto, Ryuhei Okada, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuuichiro Kume, Andres Mora, Tairo Ryotokuji, Takuta Okada, Akihiro Hoshino, Yutaka Tokairin, Yausaki Nakajima, Yusuke kiyokawa, Fuminori Nomura, Yosuke Ariizumi, Shohei Tomii, Takashi Ito, Takahiro Asakage, Yusuke Kinugasa, Tatsuyuki Kawano. A case of simultaneous triple primary cancers of the hypopharynx, esophagus and stomach which were dissected by endoscopic laryngo-pharyngeal surgery combined with endoscopic submucosal dissection *Open Journal of Gastroenterology*. 2018.03; 8(3); 94-102
5. Kobayashi M, Miyagawa M, Nishio SY, Moteki H, Fujikawa T, Ohyama K, Sakaguchi H, Miyanohara I, Sugaya A, Naito Y, Morita SY, Kanda Y, Takahashi M, Ishikawa K, Nagano Y, Tono T, Oshikawa C, Kihara C, Takahashi H, Noguchi Y, Usami SI. WFS1 mutation screening in a large series of Japanese hearing loss patients: Massively parallel DNA sequencing-based analysis. *PloS one*. 2018.03; 13(3); e0193359
6. Takeda T, Makabe A, Hirai C, Tsutsumi T.. Determination of the time course of caloric nystagmus in patients with spinocerebellar degeneration using caloric step stimulus procedure. *Acta Otolaryngol*. 2018.04; 138(1); 41-45
7. Mori Y, Kawashima Y, Takahashi M, Maruyama A, Fujikawa T, Tsutsumi T. . Bilateral cochlear ossification in a patient with Takayasu Arteritis. 2018.04;
8. Toriihara A, Nakadate M, Fujioka T, Oyama J, Tsutsumi T, Asakage T, Tsunoda A, Tateishi U. Clinical Usefulness of 18F-FDG PET/CT for Staging Cancer of the External Auditory Canal. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*. 2018.06; 39(5); e370-e375
9. Takamori Takeda, Yoshiyuki Kawashima, Chiaki Hirai, Ayane Makabe, Taku Ito, Taro Fujikawa, Katsura Yamamoto, Ayako Maruyama, Takeshi Tsutsumi. Vestibular Dysfunction in Patients With Superficial Siderosis of the Central Nervous System. *Otol. Neurotol.* 2018.07; 39(6); e468-e474
10. Takamori Takeda, Yoshiyuki Kawashima, Chiaki Hirai, Ayane Makabe, Taku Ito, Taro Fujikawa, Katsura Yamamoto, Ayako Maruyama, and Takeshi Tsutsumi. Vestibular dysfunction in patients with superficial siderosis of the central nervous system. *Otology&Neurotology*. 2018.07; 39(6); 468-474
11. Ito T, Ikeda S, Asamori T, Honda K, Kawashima Y, Kitamura K, Suzuki K, Tsutsumi T. Increased expression of pendrin in eosinophilic chronic rhinosinusitis with nasal polyps. *Brazilian journal of otorhinolaryngology*. 2018.08;
12. Ayako Maruyama, Atsunobu Tsunoda, Masatoki Takahashi, Seiji Kishimoto, Masami Suzuki. Nasopharyngeal pleomorphic adenoma presenting as otitis media with effusion: case report and literature review. *Am J Otolaryngol*. 35(1); 73-76

[Misc]

1. Benign paroxysmal positional vertigo vs malignant type vertigo. *Otolaryngology-Head and Neck Surgery*. 2018.11; 90(12); 1006-1009

[Conference Activities & Talks]

1. Takeda T, Kawashima Y, Hirai C, Makabe A, Ito T, Fujikawa T, Yamamoto K, Maruyama A, Tsutsumi T.. Peripheral Vestibular Dysfunction in Patients with Superficial Siderosis of the Central Nervous System.. 17th Korea-Japan Joint meeting of Otolaryngology-Head and Neck Surgery 2018.04
2. Tsutsumi T, Makabe A, Hirai C, Takeda T, Kawashima Y.. Power-spectral analysis of gravicorder in patients with spino-cerebellar degeneration – Linear regression on logarithmic coordinates.. 17th Korea-Japan Joint Meeting of Otorhinolaryngology-Head and Neck Surgery 2018.04.06
3. Taku Ito, Yoshihiro Noguchi, Yoshiyuki Kawashima Taro Fujikawa, Keiji Honda, Ken Kitamura, Takeshi Tsutsumi. Application of droplet digital PCR to determine copy number variation of STRC in mild to moderate hearing loss. the 6th East Asian Symposium on Otology (EASO 2018) 2018.05.25
4. Takeda T, Tasaki A, Inaba Y, Kiyokawa Y, Fujikawa T, Suzuki Y, Tsutsumi T. Evaluation of gravitational recognition in patients with spinocerebellar degeneration.. 30th Barany Society meeting 2018.06
5. Tsutsumi T, Ikeda T, Fukuoka Y.. Main sequence of torsional saccade under videooculography recordings.. 30th Barany Society Meeting 2018.06.11

Neurology and Neurological Science

Professor YOKOTA Takanori
 Associate Professor ISHIBASHI Satoru
 Junior Associate Professor NISHIDA Yoichiro
 Assistant Professor OHKUBO Takuya
 Assistant Professor OZAKI Kokoro
 Assistant Professor HATTORI Takaaki
 Assistant Professor NUMASAWA Yoshiyuki
 Assistant Professor Yagi Yohsuke
 Assistant Professor Abe Keisuke
 Project Professor SANJO Nobuo
 Project Professor UCHIHARA Toshiki
 Project Associate Professor NAGATA Tetsuya
 Project Junior Associate Professor HARA Rintaro
 Project Assistant Professor KUWAHARA Hiroya
 Project Assistant Professor YOSHIOKA Kotaro
 Project Assistant Professor SAKAUE Fumika
 Project Assistant Professor HIGASHI Miwa
 Project Assistant Professor ASADA Ken
 Graduate Student ZENIYA Satoshi
 Graduate Student IWASAWA Eri
 Graduate Student OHYAGI Masaki
 Graduate Student HASEGAWA Jyuri
 Graduate Student SHINTAKU Hiroshi
 Graduate Student FURUKAWA Fumiko
 Graduate Student MIYASHITA Akiko
 Graduate Student FUJITA Kyohe
 Graduate Student MAJIMA Takamasa
 Graduate Student ONO Daisuke
 Graduate Student HIRATA Kose
 Graduate Student KUNIEDA Taiki
 Graduate Student SANO Tatsuhiko
 Graduate Student ISHINOSE Keiko
 Graduate Student MARUOKA Hiroyuki
 Graduate Student NISHI Rieko
 Graduate Student SUZUKI Motohiro
 Graduate Student YAMADA Akane
 Graduate Student KINA Satoko
 Graduate Student SATO Takefumi
 Graduate Student IIDA Shintaro
 Graduate Student TAKAHASHI Yuko
 Graduate Student OOHARA Masahiro
 Graduate Student MIURA Motoki
 Graduate Student AOKI Hanako
 Graduate Student YAMADA Hiroki
 Research Student OOTSU Shinichi
 Research Student Matsuda Sakino
 Graduate Student SU SU Lei Mon
 Graduate Student JIA Chunyan
 Graduate Student DAIZO Kaiichi
 Graduate Student YASUDA Eiji
 Graduate Student MITSUHASHI Yuta
 Graduate Student TAMURA Keigo
 Graduate Student OOSAKI Mayu

(1) Research

- 1) Development of base technology on nucleic acid medicine and its application to neurological disorders
- 2) Discovery of biomarker in body fluid for neurological diseases
- 3) Pathogenesis of Alzheimer disease
- 4) Pathogenesis and therapies of amyotrophic lateral sclerosis (ALS)
- 5) Pathogenesis and therapies of cerebrovascular diseases
- 6) Genetical and pathomechanical studies of spinocerebellar ataxias
- 7) Regulation of blood-brain barrier
- 8) Electrophysiological studies
- 9) Leading-edge neuroradiological studies
- 10) Neuropathological studies of biopsied and autopsied samples

(2) Lectures & Courses

Neurology is a medical specialty concerned with the diagnosis and treatment of disorders of the nervous system including the brain, spinal cord, peripheral nerves, autonomic nerves and skeletal muscles. Since the nervous system extends to the whole body and regulate all the organs, neurologists have to examine and understand many symptoms of the whole brain and body.

The Department of Neurology and Neurological Science at Tokyo Medical and Dental University offers a unique “clinical neurological training for specialist” in a three-year residency program. This program is designed to provide the highest quality clinical training in the clinical practice of neurology, either in an academic or a practice career. To accomplish this, the program integrates extensive practical exposure to all aspects of current clinical neurology with a firm grounding in underlying scientific principles and methods of clinical investigations such as electrophysiology, neuromuscular pathology, stroke, dementia, neuroimaging, and neurogenetics. The faculty and staff are committed to facilitate resident education and training.

After completion of their training for three years, senior residents are equipped with a lot of clinical experience as attending doctors or teaching assistants in the university hospital and affiliated hospitals. They are eligible for the board certification by the Japanese Society of Neurology.

(3) Clinical Services & Other Works

We daily see about 100 out-patients and 36 in-patients, and offer in- and out-patient consultation services through the weekday and on weekends. We diagnose and treat patients with stroke, multiple sclerosis, Parkinson's disease, spinocerebellar ataxia, ALS, myopathies, neuropathies, meningitis/encephalitis, and hundreds of other neurological issues. We also have the “out-patients clinic specialized to patients with amnesia.” Our patients will be reliably evaluated and diagnosed with some skillful techniques, such as the electrophysiological, neuroradiological, and neuropsychological tests and pathological diagnosis of biopsied nerves and muscles.

(4) Publications**[Original Articles]**

1. Rintaro Iwara Hara, Yuta Mitsunashi, Keita Saito, Yusuke Maeda, Takeshi Wada. Solid-phase synthesis of oligopeptides containing sterically hindered amino acids on non-swellable resin using 3-nitro-1,2,4-triazol-1-yl-tris(pyrrolidin-1-yl)phosphonium hexafluorophosphate (PyNTP) as the condensing reagent ACS Combinatorial Science. 2018; 20; 132-136
2. Furukawa F, Sanjo N, Kobayashi A, Hamaguchi T, Yamada M, Kitamoto T, Mizusawa H, Yokota T. Specific amyloid- β 42 deposition in the brain of a Gerstmann-Sträussler-Scheinker disease patient with a P105L mutation on the prion protein gene. Prion. 2018; 12(5-6); 315-319
3. Yoko Ito, Nobuo Sanjo, Masaki Hizume, Atsushi Kobayashi, Tetsuya Ohgami, Katsuya Satoh, Tsuyoshi Hamaguchi Masahito Yamada, Tetsuyuki Kitamoto, Hidehiro Mizusawa, Takanori Yokota. Biochemical features of genetic Creutzfeldt-Jakob disease with valine-to-isoleucine substitution at codon 180 on the prion protein gene. Biochemical and Biophysical Research Communications. 2018.02; 496(4); 1055-1061

4. Ohara Masahiro, Ozaki Kokoro, Ohkubo Takuya, Yamada Akane, Numasawa Yoshiyuki, Tanaka Keisuke, Tomii Shohei, Ishibashi Satoru, Sanjo Nobuo, Yokota Takanori. 胸腺摘除術後、長期にわたりタクロリムス療法を行った、重症筋無力症に合併した非特定型末梢性 T 細胞リンパ腫 (PTCL-NOS)(Myasthenia Gravis Complicated with Peripheral T-cell Lymphoma, Not Otherwise Specified(PTCL-NOS), Following Thymectomy and Longstanding Tacrolimus Therapy) Internal Medicine. 2018.02; 57(4); 601-604
5. Rintaro Iwata Hara, Yuki Hisada, Yusuke Maeda, Takanori Yokota, Takeshi Wada. Artificial cationic oligosaccharides for heteroduplex oligonucleotide-type drugs. Sci Rep. 2018.03; 8(1); 4323
6. Hiroya Kuwahara, Jindong Song, Takahiro Shimoura, Kie Yoshida-Tanaka, Tadahaya Mizuno, Tatsuki Mochizuki, Satoshi Zeniya, Fuying Li, Kazutaka Nishina, Tetsuya Nagata, Shingo Ito, Hiroyuki Kusuvara, Takanori Yokota. Modulation of blood-brain barrier function by a heteroduplex oligonucleotide in vivo. Sci Rep. 2018.03; 8(1); 4377
7. Amano Eiichiro, Ozaki Kokoro, Egawa Satoru, Suzuki Motohiro, Hirai Takashi, Ishibashi Satoru, Ohkubo Takuya, Yoshii Toshitaka, Okawa Atsushi, Yokota Takanori. Dynamic spinal compression revealed by computed tomography myelography in overshunting-associated myelopathy: A case report. Medicine (Baltimore). 2018.03; 97(10); e0082
8. Hiroki Yamada, Takahiro Takeda, Toshiki Uchihara, Shizuko Sato, Susumu Kirimura, Yuka Hirota, Makoto Kodama, Masanobu Kitagawa, Katsui Hirokawa, Takanori Yokota, Shuta Toru. Macroscopic Localized Subicular Thinning as a Potential Indicator of Amyotrophic Lateral Sclerosis. Eur. Neurol.. 2018.03; 79(3-4); 200-205
9. Sugai Hiroka, Nakase Ikuhiko, Sakamoto Seiji, Nishio Akihiro, Inagaki Masahito, Nishijima Masaki, Yamayoshi Asako, Araki Yasuyuki, Ishibashi Satoru, Yokota Takanori, Inoue Yoshihisa, Wada Takehiko. Peptide Ribonucleic Acid (PRNA)-Arginine Hybrids. Effects of Arginine Residues Alternatingly Introduced to PRNA Backbone on Aggregation, Cellular Uptake, and Cytotoxicity CHEMISTRY LETTERS. 2018.03; 47(3); 381-384
10. Higashi M, Ozaki K, Hattori T, Ishii T, Soga K, Sato N, Tomita M, Mizusawa H, Ishikawa K, Yokota T. A diagnostic decision tree for adult cerebellar ataxia based on pontine magnetic resonance imaging. Journal of the neurological sciences. 2018.04; 387; 187-195
11. Hattori T, Ito K, Nakazawa C, Numasawa Y, Watanabe M, Aoki S, Mizusawa H, Ishiai S, Yokota T. Structural connectivity in spatial attention network: reconstruction from left hemispatial neglect. Brain imaging and behavior. 2018.04; 12(2); 309-323
12. Komaki H*, Nagata T*, Saito T*, Masuda S, Takeshita E, Sasaki M, Tachimori H, Nakamura H, Aoki Y, Takeda S *Equal Contribution. Systemic administration of the antisense oligonucleotide NS-065/NCNP-01 for skipping of exon 53 in patients with Duchenne muscular dystrophy. Science translational medicine. 2018.04; 10(437);
13. Eri Iwasawa, Satoru Ishibashi, Motohiro Suzuki, FuYing Li, Masahiko Ichijo, Kazunori Miki, Takanori Yokota. Sphingosine-1-Phosphate Receptor 1 Activation Enhances Leptomeningeal Collateral Development and Improves Outcome after Stroke in Mice. J Stroke Cerebrovasc Dis. 2018.05; 27(5); 1237-1251
14. Zeniya S, Kuwahara H, Daizo K, Watari A, Kondoh M, Yoshida-Tanaka K, Kaburagi H, Asada K, Nagata T, Nagahama M, Yagi K, Yokota T. Angubindin-1 opens the blood-brain barrier in vivo for delivery of antisense oligonucleotide to the central nervous system. Journal of controlled release : official journal of the Controlled Release Society. 2018.05;
15. Guo Huijia, Yoshioka Kotaro, Kunieda Taiki, Asami Yutaro, Miyata Haruka, Yoshida-Tanaka Kie, Nagata Tetsuya, Yokota Takanori. Efficacy of microRNA silencing by lipid-conjugated double-stranded antisense oligonucleotides Journal of Medical and Dental Sciences. 2018.06; 65(2); 83-88
16. Asada K, Ito K, Yui D, Tagaya H, Yokota T. Cytosolic Genomic DNA functions as a Natural Antisense. Scientific reports. 2018.06; 8(1); 8551
17. Misawa S, Kuwabara S, Sato Y, Yamaguchi N, Nagashima K, Katayama K, Sekiguchi Y, Iwai Y, Amino H, Suichi T, Yokota T, Nishida Y, Kanouchi T, Kohara N, Kawamoto M, Ishii J, Kuwahara M, Suzuki H, Hirata K, Kokubun N, Masuda R, Kaneko J, Yabe I, Sasaki H, Kaida KI, Takazaki H, Suzuki N, Suzuki S, Nodera H, Matsui N, Tsuji S, Koike H, Yamasaki R, Kusunoki S, Japanese Eculizumab Trial for GBS

- (JET-GBS) Study Group.. Safety and efficacy of eculizumab in Guillain-Barré syndrome: a multicentre, double-blind, randomised phase 2 trial. *The Lancet. Neurology*. 2018.06; 17(6); 519-529
18. Itaya Sakiko, Kobayashi Zen, Ozaki Kokoro, Sato Nozomu, Numasawa Yoshiyuki, Ishikawa Kinya, Yokota Takanori, Matsuda Hiroshi, Shintani Shuzo. Spinocerebellar Ataxia Type 31 with Blepharospasm Internal Medicine. 2018.06; 57(11); 1651-1654
 19. Li Fuying, Ishibashi Satoru, Iwasawa Eri, Suzuki Motohiro, Ichinose Keiko, Yokota Takanori. Upregulation of lipoprotein receptors on brain endothelial cells and neurons in the early phase of ischemic stroke in mice *Journal of Medical and Dental Sciences*. 2018.06; 65(2); 59-71
 20. Rintaro Iwata Hara, Aya Yaoita, Katsuya Takeda, Hiroaki Ueki, Ayumu Ishii, Hideyuki Imoto, Satoshi Kobayashi, Michi Sano, Mihoko Noro, Kazuki Sato, Takeshi Wada. Solid-Phase Synthesis of Fluorinated Analogues of Glycosyl 1-Phosphate Repeating Structures from *Leishmania* using the Phosphoramidite Method *ChemistryOpen*. 2018.06; 7; 439-446
 21. Ozaki K, Ohkubo T, Yamada T, Yoshioka K, Ichijo M, Majima T, Kudo S, Akashi T, Honda K, Ito E, Watanabe M, Sekine M, Hamagaki M, Eishi Y, Sanjo N, Ishibashi S, Mizusawa H, Yokota T. Progressive Encephalomyelitis with Rigidity and Myoclonus Resolving after Thymectomy with Subsequent Anasarca: An Autopsy Case. *Internal medicine (Tokyo, Japan)*. 2018.07;
 22. Tsutomu Nakamura, Fumika Sakaue, Yukiko Nasu-Nishimura, Yasuko Takeda, Ken Matsuura, Tetsu Akiyama. The Autism-Related Protein PX-RICS Mediates GABAergic Synaptic Plasticity in Hippocampal Neurons and Emotional Learning in Mice. *EBioMedicine*. 2018.07;
 23. Yokote H, Kamata T, Toru S, Sanjo N, Yokota T. Brain volume loss is present in Japanese multiple sclerosis patients with no evidence of disease activity. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. 2018.07;
 24. Sasaguri H, Nagata K, Sekiguchi M, Fujioka R, Matsuba Y, Hashimoto S, Sato K, Kurup D, Yokota T, Saido TC. Introduction of pathogenic mutations into the mouse *Psen1* gene by Base Editor and Target-AID. *Nature communications*. 2018.07; 9(1); 2892
 25. Honda T, Nagao S, Hashimoto Y, Ishikawa K, Yokota T, Mizusawa H, Ito M. Tandem internal models execute motor learning in the cerebellum. *Proceedings of the National Academy of Sciences of the United States of America*. 2018.07; 115(28); 7428-7433
 26. Rintaro Iwata Hara, Yusuke Maeda, Haruna Fujimaki, Takeshi Wada. Enhancement in RNase H activity of a DNA/RNA hybrid duplex using artificial cationic oligopeptides *Chemical Communications*. 2018.08; 54(61); 8526-8529
 27. Miura M, Numasawa Y, Takahisa M, Ozaki K, Irioka T, Nishida Y, Ishibashi S, Yokota T. Levodopa-responsive truncal tremor in a patient with spinocerebellar ataxia type 3. *Journal of the neurological sciences*. 2018.09; 392; 32-33
 28. Miho Akaza, Itaru Akaza, Tadashi Kanouchi, Tetsuo Sasano, Yuki Sumi, Takanori Yokota. Nerve conduction study of the association between glycemic variability and diabetes neuropathy. *Diabetol Metab Syndr*. 2018.09; 10; 69
 29. Tanihata J, Nagata T, Ito N, Saito T, Nakamura A, Minamisawa S, Aoki Y, Ruegg UT, Takeda S. Truncated dystrophin ameliorates the dystrophic phenotype of mdx mice by reducing sarcolipin-mediated SERCA inhibition. *Biochemical and biophysical research communications*. 2018.09;
 30. Naoki Watanabe*, Tetsuya Nagata*, Youhei Satou, Satoru Masuda, Takashi Saito, Hidetoshi Kitagawa, Hirofumi Komaki, Kazuchika Takagaki, Shin'ichi Takeda *Equal Contribution. NS-065/NCNP-01: An Antisense Oligonucleotide for Potential Treatment of Exon 53 Skipping in Duchenne Muscular Dystrophy. *Mol Ther Nucleic Acids*. 2018.09; 13; 442-449
 31. Sano T, Kobayashi Z, Takaoka K, Ota K, Onishi I, Iizuka M, Tomimitsu H, Shintani S. Retrobulbar optic neuropathy associated with sphenoid sinus mucormycosis. *Neurology and clinical neuroscience*. 2018.09; 6(5); 146-147
 32. Hirata K, Numasawa Y, Kobayashi Z, Yokota T. Bilateral Optic Tract Hyperintensity due to Pituitary Apoplexy. *Internal medicine (Tokyo, Japan)*. 2018.10;

33. Kenji Rowel Q Lim*, Yusuke Echigoya*, Tetsuya Nagata*, Mutsuki Kuraoka, Masanori Kobayashi, Yoshit-sugu Aoki, Terence Partridge, Rika Maruyama, Shin'ichi Takeda, Toshifumi Yokota *Equal Contribution . Efficacy of Multi-exon Skipping Treatment in Duchenne Muscular Dystrophy Dog Model Neonates. *Mol. Ther.*. 2018.10;
34. Sanjo N, Nose Y, Shishido-Hara Y, Mizutani S, Sekijima Y, Aizawa H, Tanizawa T, Yokota T. A controlled inflammation and a regulatory immune system are associated with more favorable prognosis of progressive multifocal leukoencephalopathy. *Journal of neurology*. 2018.12;
35. Otani T, Irioka T, Takahashi YK, Soga K, Igarashi S, Kaneko K, Takahashi T, Yokota T. Two cases of late-onset neuromyelitis optica spectrum disorder initially presenting with isolated cerebral white matter lesions. *eNeurologicalSci*. 2018.12; 13; 35-37
36. Yoshiaki Masaki, Keishi Yamamoto, Takeshi Inde, Keita Yoshida, Atsuya Maruyama, Tetsuya Nagata, Jun Tanihata, Shin'ichi Takeda, Mitsuo Sekine, Kohji Seio. Synthesis of 2'-O-(N-methylcarbamoyl)ethyl 5-methyl-2-thiouridine and its application to splice-switching oligonucleotides. *Bioorg. Med. Chem. Lett.*. 2018.12;
37. Ozaki Kokoro, Ohkubo Takuya, Yamada Tetsuo, Yoshioka Kotaro, Ichijo Masahiko, Majima Takamasa, Kudo Shunsuke, Akashi Takumi, Honda Keiji, Ito Eisaku, Watanabe Mayumi, Sekine Masaki, Hamagaki Miwako, Eishi Yoshinobu, Sanjo Nobuo, Ishibashi Satoru, Mizusawa Hidehiro, Yokota Takanori. Progressive Encephalomyelitis with Rigidity and Myoclonus Resolving after Thymectomy with Subsequent Anasarca: An Autopsy Case Internal Medicine. 2018.12; 57(23); 3451-3458
38. Nishida Y, Hizume M, Fumimura Y, Ichikawa T. Cerebellar Cognitive Affective Syndrome Improved by Donepezil. *Internal medicine (Tokyo, Japan)*. 2018.12;

[Misc]

1. Rintaro Iwata Hara, Takeshi Wada. New molecular technologies for stabilization and activation of nucleic acid drugs Dementia Japan. 2018; 32; 597-606

[Conference Activities & Talks]

1. Hiroya Kuwahara, Takanori Yokota. Glycemic Control Boosts Glucosylated Nanocarrier Crossing the BBB into the Brain. *AAN2018* 2018.04.22
2. Kotaro Yoshioka, Takanori Yokota. A new class of double-stranded oligonucleotide enhances in vivo potency of microRNA silencing. 第 59 回日本神経学会学術大会 2018.05.23 札幌
3. Tetsuya Nagata, Takanori Yokota. Recent progress of DNA/RNA heteroduplex oligonucleotide. 第 59 回日本神経学会学術大会 2018.05.23 札幌
4. Takaaki Hattori, Richard Reynolds, Silvina Horovitz, Codrin Lungu, Eric Wassermann, Mark Hallett. Impaired working memory network and default mode network in Parkinson's disease. 第 59 回日本神経学会学術大会 2018.05.23
5. Su Su Lei Mon, Kotaro Yoshioka, Taiki Kunieda, Yutaro Asami, Wenying Piao, Kie Tanaka, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. A novel structure of duplex antisense oligonucleotides improves potency via intraventricular route. 第 59 回日本神経学会学術大会 2018.05.24 札幌
6. Takanori Yokota, Hiroya Kuwahara, Tetsuya Nagata, Yasutaka Anraku, Makoto Nakakido, Nobuo Sanjo, Kouhei Tsumoto, Kazunori Kataoka, Etsuro Matsubara. Development of blood-brain barrier-crossing amyloid-beta oligomer antibody.. 第 59 回日本神経学会学術大会 2018.05.25 札幌
7. 横田隆徳. Development of blood-brain barrier-crossing amyloid-beta oligomer antibody. . 第 59 回日本神経学会学術大会 2018.05.25 北海道
8. Hiroya Kuwahara, Takanori Yokota. BBB-crossing delivery mechanism of glucosylated nanocarrier by glycemic control. 第 59 回日本神経学会学術大会 2018.05.25 札幌
9. Satoru Ishibashi, Eri Iwasawa, Motohiro Suzuki, Li Fuying, Masahiko Ichijo, Kazunori Miki, Takanori Yokota. S1P1 activation enhances leptomeningeal collateral development and improves outcome after stroke. *Stroke* 2018 2018.05.26

10. Takaaki Hattori, Richard Reynolds, Silvina Horovitz, Codrin Lungu, Eric Wassermann, Mark Hallett. Altered brain activations during working memory task in Parkinson's disease. 2019 Organization for Human Brain Mapping 2018.06.19
11. Takanori Yokota, Hiroya Kuwahara, Takahiro Shimoura, Jindong Song, Kie Yoshida-Tanaka, Tadahaya Mizuno, Tatsuki Mochizuki, Kazutaka Nishina, Tetsuya Nagata, Hiroyuki Kusuhashi. Modulation of blood-brain barrier function by a heteroduplex oligonucleotide in vivo. Keystone Symposia 2018.06.20 USA
12. Su Su Lei Mon, Kotaro Yoshioka, Taiki Kunieda, Yutaro Asami, Wenying Piao, Kie Tanaka, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. A novel structure of double-stranded heteroduplex oligonucleotides for intracerebroventricular application. 日本核酸医薬学会 第4回年会 2018.07.10 福岡
13. Takanori Yokota. Glycemic control enables glucosylated nanocarrier crossing the BBB into the brain. 日本核酸医薬学会 第4回年会 2018.07.11 福岡
14. Akiko Amano, Nobuo Sanjo, Makoto Nakakido, Kouhei Tsumoto, Etsuro Matsubara, Fumiko Furukawa, Tetsuya Nagata, Yoichiro Nishida, Hiroya Kuwahara, Kosei Hirata, Hiroyuki Maruoka, Takanori Yokota. Dot Blot Assay For Quantitative Measurement of Amyloid-Beta Oligomer. AAIC 2018 2018.07.22 USA
15. Nobuo Sanjo, Hiroya Kuwahara, Tetsuya Nagata, Yoichiro Nishida, Akiko Amano, Fumiko Furukawa, Kosei Hirata, Hiroyuki Maruoka, Makoto Nakakido, Tsumoto Kohei, Yasutaka Anraku, Kazunori Kataoka, Ichio Aoki, Etsuro Matsubara, Takami Tomiyama, Takanori Yokota. Molecular Imaging And Treatment of Alzheimer's Disease By Developing Amyloid- β oligomer Antibodies That Cross The Blood-Brain Barrier. AAIC 2018 2018.07.22 USA
16. Hiroya Kuwahara, Yasutaka Anraku, Kazunori Kataoka, Takanori Yokota. An efficient drug delivery system across the BBB by utilizing. 第41回日本神経科学大会 2018.07.28 神戸
17. Kotaro Yoshioka, Taiki Kunieda, Yutaro Asami, Kie Tanaka, Wenying Piao, Hiroya Kuwahara, Kazutaka Nishina, Shingo Ito, Tetsuya Nagata, Takanori Yokota. Overhanging heteroduplex oligonucleotides enable enhanced gene silencing by efficient delivery associated with transferrin. The 2018 Oligo Meeting, 14th Annual Meeting of the Oligonucleotide Therapeutics Society 2018.10.01 USA
18. Satoshi Zeniya, Hiroya Kuwahara, Kaiichi Daizo, Akihiro Watari, Masuo Kondoh, Kie Yoshida-Tanaka, Hidetoshi Kaburagi, Ken Asada, Tetsuya Nagata, Masahiro Nagahama, Kiyohito Yagi, Takanori Yokota. Angubindin-1 for an efficient in vivo delivery of antisense oligonucleotide across the blood-brain barrier into brain. The 2018 Oligo Meeting, 14th Annual Meeting of the Oligonucleotide Therapeutics Society 2018.10.01 USA
19. Takanori Yokota. Glycemic Control Boosts Glucosylated Nanocarrier Crossing the BBB into the Brain. The Oligo Meeting 2018 2018.10.03 Seattle
20. Fumiko Furukawa, Keisuke Ishizawa, Taku Hatano, Chiaki Yanagisawa, Mikiya Suzuki, Yoji Goto, Kagari Mano, Yasushi Iwasaki, Katsuya Satoh, Tetsuyuki Kitamoto, Yoshikazu Nakamura, Masahito Yamada, Tadashi Tsukamoto, Hidehiro Mizusawa, Takanori Yokota, Nobuo Sanjo. Gerstmann-Sträussler-Sheinker syndrome with P105L mutation from prospective 19-years surveillance in Japan.. the Asian Pacific Prion Symposium 2018 2018.10.04 東京
21. Zen Kobayashi, Miho Yoshioka, Keisuke Inoue, Mayumi Watanabe, Kaori Kato, Kazunori Toyoda, Yoshiyuki Numasawa, Shoichiro Ishihara, Hiroyuki Tomimitsu, Shuzo Shintani. Serial changes in Trail Making Test score after mild ischemic stroke. The 20th Congress of the International Association of Rural Health and Medicine 2018.10.11 Tokyo
22. Keisuke Inoue, Yoshiyuki Numasawa, Satoshi Sutou, Masaki Hakomori, Kazunori Toyoda, Hiroyuki Tomimitsu. The combination of Berg Balance Scale and Moss Attention Rating Scale for assessment of walking independence in acute ischemic stroke. The 20th Congress of the International Association of Rural Health and Medicine 2018.10.11 Tokyo
23. Miwa Higashi, Kokoro Ozaki, Takaaki Hattori, Takashi Ishii, Kazumasa Soga, Nozomu Sato, Makoto Tomita, Hidehiro Mizusawa, Kinya Ishikawa, and Takanori Yokota. A diagnostic decision tree for degenerative cerebellar ataxia based on pontine magnetic resonance imaging. Asian Oceanian Congress of Neurology 2018 (AOCN 2018) 2018.11.10 Seoul, Korea

[Patents]

1. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : 2791335
2. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : 2791335
3. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : 2012353330
4. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : 2012353330
5. DOUBLE-STRANDED AGENTS FOR DELIVERING THERAPEUTIC OLIGONUCLEOTIDES, Patent Number : 3004347
6. DOUBLE-STRANDED AGENTS FOR DELIVERING THERAPEUTIC OLIGONUCLEOTIDES, Patent Number : 3004347
7. DOUBLE-STRANDED AGENTS FOR DELIVERING THERAPEUTIC OLIGONUCLEOTIDES, Patent Number : 3004347

[Awards & Honors]

1. 2018 AAN Annual Meeting Abstract of Distinction Award, American Academy of Neurology 70th Annual Meeting, 2018.04
2. TMDU President's Young Researchers Award, Tokyo Medical and Dental University, 2018.09

[Others]

1. 2018.06
Journal of Controlled Release

Psychiatry and Behavioral Sciences

Professor, Chair

Toru NISHIKAWA(-Mar.2018)

Professor

Takayuki OKADA

Associate Professor

Akeo KURUMAJI

Junior Associate Professor

Takashi TAKEUCHI, Akihito UEZATO

Senior Assistant Professor

Daisuke JITOKU

Assistant Professor

Hitoshi MUTO, Takehiro TAMURA, Takako NAKANOTANI(-Sep.2017), Kazuo TAKIGUCHI(-Mar.2018)

Junior Assistant Professor

Kouhei MISE(Apr.2018-), Ryota SHIOE(Apr.2018-), Hiroki SHIWAKU(Apr.2018-)

Senior Resident

Kouhei MISE(-Mar.2018), Ryota SHIOE(-Mar.2018), Hiroki SHIWAKU(-Mar.2018),
Satoshi TAKAHASHI(-Sep.2018), Koutaro KAWAMATA(-Mar.2018), Nanase KOBAYASHI(Apr.2018-)

Clinical Psychologist

Yasuhiro OKA(-Dec.2018), Kazunori MURAKAMI, Yukari WAKAYAMA, Toshikazu SHINOTAKE,
Hisashi YAMADA(Jan.2018-Mar.2018 and Oct.2018-), Ryoko NAKAJIMA(Apr.2018-)

Psychiatric Social Worker

Yoshifumi KANEKO, Noriko NUMAGUCHI, Sayaka KOJIMA, Norikazu MONTA(-Mar.2018),
Sumiko NOGUCHI

Graduate Students

Shinichi UMINO(-Mar.2018), Kazuo TAKIGUCHI(-Mar.2018), Momoko KOBAYASHI(-Mar.2018),
Megumi GOTO, Ko FURUTA, Shigehiro OGATA, Hidetoshi KINOSHITA, Ryotaro SAITO,
Koji TAKEDA, Takehiro TAMURA(Diagnostic Radiology and Nuclear Medicine),
Yosuke SEKIGUCHI, Yoshiko NOMURA, Asami ISHIZUYA

(1) Outline

Our laboratory is committed to comprehensive research on endogenous psychosis, neurosis, and epilepsy through biological, psychological and social approaches. In collaboration with external research facilities, we are also involved in social psychiatry, child and adolescent psychiatry, and brain imaging studies.

(2) Research

1) Studies in biological psychiatry

(i) Molecular genetic studies to clarify the causes and conditions of neuropsychiatric diseases:

Using animal models with psychotic symptom-causing agents, we are involved in a study to isolate new candidate gene clusters associated with the pathogenesis and pathophysiology of neuropsychiatric disorders from the viewpoint of developmental pharmacology. We are examining the effects of candidate gene clusters in patients with neuropsychiatric disorders.

(ii) Studies in biochemical pharmacology to develop new therapeutic methods for neuropsychiatric disorders.

(iii) A study of sleep stages and behavior in neuropsychiatric diseases:

A study is being carried out to examine sleep stages and behavior using an originally developed automatic analysis device (polysomnography) in patients with various psychiatric disorders.

(iv) A study on brain functioning in psychiatric disorders by using the near-infrared spectroscopy (NIRS):

To obtain an insight into biological markers of psychiatric disorders, changes in regional brain functions during psychological tasks are examined by measuring the relative concentrations of oxyhemoglobin using NIRS in combination with MRI in the brain areas of the patients with schizophrenia and mood disorders.

2) Psychopathological studies

We are conducting psychological studies of neuropsychiatric diseases from the aspects of phenomenology, anthropology, and linguistics, while employing a psychotherapeutic approach. Other research activities include a review of basic psychiatric concepts and a basic study for the classification and diagnosis of psychiatric disorders, which are important recent issues. In addition to endogenous psychosis including schizophrenia and manic depressive disorder, we are also involved in psychoanalytic studies of neurosis and borderline personality disorder, which are attracting increasing attention, and psychotherapies for them, as well as pathological research on pathography and art therapy in terms of creativity.

3) Forensic Psychiatry Research

Our research includes projects in the development of forensic psychiatric evaluation methodology, risk assessment and management in forensic settings, exploring associations and mechanisms of criminal behavior.

(3) Education

Following the two-year period of mandatory clinical training, basic professional training in psychiatry will be provided for 6-9 months mainly in the university. In the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists, and undergo practical training at affiliated medical facilities to become qualified psychiatrists. Undergraduate education, which places emphasis on clinical clerkship training after a systematic series of lecture course and seminar-based classes, is designed to develop students' problem-solving skills, and increase their motivation to learn neuropsychiatry, with support from external facilities.

(4) Lectures & Courses

In the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment and laws and regulations related to clinical practice, and acquire other general knowledge, all being essential for biologic, psychological, social, and ethical approaches to neuropsychiatric diseases.

(5) Clinical Services & Other Works

Clinical practice

Approximately eighty new outpatients visit our department every month, about 30% of which are classified as having "mood disorders" (F3) by ICD-10, followed by "neurotic, stress-related, and somatoform disorders" (F4) and "schizophrenia, schizophrenic and paranoid disorders" (F2). We are also actively involved in consultation and liaison psychiatry for inpatients in other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance dependence, and neurosis requiring intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. Since this facility, the psychiatric department of a general hospital, is used for university education and training, most inpatients are classified as F2, followed by F4 and F3 (ICD-10). We also provide care and treatment for patients with sleep rhythm disorders and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided mECT (modified electroconvulsive therapy) for inpatients, and individual and group psychotherapy for the patients in our psychiatric ward and clinic and day care center in close collaboration with rehabilitation facilities in the community. The day care team consists of a doctor, two nurses, and a psycho-social worker or a clinical psychologist. Day care (partial hospitalization) is the transitional element between inpatient and outpatient care and its indications have a wide range of psychiatric disorders as follows: schizophrenia, depression, bipolar disorder, adjustment disorder and personality disorders. Each member has the own aim and the team gives care with different types of framework. Our day care team regards the potentiality of group very important and the group process could contribute to therapeutic effect. With this kind of experience, patients

could develop their ability to communicate with other people and readapt to social situations.

(i) A study of biological indicators in schizophrenia with eye cameras:

We are not only involved in studies of monozygotic twins, early-onset patients, and children at a high risk in Japan, but also in an international joint research project of the WHO as a center in charge of operations.

(6) Clinical Performances

Since the 2011 fiscal year, we have been conducting the clinical trial of D-cycloserine for negative symptoms such as avolition, flattening of affect, and poverty of thought and cognitive dysfunction of schizophrenia. We also have been treating patients with schizophrenia with clozapine, which has been approved for refractory schizophrenia. We have started getting systematically involved in the treatment of patients complaining of pain or dysesthesia in oral regions in liaison with the Dental Hospital, which is the unique characteristics of our university. In the 2014 fiscal year, we started the psychoeducational program for patients with bipolar disorder, which focuses on the prevention of relapse. In addition, there is an increasing number of liaison activities for the prevention of delirium especially in the surgical wards, the intervention to patients with suicide attempts in the emergency room, and the mental support for peripartum patients in cooperation with the staffs.

(7) Publications

[Original Articles]

1. Momoko Kobayashi, Daisuke Jitoku, Yoshimi Iwayama, Naoki Yamamoto, Tomoko Toyota, Katsuaki Suzuki, Mitsuru Kikuchi, Tasuku Hashimoto, Nobuhisa Kanahara, Akeo Kurumaji, Takeo Yoshikawa, Toru Nishikawa. Association studies of WD repeat domain 3 and chitobiosyldiphosphodolichol beta-mannosyltransferase genes with schizophrenia in a Japanese population. PLoS ONE. 2018.01; 13(1); e0190991
2. Ishiwata S, Hattori K Sasayama D, Teraishi T, Miyakawa T, Yokota Y, Matsumura R, Nishikawa T, Kunugi H. . Cerebrospinal fluid D-serine contents in major depressive disorder negatively correlate with depression severity. J Affect Disord.. 2018.01; (226); 155-162
3. Takagi Shunsuke, Takeuchi Takashi, Yamamoto Naoki, Fujita Munehisa, Furuta Ko, Ishikawa Hiroyo, Motohashi Nobutaka, Nishikawa Toru. 日本人における電気けいれん療法後の認知機能の短期及び長期評価 (Short- and long-term evaluation of cognitive functions after electroconvulsive therapy in a Japanese population) Psychiatry and Clinical Neurosciences. 2018.02; 72(1-2); 95-102
4. Takagi S, Terasawa Y, Takeuchi T. Asystole a Few Seconds After the Electrical Stimulation of Electroconvulsive Therapy. Psychosomatics. 2018.03;
5. Takeuchi T, Okumura Y, Uezato A, Nishikawa T. Clinical characteristics of suicidal behavior in an intensive care unit at a university hospital in Japan: A 7-year observational study. Asian journal of psychiatry. 2018.03; 33; 121-125
6. Takashi Takeuchi, Kanako Ichikura, Kanako Amano, Wakana Takeshita, Kazuho Hisamura. The degree of social difficulties experienced by cancer patients and their spouses. BMC Palliative Care. 2018.06; 17;
7. Yojiro Umezaki, Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Shiori Sugawara, Kaoru Kawasaki, Trang Th Tu, Takeshi Watanabe, Takayuki Suga, Motoko Watanabe, Miho Takenoshita, Tatsuya Yoshikawa, Akihito Uezato, Toru Nishikawa, Ken Hoshiko, Toru Naito, Haruhiko Motomura, Akira Toyofuku. Clinical characteristics and course of oral somatic delusions: a retrospective chart review of 606 cases in 5 years. Neuropsychiatr Dis Treat. 2018.08; 14; 2057-2065
8. T T H Tu, A Uezato, A Toyofuku. Psychology: Psychiatric dimension to oral pain. Br Dent J. 2018.08; 225(4); 276
9. Takashi Takeuchi, Hitoshi Muto, Hiromi Matsuoka, Kazunori Murakami. What is the expected role of general hospital psychiatrists in perinatal mental health? Japanese Journal of General Hospital Psychiatry. 2018.10; 30(4); 334-340

[Books etc]

1. Psychopharmacology and Pregnancy. 2018.06

[Conference Activities & Talks]

1. Koji Takeda, Takako Nagata, Norio Sugawara, Taro Matsuda, Akihiro Shimada, Takayuki Okada, Naot-sugu Hirabayashi. Recidivism and suicide rate of patients discharged from forensic psychiatric wards in Jap. Annual Meeting of the International Association of Forensic Mental Health Services 2018.06.13 ANTWERP, BELGIUM
2. Uezato, A. et al.. Molecular and genetic study of the discs, large homolog 1 of Drosophila (DLG1) in schizophrenia. CINP 31st World Congress 2018 2018.06.19 Vienna, Austria
3. Takashi Takeuchi. Approach to insomnia and delirium Through the activities of the psychiatry liaison team. 2018.08.03 Tokyo

Neurosurgery

Professor: Taketoshi Maehara

Associate Professor: Tadashi Nariai

Assistant Professors: Yoji Tanaka and Motoki Inaji

Hospital stuffs:

Takashi Sugawara, Kaoru Tamura, Takumi Kudo and Kazuhide Shimizu

Graduate Students: Masahumi Sasaki, Yasuhiro Ueda, Shouko Hara, Satoka Hashimoto, Kenji Yamada, Masataka Yoshimura, Akitaka Muta, Jiro Aoyama, Tomoyuki Nakano and Motoshige Yamashina

(1) Outline

There are various attracting subjects in the field of clinical or basic research. It is essential to acquire the sufficient knowledge and insight into the pathological conditions as well as normal functions of the central nervous system and spinal cord, which will directly benefit for the improvement of clinical results. Main educational purpose of neurosurgery in the graduate course is to provide students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

In the clinical practice, it is important to attach priority to the patients, considering their background. Also in surgery, it is important to preserve the normal brain functions by employing the cutting edge technique. In the research field, it is essential to introduce and develop the latest knowledge and technology by establishing the reciprocal relationship with the other laboratory institutions.

(2) Research

Brain tumors

1. Analysis of the mechanism of tumor proliferation and infiltration, and its application to treatment
2. Analysis of both proliferative and inhibitory cancer genes in cerebral and spinal tumors
3. Studies of photodynamic therapy, irradiation therapy, agents of chemotherapy, immunotherapy, and inhibition of angiogenesis
4. Development of the multi-modal navigation system integrated with anatomical, hemodynamic, and functional information for brain tumor surgery and evaluate its efficacy.

Vascular diseases in the central nervous system and spinal cord

1. Analysis of pathogenesis of vasospasm after subarachnoid hemorrhage and its application to treatment
2. Studies of circulatory disturbance in ischemic and hemorrhagic diseases, and reversibility of the brain tissue
3. Investigations of pathology of Moyamoya disease and the effects of indirect surgical anastomosis on this entity
4. Solutions of problems in the development of endovascular surgery

Neurotrauma

1. Analysis of cell damage and its reversibility, dynamic simulation in cerebrospinal injury
2. Animal experiments concerning treatment of cerebrospinal injury

Functional neurosurgery

1. Pathological analysis and treatment of temporal lobe epilepsy
2. Analysis of intracellular signal transductions

Others

1. Studies of human cerebral circulation, metabolism, and functions using PET, MRI/S, and MEG
2. Studies of receptors in the central nervous system using PET
3. Experiments of brain diseases using animal model MRI and PET

(3) Clinical Services & Other Works

Neurosurgery is a clinical department dealing with various diseases of central nervous system and spinal cord including tumors, vascular diseases, trauma, congenital malformation, functional disorders, and infection.

(4) Publications

[Original Articles]

1. Hiura M, Nariai T, Takahashi K, Muta A, Sakata M, Ishibashi K, Toyohara J, Wagatsuma K, Tago T, Ishii K, Maehara T. Dynamic Exercise Elicits Dissociated Changes Between Tissue Oxygenation and Cerebral Blood Flow in the Prefrontal Cortex: A Study Using NIRS and PET. *Advances in experimental medicine and biology*. 2018; 1072; 269-274
2. Karakama Jun, Nariai Tadashi, Hara Shoko, Hayashi Shihori, Sumita Kazutaka, Inaji Motoki, Tanaka Yoji, Wagatsuma Kei, Ishii Kenji, Nemoto Shigeru, Maehara Taketoshi. Unique Angiographic Appearances of Moyamoya Disease Detected with 3-Dimensional Rotational Digital Subtraction Angiography Imaging Showing the Hemodynamic Status *Journal of Stroke and Cerebrovascular Diseases*. 2018; 27(8); 2147-2157
3. Ohnaka Keisuke, Shimizu Kazuhide, Kobayashi Daisuke, Inaji Motoki, Maehara Taketoshi. 基底槽に伸展した胚芽異形成性神経上皮腫瘍 1 症例報告 (Dysembryoplastic Neuroepithelial Tumor with Extension to the Basal Cistern: A Case Report) *Epilepsy & Seizure*. 2018; 10(1); 87-94
4. Shihori Hayashi, Motoki Inaji, Tadashi Nariai, Keiichi Oda, Muneyuki Sakata, Jun Toyohara, Kenji Ishii, Kiichi Ishiwata, Taketoshi Maehara. Increased Binding Potential of Brain Adenosine A1 Receptor in Chronic Stages of Patients with Diffuse Axonal Injury Measured with [1-methyl-11C] 8-dicyclopropylmethyl-1-methyl-3-propylxanthine Positron Emission Tomography Imaging. *J. Neurotrauma*. 2018.01; 35(1); 25-31
5. Deepak Bhare, Kaoru Tamura, Hiroaki Wakimoto, Sung Hugh Choi, Benjamin Purow, Jeremy Debatisse, Khalid Shah. microRNA-7 upregulates death receptor 5 and primes resistant brain tumors to caspase-mediated apoptosis. *Neuro-oncology*. 2018.01; 20(2); 215-224
6. Kazuhide Shimizu, Masayuki Nitta, Takashi Komori, Takashi Maruyama, Takayuki Yasuda, Yu Fujii, Ken Masamune, Takakazu Kawamata, Taketoshi Maehara, Yoshihiro Muragaki. Intraoperative Photodynamic Diagnosis Using Talaporfin Sodium Simultaneously Applied for Photodynamic Therapy against Malignant Glioma: A Prospective Clinical Study. *Front Neurol*. 2018.01; 9; 24
7. Hiroyuki Akagawa, Maki Mukawa, Tadashi Nariai, Shunsuke Nomura, Yasuo Aihara, Hideaki Onda, Taku Yoneyama, Takumi Kudo, Kazutaka Sumita, Taketoshi Maehara, Takakazu Kawamata, Hidetoshi Kasuya. variants in Japanese pediatric patients with moyamoya disease. *Hum Genome Var*. 2018.01; 5; 17060
8. Mikio Hiura, Tadashi Nariai, Muneyuki Sakata, Akitaka Muta, Kenji Ishibashi, Kei Wagatsuma, Tetsuro Tago, Jun Toyohara, Kenji Ishii, Taketoshi Maehara. Response of Cerebral Blood Flow and Blood Pressure to Dynamic Exercise: A Study Using PET. *Int J Sports Med*. 2018.02; 39(3); 181-188
9. Yoshiki Obata, Yoshihisa Kawano, Yoji Tanaka, Taketoshi Maehara. Prognostic Impact and Post-operative Evaluation of Volumetric Measurement of the Cerebellopontine Cistern in Trigeminal Neuralgia Using 3 Tesla Magnetic Resonance Imaging. *Neurol. Med. Chir. (Tokyo)*. 2018.02; 58(2); 71-78
10. Obata Yoshiki, Kawano Yoshihisa, Tanaka Yoji, Maehara Taketoshi. 3 テスラ MRI 画像を用いた三叉神経痛における小脳橋槽の容積測定の予後予想と術後評価 (Prognostic Impact and Post-operative Evaluation of Volumetric Measurement of the Cerebellopontine Cistern in Trigeminal Neuralgia Using 3 Tesla Magnetic Resonance Imaging) *Neurologia medico-chirurgica*. 2018.02; 58(2); 71-78

11. Nakano T, Tamura K, Tanaka Y, Inaji M, Hayashi S, Kobayashi D, Nariai T, Toyohara J, Ishii K, Maehara T. Usefulness of ^{11}C -Methionine Positron Emission Tomography for Monitoring of Treatment Response and Recurrence in a Glioblastoma Patient on Bevacizumab Therapy: A Case Report. *Case reports in oncology*. 2018.05; 11(2); 442-449
12. Karakama Jun, Nariai Tadashi, Hara Shoko, Hayashi Shihori, Sumita Kazutaka, Inaji Motoki, Tanaka Yoji, Wagatsuma Kei, Ishii Kenji, Nemoto Shigeru, Maehara Taketoshi. Unique Angiographic Appearances of Moyamoya Disease Detected with 3-Dimensional Rotational Digital Subtraction Angiography Imaging Showing the Hemodynamic Status *JOURNAL OF STROKE & CEREBROVASCULAR DISEASES*. 2018.08; 27(8); 2147-2157
13. Hara S, Hori M, Murata S, Ueda R, Tanaka Y, Inaji M, Maehara T, Aoki S, Nariai T. Microstructural Damage in Normal-Appearing Brain Parenchyma and Neurocognitive Dysfunction in Adult Moyamoya Disease. *Stroke*. 2018.10; 49(10); 2504-2507
14. Akihito Sato, Sakyo Hirai, Yoshiki Obata, Taketoshi Maehara, Masaru Aoyagi. Muscular-stage Dissection during Far Lateral Approach and Its Transcondylar Extension. *J Neurol Surg B Skull Base*. 2018.10; 79(Suppl 4); S356-S361
15. Wagatsuma Kei, Oda Keiichi, Sakata Muneyuki, Inaji Motoki, Miwa Kenta, Sasaki Masayuki, Toyohara Jun, Ishii Kenji. Validation of scatter limitation correction to eliminate scatter correction error in oxygen-15 gas-inhalation positron emission tomography images *NUCLEAR MEDICINE COMMUNICATIONS*. 2018.10; 39(10); 936-944
16. Ohnaka K, Shimizu K, Kobayashi D, Inaji M, Maehara T. Dysembryoplastic Neuroepithelial Tumor with Extension to the Basal Cistern: A Case Report *Epilepsy & Seizure*. 2018.11;
17. Hara S, Hori M, Inaji M, Maehara T, Aoki S, Nariai T. Regression of White Matter Hyperintensity after Indirect Bypass Surgery in a Patient with Moyamoya Disease. *Magnetic resonance in medical sciences : MRMS : an official journal of Japan Society of Magnetic Resonance in Medicine*. 2018.12;
18. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol*. 35(3); 402-404

[Conference Activities & Talks]

1. Hara S, Hori M, Tsurushima Y, Tanaka Y, Maehara T, Aoki S, Nariai T.. Myelin imaging in Moyamoya disease. 47th annual meeting of the Japanese Society for Neuroradiology 2018.02.16 Tsukuba, Japan
2. Surgical technique of tentorium resection and oculomotor nerve peeling for IC-PC aneurysm clipping. 2018.03.15
3. Karakama Jun, Nariai Tadashi, Tanaka Yoji. Unique Angiographic Appearances of Moyamoya Disease Detected with 3-Dimensional Rotational Digital Subtraction Angiography Imaging Showing the Hemodynamic Status. The 21st Symposium Neuroradiologicum 2018.03.18
4. Takashi Sugawara, Motoki Inaji, Yoji Tanaka, Tadashi Nariai, Taketoshi Maehara. Surgical Technique for Neck Clipping of Internal Carotid Artery Supracaloid Segment Aneurysm. 2018 China-Japan Cerebrovascular Disease Forum 2018.03.31 Tokyo
5. Shoko Hara. Diversity of work style in Neurosurgery. 2nd Supporting Society for Medical Students and Residents 2018.05.20 Osaka, Japan
6. Hara S, Hori M, Murata S, Ueda R, Nakazawa M, Tanaka Y, Maehara T, Aoki S, Nariai T. Myelin imaging may reveal microstructural damage caused by chronic ischemia correlated with neurocognitive dysfunction in patients with moyamoya disease. ISMRM 26th Annual Meeting & Exhibition 2018.06.20 Paris, France
7. Clinical anatomy of cavernous sinus for transcavernous approach. 2018.07.13
8. Anatomy and skull base surgery of petrous bone -review of 15 case with mastoidectomy-. 2018.07.13

9. Takashi Sugawara, Yoji Tanaka, Yosuke Ariizumi, Kentaro Tanaka, Takahiro Asakage, Taketoshi Maehara. Total Resection of Juvenile Nasopharyngeal Angiofibroma with the combined Microscopic Transcranial and Endoscopic Transnasal Approach. WFNS foundation Endoscopic Cadaver Dissection and Live Surgery Seminar 2018.08.03 Tyumen
10. Takashi Sugawara, Masaru Aoyagi, Masashi Tamaki, Tomoyuki Yano Atsunobu Tsunoda, Kikuo Ohno, Taketoshi Maehara and Seiji Kishimoto. Surgical Technique and Long Term Outcomes of Extended Orbital Exenteration for Sinonasal Malignancy with Orbital Apex Extension. WFNS foundation Endoscopic Cadaver Dissection and Live Surgery Seminar 2018.08.03
11. Takashi Sugawara, Masaru Aoyagi, Masashi Tamaki, Tomoyuki Yano Atsunobu Tsunoda, Kikuo Ohno, Taketoshi Maehara and Seiji Kishimoto. Surgical Technique and Long Term Outcomes of Extended Orbital Exenteration for Sinonasal Malignancy with Orbital Apex Extension. 2nd Congress of Neurosurgeons of Uzbekistan WFNS FOUNDATION ACNS LIVE SEMINAR 2018.09.05 Tashkent
12. Takashi Sugawara, Yoji Tanaka, Takeshi Tsutsumi, Taketoshi Maehara. Surgical strategy of Jugular foramen tumor with consideration of nerve function preservation –focus on facial nerve function-. 2nd Congress of Neurosurgeons of Uzbekistan WFNS FOUNDATION ACNS LIVE SEMINAR 2018.09.05
13. Takashi Sugawara, Yoji Tanaka, Taketoshi Maehara. Surgical Technique for Neck Clipping of Internal Carotid Artery Supracaloid Segment Aneurysm - complete exposure of the aneurysm -. 2nd Congress of Neurosurgeons of Uzbekistan WFNS FOUNDATION ACNS LIVE SEMINAR 2018.09.05 Tashkent
14. Takashi Sugawara, Masaru Aoyagi, Masashi Tamaki, Tomoyuki Yano Atsunobu Tsunoda2, Kikuo Ohno, Taketoshi Maehara and Seiji Kishimoto. Surgical Technique and Long Term Outcomes of Extended Orbital Exenteration for Sinonasal Malignancy with Orbital Apex Extension -Surgical Technique of Anterior and Middle Cranial Fossa Exposure-. Live conference at Regional cancer centre, Trivandrum, Kerala, INDIA 2018.09.28 Kerala (Live lecture from Tokyo)
15. Takashi Sugawara, Masaru Aoyagi, Masashi Tamaki, Tomoyuki Yano Atsunobu Tsunoda2, Kikuo Ohno, Taketoshi Maehara and Seiji Kishimoto. Surgical Technique and Long Term Outcomes of Extended Orbital Exenteration for Sinonasal Malignancy with Orbital Apex Extension -Surgical Technique of Anterior and Middle Cranial Fossa Exposure-. 2018 ACNS Hanoi Skull Base Live Surgery Seminar 2018.10.05 Hanoi
16. Takashi Sugawara, Yoji Tanaka, Taketoshi Maehara. Surgical Technique for Paraclinoid Meningioma resection -Oculomotor cave exposure-. 2018 ACNS Hanoi Skull Base Live Surgery Seminar 2018.10.05
17. Shoko Hara. Bayesean analysis of perfusion-weighted imaging to estimate cerebral blood flow measured by 15O-gas positron emission tomography in patients with chronic cerebrovascular diseases. The 77th Annual Meeting of the Japan Neurosurgical Society 2018.10.12

[Awards & Honors]

1. The ISMRM Magna Cum Laude Merit Award , Joint Annual Meeting ISMRM-ESMRMB 16-21 June 2018 , 2018.06

[Social Contribution]

1. ACNS Endoscopic Cadever Dissection and Live Surgery Seminar, Asian Congress of Neurological Surgeons, 2018 WFNS Foundation ACNS Endoscopic Cadever Dissection and Live Surgery Seminar, Federal Center of Neurosurgery, Tyumen, Russia, 2018.08.03 - 2018.08.05
2. 2nd Congress of Neurosurgeons of Uzbekistan WFNS FOUNDATION ACNS LIVE SEMINAR, Asian Congress of Neurological Surgeons , Tashkent, Uzbekistan, 2018.09.05 - 2018.09.07
3. 2018 ACNS Hanoi Skull Base Live Surgery Seminar, Asian Congress of Neurological Surgeons, Hanoi, Vietnam, 2018.10.05 - 2018.10.07

Endovascular Surgery

Professor Shigeru Nemoto
 Associate Professor Kazutaka Sumita
 Assistant Professor Kazunori Miki
 Clinical Fellow Jun Karakama
 Secretary Yoko Yanagida, Hitomi Kuwahara

(1) Outline

There are various attracting subjects in the field of clinical or basic research. It is essential to acquire the sufficient knowledge and insight into the pathological conditions as well as normal functions of the vascular system, which will directly benefit for the improvement of clinical results. Main educational purpose of Endovascular Surgery in the graduate course is to provide physicians/students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

(2) Research

Our experimental research program is objected to elucidate unsolved questions derived from daily clinical experience. To treat vascular diseases of central nervous system, facial and head-neck legions, we need to understand detailed vascular anatomy, accurate function of these organs and exact pathophysiology of each disease. Our essential research target is the hemodynamics in the vascular diseases of these lesions. Especially we are interested in the integration of the fluid engineering technology into the endovascular field in an effort to open a new frontier of surgical treatment.

(3) Education

Course objects of Endovascular Surgery in the graduate course is to acquire the proper technique as well as the basic knowledge of neuroendovascular surgery.

(4) Lectures & Courses

Main educational purpose of Endovascular Surgery in the graduate course is to provide students the proper technique as well as the basic knowledge of neuroendovascular surgery.

(5) Clinical Services & Other Works

Our major clinical and extracurricular activities are as follows. 1. Endovascular surgery for diseases of central nervous system, facial and head-neck legions. 2. Analysis of cerebrovascular diseases using computational fluid dynamics (CFD). 3. Development of integrated training system for the endovascular surgery.

(6) Clinical Performances

Endovascular Surgery is a clinical department dealing with various vascular diseases of central nervous system, spinal cord, facial and head-neck lesions including tumors, congenital malformation, and functional disorders.

(7) Publications

[Original Articles]

1. Karakama Jun, Nariai Tadashi, Hara Shoko, Hayashi Shihori, Sumita Kazutaka, Inaji Motoki, Tanaka Yoji, Wagatsuma Kei, Ishii Kenji, Nemoto Shigeru, Maehara Taketoshi. Unique Angiographic Appearances of Moyamoya Disease Detected with 3-Dimensional Rotational Digital Subtraction Angiography Imaging Showing the Hemodynamic Status *Journal of Stroke and Cerebrovascular Diseases*. 2018; 27(8); 2147-2157
2. Hiroyuki Akagawa, Maki Mukawa, Tadashi Nariai, Shunsuke Nomura, Yasuo Aihara, Hideaki Onda, Taku Yoneyama, Takumi Kudo, Kazutaka Sumita, Taketoshi Maehara, Takakazu Kawamata, Hidetoshi Kasuya. variants in Japanese pediatric patients with moyamoya disease. *Hum Genome Var*. 2018.01; 5; 17060
3. Masato Inoue, Ryuichi Noda, Shoji Yamaguchi, Yuta Tamai, Makiko Miyahara, Shunsuke Yanagisawa, Koichiro Okamoto, Tetsuo Hara, Sosuke Takeuchi, Kazunori Miki, Shigeru Nemoto. Specific Factors to Predict Large-Vessel Occlusion in Acute Stroke Patients. *J Stroke Cerebrovasc Dis*. 2018.04; 27(4); 886-891
4. Eri Iwasawa, Satoru Ishibashi, Motohiro Suzuki, FuYing Li, Masahiko Ichijo, Kazunori Miki, Takanori Yokota. Sphingosine-1-Phosphate Receptor 1 Activation Enhances Leptomeningeal Collateral Development and Improves Outcome after Stroke in Mice. *J Stroke Cerebrovasc Dis*. 2018.05; 27(5); 1237-1251
5. Karakama J, Nariai T, Hara S, Hayashi S, Sumita K, Inaji M, Tanaka Y, Wagatsuma K, Ishii K, Nemoto S, Maehara T. Unique Angiographic Appearances of Moyamoya Disease Detected with 3-Dimensional Rotational Digital Subtraction Angiography Imaging Showing the Hemodynamic Status. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2018.08; 27(8); 2147-2157

[Conference Activities & Talks]

1. Shigeru Nemoto. Catheter shaping using vascular model made by 3D printer for coil embolization of cerebral aneurysms. Working Group of Interventional Neuroradiology 2018.01.17 Val d'Isere, France
2. Shigeru Nemoto. 3D vascular model is valuable in coil embolization of the cerebral aneurysms. The 13th AAFITN meeting 2018.03.08 Kota Kinabalu, Malaysia
3. Karakama Jun, Nariai Tadashi, Tanaka Yoji. Unique Angiographic Appearances of Moyamoya Disease Detected with 3-Dimensional Rotational Digital Subtraction Angiography Imaging Showing the Hemodynamic Status. The 21st Symposium Neuroradiologicum 2018.03.18
4. Shigeru Nemoto. Endovascular revascularization of chronic complete occlusion of the internal carotid artery. ESNR (European Society of Neuroradiology) 41th annual meeting 2018.09.20 Rotterdam Holland

NCNP Brain Physiology and Pathology

1. Staffs

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Hiroshi KUNUGI
Collaborative Professor	Takashi HANAKAWA
Collaborative Professor	Noritaka ICHINOHE
Collaborative Associate Professor	Yoshitsugu AOKI

(1) Research

1) Investigation of the molecular mechanisms underlying brain development.

(Mikio Hoshino; Department of Biochemistry and Cellular Biology, National Institute of Neuroscience, NCNP)

We are investigating molecular mechanisms underlying nervous system development, especially focusing on neuron-subtype specification, nervous system regionalization, neuronal migration and synaptogenesis. We are also interested in human diseases/disorders caused by disorganized development of the nervous system. We reported a novel machinery for sex differentiation of the brain (Fujiyama et al.).

2) Molecular genetic and genomic study for intellectual disability in Japan.

(Yu-ichi Goto, Department of Mental Retardation and Birth Defect Research, National Institute of Neuroscience, NCNP)

One of the major causes of intellectual disability (ID) is based on mutations in the related genes, which are timely and locally expressed in concert with one another in central nervous system. ID is a phenotype derived from the inappropriate expression of these genes. Recent advances in molecular genetics and genome medicine have pushed us on with systematic analysis of ID patients, especially on X-linked MR. Since 2013, we have investigated the genetic causes and pathophysiology of mitochondrial disease, Rett syndrome, and diseases with cortical and white matter dysplasia. We detected KRAS mutations in patients with early-onset progressive leukoencephalopathy (Itoh M, et al. Brain, 2019), and a novel intragenic deletion in Dandy-Walker malformation (Iida A, et al. Hum Genom Var, 2019) and we studied CO2-sensitive tRNA modification associated with human mitochondrial disease (Lin H, et al. Nat Commun, 2018).

3) Clinical research on mood disorders and schizophrenia

(Hiroshi Kunugi, Department of Mental Disorder Research, National Institute of Neuroscience, NCNP)

The pathogenesis and physiology of mood disorders and schizophrenia remain elusive, and their biomarkers have not yet been established. Our department, which is in collaboration with the National Center of Neurology and Psychiatry Hospital, is trying to develop objective diagnostic markers for these diseases, employing omics approach, brain imaging, and physiological studies. We also aim to develop new treatment on the basis of key molecules and nutrition. In this year, we reported that dopamine metabolite could be a biomarker for depressive disorder in a meta-analysis (J Psychiatr Res, 2018). We found, for the first time, that food allergy is associated with depression and psychological distress (J Affect Disord, 2019). As a nutritional approach, we reported that a medium-chain triglyceride-based ketogenic formula is effective on cognitive function in patients with mild-to-moderate Alzheimer's disease (Neurosci Lett, 2019).

4) Noninvasive study on pathophysiology of human higher brain function.

(Takashi Hanakawa, Department of Advanced Neuroimaging, Integrative Brain Imaging Center, NCNP)

We aim at revealing neural mechanisms underlying higher brain functions including sensory, motor, thought, emotion, and decision making functions in humans, by integrating innovative brain imaging techniques. Translational approach based on this methodological development is to find imaging biomarkers related to the pathophysiology of neuro-psychiatric disorders and to develop new diagnostic tools using the biomarkers. We also develop new rehabilitation methods using non-invasive brain stimulation and brain-machine interface(BMI).

In 2018, we developed EEG-based BMI-related methods (Tobar et al. 2018) and applied EEG-based BMI to a patient in a pilot study (Kasahara et al. 2018). We used MRI technology such as resting-state fMRI to evaluate neuro-psychiatric disorders (Kita et al. 2018; Nakamura et al. 2018; Hakamata et al. 2018). We also used brain stimulation methodology to clarify the pathophysiology of musician's dystonia (Furuya et al. 2018).

5) Primate Social brains: their development, anatomy, physiology and patho-physiology.

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, NCNP)

We are examining the pathophysiology of autism, which is pervasive developmental disorder characterized by communication and social deficit and stereotyped behaviors. For this purpose, a primate model (common marmoset) of autism has been used because similarity of social behavior and brain structures between human and marmosets. Emphases are on multi-dimensional analysis, using genome-wide analysis, anatomy, electrophysiology, *in vivo* imaging and behavior. This year, we have published papers related to this context (Yasue et al., 2018; Abe et al., 2018; Tani et al., 2018 and Komatsu et al., 2019).

6) Molecular pathogenesis and gene therapies for neuromuscular diseases

(Yoshitsugu Aoki, Department of Molecular Therapy, National, National Institute of Neuroscience, NCNP)

Our research group focuses on genetic neuromuscular diseases including fatal Duchenne muscular dystrophy (Annals of Neurology 2009, PNAS 2012, PNAS 2017) and amyotrophic lateral sclerosis (Brain 2017). Our lab integrates molecular, pharmacologic, proteomic and genomic methodologies to clarify the molecular mechanisms of disease pathogenesis and develop novel genetic therapies for the diseases. Especially, we are dedicated to the development of antisense-oligonucleotides based drugs for the diseases in collaboration with Profs. Matthew Wood, Oxford, Kevin Talbot, Oxford, Toshifumi Yokota, Alberta, Fazel Shabanpoor, Melbourne and Samir El-Andaloussi, Karolinska Institutet. The goal of the laboratory is a better understanding and improved treatment of fatal and currently untreated neuromuscular diseases.

During the academic year 2018, we reported promising results of phase 1, open-label, dose-escalation clinical trial to determine the safety, pharmacokinetics, and activity of NS-065/NCNP-01, a morpholino antisense-oligonucleotides based drug that enables skipping of exon 53 (Science Translational Medicine 2018). Furthermore, with the help of two PhD candidates at Tokyo Medical and Dental University, we reported MYOD1-converted, urine-derived cells as a novel Duchenne muscular dystrophy muscle cell model (Scientific Reports 2019). We also reported that the uptake of morpholino antisense-oligonucleotides and the efficiency of exon-skipping were promoted in dystrophin-deficient myotubes via endocytosis through a caveolin-dependent pathway (Molecular Therapy Nucleic Acid 2019).

(2) Education

The nervous system is a very fine and complex organ to elicit the higher brain function and its malfunction causes a variety of neurological and psychiatric disorders

in humans. In this course, students learn the structure, development and function of the normal nervous and muscle systems as well as pathology of developmental disorders, psychiatric disorders, neurological diseases and muscle diseases. Students also study the latest progress of advanced remedy for neuromuscular diseases.

(3) Publications

[Original Articles]

1. Ambrozkiiewicz MC, Schwark M, Kishimoto-Suga M, Borisova E, Hori K, Salazar-Lázaro A, Rusanova A, Altas B, Piepkorn L, Bessa P, Schaub T, Zhang X, Rabe T, Ripamonti S, Rosário M, Akiyama H, Jahn O, Kobayashi T, Hoshino M, Tarabykin V, Kawabe H: Polarity Acquisition in Cortical Neurons Is Driven by Synergistic Action of Sox9-Regulated Wwp1 and Wwp2 E3 Ubiquitin Ligases and Intronic miR-140.. *Neuron*, 100 (5): 1097-1115.e15, 2018
2. Fujiyama T, Miyashita S, Tsuneoka Y, Kanemaru K, Kakizaki M, Kanno S, Ishikawa Y, Yamashita M, Owa T, Nagaoka M, Kawaguchi Y, Yanagawa Y, Magnuson MA, Muratani M, Shibuya A, Nabeshima Y, Yanagisawa M, Funato H, Hoshino M: Forebrain Ptf1a Is Required for Sexual Differentiation of the Brain.. *Cell Reports*, 24 (1): 79-94, 2018
3. Inoue YU, Morimoto Y, Hoshino M, Inoue T: Generation of Pax6-IRES-EGFP knock-in mouse via the cloning-free CRISPR/Cas9 system to reliably visualize neurodevelopmental dynamics.. *Neuroscience research*, 132 : 1-7, 2018
4. Itoh M, Yamashita M, Kaneko M, Okuno H, Abe M, Yamazaki M, Natsume R, Yamada D, Kaizuka T, Suwa R, Sakimura K, Sekiguchi M, Wada K, Hoshino M, Mishina M, Hayashi T: Deficiency of AMPAR-Palmitoylation Aggravates Seizure Susceptibility. *The Journal of neuroscience*, 38 (47): 10220-10235, 2018
5. Sakikubo M, Furuyama K, Horiguchi M, Hosokawa S, Aoyama Y, Tsuboi K, Goto T, Hirata K, Masui T, Dor Y, Fujiyama T, Hoshino M, Umemoto S, Kawaguchi Y : Ptf1a inactivation in adult pancreatic acinar cells causes apoptosis through activation of the endoplasmic reticulum stress pathway. *Scientific Reports*, 8 : 15812-, 2018
6. Owa T, Taya S, Miyashita S, Yamashita M, Adachi T, Yamada K, Yokoyama M, Aida S, Nishioka T, Inoue YU, Goitsuka R, Nakamura T, Inoue T, Kaibuchi K, Hoshino M: Meis1 Coordinates Cerebellar Granule Cell Development by Regulating Pax6

- Transcription, BMP Signaling and Atoh1 Degradation. *J Neurosci*, 38 (5): 1277-1294, 2018
7. Russo D, Della Ragione F, Rizzo R, Sugiyama E, Scalabri F, Hori K, Capasso S, Sticco L, Fioriniello S, De gregorio R, Granata I, Guarracino MR, Maglione V, Johannes L, Bellenchi GC, Hoshino M, Setou M, D'Esposito M, Luini A, D'Angelo G: Glycosphingolipid metabolic reprogramming drives neural differentiation. *EMBO Journal*, 37 (7): 2018
 8. Itoh M, Dai H, Horike A, Gonzalez J, Kitami Y, Meguro-Horike M, Kuki I, Shimakawa S, Yoshinaga H, Ota Y, Okazaki T, Maegaki Y, Nabatame S, Okzaki S, Kawawaki H, Ueno N, Goto Y, Kato Y. Biallelic KARS pathogenic variants cause an early-onset progressive leukodystrophy. *Brain* 142:560-573, 2019 March
 9. Iida A, Takeshita E, Kosugi S, Kamatani Y, Momozawa Y, Kubo M, Nakagawa E, Kurosawa K, Inoue K, Goto Y. A novel intragenic deletion in *OPHN1* in a Japanese patient with Dandy-Walker malformation. *Hum Genom Var* 6:1, 2019
 10. Lin H, Miyauchi K, Harada T, Okita R, Takeshita E, Komaki H, Fujioka K, Yagasaki H, Goto Y, Yanaka K, Nakagawa S, Sakaguchi Y, Suzuki T. CO2-sensitive tRNA modification associated with human mitochondrial disease. *Nat Commun* 9:1875, 2018 May
 11. Hidese S, Nogawa S, Saito K, Kunugi H. Food allergy is associated with depression and psychological distress: A web-based study in 11,876 Japanese. *J Affect Disord*. 2019 Feb 15;245:213-218.
 12. Ota M, Matsuo J, Ishida I, Takano H, Yokoi Y, Hori H, Yoshida S, Ashida K, Nakamura K, Takahashi T, Kunugi H. Effects of a medium-chain triglyceride-based ketogenic formula on cognitive function in patients with mild-to-moderate Alzheimer's disease. *Neurosci Lett*. 2019 Jan 18;690:232-236.
 13. Hidese S, Matsuo J, Ishida I, Hiraishi M, Teraishi T, Ota M, Hattori K, Kunugi H. Relationship of Handgrip Strength and Body Mass Index With Cognitive Function in Patients With Schizophrenia. *Front Psychiatry*. 2018 Apr 25;9:156
 14. Ogawa S, Tsuchimine S, Kunugi H. Cerebrospinal fluid monoamine metabolite concentrations in depressive disorder: A meta-analysis of historic evidence. *J Psychiatr Res*. 2018 Oct;105:137-146.
 15. Kita K, Rokicki J, Furuya S, Sakamoto T, Hanakawa T: Resting-state basal ganglia connectivity codes a motor musical skill and its disruption from dystonia. *Mov Disord* 33(9): 1472-1480, 2018.
 16. Tobar AM, Ogata Y, Kambara H, Kita K, Nakamura T, Hanakawa T, Koike Y, Yoshimura N: Effect of the EEG sensor number on the current-source decoder

- performance based on a variational Bayesian method (VBMEG). *Int J Eng Res Allied Sci* 5(3), 25-29, 2018.5.
17. Kasahara K, Hoshino H, Furusawa Y, DaSalla CS, Honda M, Murata M, Hanakawa T: Initial experience with a sensorimotor rhythm-based brain-computer interface in a Parkinson's disease patient. *Brain Computer Interfaces* 5(2-3): 88-96.
18. Hakamata Y, Mizukami S, Komi S, Sato E, Moriguchi Y, Motomura Y, Maruo K, Izawa S, Kim Y, Hanakawa T, Inoue Y, Tagaya H: Attentional bias modification alters intrinsic functional network of attentional control: a randomized control trial. *J Affect Disord* 238, 42-281, 2018.6.
19. Nakamura M, Etoh S, Sakamoto T, Nakamura T, Jie LX, Miura Y, Itatani M, Hanakawa T: Potential therapeutic effect of repetitive transcranial magnetic stimulation for tremor in Minamata disease: A case report. *J Neurol Sci* 388:47-49, 2018.
20. Furuya S, Uehara K, Sakamoto T, *Hanakawa T: Aberrant cortical excitability explains the loss of hand dexterity in musicians' dystonia. *J Physiol* 596(12): 2397-2411, 2018.6 doi: 10.1113/JP275813.
21. Kurashige H, Yamashita Y, Hanakawa T, Honda M: A knowledge-based arrangement of prototypical neural representation prior to experience contributes the selectivity in upcoming knowledge acquisition. *Front Hum Neurosci* 12:111, 2018.5
22. Tobar AM, Hyodo R, Kita K, Nakamura T, Kambara H, Hanakawa T, Koike Y, Yoshimura N: Decoding of estimated cortical current sources from ankle flexion and extension using non-invasive brain activity recording methods. *Front Neurosci* 11: 733, 2018.1.
23. Yasue M, Nakagami A, Nakagaki K, Ichinohe N, Kawai N: Inequity aversion is observed in common marmosets but not in marmoset models of autism induced by prenatal exposure to valproic acid.. *Behav Brain Res.*, 343 : 36-40, 2018
24. Abe H, Tani T, Mashiko H Kitamura N, Hayami T, Watanabe S, Sakai K, Suzuki W, Mizukami H, Watakabe A, Yamamori T, Ichinohe N: Axonal Projections From the Middle Temporal Area in the Common Marmoset. *Front. Neuroanat.*, 12 (89): 1-14, 2018
25. Tani T, Abe H, Hayami T, Banno T, Miyakawa N, Kitamura N, Mashiko H, Ichinohe N, Suzuki W: Sound Frequency Representation in the Auditory Cortex of the Common Marmoset Visualized Using Optical Intrinsic Signal Imaging. *eNeuro.*, 5(2): 1-13, 2018
26. Komaki H, Nagata T, Saito T, Masuda S, Takeshita E, Sasaki M, Tachimori H,

- Nakamura H, Aoki Y, Takeda S. Systemic administration of the antisense oligonucleotide NS-065/NCNP-01 for skipping of exon 53 in patients with Duchenne muscular dystrophy. *Sci Transl Med*. 2018;10(437).
27. Lee J, Echigoya Y, Duddy W, Saito T, Aoki Y, Takeda S, Yokota T. Antisense PMO cocktails effectively skip dystrophin exons 45-55 in myotubes transdifferentiated from DMD patient fibroblasts. *PLoS One*. 2018;13(5):e0197084.
 28. Takizawa H, Hara Y, Mizobe Y, Ohno T, Suzuki S, Inoue K, Takeshita E, Shimizu-Motohashi Y, Ishiyama A, Hoshino M, Komaki H, Takeda S, Aoki Y. Modeling Duchenne muscular dystrophy in MYOD1-converted urine-derived cells treated with 3-deazaneplanocin A hydrochloride. *Sci Rep*. 2019;9(1):3807.
 29. Miyatake S, Mizobe Y, Tsoumpra MK, Lim KRQ, Hara Y, Shabanpoor F, Yokota T, Takeda S, Aoki Y. Scavenger Receptor Class A1 Mediates Uptake of Morpholino Antisense Oligonucleotide into Dystrophic Skeletal Muscle. *Mol Ther Nucleic Acids*. 2019;14:520-535.
 30. Kuraoka M, Nitahara-Kasahara Y, Tachimori H, Kato N, Shibasaki H, Shin A, Aoki Y, Kimura E, Takeda S. Accelerometric outcomes of motor function related to clinical evaluations and muscle involvement in dystrophic dogs. *PLoS One*. 2018;13(12):e0208415.
 31. Tanihata J, Nagata T, Ito N, Saito T, Nakamura A, Minamisawa S, Aoki Y, Ruegg UT, Takeda S. Truncated dystrophin ameliorates the dystrophic phenotype of mdx mice by reducing sarcolipin-mediated SERCA inhibition. *Biochem Biophys Res Commun*. 2018;505(1):51-59.
 32. Lim KRQ, Echigoya Y, Nagata T, Kuraoka M, Kobayashi M, Aoki Y, Partridge T, Maruyama R, Takeda S, Yokota T. Efficacy of Multi-exon Skipping Treatment in Duchenne Muscular Dystrophy Dog Model Neonates. *Mol Ther*. 2019;27(1):76-86.

[Review Articles • Books]

1. Zito G and Hanakawa T: Challenging the functional connectivity disruption in neurodegenerative diseases: new therapeutic perspectives through non-invasive neuromodulation and cutting-edge technologies. *Front Neurosci* 12:554, 2018
2. Hanakawa T: True value of neuroimaging. *BIO Clinica* 33(14):4-5
3. Nakamura A, Aoki Y, Tsoumpra M, Yokota T, Takeda S. In Vitro Multiexon Skipping by Antisense PMOs in Dystrophic Dog and Exon 7-Deleted DMD Patient. *Methods Mol Biol*. 2018;1828:151-163.
4. Mizobe Y, Miyatake S, Takizawa H, Hara Y, Yokota T, Nakamura A, Takeda S, Aoki

- Y. In Vivo Evaluation of Single-Exon and Multiexon Skipping in mdx52 Mice. *Methods Mol Biol.* 2018;1828:275-292.
5. Maruyama R, Aoki Y, Takeda S, Yokota T. In Vivo Evaluation of Multiple Exon Skipping with Peptide-PMOs in Cardiac and Skeletal Muscles in Dystrophic Dogs. *Methods Mol Biol.* 2018;1828:365-379.
 6. Hara Y, Mizobe Y, Miyatake S, Takizawa H, Nagata T, Yokota T, Takeda S, Aoki Y. Exon Skipping Using Antisense Oligonucleotides for Laminin-Alpha2-Deficient Muscular Dystrophy. *Methods Mol Biol.* 2018;1828:553-564.
 7. Shimizu-Motohashi Y, Komaki H, Motohashi N, Takeda S, Yokota T, Aoki Y. Restoring Dystrophin Expression in Duchenne Muscular Dystrophy: Current Status of Therapeutic Approaches. *J Pers Med.* 2019;9(1).

Molecular Virology

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Yao WEITONG SELESE DELETSU
ADIZA ABASS
Master course: Haruka YAMAGUCHI
Masanori KITAMURA
Saki KAWAMURA
Shiyu GAN
Natsuki IJIMA

(1) Outline

Microbiology covers several aspects of bacteriology, immunology and virology. Through the studies on various microbes it is expected to understand host-parasite relationship and mechanisms of pathogenicity. Unlike the past, microbiology has rapidly been drawn to the center of the biological stage.

Our laboratory mainly deals with viral oncogenesis and immunodeficiency in humans. Several projects are carried out with particular emphasis on investigation into the mechanisms of viral replication and pathogenesis induced by human retroviruses (HIV-1 and HTLV-I) and human herpes viruses. The purpose of many of the studies being undertaken is to identify critical events and molecules responsible for the efficient replication of these viruses, and in case of human retroviruses, those for transformation or destruction of normal lymphocytes. Virological, immunological and molecular approaches are being applied for this purpose.

(2) Research

The following studies have been extensively carried out in our laboratory with various biological and molecular biological techniques:

- Pathogenesis of HIV and HTLV (mutation, virulence, apoptosis, polymorphism).

- Studies on signal transduction pathways targeted by viral proteins.
- Molecular cloning by genetic approaches of components essential for virus replication in mammalian cells.

(3) Education

We are engaged in the lectures and practices on the basic aspects of infections for the 2nd year medical students and in the pre-clinical clerkship for the 4th year medical students. Students are also accepted in the Project Semester Program. Graduate course students carry out research on virology and oncology in the laboratory and join seminars and progress meetings.

(4) Lectures & Courses

Students can learn the structure, replication, function and genetics of micro-organisms as well as the host-pathogen interactions based on the front-line molecular and microbiological sciences.

(5) Publications

[Original Articles]

1. Bonney JHK, Hayashi T, Dadzie S, Agbosu E, Pratt D, Nyarko S, Asiedu-Bekoe F, Ido E, Sarkodie B, Ohta N, Yamaoka S. Molecular detection of dengue virus in patients suspected of Ebola virus disease in Ghana. *PloS one*. 2018; 13(12); e0208907
2. Hai W., Goda T., Takeuchi H., Yamaoka S., Horiguchi Y., Matsumoto A., and Miyahara Y. Human Influenza Virus Detection Using Sialyllactose-Functionalized Organic Electrochemical Transistors. *Sensors & Actuators B-Chemical*. 2018.01;
3. Hirona Ichikawa, Momoe Itsumi, Shunichi Kajioka, Tomoko Maki, Ken Lee, Makoto Tomita, Shoji Yamaoka. Overexpression of exchange protein directly activated by cAMP-1 (EPAC1) attenuates bladder cancer cell migration. *Biochem. Biophys. Res. Commun.*. 2018.01; 495(1); 64-70
4. Yuki Mizuno, Shu Shimada, Yoshimitsu Akiyama, Shuichi Watanabe, Tomomi Aida, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shigeki Arai, Shoji Yamaoka, Minoru Tanabe, Shinji Tanaka. DEPDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma. *Sci Rep*. 2018.01; 8(1); 106
5. Jin Gohda, Kazuo Suzuki, Kai Liu, Xialin Xie, Hiroaki Takeuchi, Jun-Ichiro Inoue, Yasushi Kawaguchi, Takaomi Ishida. BI-2536 and BI-6727, dual Polo-like kinase/bromodomain inhibitors, effectively reactivate latent HIV-1. *Sci Rep*. 2018.02; 8(1); 3521
6. Miho Osako, Momoe Itsumi, Haruka Yamaguchi, Hiroaki Takeuchi, Shoji Yamaoka. A20 restores phorbol ester-induced differentiation of THP-1 cells in the absence of nuclear factor- κ B activation. *J. Cell. Biochem.*. 2018.02; 119(2); 1475-1487
7. Jerry Kwame Ndzinu, Hiroaki Takeuchi, Hideki Saito, Takeshi Yoshida, Shoji Yamaoka. eIF4A2 is a host factor required for efficient HIV-1 replication. *Microbes Infect.*. 2018.05;
8. Chiyonobu Norimichi, Shimada Shu, Akiyama Yoshimitsu, Mogushi Kaoru, Itoh Michiko, Akahoshi Keiichi, Matsumura Satoshi, Ogawa Kosuke, Ono Hiroaki, Mitsunori Yusuke, Ban Daisuke, Kudo Atsushi, Arai Shigeki, Suganami Takayoshi, Yamaoka Shoji, Ogawa Yoshihiro, Tanabe Minoru, Tanaka Shinji. Fatty Acid Binding Protein 4 (FABP4) Overexpression in Intratumoral Hepatic Stellate Cells within Hepatocellular Carcinoma with Metabolic Risk Factors *AMERICAN JOURNAL OF PATHOLOGY*. 2018.05; 188(5); 1213-1224

9. Ohashi M, Amoa-Bosompem M, Kwofie KD, Agyapong J, Adegle R, Sakyamah MM, Ayertey F, Owusu KB, Tuffour I, Atchoglo P, Tung NH, Uto T, Aboagye F, Appiah AA, Appiah-Opong R, Nyarko AK, Anyan WK, Ayi I, Boakye DA, Koram KA, Edoh D, Yamaoka S, Shoyama Y, Ohta N. In vitro antiprotozoan activity and mechanisms of action of selected Ghanaian medicinal plants against Trypanosoma, Leishmania, and Plasmodium parasites. *Phytotherapy research : PTR*. 2018.05;
10. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Gold Nanoparticles with Ligand/Zwitterion Hybrid Layer for Individual Counting of Influenza A H1N1 Subtype Using Resistive Pulse Sensing. *Langmuir*. 2018.08;
11. Suzuki N., Yoshida T., Takeuchi H., Sakuma R., Sukegawa S., and Yamaoka S.. Robust enhancement of lentivirus production by promoter activation. *Scientific Reports*. 2018.09;
12. Suzuki N, Yoshida T, Takeuchi H, Sakuma R, Sukegawa S, Yamaoka S. Robust Enhancement of Lentivirus Production by Promoter Activation. *Scientific reports*. 2018.10; 8(1); 15036
13. Okuno K, Akiyama Y, Shimada S, Nakagawa M, Tanioka T, Inokuchi M, Yamaoka S, Kojima K, Tanaka S. Asymmetric dimethylation at histone H3 arginine 2 by PRMT6 in gastric cancer progression. *Carcinogenesis*. 2018.12;
14. Mizuno Yuki, Shimada Shu, Akiyama Yoshimitsu, Watanabe Shuichi, Aida Tomomi, Ogawa Kosuske, Ono Hiroaki, Mitsunori Yusuke, Ban Daisuke, Kudo Atsushi, Yamaoka Shoji, Tanaka Shinji, Tanabe Minoru. DEPDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma *CANCER SCIENCE*. 2018.12; 109; 952
15. Watanabe S, Shimada S, Akiyama Y, Ishikawa Y, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Loss of KDM6A characterizes a poor prognostic subtype of human pancreatic cancer and potentiates HDAC inhibitor lethality. *International journal of cancer*. 2018.12;

[Misc]

1. Investigation of newly identified host proteins regulating HIV-1 infection *The Journal of AIDS Research*. 2018.06; 20; 117-123

[Conference Activities & Talks]

1. 武内 寛明. Dynamics and regulation of HIV-1 uncoating and nuclear movements of HIV-1 complexes. 熊本大学エイズ学研究センター「エイズ学演習 VI」大学院セミナー 2018.07.25 熊本、日本
2. 水野 裕貴, 島田 周, 秋山 好光, 渡邊 秀一, 相田 知海, 小川 康介, 小野 宏晃, 光法 雄介, 伴 大輔, 工藤 篤, 山岡 昇司, 田中 真二, 田邊 稔. 肝細胞癌においてDEPDC5不活化はp62発現上昇を介してロイシン欠乏に対する抵抗性の獲得に寄与する (DEPDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma). *日本癌学会総会記事* 2018.09.01
3. Yoshida Takeshi, Kawamura Saki, Yamaguchi Haruka, Takeuchi Hiroaki, Yamaoka Shoji. Identification of a host factor supporting HIV-1 entry(和訳中). *日本エイズ学会誌* 2018.11.01

Immunotherapeutics

Professor: Mari KANNAGI

Associate Professor: Takao MASUDA

Assistant Professor: Atsuhiko HASEGAWA (Lecturer)

Assistant Professor: Yoshiko NAGANO

Visiting Researcher: Sayaka ITO

Research Assistant: Kuniko Katagiri

Graduate Student: Undrakh Ganbaatar, Yu-Lun HUANG, Tomokma Fujikawa, Atsushi Otsuka, ZHANG JIANCHUN, Takeru Yoneda

(1) Outline

Our research area is in between clinical and basic science, involving immunology, microbiology, and oncology. Persistent viral infection causes various diseases by inducing immunodeficiency, malignancy, autoimmunity, and inflammation. Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS), and Human T-cell leukemia virus type-I (HTLV-I) causes adult T-cell leukemia (ATL) and various chronic inflammatory autoimmune-like diseases. To understand mechanisms of these diseases, investigation on host immunity is indispensable. Immune responses are usually protective but sometimes harmful for the host, and are important determinants for disease manifestation. The goal of our research is elucidation of the role of host immunity in the diseases in order to develop effective immunotherapy. We also investigate intracellular mechanisms of viral replication to target direct molecules for therapy.

Research Subjects

1. Analysis of immunological risks for ATL development in HTLV-I-carriers.
2. Development of anti-tumor vaccine against ATL.
3. Immunological and molecular mechanism of HTLV-1-induced leukemogenesis.
4. Molecular mechanism of HIV replication especially related to HIV-1 integrase.
5. Experiments based on gene therapy to suppress HIV-1 replication.

(2) Research

① Development and clinical study of anti-ATL vaccine therapy with Tax peptide-pulsed autologous dendritic cells.

Adult T-cell leukemia/lymphoma (ATL) is a human T-cell leukemia virus type-I (HTLV-I)-infected T-cell malignancy with poor prognosis. We developed a novel therapeutic vaccine designed to augment an HTLV-I Tax-specific cytotoxic T lymphocyte (CTL) response that has been implicated in anti-ATL effects, and conducted a pilot study to investigate its safety and efficacy in collaboration of Tokyo Medical and Dental University, National Kyushu Cancer Center, and Kyushu University. The vaccine consists of autologous dendritic cells pulsed with Tax peptides corresponding to the CTL epitopes. Two of three patients administered with the vaccine achieved partial and complete remission without severe side effects. The clinical outcomes of this pilot study indicate that the Tax peptide-pulsed DC vaccine is a safe and promising immunotherapy for ATL (Suehiro, Y., Hasegawa, A., et al. *Brit J Haematol.* 169: 356-367, 2015. doi: 10.1111/bjh.13302) .

② Involvement of innate immune response in HTLV-1 pathogenesis.

The constitutive activation of NF κ B plays an important role in leukemogenesis of adult T-cell leukemia/lymphoma (ATL) caused by human T-cell leukemia virus type-1 (HTLV-1). Although HTLV-1 Tax is known to activate NF κ B, ATL cells exhibit NF κ B activities even in the absence of Tax expression, the mechanism of which has been a long-puzzling question. We demonstrate that both double-stranded RNA-dependent protein kinase (PKR) and anti-sense HTLV-1 transcripts are involved in the constitutive NF κ B activation in Tax-negative ATL cells. Our findings elucidate a novel Tax-independent mechanism of NF κ B activation underlying HTLV-1 leukemogenesis in which host antiviral responses are involved (Kinpara, S., et al. *Leukemia*, 29:1425-1444, 2015. doi: 10.1038/leu.2015.1).

(3) Education

① For under graduate students of the medical school, we participate in education of basic immunology I, and II, the project semester, and the preclinical clerkship.

② Graduate students are trained for basic skills in the field of immunology and virology to handle biohazard materials. We provide the opportunity to research for mechanisms of the retro-virus-mediated diseases and development of immunological therapeutics. All the stuffs and students participate in maintenance of the laboratory and periodical seminars to discuss about their own studies and keep up with the latest knowledge and information in the area.

(4) Lectures & Courses

We always think of the clinical significance of the results of basic research. We try to find an effective therapy by approaching from basic research to understand the disease mechanisms and solve the problem. The disease mechanisms that we study include leukemogenesis, inflammation, immunosuppression, and autoimmunity in persistent virus infection. Through these studies, we contribute to clinical therapies as well as medical sciences.

(5) Clinical Services & Other Works

We held the 5th Annual Meeting of Japanese Society of HTLV-1 Associated Diseases in Tokyo on Aug 31 through Sept 2, 2018.

(6) Clinical Performances

We developed an anti-ATL immunotherapy (Tax peptide-pulsed dendritic cell vaccine), which is under clinical studies in collaboration with National Kyushu Cancer Center and Kyushu University. We evaluate anti-tumor and anti-virus T-cell responses in HTLV-1-infected patients with or without various therapies including the immunotherapy and hematopoietic stem cell transplantation, in response to requests from clinical doctors.

(7) Publications

[Original Articles]

1. Hasegawa Atsuhiko, Iino Tadafumi, Kitauro Kazutaka, Matsutani Takaji, Suzuki Ryuji, Kannagi Mari, Suehiro Youko. Eradication of residual leukemic cells in an ATL patient after DC immunotherapy *CANCER SCIENCE*. 2018.01; 109; 195
2. Kannagi Mari, Sawada Leila, Nagano Yoshiko, Kinpara Shuichi, Hasegawa Atsuhiko. Involvement of antiviral innate responses in HTLV-1 leukemogenesis *CANCER SCIENCE*. 2018.01; 109; 414
3. 末廣 陽子, 福田 哲也, 白土 基明, 飯野 忠史, 長谷川 温彦, 安永 純一朗, 平田 明恵, 宇都宮 勇人, 大野 博文, 石田 高司, 赤司 浩一, 松岡 雅雄, 神奈木 真理. ATL に対する Tax 標的樹状細胞ワクチン療法 第 Ia/Ib 相医師主導治験 (Tax targeting dendritic cell vaccine for ATL: A phase Ia/Ib clinical study) *臨床血液*. 2018.09; 59(9); 1518

4. 長谷川 温彦, 富士川 朋夏, Ganbaatar Undrakh, 永野 佳子, 増田 貴夫, 田中 勇悦, 明里 宏文, 神奈木 真理. HTLV-1 感染における T 細胞免疫抑制の霊長類モデルとしての STLV-1 自然感染ニホンザル (Impaired T-cell responses in natural infection of STLV-1 as a primate model of immune suppression in HTLV-1 infection) 日本癌学会総会記事. 2018.09; 77 回; 983
5. Shiratsuchi Motoaki, Fukuda Tetsuya, Iino Tadafumi, Hasegawa Atsuhiko, Yasunaga Jun-ichirou, Watanabe Ken, Hirata Akie, Utsunomiya Hayato, Ohno Hirofumi, Ishida Takashi, Akashi Koichi, Matsuoka Masao, Kannagi Mari, Suehiro Youko. Tax-Targeting Dendritic Cell Therapy for ATL: A Phase Ia/Ib Clinical Study BLOOD. 2018.11; 132;
6. Hasegawa Atsuhiko, Fujikawa Tomoka, Ganbaatar Undrakh, Nagano Yoshiko, Masuda Takao, Tanaka Yuetsu, Akari Hirofumi, Kannagi Mari. Impaired T-cell responses in natural infection of STLV-1 as a primate model of immune suppression in HTLV-1 infection CANCER SCIENCE. 2018.12; 109; 643
7. Ganbaatar Undrakh, Hasegawa Atsuhiko, Miyazawa Rinsaku, Masuda Takao, Kannagi Mari. Cancer immunotherapy-2 Mitomycin C-induced HTLV-1-infected cell death leads to enhanced phagocytosis by dendritic cells and macrophages compared to Doxorubicin-induced cell death(和訳中) 日本免疫学会総会・学術集会記録. 2018.12; 47(Proceedings); 3-E

[Conference Activities & Talks]

1. Tsutomu Murakami, Masayuki Fujino, Masaru Yokoyama, Takuya Kobayakawa, Hiroaki Takeuchi, Takao Masuda, Osamu Kotani, Hirokazu Tamamura, Hironori Sato. Biological and molecular characterization of a novel anti-HIV-1 compound created by in silico design and de novo organic synthesis.. Cold Spring Harbor Laboratory Meeting, Retroviruses 2018.05.21 NY (USA)
2. 富士川朋夏、長谷川温彦、Undrakh Ganbaatar、永野佳子、増田貴夫、田中勇悦、明里宏文、神奈木真理. STLV-1 自然感染ニホンザルにおける STLV-1 特異的 T 細胞免疫の低応答性. 第 5 回日本 HTLV-1 学会学術集会 2018.09.01 東京
3. Yoko Shinohara, Takao Masuda, Gota Kawai. Structural differences of the TAR-PolyA region of the HIV-1 genomic RNA caused by the different number of G residues in its 5'-terminal. The 91st Annual Meeting of the Japan Biochemical Society 2018.09.24 Kyoto
4. Hasegawa A, Fujikawa T, Ganbaatar U, Nagano Y, Masuda T, Tanaka Y, Akari H, Kannagi M. Impaired T-cell responses in natural infection of STLV-1 as a primate model of immune suppression in HTLV-1 infection. 第 77 回日本癌学会学術総会 2018.09.27
5. Hasegawa A, Fujikawa T, Ganbaatar U, Nagano Y, Masuda T, Tanaka Y, Akari H, Kannagi M. Impaired T-cell responses in natural infection of STLV-1 as a primate model of immune suppression in HTLV-1 infection. 第 77 回日本癌学会学術集会 2018.09.28
6. Mari Kannagi . Host innate and acquired immune responses are the key factors for pathogenesis and therapy in HTLV-1 infection. The 30th International Workshop on Retroviral Pathogenesis Symposium 2018.10.11 Awaji
7. Takao Masuda, Yu-Lun Huang, Paoling Wang, Atsuhiko Hasegawa, Mari Kannagi. Evaluation of HIV-1 integrase in fusion with reverse-transcriptase in vitro.. 第 66 回日本ウイルス学会学術集会 (2018.10.28 京都
8. Takao Masuda, Yu-Lun Huang, Paoling Wang, Atsuhiko Hasegawa, Mari Kannagi.. Roles of RTIN fusion protein during reverse transcription.. 2018.12.04

Cellular and Environmental Biology

Associate Professor Masayuki HARA

(1) Research

Research Subjects

- 1) Reaction mechanisms of cellular protection systems against environmental oxidation stresses.
- 2) Modifying mechanisms in higher order structure of chromatin in cellular differentiation.
- 3) Shifting mechanisms in proteome profiles of cell organelle between pre and post conditions in environment, cell differentiation, disease, or drug exposure.

(2) Education

Living organisms were influenced their life by environment and adapted themselves to it, however, they formed environment and affected it. In other words, the species that cannot fit the changing environment were fallen and replaced by the new species which could adapt itself to. The organisms are as a part of the global environment, so it is thought that the individual structure and working of them are necessary environmental measures for their survival. It may be said that it is excessive suddenness of the change that human activity is environmentally-impacted now.

Main objective of cellular and environmental biology in the graduate course is to provide students opportunity to study the reaction and adaptation of the organisms for the environmental change at cellular level, to consider hazardous property, toxicity, or physiological activity of environmental (or man-made) factor, and to mention the biotechnical action to the environmental problems.

(3) Publications

[Original Articles]

1. Nomura K, Yunoki A, Hara M, Morito Y, Fujishima A. Development of a flexible γ -ray detector using a liquid scintillation light guide (LSLG). Applied radiation and isotopes : including data, instrumentation and methods for use in agriculture, industry and medicine. 2018.09; 139; 12-19

[Conference Activities & Talks]

1. Masayuki Hara and Kiyoshi Nomura. A cell biological explanation for general evaluation of human body effects of low dose radiation. 2018.05.24
2. NOTO, Akio ; YOKOTA, Hiratsugu ; HARA, Masayuki. About the effects of cold run in radioisotope training by our university students. 2018.07.04
3. Akio NOTO, Hiratsugu YOKOTA, Kiyoshi NOMURA, and Masayuki HARA. Estimate of the amounts of DNA break and the repair at low dose irradiation. 2018.12.05

4. Kiyoshi Nomura, Masayuki Hara, Akira Yunoki. Development of a flexible radiation detector using a liquid scintillation light guide. (Second report). 2018.12.05

Biodefense Research

Professor Toshiaki Ohteki
 Junior Associate Professor Taku Sato
 Adjunct Lecturer Nobuyuki Onai
 Assistant Professor Masashi Kanayama
 Specially Appointed Assistant Professor Jumpei Asano (to March 31)
 Specially Appointed Assistant Professor Mihoko Kajita (to Sep.30)
 Project Assistant Professor Mihoko Kajita (from Oct.1st)
 Project Researcher Shusuke Kawamura (to March 14)
 Graduate Student Minako Inazawa
 Graduate Student Kana Minamide
 Graduate Student Miwako Sase
 Graduate Student Shun Ishikawa
 Graduate Student Hirona Yamamoto
 Graduate Student Yuta Izumi
 Research Technician Shoko Kuroda
 Research Technician Kisho Shiseki
 Research Technician Minako Hanabusa (to March 31)
 Secretarial Assistant Hisako Kamioka

(1) Outline

Our research projects focus on understanding the dynamic maintenance and transfiguration of homeostasis in the living body. Our goal is to define the homeostasis mechanism under conditions of health and disease. To accomplish this goal, we are trying to clarify the molecular basis of induction and failure of homeostasis by focusing on immune cells in particular myeloid cells (dendritic cells and macrophages), tissue stem cells, and their functional interplay in the immunological and non-immunological organs. On the basis of our findings, we will further pursue our research in the hope of developing new rational therapies for prevention and treatment of disease.

(2) Research

1. Research on mononuclear phagocytes

1) Discovery of a novel source of mononuclear phagocytes

In 1968, Drs. Ralph van Fruth and Zanjil A. Cohn proposed a concept of mononuclear phagocytes that include monocytes and macrophages. In 1973, Dr. Ralph Steinman discovered dendritic cells (DCs), thereby redefining the mononuclear phagocytes as a population consisting of monocytes, macrophages and also DCs. It has been recently continuing epoch-making discoveries in the field of mononuclear phagocytes and their functions are now beyond classical Immunology and rather extend to broad life phenomenon, e.g. tissue development/regeneration, wound-healing, and establishment of various inflammatory diseases.

DCs consist of conventional DCs (cDCs) and plasmacytoid DCs (pDCs), both of which play critical regulatory roles in the immune system. cDCs exhibit prominent antigen-presenting ability, whereas pDCs are characterized by their capacity to produce large amounts of type I interferons (IFNs). We have discovered the DC progenitors in the mouse bone marrow, and named common DC progenitors (CDPs) (Immunity 2013; Nat Immunol 2007). Interestingly, CDPs are divided into 2 subpopulations. One is M-CSF receptor (R)+ CDPs mainly producing

cDCs, and the other M-CSFR-CDPs producing a large number of pDCs. In addition to CDPs, common monocyte/macrophage progenitors, cMoP, identified in the mouse bone marrow and spleen by other group in 2013.

Based on these achievements in mouse, we have been trying to identify human progenitors of mononuclear phagocytes, and most recently succeeded to identify human cMoP (in revision). Human cMoP gives rise to only monocytes but not other hematopoietic cells including DCs. Given that monocytes and monocyte-derived macrophages cause a variety of inflammatory disorders, including metabolic syndromes and tumor development, our studies shed light on possible therapeutic applications for infectious diseases, cancers and autoimmune diseases.

2) Roles of mononuclear phagocytes in inflammatory bowel disease

Breakdown of the intestinal epithelial layer's barrier function results in the inflow of commensal flora and improper immune responses against the commensal flora, leading to inflammatory bowel disease (IBD) development. Using a mouse dextran sodium sulfate (DSS)-induced colitis model, we showed that commensal Gram-positive bacteria trigger the mobilization of inflammatory monocytes and macrophages into the colon (Mucosal Immunol 2015). $\text{TNF-}\alpha$, a representative cytokine that aggravates colitis and a promising therapeutic target, was predominantly produced by monocytes/macrophages. Among macrophage subpopulations, Ly6c+ macrophages were a major colitogenic subset producing $\text{TNF-}\alpha$. In addition, $\text{IFN-}\gamma$ -Stat1 pathway was required for histone acetylation at the promoter regions of the *Tnf* loci in macrophages, indicating that $\text{IFN-}\gamma$ -dependent epigenetic regulation instructs the development of colitogenic macrophages. Our study may provide new therapeutic targets, e.g. inhibition of acetyl transferase in macrophage, for treating IBD and colon cancer (Mucosal Immunol 2018).

2. Research on tissue stem cells

1) Understanding of tissue homeostasis and its breakdown on the basis of immune cell-tissue stem cell interplay

We found that type I IFNs induce proliferation and exhaustion in hematopoietic stem cells (HSCs), and that interferon regulatory factor-2 (IRF2), a transcriptional suppressor of type I IFN signaling, preserves the self-renewal and multi-lineage differentiation capacity of HSCs (Nat Med 2009). Based on this finding, we show that type I IFN preconditioning, without irradiation or DNA alkylating agents, significantly enhanced the HSC engraftment efficiency in wild type (WT) recipient mice (Blood 2013). Based on these achievements, we have further found that physiological levels of type I IFN signaling also affect other tissue stem cells, e.g. intestinal stem cells (ISCs) and hair follicle stem cells (HFSCs). Elucidation of detailed mechanisms is currently in progress.

2) Establishment of biobank for human tongue cancer

Oral cancer has an increasing trend of 270,000 new cases per year worldwide. Two-thirds of them are tongue cancers, and in advanced cases, they become refractory to treatment and have a poor prognosis, and causal genes have not been identified. Under these backgrounds, we succeeded in establishing a human tongue cancer organoid culture system. In the future, we aim to develop fundamental technologies that lead to personalized treatment.

(3) Education

Immunology lectures in Faculty of Medicine, Masters Degree, and Doctoral Programs, Graduate School Seminar in other universities as a adjunct lecturer, and educational and research guidance for individual graduate students.

(4) Publications

[Original Articles]

1. Y Nakanishi, T Sato, K Takahashi, T Ohteki. $\text{IFN-}\gamma$ -dependent epigenetic regulation instructs colitogenic monocyte/macrophage lineage differentiation in vivo. *Mucosal Immunol.* 2018.05; 11(3); 871-880

[Misc]

1. Toshiaki Ohteki. Identification of a human progenitor strictly committed to monocytic differentiation: a counterpart of mouse cMoPs. *Rinsho Ketsueki.* 2018; 59(6); 812-818

2. Masashi Kanayama, Mari L. Shinohara. Balancing population sizes of myeloid and lymphoid cells by osteopontin isoforms 2018.03; 63(3); 219-224
3. Shunsuke Kawamura, Toshiaki Ohteki. Monopoiesis in humans and mice. Int. Immunol.. 2018.10; 30(11); 503-509

[Conference Activities & Talks]

1. Ohteki Toshiaki. Identification of human common monocyte progenitor, cMoP. KEY Forum 2018 Stem Cell Traits and Developmental Systems 2018.01.12 Kumamoto
2. Ohteki Toshiaki. From NKT cells to antigen-presenting cells and beyond. . Symposium in honor of Rob MacDonald 2018.09.12 Switzerland
3. Toshiaki Ohteki. Adaptive differentiation of dendritic cell progenitors in tissue microenviroments.. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.12 Fukuoka

Pathological Cell Biology

Professor : Shigeomi SHIMIZU

Associate Professor : Norio SHIMIZU

Junior Associate Professor : Satoko ARAKAWA

Project Associate Professor : Masatsune TSUJIOKA, Satoshi TORII

Assistant Professor : Shinya HONDA

Project Assistant Professor : Hirofumi YAMAGUCHI,

Michiko MUROHASHI, Nobuhiro FUJIKAKE, Hajime SAKURAI, Minkyon SHIN

Postdoctoral fellow (PD2) : Go Yoshida

Secretary : Hitomi Fukabori, Setsu TAMAI

Research Assistant : Ikuyo YOSHINO, Ikuko NAKANOMYO, Naomi KOJIMA,

Hikari SHIMADA, Yuta YUNOMAE

Graduate Student : Yuna SUGIMOTO, Toyokazu SEKI, Tomoyo YOSHIDA, Saori NOGUCHI, Miyuki NAKAI, Hatuki ENDO, Ryo OKUNO

(1) Outline

- 1) Analysis of apoptosis mechanism
- 2) Analysis of non-apoptotic cell death (autophagic cell death)
- 3) Physiological and pathological roles of cell death in mammals
- 4) Analysis of alternative macroautophagy mechanism
- 5) Physiological and pathological roles of autophagy in mammals
- 6) Development of novel EBV infection animal models using the hNOG mice
- 7) Development of an exhaustive pathogenic microbe screening system

(2) Research

Main objective in the graduate course is to provide students opportunity to study the molecular mechanisms of cell death and autophagy, the cell death-related diseases, the physiological and pathological roles of autophagy, and the development mechanism of Epstein-Barr virus (EBV) infection, the employment of immunodeficiency animals for the creation of virus research models and development of an exhaustive pathogenic microbial screening system.

(3) Education

Main objective in the graduate course is to provide students opportunity to study the molecular mechanisms of cell death and autophagy, the cell death-related diseases, the physiological and pathological roles of autophagy, and the development mechanism of Epstein-Barr virus (EBV) infection, the employment of immunodeficiency animals for the creation of virus research models and development of an exhaustive pathogenic microbial screening system.

(4) Publications

[Original Articles]

1. Sasaki M, Shimizu N, Zushi Y, Saito T, Tsunemine H, Itoh K, Aoyama Y, Goto Y, Kodaka T, Tsuji G, Senda E, Fujimori T, Itoh T, Takahashi T. Analysis of gastrointestinal virus infection in immunocompromised hosts by multiplex virus PCR assay. *AIMS microbiology*. 2018; 4(2); 225-239
2. Kohno Takashi, Shimizu Shigeomi. New therapeutic ways for new precision cancer medicine: Vulnerability of cancer cells *CANCER SCIENCE*. 2018.01; 109; 942
3. Tomokazu Yamaguchi, Takashi Suzuki, Teruki Sato, Akinori Takahashi, Hiroyuki Watanabe, Ayumi Kadowaki, Miyuki Natsui, Hideaki Inagaki, Satoko Arakawa, Shinji Nakaoka, Yukio Koizumi, Shinsuke Seki, Shungo Adachi, Akira Fukao, Toshinobu Fujiwara, Tohru Natsume, Akinori Kimura, Masaaki Komatsu, Shigeomi Shimizu, Hiroshi Ito, Yutaka Suzuki, Josef M Penninger, Tadashi Yamamoto, Yumiko Imai, Keiji Kuba. The CCR4-NOT deadenylase complex controls Atg7-dependent cell death and heart function. *Sci Signal*. 2018.02; 11(516);
4. Hidefumi Iwashita, Hajime Tajima Sakurai, Noriyoshi Nagahora, Munetaka Ishiyama, Kosei Shioji, Kazumi Sasamoto, Kentaro Okuma, Shigeomi Shimizu, Yuichiro Ueno. Small fluorescent molecules for monitoring autophagic flux. *FEBS Lett.* 2018.02; 592(4); 559-567
5. Takasawa Kei, Nakagawa Ryuichi, Takishima Shigeru, Moriyama Kengo, Watanabe Ken, Kiyohara Koji, Hasegawa Takeshi, Shimohira Masahiro, Kashimada Kenichi, Shimizu Norio, Morio Tomohiro. Cause of acute encephalitis/encephalopathy in Japanese children diagnosed by a rapid and comprehensive virological detection system and differences in their clinical presentations *Brain & Development*. 2018.02; 40(2); 107-115
6. Meruna Nagata, Satoko Arakawa, Hirofumi Yamaguchi, Satoru Torii, Hazuki Endo, Masatsune Tsujioka, Shinya Honda, Yuya Nishida, Akimitsu Konishi, Shigeomi Shimizu. Dram1 regulates DNA damage-induced alternative autophagy *Cell Stress*. 2018.03; 2(3); 55-65
7. Ken Watanabe, Koji Otabe, Norio Shimizu, Keiichirou Komori, Mitsuru Mizuno, Hisako Katano, Hideyuki Koga, Ichiro Sekiya. High-sensitivity virus and mycoplasma screening test reveals high prevalence of parvovirus B19 infection in human synovial tissues and bone marrow. *Stem Cell Res Ther*. 2018.03; 9(1); 80
8. Setsuko Shioda, Fumio Kasai, Ken Watanabe, Kohei Kawakami, Azusa Ohtani, Masashi Iemura, Midori Ozawa, Akemi Arakawa, Noriko Hirayama, Eiko Kawaguchi, Tomoko Tano, Sayaka Miyata, Motonobu Satoh, Norio Shimizu, Arihiro Kohara. Screening for 15 pathogenic viruses in human cell lines registered at the JCRB Cell Bank: characterization of in vitro human cells by viral infection. *R Soc Open Sci*. 2018.05; 5(5); 172472
9. Masaaki Yoshida, Takehiro Hariya, Shunji Yokokura, Kazuichi Maruyama, Kota Sato, Sunao Sugita, Yasuhiro Tomaru, Norio Shimizu, Toru Nakazawa. Diagnosing superinfection keratitis with multiplex polymerase chain reaction. *J. Infect. Chemother.* 2018.07;
10. Erika Onozawa, Haruna Shibayama, Honami Takada, Ken-Ichi Imadome, Sho Aoki, Mayumi Yoshimori, Norio Shimizu, Shigeyoshi Fujiwara, Takatoshi Koyama, Osamu Miura, Ayako Arai. STAT3 is constitutively activated in chronic active Epstein-Barr virus infection and can be a therapeutic target. *Oncotarget*. 2018.07; 9(57); 31077-31089
11. Nakano Satoko, Tomaru Yasuhiro, Takase Hiroshi, Kubota Toshiaki, Mochizuki Manabu, Shimizu Norio, Sugita Sunao. Evaluation of a multiplex Strip PCR examination for infectious uveitis and endophthalmitis: A prospective multi-center study *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE*. 2018.07; 59(9);
12. Shiori Kinoshita, Takashi Ishida, Asahi Ito, Tomoko Narita, Ayako Masaki, Susumu Suzuki, Takashi Yoshida, Masaki Ri, Shigeru Kusumoto, Hirokazu Komatsu, Norio Shimizu, Hiroshi Inagaki, Taruho Kuroda, Arne Scholz, Ryuzo Ueda, Takaomi Sanda, Shinsuke Iida. Cyclin-dependent kinase 9 as a potential specific molecular target in NK cell leukemia/lymphoma. *Haematologica*. 2018.08;

13. Okuno Y, Murata T, Sato Y, Muramatsu H, Ito Y, Watanabe T, Okuno T, Murakami N, Yoshida K, Sawada A, Inoue M, Kawa K, Seto M, Ohshima K, Shiraishi Y, Chiba K, Tanaka H, Miyano S, Narita Y, Yoshida M, Goshima F, Kawada JI, Nishida T, Kiyoi H, Kato S, Nakamura S, Morishima S, Yoshikawa T, Fujiwara S, Shimizu N, Isobe Y, Noguchi M, Kikuta A, Iwatsuki K, Takahashi Y, Kojima S, Ogawa S, Kimura H.. defective epstein-barr virus in chronic active infection and haematological malignancy. *Clinical blood*. 2018.09; 59(9); 1484
14. 清水 重臣, 成田 匡司, 荒川 聡子. がんと細胞老化シグナル (Cancer and cellular senescence signaling Relationship between autophagy and cellular senescence Relationship between autophagy and cellular senescence) *日本癌学会総会記事*. 2018.09; 77 回; 1120
15. 渡辺 雄一郎, 本田 真也, 小西 昭充, 田邊 稔, 田中 真二, 清水 重臣. オートファジーは Cep63 を介して中心体数を制御する (Autophagy controls centrosome number by degrading Cep63) *日本癌学会総会記事*. 2018.09; 77 回; 63
16. Tsurusaki Shinya, Matsuda Michitaka, Shimizu Shigeomi, Nakano Hiroyasu, Miyajima Atsushi, Tanaka Minoru. Elucidation of the Type of Cell Death at the Onset of Non-Alcoholic Steatohepatitis (NASH) *HEPATOLOGY*. 2018.10; 68; 1023A-1024A
17. Okuno Yusuke, Murata Takayuki, Sato Yoshitaka, Muramatsu Hideki, Ito Yoshinori, Watanabe Takahiro, Okuno Tatsuya, Murakami Norihiro, Yoshida Kenichi, Sawada Akihisa, Inoue Masami, Kawa Keisei, Seto Masao, Ohshima Koichi, Shiraishi Yuichi, Chiba Kenichi, Tanaka Hiroko, Miyano Satoru, Narita Yohei, Yoshida Masahiro, Goshima Fumi, Kawada Junichi, Nishida Tetsuya, Kiyoi Hitoshi, Kato Seiichi, Nakamura Shigeo, Morishima Satoko, Fujiwara Shigeyoshi, Shimizu Norio, Isobe Yasushi, Noguchi Masaaki, Kikuta Atsushi, Iwatsuki Keiji, Takahashi Yoshiyuki, Kojima Seiji, Ogawa Seishi, Kimura Hiroshi. The Presence of Defective Epstein-Barr Virus (EBV) Infection in Patients with EBV-Associated Hematological Malignancy *BLOOD*. 2018.11; 132;
18. Yoshida Masaaki, Hariya Takehiro, Yokokura Shunji, Maruyama Kazuichi, Sato Kota, Sugita Sunao, Tomaru Yasuhiro, Shimizu Norio, Nakazawa Toru. Diagnosing superinfection keratitis with multiplex polymerase chain reaction(和訳中) *Journal of Infection and Chemotherapy*. 2018.12; 24(11-12); 1004-1008
19. Ng SB, Ohshima K, Selvarajan V, Huang G, Choo SN, Miyoshi H, Shimizu N, Reghunathan R, Chua HC, Yeoh AE, Quah TC, Koh LP, Tan PL, Chng WJ. . Epstein-Barr virus-associated T/natural killer-cell lymphoproliferative disorder in children and young adults has similar molecular signature to extranodal nasal natural killer/T-cell lymphoma but shows distinctive stem cell-like phenotype. *Leuk Lymphoma*.. 56; 2408-2415
20. Wu T, Wang S, Wu J, Lin Z, Sui X, Xu X, Shimizu N, Chen B, Wang X.. Icaritin induces lytic cytotoxicity in extranodal NK/T-cell lymphoma. *J Exp Clin Cancer Res*. . 34; 17
21. Kozaki T, Komano J, Kanbayashi D, Takahama M, Misawa T, Satoh T, Takeuchi O, Kawai T, Shimizu S, Matsuura Y, Akira S, Saitoh T.. Mitochondrial damage elicits a TCDD-inducible poly(ADP-ribose) polymerase-mediated antiviral response. *PNAS*..

[Books etc]

1. Shimizu S. Autophagic Cell Death and Cancer Chemotherapeutics. . Springer,

[Misc]

1. Shigeomi Shimizu. Biological Roles of Alternative Autophagy. *Mol. Cells*. 2018.01; 41(1); 50-54
2. Nobuhiro Fujikake, Minkyung Shin, Shigeomi Shimizu. Association Between Autophagy and Neurodegenerative Diseases. *Front Neurosci*. 2018.09; 12; 255
3. shigeomi shimizu. Organelle zones in mitochondria *The Journal of Biochemistry*. 2018.12;
4. Arakawa S, Honda S, Torii S, Tsujioka M, Shimizu S.. Monitoring of Atg5-independent Mitophagy. *Methods in Molecular Biology,"Mitophagy"*.

[Conference Activities & Talks]

1. Watanabe k, Shimada H, Yunomae Y, Shimizu N, Sekiya I. . Ensuring microbiol safety in regenerative medicine: Development of rapid detection method for live or dead bacteria selection.. 17th The Japanese Society for Regenerative Medicine 2018.03.21 Yokohama,Japan.
2. shigeomi shimizu. Mechanisms and Biological Roles of Golgi Stress-induced Mitophagy. Keystone Symposia 2018.04.26
3. shigeomi shimizu. Molecular mechanisms and physiological roles of Atg5-independent autophagy. EMBO meeting "Lysosome" 2018.05.09 Naples
4. shigeomi shimizu. Molecular mechanisms and physiological roles of Atg5-independent autophagy. Australia-Japan Cell Death meeting 2018.05.21 Tokyo
5. Sugita N, Takase H, Nakako S, Takarano A, Tomaru Y, Shimizu N, Mochizuki M.. PCR diagnostic of uveitis.. 2th Annual Congress of Japan Clinical Ophthalmology. 2018.10.11 Tokyo Japan.

Lipid Biology

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Associate Professor Junko Sasaki
Assistant Professor Junya Hasegawa
Technical Assistant Toshiyoshi Yamamoto
Technical Assistant Emi Tokuda
JSPS Research Fellow Morioka Shin
Graduate student (master) Takumi Ikeda
Graduate research student Yixin Zhang
Secretary Masayo Mita

(1) Outline

Lipids are biological molecules essential for the integrity of cell membranes, energy storage, and intra/extracellular signal transduction. What our group is mostly focused on now is the roles of phosphoinositide metabolism in health and disease. Phosphoinositides (PIPs) are bipolar lipids that contain a phosphatidylinositol (PI). PI has a glycerol backbone, an inositol head group linked to the glycerol through a phosphate group, and two long-chain fatty acids linked to the glycerol through ester bonds. Phosphorylation patterns of the hydroxyls of the inositol moiety give rise to seven other PIPs classes. In humans and mice, there are 18 interconversion reactions involving all eight PIPs classes, and these reactions are orchestrated by as many as 48 genes encoding 19 lipid kinases and 29 phosphatases. Three acyltransferases that modify the acyl moiety of phosphoinositides have also been identified.

Our goal is to achieve a comprehensive understanding of this whole metabolic system to propose new strategies for the treatment and diagnosis of incurable diseases. To this end, we have been systematically generating and characterizing knockout mouse mutants for each PIPs metabolizing enzyme. Another unique strength of the group is our original methods for lipid profiling based on LC-MS/MS technique, which will help explore novel therapeutic targets as well as biomarkers.

(2) Research

We are proposing the "**Department of Lipid Biology's Four Postulates**" to find out the relationship between lipids and diseases, and proceed with basic research to prove it scientifically.

1. Find specific lipid changes (deficiency/accumulation) in certain human pathological conditions.
2. Identify the lipid metabolizing (production/degradation) enzyme.
3. Cause the same disease state by deleting/expressing the metabolizing enzyme in mice.
4. Find the same lipid changes as in 1.

Based on this basic concept, we are trying to elucidate the true nature of the following various pathologies and to develop medical applications based on these new findings.

- Stratification method of lymphomas based on lipid acyl group composition
- Prediction method for the sensitivity of cancers (breast cancer, pancreatic cancer, lymphoma) to molecular target drugs by lipid profile.
- Identification of phospholipids involved in the pathogenesis of inflammatory diseases (pneumonia, colitis, and non-alcoholic steatohepatitis).
- Identification of phospholipids involved in basal ganglia neurodegeneration.

- Discovery of new phospholipids, their metabolic enzymes, and target proteins.
- Elucidation of target protein activation mechanism by phospholipid (MD simulation, Shotgun proteomics)

(3) Education

Topics of research for graduate student

1. Exploring bioactive lipids that cause disease conditions
2. Exploring bioactive lipids that reflect disease conditions
3. Elucidation of the true nature of cancer, inflammatory diseases, and neurodegenerative diseases by lipid profiling
4. Development of lipid analysis technology based on mass spectrometry
5. Pathological analysis of mice lacking lipid metabolizing enzymes (PI3K, PTEN, etc.)

(4) Lectures & Courses

Each student has an independent research theme.

Systematically teach experimental science knowledge and skills through research and practice, including cell culture, genome editing, and how to use knockout mice, multivariate analysis, chromatography, and mass spectrometer technology.

It is aiming for scientifically original discovery that is useful for medical progress.

The goal is to be able to plan, execute, and present original research in cooperation with other researchers.

(5) Publications

[Original Articles]

1. Fei Yang, Lingli Yang, Mari Wataya-Kaneda, Junya Hasegawa, Tamotsu Yoshimori, Atsushi Tanemura, Daisuke Tsuruta, Ichiro Katayama. Dysregulation of autophagy in melanocytes contributes to hypopigmented macules in tuberous sclerosis complex. *J. Dermatol. Sci.*. 2018.02; 89(2); 155-164
2. Shin Morioka, Kiyomi Nigorikawa, Eri Okada, Yoshimasa Tanaka, Yoshihiro Kasuu, Miho Yamada, Satoshi Kofuji, Shunsuke Takasuga, Hiroki Nakanishi, Takehiko Sasaki, Kaoru Hazeki. TMEM55a localizes to macrophage phagosomes to downregulate phagocytosis. *J. Cell. Sci.*. 2018.03; 131(5);
3. Marc C Liggins, Jessica L Flesher, Sohail Jahid, Priya Vasudeva, Victoria Eby, Shunsuke Takasuga, Junko Sasaki, Takehiko Sasaki, Raymond E Boissy, Anand K Ganesan. PIKfyve regulates melanosome biogenesis. *PLoS Genet.*. 2018.05; 14(3); e1007290
4. Hirotaka Kimura, Yasushi Matsuyama, Sachiko Araki, Atsushi Koizumi, Yumi Kariya, Shunsuke Takasuga, Satoshi Eguchi, Hiroki Nakanishi, Junko Sasaki, Takehiko Sasaki. The effect and possible clinical efficacy of in vivo inhibition of neutrophil extracellular traps by blockade of PI3K-gamma on the pathogenesis of microscopic polyangiitis. *Mod Rheumatol.* 2018.05; 28(3); 530-541
5. Hideki Makinoshima, Shigeki Umemura, Ayako Suzuki, Hiroki Nakanishi, Ami Maruyama, Hibiki Udagawa, Sachiyo Mimaki, Shingo Matsumoto, Seiji Niho, Genichiro Ishii, Masahiro Tsuboi, Atsushi Ochiai, Hiroyasu Esumi, Takehiko Sasaki, Koichi Goto, Katsuya Tsuchihara. Metabolic Determinants of Sensitivity to Phosphatidylinositol 3-Kinase Pathway Inhibitor in Small-Cell Lung Carcinoma. *Cancer Res.* 2018.05; 78(9); 2179-2190
6. Kimura Hirotaka, Matsuyama Yasushi, Araki Sachiko, Koizumi Atsushi, Kariya Yumi, Takasuga Shunsuke, Eguchi Satoshi, Nakanishi Hiroki, Sasaki Junko, Sasaki Takehiko. 顕微鏡的多発血管炎の病因に対するPI3K-ガンマの遮断による好中球細胞外トラップの in vivo 阻害の影響と潜在的な臨床作用 (The effect and possible clinical efficacy of in vivo inhibition of neutrophil extracellular traps by blockade of PI3K-gamma on the pathogenesis of microscopic polyangiitis) *Modern Rheumatology.* 2018.05; 28(3); 530-541
7. 小泉 淳, 成田 伸太郎, 中西 広樹, 奈良 健平, 神田 壮平, 沼倉 一幸, 黄 明国, 齋藤 満, 井上 高光, 佐藤 滋, 吉岡 年明, 羽瀨 友則, 佐々木 雄彦. 前立腺癌におけるホスファチジルイノシトールリン酸プロファイルの解析 (Phosphatidylinositol phosphate profiles in pre-clinical and clinical prostate cancer) *日本癌学会総会記事.* 2018.09; 77 回; 1444

[Conference Activities & Talks]

1. 山本詠士、佐々木純子、Mark S.P. Sansom、佐々木雄彦. リポクオリティがプレクストリン相同ドメインと生体膜の相互作用に与える影響. 第 60 回 日本脂質生化学会 2018.05.31
2. 佐々木 雄彦 (計画班) 青木 淳賢 (分担者) . 膜リン脂質クオリティ分析技術の開発と生命現象への適用. 第 4 回リポクオリティ領域会議 2018.06.17
3. 阿部史人、中西広樹、池田翔、田川博之、佐々木雄彦. イノシトールリン脂質プロファイルに基づく 悪性リンパ腫の新たな治療戦略. 第 17 回生命科学研究会 2018.06.30
4. 佐々木雄彦. 細胞膜リン脂質動態の生理と病態：An overview. 第 91 回日本生化学会大会 2018.09.25
5. 佐々木雄彦. ホスホイノシタイドの異常と疾患. 第 176 回 東京脂質談話会 2018.10.10
6. Takehiko Sasaki, Satoshi Kofuji, Shunsuke Takasuga, Junko Sasaki. The lipid phosphatase INPP4B is a tumor suppressor in the context of PTEN insufficiency. Workshop on Frontiers in Phosphatase Research and Drug Discovery 2018.10.24

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Department of Pediatrics, Neonatal and Maternal Medicine

Professor: Shozaburo DOI (~ September, 2019)

Associate Professor: Kohsuke IMAI

Project Assistant Professor: Susumu HOSOKAWA, Tomohiro WATANABE

Department of Lifecourse Clinical Immunology

Professor: Masaaki MORI

Project Assistant Professor: Takahiro KAMIYA

(1) Outline

Our department is providing advanced medical service for infants, children, adolescents and young adults. The specialties cover most pediatric diseases, including hematology-oncology, immunology, cardiology, neurology, endocrinology, nephrology, neonatology, allergy and rheumatology. On the other hand, our scientific and academic activities encompass a wide spectrum, from basic to clinical research. By focusing on innovative strategies for clarifying pathogenesis, diagnostic tests, and therapeutic interventions, we are looking at comprehensive resolution of the child's health problems, improving their future.

(2) Research

Our research covers many specialties of pediatric diseases, and the research spans from bench to bedside. Our current main projects are

1. Identification of responsible genes for primary immunodeficiency (PID).
2. Development of therapeutic approach for PID

3. Research in autoimmune lymphoproliferative syndrome (ALPS) and RAS-associated ALPS like syndrome
4. Quality assessment of iPS cells for clinical application
5. Regulation of granulocyte activation and apoptosis
6. Development of innovative techniques for ex vivo cell therapy after hematopoietic stem cell transplantation.
7. Effect of dexmedetomidine on progress of pulmonary hypertension
8. Evaluation of fetal left ventricular twist using two-dimensional speckle-tracking analysis
9. Registry study on Kawasaki Disease with coronary aneurysm
10. Study on detection standard of electrocardiogram and echocardiogram associated with genetic examination in pediatric cardiomyopathy
11. Identifying the pathological mechanisms of periventricular leukomalacia and pulmonary damage using model rats
12. Elucidating the molecular mechanisms of gonadal development
13. Molecular pathology of congenital adrenal diseases and disorder of sex development
14. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
15. Elucidating the role of ATM in cellular differentiation
16. Identifying pathological mechanisms of neurological diseases caused by defective DNA damage response
17. Investigation of molecule marker determine the prognosis of infant leukemia
18. Development of therapeutic strategy targeting homologous recombination repair
19. Genetic background of leukemia development
20. Genetic analysis and development of therapeutic approach for epilepsy syndrome
21. Developing data base of JIA (juvenile inflammatory arthritis), CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan)
22. Clarifying immunological profiles of the patients with autoimmune diseases
23. Developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Science, Hiroshima University, Istituto Nazionale Tumori (Dr. D. Delia), University of Queensland (Prof. Peter Koopman), Erasmus University (Prof. Jacques van Dongen), Yonsei University (Profs. H. Kim, and SK Lee), Sony Life Science Laboratories, National Institute for Longevity Sciences, National Research Institute for Child Health and Development, RIKEN Center for Integrative Medical Science, Kazusa DNA Research Institute, Tokyo Metropolitan Institute for Medical Science, Juntendo University, and many other laboratories.

● Hematology/Oncology/Immunology Group (Basic Research)

Hematology/Oncology/Immunology group includes 9 staff members, 3 medical staff, 10 graduate students, collaborating researchers, and several technical assistants.

Identifying the pathophysiology of primary immunodeficiency (PID)

We are performing candidate gene hunting of PID using whole exon sequencing analysis by a next generation sequencer and identified several responsive or candidate genes, and we will also analyze further pathogenesis. Among them, in 2018, Kanegane et al studied with ZAP70 deficiency, X linked lymphoproliferative disorder, and CTLA4 deficiency from the view from EBV infection, and reported in a scientific journal. We also reported about application methods such as flow cytometric analysis method and digital PCR necessary for PID diagnosis and/or treatment standardization. As clinical research, the results of a nationwide survey of hematopoietic cell transplantation to PI3K δ abnormality was reported. Sugawara et al. reported the usefulness of cimetidine for Aicardi - Goutières syndrome with IFIH1 mutation.

As the ongoing study, research of PAPA syndrome, PID with lymphoma susceptibility, PID with pulmonary alveolar proteinosis a disease with immunoglobulin class switch abnormality. Takagi and associate professor Otsu in the University of Tokyo Medical Science Institute engage in the study of RAS-associated ALPS-like diseases (RALD). They established iPS cells and are developing drug discovery for therapeutic purposes. Imai pursues the research on the execution of nationwide neonatal mass screening using TREC/KREC test for PID, and research using early diagnosis and patient registration database. Development of adoptive immunotherapy, virus-specific T cell therapy, to promote immunological reconstitution after hematopoietic transplantation was performed by Mori and Yanagimachi. The clinical trial of specific T cell therapy was launched this year.

Regenerative medicine

Morio organized a research group to evaluate the quality of the clinical uses of iPS cell. The comprehensive microbe monitoring system has been developing in collaboration with Dr. Shimizu at TMDU Medical research institute, and non-invasive genomic alteration detection system has been in development in collaboration with

Dr. Inazawa at TMDU Medical research institute and Dr. Ohara at Kazusa genome institute.

Oncology

TCF3-PBX1 chimeric gene is known to be a responsible gene for B progenitor leukemia development. In our research, it also revealed that TCF3-PBX1 chimeric gene is also involved in the development of B cell lymphoblastic lymphoma. We are focusing on identifying the mechanisms that suppress oncogenic transformation by DNA damage response. In addition, the development of therapeutics targeting DNA damage and repair pathway is conducted. Comprehensive genome research for leukemia has been conducted. This research will lead to the identification of novel therapeutic approaches for pediatric leukemia and neuroblastoma. The research was expanded to Phase I clinical trial of Olaparib for refractory solid tumor. In addition, a graduate student, Nishii, created NUDT15 knockout mice under the supervision of Dr. Yang at St. Jude Children's research hospital, analyzing the mechanism of 6MP high sensitivity in NUDT15 knockout mice.

● Cardiology and Intensive Care Group

One graduate student was studying the mechanism of dexmedetomidine effect on progress of rat pulmonary hypertension induced by monocrotaline, and the other was engaged in evaluation of fetal left ventricular twist using two-dimensional speckle-tracking analysis and published manuscript.

Group staffs joined multicenter clinical studies, one of which was registry study of Kawasaki Disease with coronary aneurysms, and the other of which was study on detection standard of electrocardiogram and echocardiogram associated with genetic examination in pediatric cardiomyopathy.

● Neurology Group

< Basic research >

· Ataxia-telangiectasia (AT) is one of the major neurodegenerative diseases, and we established iPS cell lines from AT patients for elucidating the neuropathological mechanism. Further, we are exploring to discover unidentified genetic diseases with DNA repair-deficiency disorders using next-generation sequencing technology. We had identified the pathological mechanisms of a disease associated with ER (Endoplasmic Reticulum) stress, Marinesco-Sjögren syndrome at the cellular level and provided therapeutic approach. We are investigating the pathological mechanism of Moyamoya syndrome.

· Elucidating immunological roles of the purinergic receptor signal for microglial inflammatory reaction is another target of our research. We have established P2RY12 KO microglial cell line that enabled us to investigate purinergic receptor signals on inflammatory cytokine production from microglia (collaborative project with Hiroshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

< Clinical research >

“Genetic analysis and development of therapeutic approach for epilepsy syndrome” (collaboration with Showa University)

“Research for rare epilepsy syndrome” (collaboration with Institute of Epilepsy and Neurological Disorders)

“Systematic measurement and functional analysis of autoantibody in immunologic neurological diseases” (collaboration with Tokyo Metropolitan Institute of Medical Science)

“Evaluation of adrenocortical function in the patients with West syndrome treated with ACTH therapy”

● Endocrinology Group

Molecular mechanisms of gonadal development

We are trying to elucidate the molecular mechanisms of gonadal development, especially, focusing on elucidating transcriptional network of gonadal development and gonadal cell differentiation. Our projects also include identifying the precise function of transcription factors, such as NR5A1 (SF1), FOXL2 and SOX9.

Elucidating the mechanisms of de-methylation during primordial germ cells differentiation

This project is carried out in collaboration with Prof. Ishino (XXXX).

Molecular analysis of pathological mechanisms in congenital adrenal hyperplasia (CAH)

Including the relationships between genotype and phenotype, we are trying to elucidate the pathological mechanisms of the disease.

Identifying novel molecules of congenital endocrinological diseases

Including insulin resistance, we are aiming to identify novel molecules that is responsible for congenital endocrinological diseases. Current ongoing projects will be integrated systematically, and will be applicable to develop innovative approach for the treatment of congenital endocrine disorder, including regenerative medicine.

● Collagen/Rheumatoid disease group

We are establishing an evidence based guideline of pediatric rheumatoid diseases including juvenile idiopathic arthritis: JIA. Developing a novel database system, CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan) , clarifying immunological profiles of the patients with autoimmune diseases, and developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker are other our current projects.

● Neonatology group

We are examining changes of profile in umbilical cord-derived mesenchymal stem cells due to the intrauterine environment in humans through joint clinical research with related hospitals.

We are trying to elucidate the mechanism and effect of umbilical cord-derived mesenchymal stem cell therapy for diseases in preterm infant and the involvement of mesenchymal stem cells in the establishment of diseases.

● Allergy Group

One of our main project goals is to elucidate the immunological mechanisms of food allergy such as that against milk and eggs. In addition, we carry out epidemiological studies of food allergy.

In collaboration with the Japanese Society of Pediatric Allergy and Clinical Immunology, we are conducting several clinical studies to refine pharmacologic therapy listed in the Japanese pediatric guideline for the treatment and management of asthma.

(3) Education

Block Lecture

The systematic lecture was performed for M4 students. One third of lectures “were performed using an active-learning” style. The number of frames of the active-learning from nine frames in the previous fiscal year to 12 frames. Two frames of team -based learning (TBL) were also provided. Although one frame of active-learning alone cannot cover the whole area of pediatrics, about 85% of students reach the passing point in the final test covering the whole area of pediatrics by student self-study. At this point, we believe that the usefulness of active learning has been demonstrated.

Project semester

This provides the opportunities of basic research for the 4th grade students for half a year. This year, one student was committed to the research of our department and presented at a scientific meeting.

Pre-clinical clerkship (PCC).

We proposed 6 programs providing the opportunities to learn the logical skills of clinical practice.

After the curriculum, The students undertake the examination of clinical practice, i.e., OSCE , CBT.

Clinical clerkship (CC)

Clinical clerkship (CC) is a compulsory course for one month. The practical training of medicine, and every month, approximately 10 students have the training in our department. The students involved in each group of sub-specialty (Hematology, Oncology, Immunology, Cardiology, Neurology, Nephrology, Rheumatology, Endocrinology, Neonatology). In addition to our university hospital, the students visit the satellite hospitals for the training of common diseases.

Once a week, the students round the pediatric ward of the hospital with the professor to learn the physical examination skills. This fiscal year, we made an effort to eliminate the disparity between inside and outside clinical practice among students by increasing the facilities performing extracurricular clinical training from five to six institutes (NICU at Kawaguchi Municipal Medical Center, Musashino Red Cross Hospital, Soka Municipal Hospital, Tokyo North Medical Center, Tsuchiura Kyodo General Hospital ot Tokyo Metropolitan Bokuto Hospital). Every Friday, we made a practical training program to conduct student conferences for further understanding of clinical practice.

Training of junior clinical fellows

We provide clinical training courses in cooperation with satellite hospitals (Musashino Red Cross Hospital, Soka Municipal Hospital or Tokyo North Medical Center). Depending on the individuals, they could select the advanced training at the pediatric ward in The University Hospital for two to eight months.

(4) Lectures & Courses

Primary care of pediatrics covers a wide spectrum of health care and clinical problems in children, and all pediatricians should be well trained in those subjects. Further, Tokyo Medical and Dental University is one of the top ranked national medical universities in Japan, and achieving cutting edge research is another social responsibility. For students, we provide educational programs to learn primary pediatric care, management of the diseases in every organ during neonatal period childhood, and basic science. For residents, our educational program is mainly focused on producing physician scientists who possess the skills of pediatrics for primary care, of physician specialist and of basic researcher.

(5) Clinical Services & Other Works

● Hematology/Oncology/Immunology Group

Treating children with primary immunodeficiency, hematological malignancies, hematological disorders, and malignant solid tumors.

Collaboration with other professional facilities including St. Luke' s International Hospital and Juntendo University Hospital. Joint clinical conference and trainee exchange program are regularly held in the collaborating system.

Medical care

By collaborating with national co-operative clinical research group, such as the Tokyo Children' s Cancer Study Group (TCCSG) and Japanese Children' s Cancer Study Group (JCCG), we offer our patients opportunities to participate in the latest clinical trials, contributing to establishment of both standard and novel therapies for childhood cancers and other non-malignant diseases.

In 2018, we performed HCT for 7, and 4 cases were for PID patients. Our experience of HCT exceeds 222 cases including more than 99 cases with primary immunodeficiency diseases, so far.

Clinical trial

Three doctor-initiated clinical trials led by the pediatric department of Tokyo Medical and Dental University are ongoing.

"Phase I Clinical Study of Oral Olaparib in Pediatric Patients with Refractory Solid Tumors "

" Multi-virus (Cytomegalovirus, EB virus, Adenovirus, BK virus, and HHV-6) specific Cytotoxic T-Lymphocytes from HLA-haploidentical or more HLA-matched relative donor to persistent viral infection after hematopoietic cell transplantation (multi-center, prospective phase I/II study) "

" Clinical Phase II Study of hematopoietic stem cell transplantation for ataxia telangiectasia and related diseases " is carried out.

● Cardiology and Intensive Care Group

We provide medical care in a wide range of pediatric cardiovascular diseases. Especially, our department is one of the major center hospitals providing medical care of pediatric pulmonary hypertension.

In 2018, the number of inpatients was 112, which consisted of 59 congenital heart disease, 15 Kawasaki Disease, 13 pulmonary hypertension, 12 arrhythmia, 4 cardiomyopathy and 9 others. Cardiac catheterizations were performed in 55 patients and cardiac surgery was performed in 21 patients (19 open-heart surgery), which consisted of 10 VSDs, 8 ASDs, 1 PDAs, 2 aortic repairs. The number of outpatients was 2,044, echocardiogram was performed in 1,930, Treadmill exercise-induced electrocardiogram was performed in 103, and Holter 24hr electrocardiogram was performed in 119 patients.

● Neurology Group

We provide medical care in a wide range of pediatric neurologic diseases.

In particular, collaborating with the department of neurosurgery, we run an epilepsy center, providing advanced medical care for pediatric patients with intractable epilepsy.

The medical services in our department are long-term video EEG monitoring, high magnetic field MRI/PET, ACTH therapy, ketogenic diet, vagus nerve stimulation and surgical operation, such as focal brain resection and callosotomy.

● Endocrinology Group

We provide highly specific diagnostic approach and therapy in a wide range of pediatric endocrine disorders.

Among many pediatric endocrine disorders, we are directing our effort at the disorders of adrenal gland and sex

development (DSD), and diabetes mellitus. We are looking at establishing the clinical center for those patients with pediatric-urologist and other co-medical staffs.

● Nephrology Group

Nephrology Group provides diagnosis and treatment for patients with various kidney diseases. We perform kidney biopsy (30/year) and imaging examination.

We performed peritoneal dialysis for low-body-weight children and provided acute hemodialysis for children who developed acute kidney injury and for children with collagen diseases.

● Neonatology group

Collaborating with other medical departments or special care groups in pediatrics, we are treating preterm infants (≥ 28 weeks gestation, birth weight $\geq 1,000$ g), neonates with complications and babies born from mothers with complication.

● Allergy Group

The qualified allergists of the group attend both inpatient and outpatient care units for allergic diseases in the allergy medical center of our university and extramural, affiliated hospitals, where not only the standard medical services following clinical guidelines for allergic diseases are provided, but also highly advanced treatment such as oral immunotherapy for food allergy as well.

(6) Clinical Performances

● Hematology-Oncology/ Immunology Group

Hematology-Oncology/ Immunology Group provides diagnosis, treatment and pathological analysis of hematological malignancies and primary immunodeficiency diseases. We perform hematopoietic stem cell transplantation for refractory diseases. Specifically, we treat the largest number of primary immunodeficiency disease patients in Japan. We participate in multi-center cooperative clinical research to establish both standard and novel therapies for childhood cancers, and also participate in the approval of industry-based clinical trials for drugs (such as anticancer drugs).

● Cardiology and Intensive Care Group

Cardiology and intensive care group perform diagnosis, evaluation of treatment and decision of treatment strategy for PH patients. We positively treat severe idiopathic/hereditary pulmonary arterial hypertension (IPAH/HPAH) patients by up-front combination therapy (uCT) with two or three kinds of disease targeted drugs including continuous venous infusion of epoprostenol. We made considerable achievements of treatment in severe IPAH/HPAH patients with epoprostenol/treprostinil.

● Neurology Group

Neurology group provide highly specialized diagnostic approach and medical care for neurological disorders such as intractable epilepsy, cerebellar ataxia, involuntary movement, immune-mediated neurological disease, perinatal brain damage, infection of nervous system, acute encephalopathy/encephalitis, neurodegenerative disease and neuromuscular disorder.

● Endocrinology Group

The leader of our endocrinology group is a supervisor of congenital adrenal hyperplasia (CAH) newborn screening in Tokyo. We treat many CAH (21-OHD) patients and performed couples of clinical studies. We also focus on disorder of sex development (DSD) and long-term follow-up for childhood cancer survivors (CSS). We are managing a Type 1 DM patients' association (Wakamatsu-kai) and organize the summer camp every year.

● Nephrology Group

We treat various pediatric kidney diseases, such as congenital nephrotic syndrome, refractory nephrotic syndrome, IgA nephropathy, etc. Kidney biopsy is performed to more than 40 patients. We provide acute hemodialysis treatment and peritoneal dialysis for low-body-weight patients (under 10kg) in cooperation with department of blood purification.

● Collagen/Rheumatoid disease group

Clinically, our target is not only pediatric collagen and rheumatic disease, but also inflammatory diseases which require biopharmaceutical medicine, such as periodic fever unknown origin, and repeated arthritis affecting mul-

tiple joints. Further, for developing a therapeutic approach, we are planning to register international clinical trials of a novel biopharmaceutical medicine, such as belimumab for pediatric SLE.

● Neonatology Group

Our NICU provides intensive care for preterm infants and critically ill newborns. As a designated perinatal medical center in Tokyo, we accept maternal and neonatal transfer from various areas in Tokyo and contribute to perinatal medicine in Tokyo.

● Allergy Group

We focus on clinical care of severe and complicated allergic diseases such as food allergy-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, food protein-induced enterocolitis syndrome and oral allergy syndrome induced by cross-reactivity between food, inhalant and contact allergens. We extensively perform food challenge tests not only for correct diagnosis of food allergy but for preparation of oral immunotherapy in cooperation with the affiliated hospitals.

(7) Publications

[Original Articles]

1. Matsuura Y, Daimon M, Doi S, Miyasaka N, Fujita H, Morio T. Feasibility and Reproducibility of Fetal Left Ventricular Twist using Two-Dimensional Speckle-Tracking Analysis in a Japanese Population International Heart Journal. 2018;
2. Taiki Shima, Hiroshi Sakuma, Tomonori Suzuki, Kuniko Kohyama, Takako Matsuoka, Masaharu Hayashi, Akihisa Okumura, Toshiaki Shimizu. Effects of antiepileptic drugs on microglial properties Epilepsy & Seizure. 2018; 10; 22-32
3. Kurokami Tsunehiko, Takasawa Reiko, Takeda Sayaka, Kurobe Masashi, Takasawa Kei, Nishioka Masato, Shimohira Masayuki. Venous thromboembolism in two adolescents with Down syndrome TURKISH JOURNAL OF PEDIATRICS. 2018; 60(4); 429-432
4. Toshihiro Matsui, Takumi Matsumoto, Fumio Hirano, Fumika Tokunaga, Keisuke Okamoto, Shigeto Tohma, Tomohiro Morio, Hitoshi Kohsaka, Masaaki Mori. Survey of the awareness of adult rheumatologists regarding transitional care for patients with juvenile idiopathic arthritis in Japan Mod Rheumatol. 2018.01; 28(6); 981-985
5. Kaneko R, Yamamoto S, Okamoto N, Akiyama K, Matsuno R, Toyama D, Hoshino A, Imai K, Isoyama K. Wiskott-Aldrich syndrome that was initially diagnosed as immune thrombocytopenic purpura secondary to a cytomegalovirus infection SAGE Open Med Case Rep. 2018.01; 6; 2050313X17753788
6. Kei Takasawa, Maki Igarashi, Makoto Ono, Akira Takemoto, Shuji Takada, Atsuyuki Yamataka, Tsutomu Ogata, Tomohiro Morio, Maki Fukami, Kenichi Kashimada. Phenotypic Variation in 46,XX Disorders of Sex Development due to the NR5A1 p.R92W Variant: A Sibling Case Report and Literature Review Sex Dev. 2018.01; 11(5-6); 284-288
7. Yuko Shimosato, Reo Tanoshima, Shin-Ichi Tsujimoto, Masanobu Takeuchi, Koji Sasaki, Ryosuke Kajiwara, Hiroaki Goto, Junichi Nagai, Masakatsu D Yanagimachi, Shuichi Ito, Shumpei Yokota. Association of isochromosome (7)(q10) in Shwachman-Diamond syndrome with the severity of cytopenia. Clin Case Rep. 2018.01; 6(1); 125-128
8. Kevin Y Urayama, Masatoshi Takagi, Takahisa Kawaguchi, Keitaro Matsuo, Yoichi Tanaka, Yoko Ayukawa, Yuki Arakawa, Daisuke Hasegawa, Yuki Yuza, Takashi Kaneko, Yasushi Noguchi, Yuichi Taneyama, Setsuo Ota, Takeshi Inukai, Masakatsu Yanagimachi, Dai Keino, Kazutoshi Koike, Daisuke Toyama, Yozo Nakazawa, Hidemitsu Kurosawa, Kozue Nakamura, Koichi Moriwaki, Hiroaki Goto, Yujin Sekinaka, Daisuke Morita, Motohiro Kato, Junko Takita, Toshihiro Tanaka, Johji Inazawa, Katsuyoshi Koh, Yasushi Ishida, Akira Ohara, Shuki Mizutani, Fumihiko Matsuda, Atsushi Manabe. Regional evaluation of childhood acute lymphoblastic leukemia genetic susceptibility loci among Japanese. Sci Rep. 2018.01; 8(1); 789
9. Honda-Ozaki F, Terashima M, Niwa A, Saiki N, Kawasaki Y, Ito H, Hotta A, Nagahashi A, Igura K, Asaka I, Li HL, Yanagimachi M, Furukawa F, Kanazawa N, Nakahata T, Saito MK. Pluripotent Stem

- Cell Model of Nakajo-Nishimura Syndrome Untangles Proinflammatory Pathways Mediated by Oxidative Stress Stem Cell Reports. 2018.01; 10(6); 1835-1850
10. Perinatal factors affecting growth and development at age 3 years in extremely low birth weight infants born small for gestational age 2018.01; 27(1); 31-38
11. Masatoshi Takagi, Akihiro Hoshino, Kenichi Yoshida, Hiroo Ueno, Kohsuke Imai, Jinhua Piao, Hirokazu Kanegane, Motoi Yamashita, Tsubasa Okano, Hideki Muramatsu, Yusuke Okuno, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seishi Ogawa, Yasuhide Hayashi, Seiji Kojima, Tomohiro Morio. Genetic heterogeneity of uncharacterized childhood autoimmune diseases with lymphoproliferation. *Pediatr Blood Cancer*. 2018.02; 65(2);
12. Ryuichi Nakagawa, Kei Takasawa, Tzu-Wen Yeh, Kohsuke Imai, Kenichi Kashimada, Tomohiro Morio. Type 1 Diabetes Mellitus Associated with Activated Phosphoinositide-3-kinase Delta Syndrome, Type 2. *J Diabetes*. 2018.02; 10(5); 421-422
13. Ayako Kashimada, Setsuko Hasegawa, Takeo Isagai, Tsuyoshi Uchiyama, Muneaki Matsuo, Motoharu Kawai, Masahide Goto, Tomohiro Morio, Yukiko K Hayashi, Masatoshi Takagi. Targeting the enhanced ER stress response in Marinesco-Sjögren syndrome *J. Neurol. Sci.*. 2018.02; 385; 49-56
14. Toshiaki Ono, Yuriko Fujita, Tetsuro Matano, Satoshi Takahashi, Tomohiro Morio, Ai Kawana-Tachikawa. Characterization of in vitro expanded virus-specific T cells toward adoptive immunotherapy against virus infection *Jpn. J. Infect. Dis.*. 2018.02; 71(2); 122-128
15. Takasawa Kei, Nakagawa Ryuichi, Takishima Shigeru, Moriyama Kengo, Watanabe Ken, Kiyohara Koji, Hasegawa Takeshi, Shimohira Masahiro, Kashimada Kenichi, Shimizu Norio, Morio Tomohiro. Cause of acute encephalitis/encephalopathy in Japanese children diagnosed by a rapid and comprehensive virological detection system and differences in their clinical presentations *Brain & Development*. 2018.02; 40(2); 107-115
16. Jennifer W Leiding, Satoshi Okada, David Haginn E Sullivan, Nancy Bunin, Sara Sebnem Kilic, Fikret Arpacı, Oscar , Mario Abinun, Anna Shcherbina, Dmitry N Balashov, Vy H D Kim, Adi Ovadia, Stephen L Guthery, Michael Pulsipher, Desa Lilic, Lisa A Devlin, Sharon Christie, Mark Depner, Sebastian Fuchs, Annet van Royen-Kerkhof, Caroline Lindemans, Aleksandra Petrovic, Kathleede la Calle-Martin, Laura Martinez-Martinez, Juan Carlos Aldave, Masao Kobayashi, Teppei Ohkawa, Kohsuke Imai, Akihiro Iguchi, Chaim M Roifman, Andrew R Gennery, Mary Slatter, Hans D Ochs, Tomohiro Morio, Troy R Torgerson, . Hematopoietic stem cell transplantation in patients with gain-of-function signal transducer and activator of transcription 1 mutations. *J. Allergy Clin. Immunol.*. 2018.02; 141(2); 704-717.e5
17. Tomohiro Ishii, Masanori Adachi, Kei Takasawa, Satoshi Okada, Hotaka Kamasaki, Takuo Kubota, Hiromori Kobayashi, Hirotake Sawada, Keisuke Nagasaki, Chikahiko Numakura, Shohei Harada, Kanshi Minamitani, Shigetaka Sugihara, Toshihiro Tajima. Incidence and Characteristics of Adrenal Crisis in Children Younger than 7 Years with 21-Hydroxylase Deficiency: A Nationwide Survey in Japan. *Horm Res Paediatr*. 2018.02; 89(3); 166-171
18. Daniel Petersheim, Michel J Massaad, Saetbyul Lee, Alessia Scarselli, Caterina Cancrini, Kunihiko Moriya, Yoji Sasahara, Arjan C Lankester, Morna Dorsey, Daniela Di Giovanni, Liliana Bezrodnik, Hidenori Ohnishi, Ryuta Nishikomori, Kay Tanita, Hirokazu Kanegane, Tomohiro Morio, Erwin W Gelfand, Ashish Jain, Elizabeth Secord, Capucine Picard, Jean-Laurent Casanova, Michael H Albert, Troy R Torgerson, Raif S Geha. Mechanisms of genotype-phenotype correlation in autosomal dominant anhidrotic ectodermal dysplasia with immune deficiency. *J. Allergy Clin. Immunol.*. 2018.03; 141(3); 1060-1073.e3
19. Yasuyoshi Ishiwata, Masashi Nagata, Kohta Tsuge, Hiromitsu Takahashi, Sayo Suzuki, Kohsuke Imai, Masatoshi Takagi, Hirokazu Kanegane, Tomohiro Morio, Masato Yasuhara. Population Pharmacokinetics of Intravenous Busulfan in Japanese Pediatric Patients With Primary Immunodeficiency Diseases. *J Clin Pharmacol*. 2018.03; 58(3); 327-331
20. Federica Barzaghi, Laura Cristina Amaya Hernandez, Benedicte Neven, Silvia Ricci, Zeynep Yesim Kucuk, Jack J Bleasing, Zohreh Nademi, Mary Anne Slatter, Erlinda Rose Ulloa, Anna Shcherbina, Anna Roppelt, Austen Worth, Juliana Silva, Alessandro Aiuti, Luis Murguia-Favela, Carsten Speckmann, Magda Carneiro-Sampaio, Juliana Folloni Fernandes, Safa Baris, Ahmet Ozen, Elif Karakoc-Aydiner, Ayca Kiykim, Ansgar Schulz, Sandra Steinmann, Lucia Dora Notarangelo, Eleonora Gambineri, Paolo Lionetti, William Thomas Shearer, Lisa R Forbes, Caridad Martinez, Despina Moshous, Stephane Blanche,

- Alain Fisher, Frank M Ruemmele, Come Tissandier, Marie Ouachee-Chardin, Frédéric Rieux-Laucat, Marina Cavazzana, Waseem Qasim, Barbarella Lucarelli, Michael H Albert, Ichiro Kobayashi, Laura Alonso, Cristina Diaz De Heredia, Hirokazu Kanegane, Anita Lawitschka, Jong Jin Seo, Marta Gonzalez-Vicent, Miguel Angel Diaz, Rakesh Kumar Goyal, Martin G Sauer, Akif Yesilipek, Minsoo Kim, Yesim Yilmaz-Demirdag, Monica Bhatia, Julie Khlevner, Erick J Richmond Padilla, Silvana Martino, Davide Montin, Olaf Neth, Agueda Molinos-Quintana, Justo Valverde-Fernandez, Arnon Broides, Vered Pinsk, Antje Ballauf, Filomeen Haerynck, Victoria Bordon, Catharina Dhooge, Maria Laura Garcia-Lloret, Robert G Bredius, Krzysztof Kalwak, Elie Haddad, Markus Gerhard Seidel, Gregor Duckers, Sung-Yun Pai, Christopher C Dvorak, Stephan Ehl, Franco Locatelli, Frederick Goldman, Andrew Richard Gennery, Mort J Cowan, Maria-Grazia Roncarolo, Rosa Bacchetta, . Long-term follow-up of IPEX syndrome patients after different therapeutic strategies: An international multicenter retrospective study. *J. Allergy Clin. Immunol.* 2018.03; 141(3); 1036-1049.e5
21. Yasuo Horikoshi, Katsutsugu Umeda, Kohsuke Imai, Hiromasa Yabe, Yoji Sasahara, Kenichiro Watanabe, Yukiyasu Ozawa, Yoshiko Hashii, Hidemitsu Kurosawa, Shigeaki Nonoyama, Tomohiro Morio. Allogeneic Hematopoietic Stem Cell Transplantation for Leukocyte Adhesion Deficiency. *J. Pediatr. Hematol. Oncol.* 2018.03; 40(2); 137-140
 22. Kazutoshi Cho, Masafumi Yamada, Kazunaga Agematsu, Hirokazu Kanegane, Noriko Miyake, Masahiro Ueki, Takuma Akimoto, Norimoto Kobayashi, Satoru Ikemoto, Mishie Tanino, Atsushi Fujita, Itaru Hayasaka, Satoshi Miyamoto, Mari Tanaka-Kubota, Koh Nakata, Masaaki Shiina, Kazuhiro Ogata, Hisanori Minakami, Naomichi Matsumoto, Tadashi Ariga. Heterozygous Mutations in OAS1 Cause Infantile-Onset Pulmonary Alveolar Proteinosis with Hypogammaglobulinemia. *Am. J. Hum. Genet.* 2018.03; 102(3); 480-486
 23. Rin Asao, Takuto Seki, Miyuki Takagi, Hiroyuki Yamada, Fumiko Kodama, Yoshiko Hosoe-Nagai, Eriko Tanaka, Juan Alejandro Oliva Trejo, Kanae Yamamoto-Nonaka, Yu Sasaki, Teruo Hidaka, Takashi Ueno, Motoko Yanagita, Yusuke Suzuki, Yasuhiko Tomino, Katsuhiko Asanuma. Rac1 in podocytes promotes glomerular repair and limits the formation of sclerosis. *Sci Rep.* 2018.03; 8(1); 5061
 24. Oshima K, Saiki N, Tanaka M, Imamura H, Niwa A, Tanimura A, Nagahashi A, Hirayama A, Okita K, Hotta A, Kitayama S, Osawa M, Kaneko S, Watanabe A, Asaka I, Fujibuchi W, Imai K, Yabe H, Kamachi Y, Hara J, Kojima S, Tomita M, Soga T, Noma T, Nonoyama S, Nakahata T, Saito MK.. Human AK2 links intracellular bioenergetic redistribution to the fate of hematopoietic progenitors. *Biochem. Biophys. Res. Commun.* 2018.03; 497(2); 719-725
 25. Takeuchi M., Kobayashi T., Biss T., Kamali F., Vear S., Ho R., Bajolle F., Lorient M. -A., Shaw K., Carleton B., Hamberg A. -K., Wadelius M., Hirono K., Taguchi M., Wakamiya T., Yanagimachi M., Hirai K., Itoh K., Brandao L., Ito S.. EFFECT OF CYP2C9, VKORC1, AND CYP4F2 ON WARFARIN MAINTENANCE DOSE IN CHILDREN AGED LESS THAN 18 YEAR OF AGE; SYSTEMATIC REVIEW AND META-ANALYSIS. *CLINICAL PHARMACOLOGY & THERAPEUTICS.* 2018.03; 103; S52
 26. Tomonori Kadowaki, Hidenori Ohnishi, Norio Kawamoto, Tomohiro Hori, Kenichi Nishimura, Chie Kobayashi, Tomonari Shigemura, Shohei Ogata, Yuzaburo Inoue, Tomoki Kawai, Eitaro Hiejima, Masatoshi Takagi, Kohsuke Imai, Ryuta Nishikomori, Shuichi Ito, Toshio Heike, Osamu Ohara, Tomohiro Morio, Toshiyuki Fukao, Hirokazu Kanegane. Haploinsufficiency of A20 causes autoinflammatory and autoimmune disorders. *J. Allergy Clin. Immunol.* 2018.04; 141(4); 1485-1488.e11
 27. Asano T, Okada S, Tsumura M, Yeh TW, Mitsui-Sekinaka K, Tsujita Y, Ichinose Y, Shimada A, Hashimoto K, Wada T, Imai K, Ohara O, Morio T, Nonoyama S, Kobayashi M.. Enhanced AKT Phosphorylation of Circulating B Cells in Patients With Activated PI3K δ Syndrome. *Front Immunol.* 2018.04; 9; 568
 28. Okano T, Tsujita Y, Kanegane H, Mitsui-Sekinaka K, Tanita K, Miyamoto S, Yeh TW, Yamashita M, Terada N, Ogura Y, Takagi M, Imai K, Nonoyama S, Morio T.. Droplet Digital PCR-Based Chimerism Analysis for Primary Immunodeficiency Diseases. *J. Clin. Immunol.* 2018.04;
 29. Ryuichi Nakagawa, Atsumi Hosokawa-Tsuji, Yuki Aoki, Kei Takasawa, Mitsue Maru, Keisuke Nakajima, Akito Sutani, Yuichi Miyakawa, Daisuke Tomizawa, Kenichi Kashimada, Tomohiro Morio. Total body irradiation for hematopoietic stem cell transplantation during early childhood is associated with the risk for diabetes mellitus. *Endocrine.* 2018.04; 61(1); 76-82

30. Akihiro Hoshino, Takehiro Takashima, Kenichi Yoshida, Akira Morimoto, Yuta Kawahara, Tzu-Wen Yeh, Tsubasa Okano, Motoi Yamashita, Noriko Mitsuiki, Kohsuke Imai, Takashi Sakatani, Atsuko Nakazawa, Yusuke Okuno, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seishi Ogawa, Seiji Kojima, Tomohiro Morio, Hirokazu Kanegane. Dysregulation of Epstein-Barr virus infection in hypomorphic ZAP70 mutation *J. Infect. Dis.*. 2018.04; 218(5); 825-834
31. Teruyoshi Shimoyama, Nozomi Matsuda, Masashi Kurobe, Takehiko Hayakawa, Masato Nishioka, Masayuki Shimohira, Kei Takasawa. Colonoscopic diagnosis and reduction of recurrent intussusception owing to Henoch-Schönlein purpura without purpura. *Paediatr Int Child Health*. 2018.04; 1-5
32. Mari Tanaka-Kubota, Koji Shinozaki, Satoshi Miyamoto, Masakatsu Yanagimachi, Tsubasa Okano, Noriko Mitsuiki, Masahiro Ueki, Masafumi Yamada, Kohsuke Imai, Masatoshi Takagi, Kazunaga Agematsu, Hirokazu Kanegane, Tomohiro Morio. Hematopoietic stem cell transplantation for pulmonary alveolar proteinosis associated with primary immunodeficiency disease. *Int. J. Hematol.*. 2018.05; 107(5); 610-614
33. Rina Nishii, Takaya Moriyama, Laura J Janke, Wenjian Yang, Chase C Suiter, Ting-Nien Lin, Lie Li, Kentaro Kihira, Hidemi Toyoda, Ute Hofmann, Matthias Schwab, Masatoshi Takagi, Tomohiro Morio, Atsushi Manabe, Shirley Kham, Nan Jiang, Karen R Rabin, Motohiro Kato, Katsuyoshi Koh, Allen Eng-Juh Yeoh, Hiroki Hori, Jun J Yang. Preclinical evaluation of NUDT15-guided thiopurine therapy and its effects on toxicity and antileukemic efficacy. *Blood*. 2018.05; 131(22); 2466-2474
34. Schwab C, Gabrysch A, Olbrich P, Patiño V, Warnatz K, Wolff D, Hoshino A, Kobayashi M, Imai K, Takagi M, Dybedal I, Haddock JA, Sansom D, Lucena JM, Seidl M, Schmitt-Gräff A, Reiser V, Emmerich F, Frede N, Bulashevskaya A, Salzer U, Schubert D, Hayakawa S, Okada S, Kanariou M, Kucuk ZY, Chapdelaine H, Petruzalkova L, Sumnik Z, Sediva A, Slatter M, Arkwright PD, Cant A, Lorenz HM, Giese T, Lougaris V, Plebani A, Price C, Sullivan KE, Moutschen M, Litzman J, Freiburger T, van de Veerdonk FL, Recher M, Albert MH, Hauck F, Seneviratne S, Schmid JP, Kolios A, Unglik G, Klemann C, Speckmann C, Ehl S, Leichtner A, Blumberg R, Franke A, Snapper S, Zeissig S, Cunningham-Rundles C, Giulino-Roth L, Elemento O, Dückers G, Niehues T, Fronkova E, Kanderová V, Platt CD, Chou J, Chatila T, Geha R, McDermott E, Bunn S, Kurzai M, Schulz A, Alsina L, Casals F, Deyà-Martinez A, Hambleton S, Kanegane H, Taskén K, Neth O, Grimbacher B.. Phenotype, penetrance, and treatment of 133 CTLA-4-insufficient individuals. *J. Allergy Clin. Immunol.*. 2018.05;
35. Okano T, Imai K, Tsujita Y, Mitsuiki N, Yoshida K, Kamae C, Honma K, Mitsui-Sekinaka K, Sekinaka Y, Kato T, Hanabusa K, Endo E, Takashima T, Hiroki H, Yeh TW, Tanaka K, Nagahori M, Tsuge I, Bando Y, Iwasaki F, Shikama Y, Inoue M, Kimoto T, Moriguchi N, Yuza Y, Kaneko T, Suzuki K, Matsubara T, Maruo Y, Kunitsu T, Waragai T, Sano H, Hashimoto Y, Tasaki K, Suzuki O, Shirakawa T, Kato M, Uchiyama T, Ishimura M, Tauchi T, Yagasaki H, Jou ST, Yu HH, Kanegane H, Kracker S, Durandy A, Kojima D, Muramatsu H, Wada T, Inoue Y, Takada H, Kojima S, Ogawa S, Ohara O, Nonoyama S, Morio T.. Hematopoietic Stem Cell Transplantation for Progressive Combined Immunodeficiency and Lymphoproliferation in Activated PI3K δ Syndrome Type 1. *J. Allergy Clin. Immunol.*. 2018.05;
36. Ono S, Nakayama M, Kanegane H, Hoshino A, Shimodera S, Shibata H, Fujino H, Fujino T, Yunomae Y, Okano T, Yamashita M, Yasumi T, Izawa K, Takagi M, Imai K, Zhang K, Marsh R, Picard C, Latour S, Ohara O, Morio T.. Comprehensive molecular diagnosis of Epstein-Barr virus-associated lymphoproliferative diseases using next-generation sequencing. *Int. J. Hematol.*. 2018.05;
37. Yoshinori Kawabe, Takahiro Morio, Yoshimasa Tanaka, Pauline Schaap. Glycogen synthase kinase 3 promotes multicellular development over unicellular encystation in encysting *Dictyostelia*. *Evodevo*. 2018.05; 9; 12
38. Asami Shimbo, Kei Takasawa, Masato Nishioka, Tomohiro Morio, Masayuki Shimohira. Complications of *Listeria meningitis* in two immunocompetent children. *Pediatr Int*. 2018.05; 60(5); 491-492
39. Masaru Miura, Tohru Kobayashi, Tetsuji Kaneko, Mamoru Ayusawa, Ryuji Fukazawa, Naoya Fukushima, Shigeto Fuse, Kenji Hamaoka, Keiichi Hirono, Taichi Kato, Yoshihide Mitani, Seiichi Sato, Shinya Shimoyama, Junko Shiono, Kenji Suda, Hiroshi Suzuki, Jun Maeda, Kenji Waki, , Hitoshi Kato, Tsutomu Saji, Hiroyuki Yamagishi, Aya Ozeki, Masako Tomotsune, Makiko Yoshida, Yohei Akazawa, Kentaro Aso, Shouzaburoh Doi, Yoshi Fukasawa, Kenji Furuno, Yasunobu Hayabuchi, Miyuki Hayashi, Takafumi Honda, Norihisa Horita, Kazuyuki Ikeda, Masahiro Ishii, Satoru Iwashima, Masahiro Kamada, Masahide Kaneko, Hiroshi Katayama, Yoichi Kawamura, Atushi Kitagawa, Akiko Komori, Kenji Kuraishi, Hiroshi Masuda, Shinichi Matsuda, Satoshi Matsuzaki, Sayaka Mii, Tomoyuki Miyamoto, Yuji Moritou, Noriko

- Motoki, Kiyoshi Nagumo, Tsuneyuki Nakamura, Eiki Nishihara, Yuichi Nomura, Shohei Ogata, Hiroyuki Ohashi, Kenichi Okumura, Daisuke Omori, Tetsuya Sano, Eisuke Suganuma, Tsutomu Takahashi, Shinichi Takatsuki, Atsuhito Takeda, Masaru Terai, Manatomo Toyono, Kenichi Watanabe, Makoto Watanabe, Masaki Yamamoto, Kenichiro Yamamura. Association of Severity of Coronary Artery Aneurysms in Patients With Kawasaki Disease and Risk of Later Coronary Events. *JAMA Pediatr.* 2018.05; 172(5); e180030
40. Susumu Hosokawa, Rebecca R Vanderpool, Taku Ishii, Mitsunori Nishiyama, Shozaburo Doi. What Causes Pulmonary Arterial Hypertension in Down Syndrome With Congenital Heart Disease? *Circ. J.* 2018.05; 82(6); 1513-1514
41. Noguchi Y, Tomizawa D, Hiroki H, Miyamoto S, Tezuka M, Miyawaki R, Tanaka-Kubota M, Okano T, Kobayashi C, Mitsuiki N, Aoki Y, Imai K, Kajiwara M, Kanegane H, Morio T, Takagi M.. Hematopoietic cell transplantation for myeloid/NK cell precursor acute leukemia in second remission. *Clin Case Rep.* 2018.06; 6(6); 1023-1028
42. Kenji Kubara, Kazuto Yamazaki, Yasuharu Ishihara, Takuya Naruto, Huan-Ting Lin, Ken Nishimura, Manami Ohtaka, Mahito Nakanishi, Masashi Ito, Kappei Tsukahara, Tomohiro Morio, Masatoshi Takagi, Makoto Otsu. Status of KRAS in iPSCs Impacts upon Self-Renewal and Differentiation Propensity. *Stem Cell Reports.* 2018.06; 11(2); 380-394
43. David Boutboul, Hye Sun Kuehn, Zoé Van de Wyngaert, Julie E Niemela, Isabelle Callebaut, Jennifer Stoddard, Christelle Lenoir, Vincent Barlogis, Catherine Farnarier, Frédéric Vely, Nao Yoshida, Seiji Kojima, Hirokazu Kanegane, Akihiro Hoshino, Fabian Hauck, Ludovic Lhermitte, Vahid Asnafi, Philip Roehrs, Shaoying Chen, James W Verbsky, Katherine R Calvo, Ammar Husami, Kejian Zhang, Joseph Roberts, David Amrol, John Sleasman, Amy P Hsu, Steven M Holland, Rebecca Marsh, Alain Fischer, Thomas A Fleisher, Capucine Picard, Sylvain Latour, Sergio D Rosenzweig. Dominant-negative IKZF1 mutations cause a T, B, and myeloid cell combined immunodeficiency. *J. Clin. Invest..* 2018.07; 128(7); 3071-3087
44. Akihiro Hoshino, Kay Tanita, Kenji Kanda, Ken-Ichi Imadome, Yoshiaki Shikama, Takahiro Yasumi, Kohsuke Imai, Masatoshi Takagi, Tomohiro Morio, Hirokazu Kanegane. High frequencies of asymptomatic Epstein-Barr virus viremia in affected and unaffected individuals with CTLA4 mutations. *Clin. Immunol..* 2018.07; 195; 45-48
45. Kunihiko Moriya, Yoji Sasahara, Hidenori Ohnishi, Tomoki Kawai, Hirokazu Kanegane. IKBA S32 Mutations Underlie Ectodermal Dysplasia with Immunodeficiency and Severe Noninfectious Systemic Inflammation. *J. Clin. Immunol..* 2018.07; 38(5); 543-545
46. Rawat A, Mathew B, Pandiarajan V, Jindal A, Sharma M, Suri D, Gupta A, Goel S, Karim A, Saikia B, Minz RW, Imai K, Nonoyama S, Ohara O, Giliani SC, Notarangelo LD, Chan KW, Lau YL, Singh S.. Clinical and molecular features of X-linked hyper IgM syndrome - An experience from North India. *Clin. Immunol..* 2018.07; 195; 59-66
47. Nishiyama-Fujita Y, Kawana-Tachikawa AI, Ono T, Tanaka Y, Kato T, Heslop HE, Morio T, Takahashi S. Generation of multivirus-specific T cells by a single stimulation of peripheral blood mononuclear cells with a peptide mixture using serum-free medium. *Tanaka Y.* 2018.08;
48. Wada-Shimosato Y, Ikeda J, Tsujimoto SI, Sasaki K, Yanagimachi M, Kajiwara R, Shiba N, Murata H, Kawahara N, Yamanaka S, Tanoshima R, Ito S. Intraventricular Rituximab in Pediatric CD20-positive Refractory Primary Central Nervous System Lymphoma. *Journal of pediatric hematology/oncology.* 2018.08;
49. Mako Okabe, Keiichi Hirono, Kentaro Tamura, Fukiko Ichida, Hirokazu Kanegane. Reactive peripheral blood plasmacytosis in Kawasaki disease. *Pediatr Int.* 2018.09; 60(9); 884-885
50. Atsumi Tsuji-Hosokawa, Kenichi Kashimada, Tomoko Kato, Yuya Ogawa, Risa Nomura, Kei Takasawa, Rowena Lavery, Andrea Coschiera, David Schlessinger, Vincent R Harley, Shuji Takada, Tomohiro Morio. Peptidyl arginine deiminase 2 (Padi2) is expressed in Sertoli cells in a specific manner and regulated by SOX9 during testicular development. *Sci Rep.* 2018.09; 8(1); 13263

51. Sumitomo N, Baba R, Doi S, Higaki T, Horigome H, Ichida F, Ishikawa H, Iwamoto M, Izumida N, Kasamaki Y, Kuga K, Mitani Y, Musha H, Nakanishi T, Yoshinaga M, Abe K, Ayusawa M, Hokosaki T, Kato T, Kato Y, Ohta K, Sawada H, Ushinohama H, Yoshiba S, Atarashi H, Hirayama A, Horie M, Nagashima M, Niwa K, Ogawa S, Okumura K, Tsutsui H. Guidelines for Heart Disease Screening in Schools (JCS 2016/JSPCCS 2016) - Digest Version. *Circ. J.* 2018.09; 82(9); 2385-2444
52. Chelisa Cardinez, Bahar Miraghazadeh, Kay Tanita, Elizabeth da Silva, Akihiro Hoshino, Satoshi Okada, Rochna Chand, Takaki Asano, Miyuki Tsumura, Kenichi Yoshida, Hidenori Ohnishi, Zenichiro Kato, Masahide Yamazaki, Yusuke Okuno, Satoru Miyano, Seiji Kojima, Seishi Ogawa, T Daniel Andrews, Matthew A Field, Gaetan Burgio, Tomohiro Morio, Carola G Vinuesa, Hirokazu Kanegane, Matthew C Cook. Gain-of-function IKBKB mutation causes human combined immune deficiency. *J. Exp. Med.* 2018.10; 215(11); 2715-2724
53. Akihiro Hoshino, Xi Yang, Kay Tanita, Kenichi Yoshida, Toshiaki Ono, Naonori Nishida, Yusuke Okuno, Takeyuki Kanzaki, Kumiko Goi, Hisanori Fujino, Koichi Ohshima, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Seishi Ogawa, Seiji Kojima, Tomohiro Morio, Hirokazu Kanegane. Modification of cellular and humoral immunity by somatically reverted T cells in X-linked lymphoproliferative syndrome type 1. *J. Allergy Clin. Immunol.* 2018.10; 413(1); 421-424
54. Chikako Kamae, Kohsuke Imai, Tamaki Kato, Tsubasa Okano, Kenichi Honma, Noriko Nakagawa, Tzu-Wen Yeh, Emiko Noguchi, Akira Ohara, Tomonari Shigemura, Hiroshi Takahashi, Shunichi Takakura, Masatoshi Hayashi, Aoi Honma, Seiichi Watanabe, Tomoko Shigemori, Osamu Ohara, Hiroyuki Sasaki, Takeo Kubota, Tomohiro Morio, Hirokazu Kanegane, Shigeaki Nonoyama. Clinical and Immunological Characterization of ICF Syndrome in Japan. *J. Clin. Immunol.* 2018.10; 38(8); 927-937
55. Isoda T, Nishimura A, Miyamoto S, Morio T, Takagi M, Murre C. Non-Coding RNA ThymoD Transcription Modulates Nuclear Architecture to Orchestrate T-Cell Fate and Block T-Cell Malignancies. *PEDIATRIC BLOOD & CANCER*. 2018.11; 65; S4
56. Jolles S, Rojavin MA, Lawo JP, Nelson R Jr, Wasserman RL, Borte M, Tortorici MA, Imai K, Kanegane H.. Long-Term Efficacy and Safety of Hizentra® in Patients with Primary Immunodeficiency in Japan, Europe, and the United States: a Review of 7 Phase 3 Trials. *J. Clin. Immunol.* 2018.11;
57. Nagatsuma M, Takasawa K, Yamauchi T, Nakagawa R, Mizuno T, Tanaka E, Yamamoto K, Uemura N, Kashimada K, Morio T. A postzygotic KRAS mutation in a patient with Schimmelpenning syndrome presenting with lipomatosis, renovascular hypertension, and diabetes mellitus. *Journal of human genetics*. 2018.11;
58. Akihiro Tamura, Suguru Uemura, Nobuyuki Yamamoto, Atsuro Saito, Aiko Kozaki, Kenji Kishimoto, Toshiaki Ishida, Daiichiro Hasegawa, Haruka Hiroki, Tsubasa Okano, Kohsuke Imai, Tomohiro Morio, Hirokazu Kanegane, Yoshiyuki Kosaka. Hematopoietic cell transplantation for asymptomatic X-linked lymphoproliferative syndrome type 1. *Allergy Asthma Clin Immunol*. 2018.11; 14; 82
59. Rajiv Mallick, Stephen Jolles, Hirokazu Kanegane, Dominique Agbor-Tarh, Mikhail Rojavin. Treatment Satisfaction with Subcutaneous Immunoglobulin Replacement Therapy in Patients with Primary Immunodeficiency: a Pooled Analysis of Six Hizentra® Studies. *J. Clin. Immunol.* 2018.11; 38(8); 886-897
60. Acerini CL, Segal D, Criseno S, Takasawa K, Nedjatian N, Röhrich S, Maghnie M.. Shared Decision-Making in Growth Hormone Therapy – Implications for Patient Care *Front Endocrinol (Lausanne)*. 2018.11; 22(9); 688
61. Acerini Carlo L., Segal David, Criseno Sherwin, Takasawa Kei, Nedjatian Navid, Rohrich Sebastian, Maghnie Mohamad. Shared Decision-Making in Growth Hormone Therapy-Implications for Patient Care *FRONTIERS IN ENDOCRINOLOGY*. 2018.11; 9; 688
62. Shigeta N, Nakamura H, Kumasawa K, Imai K, Saito S, Sakaguchi S, Kimura T.. Are naïve T cells and class-switched memory (IgD- CD27+) B cells not essential for establishment and maintenance of pregnancy? Insights from a case of common variable immunodeficiency with pregnancy. *Med. Hypotheses*. 2018.12; 121; 36-41
63. Isoda Takeshi, Takagi Masatoshi. Non-coding RNA transcription modulates nuclear architecture to specify T-cell fate and blocks T-cell malignancies. *CANCER SCIENCE*. 2018.12; 109; 346
64. Takai S, Takasawa K, Doi S. Atypical coronary artery aneurysms due to Kawasaki disease in Noonan syndrome with a novel PTPN11 mutation. *Cardiol Young*. 2018.12; 4; 1-3

[Books etc]

1. Guidelines for Treatment of Pulmonary Hypertension(JCS 2017/JPCPHS 2017). 2018.11

[Misc]

1. Kanegane H, Hoshino A, Takagi M. Primary immunodeficiencies and hematological malignancies Rinsho Ketsueki (The Japanese journal of clinical hematology). 2018.12; 59(11); 2459-2467

[Conference Activities & Talks]

1. Tomohiro Morio. Multi-virus specific T cell therapy for drug-resistant viral infection following hematopoietic cell transplantation. The 5th IMSUT-CGCT Symposium 2018.01.30 Tokyo
2. Tsuji-Hosokawa A, Kato T, Ogawa Y, Nomura R, Lavery R, Takasawa K, Harley V, Morio T, Takeda S, Kashimada K. SOX9 and FOXL2 Antagonistically Regulate Peptidyl Arginine Deiminase 2 (PADI2) Expression during testicular Development. 8th International Symposium on the Biology of Vertebrate Sex determination 2018.04.16 Kona
3. Imai K. HSCT for radiosensitive SCID. APSID2018 Summer School 2018.05.05 Chongqing
4. Okamoto K, Shigemizu D, Okano T, Yeh TW, Takashima T, Yamashita M, Ono S, Mitsui N, Takagi M, Mori M, Kanegane H, Tsunoda T, Imai K, Morio T. Whole exome sequence analysis using the known and candidate genes for primary immunodeficiency diseases. The 2nd APSID Scientific Congress 2018.05.07 Chongqing, China
5. Yeh TW, Okano T, Okamoto K, Yamashita M, Takashima T, Mitsui N, Okada S, Kanegane H, Imai K, Morio T. APRIL deficiency as a cause of common variable immunodeficiency. The 2nd APSID Scientific Congress 2018.05.07 Chongqing, China
6. Kanegane H. EBV associated PID. The 2nd APSID Scientific Congress 2018.05.07 Chongqing, China
7. Kanegane H. Management of HLH and XLP. APSID 2018 Summer School 2018.05.07 Chongqing, China
8. Imai K. PID research and clinical care in Japan. 2018 Samsung Medical Center Primary Immunodeficiency Symposium. 2018.05.08 Chongqing
9. Imai K. Hematopoietic stem cell transplantation for radiosensitive severe combined immunodeficiency. APSID 2018 Summer School 2018.05.08 Chongqing
10. Kanegane H. Chronic Active Epstein-Barr Virus & Epstein-Barr Virus associated with Haemophagocytic Lymphohistiocytosis. CME Lecture 2018.05.21 Singapore
11. Kanegane H. Epstein-Barr related Primary Immunodeficiency. CME Lecture 2018.05.21 Singapore
12. Imai K. Newborn Screening of PID in Japan. 7th Singapore Paediatric and Perinatal Annual Congress (SiPPAC) 2018.06.27 Singapore
13. Imai K. Primary Antibody Deficiencies. 7th Singapore Paediatric and Perinatal Annual Congress (SiPPAC). 2018.06.27 Singapore
14. 6th World symposium on PH 2018. 2018.07.05
15. Tomohiro Morio. Overview and Updates on PID. 2018 Samsung Medical Center Primary Immunodeficiency Symposium 2018.07.14 Seoul, Korea
16. Imai K. PIDJ: primary immunodeficiency in Japan project. 2018 Samsung Medical Center Primary Immunodeficiency Symposium. 2018.07.14 Seoul
17. Morio T, Nakajima K, Okado H. Benzodiazepine-resistant status epilepticus in children: Alteration in GABAAR signal in children and its potential preventive measure. The World Federation of Societies of Biological Psychiatry (WFSBP). 2018.09.07 Kobe

18. Yuji Sugawara, Takeshi Hasegawa, Toshihiro Nomura, Kengo Moriyama, Tomoko Mizuno, Daisuke Kobayashi, Motoki Inaji, Taketoshi Maehara. Temporo-polar gray/white matter blurring prior to febrile seizure status in temporal lobe epilepsy. 19th annual Meeting of Infantile Seizure Society (ISSET International Symposium on Severe Infantile Epilepsy Treatment) 2018.09.22 Roma, Italy
19. Imai K. Newborn Screening for primary immunodeficiency (PID) in Japan and Asia. European Society for Blood and Marrow Transplantation 2018.09.27 Leiden
20. Imai K. Antibody deficiency: a diagnostic and management challenge. APSID Autumn School 2018.10.11 Bangkok
21. Okano T, Cho K, Kwamura S, Onai N, Fujii W, Kakuta S, Kanai-Azuma M, Ohteki T, Otsu M, Ariga T, Morio T. . Induced Pluripotent Stem Cell (iPSC)-Derived Macrophages Recapitulate the Pathological Features of Pulmonary Alveolar Proteinosis Caused by OAS1 Mutation.. 18th Biennial Meeting of the European Society of Immunodeficiencies (ESID2018) 2018.10.25 Lisbon
22. Yeh T. W, Okano T, Okamoto K, Yamashita M, Takashima T, Mitsuki N, Okada S, Kanegane H, Imai K, Morio T.. April Deficiency as a Cause of Common Variable Immunodeficiency. . 18th Biennial Meeting of the European Society of Immunodeficiencies (ESID2018) 2018.10.25 Lisbon
23. Leiding J, Vogel T, Heimall J, Gignon Jadoul V, Mhaskar R, Cooper M, O'Sullivan M, Giovannini-Chami L, Thatayatikom B, Bauer C, Hamalainen S, Taskinen M, Seppanen M, Adeli M, Formankova R, Heeg M, Pozos T, Szabolcs P, Morio T, Chua I, Hague R, Hambleton S, Tangye S, Gennery A, Cunningham-Rundles C, Su H, Rao K, Milner J, Ehl S, Forbes L.. The Natural History of STAT3-GOF-The Range of Clinical Manifestations and Treatment Options.. 18th Biennial Meeting of the European Society of Immunodeficiencies (ESID2018) 2018.10.25 Lisbon
24. Taiki Shima, Hiroshi Sakuma, Tomonori Suzuki, Kuniko Kohyama, Takako Matsuoka, Masaharu Hayashi, Akihisa Okumura. Effect of Antiepileptic Drugs on Microglia Property. 2018.10.26
25. Kanegane H.. Modification of cellular and humoral immunity by somatically reverted T cells in XLP1. XLP Symposium 2018. 2018.10.29 London
26. TCF3 inherited variants in children with B-cell precursor acute lymphoblastic leukemia. 2018.11.15
27. Isoda T, Nishimura A, Miyamoto S, Morio T, Takagi M, Murre C. Non-Coding RNA thymic transcription modulates nuclear architecture to orchestrate cell fate and block T-Cell malignancies. SIOP2018 2018.11.17 Kyoto
28. Lin HT, Kubara K, Yamazaki K, Takagi M, Naruto T, Morio T, Okumura T, Otsu M. Enhanced Selective Inhibition of KRAS Mutant Hematopoietic Progenitor Cell Expansion By MEK and Bcl-2 Inhibition . 60st American society of Hematology Annual Meeting & Exposition 2018.12.01 San Diego
29. Nishimura A, Yokoyama K, Yamagishi C, Naruto T, Morio T, Kanai A, Matsui H, Higuchi N, Takada A, Okuno H, Saito S, Karakawa S, Kobayashi S, Sano H, Koike T, Hasegawa D, Fujisaki H, Hasegawa D, Koike K, Ogawa A, Kinoshita A, Shiba N, Miki M, Nakayama H, Nakazawa Y, Imamura T, Taga T, Adachi S, Koh K, Manabe A, Taki T, Ishida Y, Tojo A, Takagi M. Clinical Feature and Genetic Alterations in Myeloid/Natural Killer (NK) Cell Precursor Acute Leukemia and Myeloid/NK Cell Acute Leukemia. 60st American society of Hematology Annual Meeting & Exposition 2018.12.02 San Diego
30. Doi S. Therapeutic approach to pulmonary hypertension associated with congenital heart disease. Joint Session-JSPCCS, Annual meeting of Taiwan Society of Pediatric Cardiology 2018.12.09 Taipei, Taiwan

Rheumatology

Professor emeritus	Nobuyuki MIYASAKA
Professor	Masaaki MORI (1) Tetsuo KUBOTA (2) Kazuki TAKADA (3) Ryuji KOIKE (2)
Junior Associate Professor	Hideyuki IWAI
Assistant Professor	Fumitaka MIZOGUCHI, Tadashi HOSOYA, Naoki KIMURA, Hisanori HASEGAWA, Natsuka UMEZAWA, Hirokazu SASAKI
Visiting Lecturer	Kimito KAWAHATA, Kenji NAGASAKA, Akito TAKAMURA, Makoto SOEJIMA, Hiroyuki HAGIYAMA, Yusuke MATSUO, Takahiko SUGIHARA, Fumihito SUZUKI, Reiko TSUBATA, Kaori IMAI, Jyunko NISHIO, Mari KIHARA, Toshihiro MATSUI
Affiliated Hospital	Fumiaki KONDO, Takeshi KUSUDA, Wakako KAWSAKI, Tatsuhiko SHINOHARA, Marina TSUCHIDA, Ayaka MAEDA, Masami TOKURA, Yuriko YAGYU, Tomoko NIWANO, Yoichi IMAI, Motohiko SATO, Seiya OBA, Takahiro NAKAHARA, Daisuke KAWADA
Resident	Akiou YAMAMOTO, Tatsuya KAWASAKI, Hiroyuki BABA, Takuji ITAKURA, Kanae ITO, Yuichi KIRI
Graduate Student	Akiou YAMAMOTO, Hirokazu SASAKI, Mari KAMIYA, Yasuhiro TAGAWA, Tatsuhiko SHINOHARA, Youji KOMIYA, Takumi MATSUMOTO, Seiji NODA, Sahoko TAMURA, Tasuku SASAKI
Researcher	Nao TANAKA
Office Administrator	Kaori KONNO, Tomoko TAKAHASHI (1)
Technical Staff	Kazuko YAMAZAKI, Naoko FUJITA

(1) Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,
(3) Curricular Management Division, Institute of Education,

(1) Research

Following studies have been extensively carried out in our laboratory with various biochemical, immunological, molecular biological and statistical techniques:

1) Investigation of mechanism and development of new therapeutics for the treatment of rheumatoid arthritis and dermato/polymyositis.

2) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies. We collaborate with department of lifetime clinical immunology and pediatrics.

(2) Education

We have provided medical students and graduates with the opportunity to obtain the ability to identify important clinical problems and to solve them by clinical reasoning through their active participation into the diagnosis and management of various rheumatic diseases.

(3) Clinical Services & Other Works

We have provided care to many patients with diverse rheumatic diseases. We have aimed to practice evidence-based medicine and to provide care that is in accordance with the global standard. We have contributed to the development of potential new drugs and treatments through participation into industry- as well as investigator-initiated clinical trials for chemical and biological agents. We have also contributed to the refinement of the care of rheumatic disease patients through the conduct of various pharmacovigilance studies.

We cooperate with department of lifetime clinical immunology and pediatrics.

(4) Publications

[Original Articles]

1. Mizoguchi F, Slowikowski K, Wei K, Marshall JL, Rao DA, Chang SK, Nguyen HN, Noss EH, Turner JD, Earp BE, Blazar PE, Wright J, Simmons BP, Donlin LT, Kalliolias GD, Goodman SM, Bykerk VP, Ivashkiv LB, Lederer JA, Hachohen N, Nigrovic PA, Filer A, Buckley CD, Raychaudhuri S, Brenner MB.. Functionally distinct disease-associated fibroblast subsets in rheumatoid arthritis. *Nature Communications*. 2018.02; 9(1); 789
2. Honda Suguru, Hirano Fumio, Mouri Mariko, Hasegawa Hisanori, Kohsaka Hitoshi. Aneurysm formation after stent grafting in vascular Behcet's disease *ARTHRITIS & RHEUMATOLOGY*. 2018.02; 70(2); 322
3. Shinji Ogihara, Ryoichi Saito, Etsuko Sawabe, Takahiro Kozakai, Mari Shima, Yoshibumi Aiso, Toshihide Fujie, Yoko Nukui, Ryuji Koike, Michio Hagihara, Shuji Tohda. Molecular typing of methicillin-resistant *Staphylococcus aureus*: Comparison of PCR-based open reading frame typing, multilocus sequence typing, and *Staphylococcus* protein A gene typing. *J. Infect. Chemother.*. 2018.04; 24(4); 312-314
4. Umezawa Natsuka, Kawahata Kimito, Mizoguchi Fumitaka, Kimura Naoki, Yoshihashi-Nakazato Yoko, Miyasaka Nobuyuki, Kohsaka Hitoshi. Interleukin-23 as a therapeutic target for inflammatory myopathy *SCIENTIFIC REPORTS*. 2018.04; 8(1); 5498
5. Ryoko Sakai, Shoko Kasai, Fumio Hirano, Sayoko Harada, Mari Kihara, Waka Yokoyama, Michi Tsutsumino, Kenji Nagasaka, Ryuji Koike, Hisashi Yamanaka, Nobuyuki Miyasaka, Masayoshi Harigai. No increased risk of herpes zoster in TNF inhibitor and non-TNF inhibitor users with rheumatoid arthritis: epidemiological study using the Japanese health insurance database. *Int J Rheum Dis*. 2018.04;
6. Ogihara Shinji, Saito Ryoichi, Sawabe Etsuko, Kozakai Takahiro, Shima Mari, Aiso Yoshibumi, Fujie Toshihide, Nukui Yoko, Koike Ryuji, Hagihara Michio, Tohda Shuji. Molecular typing of methicillin-resistant *Staphylococcus aureus*: Comparison of PCR-based open reading frame typing, multilocus sequence typing, and *Staphylococcus* protein A gene typing *Journal of Infection and Chemotherapy*. 2018.04; 24(3-4); 312-314
7. Nikunj M Shukla, Kei-Ichiro Arimoto, Shiyin Yao, Jun-Bao Fan, Yue Zhang, Fumi Sato-Kaneko, Fitzgerald S Lao, Tadashi Hosoya, Karen Messer, Minya Pu, Howard B Cottam, Dennis A Carson, Tomoko Hayashi, Dong-Er Zhang, Maripat Corr. Identification of Compounds That Prolong Type I Interferon Signaling as Potential Vaccine Adjuvants. *SLAS Discov*. 2018.05; 2472555218774308
8. Donlin Laura T., Rao Deepak A., Wei Kevin, Slowikowski Kamil, McGeachy Mandy J., Turner Jason D., Meednu Nida, Mizoguchi Fumitaka, Gutierrez-Arcelus Maria, Lieb David J., Keegan Joshua, Muskat Kaylin, Hillman Joshua, Roza Cristina, Ricker Edd, Eisenhaure Thomas M., Li Shuqiang, Browne Edward P., Chicoine Adam, Sutherby Danielle, Noma Akiko, Nusbaum Chad, Kelly Stephen, Pernis Alessandra B.,

- Ivashkiv Lionel B., Goodman Susan M., Robinson William H., Utz Paul J., Lederer James A., Gravalles Ellen M., Boyce Brendan F., Hachohen Nir, Pitzalis Costantino, Gregersen Peter K., Firestein Gary S., Raychaudhuri Soumya, Moreland Larry W., Holers V. Michael, Bykerk Vivian P., Filer Andrew, Boyle David L., Brenner Michael B., Anolik Jennifer H.. Methods for high-dimensional analysis of cells dissociated from cryopreserved synovial tissue ARTHRITIS RESEARCH & THERAPY. 2018.07; 20(1); 139
9. Tadashi Hosoya, Fumi Sato-Kaneko, Alast Ahmadi, Shiyin Yao, Fitzgerald Lao, Kazutaka Kitaura, Takaji Matsutani, Dennis A Carson, Tomoko Hayashi. Induction of oligoclonal CD8 T cell responses against pulmonary metastatic cancer by a phospholipid-conjugated TLR7 agonist. Proc. Natl. Acad. Sci. U.S.A.. 2018.07; 115(29); E6836-E6844
10. Kenji Oku, Tatsuya Atsumi, Yuji Akiyama, Hirofumi Amano, Naoto Azuma, Toshiyuki Bohgaki, Yu Funakubo Asanuma, Tetsuya Horita, Tadashi Hosoya, Kunihiro Ichinose, Masaru Kato, Yasuhiro Katsumata, Yasushi Kawaguchi, Atsushi Kawakami, Tomohiro Koga, Hitoshi Kohsaka, Yuya Kondo, Kanae Kubo, Masataka Kuwana, Akio Mimori, Tsuneyo Mimori, Toshihide Mimura, Kosaku Murakami, Kazuhisa Nakano, Shingo Nakayamada, Hiroshi Ogishima, Kazumasa Ohmura, Kazuyoshi Saito, Hajime Sano, Mihoko Shibuya, Yuko Takahashi, Yoshinari Takasaki, Tsutomu Takeuchi, Naoto Tamura, Yoshiya Tanaka, Hiroto Tsuboi, Shinichiro Tsunoda, Naoichiro Yukawa, Noriyuki Yamakawa, Kazuhiko Yamamoto, Takayuki Sumida. Evaluation of the alternative classification criteria of systemic lupus erythematosus established by Systemic Lupus International Collaborating Clinics (SLICC). Mod Rheumatol. 2018.07; 28(4); 642-648
11. Fumi Sato-Kaneko, Xiaodong Wang, Shiyin Yao, Tadashi Hosoya, Fitzgerald S. Lao, Karen Messer, Minya Pu, Nikunj M. Shukla, Howard B. Cottam, Michael Chan, Dennis A. Carson, Maripat Corr, and Tomoko Hayashi. Discovery of a Novel Microtubule Targeting Agent as an Adjuvant for Cancer Immunotherapy BioMed Research International. 2018.09;
12. Sugihara Takahiko, Ishizaki Tatsuro, Baba Hiroyuki, Matsumoto Takumi, Iga Shoko, Kusuda Takeshi, Tsuchida Marina, Kamiya Mari, Komiya Yoji, Hirano Fumio, Hosoya Tadashi, Miyasaka Nobuyuki, Harigai Masayoshi. Three Year Outcomes of Patients with Elderly-Onset Rheumatoid Arthritis Treated with a Therapeutic Strategy Targeting Low Disease Activity, and Impact of Adverse Events on Physical Function ARTHRITIS & RHEUMATOLOGY. 2018.09; 70;
13. Kasai S, Sakai R, Koike R, Kohsaka H, Miyasaka N, Harigai M. Higher risk of hospitalized infection, cardiovascular disease, and fracture in patients with rheumatoid arthritis determined using the Japanese health insurance database. Modern rheumatology. 2018.11; 1-7
14. H Sasaki, A Takamura, K Kawahata, T Takashima, K Imai, T Morio, H Kohsaka. Peripheral blood lymphocyte subset repertoires are biased and reflect clinical features in patients with dermatomyositis. Scand. J. Rheumatol.. 2018.12; 1-5

[Misc]

1. Hideto Kameda, Takao Fujii, Ayako Nakajima, Ryuji Koike, Akira Sagawa, Katsuaki Kanbe, Tetsuya Tomita, Masayoshi Harigai, Yasuo Suzuki, . Japan College of Rheumatology guideline for the use of methotrexate in patients with rheumatoid arthritis. Mod Rheumatol. 2018.05; 1-10
2. Yusuke Matsuo, Tetsuya Saito, Akio Yamamoto, Hitoshi Kohsaka. Origins of fibroblasts in rheumatoid synovial tissues: Implications from organ fibrotic models. Mod Rheumatol. 2018.07; 28(4); 579-582
3. Fumitaka Mizoguchi. Therapeutic strategies to prevent joint destruction in rheumatoid arthritis CLINICIAN. 2018.10; 65(668); 23-30
4. Hirokazu Sasaki, Hitoshi Kohsaka. Current diagnosis and treatment of polymyositis and dermatomyositis. Mod Rheumatol. 2018.11; 28(6); 913-921
5. Fumitaka Mizoguchi. Molecular and cellular deconstruction of tissue pathology in rheumatoid arthritis Rheumatology. 2018.12; 60(6); 628-634

[Conference Activities & Talks]

1. Mari Kamiya, Fumitaka Mizoguchi, Naoki Kimura, Akito Takamura, Kimito Kawahata, Hitoshi Kohsaka
. In-vitro study of cytotoxic T lymphocyte-mediated muscle injury in polymyositis.. 2018.04.26
2. Mari Kamiya, Naoki Kimura, Akito Takamura, Fumitaka Mizoguchi, Kimito Kawahata, Hitoshi Kohsaka.
Cytotoxic T lymphocytes induced perforin/granzyme-dependent apoptosis of myoblasts and Fas/FasL-
dependent necroptosis of myotubes in in vitro model of myositis.. JCR international School 2018 2018.08.02

Dermatology

Professor: Hiroo YOKOZEKI

Associate Professor: Takeshi NAMIKI

Junior Associate Professor: Tsukasa UGAJIN, Makiko NISHIDA

Project Junior Associate Professor: Kaoru TAKAYAMA

Assistant Professor: Shown TOKORO, Takashi HASHIMOTO,

Shinnji OGAWA, Yusuke YOSHIOKA

Senior Resident: Takuya WAKASA, Masahiro KATAGIRI, Tadatune IIDA, Chie UCHIDA

Resident: Hsieh Ming hsiu

Doctoral Student: Minako INAZAWA, Aiko FURUI, Kohei NOJIMA, Kohei KATO, Michiko NAKAMURA

Sally ESHIBA, Rumi SUZUKI, Takahiro ISHIKAWA, Al-Busani Hind Abdullah Ahmed,

Hazuki IJIMA, Yukari MORIKAWA

Technical Assistant: Chiyako MIYAGISHI, Ayumi FUJIKAWA

Staff Assistant: Masae SAKATA, Mayuko HAYASHI,

(1) Outline

Dermatology is a department of medical science which educates students to make a diagnosis and treatment for skin diseases. Main objective of Dermatology in the graduate course is to provide students opportunity to study advanced Immunodermatology, physiology, pathology and allergology, and also to study making diagnosis of skin diseases and operation techniques. Students are also taught on skin oncology (melanoma, angiosarcoma) and its related laboratory technology depending on their research project.

(2) Research

- 1) Mechanisms of contact hypersensitivity
- 2) Pathological etiology of atopic dermatitis
- 3) Mechanisms of eosinophil recruitment to the skin
- 4) Roles of basophils in human skin diseases
- 5) Functional roles of PGD2 and its receptors in allergic inflammation
- 6) Therapeutic approach for skin diseases by stable form of galectin-9
- 7) Analysis of pathological mechanisms' of hyperhidrosis
- 8) Investigation of mediators for itch
- 9) Pathological etiology of chronic prurigo
- 10) Therapeutic approach for angiosarcoma with HVJ-E.
- 11) To establish the in vitro diseases model of dermatological disorders using human induced pluripotent stem cell
- 12) Murine food allergy model with transcutaneous sensitization

(3) Clinical Performances

Dermatology clinic provides an advanced treatment for skin diseases; skin tumors, infectious diseases, skin allergy, collagen diseases and psoriasis. Recently, we established the gene therapies (STAT6 decoy ODN) for severe atopic dermatitis in the clinic.

(4) Publications

[Original Articles]

1. Takeshi Namiki, Takashi Hashimoto, Takaaki Hanafusa, Keiko Miura, Hiroo Yokozeki. Case of dermatomyositis with Gottron papules and mechanic's hand: Dermoscopic features. *J. Dermatol.* 2018.01; 45(1); e19-e20
2. Takeshi Namiki, Chika Omigawa, Kohei Nojima, Takuya Wakasa, Shown Tokoro, Takaaki Hanafusa, Keiko Miura, Hiroo Yokozeki. Case of cetuximab-induced disseminated necrotic and maculopapular eruptions: Involvement of an epidermal growth factor receptor inhibitor with epidermal necrosis. *J. Dermatol.* 2018.01; 45(1); e3-e4
3. Nishida M, Namiki T, Sone Y, Hashimoto T, Tokoro S, Hanafusa T, Yokozeki H. Acquired anhidrosis associated with systemic sarcoidosis: quantification of nerve fibres around eccrine glands by confocal microscopy. *Br J Dermatol.* 2018.01; 178(1); e59-e61
4. Namiki Takeshi, Hashimoto Takashi, Hanafusa Takaaki, Miura Keiko, Yokozeki Hiroo. Gottron 丘疹と機械工の手を伴う皮膚筋炎の1例 皮膚鏡検査所見 (Case of dermatomyositis with Gottron papules and mechanic's hand: Dermoscopic features) *The Journal of Dermatology.* 2018.01; 45(1); e19-e20
5. Namiki Takeshi, Omigawa Chika, Nojima Kohei, Wakasa Takuya, Tokoro Shown, Hanafusa Takaaki, Miura Keiko, Yokozeki Hiroo. セツキシマブ誘発性の播種性壊死性および斑丘疹性発疹の1症例 表皮壊死に対する表皮成長因子受容体阻害剤の関与 (Case of cetuximab-induced disseminated necrotic and maculopapular eruptions: Involvement of an epidermal growth factor receptor inhibitor with epidermal necrosis) *The Journal of Dermatology.* 2018.01; 45(1); e3-e4
6. Takeshi Namiki, Kohei Nojima, Takaaki Hanafusa, Keiko Miura, Hiroo Yokozeki. Superficial basal cell carcinoma: Dermoscopic and histopathological features of multiple small erosions. *Australas. J. Dermatol.* 2018.02; 59(1); 69-71
7. Keiko Miura, Takeshi Namiki, Takumi Akashi, Noriko Uemura, Hiroki Mori, Hiroo Yokozeki, Mutsumi Okazaki. Desmoplastic transformation of a nodular melanoma arising from a speckled lentiginous nevus. *J. Dermatol.* 2018.02;
8. Takeshi Namiki, Yumiko Sone, Keiko Miura, Masaru Tanaka, Hiroo Yokozeki. Methotrexate-Associated Lymphoproliferative Disorder: Dermoscopic Features. *Case Rep Dermatol.* 2018.02; 10(2); 149-153
9. Yoko KOMURA, Takamichi KOGURE, Kazuo KAWAHARA, Hiroo YOKOZEKI. Economic assessment of actual prescription of drugs for treatment of atopic dermatitis: Differences between dermatology and pediatrics in large-scale receipt data *The Journal of DERMATOLOGY.* 2018.02; 45; 165-174
10. Komura Yoko, Kogure Takamichi, Kawahara Kazuo, Yokozeki Hiroo. アトピー性皮膚炎治療のための実際の薬物処方を経済的評価 大規模レセプトデータにおける皮膚科と小児科の差異 (Economic assessment of actual prescription of drugs for treatment of atopic dermatitis: Differences between dermatology and pediatrics in large-scale receipt data) *The Journal of Dermatology.* 2018.02; 45(2); 165-174
11. Makiko Ueno, Takeshi Namiki, Madoka Iikawa, Maki Amano, Kohei Nojima, Takashi Hashimoto, Takaaki Hanafusa, Keiko Miura, Hiroo Yokozeki. Case of tumoral melanosis with a massive infiltration of CD163+ and CD68+ macrophages. *J. Dermatol.* 2018.03; 45(3); 368-370
12. Kohei Nojima, Takeshi Namiki, Keiko Miura, Masaru Tanaka, Hiroo Yokozeki. A case of CD8+ and CD56+ cytotoxic variant of poikiloderma with mycosis fungoides: Dermoscopic features of reticular pigmentation and vascular structures. *Australas. J. Dermatol.* 2018.03;

13. Ueno Makiko, Namiki Takeshi, Iikawa Madoka, Amano Maki, Nojima Kohei, Hashimoto Takashi, Hanafusa Takaaki, Miura Keiko, Yokozeki Hiroo. CD163 陽性および CD68 陽性マクロファージの大量浸潤を伴う腫瘍性メラノシスの症例 (Case of tumoral melanosis with a massive infiltration of CD163+ and CD68+ macrophages) *The Journal of Dermatology*. 2018.03; 45(3); 368-370
14. Takeshi Namiki, Kohei Nojima, Keiko Miura, Masaru Tanaka, Hiroo Yokozeki. Pigmented Bowen disease: A challenging dermoscopic feature due to a traumatic disfigurement. *J. Dermatol.* 2018.04; 45(4); e88-e89
15. Takeshi Namiki, Takashi Hashimoto, Makiko Nishida, Tsukasa Ugajin, Keiko Miura, Hiroo Yokozeki. A case of peripheral T-cell lymphoma, not otherwise specified, with rapid progression to erythroderma. *Eur J Dermatol*. 2018.04; 28(2); 240-241
16. Hashimoto Takashi, Satoh Takahiro, Yokozeki Hiroo. Toe Gangrene Associated with Macroangiopathy in Systemic Sclerosis: A Case Series on the Unreliability of the Ankle-brachial Pressure Index. *Acta Derm Venereol*. 2018.04; 98(5); 532-533
17. Omigawa Chika, Hashimoto Takashi, Hanafusa Takaaki, Namiki Takeshi, Igawa Ken, Yokozeki Hiroo. Generalized Purpura as an Atypical Skin Manifestation of Adult-onset Still's Disease in a Patient with Behcet's Disease. *Acta Derm Venereol*. 2018.04; 98(4); 452-453
18. Ono Emi, Murota Hiroyuki, Mori Yuki, Yoshioka Yoshichika, Nomura Yuko, Munetsugu Takichi, Yokozeki Hiroo, Katayama Ichiro. Sweat glucose and GLUT2 expression in atopic dermatitis: Implication for clinical manifestation and treatment *PLOS ONE*. 2018.04; 13(4); e0195960
19. Namiki Takeshi, Nojima Kohei, Miura Keiko, Tanaka Masaru, Yokozeki Hiroo. 色素性 Bowen 病 外傷のため検査が困難なダーモスコピー所見 (Pigmented Bowen disease: A challenging dermoscopic feature due to a traumatic disfigurement) *The Journal of Dermatology*. 2018.04; 45(4); e88-e89
20. Takeshi Namiki, Keiko Miura, Hiroo Yokozeki, Shin-Ichi Ansai. Bowen Disease With Sebaceous Differentiation: A Case Report and Immunohistochemical Analysis of Adipophilin and Cytokeratin 1. *Am J Dermatopathol*. 2018.05;
21. Kohei Kato, Takeshi Namiki, Kohei Nojima, Takashi Hashimoto, Makiko Ueno, Takaaki Hanafusa, Keiko Miura, Hiroo Yokozeki. Case of subungual tumoral melanosis: The detection of melanoma cells and dermoscopic features. *J. Dermatol.* 2018.06; 45(6); e161-e162
22. T Namiki, K Nojima, T Hashimoto, T Hanafusa, S Tokoro, K Miura, M Tanaka, H Yokozeki. Borst-Jadassohn phenomenon arising from a seborrheic keratosis and its characteristic dermoscopic features. *Clin. Exp. Dermatol.* 2018.06;
23. Hashimoto Takashi, Rosen Jordan D, Sanders Kristen M, Yosipovitch Gil. Possible roles of basophils in chronic itch. *Exp Dermatol*. 2018.06;
24. Kato Kohei, Namiki Takeshi, Nojima Kohei, Hashimoto Takashi, Ueno Makiko, Hanafusa Takaaki, Miura Keiko, Yokozeki Hiroo. 爪下腫瘍性メラノシスの 1 例 黒色腫細胞の検出とダーモスコピー所見 (Case of subungual tumoral melanosis: The detection of melanoma cells and dermoscopic features) *The Journal of Dermatology*. 2018.06; 45(6); e161-e162
25. Wataya-Kaneda Mari, Ohno Yuuki, Fujita Yasuyuki, Yokozeki Hiroo, Niizeki Hironori, Ogai Masaaki, Fukai Kazuyoshi, Nagai Hiroshi, Yoshida Yuichi, Hamada Izumi, Hio Taihei, Shimizu Kenji, Murota Hiroyuki. Sirolimus Gel Treatment vs Placebo for Facial Angiofibromas in Patients With Tuberous Sclerosis Complex A Randomized Clinical Trial *JAMA DERMATOLOGY*. 2018.07; 154(7); 781-788
26. Omigawa Chika, Namiki Takeshi, Hashimoto Takashi, Miura Keiko, Yokozeki Hiroo. Cetuximab-induced epidermolysis revealed by multiple erosions. *Eur J Dermatol*. 2018.08; 28(4); 524-525
27. Miura Keiko, Namiki Takeshi, Akashi Takumi, Uemura Noriko, Mori Hiroki, Yokozeki Hiroo, Okazaki Mutsumi. Desmoplastic transformation of a nodular melanoma arising from a speckled lentiginous nevus(和訳中) *The Journal of Dermatology*. 2018.08; 45(8); e230-e231
28. Sanders Kristen M, Hashimoto Takashi, Sakai Kent, Akiyama Tasuku. Modulation of Itch by Localized Skin Warming and Cooling. *Acta Derm Venereol*. 2018.10; 98(9); 855-861
29. Hashimoto Takashi, Namiki Takeshi, Wakasa Takuya, Shimokata Miho, Yokozeki Hiroo. Dacryocystitis mimicking erysipelas due to a giant dacryolith. *J Dermatol*. 2018.10; 45(10); e272-e274

30. Ugajin T, Inazawa M, Inui K, Namiki T, Yokozeki H. A case of chronic prurigo successfully treated with omalizumab. *European journal of dermatology : EJD*. 2018.10; 28(5); 691-692
31. Hashimoto Takashi, Namiki Takeshi, Wakasa Takuya, Shimokata Miho, Yokozeki Hiroo. Dacryocystitis mimicking erysipelas due to a giant dacryolith(和訳中) *The Journal of Dermatology*. 2018.10; 45(10); e272-e274
32. Ogawa S, Namiki T, Uchida C, Nojima K, Miura K, Tanaka M, Yokozeki H. Hypomelanotic melanoma simulating pigmented Bowen's disease and its challenging dermoscopic features. *The Journal of dermatology*. 2018.10;
33. Yokozeki Hiroo, Izuhara Kenji. Two facets of sweat: A defensive factor in skin tissues and an accelerating factor for allergic skin diseases *ALLERGOLOGY INTERNATIONAL*. 2018.10; 67(4); 433-434
34. Hashimoto Takashi, Sakai Kent, Sanders Kristen M, Yosipovitch Gil, Akiyama Tasuku. Antipruritic Effects of Janus Kinase Inhibitor Tofacitinib in a Mouse Model of Psoriasis. *Acta Derm Venereol*. 2018.11;
35. Namiki Takeshi, Hashimoto Takashi, Omigawa Chika, Fujimoto Tomoko, Ugajin Tsukasa, Miura Keiko, Satoh Takahiro, Nakano Hajime, Yokozeki Hiroo. Case of generalized anhidrosis associated with diffuse reticular hyperpigmentation and syndactyly. *J Dermatol*. 2018.11;
36. Yosipovitch Gil, Rosen Jordan Daniel, Hashimoto Takashi. Itch: From mechanism to (novel) therapeutic approaches. *J Allergy Clin Immunol*. 2018.11; 142(5); 1375-1390
37. Namiki T, Nojima K, Chikazawa S, Iwamoto Y, Otsuki Y, Albusani H, Miura K, Kiyokawa Y, Asakage T, Yokozeki H. Dramatic effect of nivolumab against melanoma and immune-related liver toxicity: A detailed histopathological and immunohistochemical analysis of nivolumab-induced liver toxicity. *The Journal of dermatology*. 2018.11;
38. Tokoro S, Namiki T, Miura K, Yokozeki H. A case of isoniazid-induced pellagra aggravated by secondary anorexia presenting with an amino acid and vitamin-deficient profile. *European journal of dermatology : EJD*. 2018.12; 28(6); 832-833
39. Shimokata Miho, Namiki Takeshi, Tokoro Shown, Ugajin Tsukasa, Miura Keiko, Yokozeki Hiroo. Case of psoriasiform and pustular eruptions in addition to alopecia as a paradoxical reaction induced by infliximab *JOURNAL OF DERMATOLOGY*. 2018.12; 45(12); E331-E333
40. Shimokata Miho, Namiki Takeshi, Tokoro Shown, Ugajin Tsukasa, Miura Keiko, Yokozeki Hiroo. Case of psoriasiform and pustular eruptions in addition to alopecia as a paradoxical reaction induced by infliximab(和訳中) *The Journal of Dermatology*. 2018.12; 45(12); e331-e333
41. Hashimoto T, Yokozeki H. Occupational contact dermatitis caused by Eucalyptus species and Tanacetum parthenium. *Contact dermatitis*. 2018.12;
42. Oka Keiko, Ohtaki Noriko, Igawa Ken, Yokozeki Hiroo. Study on the correlation between age and changes in mosquito bite response *JOURNAL OF DERMATOLOGY*. 2018.12; 45(12); 1471-1474
43. Oka Keiko, Ohtaki Noriko, Igawa Ken, Yokozeki Hiroo. Study on the correlation between age and changes in mosquito bite response(和訳中) *The Journal of Dermatology*. 2018.12; 45(12); 1471-1474
44. Furusawa Emi, Noda Taisei, Komiyama Takuya, Ohno Tatsukuni, Yokozeki Hiroo, Kobayashi Katsunori, Hamamoto Hidetoshi, Miyashin Michiyo, Azuma Miyuki. Tolerance and Immune suppression-2: Antigen presentation and co-stimulation in Tolerance Silencing effects of B7-DC in cutaneous DCs on allergic skin diseases(和訳中) *日本免疫学会総会・学術集会記録*. 2018.12; 47(Proceedings); 3-C

[Books etc]

1. Takashi Hashimoto, Takahiro Satoh. *Evolution of Atopic Dermatitis in the 21st Century*. Springer Singapore, 2018.08 (ISBN : 978-981-10-5540-9)

NCCHD Child Health and Development

1. Staffs and Students

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Matsumoto, Kenji

2. Purpose of Education

The goal of this course is to learn the developmental process of human life from the viewpoints of latest molecular biology and genetics. Medical science for child health and development is the study to comprehensively grasp various health problems related to “human life cycle” to begin with the fertilization and to continue to the next generation through generation and development. Students of this course are required to understand a role and a function of medical care for child health and development, to acquire ability to handle such health problems and support relevant person with specialized theory and technique.

3. Research Subjects

1) Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells
Application studies for reproductive medicine and regenerative medicine

(Akutsu, Hidenori; Center for Regenerative Medicine, National Institute for Child Health and Development)

Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells.
Application studies for reproductive medicine and regenerative medicine.

2) Studying for cellular model in human severe disease by advancing flow cytometry

(Onodera, Masashi; Dept. of Human Genetics, National Institute for Child Health and Development)

We aim to identify causative genes for child intractable hereditary diseases and analyze their functions to develop new gene-based therapeutic options. We also establish iPS cells from peripheral blood or skin fibroblasts obtained from patients with intractable hereditary diseases such as primary immunodeficiencies and congenital metabolic disorders.

3) Elucidation of genetic abnormality in congenital severe metabolic diseases using advanced genetic analysis

(Fukami, Maki; Dept. of Molecular Endocrinology, National Institute for Child Health and Development)

Our objective is to clarify the molecular basis of congenital endocrine-related disorders and apply our findings to new innovations in clinical medicine. We investigate the molecular basis of single gene disorders, epigenetic/inprinting disorders, and multifactorial disorder.

4) Elucidating for molecular mechanism of perinatal abnormality using system biology

(Hata, Kenichiro; Dept. of Maternal-Fetal Biology, National Institute for Child Health and Development)

We aim to clarify mechanisms underlying abnormalities in fetal development and placentation, and/or perinatal diseases with developmental defects. To identify the underlying mechanisms of perinatal diseases, we take advantage of post-genomic technologies and investigate etiologies using an integrated genomic and epigenomic approach.

5) Identification of target molecules in severe diseases and establishment of disease model mice by studying molecular mechanisms of genomic imprinting, gametogenesis and sexual differentiation

(Takada, Shuji; Dept. of Systems Biomedicine, National Institute for Child Health and Development)

Our aim is to reveal the molecular mechanisms underlying embryonic development, cell differentiation and tissue formation and apply our findings to understand the causes of developmental diseases.

6) Elucidation for allergic disease mechanism and target molecules using molecular biology and ‘omics’ technology

(Matsumoto, Kenji; Dept. of Allergy and Clinical Immunology, National Institute for Child Health and Development)

Our mission is to clarify the precise pathogenic mechanisms of various immunological and allergic diseases, such as Kawasaki disease, various allergic diseases, allogeneic immune tolerance, congenital viral infections and severe infectious diseases. To achieve this, we employ various experimental approaches, including epidemiology, clinical and basic research. Our ultimate aim is to develop better means of preventing, diagnosing and treating allergic and immunological and infectious diseases based on our research findings and cumulative knowledge.

4. Publications

[Original Articles]

1. Takasawa K, Arai Y, Yamazaki-Inoue M, Toyoda M, Akutsu H, Umezawa A, Nishino K. DNA hypermethylation enhanced telomerase reverse transcriptase expression in human-induced pluripotent stem cells. *Hum Cell*. 2018; 31(1): 78-86.
2. Sugawara T, Sasaki K, Akutsu H. Organoids recapitulate organs? *Stem Cell Investig*. 2018; 5: 3.
3. Fukuda A, Umezawa A, Akutsu H. Manipulation of Xist Imprinting in Mouse Preimplantation Embryos. *Methods Mol Biol*. 2018; 1861: 47-53.
4. Nishino K, Arai Y, Takasawa K, Toyoda M, Yamazaki-Inoue M, Sugawara T, Akutsu H, Nishimura K, Ohtaka M, Nakanishi M, Umezawa A. Epigenetic-scale comparison of human iPSCs generated by retrovirus, Sendai virus or episomal vectors. *Regen Ther*. 2018; 9: 71-78.
5. Ushijima K, Yatsuga S, Matsumoto T, Nakamura A, Fukami M, Kagami M. A severely short-statured girl with 47,XX,+14/46,XX,upd(14)mat, mosaicism. *J Hum Genet*. 63(3):377-381, 2018
6. Ohsako S, Aiba T, Miyado M, Fukami M, Ogata T, Hayashi Y, Mizuno K, Kojima Y. Expression of xenobiotic biomarkers CYP1 family in preputial tissue of patients with hypospadias and its association with DNA methylation level of SRD5A2 minimal promoter. *Arch Environ Contam Toxicol*. 74(2):240-247, 2018
7. Ayabe T, Yamamoto-Hanada K, Mezawa H, Konishi M, Ishitsuka K, Saito M, Fukami M, Michikawa T, Yamazaki S, Senju A, Kusuhashi K, Kawamoto T, Sanefuji M, Kato K, Oda M, Mitsubuchi H, Katoh T, Monden Y, Mise N, Kayama F, Saito H, Ohya Y. Regional difference of infant 25OHD levels in Pilot Study of Japan Environment and Children's Study. *Pediatr Int*. 60(1):30-34, 2018
8. Shima H, Koehler K, Nomura Y, Sugimoto K, Satoh A, Ogata T, Fukami M, Jühlen R, Schuelke M, Mohnike K, Huebner A, Narumi S. Two patients with MIRAGE syndrome lacking haematological features: role of somatic second-site reversion SAMD9 mutations. *J Med Genet*. 55(2):81-85, 2018
9. Yamoto K, Okamoto S, Fujisawa Y, Fukami M, Saito H, Ogata T. FGFR1 disruption identified by whole genome sequencing in a male with a complex chromosomal rearrangement and hypogonadotropic hypogonadism. *Am J Med Genet A*. 176(1):139-143, 2018
10. Yoshii K, Naiki Y, Terada Y, Fukami M, Horikawa R. Mismatch between fetal sexing and birth phenotype: a case of complete androgen insensitivity syndrome. *Endocr J*. 65(2):221-225, 2018
11. Okuno M, Ayabe T, Yokota I, Musha I, Shiga K, Kikuchi T, Kikuchi N, Ohtake A, Nakamura A, Nakabayashi K, Okamura K, Momozawa Y, Kubo M, Suzuki J, Urakami T, Kawamura T, Amemiya S, Ogata T, Sugihara S, Fukami M. Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes. Protein-altering variants of PTPN2 in childhood-onset type 1A diabetes. *Diabet Med*. 35(3):376-380, 2018
12. Ono H, Numakura C, Homma K, Hasegawa T, Tsutsumi S, Kato F, Fujisawa Y, Fukami M, Ogata T. Longitudinal serum and urine steroid metabolite profiling in a 46,XY infant with prenatally identified POR deficiency. *J Steroid Biochem Mol Biol*. 178:177-184, 2018
13. Horikawa Y, Enya M, Komagata M, Hashimoto KI, Kagami M, Fukami M, Takeda J. Effectiveness of sodium-glucose cotransporter-2 inhibitor as an add-on drug to GLP-1 receptor agonists for glycemic control of a patient with Prader-Willi syndrome: A case report. *Diabetes Ther*. 9(1):421-426, 2018
14. Katoh-Fukui Y, Yatsuga S, Shima H, Hattori A, Nakamura A, Okamura K, Yanagi K, Iso M, Kaname T, Matsubara Y, Fukami M. An unclassified variant of CHD7 activates a cryptic splice site in a patient with CHARGE syndrome. *Hum Genome Var*. 5:18006, 2018
15. Miyado M, Muroya K, Katsumi M, Saito K, Kon M, Fukami M. Somatic acquired idic(Y) and mosaic loss of chromosome Y in a boy with hypospadias. *Cytogenet Genome Res* 154(3):122-125, 2018
16. Sekiguchi K, Itonaga T, Tomoki M, Fukami M, Yorifuji T, Ihara K. A case of CHARGE syndrome associated with hyperinsulinemic hypoglycemia in infancy. *Eur J Med Genet*. 61(6):312-314, 2018
17. Takeuchi T, Yoto Y, Ishii A, Tsugawa T, Yamamoto M, Hori T, Kamasaki H, Nogami K, Oda T, Nui A, Kimura S, Yamagishi T, Homma K, Hasegawa T, Fukami M, Watanabe Y, Sasamoto H, Tsutsumi H. Adrenocortical carcinoma characterized by gynecomastia: A case report. *Clin Pediatr Endocrinol*. 27(1):9-18, 2018
18. Ono H, Saito H, Horikawa R, Nakashima S, Ohkubo Y, Yanagi K, Nakabayashi K, Fukami M, Fujisawa Y, Ogata T. Partial androgen insensitivity syndrome caused by a deep intronic mutation creating an alternative splice acceptor site of the AR gene. *Sci Rep*. 8(1):2287, 2018
19. Igarashi M, Mizuno K, Kon M, Narumi S, Kojima Y, Hayashi Y, Ogata T, Fukami M. GATA4 mutations are uncommon in patients with 46,XY disorders of sex development without heart anomaly. *Asian J Androl*. 6(11):2229-2233, 2018
20. Nakamura A, Muroya K, Ogata-Kawata H, Nakabayashi K, Matsubara K, Ogata T, Kurosawa K, Fukami M, Kagami M. A case of paternal uniparental isodisomy for chromosome 7 associated with overgrowth. *J Med Genet*. 55(8):567-570, 2018
21. Nakamura S, Kobori Y, Ueda Y, Tanaka Y, Ishikawa H, Yoshida A, Katsumi M, Saito K, Nakamura A, Ogata T, Okada H, Nakai H, Miyado M, Fukami M. STX2 is a causative gene for non-obstructive azoospermia. *Hum Mutat*. 39(6):830-833, 2018

22. Kawasima S, Nakmura A, Inoue T, Matsubara K, Horikawa R, Wakui K, Takano K, Fikushima Y, Tatematsu T, Mizuno S, Tsubaki J, Kure S, Matsubara Y, Ogata T, [Fukami M](#), Kagami M. Maternal uniparental disomy for chromosome 20: physical and endocrinological characteristics of five patient. *J Clin Endocrinol Metab* 103(6):2083-2088, 2018
23. Montalbano A, Juergensen L, [Fukami M](#), Thiel CT, Hauer NH, Roeth R, Weiss B, Naiki Y, Ogata T, Hassel D, Rappold GA. Functional missense and splicing variants in the retinoic acid catabolizing enzyme CYP26C1 in idiopathic short stature. *Eur J Hum Genet.* 26(8):1113-1120, 2018
24. Hosono K, Nishina S, Yokoi T, Katagiri S, Saitsu H, Kurata K, Miyamichi D, Hikoya A, Mizobuchi K, Nakano T, Minoshima S, [Fukami M](#), Kondo H, Sato M, Hayashi T, Azuma N, Hotta Y. Molecular diagnosis of 34 Japanese families with Leber congenital amaurosis using targeted next generation sequencing. *Sci Rep.* 8(1):8279, 2018
25. Yoshida T, Matsuzaki T, Miyado M, Saito K, Iwasa T, Matsubara Y, Ogata T, Irahara M, [Fukami M](#). 11-oxygenated C19 steroids as circulating androgens in women with polycystic ovary syndrome. *Endocr J.* 65(10):979-990. 2018
26. Fukuhara Y, Cho SY, Miyazaki O, Hattori A, Seo JH, Mashima R, Kosuga M, [Fukami M](#), Jin DK, Okuyama T, Nishimura G. The second report on spondyloepimetaphyseal dysplasia, aggrecan type: a milder phenotype than originally reported. *Clin Dysmorphol.* 28(1):26-29, 2018.
27. [Fukami M](#). Long-term healthcare of people with disorders of sex development: Predictors of pubertal outcomes of partial androgen insensitivity syndrome. *EbioMedicine.* 37:29-30, 2018
28. Katoh-Fukui Y, Baba T, Sato T, Otake H, Nagakui-Noguchi Y, Shindo M, Suyama M, Ohkawa Y, Tsumura H, Morohashi KI, [Fukami M](#). Mouse polycomb group gene Cbx2 promotes osteoblastic but suppresses adipogenic differentiation in postnatal long bones. *Bone.* 120:219-231, 2019
29. Shima H, Hayashi M, Tachibana T, Oshiro M, Amano N, Ishii T, Haruna H, Igarashi M, Kon M, Fukuzawa R, Tanaka Y, [Fukami M](#), Hasegawa T, Narumi S. MIRAGE syndrome is a rare cause of 46,XY DSD born SGA without adrenal insufficiency. *PLoS One.* 13(11):e0206184, 2018
30. Shimizu D, Iwashima S, Sato K, Hayano S, [Fukami M](#), Saitsu H, Ogata T. GATA4 variant identified by whole-exome sequencing in a Japanese family with atrial septal defect: Implications for male sex development. *Clin Case Rep.* 6(11):2229-2233, 2018
31. Shoji K, Kawai T, [Onodera M](#), Tsutsumi Y, Nosaka S, Miyairi I. Multiple osteolytic lesions on the skull of a girl with Mendelian susceptibility to mycobacterial disease. *Pediatr Int.* 60: 1043-1044, 2018.
32. Tomono T, Hirai Y, Okada H, Miyagawa Y, Adachi K, Sakamoto S, Kawano Y, Chono H, Mineno J, Ishii A, Shimada T, [Onodera M](#), Tamaoka A, Okada T. Highly Efficient Ultracentrifugation-free Chromatographic Purification of Recombinant AAV Serotype 9. *Mol Ther Methods Clin Dev.* 11: 180-190, 2018.
33. Osumi T, Tomizawa D, Kawai T, Sako M, Inoue E, Takimoto T, Tamura E, Uchiyama T, Imadome KI, Taniguchi M, Shirai R, Yoshida M, Ando R, Tsumura Y, Fuji H, Matsumoto K, Shioda Y, Kiyotani C, Terashima K, [Onodera M](#), Matsumoto K, Kato M. A prospective study of allogeneic transplantation from unrelated donors for chronic granulomatous disease with target busulfan-based reduced-intensity conditioning. *Bone Marrow Transplant.* 2018 Jun 29. doi: 10.1038/s41409-018-0271-9. [Epub ahead of print]
34. Kamei K, Miyairi I, Ishikura K, Ogura M, Shoji K, Funaki T, Ito R, Arai K, Abe J, Kawai T, [Onodera M](#), Ito S. Prospective Study of Live Attenuated Vaccines for Patients with Nephrotic Syndrome Receiving Immunosuppressive Agents. *J Pediatr.* S0022-3476 (17) 31756-0, 2018.
35. Nishi K, Kawai T, Kubota M, Ishiguro A, [Onodera M](#). X-linked agammaglobulinemia complicated with pulmonary aspergillosis. *Pediatr Int* 1: 90-92, 2018.
36. Yamaoka M, Akiyama M, Ohyama W, Tachimoto H, [Matsumoto K](#). Acute lymphoblastic leukemia with hypereosinophilia in a 3-year-old boy. *Pediatr Int* 2018;60:88-90.
37. Yamamoto-Hanada K, Ishitsuka K, Pak K, Saito M, Ayabe T, Mezawa H, Konishi M, Yang L, [Matsumoto K](#), Saito H, Ohya Y. Allergy and mental health among pregnant women in the Japan Environment and Children's Study. *J Allergy Clin Immunol Pract* 2018;6:1421-4.
38. Yamaguchi S, Nambu A, Numata T, Yoshizaki T, Narushima S, Shimura E, Hiraishi Y, Arae K, Morita H, [Matsumoto K](#), Hisatome I, Sudo K, Nakae S. The roles of IL-17C in T cell-dependent and -independent inflammatory diseases. *Sci Rep* 2018;8:15750.
39. Tamari M, Orimo K, Motomura K, Arae K, Matsuda A, Nakae S, Saito H, Morita H, [Matsumoto K](#). The optimal age for epicutaneous sensitization following tape-stripping in BALB/c mice. *Allergol Int* 2018;67:380-7.
40. Takamori A, Nambu A, Sato K, Yamaguchi S, Matsuda K, Numata T, Sugawara T, Yoshizaki T, Arae K, Morita H, [Matsumoto K](#), Sudo K, Okumura K, Kitaura J, Matsuda H, Nakae S. IL-31 is crucial for induction of pruritus, but not inflammation, in contact hypersensitivity. *Sci Rep* 2018;8:6639.
41. Suto H, Nambu A, Morita H, Yamaguchi S, Numata T, Yoshizaki T, Shimura E, Arae K, Asada Y, Motomura K, Kaneko M, Abe T, Matsuda A, Iwakura Y, Okumura K, Saito H, [Matsumoto K](#), Sudo K, Nakae S. IL-25 enhances TH17 cell-mediated contact dermatitis by promoting IL-1beta production by dermal dendritic cells. *J Allergy Clin Immunol* 2018;142:1500-9.
42. Sugita K, Steer CA, Martinez-Gonzalez I, Altunbulakli C, Morita H, Castro-Giner F, Kubo T, Wawrzyniak P, Ruckert B, Sudo K, Nakae S, [Matsumoto K](#), O'Mahony L, Akdis M, Takei F, Akdis CA. Type 2 innate lymphoid

- cells disrupt bronchial epithelial barrier integrity by targeting tight junctions through IL-13 in asthmatic patients. *J Allergy Clin Immunol* 2018;141:300-10 e11.
43. Saito M, Yamamoto-Hanada K, Pak K, Ayabe T, Mezawa H, Ishitsuka K, Konishi M, Yang L, Matsumoto K, Saito H, Ohya Y. Having small-for-gestational-age infants was associated with maternal allergic features in the JECS birth cohort. *Allergy* 2018;73:1908-11.
44. Okada N, Nakayama T, Asaka D, Inoue N, Tsurumoto T, Takaishi S, Otori N, Kojima H, Matsuda A, Oboki K, Saito H, Matsumoto K, Yoshikawa M. Distinct gene expression profiles and regulation networks of nasal polyps in eosinophilic and non-eosinophilic chronic rhinosinusitis. *Int Forum Allergy Rhinol* 2018;8:592-604.
45. Matsumoto Y, Yokoi H, Kimura T, Kawada M, Arae K, Nakae S, Ikeda T, Matsumoto K, Sakurai H, Saito K. Gastrin-Releasing Peptide Is Involved in the Establishment of Allergic Rhinitis in Mice. *Laryngoscope* 2018;128:E377-E84.
46. Hiraishi Y, Yamaguchi S, Yoshizaki T, Nambu A, Shimura E, Takamori A, Narushima S, Nakanishi W, Asada Y, Numata T, Suzukawa M, Yamauchi Y, Matsuda A, Arae K, Morita H, Hoshino T, Suto H, Okumura K, Matsumoto K, Saito H, Sudo K, Iikura M, Nagase T, Nakae S. IL-33, IL-25 and TSLP contribute to development of fungal-associated protease-induced innate-type airway inflammation. *Sci Rep* 2018;8:18052.
47. Higaki S, Muramatsu M, Matsuda A, Matsumoto K, Satoh JI, Michikawa M, Niida S. Defensive effect of microRNA-200b/c against amyloid-beta peptide-induced toxicity in Alzheimer's disease models. *PLoS ONE* 2018;13:e0196929.
48. Fujiwara T, Weisman O, Ochi M, Shirai K, Matsumoto K, Noguchi E, Feldman R. Genetic and peripheral markers of the oxytocin system and parental care jointly support the cross-generational transmission of bonding across three generations. *Psychoneuroendocrinology* 2018;102:172-81.
49. Emi-Sugie M, Toyama S, Matsuda A, Saito H, Matsumoto K. IL-33 induces functional CCR7 expression in human mast cells. *J Allergy Clin Immunol* 2018;142:1341-4.
50. Demeais F, Margaritte-Jeannin P, Barnes KC, Cookson WOC, Altmüller J, Ang W, Barr RG, Beaty TH, Becker AB, Beilby J, Bisgaard H, Björnsdóttir US, Bleecker E, Bønnelykke K, Boomsma DI, Bouzigon E, Brightling CE, Brossard M, Brusselle GG, Burchard E, Burkart KM, Bush A, Chan-Yeung M, Chung KF, Couto Alves A, Curtin JA, Custovic A, Daley D, de Jongste JC, Del-Rio-Navarro BE, Donohue KM, Duijts L, Eng C, Eriksson JG, Farrall M, Fedorova Y, Feenstra B, Ferreira MA, Freidin MB, Gajdos Z, Gauderman J, Gehring U, Geller F, Genuneit J, Gharib SA, Gilliland F, Granell R, Graves PE, Gudbjartsson DF, Hahtela T, Heckbert SR, Heederik D, Heinrich J, Heliövaara M, Henderson J, Himes BE, Hirose H, Hirschhorn JN, Hofman A, Holt P, Hottenga J, Hudson TJ, Hui J, Imboden M, Ivanov V, Jaddoe VWV, James A, Janson C, Jarvelin M-R, Jarvis D, Jones G, Jonsdóttir I, Jousilahti P, Kabesch M, Kähönen M, Kantor DB, Karunas AS, Khusnutdinova E, Koppelman GH, Kozlarskyj AL, Kreiner E, Kubo M, Kumar R, Kumar A, Kuokkanen M, Lahousse L, Laitinen T, Laprise C, Lathrop M, Lau S, Lee Y-A, Lehtimäki T, Letort S, Levin AM, Li G, Liang L, Loefer LR, London SJ, Loth DW, Manichaikul A, Marenholz I, Martinez FJ, Matheson MC, Mathias RA, Matsumoto K, Mbarek H, McArdle WL, Melbye M, Melén E, Meyers D, Michel S, Mohamdi H, Musk AW, Myers RA, Nieuwenhuis MAE, Noguchi E, O'Connor GT, Ogorodova LM, Palmer CD, Palotie A, Park JE, Pennell CE, Pershagen G, Polonikov A, Postma DS, Probst-Hensch N, Puzyrev VP, Raby BA, Raitakari OT, Ramasamy A, Rich SS, Robertson CF, Romieu I, Salam MT, Salomaa V, Schlönsen V, Scott R, Selivanova PA, Sigsgaard T, Simpson A, Siroux V, Smith LJ, Solodilova M, Standl M, Stefansson K, Strachan DP, Stricker BH, Takahashi A, Thompson PJ, Thorleifsson G, Thorsteinsdóttir U, Tiesler CMT, Torgerson DG, Tsunoda T, Uitterlinden AG, van der Valk RJP, Vaysse A, Vedantam S, von Berg A, von Mutius E, Vonk JM, Waage J, Wareham NJ, Weiss ST, White WB, Wickman M, Widén E, Willemsen G, Williams LK, Wouters IM, Yang JJ, Zhao JH, Moffatt MF, Ober C, Nicolae DL. Multiancestry association study identifies new asthma risk loci that colocalize with immune-cell enhancer marks. *Nature Genetics* 2018;50:42-53.
51. Arae K, Morita H, Unno H, Motomura K, Toyama S, Okada N, Ohno T, Tamari M, Orimo K, Mishima Y, Suto H, Okumura K, Sudo K, Miyazawa H, Taguchi H, Saito H, Matsumoto K, Nakae S. Chitin promotes antigen-specific Th2 cell-mediated murine asthma through induction of IL-33-mediated IL-1beta production by DCs. *Sci Rep* 2018;8:11721.
52. Morita H, Kubo T, Rückert B, Ravindran A, Soyka M, Rinaldi A, Sugita K, Wawrzyniak M, Wawrzyniak P, Motomura K, Tamari M, Orimo K, Okada N, Arae K, Saito K, Altunbulakli C, Castro-Giner F, Tan G, Neumann A, Sudo K, O'Mahony L, Honda K, Nakae S, Saito H, Mjösberg J, Nilsson G, Matsumoto K, Akdis M, Akdis CA. Induction of human regulatory innate lymphoid cells from group 2 innate lymphoid cells by retinoic acid. *J Allergy Clin Immunol*. 2018 accepted.
53. Morita H, Tamari M, Fujiwara M, Motomura K, Koezuka Y, Ichien G, Matsumoto K, Ishizaka K, Saito H. IgE-class-specific immunosuppression in offspring by administration of anti-IgE to pregnant mice. *J Allergy Clin Immunol*. 2018 in press. doi:10.1016/j.jaci.2018.11.008.
54. Sato T, Migita O, Hata H, Okamoto A, Hata K : Analysis of Chromosome Microstructures in Products of Conception Associated with Recurrent Miscarriage. *Reprod Biomed Online*. 2018. doi: 10.1016/j.rbmo.2018.12.010. [Epub ahead of print]
55. Kabata R, Okuda H, Noguchi A, Kondo D, Fujiwara M, Hata K, Kato Y, Ishikawa K, Tanaka M, Sekine Y, Hishikawa N, Mizukami T, Ito J, Akasaka M, Sakurai K, Yoshida T, Minoura H, Hayashi T, Inoshita K, Matsuyama

- M, Kinjo N, Cao Y, Inoue S, Kobayashi H, Harada KH, Youssefian S, Takahashi T, Koizumi A : Familial episodic limb pain in kindreds with novel Nav1.9 mutations. *PLoS One*. 2018;13:e0208516
56. Narumi-Kishimoto Y, Araki N, Migita O, Kawai T, Okamura K, Nakabayashi K, Kaname T, Ozawa Y, Ozawa H, Takada F, Hata K : Novel SIN3A mutation identified in a Japanese patient with Witteveen-Kolk syndrome. *Eur J Med Genet*. 2018. doi: 10.1016/j.ejmg.2018.09.014. [Epub ahead of print]
 57. Kasuga Y, Miyakoshi K, Tajima A, Saisho Y, Ikenoue S, Ochiai D, Matsumoto T, Arata N, Hata K, Tanaka M : Clinical and Genetic Characteristics of Abnormal Glucose Tolerance in Japanese Women in the First Year after Gestational Diabetes Mellitus. *J Diabetes Investig*. 2018. doi: 10.1111/jdi.12935. [Epub ahead of print]
 58. Katoh N, Kuroda K, Tomikawa J, Ogata-Kawata H, Ozaki R, Ochiai A, Kitade M, Takeda S, Nakabayashi K, Hata K : Reciprocal changes of H3K27ac and H3K27me3 at the promoter regions of the critical genes for endometrial decidualization. *Epigenomics*. 2018;10:1243-1257
 59. Sato T, Samura O, Matsuoka T, Yoshida M, Aoki H, Migita O, Okamoto A, Hata K : Molecular genetic analysis reveals atypical confined placental mosaicism with a small supernumerary marker chromosome derived from chromosome 18: A clinical report of discordant results from three prenatal tests. *Eur J Med Genet*. 2018. doi: 10.1016/j.ejmg.2018.08.014. [Epub ahead of print]
 60. Hernandez Mora JR, Tayama C, Sánchez-Delgado M, Monteagudo-Sánchez A, Hata K, Ogata T, Medrano J, Poo-Llanillo ME, Simón C, Moran S, Esteller M, Tenorio J, Lapunzina P, Kagami M, Monk D, Nakabayashi K : Characterization of parent-of-origin methylation using the Illumina Infinium MethylationEPIC array platform. *Epigenomics*. 2018;10:941-954
 61. Osumi T, Tsujimoto SI, Tamura M, Uchiyama M, Nakabayashi K, Okamura K, Yoshida M, Tomizawa D, Watanabe A, Takahashi H, Hori T, Yamamoto S, Hamamoto K, Migita M, Ogata-Kawata H, Uchiyama T, Kizawa H, Ueno-Yokohata H, Shirai R, Seki M, Ohki K, Takita J, Inukai T, Ogawa S, Kitamura T, Matsumoto K, Hata K, Kiyokawa N, Goyama S, Kato M : Recurrent RARB Translocations in Acute Promyelocytic Leukemia lacking RARA Translocation. *Cancer Res*. 2018;78:4452-4458
 62. Okano S, Miyamoto A, Fukuda I, Tanaka H, Hata K, Kaname T, Matsubara Y, Makita Y : Genitopatellar syndrome: the first reported case in Japan. *Hum Genome Var*. 2018;5:8
 63. Sato T, Samura O, Kato N, Taniguchi K, Takahashi K, Ito Y, Aoki H, Kobayashi M, Migita O, Okamoto A, Hata K : Novel TFAP2A mutation in a Japanese family with Branchio-oculo-facial syndrome. *Hum Genome Var*. 2018;5:5
 64. Usui H, Nakabayashi K, Kaku H, Maehara K, Hata K, Shozu M : Elucidation of the developmental mechanism of ovarian mature cystic teratomas using B allele-frequency plots of single nucleotide polymorphism array data. *Genes Chromosomes Cancer*. 2018;57:409-419
 65. Matsushita J, Okamura K, Nakabayashi K, Suzuki T, Horibe Y, Kawai T, Sakurai T, Yamashita S, Higami Y, Ichihara G, Hata K, Nohara K : The DNA methylation profile of liver tumors in C3H mice and identification of differentially methylated regions involved in the regulation of tumorigenic genes. *BMC Cancer*. 2018;18:317
 66. Yoshida W, Saikyo H, Nakabayashi K, Yoshioka H, Bay DH, Iida K, Kawai T, Hata K, Ikebukuro K, Nagasawa K, Karube I : Identification of G-quadruplex clusters by high-throughput sequencing of whole-genome amplified products with a G-quadruplex ligand. *Sci Rep*. 2018;8:3116
 67. Mizuguchi T, Nakashima M, Kato M, Okamoto N, Kurahashi H, Ekhilevitch N, Shiina M, Nishimura G, Shibata T, Matsuo M, Ikeda T, Ogata K, Tsuchida N, Mitsuhashi S, Miyatake S, Takata A, Miyake N, Hata K, Kaname T, Matsubara Y, Saitsu H, Matsumoto N : Loss-of-function and gain-of-function mutations in PPP3CA cause two distinct disorders. *Hum Mol Genet*. 2018;27:1421-1433
 68. Miyashita N, Onozawa M, Hayasaka K, Yamada T, Migita O, Hata K, Okada K, Goto H, Nakagawa M, Hashimoto D, Kahata K, Kondo T, Kunishima S, Teshima T : A novel heterozygous ITGB3 p.T720del inducing spontaneous activation of integrin α IIb β 3 in autosomal dominant macrothrombocytopenia with aggregation dysfunction. *Ann Hematol*. 2018;97:629-640
 69. Osumi T, Tsujimoto SI, Nakabayashi K, Taniguchi M, Shirai R, Yoshida M, Uchiyama T, Nagasawa J, Goyama S, Yoshioka T, Tomizawa D, Kurokawa M, Matsubara Y, Kiyokawa N, Matsumoto K, Hata K, Kato M : Somatic MECOM mosaicism in a patient with congenital bone marrow failure without a radial abnormality. *Pediatr Blood Cancer*. 2018;65:e26959
 70. Isobe T, Seki M, Yoshida K, Sekiguchi M, Shiozawa Y, Shiraishi Y, Kimura S, Yoshida M, Inoue Y, Yokoyama A, Kakiuchi N, Suzuki H, Kataoka K, Sato Y, Kawai T, Chiba K, Tanaka H, Shimamura T, Kato M, Iguchi A, Hama A, Taguchi T, Akiyama M, Fujimura J, Inoue A, Ito T, Deguchi T, Kiyotani C, Iehara T, Hosoi H, Oka A, Sanada M, Tanaka Y, Hata K, Miyano S, Ogawa S, Takita J : Integrated molecular characterization of the lethal pediatric cancer pancreatoblastoma. *Cancer Res*. 2018;78:865-876
 71. Ushijima K, Fukami M, Ayabe T, Narumi S, Okuno M, Nakamura A, Takahashi T, Ihara K, Ohkubo K, Tachikawa E, Nakayama S, Arai J, Kikuchi N, Kikuchi T, Kawamura T, Urakami T, Hata K, Nakabayashi K, Matsubara Y, Amemiya S, Ogata T, Yokota I, Sugihara S; Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes. : Comprehensive screening for monogenic diabetes in 89 Japanese children with insulin-requiring antibody-negative type 1 diabetes. *Pediatr Diabetes*. 2018;19:243-250
 72. Takasawa K, Gau M, Sutani A, Igarashi M, Ono M, Takemoto A, Takada S, Yamataka A, Ogata T, Morio T, Fukami M, Kashimada K: Phenotypic variation in 46,XX disorders of sex development due to the NR5A1 p.R92W variant: a sibling case report and literature review. *Sexual Development*, 11(5-6):284-288 (2018).

73. Inui M, Mokuda S, Sato T, Tamano M, Takada S, Asahara H: Dissecting the roles of miR-140 and its host gene. *Nature Cell Biology*, 20(5):516-518 (2018).
74. Saito T, Hara S, Kato T, Tamano M, Muramatsu A, Asahara H, Takada S: A tandem repeat array in IG-DMR is essential for imprinting of paternal allele at the Dlk1-Dio3 domain during embryonic development. *Human Molecular Genetics*, 27(18):3283-3292 (2018).
75. Tsuji-Hosokawa A, Kashimada K, Kato T, Ogawa Y, Nomura R, Takasawa K, Lavery R, Coschiera A, Schlessinger D, Harley VR, Takada S, Morio T: Peptidyl arginine deiminase 2 (Padi2) is expressed in Sertoli cells in a specific manner and regulated by SOX9 during testicular development. *Scientific Reports*, 8(1):13263 (2018).
76. Ogawa Y, Terao M, Hara S, Tamano M, Okayasu H, Kato T, Takada S: Mapping of a responsible region for sex reversal upstream of Sox9 by production of mice with serial deletion in a genomic locus. *Scientific Reports*, 8(1):17514 (2018).

[Review Articles]

1. Fukami M, Suzuki E, Igarashi M, Miyado M, Ogata T. Gain-of-function mutations in G-protein coupled receptor genes associated with human endocrine disorders. *Clin Endocrinol*. 88(3):351-359, 2018
2. Matsubara K, Kagami M, Fukami M. Uniparental disomy as a cause of pediatric endocrine disorders. *Clin Pediatr Endocrinol* ;27(3):113-121, 2018
3. Hara S, Takada S: Genome editing for the reproduction and remedy of human diseases in mice. *Journal of Human Genetics*, 63(2):107-113 (2018).

[Books]

1. Fukami M, Kurahashi H. Clinical consequences of chromothripsis and other catastrophic cellular events. In Pellestor F ed. *Chromothripsis*. Springer 2017

[Conference Activities & Talks]

1. Fukami M. Delayed puberty. In: Meet-the-Expert session. 16th Asia-Oceania Congress of Endocrinology, 29 September 2018, Yogyakarta, Indonesia.
2. Fukami M. Molecular basis of disorders of sex development. In: Meet-the-Expert session. 16th Asia-Oceania Congress of Endocrinology, 30 September 2018, Yogyakarta, Indonesia.
3. Fukami M. Molecular basis of disorders of sex development. In: International Workshop for Sex Development. 23 July 2018 Tokyo

Human Pathology

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(1) Outline

Pathology in a medical department used to be the general study field about human disease. Later, Microbiology and Parasitology had been separated from the field of Pathology. Lately, interdisciplinary of traditional study field had been advanced and new specific academic disciplines are developed. Pathology is currently under the same trend. Basic divisions such as Experimental and Cell Biological pathology are becoming independent from the clinicopathological field. Thus, Human Pathology has become the main category of pathology.

The principles of Human Pathology are to educate clinical pathologists with accurate pathological diagnosis skills of human disease, to research theses that are directly related to human disease, and to educate pathological researchers with ability to perform such research.

(2) Research

1) Endogenous infection (diseases caused by indigenous microorganisms in susceptible hosts)

2) Cancer research (histopathology, carcinogenesis, prognostic factors, and so on)

(3) Education

In the course, they usually spend the first two years for anatomical pathology training, searching for their own research theme and another two years for researches and thesis-writing.

(4) Lectures & Courses

Department of Human Pathology provides a graduate course for future pathologists to train the skills and knowledge of anatomical pathology and develop the abilities for medical researches. Graduate students are educated to associate their researches with problems in diagnosis and treatment of diseases and etiologies of the diseases of unknown causes.

(5) Clinical Performances

After the Meiji Era, the department of Human Pathology in medical faculty belonged under the basic medical sciences; however, Pathology in the existing hospitals is essentially the clinical medicine. Diagnosis of patients in each clinical department is done by taking the biopsy of diseased tissues or collecting the cell samples by either endoscope or surgery. Then, the lesions are analyzed with the microscope, and pathological diagnosis is reported to the clinical departments. The samples of organs and tissues taken from the surgery are used to study the spread of the lesion and its characteristics, and also to examine the adequacy of surgery. It is also used to determine future treatment policy. During the course of patients' treatments, sample tissues are taken periodically and are analyzed pathologically to see therapeutic effect. If a patient has unfortunately joined the majority, morbid anatomy is done by the pathologists along with the patient's attending physician. They study the resulting effects of laboratory findings and choice of treatment, and improve the future diagnosis and treatments. The department of Human Pathology and Surgical Pathology technically work as one although they are separated in this university's organizational structure. Human Pathology does not directly work with the patients; however, it is involved directly with the diagnosis as well as the treatments. Strong cooperation between clinicians and pathologists is essential for the best practice, and is required for the university hospital as an "advanced treatment hospital." Therefore, doctors of Human Pathology study, research and practice pathology to be the great pathologists so-called the "doctor of doctors."

(6) Publications

[Original Articles]

1. Yoshimi Suzuki, Keisuke Uchida, Tamiko Takemura, Masaki Sekine, Tomoki Tamura, Asuka Furukawa, Akira Hebisawa, Yumi Sakakibara, Nobuyasu Awano, Tomonari Amano, Daisuke Kobayashi, Mariko Negi, Tomoya Kakegawa, Yuriko Wada, Takashi Ito, Takashige Suzuki, Takumi Akashi, Yoshinobu Eishi. Propionibacterium acnes-derived insoluble immune complexes in sinus macrophages of lymph nodes affected by sarcoidosis. PLoS ONE. 2018.02; 13(2); e0192408
2. Yamada Ichiro, Sakamoto Junichiro, Kobayashi Daisuke, Miyasaka Naoyuki, Wakana Kimio, Oshima Noriko, Wakabayashi Akira, Saida Yukihisa, Tateishi Ukihide, Eishi Yoshinobu. 子宮及び子宮内膜癌の Diffusion Kurtosis Imaging による評価 病理組織学的所見との対比 (Diffusion Kurtosis Imaging of the Uterus and Endometrial Carcinoma: Correlation with Histopathologic Findings) 日本医学放射線学会学術集会抄録集. 2018.02; 77 回; S296
3. Yamada Ichiro, Wakana Kimio, Kobayashi Daisuke, Miyasaka Naoyuki, Oshima Noriko, Wakabayashi Akira, Saida Yukihisa, Tateishi Ukihide, Eishi Yoshinobu. 子宮及び子宮内膜癌の Diffusion-Tensor Imaging による評価 免疫組織化学的所見との比較 (Diffusion-Tensor Imaging of the Uterus and Endometrial Carcinoma: Comparison with Immunohistochemical Findings) 日本医学放射線学会学術集会抄録集. 2018.02; 77 回; S193
4. Yamada I, Hikishima K, Yoshino N, Sakamoto J, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using q-space imaging; correlation with histopathologic findings. J Magn Reson Imaging. 2018.03; 48(4); 1059-1068
5. Shintaro Akiyama, Masakazu Nagahori, Shinya Oooka, Mariko Negi, Takashi Ito, Kento Takenaka, Kazuo Ohtsuka, Mamoru Watanabe. Small intestinal obstruction due to the metastasis of intrahepatic cholangiocarcinoma: A case report. Medicine (Baltimore). 2018.03; 97(12); e0190
6. Kenro Kawada, Taro Sugimoto, Ryuhei Okada, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuuichiro Kume, Andres Mora, Tairo Ryotokuji, Takuta Okada, Akihiro Hoshino, Yutaka Tokairin, Yausaki

- Nakajima, Yusuke Kiyokawa, Fuminori Nomura, Yosuke Ariizumi, Shohei Tomii, Takashi Ito, Takahiro Asakage, Yusuke Kinugasa, Tatsuyuki Kawano. A case of simultaneous triple primary cancers of the hypopharynx, esophagus and stomach which were dissected by endoscopic laryngo-pharyngeal surgery combined with endoscopic submucosal dissection *Open Journal of Gastroenterology*. 2018.03; 8(3); 94-102
7. Manabu Sema, Yasunari Miyazaki, Toshiharu Tsutsui, Makoto Tomita, Yoshinobu Eishi, Naohiko Inase. Environmental levels of avian antigen are relevant to the progression of chronic hypersensitivity pneumonitis during antigen avoidance. *Immun Inflamm Dis*. 2018.03; 6(1); 154-162
 8. Yuriko Wada, Kosuke Takemura, Padmaja Tummala, Keisuke Uchida, Keisuke Kitagaki, Asuka Furukawa, Yuuki Ishige, Takashi Ito, Yukichi Hara, Takashige Suzuki, Hitomi Mimuro, Philip G Board, Yoshinobu Eishi. *Helicobacter pylori* induces somatic mutations in TP53 via overexpression of CHAC1 in infected gastric epithelial cells. *FEBS Open Bio*. 2018.03; 8(4); 671-679
 9. Guang Yang, Yoshinobu Eishi, Anwar Raza, Heather Rojas, Adina Achiriloaie, Kenneth De Los Reyes, Ravi Raghavan. *Propionibacterium acnes*-associated neurosarcoidosis: A case report with review of the literature. *Neuropathology*. 2018.04; 38(2); 159-164
 10. Takuya Okada, Kenro Kawada, Taro Sugimoto, Takashi Ito, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuichiro Kume, Tairo Ryotokuji, Akihiro Hoshino, Yutaka Tokairin & Yasuaki Nakajima. Asymptomatic marginal zone lymphoma of mucosa-associated lymphoid tissue in the hypopharynx, detected with esophagogastroduodenoscopy *Acta Oto-Laryngologica Case Reports*. 2018.05; 3(1); 19-23
 11. Nakano T, Tamura K, Tanaka Y, Inaji M, Hayashi S, Kobayashi D, Nariai T, Toyohara J, Ishii K, Maehara T. Usefulness of ^{11}C -Methionine Positron Emission Tomography for Monitoring of Treatment Response and Recurrence in a Glioblastoma Patient on Bevacizumab Therapy: A Case Report. *Case reports in oncology*. 2018.05; 11(2); 442-449
 12. Keiko Miura, Takumi Akashi, Noboru Ando, Shinya Ayabe, Kou Kayamori, Takeshi Namiki, Yoshinobu Eishi. Homeobox transcriptional factor engrailed homeobox 1 is expressed specifically in normal and neoplastic sweat gland cells. *Histopathology*. 2018.06; 72(7); 1199-1208
 13. Maki Kobayashi; Hiroshi Kawachi; Samara Pasternak; Carlos Delgado; Pablo Pinto; Takashi Ito; Stanko Karelovic; Hernan Carrasco; Koji Tanaka; Takuya Okada; Tomoyuki Odagaki; Alejandro J. Zárate; Alejandra Ponce; Udo Kronberg; Francisco López-Köstner; Masahiro Tsubaki; Tatsuyuki Kawano; Yoshinobu Eishi. Histopathologic study from a colorectal cancer screening in Chile *European Journal of Cancer Prevention*. 2018.06; Epub ahead;
 14. G Amodini Rajakaruna, Mariko Negi, Keisuke Uchida, Masaki Sekine, Asuka Furukawa, Takashi Ito, Daisuke Kobayashi, Yoshimi Suzuki, Takumi Akashi, Makoto Umeda, Walter Meinzer, Yuichi Izumi, Yoshinobu Eishi. Localization and density of *Porphyromonas gingivalis* and *Tannerella forsythia* in gingival and subgingival granulation tissues affected by chronic or aggressive periodontitis. *Sci Rep*. 2018.06; 8(1); 9507
 15. Pathological features of carcinoma within anal fistula *Stomach and Intestine*. 2018.06; 53(7); 967-973
 16. Ozaki K, Ohkubo T, Yamada T, Yoshioka K, Ichijo M, Majima T, Kudo S, Akashi T, Honda K, Ito E, Watanabe M, Sekine M, Hamagaki M, Eishi Y, Sanjo N, Ishibashi S, Mizusawa H, Yokota T. Progressive Encephalomyelitis with Rigidity and Myoclonus Resolving after Thymectomy with Subsequent Anasarca: An Autopsy Case. *Internal medicine (Tokyo, Japan)*. 2018.07;
 17. Kobayashi M, Kawachi H, Hurtado C, Wielandt AM, Ponce A, Karelovic S, Pasternak S, Delgado C, Pinto P, Carrasco H, Ito T, Okada T, Tanaka K, Odagaki T, Zárate AJ, Kronberg U, López-Köstner F, Tsubaki M, Kawano T, Eishi Y.. A Pilot Trial to Quantify Plasma Exosomes in Colorectal Cancer Screening from the International Collaborative Study between Chile and Japan *Digestion*. 2018.08; 98(4); 270-274
 18. Hiroyuki Takama, Takeshi Yanagishita, Jun Muto, Yuichiro Ohshima, Emiko Takahashi, Toyonori Tsuzuki, Keisuke Uchida, Yoshinobu Eishi, Masashi Akiyama, Daisuke Watanabe. Granulomatous pigmented purpuric dermatosis containing *Propionibacterium acnes*. *Eur J Dermatol*. 2018.08; 28(4); 540-542
 19. Makoto Kodama, Daisuke Kobayashi, Kuniko Iihara, Keiko Abe, Rikisaburo Sahara, Motoki Sassa, Tetsuo Yamana, Satomi Furukawa, Takashi Yao, Keisuke Uchida, Tomoki Tamura, Mariko Negi, Yoshinobu Eishi. Adenocarcinoma within anorectal fistulae: different clinicopathological characteristics between Crohn's disease-associated type and the usual type. *Mod. Pathol.*. 2018.09;

20. Kohei Ishibashi, Yoshinobu Eishi, Nobuhiro Tahara, Masanori Asakura, Naka Sakamoto, Kazufumi Nakamura, Yoichi Takaya, Tomohisa Nakamura, Yoshikazu Yazaki, Tetsuo Yamaguchi, Koko Asakura, Toshihisa Anzai, Teruo Noguchi, Satoshi Yasuda, Fumio Terasaki, Toshimitsu Hamasaki, Kengo Kusano. Japanese Antibacterial Drug Management for Cardiac Sarcoidosis (J-ACNES): A multicenter, open-label, randomized, controlled study. *J Arrhythm.* 2018.10; 34(5); 520-526
21. Ichiro Yamada, Kimio Wakana, Daisuke Kobayashi, Naoyuki Miyasaka, Noriko Oshima, Akira Wakabayashi, Yukihisa Saida, Ukihide Tateishi, Yoshinobu Eishi. Endometrial carcinoma: Evaluation using diffusion-tensor imaging and its correlation with histopathologic findings. *J Magn Reson Imaging.* 2018.11;
22. Mitsumura T, Ito Y, Chiba T, Matsushima T, Kurimoto R, Tanaka Y, Kato T, Uchida K, Ito T, Yamamoto K, Eishi Y, Kitagawa M, Miyazaki Y, Inase N, Asahara H. Ablation of miR-146b in mice causes hematopoietic malignancy. *Blood advances.* 2018.12; 2(23); 3483-3491
23. Maiko Motobayashi, Katsuyoshi Matsuoka, Kento Takenaka, Toshimitsu Fujii, Masakazu Nagahori, Kazuo Ohtsuka, Fumihiko Iwamoto, Kiichiro Tsuchiya, Mariko Negi, Yoshinobu Eishi, Mamoru Watanabe. Predictors of mucosal healing during induction therapy in patients with acute moderate-to-severe ulcerative colitis.[Epub ahead of print] *J. Gastroenterol. Hepatol.* 2018.12;

Physiology and Cell Biology

Junior associate professor: Shingo Sato

Assistant professor: Hiroki Ochi

Assistant professor: Satoko Sunamura

(1) Outline

Recent progress in molecular biology and genetics advanced our understanding of molecular basis of physiological function and pathophysiological mechanisms of various diseases. Besides, signal transduction system using intercellular, intersystem, and inter-organ networks has been shown to be essential for whole-body homeostatic function. In our department, we are studying on the inter-organ regulatory networks of metabolism, especially between bone and the other organs.

(2) Research

1. Studies on the regulatory network of metabolism between bone and the other internal organs: It had been believed that bone is controlled by local environment through the action of hormones and cytokines, independently of the other organs. However, our discovery that leptin regulates bone formation through the central nervous system shed light on a new regulatory system of bone metabolism, i.e., neuronal control (Takeda S, Cell, 2002, Nature, 2005). In addition, we have also demonstrated that neuromedin U, an anorexigenic neuropeptide, regulates bone formation through the central nervous system (Sato S, Nat Med, 2007). Moreover, recent studies have revealed that FGF23 or osteocalcin, which is secreted by bone, regulates the metabolism of kidney or pancreas. Thus, bone is now considered as a major player for whole-body homeostasis, and forms a regulatory network of metabolism together with the other organs. We are now conducting further experiments to clarify a comprehensive network between bone and the other organs.

2. Studies on the regulation of bone metabolism by sensory nerves: We have recently revealed that sensory nerves inside bones have a crucial role in regulating bone mass, and that the penetration of sensory nerves into bones is necessary for normal bone development or fracture healing (Fukuda T, Nature, 2013). Based on these findings, we are now conducting further experiments to develop novel therapeutic approaches to osteoporosis.

3. Studies on the regulation of bone metabolism and bone metastasis by microRNA: microRNA (miRNA) is a small non-coding RNA molecule, and regulates various developmental and homeostatic events in vertebrates and invertebrates. Aberrant expression of miRNA has been implicated in numerous disease states, and miRNA-based therapies are under investigation. We have previously demonstrated the physiological role of miRNA in osteoblast differentiation (PNAS, 2009). We also investigated the role of miRNA in bone metastatic microenvironment and recently demonstrated that bone metastatic lesions could be regulated by miRNAs secreted by cancer cells (Sato S, Hashimoto K, PNAS, 2018). We are now conducting further experiments to identify novel miRNAs regulating bone metabolism or bone metastasis and to develop new diagnostic or therapeutic approaches.

4. Studies on the mechanical regulation of musculoskeletal system: In Japan, the number of patients with osteoporosis or sarcopenia have rapidly increased. Mechanical stress is known to be essential for the maintenance of bone volume or muscle strength. However, the mechanism of the mechanical regulation remains elusive. We are now elucidating the role of gravity on bone or muscle homeostasis as well as on neurovascular formation in

bone or muscle tissues by utilizing a tail suspension mouse model.

5. Studies on the mechanism in the development of bone and soft tissue sarcomas: Sarcomas are malignancies derived from mesenchymal tissues such as bone, muscle, fat, and cartilage. Molecular mechanisms in the occurrence and growth of sarcomas have yet to be elucidated. Even the cell of origin for most sarcomas still remains unclear. We have recently established a novel mouse model for osteosarcoma and also demonstrated that sarcomas could be derived from pericytes with mutations of crucial genes. Based on these findings, we are now conducting further experiments to elucidate the detailed mechanism of sarcoma development.

(3) Education

We give lectures and laboratory teachings about physiology to sophomore medical students. We also teach experimental techniques to undergraduate students to develop young basic scientists. PhD students are required to join our research team and learn various experimental techniques including molecular biology, cellular biology, and physiology.

(4) Lectures & Courses

All students are expected to understand the background of the research field and bring up relevant scientific questions to verify the hypothesis. They are also expected to develop their scientific thinking with effective questions and cultivate their abilities to analyze obtained results objectively, discuss them logically and scientifically, and present them effectively.

(5) Publications

[Original Articles]

1. H Tanoue, J Morinaga, T Yoshizawa, M Yugami, H Itoh, T Nakamura, Y Uehara, T Masuda, H Odagiri, T Sugizaki, T Kadomatsu, K Miyata, M Endo, K Terada, H Ochi, S Takeda, K Yamagata, T Fukuda, H Mizuta, Y Oike. Angiopoietin-like protein 2 promotes chondrogenic differentiation during bone growth as a cartilage matrix factor. *Osteoarthr. Cartil.* 2018.01; 26(1); 108-117
2. Kyoko Hashimoto, Hiroki Ochi, Satoko Sunamura, Nobuyoshi Kosaka, Yo Mabuchi, Toru Fukuda, Kenta Yao, Hiroaki Kanda, Keisuke Ae, Atsushi Okawa, Chihiro Akazawa, Takahiro Ochiya, Mitsuru Futakuchi, Shu Takeda, Shingo Sato. Cancer-secreted hsa-miR-940 induces an osteoblastic phenotype in the bone metastatic microenvironment via targeting ARHGAP1 and FAM134A. *Proc. Natl. Acad. Sci. U.S.A.* 2018.02; 115(9); 2204-2209
3. Guangwen Jin, Alkebaier Aobulikasimu, Jinying Piao, Zulipiya Aibibula, Daisuke Koga, Shingo Sato, Hiroki Ochi, Kunikazu Tsuji, Tetsuo Nakabayashi, Toshio Miyata, Atsushi Okawa, Yoshinori Asou. A small-molecule PAI-1 inhibitor prevents bone loss by stimulating bone formation in a murine estrogen deficiency-induced osteoporosis model. *FEBS Open Bio.* 2018.02; 8(4); 523-532
4. Shingo Sato. New findings of the mechanism of bone metastasis and possibility for drug discovery PHARM STAGE. 2018.06; 18(3); 54-58
5. Jin Guangwen, Aobulikasim Alkebaier, Piao Jinying, Aibibula Zulipiya, Koga Daisuke, Ochi Hiroki, Ishiyama Kirika, Kanno Taro, Niwano Yoshimi, Okawa Atsushi, Asou Yoshinori. Proanthocyanidin-rich grape seed extract prevent estrogen deficiency-induced metabolic disorders *Journal of Medical and Dental Sciences.* 2018.06; 65(2); 45-50
6. S Arima, H Ochi, M Mitsuhashi, R Kibe, K Takahashi, Y Kataoka. *Staphylococcus pseudintermedius* biofilms secrete factors that induce inflammatory reactions in vitro. *Lett. Appl. Microbiol.* 2018.09; 67(3); 214-219
7. Shingo Sato. Cancer-secreted microRNAs induce osteoblastic bone metastasis *Orthopedic Surgery.* 2018.09; 69(11); 1124

8. Aobulikasimu Aikebaier, Aibibula Zulipiya, Piao Jinying, Sato Shingo, Ochi Hiroki, Tsuji Kunikazu, Okawa Atsushi, Asou Yoshinori. Osteocyte Sirt6 has crucial roles in bone and phosphate metabolism JOURNAL OF BONE AND MINERAL RESEARCH. 2018.11; 33; 97-98
9. Akira Takahashi, Mieradili Mulati, Masanori Saito, Hoashi Numata, Yutaka Kobayashi, Hiroki Ochi, Shingo Sato, Philipp Kaldis, Atsushi Okawa, Hiroyuki Inose. Loss of cyclin-dependent kinase 1 impairs bone formation, but does not affect the bone-anabolic effects of parathyroid hormone. J. Biol. Chem.. 2018.12; 293(50); 19387-19399

[Conference Activities & Talks]

1. Shingo Sato, Kyoko Hashimoto, Hiroki Ochi, Satoko Sunamura, Atsushi Okawa, Mitsuru Futakuchi, Shu Takeda. Cancer-secreted Hsa-miR-940 Induces Osteoblastic Phenotype in the Bone Metastatic Microenvironment. Orthopaedic Research Society Annual Meeting 2018 2018.03.10 New Orleans, USA
2. Shingo Sato. Tumor-stromal interaction during bone metastasis.. 8th Seoul Breast Cancer 2018 2018.06.16 Seoul National University Hospital, Korea
3. Shingo Sato. Early treatment for bone metastasis by orthopaedics-centered multidisciplinary treatment approach. The 51th Annual Musculoskeletal Tumor Meeting of the Japanese Orthopaedic Association 2018.07.13 Shizuoka
4. Shingo Sato. The preventive effect of jaw osteonecrosis by medical and dental combined bone metastasis treatment approach. The 51th Annual Musculoskeletal Tumor Meeting of the Japanese Orthopaedic Association 2018.07.13 Shizuoka
5. Alkebaier Aobulikasimu, Zulipiya Aibibula, Jinying Piao, Shingo Sato, Hiroki Ochi, Kunikazu Tsuji, Atsushi Okawa, Yoshinori Asou. Osteocyte Sirt6 has crucial roles in bone and phosphate metabolism. American Society for Bone and Mineral Research (ASBMR) 2018 Annual Meeting 2018.09.28 Montreal, Quebec, Canada
6. Shingo Sato. Bone metastasis. Juntendo Orthopedic Oncology Collaboration (JOOC) 2018.12.08 Juntendo University, Tokyo

Molecular Cellular Cardiology

Professor	Tetsushi Furukawa
Associate professor	Jun Takeuchi
Assistant professor	Kensuke Ihara
Post-doc (PD)	Yoshitake Higashijima
Post-doc	Masahiro Yamazoe
Post-doc	Hiroko Kushige
D3	Xiaoki Yang
D3(Department of Pediatrics)	Yohei Yamaguchi
D2(Department of Dental Anesthetics)	Keiko Abe
D1	Sun Yihan
D1	Nodoka Yanagi
M1	Sae Kakeno
M1	Hiroaki Komuro
Technician	Reiko Kimura
Secretary	Yukiko Takakura
Secretary	Akemi Oshikiri

(1) Outline

This laboratory focuses on understanding pathogenesis of intractable and common cardiovascular diseases using multidisciplinary approach (patch-clamp, cell biology, optical recording, genetic analysis, and computational analysis). Our ultimate goal is to improve diagnosis and management of intractable and common cardiovascular diseases.

(2) Research

1. Highlight: Electrophysiological Assessment of Murine heart with High-Resolution Optical Mapping

Conventional optical mapping of murine heart, especially of its atria, has some critical problems due to its small size. To overcome them, we developed the novel electrophysiological assessment method for elucidating the underlying mechanism of arrhythmogenesis using murine heart by combining high spatial and temporal resolution optical mapping system and precise electrophysiological study (J. Vis. Exp 2018). This novel method will contribute to assessing the onset and maintenance mechanism of arrhythmias precisely in various mouse models.

2. Biological pacemaker utilizing in vivo genome editing

In the current clinical medicine, the only therapy for bradycardia is the electrical pacemaker, which has many serious problems such as battery longevity, device infection. As an alternative, biological pacemaker has been studied for decades. Previous attempts to make biological pacemaker by gene delivery had a limitation that the effect was transient. Application of genome editing by CRISPR/Cas9 is expected to generate permanent gene knockout. We found that in vivo genome editing can generate pacemaker activity, and are now optimizing this technique for better efficacy.

3. Systemic inflammation accompanied with atrial fibrillation

Various inflammatory markers and mediators such as c-reactive protein (CRP) and pro-inflammatory cytokines have been reported to be linked with the presence and outcome of atrial fibrillation (AF). These systemic inflammatory responses could cause and worsen not only AF related systemic dysfunctions including coagulation activity and endothelial dysfunctions, but also AF pathogenesis through atrial electrical and structural remodeling. However, the underlying mechanism why AF is accompanied with systemic inflammation remains to be elucidated.

We focused the nucleic acid circulating in blood as potential contributor for systemic inflammation accompanied with AF. First, we found that AF patients had higher nucleic acid levels in plasma compared with non-AF subjects. We also confirmed this finding in AF mimicking models; rapid tachycardia stimulation for cultured atrial cardiomyocytes, and murine right atrium. Second, we observed that nucleic acid promoted IL-1 β and IL-6 expression in macrophages and clarified its signal pathway. Additionally, we identified the essential characters of nucleic acids in inducing pro-inflammatory cytokines in macrophages. Taken together, we revealed the potential contributor for systemic inflammation accompanied with AF, suggesting the circulating nucleic acid might be the novel biomarker for AF occurrence and development.

4. Understanding the mechanisms of heart induction and its compartment

The mammalian heart has systematic four-chamber structures including the left-right/atria-ventricular with functional differences. These complicated morphologies in mammals create difficult questions in addressing the mechanisms of human heart diseases. To answer these questions, many scientists initially generated knockout mice, before establishing the methods for in vitro CM induction from embryonic stem cells (ESCs) or induced pluripotency stem cells (iPSCs). However, the general methods for cardiac cell induction are insufficient to completely produce the chamber-like heart structures with regional identities like the embryonic heart. Furthermore, no information has been reported about the differences of the heart structures, physiological functions and transcriptional regulations between in human and in mice. To address these questions, we performed two projects; 1. the cardiac induction and 2. the heart chamber formation.

5. Epigenetic transcription regulation of inflammation-related genes in vascular endothelial cells

The spatial organization of the genome is functionally linked to gene expression programs. Pro-inflammatory stimuli elicit rapid transcriptional responses via transduced signals to master transcription factors, but it is largely unknown how the genome and epigenome spatially control gene expression during early inflammation. Here, we performed Hi-C in combination with chromatin interaction analysis by paired-end tag sequencing (ChIA-PET) using anti-active RNA polymerase II antibody and found that inflammatory gene expression in human endothelial cells (ECs) is controlled by newly formed chromatin interactions between tumor necrosis factor alpha (TNF- α)-induced super-enhancers (SEs). Importantly, these SE-SE loops (approximately 200 to 500 kb length) are formed within 1 hour after TNF- α -treatment although megabase-size topologically associating domains (long interactions) are unchanged. We also found that lysine demethylase 7A (KDM7A) and 6A (UTX) are rapidly mobilized to TNF- α -induced SEs where nuclear factor kappa-B are highly occupied, and demethylate their H3K9me2 and H3K27me3 marks, respectively, and are responsible for rapid formation of SE-SE loops. Collectively, these findings suggest that erasing of repressive histone marks by KDM7A and UTX within NF κ B-related elements might functionally associate with formation of SE-SE loops and could be a cue signal during inflammatory responses in human endothelial cells.

(3) Education

School of Medicine

2nd grade Introduction to Neurophysiology (2 units)

2nd grade Physiology (6 units)

3rd grade Cardiology (1 unit)

4th grade Project semester

School of Dentistry

3rd grade Pharmacology III(2 units)

3rd grade Practice for Pathophysiological Sciences (2 units)

School of Health Care Medicine

3rd/4th grade Cardiac physiology (8 units)

(4) Publications

[Original Articles]

1. Kensuke Ihara, Koji Sugiyama, Kentaro Takahashi, Masahiro Yamazoe, Tetsuo Sasano, Tetsushi Furukawa. Electrophysiological Assessment of Murine Atria with High-Resolution Optical Mapping Journal of Visualized Experiments. 2018.02;
2. Ihara Kensuke, Sugiyama Koji, Takahashi Kentaro, Yamazoe Masahiro, Sasano Tetsuo, Furukawa Tetsushi. Electrophysiological Assessment of Murine Atria with High-Resolution Optical Mapping JOVE-JOURNAL OF VISUALIZED EXPERIMENTS. 2018.02; (132);
3. Yu Natsume, Kasumi Oaku, Kentaro Takahashi, Wakana Nakamura, Ai Oono, Satomi Hamada, Masahiro Yamazoe, Kensuke Ihara, Takeshi Sasaki, Masahiko Goya, Kenzo Hirao, Tetsushi Furukawa, Tetsuo Sasano. Combined Analysis of Human and Experimental Murine Samples Identified Novel Circulating MicroRNAs as Biomarkers for Atrial Fibrillation. Circulation Journal. 2018.03; 82; 965-973
4. Natsume Yu, Oaku Kasumi, Takahashi Kentaro, Nakamura Wakana, Oono Ai, Hamada Satomi, Yamazoe Masahiro, Ihara Kensuke, Sasaki Takeshi, Goya Masahiko, Hirao Kenzo, Furukawa Tetsushi, Sasano Tetsuo. ヒト由来試料と実験マウス由来試料の統合解析により心房細動のバイオマーカーとして新たな循環 microRNA を特定した (Combined Analysis of Human and Experimental Murine Samples Identified Novel Circulating MicroRNAs as Biomarkers for Atrial Fibrillation) Circulation Journal. 2018.03; 82(4); 965-973
5. Ihara Kensuke, Sasano Tetsuo, Takahashi Kentaro, Yamazoe Masahiro, Furukawa Tetsushi. マウスでは pannexin-1 が電氣的ペースングおよび/または低酸素症下の心機能を維持する (Pannexin-1 Maintains Cardiac Function under the Electrical Pacing and/or Hypoxia in Mice) 日本循環器学会学術集会抄録集. 2018.03; 82 回; PE033-7
6. Yamazoe Masahiro, Sasano Tetsuo, Nakamura Wakana, Takahashi Kentaro, Ihara Kensuke, Hirao Kenzo, Furukawa Tetsushi. 心房細動患者における無細胞 DNA はマクロファージにおける炎症性サイトカインの発現を促進する (Cell Free DNA in Patients with Atrial Fibrillation Promotes Pro-Inflammatory Cytokine Expression in Macrophages) 日本循環器学会学術集会抄録集. 2018.03; 82 回; FRS1-4
7. Jun-Ichi Okada, Takashi Yoshinaga, Junko Kurokawa, Takumi Washio, Tetsushi Furukawa, Kohei Sawada, Seiryu Sugiura, Toshiaki Hisada. Arrhythmic hazard map for a 3D whole-ventricle model under multiple ion channel block. Br. J. Pharmacol.. 2018.09; 175(17); 3435-3452
8. Hamada Satomi, Hasegawa Yuki, Oono Ai, Suzuki Anna, Takahashi Naomi, Nishimura Takuro, Koyama Takatoshi, Hagihara Michio, Tohda Shuji, Furukawa Tetsushi, Hirao Kenzo, Sasano Tetsuo. Differential Assessment of Factor Xa Activity and Global Blood Coagulability Utilizing Novel Dielectric Coagulometry SCIENTIFIC REPORTS. 2018.10; 8(1); 16129
9. Hori Yutaro, Tanimoto Yoko, Takahashi Satoru, Furukawa Tetsushi, Koshiba-Takeuchi Kazuko, Takeuchi Jun K.. Important cardiac transcription factor genes are accompanied by bidirectional long non-coding RNAs BMC GENOMICS. 2018.12; 19(1); 967

[Misc]

1. Tetsushi Furukawa. Atrial fibrillation and inflammation 2018.02; 7(1); 24-28

[Conference Activities & Talks]

1. Furukawa T, Okata S, Yuasa S, Suzuki T, Makita N, Kurokawa J, Egashira T, Yamakawa H, Seki T, Aizawa T, Hashimoto H, Kuroda Y, Tanaka A, Yae K, Murata M, Aiba T, Shimizu W, Horie M, Kodama I, Ogawa S, Fukuda K. Disease modeling using iPS cells. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
2. Sato Y, Satoh A, Nitta J, Honda Y, Kuroda S, Sekigawa M, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Impact of SNP on IL6R (rs7514452) for age at onset of atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

3. Sekigawa M, Satoh A, Nitta J, Sato Y, Honda Y, Kuroda S, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Effect of SNP on 9q22 (rs6479562) on the progression from paroxysmal atrial fibrillation to persistent atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

Stem Cell Regulation

Professor Tetsuya TAGA

Associate Professor Ikuo NOBUHISA

Assistant Professor Kouichi TABU

Technical Assistant/Administrative Assistant Kazuko INOUE

(1) Outline

Research in this department has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. Particular attention is given to cell-external cues (such as cytokines) and cell-intrinsic programs (including epigenetic modification), taking cross-interactions of transcriptional regulatory signals into consideration.

(2) Research

Research Subjects in this department are as follows:

- 1) Molecular basis for the maintenance of neural stem cells
- 2) Regulation of the neural stem cell fate
- 3) Characterization of hematopoietic stem cells in fetal hematopoietic organs
- 4) Characterization of cancer stem cells and their niche
- 5) Epigenetic regulation of neural development

(3) Education

Our education has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. The projects have been performed, for instance by elucidation of stem cell characteristics, analysis of transcriptional regulatory signaling pathways, and identification of niche signals.

(4) Lectures & Courses

Under our education program, students will learn the molecular basis of stem cell regulation in view of cell-extrinsic signals and cell intrinsic-programs during tissue development, maintenance, and regeneration from molecular to whole-body levels. Students will receive exposure to cutting edge concepts and research technologies, and study regulatory mechanisms in neural, hematopoietic, and cancer stem cells. With emphasis also on physiological and pathological conditions surrounding the stem cells, we aims to improve student's understanding of stem cells from multiple viewpoints.

(5) Publications**[Original Articles]**

1. Ito K, Noguchi A, Uosaki Y, Taga T, Arakawa H, Takizawa.. Gfap and Osmr regulation by BRG1 and STAT3 via interchromosomal gene clustering in astrocytes. *Mol Biol Cell*. 2018.01; 29; 209-219
2. Saito K, Nobuhisa I, Harada K, Takahashi S, Anani M, Lickert H, Kanai-Azuma M, Kanai Y, and Taga T . Maintenance of hematopoietic stem and progenitor cells in fetal intra-aortic hematopoietic clusters by the Sox17-Notch1-Hes1 axis *Exp Cell Res*. 2018.04; 365(1); 145-155

[Conference Activities & Talks]

1. Tabu K and Taga T. Abilities of cancer stem cells to organize the self-advantageous microenvironment niche. TMU-TMDU Joint Symposium 2018 2018.03.24 Tokyo Medical and Dental University, Tokyo, Japan
2. Nobuhisa I, Saito K, and Taga T. Expression of TET family members in hematopoietic stem cell-containing clusters of the dorsal aorta in midgestation mouse embryo. The 16th Stem Cell Research Symposium 2018.06.02 Centennial Hall, Kyushu University School of Medicine
3. Tabu K and Taga T. Identification of a subpopulation of glioma cells with a potential for tumor niche development involving myeloid cells. The 16th Stem Cell Research Symposium 2018.06.02 Centennial Hall, Kyushu University, Fukuoka, Japan
4. Tabu K and Taga T. A monocyte-recruiting phenotype defines functional heterogeneity of glioma cells with stemness and chemoresistance. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.29 Osaka International Convention Center, Osaka
5. Azuma K, Nobuhisa I, Saito K, Iizuka N, and Taga T. The role of an epigenetic factor TET1 in undifferentiated hematopoietic cell clusters in the embryonic AGM region where definitive hematopoiesis arises. The 41th Annual Meeting of the Molecular Biology Society of Japan 2018.11.29 Pacifico Yokohama, Yokohama, Japan
6. Iizuka N, Nobuhisa I Saito K, Azuma K, and Taga T. Involvement of an NF- κ B signal pathway in the maintenance of an undifferentiated state of hematopoietic stem cell-containing clusters in the midgestation mouse dorsal aorta. The 41th Annual Meeting of the Molecular Biology Society of Japan 2018.11.29 Pacifico Yokohama, Yokohama, Japan
7. Saito K, Nobuhisa I, and Taga T. Expression analysis of Tet family members in AGM region. The 41th Annual Meeting of the Molecular Biology Society of Japan 2018.11.29 Pacifico Yokohama, Yokohama, Japan
8. Nobuhisa I, Saito K, Azuma K, Iizuka N, and Taga T. The contribution of TET1 to the maintenance of the hematopoietic capacity in hematopoietic stem cell-containing clusters in the dorsal aorta in midgestation mouse embryo. The 47th Annual Meeting of The Japanese Society for Immunology 2018.12.10 Fukuoka International Congress Center, Fukuoka, Japan

Molecular Pharmacology

Associate Professor: Yoichi Ezura, M.D., Ph.D.

(1) Outline

In order to contribute to the establishment of therapy and prevention for osteoporosis and the other calcium-related disorders, we are elucidating molecular mechanisms underlying regulation of calcium metabolism with emphases on bone formation and resorption. Skeletal system is the largest storage site for calcium in a living body and its metabolism is conducted by a complex cell society consisting of bone-forming osteoblasts and bone-resorbing osteoclasts as well as stromal cells and chondrocytes. In our department, we take molecular and cellular biological approaches to study the mechanisms underlying regulation of development, differentiation, and function of these cells.

(2) Research

Bone is the major organ for calcium metabolism in our body. The regulation of bone metabolism is mediated by a balance between osteoblastic bone formation and osteoclastic bone resorption. These activities are maintained in balance and called bone remodeling. Imbalance of the remodeling results in development of bone disorders, such as osteoporosis. Osteoblasts are differentiated from mesenchymal stem cells. These cells are under the regulation by local and systematic factors, such as growth factors and hormones. These factors activate intracellular signaling, which promotes transcription factors thereby delineates cell differentiation. In our laboratory, we are studying the process from various aspects of bone cell regulation including transcription factors, cytokines and hormones. To promote our study, knockout and transgenic mice, gene introduction via virus, global analysis of gene expression, and genome database analysis are used. Our study will provide the basic understandings of bone homeostasis, which will contribute the development of measures for diagnosis and treatment of bone disorders.

(3) Publications

[Original Articles]

1. Lin W, Izu Y, Smriti A, Kawasaki M, Pawaputanon C, Böttcher RT, Costell M, Moriyama K, Noda M, Ezura Y. Profilin1 is expressed in osteocytes and regulates cell shape and migration. *Journal of Cellular Physiology*. 2018.01; 233(1); 259-268
2. Kajikawa Shuhei, Taguchi Yuu, Hayata Tadayoshi, Ezura Yoichi, Ueta Ryo, Arimura Sumimasa, Inoue Jun-ichiro, Noda Masaki, Yamanashi Yuji. Dok-3 and Dok-1/-2 adaptors play distinctive roles in cell fusion and proliferation during osteoclastogenesis and cooperatively protect mice from osteopenia *BIO-CHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS*. 2018.04; 498(4); 967-974
3. Hayata Tadayoshi, Chiga Masahiko, Ezura Yoichi, Asashima Makoto, Katabuchi Hidetaka, Nishinakamura Ryuichi, Noda Masaki. Dullard deficiency causes hemorrhage in the adult ovarian follicles *GENES TO CELLS*. 2018.05; 23(5); 345-356

4. Shimada Akemi, Ideno Hisashi, Arai Yoshinori, Komatsu Koichiro, Wada Satoshi, Yamashita Teruhito, Amizuka Norio, Poschl Ernst, Brachvogel Bent, Nakamura Yoshiki, Nakashima Kazuhisa, Mizukami Hiroaki, Ezura Yoichi, Nifuji Akira. Annexin A5 Involvement in Bone Overgrowth at the Enthesis JOURNAL OF BONE AND MINERAL RESEARCH. 2018.08; 33(8); 1532-1543

Stem Cell Biology

Professor : Emi Nishimura, M.D., Ph.D.
Associate Professor: Daisuke Nanba, Ph.D
Assistant Professor : Hiroyuki Matsumura, Ph.D.
Project Assistant Professor :Yasuaki Mohri, Ph.D.
Hironobu Morinaga, Ph.D.
Kyosuke Asakawa, Ph.D.

(1) Outline

Stem cell systems play fundamental roles in sustaining tissue turnover and homeostasis. Our goal is to understand the mechanisms of tissue homeostasis driven by stem cell systems in mammals and to apply that knowledge to better understand the mechanisms underlying tissue/organ aging, cancer development and other diseases associated with aging. We further aim to apply this knowledge to drug discovery, regenerative medicine and the prevention and treatment of age-associated diseases.

(2) Research

1) Identification of stem cells in the skin

The skin is the largest organ in the body. Hair follicles are mini-organs located in the skin that constantly renew themselves by alternate phases of growth, regression and rest. During this process, mature melanocytes (pigment cells) in hair follicles are replaced by a new cell population in each hair cycle. We previously identified the source of those melanocytes, “melanocyte stem cells” (McSCs), which are located in the hair follicle bulge and supply mature melanocytes required for hair and skin pigmentation (Nishimura EK et al. *Nature*, 2002). Subsequently, we identified similar McSCs in non-hair-bearing skin areas (Okamoto N et al. *PCMR*, 2014). Further, we recently succeeded in identifying epidermal stem cells with sufficient self-renewing potential by using genetic tracing of stem cell clones (Liu N et al. *Nature*, in press).

2) Mechanisms of stem cell maintenance

The underlying mechanisms of stem cell maintenance are a fundamental issue in stem cell biology and medicine. We previously found that the niche microenvironment plays a dominant role in the fate determination of McSCs (Nishimura EK et al. *Nature*, 2002). That finding prompted us to further study the mechanisms involved and led us to demonstrate that hair follicle stem cells (HFSCs), which reside in the hair follicle bulge, serve as a functional niche for the maintenance of McSCs (Nishimura EK et al. *Cell Stem Cell*, 2010)(Tanimura S et al. *Cell Stem Cell*, 2011). The niche functions of HFSCs are mediated by extrinsic niche factors, including transforming growth factor β (TGF- β), that are secreted from HFSCs to maintain McSCs in a quiescent and immature state. Meanwhile, intrinsic defects in stem cells, such as those caused by *Mitf* or *Bcl2* deficiencies in mice, also induce the depletion of McSCs, which leads to the progressive expression of the hair graying phenotype. Therefore, we concluded that the incomplete maintenance of McSCs either by defective signaling from

the stem cell niche or by intrinsic defects in stem cells, results in an insufficient supply of mature melanocytes for hair pigmentation in mice expressing the progressive hair graying phenotype.

3) A stemness checkpoint underlies the quality maintenance of tissues

Physiological hair graying and hair thinning are typical outward signs of aging in mammals, yet the mechanisms underlying those phenotypes had been largely unclear. We found that the incomplete maintenance of McSCs during the course of aging causes hair graying (Nishimura EK et al. *Science*, 2004). We then showed that genotoxic stress triggers/accelerates the aging process and abrogates the self-renewal of McSCs by triggering their differentiation without inducing cellular senescence. Further study of aged wild-type mice and progeroid mouse models, including ATM-deficient mice, revealed that a “stemness checkpoint”, which determines whether stem cells are qualified to self-renew or rather are forced to differentiate, maintains the quality of the stem cell pool and eliminates stressed/damaged stem cells from tissues (Inomata K et al. *Cell*, 2009). Similar checkpoint mechanisms have been found in HFSCs (Matsumura H et al. *Science*, 2016) and in epidermal stem cells (Liu N et al. *Nature*, 2019 in press) by us and also in other somatic stem cells by other groups. We are currently studying the underlying molecular mechanism.

4) Dynamic elimination of aged stem cells causes hair follicle aging

To study the fate and dynamics of aged somatic stem cells, we performed in vivo fate tracing analysis of HFSCs and demonstrated that the dynamic elimination of HFSCs through their epidermal differentiation causes the stepwise miniaturization of hair follicles and eventual hair loss in mice. The DNA damage response in HFSCs causes proteolysis of Type XVII Collagen (COL17A1/BP180), a critical molecule for HFSC maintenance, to trigger HFSC aging that is characterized by the loss of stemness signatures and epidermal differentiation. Aged HFSCs are thus cyclically eliminated from the skin through their epidermal differentiation-mediated shedding from the skin surface, thereby causing hair follicle miniaturization. The aging process can be recapitulated by Col17a1-deficiency and prevented by the forced maintenance of COL17A1 in HFSCs, demonstrating that COL17A1 in HFSCs orchestrates the stem cell-centric aging program of the epithelial mini-organ (Matsumura H et al. *Science*, 2016). We are currently trying to identify the stem cell division program for organ aging.

5) Stem cell competition in the epidermis underlies skin homeostasis and aging

The skin protects living organisms from the outside world by acting as a barrier throughout the life-span, suggesting that the skin has more robust and flexible anti-aging mechanisms than mini-organs such as hair follicles. We have performed in vivo clonal analysis in mice by focusing on the expression of the hemidesmosomal protein COL17A1 by epidermal stem cells. Those studies revealed that the expression of COL17A1 fluctuates physiologically through genomic/oxidative stress-induced proteolysis, and that the resulting differential expression of COL17A1 in individual stem cells generates a driving force for cell competition. Clones that express high levels of COL17A1 divide symmetrically and outcompete/eliminate adjacent stressed clones that express low levels of COL17A1 and divide asymmetrically. Stem cells with higher potential or quality are thus selected for homeostasis, but their eventual loss of COL17A1 limits their competition, thereby causing aging. The resulting hemidesmosome fragility and stem cell delamination depletes adjacent melanocytes and fibroblasts to promote skin aging. Conversely, the forced maintenance of COL17A1 rescues skin organ aging, thereby indicating potential new approaches for anti-aging therapeutic intervention. We are searching for small molecules that provide somatic stem cells with high regenerative potential and quality that have clinical application.

(3) Publications

[Original Articles]

1. Sasaki M, Shinozaki S, Morinaga H, Kaneki M, Nishimura EK, Shimokado K. iNOS inhibits hair regeneration in obese diabetic (ob/ob) mice. *Biochemical and Biophysical Research Communications*. 2018.07; 501(4); 893-897

[Conference Activities & Talks]

1. Emi K. Nishimura. Stem cells orchestrates hair follicle aging program. JSPS&NUS Joint 2nd Symposium "New Horizons in Normal and Cancer Stem Cell Research" 2018.01.18 Kumamoto, Japan
2. Emi K. Nishimura. Stem cells orchestrates hair follicle aging program. International Meeting on RECQ Helicases and Related Disease 2018 2018.02.16 Chiba, Japan
3. Emi K. Nishimura. Stem cell-centric mechanisms of hair follicle aging. Gordon Research Conference- Cornea and Ocular Surface Biology and Pathology- 2018.02.18 California, USA
4. Emi K. Nishimura. Melanocyte stem cells and melanoma. Montagna Symposium on the Biology of Skin 2018.08.19
5. Emi K. Nishimura. Stem cell and niche dynamics in aging skin. Gordon Research Conferences-Issue niches and resident stem cells in adult epithelia- 2018.08.19 New Hampshire, USA
6. 西村 栄美. 毛包をモデルとした器官の再生と老化. NCGMRI Science Forum 2018.10.03 東京
7. 西村 栄美. Cell fate determination in aging organs:stem cell aging vs cellular senescence. 第41回日本分子生物学会年会 2018.11.29 パシフィコ横浜

Respiratory Medicine

Professor: Yasunari Miyazaki

Respiratory and Nervous System Science, Graduate School of Professor Department of Medical and Dental Sciences:
Yuki Sumi

Assistant professor Department of Clinical Oncology: Hiroyuki Sakashita

Associate professor, RESPIRATORY Physiology and Sleep Medicine: Meiyo Tamaoka

Associate professor Health Administration Center : Toshihide Fujie

Assistant Professor: Tomoya Tateishi, Masahiro Ishizuka, Yoshihisa Nukui, Tuyoshi Shirai

Assistant Professor Health Administration Center: Manabu Sema

Clinical Fellow: Hikaru Aoki, Akifumi Mochizuki, Rei Sagawa, Ryusaku Hosoya, Yuki Iijima, Seiko Takazawa

Project Professor: Kyoko Shimizu, Rie Sakakibara, Takayuki Honda

Ph.D. student: Syo Shibata, Hiroaki Saito, Satoshi Hanzawa, Yukihiro Inoue, Takashi Yamana, Naoki Nishiyama,
Shinji Katayanagi, Masaru Ejima, Takafumi Suzuki, Tatuo Kawahara, Yuri Tasaka,

Specially-appointed Professor: Yasunari Setoguchi

(1) Outline

Respiratory Medicine deals with a variety of pulmonary diseases including tumors, infectious diseases, allergic diseases, non-allergic inflammatory diseases, and genetic disorders.

(2) Research

1. Pathogenesis of hypersensitivity pneumonitis and identification of environmental causative antigens
2. Airway remodeling in bronchial asthma model
3. Acute exacerbation in pulmonary fibrosis
4. Proteomics of pulmonary fibrosis
5. Pathogenesis of pulmonary fibrosis and emphysema
6. Sleep apnea
7. Treatment of drug-resistance bacteria

(3) Education

Main objective in the graduate course is to provide our students to study specific diagnostic modalities as well as basic scientific findings regarding the pathogenesis of pulmonary diseases. Students are also taught on basic science and its related laboratory technology depending upon their research subject.

(4) Lectures & Courses

Students should try to understand a variety of pulmonary diseases in terms of scientific aspect and make an appropriate plan to examine unsolved research questions.

(5) Clinical Services & Other Works

Our clinic provides a full spectrum of diagnosis and treatment of a variety of pulmonary diseases. Consultant system is open to all departments in this hospital and daily clinical conference regarding inpatients is organized by professors of the department. In outpatient clinic, chemotherapy, home oxygen therapy, management of sleep apnea, and arrange of clinical studies are provided.

(6) Clinical Performances

We have immunological tools to examine hypersensitivity pneumonitis including antigen inhalation challenge test, specific antibody against causative antigen, and lymphocyte proliferation test. Many patients with interstitial lung diseases in Japan are referred to our clinic.

(7) Publications

[Original Articles]

1. Nukui Yoshihisa, Miyazaki Yasunari, Suhara Kozo, Okamoto Tsukasa, Furusawa Haruhiko, Inase Naohiko. IDENTIFICATION OF APOLIPOPROTEIN A-I IN BALF AS A BIOMARKER OF SARCOIDOSIS SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES. 2018; 35(1); 5-15
2. Kanke Y, Shimomura A, Saito M, Honda T, Shiraishi K, Shimada Y, Watanabe R, Yoshida H, Yoshida M, Shimizu C, Takahashi K, Totsuka H, Ogiwara H, Hirose S, Kono K, Tamura K, Okamoto A, Kinoshita T, Kato T, Kohno T. Gene aberration profile of tumors of adolescent and young adult females. *Oncotarget*. 2018.01; 9(5); 6228-6237
3. Honda Takayuki, Shiraishi Kouya, Mimaki Sachiyo, Sakashita Hiroyuki, Kobayashi Masashi, Motoi Noriko, Tsuchihara Katsuya, Kohno Takashi. Mutational signatures and their association with clinicopathological features in lung adenocarcinoma of smokers *CANCER SCIENCE*. 2018.01; 109; 442
4. Ohno T, Zhang C, Kondo Y, Kang S, Furusawa E, Tsuchiya K, Miyazaki Y, Azuma M. The immune checkpoint molecule VISTA regulates allergen-specific Th2-mediated immune responses. *Int Immune*. 2018.02; 30(1); 3-11
5. Manabu Sema, Yasunari Miyazaki, Toshiharu Tsutsui, Makoto Tomita, Yoshinobu Eishi, Naohiko Inase. Environmental levels of avian antigen are relevant to the progression of chronic hypersensitivity pneumonitis during antigen avoidance. *Immun Inflamm Dis*. 2018.03; 6(1); 154-162
6. Yu Kusaka, Chiaki Kajiwara, Sho Shimada, Yoshikazu Ishii, Yasunari Miyazaki, Naohiko Inase, Theodore J Standiford, Kazuhiro Tateda. Potential Role of Gr-1+ CD8+ T Lymphocytes as a Source of Interferon- γ and M1/M2 Polarization during the Acute Phase of Murine *Legionella pneumophila* Pneumonia. *J Innate Immun*. 2018.04; 10(4); 328-338
7. Sonoda S, Yamaguchi T, Aoki K, Ono D, Sato A, Kajiwara C, Kimura S, Akasaka Y, Ishii Y, Miyazaki Y, Inase N, Tateda K. Evidence of latent molecular diversity determining the virulence of community-associated MRSA USA300 clones in mice. *Immunity, inflammation and disease*. 2018.09; 6(3); 402-412
8. Fujioka T, Kubota K, Kikuchi Y, Tsuchiya J, Tateishi U, Kasaharak M, Oda G, Ishiba T, Nakagawa T. The feasibility of using 18F-FDG-PET/CT in patients with mucinous breast carcinoma. *Nuclear medicine communications*. 2018.09;
9. Shibata S, Miyake K, Tateishi T, Yoshikawa S, Yamanishi Y, Miyazaki Y, Inase N, Karasuyama H. Basophils trigger emphysema development in a murine model of COPD through IL-4-mediated generation of MMP-12-producing macrophages. *Proceedings of the National Academy of Sciences of the United States of America*. 2018.12;
10. Mitsumura T, Ito Y, Chiba T, Matsushima T, Kurimoto R, Tanaka Y, Kato T, Uchida K, Ito T, Yamamoto K, Eishi Y, Kitagawa M, Miyazaki Y, Inase N, Asahara H. Ablation of miR-146b in mice causes hematopoietic malignancy. *Blood advances*. 2018.12; 2(23); 3483-3491

11. Saito H, Tsuchiya K, Chiba S, Ogata T, Imase R, Yagi T, Mishima Y, Jinta T, Saito K, Taki R, Isogai S, Jin Y, Kawasaki T, Natsume I, Miyashita Y, Takagiwa J, Ishiwata N, Chiaki T, Kishi M, Tsukada Y, Yamasaki M, Inase N, Miyazaki Y. Treatment of asthma in smokers: A questionnaire survey in Japanese clinical practice. *Respiratory investigation*. 2018.12;
12. Hanzawa S, Tateishi T, Takemura T, Okada Y, Yamada Y, Noda M, Miyazaki Y, Inase N. The Analysis of Surgical Lung Biopsy and Explanted Lung Specimens Sheds Light on the Pathological Progression of Chronic Bird-related Hypersensitivity Pneumonitis. *Internal medicine (Tokyo, Japan)*. 2018.12;

[Misc]

1. Kolb M, Bondue B, Pesci A, Miyazaki Y, Song JW, Bhatt NY, Huggins JT, Oldham JM, Padilla ML, Roman J, Shapera S. Acute exacerbations of progressive-fibrosing interstitial lung diseases. *European respiratory review : an official journal of the European Respiratory Society*. 2018.12; 27(150);

Gastroenterology and Hepatology

Professor Mamoru WATANABE

Professor Yasuhiro ASAHINA (Department for Hepatitis Control)
Kazuo OHTSUKA (Department of Endoscopy)
Ryuichi OKAMOTO (Center for Stem Cell and Regenerative Medicine)
Tetsuya NAKAMURA
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Associate Professor

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Sei KAKINUMA (Department for Hepatitis Control)
Kiichiro TSUCHIYA (Gastroenterology and Hepatology)
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Takashi NAGAISHI
(Department of Advanced Therapeutics in Gastrointestinal Diseases)
Katsuyoshi MATSUOKA
(Department of Advanced Therapeutics in Gastrointestinal Diseases)
Masakazu NAGAHORI (Clinical Research Center)
Seishin AZUMA
(Department of Collaborative Medicine for Gastroenterology and Hepatology (CMGH))

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(Department of Advanced Therapeutics in Gastrointestinal Diseases)
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Miyako MURAKAWA (Clinical Laboratory)
Masayoshi FUKUDA (Department of Endoscopy)
Kento TAKENAKA
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Project Assistant Professor

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Takashi FUJII, Hroko NAGATA, Syun KANEKO, Youichi NIBE, Ayako WATANABE,
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Ami KAWAMOTO, Masato MIYOSHI, Tomoyuki TSUNODA, Yuria TAKEL, JOSE Nisha,
Sho ANZAI, Tomoaki SHIRASAKI, Shohei TANAKA, Reiko KUNO, Kana OTSUBO,
Ayako Sato, Sho WARANABE, Maiko MOTOHASHI, Konomi KUWABARA,
Hiroki MATSUDA, Takehito ASAKAWA, Ai MINAMIDATE, Ryo MORIKAWA,
Emi AONUMA, Mao KAWAI, Junichi TAKAHASHI, Naoya TSUGAWA,
Yuta KOJIMA, Minami HAMA, Akiko TANURA, Atsushi Tuchiya

(1) Outline

Research project is selected from the clinical problems in the Gastroenterology and Hepatology to understand the research policy, as clinical science that the results of research project finally should be restored to clinical medicine.

The purpose of this course is the understanding the situation of inflammatory bowel disease (IBD) in Japan and the problems about the pathogenesis and intractable cause of IBD. In addition, the understanding the pathogenesis and problems about the liver diseases such as viral hepatitis, cirrhosis and hepatocellular carcinoma is the purpose of this course.

(2) Research

Basic Research Projects

Systemic Organ Regulation

- Elucidating the pathophysiology of inflammatory bowel diseases and development of treatment by diseasespecific immune regulation.
- Development of novel therapeutics for inflammatory and allergic diseases based on gut-specific mucosal immune regulation.
- Basic research and clinical application of regenerative medicine in gastrointestinal diseases.
- Analysis of interferon-resistant hepatitis C virus.
- Comprehensive analysis of susceptibility genes for various gastrointestinal diseases.
- Crosstalk of the signaling pathways in intestinal epithelial cells.
- Functional analysis of the intestine using primary cell culture in vitro.

(3) Education

We believe that the central role of clinical departments in the graduate school is to establish basis for the innovative medicine / medical treatment in the next generation. Basic research lead by clinical concepts, and development of novel therapeutics established upon basic research are both critically required to achieve our mission. Therefore, our primary goal is set to train highly educated and experienced clinician-researchers in the field of gastroenterology and hepatology.

In the clinical area, we pursue development and application of highly advanced technologies, including novel endoscopic procedures, for sophisticated diagnosis and treatment of gastrointestinal and liver diseases. In basic research, our principle is to achieve "clinical science", a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice. Based on these principals, we are running research projects to 1) develop novel therapy for refractory inflammatory bowel diseases, 2) prevent progression of liver failure in chronic hepatitis patients and 3) improve anti-cancer therapy for the treatment of gastrointestinal malignancies, by expanding our distinct basic research findings in the area of mucosal immunology, liver immunology, regenerative medicine and virology, to various clinical settings. Moreover, we promote both intra- and inter-national exchanges of researchers, and provide good opportunities to study abroad. The final goal of our education is to promote students to become a well-developed clinician researcher, and also a leading expert in the field of gastroenterology and hepatology.

(4) Lectures & Courses

Research Conference	every Tuesday 18:00 19:30
Journal Club	every Tuesday 18:00 19:30

(5) Clinical Services & Other Works

Expert Areas in Clinical Practice

- Immune-regulation based treatment of inflammatory bowel diseases.
- Prevention of chronic hepatitis progression to hepatocellular cancer and liver failure, by virology-based treatment strategy.

- Clinical trial of innovative treatment for hepatocellular cancer.
- Diagnosis and treatment of small intestinal diseases by balloon assisted enteroscopy and capsule enteroscopy.
- Advanced diagnosis and treatment of colonic diseases by colonoscopy.
- Development of minimally-invasive diagnostic modalities for gastrointestinal diseases (i.e. MR enterography).
- Improved chemotherapy for gastric and pancreatic malignancies.

(6) Clinical Performances

Therapeutics of inflammatory bowel diseases by corrections of immunological disfunctions.

Diagnostic and interventional gastrointestinal endoscopy.

Antiviral therapies against chronic viral hepatitis and preventions of hepatic malignancy novel interventions of hepatic malignancy.

(7) Publications

[Original Articles]

1. Dong Il Park, Tadakazu Hisamatsu, Minhu Chen, Siew Chien Ng, Choon Jin Ooi, Shu Chen Wei, Rupa Banerjee, Ida Normiha Hilmi, Yoon Tae Jeon, Dong Soo Han, Hyo Jong Kim, Zhihua Ran, Kaichun Wu, Jiaming Qian, Pin-Jin Hu, Katsuyoshi Matsuoka, Akira Andoh, Yasuo Suzuki, Kentaro Sugano, Mamoru Watanabe, Toshifumi Hibi, Amarendra S Puri, Suk-Kyun Yang. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 2: Management. *J. Gastroenterol. Hepatol.* 2018.01; 33(1); 30-36
2. Dong Il Park, Tadakazu Hisamatsu, Minhu Chen, Siew Chien Ng, Choon Jin Ooi, Shu Chen Wei, Rupa Banerjee, Ida Normiha Hilmi, Yoon Tae Jeon, Dong Soo Han, Hyo Jong Kim, Zhihua Ran, Kaichun Wu, Jiaming Qian, Pin-Jin Hu, Katsuyoshi Matsuoka, Akira Andoh, Yasuo Suzuki, Kentaro Sugano, Mamoru Watanabe, Toshifumi Hibi, Amarendra S Puri, Suk-Kyun Yang. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 1: Risk assessment. *J. Gastroenterol. Hepatol.* 2018.01; 33(1); 20-29
3. Shiro Yui, Luca Azzolin, Martti Maimets, Marianne Terndrup Pedersen, Robert P Fordham, Stine L Hansen, Hjalte L Larsen, Jordi Guiu, Mariana R P Alves, Carsten F Rundsten, Jens V Johansen, Yuan Li, Chris D Madsen, Tetsuya Nakamura, Mamoru Watanabe, Ole H Nielsen, Pawel J Schweiger, Stefano Piccolo, Kim B Jensen. YAP/TAZ-Dependent Reprogramming of Colonic Epithelium Links ECM Remodeling to Tissue Regeneration. *Cell Stem Cell.* 2018.01; 22(1); 35-49.e7
4. Sugiyama R, Murayama A, Nitta S, Yamada N, Tasaka-Fujita M, Masaki T, Aly HH, Shiina M, Ryo A, Ishii K, Wakita T, Kato T. Interferon sensitivity-determining region of hepatitis C virus influences virus production and interferon signaling. *Oncotarget.* 2018.01; 9(5); 5627-5640
5. Dong Il Park, Tadakazu Hisamatsu, Minhu Chen, Siew Chien Ng, Choon Jin Ooi, Shu Chen Wei, Rupa Banerjee, Ida Normiha Hilmi, Yoon Tae Jeon, Dong Soo Han, Hyo Jong Kim, Zhihua Ran, Kaichun Wu, Jiaming Qian, Pin-Jin Hu, Katsuyoshi Matsuoka, Akira Andoh, Yasuo Suzuki, Kentaro Sugano, Mamoru Watanabe, Toshifumi Hibi, Amarendra S Puri, Suk-Kyun Yang. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 2: management. *Intest Res.* 2018.01; 16(1); 17-25
6. Matsuda K, Tanaka K, Fujishiro M, Saito Y, Ohtsuka K, Oda I, Katada C, Kato M, Kida M, Kobayashi K, Hoteya S, Horimatsu T, Kodashima S, Matsuda T, Muto M, Yamamoto H, Ryozaawa S, Iwakiri R, Kutsumi H, Miyata H, Kato M, Haruma K, Fujimoto K, Uemura N, Kaminishi M, Tajiri H. Design paper: Japan Endoscopy Database (JED): A prospective, large database project related to gastroenterological endoscopy in Japan. *Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society.* 2018.01; 30(1); 5-19
7. Kodashima S, Tanaka K, Matsuda K, Fujishiro M, Saito Y, Ohtsuka K, Oda I, Katada C, Kato M, Kida M, Kobayashi K, Hoteya S, Horimatsu T, Matsuda T, Muto M, Yamamoto H, Ryozaawa S, Iwakiri R,

- Kutsumi H, Miyata H, Kato M, Haruma K, Fujimoto K, Uemura N, Kaminishi M, Tajiri H. First progress report on the Japan Endoscopy Database project. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society. 2018.01; 30(1); 20-28
8. Dong Il Park, Tadakazu Hisamatsu, Minhu Chen, Siew Chien Ng, Choon Jin Ooi, Shu Chen Wei, Rupa Banerjee, Ida Normiha Hilmi, Yoon Tae Jeon, Dong Soo Han, Hyo Jong Kim, Zhihua Ran, Kaichun Wu, Jiaming Qian, Pin-Jin Hu, Katsuyoshi Matsuoka, Akira Andoh, Yasuo Suzuki, Kentaro Sugano, Mamoru Watanabe, Toshifumi Hibi, Amarendra S Puri, Suk-Kyun Yang. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 1: risk assessment. Intest Res. 2018.01; 16(1); 4-16
9. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Katsuyoshi Matsuoka, Masakazu Nagahori, Toshimitsu Fujii, Eiko Saito, Maiko Kimura, Tomoyuki Fujioka, Mamoru Watanabe. Utility of Magnetic Resonance Enterography For Small Bowel Endoscopic Healing in Patients With Crohn's Disease Am. J. Gastroenterol. 2018.02; 113(2); 283-294
10. Shinya Sugimoto, Yuki Ohta, Masayuki Fujii, Mami Matano, Mariko Shimokawa, Kosaku Nanki, Shoichi Date, Shingo Nishikori, Yoshihiro Nakazato, Tetsuya Nakamura, Takanori Kanai, Toshiro Sato. Reconstruction of the Human Colon Epithelium In Vivo. Cell Stem Cell. 2018.02; 22(2); 171-176.e5
11. Taro Watabe, Takashi Nagaishi, Naoya Tsugawa, Yudai Kojima, Nisha Jose, Akinori Hosoya, Michio Onizawa, Yasuhiro Nemoto, Shigeru Oshima, Tetsuya Nakamura, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. B cell activation in the cecal patches during the development of an experimental colitis model. Biochem. Biophys. Res. Commun. 2018.02; 496(2); 367-373
12. Fumihito Hirai, Akira Andoh, Fumiaki Ueno, Kenji Watanabe, Naoki Ohmiya, Hiroshi Nakase, Shingo Kato, Motohiro Esaki, Yutaka Endo, Hironori Yamamoto, Toshiyuki Matsui, Mitsuo Iida, Toshifumi Hibi, Mamoru Watanabe, Yasuo Suzuki, Takayuki Matsumoto. Efficacy of endoscopic balloon dilation for small bowel strictures in patients with Crohn's disease: A nationwide, multi-center, open-label, prospective cohort study. J Crohns Colitis. 2018.03; 12(4); 394-401
13. Makoto Naganuma, Shinya Sugimoto, Keiichi Mitsuyama, Taku Kobayashi, Naoki Yoshimura, Hidehisa Ohi, Shinji Tanaka, Akira Andoh, Naoki Ohmiya, Keiichi Saigusa, Takayuki Yamamoto, Yuichi Morohoshi, Hitoshi Ichikawa, Katsuyoshi Matsuoka, Tadakazu Hisamatsu, Kenji Watanabe, Shinta Mizuno, Wataru Suda, Masahira Hattori, Shinji Fukuda, Akiyoshi Hirayama, Takayuki Abe, Mamoru Watanabe, Toshifumi Hibi, Yasuo Suzuki, Takanori Kanai, . Efficacy of Indigo Naturalis in a Multicenter Randomized Controlled Trial of Patients With Ulcerative Colitis. Gastroenterology. 2018.03; 154(4); 935-947
14. Shintaro Akiyama, Masakazu Nagahori, Shinya Oooka, Mariko Negi, Takashi Ito, Kento Takenaka, Kazuo Ohtsuka, Mamoru Watanabe. Small intestinal obstruction due to the metastasis of intrahepatic cholangiocarcinoma: A case report. Medicine (Baltimore). 2018.03; 97(12); e0190
15. Ogata N, Ohtsuka K, Sasanuma S, Ogawa M, Maeda Y, Ichimasa K, Mori Y, Misawa M, Kudo T, Hisayuki T, Hayashi T, Wakamura K, Miyachi H, Baba T, Ishida F, Kudo SE. White light-emitting contrast image capsule endoscopy for visualization of small intestine lesions: a pilot study. Endoscopy international open. 2018.03; 6(3); E315-E321
16. Vishnu Mohanan, Toru Nakata, A Nicole Desch, Chloé Lévesque, Angela Borroughs, Gaelen Guzman, Zhifang Cao, Elizabeth Creasey, Junmei Yao, Gabrielle Boucher, Guy Charron, Atul K Bhan, Monica Schenone, Steven A Carr, Hans-Christian Reinecker, Mark J Daly, John D Rioux, Kara G Lassen, Ramnik J Xavier. Clorf106 is a colitis risk gene that regulates stability of epithelial adherens junctions. Science. 2018.03; 359(6380); 1161-1166
17. Makoto Naganuma, Nobuo Aoyama, Tomohiro Tada, Kiyonori Kobayashi, Fumihito Hirai, Kenji Watanabe, Mamoru Watanabe, Toshifumi Hibi. Complete mucosal healing of distal lesions induced by twice-daily budesonide 2-mg foam promoted clinical remission of mild-to-moderate ulcerative colitis with distal active inflammation: double-blind, randomized study. J. Gastroenterol. 2018.04; 53(4); 494-506
18. Makoto Naganuma, Nobuo Aoyama, Tomohiro Tada, Kiyonori Kobayashi, Fumihito Hirai, Kenji Watanabe, Mamoru Watanabe, Toshifumi Hibi. Correction to: Complete mucosal healing of distal lesions induced by twice-daily budesonide 2-mg foam promoted clinical remission of mild-to-moderate ulcerative

- colitis with distal active inflammation: double-blind, randomized study. *J. Gastroenterol.* 2018.04; 53(4); 579-581
19. Yoshiki Wada, Masayoshi Fukuda, Kazuo Ohtsuka, Mamoru Watanabe, Yumiko Fukuma, Yoko Wada, Masahiro Wada. Efficacy of Endocuff-assisted colonoscopy in the detection of colorectal polyps. *Endosc Int Open.* 2018.04; 6(4); E425-E431
20. Emma Calabrese, Torsten Kucharzik, Christian Maaser, Giovanni Maconi, Deike Strobel, Stephanie R Wilson, Francesca Zorzi, Kerri L Novak, David H Bruining, Marietta Iacucci, Mamoru Watanabe, Elisabetta Lolli, Carlo Chiaramonte, Stephen B Hanauer, Remo Panaccione, Francesco Pallone, Subrata Ghosh, Giovanni Monteleone. Real-time Interobserver Agreement in Bowel Ultrasonography for Diagnostic Assessment in Patients With Crohn's Disease: An International Multicenter Study. *Inflamm. Bowel Dis.* 2018.04;
21. Satoshi Motoya, Mamoru Watanabe, Hyo Jong Kim, Young Ho Kim, Dong Soo Han, Hirotoshi Yuasa, Junichi Tabira, Naoki Isogawa, Shoko Arai, Isao Kawaguchi, Toshifumi Hibi. Tofacitinib induction and maintenance therapy in East Asian patients with active ulcerative colitis: subgroup analyses from three phase 3 multinational studies. *Intest Res.* 2018.04; 16(2); 233-245
22. Taku Kobayashi, Tadakazu Hisamatsu, Yasuo Suzuki, Haruhiko Ogata, Akira Andoh, Toshimitsu Araki, Ryota Hokari, Hideki Iijima, Hiroki Ikeuchi, Yoh Ishiguro, Shingo Kato, Reiko Kunisaki, Takayuki Matsumoto, Satoshi Motoya, Masakazu Nagahori, Shiro Nakamura, Hiroshi Nakase, Tomoyuki Tsujikawa, Makoto Sasaki, Kaoru Yokoyama, Naoki Yoshimura, Kenji Watanabe, Miiko Katafuchi, Mamoru Watanabe, Toshifumi Hibi. Predicting outcomes to optimize disease management in inflammatory bowel disease in Japan: their differences and similarities to Western countries. *Intest Res.* 2018.04; 16(2); 168-177
23. Shunsuke Komoto, Masaaki Higashiyama, Chikako Watanabe, Yasuo Suzuki, Mamoru Watanabe, Toshifumi Hibi, Toru Takebayashi, Keiko Asakura, Yuji Nishiwaki, Soichiro Miura, Ryota Hokari. Clinical differences between elderly-onset ulcerative colitis and non-elderly-onset ulcerative colitis: A nationwide survey data in Japan. *J. Gastroenterol. Hepatol.* 2018.04;
24. Naoki Hosoe, Masaru Nakano, Ken Takeuchi, Yutaka Endo, Katsuyoshi Matsuoka, Takayuki Abe, Teppei Omori, Mari Hayashida, Taku Kobayashi, Atsushi Yoshida, Shinta Mizuno, Nakazato Yoshihiro, Makoto Naganuma, Takanori Kanai, Mamoru Watanabe, Fumiaki Ueno, Yasuo Suzuki, Toshifumi Hibi, Haruhiko Ogata. Establishment of a Novel Scoring System for Colon Capsule Endoscopy to Assess the Severity of Ulcerative Colitis-Capsule Scoring of Ulcerative Colitis. *Inflamm. Bowel Dis.* 2018.05;
25. Sasanuma S, Ohtsuka K, Kudo SE, Ogata N, Maeda Y, Misawa M, Mori Y, Kudo T, Hisayuki T, Wakamura K, Hayashi T, Katagiri A, Miyachi H, Baba T, Ishida F. Narrow band imaging efficiency in evaluation of mucosal healing/relapse of ulcerative colitis. *Endoscopy international open.* 2018.05; 6(5); E518-E523
26. Yutaka Yasui, Kaoru Tsuchiya, Masayuki Kurosaki, Takaya Takeguchi, Yuko Takeguchi, Mao Okada, Wan Wang, Yohei Kubota, Tomoyuki Goto, Yasuyuki Komiyama, Mayu Higuchi, Kenta Takaura, Tsuguru Hayashi, Hitomi Takada, Nobuharu Tamaki, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Yasuhiro Asahina, Nobuyuki Enomoto, Yoshiro Himeno, Namiki Izumi. Up-to-seven criteria as a useful predictor for tumor downstaging to within Milan criteria and Child-Pugh grade deterioration after initial conventional transarterial chemoembolization. *Hepatol. Res.* 2018.05; 48(6); 442-450
27. Kouhei Fukushima, Akira Sugita, Kitaro Futami, Ken-Ichi Takahashi, Satoshi Motoya, Hideaki Kimura, Shusaku Yoshikawa, Yoshitaka Kinouchi, Hideki Iijima, Katsuya Endo, Toshihumi Hibi, Mamoru Watanabe, Iwao Sasaki, Yasuo Suzuki, . Postoperative therapy with infliximab for Crohn's disease: a 2-year prospective randomized multicenter study in Japan. *Surg. Today.* 2018.06; 48(6); 584-590
28. Fumihiko Iwamoto, Katsuyoshi Matsuoka, Maiko Motobayashi, Kento Takenaka, Toru Kuno, Keisuke Tanaka, Yuya Tsukui, Shoji Kobayashi, Takashi Yoshida, Toshimitsu Fujii, Eiko Saito, Tatsuya Yamaguchi, Masakazu Nagahori, Tadashi Sato, Kazuo Ohtsuka, Nobuyuki Enomoto, Mamoru Watanabe. Prediction of disease activity of Crohn's disease through fecal calprotectin evaluated by balloon-assisted endoscopy. *J. Gastroenterol. Hepatol.* 2018.06;
29. Maekawa Shinya, Sato Mitsuaki, Kuratomi Natsuhiko, Inoue Taisuke, Suzuki Yuichiro, Tatsumi Akihisa, Miura Mika, Matsuda Shuya, Muraoka Masaru, Nakakuki Natsuko, Amemiya Fumitake, Takano Shinichi, Fukasawa Mitsuharu, Nakayama Yasuhiro, Yamaguchi Tatsuya, Sato Tadashi, Sakamoto Minoru, Murakawa Miyako, Nakagawa Mina, Asahina Yasuhiro, Enomoto Nobuyuki. Association between alanine

- aminotransferase elevation and UGT1A1*6 polymorphisms in daclatasvir and asunaprevir combination therapy for chronic hepatitis C *J. Gastroenterol.* 2018.06; 53(6); 780-786
30. Wai-Kay Seto, Yasuhiro Asahina, Todd T Brown, Cheng-Yuan Peng, Carol Stanciu, Dzhamal Abdurakhmanov, Fehmi Tabak, Tuan T Nguyen, Wan-Long Chuang, Tetsuro Inokuma, Fusao Ikeda, Teresa Antonia Santantonio, François Habersetzer, Alnoor Ramji, Audrey H Lau, Vithika Suri, John F Flaherty, Hongyuan Wang, Anuj Gaggar, G Mani Subramanian, Shrikant Mukewar, Maurizia R Brunetto, Scott Fung, Henry Lik-Yuen Chan. Improved Bone Safety of Tenofovir Alafenamide Compared to Tenofovir Disoproxil Fumarate Over 2 Years in Patients With Chronic HBV Infection.[Epub ahead of print] *Clin. Gastroenterol. Hepatol.* 2018.06;
 31. Michael G Kattah, Ling Shao, Yenny Y Rosli, Hiromichi Shimizu, Michael I Whang, Rommel Advincula, Philip Achacoso, Sanjana Shah, Bao H Duong, Michio Onizawa, Priscilia Tanbun, Barbara A Malynn, Averil Ma. A20 and ABIN-1 synergistically preserve intestinal epithelial cell survival. *J. Exp. Med.* 2018.07; 215(7); 1839-1852
 32. Meng-Tzu Weng, Sang Hyoung Park, Katsuyoshi Matsuoka, Chien-Chih Tung, Jae Yong Lee, Chin-Hao Chang, Suk-Kyun Yang, Mamoru Watanabe, Jau-Min Wong, Shu-Chen Wei. Incidence and Risk Factor Analysis of Thromboembolic Events in East Asian Patients With Inflammatory Bowel Disease, a Multinational Collaborative Study. *Inflamm. Bowel Dis.* 2018.07; 24(8); 1791-1800
 33. Tadakazu Hisamatsu, Reiko Kunisaki, Shiro Nakamura, Tomoyuki Tsujikawa, Fumihito Hirai, Hiroshi Nakase, Kenji Watanabe, Kaoru Yokoyama, Masakazu Nagahori, Takanori Kanai, Makoto Naganuma, Hirofumi Michimae, Akira Andoh, Akihiro Yamada, Tadashi Yokoyama, Noriko Kamata, Shinji Tanaka, Yasuo Suzuki, Toshifumi Hibi, Mamoru Watanabe, . Effect of elemental diet combined with infiximab dose escalation in patients with Crohn's disease with loss of response to infiximab: CERISIER trial. *Intest Res.* 2018.07; 16(3); 494-498
 34. Kohei Suzuki, Tatsuro Murano, Hiromichi Shimizu, Go Ito, Toru Nakata, Satoru Fujii, Fumiaki Ishibashi, Ami Kawamoto, Sho Anzai, Reiko Kuno, Konomi Kuwabara, Junichi Takahashi, Minami Hama, Sayaka Nagata, Yui Hiraguri, Kento Takenaka, Shiro Yui, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Mamoru Watanabe, Ryuichi Okamoto. Single cell analysis of Crohn's disease patient-derived small intestinal organoids reveals disease activity-dependent modification of stem cell properties. *J. Gastroenterol.* 2018.09; 53(9); 1035-1047
 35. Yasuhiro Asahina, Yoshito Itoh, Yoshiyuki Ueno, Yasushi Matsuzaki, Yasuhiro Takikawa, Hiroshi Yatsushashi, Takuya Genda, Fusao Ikeda, Takuma Matsuda, Hadas Dvory-Sobol, Deyuan Jiang, Benedetta Massetto, Anu O Osinusi, Diana M Brainard, John G McHutchison, Norifumi Kawada, Nobuyuki Enomoto. Ledipasvir-sofosbuvir for treating Japanese patients with chronic hepatitis C virus genotype 2 infection. *Liver Int.* 2018.09; 38(9); 1552-1561
 36. Yuichi Mori, Shin-Ei Kudo, Masashi Misawa, Yutaka Saito, Hiroaki Ikematsu, Kinichi Hotta, Kazuo Ohtsuka, Fumihiko Urushibara, Shinichi Kataoka, Yushi Ogawa, Yasuharu Maeda, Kenichi Takeda, Hiroki Nakamura, Katsuro Ichimasa, Toyoki Kudo, Takemasa Hayashi, Kunihiro Wakamura, Fumio Ishida, Haruhiro Inoue, Hayato Itoh, Masahiro Oda, Kensaku Mori. Real-Time Use of Artificial Intelligence in Identification of Diminutive Polyps During Colonoscopy: A Prospective Study. *Ann. Intern. Med.* 2018.09; 169(6); 357-366
 37. Shinichiro Shinzaki, Toshimitsu Fujii, Shigeki Bamba, Maiko Ogawa, Taku Kobayashi, Masahide Oshita, Hiroki Tanaka, Keiji Ozeki, Sakuma Takahashi, Hiroki Kitamoto, Kazuhito Kani, Sohachi Nanjo, Takeshi Sugaya, Yuko Sakakibara, Toshihiro Inokuchi, Kazuki Kakimoto, Akihiro Yamada, Hisae Yasuhara, Yoko Yokoyama, Takuya Yoshino, Akira Matsui, Misaki Nakamura, Taku Tomizawa, Ryosuke Sakemi, Noriko Kamata, Toshifumi Hibi. Seven days triple therapy for eradication of *Helicobacter pylori* does not alter the disease activity of patients with inflammatory bowel disease. *Intest Res.* 2018.10; 16(4); 609-618
 38. Yamazaki K, Takenaka K, Ohtsuka K. Laterally Spreading Tumor-like Early Cancer in Ileum.[Epub ahead of print] *Intern Med.* 2018.10;
 39. Hosoe N, Ohtsuka K, Endo Y, Naganuma M, Ogata N, Kuroki Y, Sasanuma S, Takabayashi K, Kudo SE, Takahashi H, Ogata H, Kanai T. Insertability comparison of passive bending single-balloon prototype versus standard single-balloon enteroscopy: a multicenter randomized non-blinded trial. *Endoscopy international open.* 2018.10; 6(10); E1184-E1189

40. Ami Kawamoto, Sayaka Nagata, Sho Anzai, Junichi Takahashi, Mao Kawai, Minami Hama, Daichi Nogawa, Kohei Yamamoto, Reiko Kuno, Kohei Suzuki, Hiromichi Shimizu, Yui Hiraguri, Shiro Yui, Shigeru Ohshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Masanobu Kitagawa, Ryuichi Okamoto, Mamoru Watanabe. Ubiquitin D is up-regulated by synergy of Notch signalling and TNF- α in the inflamed intestinal epithelia of IBD patients. [Epub ahead of print] *J Crohns Colitis*. 2018.11;
41. Ozaki R, Kobayashi T, Okabayashi S, Nakano M, Morinaga S, Hara A, Ohbu M, Matsuoka K, Toyonaga T, Saito E, Hisamatsu T, Hibi T. Histological Risk Factors to Predict Clinical Relapse in Ulcerative Colitis With Endoscopically Normal Mucosa. *Journal of Crohn's & colitis*. 2018.11; 12(11); 1288-1294
42. Niikura R, Yamada A, Fujishiro M, Tanaka K, Matsuda K, Saito Y, Ohtsuka K, Oda I, Katada C, Kato M, Kida M, Kobayashi K, Hoteya S, Horimatsu T, Kodashima S, Matsuda T, Muto M, Yamamoto H, Ryozaawa S, Iwakiri R, Kutsumi H, Miyata H, Kato M, Haruma K, Fujimoto K, Uemura N, Kaminishi M, Shinozaki T, Tajiri H, Koike K. The Effects of Direct Oral Anticoagulants, Warfarin, Aspirin and Thienopyridine on the Performance of Immunochemical, Faecal, Occult Blood Tests. *Digestion*. 2018.11; 1-10
43. Maiko Motobayashi, Katsuyoshi Matsuoka, Kento Takenaka, Toshimitsu Fujii, Masakazu Nagahori, Kazuo Ohtsuka, Fumihiko Iwamoto, Kiichiro Tsuchiya, Mariko Negi, Yoshinobu Eishi, Mamoru Watanabe. Predictors of mucosal healing during induction therapy in patients with acute moderate-to-severe ulcerative colitis.[Epub ahead of print] *J. Gastroenterol. Hepatol*. 2018.12;

[Books etc]

1. Toshimitsu Fujii. Current Progress of Endoscopy in Inflammatory Bowel Disease:MR Enterography. Springer, 2018.11
2. Kazuo Ohtsuka. Difficulty in Diagnosing Inflammatory Bowel Disease : A Case Study. Springer, 2018.11
3. Masakazu Nagahori. Diagnosis of Ulcerative Colitis:Typical Findings and Diagnostic Criteria. Springer, 2018.11
4. Mamoru Watanabe. Endoscopy in Inflammatory Bowel Disease: Asian Perspectives with Respect to Japan. Springer, 2018.11

[Misc]

1. Hiroko Nagata, Mina Nakagawa, Yasuhiro Asahina. Reply to: "Imaging Basis of AFP and WFA+M2BP as Indicators of the risk of HCC after SVR". *J. Hepatol*. 2018.03; 68(3); 607-608
2. Tetsuya Nakamura. Recent progress in organoid culture to model intestinal epithelial barrier functions. *Int. Immunol*. 2018.10;

[Conference Activities & Talks]

1. Asahina Y. Host genome mutations and HBV integration in HCC patients with HBV infection. 36th US-Japan Hepatitis Panel Meeting 2018.01.10 Shenzhen (China)
2. Aonuma E, Nibe Y, Matsuda H, Otsubo K, Maeyashiki C, Kobayashi M, Matsuzawa Y, Watanabe M, Oshima S. Necroptosis stimulation regulates SQSTM1/p62-LC3 complex formation and polyubiquitination. Keystone Symposia - Ubiquitin Signaling (A8) 2018.01.29 Tahoe(USA)
3. Matsuda H, Nibe Y, Aonuma E, Otsubo K, Maeyashiki C, Kobayashi M, Matsuzawa Y, Nakada S, Watanabe M, Oshima S. K33-linked polyubiquitin is recruited by SQSTM1/p62. Keystone Symposia - Ubiquitin Signaling (A8) 2018.01.30 Tahoe(USA)
4. Nibe Y, Matsuda H, Aonuma E, Otsubo K, Maeyashiki C, Kobayashi M, Matsuzawa Y, Nakada S, Watanabe M, Oshima S. Novel polyubiquitin imaging system, PolyUb-FC, visualized atypical polyubiquitin chain in living cells. Keystone Symposia - Ubiquitin Signaling (A8) 2018.01.30 Tahoe(USA)
5. Otsubo K, Maeyashiki C, Aonuma E, Matsuda H, Nibe Y, Kobayashi M, Matsuzawa Y, Watanabe M, Oshima S. Long-chain fatty acid regulates autophagy and polyubiquitination in intestinal epithelial cells. Keystone Symposia - Ubiquitin Signaling (A8) 2018.01.30 Tahoe(USA)

6. Nishimura R, Tsuchiya K, Shirasaki T, Watanabe S, Hibiya S, Okamoto R, Nakamura T, Watanabe M.. The identification of lesion-specific gene expression in intestinal epithelial cells of Ulcerative Colitis by comparing colonic organoids from lesion and non-lesion parts of same patients. The 13th Congress of ECCO 2018.02.16 Vienna (Austria)
7. Matsuoka K, Naganuma M, Tanida S, Kitamura K, Matsui T, Arai M, Fujiya M, Horiki N, Nebiki H, Kinjo F, Miyazaki T, Matsumoto T, Esaki M, Mitsuyama K, Saruta M, Ido A, Hojo S, Takenaka O, Oketani K, Imai T, Tsubouchi H, Hibi T, Kanai T. Efficacy and safety of anti-fraktalkine monoclonal antibody, E6011, for the patients with Crohn' s disease who had lost response to anti-TNF α antibody : a multi-center, open-label, Phase 1/2 study. The 13th Congress of ECCO 2018.02.16 Vienna (Austria)
8. Hibiya S, Tsuchiya K, Watanabe S, Nishimura R, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Establishment of in vitro human model for Ulcerative Colitis by using human colon organoid culture. 13th Congress of ECCO 2018.02.16 Vienna (Austria)
9. Asahina Y, Liu CJ, Gane E, Itoh Y, Kawada N, Ueno Y, Wang CY, Llewellyn J, Osinusi A, Svarovskaia J, Mo H, Crans G, Chuang WL, Chen PJ, Enomoto N. Ledipasvir/Sofosbuvir All-oral Regimen for Patients with Chronic Hepatitis C Genotype 2 Infection: Integrated Analysis of Three Clinical Studies. 27th Annual Conference of the Asian Pacific Association for the Study of the Liver 2018.03.15 Dehli (India)
10. Kano Y. Tyrosyl phosphorylation of KRAS disrupts the GTPase cycle and inhibits pancreatic cancer cell growth. Pizza Talk of Department of Biochemistry 2018.03.21 Toronto(Canada)
11. Watanabe M. Organoids as a therapy resource from clinical trail in a dish to engraftment. Internarional Cluster Symposium 2018 2018.03.22 Hamburg (Germany)
12. Ohtsuka K. Small Bowel Bleeding-Japan experience. Taiwan Association for the Study of Small Intestinal Diseases (TASSID) Annual Meeting 2018 2018.03.24 Taipei (Taiwan)
13. Ohtsuka K. Tips of Enteroscopy -Single Balloon Endoscopy-. Taiwan Association for the Study of Small Intestinal Diseases (TASSID) Annual Meeting 2018 2018.03.25 Taipei (Taiwan)
14. Ohtsuka K. Balloon-assisted Endoscopy. Tips and Trick. Endoscopy 2018 2018.04.07 Kuala Lumpur (Malaysia)
15. Ohtsuka K. Live demonstrations. (Single-balloon Endoscopy). Endoscopy 2018 2018.04.07 Kuala Lumpur (Malaysia)
16. Ohtsuka K. Live demonstrations. (Single-balloon Endoscopy). Endoscopy 2018 2018.04.08 Kuala Lumpur (Malaysia)
17. Asahina Y, Kakinuma S . HBV reactivation and changes in interferon-stimulated gene expression during treatment of direct-acting antivirals for HCV: Analyses in a novel in vitro model for HBV-HCV coinfection using human induced pluripotent stem cell-derived hepatic cells . EASL, The International Liver Congress 2018 2018.04.14 Paris (France)
18. Kitahata-kawai F, Asahina Y, KakinumaS, Murakawa M, Nitta S, Nagata H, Kaneko S, Inoue E, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N and Watanabe M. Difference of gene mutational profile among viral- and non-viral HCC with or without prior HBV infection: Results of comprehensive deep sequencing analyses of cancer genes and HBV/A AV integration. EASL, The International Liver Congress 2018 2018.04.14 Paris (France)
19. Shiro Yui, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. Fetalization of colonic epithelium mediated by YAP/TAZ links ECM remodeling to tissue regeneration. GI Research Academy 2018 2018.05.25 Tokyo (Japan)
20. Shiro Yui,Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. Fetalization of colonic epithelium mediated by YAP/TAZ links ECM remodeling to tissue regeneration. 16th Stem Cell Research Symposium 2018.06.02 Hyakunenn-Koudou, Kyushu University, Fukuoka (Japan)
21. C. Maeyashiki, H. Melhem, K. Baebler, S. Lang, M. Scharl, G. Rogler, C. de Valliere. Activation of pH-Sensing Receptor OGR1 (GPR68) Induces ER Stress and Autophagy in an Intestinal Epithelial Cell Model. DDW2018 2018.06.02 Washington D.C (USA)

22. Ohtsuka K, Takenaka K, Suzuki K, Fujii T, Nagahori M, Matsuoka K, Saito E, Katsukura N, Fukuda M, Araki A, Watanabe M. Usefulness of single-balloon enteroscopy: from a single center 990 experiences. DDW2018 2018.06.03 Washington D.C (USA)
23. Suzuki K, Kuwabara K, Takahashi J, Anzai S, Kuno R, Kawamoto A, Ishibashi F, Nagata S, Hiraguri Y, Yui S, Tsuchiya K, Nakamura T, Ohtsuka K, Okamoto R, Watanabe M. Single-cell level analysis of organoids derived from CD patients reveals disease-status related modifications of small intestinal stem cells. DDW2018 2018.06.04 Washington D.C (USA)
24. Shirasaki T, Tsuchiya K, Nishimura R, Watanabe S, Hibiya S, Katsukura N, Okamoto R, Nakamura T, Watanabe M. Identification of lesion-specific epithelial function of ulcerative colitis by comparing colonic organoids from lesion and non-lesion parts of same patients. DDW2018 2018.06.05 Washington D.C (USA)
25. Hibiya S, Tsuchiya K, Watanabe S, Nishimura R, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Human colonic organoid treated with inflammatory factors might mimic the pathophysiology of epithelial cells in ulcerative colitis. DDW2018 2018.06.05 Washington D.C (USA)
26. Taro Watabe, Takashi Nagaishi, Naoya Tsugawa, Yudai Kojima, Nisha Jose, Akinori Hosoya, Takahiro Adachi, Mamoru Watanabe. Analysis of ileocecal immune response in an animal model of colitis using intra-vital imaging. DDW 2018 2018.06.05 Washington D.C (USA)
27. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Mice overexpressing MKL1 in macrophages are susceptible to the development of colitis. DDW 2018 2018.06.05 Washington D.C (USA)
28. Ishibashi F, Shimizu H, Kawamoto A, Suzuki K, Anzai S, Kuwabara K, Takahashi J, Nagata S, Oshima S, Tsuchiya K, Nakamura T, Watanabe M, Okamoto R. Mouse colonic secretory cells de-differentiate into intestinal stem cells and promote mucosal repair through activation of NF-KB signalin. ISSCR2018 2018.06.20 Melbourne (Australia)
29. Takashi Nagaishi, Taro Watabe, Tsugawa, Yudai Kojima, Nisha Jose, Daiki Yamada, Takahiro Adachi, Mamoru Watanabe. Analysis of cecal immune response in a murine model of colitis using intravital imaging. FOCIS 2018 2018.06.20 San Francisco (USA)
30. Saito E, Suzuki K, Shimizu H, Motobayashi M, Takenaka K, Onizawa M, Fujii T, Nagahori M, Ohtsuka K, Watanabe M. The clinical efficacy of switching cases between Infliximab(IFX) and Adalimumab(ADA) in patients with ulcerative colitis. AOCC2018 2018.06.22 Shanghai (China)
31. Yasuhiro Nemoto. Colonic regulatory T Cells function during the ulcerative colitis. AOCC2018 2018.06.22 Shanghai (China)
32. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Mice overexpressing MKL1 in macrophages are susceptible to DSS-induced colitis. FOCIS 2018 2018.06.22 San Francisco (USA)
33. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Overexpression of MKL1 in Macrophages leads to the development of murine colitis. MICS 2018 2018.07.19 Oxford (UK)
34. Kazuo Ohtsuka. Immunological Implication in the Development of IBD Medications. TASSID 3rd Academic Meeting of 2018 2018.09.01 Taipei (Taiwan)
35. Yuka Matsumoto, Mamoru Watanabe, Tetsuya Nakamura. Development of a new mouse model of short bowel syndrome that may allow for the assessment of therapeutic efficacy of heterotopic transplantation of small intestinal organoids. 5th TERMIS World Congress 2018.09.04 Kyoto (JAPAN)
36. Suzuki K, Murano T, Hiraguri Y, Takahashi J, Shimizu H, Anzai S, Kuwabara K, Kawamoto A, Ishibashi F, Yui S, Tsuchiya K, Nakamura T, Ohtsuka K, Watanabe M, Okamoto R. Crohn's disease patient-derived small intestinal organoids reveal disease-status related modification of stem cell properties. 5th TERMIS World Congress 2018 2018.09.06 Kyoto (JAPAN)
37. Okamoto R, Watanabe M. Regenerative medicine for the treatment of inflammatory bowel disease. 5th TERMIS World Congress 2018 2018.09.07 Kyoto (JAPAN)

38. Takenaka K, Ohtsuka K, Fujii T, Nagahori M, Saito E, Motobayashi M, Suzuki K, Watanabe M. Small bowel mucosal healing of Crohn's disease treated with anti-TNF antibodies. FALKsymposium 2018.09.07 Kyoto (JAPAN)
39. Suzuki K, Takahashi J, Hiraguri Y, Yui S, Shimizu H, Tsuchiya K, Nakamura T, Ohtsuka K, Okamoto R, Watanabe M. Crohn's disease patient-derived small intestinal organoids reveal disease status related modification of stem cell properties. FALKsymposium 2018.09.08 Kyoto (JAPAN)
40. Nitta S, Kato T, Tsuchiya J, Shinomiya-Inoue E, Sato A, Tsunoda T, Miyoshi M, Kitahata-Kawai F, Murakawa M, Itsui Y, Azuma S, Nakagawa M, Kakinuma S, Asahina Y. The in vitro analysis of NS5A resistance-associated substitutions (RAS) observed in DAA treatment failure patients. 25th International Symposium on Hepatitis C Virus and Related Viruses 2018.10.09 Dublin (Ireland)
41. Kazuo Ohtsuka . State of the art for single balloon enteroscopy; Secrets of troubleshooting during insertion and therapeutic management. The 6th GSTECC 2018 2018.10.13 Seoul (Korea)
42. Yudai Kojima, Takashi Nagaishi, Taro Watabe, Naoya Tsugawa, Nisha Jose, Daiki Yamada, Akinori Hosoya, Takahiro Adachi, Mamoru Watanabe. B cell-mediated ileocecal immune response is activated in the early phase of colitis development. UEGW 2018 2018.10.22 Vienna (Austria)
43. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Mice overexpressing MKL1 in macrophages experience fulminant colitis. UEGW 2018 2018.10.22 Vienna (Austria)
44. Hibiya S, Tsuchiya K, Nishimura R, Shirasaki T, Watanabe S, Katsukura N, Okamoto R, Nakamura T, Watanabe M. Lesion-specific gene expression in the Epithelial cells of Crohn's disease by comparing Small intestinal organoids from active and inactive Lesion in the same patient. UEGW 2018 2018.10.22 Vienna (Austria)
45. Ishibashi F, Kuwabara K, Kawamoto A, Anzai S, Takahashi J, Nagata S, Shimizu H, Yui S, Oshima S, Tsuchiya K, Nakamura T, Watanabe M, Okamoto R. Ectopic expression of reg3a in the mice distal Colon is mediated by interactions between notch and Il-22 signaling pathways, and promotes tissue repair By the augmentation of EGFR signaling. UEGW 2018 2018.10.22 Vienna (Austria)
46. Kuwabara K, Ishibashi F, Kawamoto A, Anzai S, Takahashi J, Nagata S, Shimizu H, Yui S, Oshima S, Tsuchiya K, Nakamura T, Watanabe M, Okamoto R. Long-lived secretory cells residing in the mouse proximal colon serve as reserve stem cells under DNA damage-induced mucosal injury. UEGW 2018 2018.10.22 Vienna (Austria)
47. Motoya S, Watanabe K, Ogata H, Kanai T, Matsui T, Suzuki Y, Shikamura M, Sugiura K, Oda K, Hori T, Araki T, Watanabe M, Hibi T. A phase 3 study of vedolizumab in Japanese patients with ulcerative colitis: effects on time to disease worsening and treatment failure. UEGW 2018 2018.10.22 Vienna (Austria)
48. Watanabe S, Tsuchiya K, Shirasaki T, Hibiya S, Nishimura S, Katsukura N, Oshima S, Okamoto R, Tetsuya N, Watanabe M. Tp53 mutation enhances cell proliferation and stemness in human colon epithelial organoids and promotes a resistance against long-term inflammation. UEGW 2018 2018.10.22 Vienna (Austria)
49. Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Nakagawa M, Kakinuma S, Watanabe M. Gene Mutational Profile and Viral Integration in Hepatocellular Carcinoma with or without HBV/HCV Suppression. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
50. Nakagawa M, Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tomita M, Watanabe M. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
51. Nitta S, Kato T, Tsuchiya J, Sato A, Tsunoda T, Miyoshi M, Inoue- Shinomiya E, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The Characteristic and the Anti-HCV Reagents Susceptibility Analysis of NS5A Resistance-Associated Substitutions (RAS) Detected after Daa Treatment Failure Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
52. Asahina Y. Increased risk of HCC following DAA: fact or fiction? / Follow up strategy after SVR in chronic hepatitis C. Asian Pacific Digestive Week 2018 2018.11.16 Seoul (Korea)

Specialized Surgeries

< Division of Specialized Surgeries >

Professor: Hiroyuki UETAKE

Associate Professor: Toshifumi KUDO, Toshiaki ISHIKAWA

Junior Associate Professor: Tsuyoshi NAKAGAWA, Kentaro OKAMOTO, Satoshi OKAZAKI

Assistant Professor: Kimihiro IGARI

Attending staff:

Masato NISHIZAWA, Sotaro KATSUI, Kei OGINO, Yuichi KUMAKI, Tokuko HOSOYA

< Department of Translational Oncology/Clinical Research Center >

Associate Professor: Megumi ISHIGURO

< Facility of Medical Informatics >

Junior Associate Professor: Goshi ODA

(1) Outline

Division of Specialized Surgeries have been launched in April 2015, which consists of 4 clinical departments in the Medical Hospital:

- Division of Chemotherapy and Oncosurgery
- Division of Vascular Surgery
- Division of Breast Surgery
- Division of Pediatric surgery

(2) Research

Main themes of our research activities

- Identification of prognostic factors and the predictive factors for chemo-responsiveness in gastrointestinal and breast cancer, by molecular biological technique and immuno-histochemical approach
- Micro circulation in severe ischemic extremity
- Relation between vascular disease and periodontitis
- Development of new device for evaluating hemodynamics
- Development of safety central venous catheterization
- Establishment of telemedicine

(3) Education

Main objective in the graduate course is to bring up the well-rounded surgeons who has international and scientific feelings.

(4) Publications

[Original Articles]

1. Toshikazu Moriwaki, Shota Fukuoka, Hiroya Taniguchi, Atsuo Takashima, Yusuke Kumekawa, Takeshi Kajiwar, Kentaro Yamazaki, Taito Esaki, Chinatsu Makiyama, Tadamichi Denda, Hironaga Satake, Takeshi Suto, Naotoshi Sugimoto, Masanobu Enomoto, Toshiaki Ishikawa, Tomomi Kashiwada, Masahiko Sugiyama, Yoshito Komatsu, Hiroyuki Okuyama, Eishi Baba, Daisuke Sakai, Tomoki Watanabe, Takao Tamura, Kimihiro Yamashita, Masahiko Gosh, Yasuhiro Shimada. Propensity Score Analysis of Regorafenib Versus Trifluridine/Tipiracil in Patients with Metastatic Colorectal Cancer Refractory to Standard Chemotherapy (REGOTAS): A Japanese Society for Cancer of the Colon and Rectum Multicenter Observational Study. *Oncologist*. 2018.01; 23(1); 7-15
2. Yohei Yamamoto, Yoshinori Inoue, Tsuyoshi Ichinose, Masato Nishizawa, Kimihiro Igari, Takahiro Toyofuku, Toshifumi Kudo. Multiple Recurrent Pseudoaneurysms after Endovascular Repair of Abdominal Aortic Aneurysm in a Patient with Behçet's Disease. *Ann Thorac Cardiovasc Surg*. 2018.01;
3. Hideki Ueno, Shigeki Sekine, Taihei Oshiro, Yukihide Kanemitsu, Tetsuya Hamaguchi, Dai Shida, Atsuo Takashima, Megumi Ishiguro, Eisaku Ito, Yojiro Hashiguchi, Fukuo Kondo, Hideyuki Shimazaki, Satsuki Mochizuki, Yoshiki Kajiwar, Eiji Shinto, Junji Yamamoto, Yasuhiro Shimada. Disentangling the prognostic heterogeneity of stage III colorectal cancer through histologic stromal categorization. *Surgery*. 2018.04; 163(4); 777-783
4. Tomoki Yamano, Shinichi Yamauchi, Kiyoshi Tsukamoto, Masafumi Noda, Masayoshi Kobayashi, Michiko Hamanaka, Akihito Babaya, Kei Kimura, Chihyon Son, Ayako Imada, Shino Tanaka, Masataka Ikeda, Naohiro Tomita, Kenichi Sugihara, . Evaluation of appropriate follow-up after curative surgery for patients with colorectal cancer using time to recurrence and survival after recurrence: a retrospective multicenter study. *Oncotarget*. 2018.05; 9(39); 25474-25490
5. Matsuda C, Ishiguro M, Teramukai S, Kajiwar Y, Fujii S, Kinugasa Y, Nakamoto Y, Kotake M, Sakamoto Y, Kurachi K, Maeda A, Komori K, Tomita N, Shimada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Nakagawa Y, Sugihara K.. A randomised-controlled trial of 1-year adjuvant chemotherapy with oral tegafur-uracil versus surgery alone in stage II colon cancer: SACURA trial. *Eur. J. Cancer*. 2018.06; 96; 54-63
6. Chu Matsuda, Megumi Ishiguro, Satoshi Teramukai, Yoshiki Kajiwar, Shoichi Fujiie, Yusuke Kinugasa, Yoshihiko Nakamoto, Masanori Kotake, Yoshiyuki Sakamoto, Kiyotaka Kurachi, Atsuyuki Maeda, Koji Komori, Naohiro Tomita, Yasuhiro Shimada, Keiichi Takahashi, Kenjiro Kotake, Masahiko Watanabe, Hidetaka Mochizuki, Yoko Nakagawa, Kenichi Sugihara on behalf of the SAKURA Study Group. A randomised-controlled trial of 1-year adjuvant chemotherapy with oral tegafur-uracil versus surgery alone in stage II colon cancer: SACURA trial *Eur J Cancer*. 2018.06; 96; 54-63
7. Raju Kandimalla, Feng Gao, Takatoshi Matsuyama, Toshiaki Ishikawa, Hiroyuki Uetake, Naoki Takahashi, Yasuhide Yamada, Carlos R Becerra, Scott Kopetz, Xin Wang, Ajay Goel. Genome-wide discovery and identification of a novel miRNA signature for recurrence prediction in stage II and III colorectal cancer. *Clin. Cancer Res.*. 2018.08; 24(16); 3867-3877
8. Fujioka T, Kubota K, Kikuchi Y, Tsuchiya J, Tateishi U, Kasaharak M, Oda G, Ishiba T, Nakagawa T. The feasibility of using 18F-FDG-PET/CT in patients with mucinous breast carcinoma. *Nuclear medicine communications*. 2018.09;
9. Imataka G, Yamaguchi T, Ishii J, Ogino K, Okamoto K, Tsuchioka T, Yoshihara S. MERS associated with bacterial translocation in a pediatric patient with congenital portal vein hypoplasia: A case report *Experimental and Therapeutic*. 2018.10; 16(4); 2831-2834
10. Kusumoto T, Ishiguro M, Nakatani E, Yoshida M, Inoue T, Nakamoto Y, Shiomi A, Takagane A, Sunami E, Shinozaki H, Takii Y, Maeda A, Ojima H, Hashida H, Mukaiya M, Yokoyama T, Nakamura M, Munemoto Y, Sugihara K. Updated 5-year survival and exploratory T x N subset analyses of ACTS-CC trial: a randomised controlled trial of S-1 versus tegafur-uracil/leucovorin as adjuvant chemotherapy for stage III colon cancer. *ESMO Open*. 2018.10; 3(6); e000428
11. Yamamoto Y, Kudo T, Ichinose T, Nishizawa M, Toyofuku T. Bilateral external iliac venous aneurysm in a long-distance runner *Ann Vasc Surg*. 2018.11; doi.org/10.1007/s10147-018-01393-8

12. Ishiguro M, Ueno H, Kanemitsu Y, Hamaguchi T, Shida D, Simada Y. Current clinical practice of adjuvant chemotherapy for patients with 'high-risk' Stage II colorectal cancer in Japan: a questionnaire survey in the JCOG Study Group. *Jpn. J. Clin. Oncol.* 2018.12; 48(12); 1109-1112

[Misc]

1. Ishida H, Yamaguchi T, Tanakaya K, Akagi K, Inoue Y, Kumamoto K, Shimodaira H, Sekine S, Tanaka T, Chino A, Tomita N, Nakajima T, Hasegawa H, Hinoi T, Hirasawa A, Miyakura Y, Murakami Y, Muro K, Ajioka Y, Hashiguchi Y, Ito Y, Saito Y, Hamaguchi T, Ishiguro M, Ishihara S, Kanemitsu Y, Kawano H, Kinugasa Y, Kokudo N, Murofushi K, Nakajima T, Oka S, Sakai Y, Tsuji A, Uehara K, Ueno H, Yamazaki K, Yoshida M, Yoshino T, Boku N, Fujimori T, Itabashi M, Koinuma N, Morita T, Yamaguchi H, Sugihara K, Watanabe T.. Japanese Society for Cancer of the Colon and Rectum(JSCCR) Guidelines 2016 for the Clinical Practice of Hereditary Colorectal Cancer(Translated Version). *J Anus Rectum Colon.* 2018.01; 2(Suppl 1); 1-51

[Conference Activities & Talks]

1. Shinichi Yamauchi, Ayumi Takaoka, Yuriko Matsumiya, Ryota Seki, Fukuichiro Orita, Megumi Sasaki, Tomiyuki Miura, Akifumi Kikuchi, Takatoshi Matsuyama, Megumi Ishiguro, Toshiaki Ishikawa, Masamichi Yasuno, Hiroyuki Uetake, Yusuke Kinugasa, Kenichi Sugihara. Indication of Extended Lateral Lymph Node Dissection for Patients with Lower Rectal Cancer. SSO 2018 Annual Cancer Symposium 2018.03.23 Chicago, US
2. Tomiyuki Miura, Shinichi Yamauchi, Takatoshi Matsuyama, Megumi Ishiguro, Toshiaki Ishikawa, Yasuaki Nakajima, Kazuyuki Kojima, Masamichi Yasuno, Hiroyuki Uetake, Yusuke Kinugasa. A case of Incarcerated Internal Hernia through a Defect of the Falciform Ligament. International Association of Surgeons, Gastroenterologists and Oncologists (IASGO2018) 2018.04.04 Tokyo
3. Shinichi Yamauchi, Takatoshi Matsuyama, Ayumi Takaoka, Yuriko Matsumiya, Ryota Seki, Fukuichiro Orita, Megumi Sasaki, Tomiyuki Miura, Akifumi Kikuchi, Megumi Ishiguro, Toshiaki Ishikawa, Hiroyuki Uetake, Masamichi Yasuno, Yasuaki Nakajima, Kazuyuki Kojima, Yusuke Kinugasa. Laparoscopic and open surgery for ulcerative colitis. International Association of Surgeons, Gastroenterologists and Oncologists (IASGO2018) 2018.04.12 Tokyo
4. Takatoshi Matsuyama, Raju Kandimalla, Xuan Wang, Toshiaki Ishikawa, Naoki Uetake, Yasuhide Yamada, Masamichi Yasuno, Yusuke Kinugasa, Hiroyuki Uetake, Ajay Goel. A mesenchymal-associated transcriptomic signature has a prognostic and predictive potential in stage II and III colorectal cancer patients. American Association for Cancer Research (AACR 2018) 2018.04.16 Chicago (USA)
5. Okamoto K, Itoh Y, Ogino K. Insertion of peripherally inserted central venous catheter using venous visualization equipment of near infra-red light. the 51st Pacific Association of Pediatric Surgeons 2018.05.15 Sapporo
6. Ichinose T. A Case of T-banding for 4.6 L/min A-V fistula for Hemodialysis. The Asia-Pacific Angiology Academic Alliance Conference 2018 2018.05.26 Macau (China)
7. Uetake H. 【Opening Remarks】. Gastrointestinal Cancer in CHICAGO 2018.06.26 Chicago (USA)
8. Ichinose T, Yamamoto Y, Nakamura M, Nishizawa M, Yonekura K, Toyofuku T, Iwasaki T, Kudo T, Sugano N, Inoue Y. Strategy and prevention for high flow A-V fistula for hemodialysis. 10th Conference of the German-Japanese Society of Vascular Surgery 2018 2018.08.18 Frankfurt (Germany)
9. Ishikawa T, Ishiguro M, Nakatani E, Ueno H, Uetake H, Murotani K, Matsui S, Tomita N, Shimada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Teramukai S, Sugihara K. Prognostic impact of MSI and 18qLOH in Stage II colon cancer: A prospective biomarker study in the SACURA trial. ESMO 2018 2018.10.21 Munich (Germany)
10. Kumaki Y, Ikeda S, Rich TA, Shiotsu Y, Franovic A, Raymond VM, Kurzrock R, Lanman RB, Lee J, Mok TSK. Circulating cell-free DNA molecular profiling among East Asian patients reveals activating MET alterations are common in diverse advanced cancer types. ESMO Asia 2018 Congress 2018.11.24

Cardiovascular Medicine

Professor

Kenzo Hirao

Endowed Professor

Takashi Ashikaga

Associate Professor

Masahiko Goya

Tetsuo Sasano (Graduate School of Health Care Sciences,
Biofunctional Informatics)

Kiyoshi Nobori (Clinical Research Center)

Junior Associate Professor

Yasuhiro Maejima, Mihoko Kawabata, Yusuke Ebana (Medical Research Institute
Bio-informational Pharmacology)

Assistant Professor

Takanobu Yamamoto, Yoshihide Takahashi, Taro Sasaoka,,

Yu Hatano, Hidenori Arima, Masanori Konishi

Specially-Appointed Professor

Shingo Maeda, Kentaro Takahashi

Endowed Assistant Professor

Tomoyuki Umemoto

Joint Research Assistant Professor

Atsuhiko Yagishita

Graduate Student

Yusuke Ito, Kei Takayama, Ryota Iwatsuka, Tatsuya Fujinami, Osamu Inaba, Rena

Nakamura, Riri Watanabe, Naoyuki Miwa, Tomoyuki Umemoto, Takashi Nakagawa,

Yasuaki Tanaka, Tetsumin Lee, Yukihiro Inamura, Mie Ochida, Tomomasa Takamiya,

Kensuke Hirasawa, Yuki Osaka, Ohnishi Kentaro, Mituhisa Asano, Nobutaka Kato,

Yasuhiro Shirai, Naohiko Kawaguchi, Shinsuke Iwai, Shunsuke Kuroda, Nobuyuki

Kagiyama, Takuro Nisimura, Junji Matuda, Makoto Araki, Shigeki Kusa, Kazuya Yamao,

Takamitsu Takagi, Yoshihisa Kanaji, Sho Nagamine, Rei Masuda, Eisuke Usui, Naoko Kato,

Takashi Niida, Akira, Mizukami, Masakazu Kaneko, Tatsuhiko Hirao, Takakatu Yoshitake,

Taku Fukushima, Yuichiro Sagawa, Tadashi Fukuda

(1) Outline

The Department of Cardiovascular Medicine at Tokyo Medical and Dental University aims to elucidate the cause of the cardiovascular diseases, including ischemic heart diseases, arrhythmia and heart failure, and to develop their novel therapeutic strategies by assessing both basic and clinical research approaches.

We encourage young doctors to be well-balanced physicians who focus on medical therapy as well as on research. Students are encouraged and being trained to take an active role at global level, as well. We strive to make high contributions in the area of cardiovascular medicine within Japan.

(2) Research

The purposes of our investigation are to reveal the etiology and pathophysiology of cardiovascular diseases, thereby developing novel technologies for diagnosis and treatment. For that purpose we investigate clinical cases and experimental animal models. Our faculty members pursue a wide variety of basic research, ranging from investigations on the molecular mechanism of heart failure to the development of novel interventional devices for patients with angina pectoris. Current strengths of the program include molecular cardiology under Yasuhiro Maejima MD, PhD. We also actively investigate immunocardiology, the molecular mechanism of pulmonary hypertension and periodontitis-associated cardiovascular diseases.

- 1) System of origin with tachyarrhythmias (particularly supraventricular tachycardia) (Hirao)
- 2) Medical therapy and ablation for tachyarrhythmias (Hirao)
- 3) Research for the conduction of atrio-ventricular node (Hirao)
- 4) Research and Therapy for arrhythmia by using cardioendoscopy (Hirao)
- 5) Research of atrial fibrillation from origin of pulmonary vein (Hirao)
- 6) Research of genetic factor with atrial fibrillation (Hirao)
- 7) Research of ablation for atrial fibrillation (Hirao, Goya)
- 8) Clinical study for treatment of acute coronary syndrome (Ashikaga, Yamamoto, Umemoto, Sasaoka, Hatano)
- 9) Molecular mechanism and treatment of myocardial ischemia and reperfusion injury (Maejima, Hatano)
- 10) Molecular mechanism and treatment of coronary restenosis and vascular disease (Maejima, Hatano)
- 11) Treatment of heart failure and cardiomyopathy by myocardial regeneration (Maejima)
- 12) Regulation of arteriosclerosis by targeting transcription factors (Maejima)
- 13) Diagnostic imaging of aortitis (Tezuka)
- 14) Assessment by imaging of coronary artery and cardiac function (Tezuka)
- 15) Molecular mechanism and treatment of aortitis (Maejima)
- 16) Assessment of vascular endothelial dysfunction in vasculitis, heart failure and arrhythmia (Maejima)
- 17) Application in gene therapy for heart failure and cardiomyopathy (Maejima)
- 18) Molecular system of myocardial remodeling in heart failure and ventricular hypertrophy (Maejima)

There are many fruitful collaborative efforts between our department and other departments with the TMDU, such as the Department of Bio-informational Pharmacology, Medical Research Institute. Collaborations with other institutions are also common. Especially, we closely collaborate with the Department of Cell Biology and Molecular Medicine, Rutgers-New Jersey Medical School (Newark, NJ, USA; Junichi Sadoshima MD, PhD). Our cardiologists continuously contribute to establish evidence-based cardiovascular medicine through clinical researches. So far, we are engaged in over ten clinical studies. The targets of our clinical research include heart failure, ischemic heart disease, arrhythmia, cardiac imaging and Takayasu arteritis.

(3) Education

The Department of Cardiovascular Medicine at Tokyo Medical and Dental University (TMDU) primarily aims at offering patient-centered care for every person who suffer from cardiovascular diseases, including ischemic heart diseases, arrhythmia, heart failure, valvular disorders and vasculitis. Our cardiologists are experts in electrophysiology, interventional cardiology, heart failure, and cardiac imaging who make full use of state-of-the-art diagnostic tests and therapeutic procedures to provide high-quality care for every patient. We also actively engage in basic and clinical research to elucidate the mechanism of heart & vessel disorders for providing novel therapeutic strategies to the patients of cardiovascular diseases. In addition to high-quality patient care and innovative research, our faculty members are vigorously involved in the education and training to the young physicians and researchers specializing in cardiovascular medicine. Thus, we are continuously making every effort to serve the highest quality of patient care, education and innovative research of cardiovascular medicine.

(4) Clinical Services & Other Works

Our clinical training program provides the trainee with outstanding skills in clinical cardiology. The trainees will develop their clinical knowledge, clinical judgment, procedural skills and interpersonal skills required as a specialist in cardiovascular diseases. The program provides clinical cardiology training not only at the University Hospital but also at our outstanding affiliate hospitals (N=22), including Kameda General Hospital, Musashino Red-Cross Hospital, Tsuchiura Kyodo Hospital and Yokosuka Kyosai Hospital. Our training program for re-

search emphasizes developing academic cardiologists who will become leaders in cardiovascular research. The program offers training of basic, clinical and translational researches not only at the Graduate School of our department but also at other departments with the TMDU and at other institutions described above.

(5) Publications

[Original Articles]

1. Araki Makoto, Yonetsu Taishi, Lee Tetsumin, Murai Tadashi, Kanaji Yoshihisa, Usui Eisuke, Matsuda Junji, Hoshino Masahiro, Niida Takayuki, Hada Masahiro, Ichijo Sadamitsu, Hamaya Rikuta, Kanno Yoshinori, Isobe Mitsuaki, Kakuta Tsunekazu. Relationship between optical coherence tomography-defined in-stent neoatherosclerosis and out-stent arterial remodeling assessed by serial intravascular ultrasound examinations in late and very late drug-eluting stent failure JOURNAL OF CARDIOLOGY. 2018; 71(3-4); 244-250
2. Matsuda J, Ikenouchi T, Nitta G, Kato S, Murata K, Kanoh M, Inamura Y, Kato N, Takamiya T, Negi K, Sato A, Yamato T, Matsumura Y, Nitta J. Successful Percutaneous Coronary Intervention for Atherosclerotic Coronary Lesion with Anomalous Origin of the Right Coronary Artery. Case reports in medicine. 2018; 2018; 4232941
3. Aoyama N, Suzuki JI, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, Shiheido Y, Sato H, Minabe M, Izumi Y, Isobe M. Associations among tooth loss, systemic inflammation and antibody titers to periodontal pathogens in Japanese patients with cardiovascular disease. Journal of Periodontal Research. 2018.02; 53(1); 117-122
4. Yu Natsume, Kasumi Oaku, Kentaro Takahashi, Wakana Nakamura, Ai Oono, Satomi Hamada, Masahiro Yamazoe, Kensuke Ihara, Takeshi Sasaki, Masahiko Goya, Kenzo Hirao, Tetsushi Furukawa, Tetsuo Sasano. Combined Analysis of Human and Experimental Murine Samples Identified Novel Circulating MicroRNAs as Biomarkers for Atrial Fibrillation. Circulation Journal. 2018.03; 82; 965-973
5. Aoyama Norio, Suzuki Jun-ichi, Kobayashi Naho, Hanatani Tomoya, Ashigaki Norihiko, Yoshida Asuka, Shiheido Yuka, Sato Hiroki, Kumagai Hidetoshi, Ikeda Yuichi, Akazawa Hiroshi, Komuro Issei, Minabe Masato, Izumi Yuichi, Isobe Mitsuaki. 日本人糖尿病合併心血管疾患患者は糖尿病非合併患者と比較して歯牙欠損が増加する 横断研究 (Japanese Cardiovascular Disease Patients with Diabetes Mellitus Suffer Increased Tooth Loss in Comparison to Those without Diabetes Mellitus: A Cross-sectional Study) Internal Medicine. 2018.03; 57(6); 777-782
6. 篠岡 太郎, 福島 啄, 中釜 瞬, 仁井田 崇志, 仲村 太一, 松田 祐治, 平澤 憲祐, 秦野 雄, 梅本 朋幸, 山本 貴信, 前嶋 康浩, 合屋 雅彦, 足利 貴志, 平尾 見三. エキシマレーザーによる粥腫切除術を要する冠病変の包括的 OCT/OFDI 解析 (Comprehensive OCT/OFDI Analysis of the Excimer Laser Atherectomy Required Coronary Lesions) 日本循環器学会学術集会抄録集. 2018.03; 82 回; PJ022-2
7. Sasaoka Taro, Nakagama Shun, Niida Takayuki, Nakamura Taichi, Matsuda Yuji, Hirasawa Kensuke, Hatano Yu, Umemoto Tomoyuki, Yamamoto Takanobu, Maejima Yasuhiro, Goya Masahiko, Ashikaga Takashi, Hirao Kenzo. エキシマレーザー冠動脈粥腫切除術 (ELCA) の臨床的特徴と転帰 実診療の経験から (Clinical Characteristics and Outcomes of Excimer Laser Coronary Atherectomy(ELCA): from the Real-world Experiences) 日本循環器学会学術集会抄録集. 2018.03; 82 回; OE63-8
8. Hatano Yu, Ashikaga Takashi, Niida Takayuki, Nakamura Taichi, Matsuda Yuji, Hirasawa Kensuke, Sasaoka Taro, Umemoto Tomoyuki, Yamamoto Takanobu, Maejima Yasuhiro, Hirao Kenzo. ステント内再狭窄病変と新規狭窄病変で比較した薬剤コーティングバルーンによる中期的効果の差 (The Difference of Mid-term Effect of a Drug-coated Balloon between In-stent Restenosis Lesions and de Novo Lesions) 日本循環器学会学術集会抄録集. 2018.03; 82 回; OE71-7
9. Matsuda Yuji, Ashikaga Takashi, Nakamura Taichi, Hirasawa Kensuke, Hatano Yu, Sasaoka Taro, Umemoto Tomoyuki, Yamamoto Takanobu, Maejima Yasuhiro, Hirao Kenzo. 回転式アテレクトミーを必要とした重度石灰化病変への第 2 世代 DES に関する連続 OFDI/OCT 解析 Xience 対 Synergy(The Serial OFDI/OCT Analysis of the 2nd Generation DES at Severe Calcified Lesion with Rotational Atherectomy Required: Xience vs Synergy) 日本循環器学会学術集会抄録集. 2018.03; 82 回; PE126-5

10. Matsuda Yuji, Ashikaga Takashi, Nakamura Taichi, Hirasawa Kensuke, Hatano Yu, Sasaoka Taro, Umemoto Tomoyuki, Yamamoto Takanobu, Maejima Yasuhiro, Hirao Kenzo. 回転式アテレクトミーを要した重度石灰化病変に対する第二世代 DES の連続的 OFDI/OCT 解析 Xience と Promus の比較 (The Serial OFDI/OCT Analysis of the 2nd Generation DES at Severely Calcified Lesion with Rotational Atherectomy Required: Xience vs Promus) 日本循環器学会学術集会抄録集. 2018.03; 82 回; PE030-6
11. Umemoto Tomoyuki, Ueshima Daisuke, Yoshikawa Shunji, Sasaoka Taro, Hatano Yu, Kurihara Ken, Maejima Yasuhiro, Isobe Mitsuaki, Ashikaga Takashi, Hirao Kenzo. 経皮的冠動脈インターベンションにおける逆説的高コレステロール血症 多施設共同 PCI レジストリの解析 (The Hypercholesterolemia Paradox in Percutaneous Coronary Intervention: Analysis of A Multicenter PCI Registry) 日本循環器学会学術集会抄録集. 2018.03; 82 回; PE004-5
12. Araki Makoto, Yonetsu Taishi, Lee Tetsumin, Murai Tadashi, Kanaji Yoshihisa, Usui Eisuke, Matsuda Junji, Hoshino Masahiro, Niida Takayuki, Hada Masahiro, Ichijo Sadamitsu, Hamaya Rikuta, Kanno Yoshinori, Isobe Mitsuaki, Kakuta Tsunekazu. 薬剤溶出性ステントの晩期および超晩期失敗におけるステント内新生アテローム性動脈硬化の OCT 像と血管内超音波で経時的に評価したステント外の動脈リモデリングとの関係 (Relationship between optical coherence tomography-defined in-stent neoatherosclerosis and out-stent arterial remodeling assessed by serial intravascular ultrasound examinations in late and very late drug-eluting stent failure) Journal of Cardiology. 2018.04; 71(3-4); 244-250
13. Yusuke Ito, Yasuhiro Maejima, Natsuko Tamura, Yuka Shiheido-Watanabe, Masanori Konishi, Takashi Ashikaga, Kenzo Hirao, Mitsuaki Isobe. Synergistic effects of HMG-CoA reductase inhibitor and angiotensin II receptor blocker on load-induced heart failure. FEBS Open Bio. 2018.05; 8(5); 799-816
14. Yuji Matsuda, Takashi Ashikaga, Taro Sasaoka, Yu Hatano, Tomoyuki Umemoto, Takanobu Yamamoto, Yasuhiro Maejima, Kenzo Hirao. Effectiveness of the proximal optimization technique for longitudinal stent elongation caused by post-balloon dilatation. Journal of Interventional Cardiology. 2018.07;
15. Daisuke Ueshima, Shunji Yoshikawa, Taro Sasaoka, Yu Hatano, Ken Kurihara, Yasuhiro Maejima, Mitsuaki Isobe, Takashi Ashikaga. Obesity paradox in the era of percutaneous coronary intervention with 2nd-generation drug-eluting stents: an analysis of a multicenter PCI registry. Heart Vessels. 2018.07;
16. Aoyama Norio, Suzuki Jun-ichi, Kobayashi Naho, Hanatani Tomoya, Ashigaki Norihiko, Yoshida Asuka, Shiheido Yuka, Sato Hiroki, Izumi Yuichi, Isobe Mitsuaki. Increased Oral Porphyromonas gingivalis Prevalence in Cardiovascular Patients with Uncontrolled Diabetes Mellitus INTERNATIONAL HEART JOURNAL. 2018.07; 59(4); 802-807
17. Aoyama Norio, Suzuki Jun-ichi, Kobayashi Naho, Hanatani Tomoya, Ashigaki Norihiko, Yoshida Asuka, Shiheido Yuka, Sato Hiroki, Izumi Yuichi, Isobe Mitsuaki. Increased Oral Porphyromonas gingivalis Prevalence in Cardiovascular Patients with Uncontrolled Diabetes Mellitus(和訳中) International Heart Journal. 2018.07; 59(4); 802-807
18. 仲村 太一, 篠岡 太郎, 仁井田 崇志, 松田 祐治, 平澤 憲祐, 秦野 雄, 梅本 朋幸, 山本 貴信, 足利 貴志. OCT/OFDI による石灰化ブランク分布の検討 日本心血管インターベンション治療学会抄録集. 2018.08; 27 回; MO522
19. 梅本 朋幸, 仁井田 崇志, 仲村 太一, 松田 祐治, 平澤 憲祐, 秦野 雄, 篠岡 太郎, 山本 貴信, 足利 貴志. 急性期および慢性期における急性冠症候群患者の脂質管理の現状とリピッドパドックスについて 日本心血管インターベンション治療学会抄録集. 2018.08; 27 回; MO048
20. 松田 祐治, 足利 貴志, 中釜 瞬, 仁井田 崇志, 仲村 太一, 平澤 憲祐, 秦野 雄, 篠岡 太郎, 梅本 朋幸, 山本 貴信, 前嶋 康浩, 平尾 見三. 石灰化病変に対する PCI イメージングと各種デバイス選択 回転性粥腫切除術を要する高度石灰化病変に対する第 2 世代 DES の OCT によるシリアル解析 Xience vs Promus vs Synergy 日本心血管インターベンション治療学会抄録集. 2018.08; 27 回; PD8-1
21. 宮崎 徹, 足利 貴志, 福島 琢, 秦野 雄, 栗原 顕. いかに再狭窄病変での DCB の効果を高めるか ステント再狭窄症例に対するエキシマレーザー後の薬剤溶出型バルーン治療に関する OCT を用いた比較検討 日本心血管インターベンション治療学会抄録集. 2018.08; 27 回; PD17-1
22. Daisuke Ueshima, Shunji Yoshikawa, Taro Sasaoka, Yu Hatano, Ken Kurihara, Yasuhiro Maejima, Mitsuaki Isobe, Takashi Ashikaga. The Hypercholesterolemia Paradox in Percutaneous Coronary Intervention: An Analysis of a Multicenter PCI Registry. Intern. Med.. 2018.09;

23. Natsuko Tamura, Yasuhiro Maejima, Takayoshi Matsumura, Rick B Vega, Eisuke Amiya, Yusuke Ito, Yuka Shiheido-Watanabe, Takashi Ashikaga, Issei Komuro, Daniel P Kelly, Kenzo Hirao, Mitsuki Isobe. Single-Nucleotide Polymorphism of the MLX Gene Is Associated With Takayasu Arteritis Circ Genom Precis Med. 2018.10; 11(10); e002296
24. Yasuhiro Maejima. Everything in Moderation. Int Heart J. 2018.10; 59(5); 917-919
25. Kikuchi H, Sasaki E, Nomura N, Mori T, Minamishima YA, Yoshizaki Y, Takahashi N, Furusho T, Arai Y, Mandai S, Yamashita T, Ando F, Maejima Y, Isobe K, Okado T, Rai T, Uchida S, Sohara E. Failure to sense energy depletion may be a novel therapeutic target in chronic kidney disease. Kidney International. 2018.11;
26. Aoyama N, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, Shiheido Y, Sato H, Takamura C, Yoshikawa S, Matsuo K, Izumi Y, Isobe M. Periodontal condition in Japanese coronary heart disease patients: A comparison between coronary and non-coronary heart diseases. Journal of periodontal research. 2018.11;
27. Chikashi Terao, Hajime Yoshifuji, Takayoshi Matsumura, Taeko K Naruse, Tomonori Ishii, Yoshikazu Nakaoka, Yohei Kirino, Keitaro Matsuo, Tomoki Origuchi, Masakazu Shimizu, Yasuhiro Maejima, Eisuke Amiya, Natsuko Tamura, Takahisa Kawaguchi, Meiko Takahashi, Kazuya Setoh, Koichiro Ohmura, Ryu Watanabe, Tetsuya Horita, Tatsuya Atsumi, Mitsuru Matsukura, Tetsuro Miyata, Yuta Kochi, Toshio Suda, Kazuo Tanemoto, Akira Meguro, Yukinori Okada, Akiyoshi Ogimoto, Motohisa Yamamoto, Hiroki Takahashi, Shingo Nakayamada, Kazuyoshi Saito, Masataka Kuwana, Nobuhisa Mizuki, Yasuharu Tabara, Atsuhisa Ueda, Issei Komuro, Akinori Kimura, Mitsuki Isobe, Tsuneyo Mimori, Fumihiko Matsuda. Genetic determinants and an epistasis of LILRA3 and HLA-B*52 in Takayasu arteritis Proc. Natl. Acad. Sci. U.S.A.. 2018.11;
28. Niida Takayuki, Murai Tadashi, Yonetsu Taishi, Kanaji Yoshihisa, Usui Eisuke, Matsuda Junji, Hoshino Masahiro, Araki Makoto, Yamaguchi Masao, Hada Masahiro, Ichijo Sadamitsu, Hamaya Rikuta, Kanno Yoshinori, Isobe Mitsuki, Kakuta Tsunekazu. Coronary physiological assessment combining fractional flow reserve and index of microcirculatory resistance in patients undergoing elective percutaneous coronary intervention with grey zone fractional flow reserve CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS. 2018.11; 92(6); 1077-1087
29. Ikenouchi T, Nitta J, Nitta G, Kato S, Iwasaki T, Murata K, Junji M, Hirao T, Kanoh M, Takamiya T, Kato N, Inamura Y, Negi K, Sato A, Yamato T, Matsumura Y, Takahashi Y, Goya M, Hirao K. Propensity-matched comparison of cryoballoon and radiofrequency ablation for atrial fibrillation in elderly patients. Heart rhythm. 2018.12;

[Misc]

1. Sebastiano Sciarretta, Yasuhiro Maejima, Daniela Zablocki, Junichi Sadoshima. The Role of Autophagy in the Heart. Annu. Rev. Physiol.. 2018.02; 80; 1-26
2. Yasuhiro Maejima. The critical role of autophagy in heart failure Nippon Yakurigaku Zasshi. 2018.03; 151(3); 100-105

[Conference Activities & Talks]

1. Ikenouchi Takashi, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiko, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 左房サイズが肺静脈隔離法の選択に及ぼす影響 クライオバルーンか高周波カテーテルアブレーションか (Impact of Left Atrium Size on Selection of Pulmonary Vein Isolation Method: Cryoballoon or Radiofrequency Catheter Ablation). 日本循環器学会学術集会抄録集 2018.03.01
2. Matsuda Junji, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiko, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Nitta Junichi. 心停止後の患者において SOFA 評価スコアは死亡率および神経転帰の予測因子である (The Assessment of SOFA Score Predicts Mortality and Neurogenic Outcome in Post-Cardiac Arrest Patients). 日本循環器学会学術集会抄録集 2018.03.01

3. Kato Nobutaka, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 心房細動に対する第2世代クライオバルーンアブレーションの学習曲線 (Learning Curve of 2nd Generation Cryoballoon Ablation for Atrial Fibrillation). 日本循環器学会学術集会抄録集 2018.03.01
4. Kato Nobutaka, Nitta Junichi, Nitta Giichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 心房細動に対する第2世代クライオバルーンカテーテルアブレーションの有効性 単一施設における1000症例を超える経験 (Efficacy of 2nd Generation Cryoballoon Catheter Ablation for Atrial Fibrillation: Single Center, over 1000 Cases Experience). 日本循環器学会学術集会抄録集 2018.03.01
5. Kato Shunichi, Nitta Junichi, Nitta Giichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Negi Ken, Yamato Tsunehiro, Satoh Akira, Matsumura Yutaka. 心房細動再発の臨床的予測因子 第2世代クライオバルーンによる肺静脈隔離後の2年追跡 (Clinical Predictors of Atrial Fibrillation Recurrence: Two-year Follow-up after Pulmonary Vein Isolation by Secondgeneration Cryoballoon). 日本循環器学会学術集会抄録集 2018.03.01
6. Inamura Yukihiro, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 心房細動患者における非肺静脈病変の予測因子 (The Predictor of Non-pulmonary Vein Foci in the Patients with Atrial Fibrillation). 日本循環器学会学術集会抄録集 2018.03.01
7. Inamura Yukihiro, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 持続性心房細動に対するクライオバルーンアブレーションの適応 1施設におけるレトロスペクティブ研究 (Indication of Cryoballoon Ablation for Persistent Atrial Fibrillation: A Single-center Retrospective Study). 日本循環器学会学術集会抄録集 2018.03.01
8. Hirao Tatsuhiko, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 持続性心房細動のクライオバルーンアブレーション 高度構造的リモデリング合併・非合併患者間でのアブレーション転帰の有意差 (Cryoballoon Ablation of Persistent Atrial Fibrillation: Significant Difference in the Ablation Outcome between Patients with and without Advanced Structural Remodeling). 日本循環器学会学術集会抄録集 2018.03.01
9. Kato Shunichi, Matsumura Yutaka, Nitta Giichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Negi Ken, Satoh Akira, Yamato Tsunehiro, Nitta Junichi. 救急対応ドクターカーによりST上昇型心筋梗塞患者におけるDoor-to-balloon Timeを短縮できる (Emergency Rapid Response Doctor Car can Reduce Door-to-balloon Time in Patients with ST-elevated Myocardial Infarction). 日本循環器学会学術集会抄録集 2018.03.01
10. 佐藤 明, 新田 義一, 加藤 駿一, 岩崎 司, 池ノ内 孝, 村田 和也, 松田 隼治, 平尾 龍彦, 狩野 実希, 高宮 智正, 加藤 信孝, 稲村 幸洋, 根本 謙, 大和 恒博, 松村 稔, 新田 順一. 植込み型心臓除細動器装着患者における心室細動と心室性頻脈の予後の差の影響 (Impact of Difference of Prognosis between Ventricular Fibrillation and Ventricular Tachycardia in Patients with Implantable Cardioverter Defibrillator). 日本循環器学会学術集会抄録集 2018.03.01
11. Murata Kazuya, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 発作性心房細動に対するクライオバルーンおよび高周波カテーテルアブレーション間でのブランキングピリオドにおける再発様式の差 (The Difference of Recurrence Modality in the Blanking Period between Cryoballoon and Radiofrequency Catheter Ablation for Paroxysmal Atrial Fibrillation). 日本循環器学会学術集会抄録集 2018.03.01

12. Kato Nobutaka, Nitta Junichi, Nitta Giichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 発作性心房細動に対する第二世代クライオバルーン肺静脈隔離後に誘発された非肺静脈起源心房細動がもたらす影響 (Impact of Non-pulmonary Vein Foci Induced after 2nd-generation Cryoballoon Pulmonary Vein Isolation for Paroxysmal Atrial Fibrillation). 日本循環器学会学術集会抄録集 2018.03.01
13. Murata Kazuya, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 発作性心房細動アブレーション後の肺静脈隔離耐久性の指標 高周波対クライオバルーン (Indicators of Pulmonary Vein Isolation Durability after the Ablation of Paroxysmal Atrial Fibrillation: Radiofrequency vs Cryoballoon). 日本循環器学会学術集会抄録集 2018.03.01
14. Ikenouchi Takashi, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 発作性心房細動患者におけるクライオバルーンアブレーションの合併症に対する BMI の影響 (The Impact of Body Mass Index on Complication in Cryoballoon Ablation for Paroxysmal Atrial Fibrillation Patients). 日本循環器学会学術集会抄録集 2018.03.01
15. Inamura Yukihiro, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 発作性心房細動患者に対するクライオバルーンおよび高周波肺静脈隔離間での 2 回目アブレーションに関する臨床的な差 (Clinical Difference about Second Session Ablation between Cryoballoon and Radiofrequency Pulmonary Vein Isolation for the Patients with Paroxysmal Atrial Fibrillation). 日本循環器学会学術集会抄録集 2018.03.01
16. Ikenouchi Takashi, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 肺静脈以外の起源の有無による発作性心房細動に対するクライオバルーンおよび高周波アブレーションの有効性 (The Efficacy of Cryoballoon and Radiofrequency Ablation for Paroxysmal Atrial Fibrillation with or without Nonpulmonary Vein Foci). 日本循環器学会学術集会抄録集 2018.03.01
17. Hirao Tatsuhiko, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 若年者における異所性心房頻拍の起源分布と他との心耳起源の比較 (Distribution of Origin of Ectopic Atrial Tachycardia in Young People and Compared the Atrial Appendage Origin with the Other). 日本循環器学会学術集会抄録集 2018.03.01
18. Matsuda Junji, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Hirao Tatsuhiko, Kanoh Miki, Takamiya Tomomasa, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Nitta Junichi. 薬剤コーティングバルーンによるステント内再狭窄治療にエキシマレーザー冠動脈形成術がもたらす補助的効果 (Adjunctive Effect of Excimer Laser Coronary Angiography for Treatment of In-stent Restenosis with Drug-coated Balloon). 日本循環器学会学術集会抄録集 2018.03.01
19. Takamiya Tomomasa, Nitta Junichi, Nitta Giichi, Kato Shunichi, Iwasaki Tsukasa, Ikenouchi Takashi, Murata Kazuya, Matsuda Junji, Hirao Tatsuhiko, Kanoh Miki, Kato Nobutaka, Inamura Yukihiro, Satoh Akira, Yamato Tsunehiro, Matsumura Yutaka, Takahashi Yoshihide, Goya Masahiko, Hirao Kenzo. 長期持続性心房細動に対する非肺静脈トリガーアブレーションによる肺静脈および後壁の隔離 (Isolation of Pulmonary Veins and Posterior Wall with Non Pulmonary Vein Triggers Ablation for Long Standing Persistent Atrial Fibrillation). 日本循環器学会学術集会抄録集 2018.03.01
20. Kensuke Hirasawa, Masaki Izumo, Taro Sasaoka, Tomoyuki Umemoto, Kengo Suzuki, Tomoo Harada, Takashi Ashikaga, Kenzo Hirao, Yoshihiro J Akashi. Prognostic Significance of Cardiac Index Reserve During Exercise in Asymptomatic Patients with Aortic Stenosis.. 2018.03.25

21. Kensuke Hirasawa, Masaki Izumo, Tomoyuki Umemoto, Takashi Ashikaga, Kengo Suzuki, Tomoo Harada, Hirokuni Arai, Mitsuaki Isobe, Yasuhiro J Akashi. Tricuspid Valve Morphological Assessment of Barlow Disease using Three-Dimensional Transesophageal Echocardiography and the Impact on Residual Regurgitation after Tricuspid Annuloplasty.. 2018.03.25
22. Yasuhiro Maejima, Yuka Shiheido-Watanabe, Natsuko Tamura, Yusuke Ito, Kenzo Hirao, Mitsuaki Isobe. Critical role for dipeptidyl peptidase-4 activity in the pathogenesis of experimental autoimmune myocarditis. Heart Failure Congress 2018 2018.05.29 Viena, Austria
23. Kensuke Hirasawa, Masaki Izumo, Tomoyuki Umemoto, Kengo Suzuki, Yosuke Kitasaka, Keiji Oi, Tomohiro Mizuno, Tomoo Harada, Takashi Ashikaga, Takeshi Miyairi, Hirokuni Arai, Kenzo Hirao, Yoshihiro J Akashi. Geometry of tricuspid valve apparatus in patients with mitral regurgitation due to fibroelastic deficiency versus Barlow disease: A real-time three-dimensional transesophageal echocardiography study.. American Society of Echocardiography 2018.06.25
24. 松田 隼治, 新田 義一, 加藤 駿一, 岩崎 司, 池ノ内 孝, 村田 和也, 平尾 龍彦, 狩野 実希, 稲村 幸洋, 加藤 信孝, 高宮 智正, 根木 謙, 佐藤 明, 大和 恒博, 松村 穰, 新田 順一. ISR 病変に対して DCB を施行する前に ELCA を施行した追加効果の観察研究. 日本心血管インターベンション治療学会抄録集 2018.08.01
25. 加藤 駿一, 新田 義一, 池ノ内 孝, 村田 和也, 松田 隼治, 狩野 実希, 稲村 幸洋, 高宮 智正, 加藤 信孝, 根木 謙, 佐藤 明, 大和 恒博, 松村 穰, 新田 順一, 江川 裕子, 五木田 昌士, 勅使河原 勝伸, 八坂 剛一, 田口 茂正, 清田 和也. ドクターカー活動中病院前 12 誘導心電図の伝送は ST 上昇型急性心筋梗塞患者の Door-to-Device time と FMC-to-Device time を短縮する. 日本心血管インターベンション治療学会抄録集 2018.08.01
26. 松田 隼治, 新田 義一, 加藤 駿一, 岩崎 司, 池ノ内 孝, 村田 和也, 平尾 龍彦, 狩野 実希, 稲村 幸洋, 加藤 信孝, 高宮 智正, 根木 謙, 佐藤 明, 大和 恒博, 松村 穰, 新田 順一. 心原性院外心停止患者の院内死亡率と神経学的予後の予測における冠動脈造影、血行再建、冠動脈病変の有無の影響をみた観察研究. 日本心血管インターベンション治療学会抄録集 2018.08.01
27. 新田 義一, 加藤 駿一, 池ノ内 孝, 村田 和也, 松田 隼治, 狩野 実希, 高宮 智正, 加藤 信孝, 稲村 幸洋, 根木 謙, 佐藤 明, 大和 恒博, 松村 穰, 新田 順一. 急性冠症候群による心原性ショック後に急性呼吸窮迫症候群を合併した一例. 日本心血管インターベンション治療学会抄録集 2018.08.01
28. Yasuhiro Maejima. The single nucleotide polymorphism of MLX gene is involved in the development of Takayasu Arteritis. The 2nd JCS Council Forum on Basic Cardiovascular Research 2018.09.23 Nara, Japan

[Awards & Honors]

1. Star Reviewer 2017, American Physiological Society, American Physiological Society, 2018.11

Anesthesiology

Professor: Tokujiro Uchida

Junior Associate Professor: Jiro Kurata

Assistant Professor: Akio Masuda, Atsushi Ito, Hiroto Yamamoto, Hiroki Yamamoto, Ken Shinoda, Takafumi Omori, Aya Takemoto, Akiko Kitajo, Hitomi Kanamori, Tsubasa Akune, Sayomi Tsukada, Arisa Fukagawa, Yudai Yamamoto

Staff: Tomoko Ishibasi, Mamiko Yoshida

Resident: Junpei Shibata, Hiromichi Suzuki, Shiho Tanaka,

Mizuki Motomura, Sayaka Yamashita, Sho Watanabe, Shoko Imamura, Shoko Akahoshi, Takayuki Iida, Yurie Kamiseki, Momoko Hirai, Eisaku Nashiki

Postgraduate Student: Tomoko Ishibashi, Yudai Yamamoto, Tianjiao Li, Tsuyoshi Kanma, Hirotsugu Ota, Eri Shinto, Ayumi Maeda, Kenta Takeishi

(1) Outline

A comprehensive understanding of research trends, research methods, and analysis of results by introducing the latest papers published in prestigious journals related to anesthesiology.

(2) Research

- 1) Discovering most effective ventilation methods for injury lungs.
- 2) Therapeutic mechanism of mesenchymal stem cell for lung injury (rat and mouse model)
- 3) Studies on the central nervous system effects of general anesthetics by human electrocorticogram and functional neuroimaging.
- 4) Studies on the mechanisms of cerebral pain processing and pain chronification by human functional magnetic resonance imaging and positron emission tomography.
- 5) Studies on the effects of protective one-lung ventilation on ventilatory mechanics.
- 6) Epidemiologic studies to identify incidence of, and risk factors for postoperative acute kidney injury in patients undergoing liver resection.

(3) Publications

[Original Articles]

1. Mitsui Y., Dea K. P. O., Uchida T., Takata M., Wakabayashi K.. Pro-Inflammatory Activity of Granulocyte-Derived Microvesicles Is Potentiated by Endotoxin Pre-Stimulation AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2018; 197;
2. Kurata Jiro. Neural Mechanisms of Offset Analgesia. Adv Exp Med Biol. 2018; 1099; 141-146
3. Shuo Zhang, Tianjiao Li, Hiroyuki Kobinata, Eri Ikeda, Takashi Ota, Jiro Kurata. Attenuation of offset analgesia is associated with suppression of descending pain modulatory and reward systems in patients with chronic pain. Molecular Pain. 2018.01; 14; 1-15

4. Koji Kido, Hiroyuki Ito, Yudai Yamamoto, Koshi Makita, Tokujiro Uchida. Cytotoxicity of propofol in human induced pluripotent stem cell-derived cardiomyocytes. *J Anesth.* 2018.02; 32(1); 120-131
5. E Ikeda, T Li, H Kobinata, S Zhang, J Kurata. Anterior insular volume decrease is associated with dysfunction of the reward system in patients with chronic pain. *European Journal of Pain.* 2018.02;
6. Kido Koji, Ito Hiroyuki, Yamamoto Yudai, Makita Koshi, Uchida Tokujiro. ヒト人工多能性幹細胞由来心筋細胞におけるプロポフォールの細胞毒性 (Cytotoxicity of propofol in human induced pluripotent stem cell-derived cardiomyocytes) *Journal of Anesthesia.* 2018.02; 32(1); 120-131
7. Yohei Matsuo, Jiro Kurata, Miho Sekiguchi, Katsuhiro Yoshida, Takuya Nikaido, Shin-Ichi Konno. Correction to: Attenuation of cortical activity triggering descending pain inhibition in chronic low back pain patients: a functional magnetic resonance imaging study. *Journal of Anesthesia.* 2018.04; 32(2); 311-312
8. Tianjiao Li, Shuo Zhang, Jiro Kurata. Suppressed descending pain modulatory and enhanced sensorimotor networks in patients with chronic low back pain. *Journal of Anesthesia.* 2018.09;
9. Araki S, Kijima T, Waseda Y, Komai Y, Nakanishi Y, Uehara S, Yasuda Y, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Nakano Y, Yoshimoto T, Uchida T, Fujii Y. Incidence and predictive factors of hypoglycemia after pheochromocytoma resection. *International journal of urology : official journal of the Japanese Urological Association.* 2018.11;
10. Asada M, Nagata M, Mizuno T, Uchida T, Kurashima N, Takahashi H, Makita K, Arai H, Echizen H, Yasuhara M. Effects of cardiopulmonary bypass on the disposition of cefazolin in patients undergoing cardiothoracic surgery. *Pharmacology research & perspectives.* 2018.12; 6(6); e00440

[Books etc]

1. Lohser J, Ishikawa S. Chapter 6, Clinical management of one-lung ventilation. Slinger P Ed., Principles and practice of anesthesia for thoracic surgery. Springer, 2011, pp 83-101..
2. Lohser J, Ishikawa S. Chapter 5, Physiology of the lateral decubitus position, open chest, and one-lung ventilation. Slinger P Ed., Principles and practice of anesthesia for thoracic surgery. Springer, 2011, pp 71-82..

[Conference Activities & Talks]

1. Jiro Kurata. Supraspinal mechanisms of pain chronification. The 29th Annual Meeting of the Tokai Chapter of the Japanese Society of Pain Clinicians 2018.04.28 Shinagawa City, Tokyo, Japan
2. Jiro Kurata. Subconscious self and general anesthesia. The 65th Annual Meeting of the Japanese Society of Anesthesiologists 2018.05.18 Yokohama, Kanagawa-ken, Japan
3. Comparison of the cerebral circulation time during sevoflurane versus propofol anesthesia for neuroendovascular surgery. 2018.05.18
4. 李 天嬌, 張 碩, 太田 隆嗣, 菅間 剛, 牧瀬 杏子, 倉田 二郎. The superior parietal lobule shows cortical thinning and gray matter volume reduction in patients with chronic pain . 日本麻酔科学会第 65 回学術集会 2018.05.18 神奈川県横浜市
5. Jiro Kurata. Brain mechanisms of pain chronification. The 52nd Annual Meeting of the Japanese Society of Pain Clinicians 2018.07.19 Shinagawa City, Tokyo, Japan
6. Jiro Kurata. Target of general anaesthesia: brain or soul?. World Congress of SIVA-TCI 2018.08.17 Kuala Lumpur, Malaysia
7. Jiro Kurata. Cortical atrophy in chronic pain: myth or reality. 2018.08.26 Shinagawa City, Tokyo, Japan

Cardiovascular Surgery

Professor: Hirokuni ARAI

Associate Professor: Tomohiro MIZUNO

Junior Associate Professor: Keiji OI

Assistant Professor:

Masafumi YASHIMA, Tsuyoshi HACHIMARU (until March), Eiki NAGAOKA(sabbatical leave),
Hidehito KUROKI, Tatsuki FUJIWARA, Kiyotoshi OISHI(from April), Masashi TAKESHITA

Graduate Student:

Hidehito KUROKI, Dai TASAKI, Kenji SAKAI,

Ryoji KINOSHITA, Kiyotoshi OISHI, Kenji YOKOYAMA

Hospital Staff: 4

Department of Advanced Surgical Technology Research and Development

Associate Professor: Katsuhiro OUCHI

(1) Research

- 1) Developing safe and high quality surgical strategy in coronary artery bypass grafting surgery.
- 2) Developing new surgical technique for ischemic heart disease
- 3) Developing new surgical technique for beating mitral valve surgery
- 4) Clinical research for artificial heart
- 5) Research for new regenerative therapy for failing heart to recover cardiac function

(2) Education

Cardiovascular Surgery is a branch of surgery which deals with heart and vascular (mainly aortic) disease. Main objective of our department in the graduate course is to provide medical students an opportunity to study surgical anatomy, pathophysiology, pharmacology, and advanced surgical treatment for heart and aortic disease. Students are also taught basic research for the surgical treatment for heart and aortic disease. We also provide clinical training program for young surgeon to obtain Japanese cardiovascular surgical board.

(3) Clinical Performances

Our department provides well-advanced surgical treatment of heart and aortic surgery. We perform off-pump coronary artery bypass grafting for more than 90% of patients with coronary artery disease, mitral valve repair, not valve replacement, for almost all patients with mitral valve regurgitation. New surgical reconstruction technique is provided for patients with functional mitral regurgitation due to severe heart failure. For elderly patients, we offer minimally invasive aortic surgery such as thoracic endovascular aortic repair (TEVAR) and hybrid aortic surgery without cardiopulmonary bypass for aortic arch and thoracoabdominal aortic disease.

(4) Publications

[Original Articles]

1. Mizuno T, Goya M, Hirao K, Arai H.. Implantable epicardial cardioverter-defibrillator-induced localized constrictive pericarditis. *Interact Cardiovasc Thorac Surg.* 2018.01; 26(1); 158-160
2. Daisuke Yoshioka, Koichi Toda, Minoru Ono, Takeshi Nakatani, Akira Shiose, Yoshiro Matsui, Kenji Yamazaki, Yoshikatsu Saiki, Akihiko Usui, Hiroshi Niinami, Goro Matsumiya, Hirokuni Arai, Yoshiki Sawa, . Clinical Results, Adverse Events, and Change in End-Organ Function in Elderly Patients With HeartMateII Left Ventricular Assist Device - Japanese Multicenter Study. *Circulation Journal.* 2018.01; 82(2); 409-418
3. Sakota Daisuke, Fujiwara Tatsuki, Ohuchi Katsuhiro, Kuwana Katsuyuki, Yamazaki Hiroyuki, Kosaka Ryo, Nishida Masahiro, Mizuno Tomohiro, Arai Hirokuni, Maruyama Osamu. Development of a real-time and quantitative thrombus sensor for an extracorporeal centrifugal blood pump by near-infrared light BIOMEDICAL OPTICS EXPRESS. 2018.01; 9(1); 190-201
4. Tomohiro Mizuno, Keiji Oi, Hirokuni Arai. Enhanced computed tomography showing dissection-like features in an extracorporeal membrane oxygenation-supported patient with no cardiac output: Can acute type A aortic dissection be excluded? *J. Thorac. Cardiovasc. Surg.*. 2018.04; 155(4); 1637-1639
5. Susumu Manabe, Hitoshi Kasegawa, Hirokuni Arai, Shuichiro Takanashi. Management of systolic anterior motion of the mitral valve: a mechanism-based approach. *Gen Thorac Cardiovasc Surg.* 2018.07; 66(7); 379-389
6. Sakai K, Mizuno T, TWatanabe T, Nagaoka E, Oi K, Yashima M, Hachimaru T, Kuroki H, Fujiwara T, Takeshita M, Tanabe M, Arai H.. Management of Right Gastroepiploic Arterial Coronary Grafts in Subsequent Abdominal Surgeries. *Ann. Thorac. Surg.*. 2018.07; 106(1); 52-57
7. Takeshita M, Arai H, Mizuno T, Yashima M. Successful mitral valve repair involving division of bridging tissue in a patient with double orifice mitral valve. *The Journal of thoracic and cardiovascular surgery.* 2018.11;

[Conference Activities & Talks]

1. Sakota D, Fujiwara T, Ohuchi K, Kuwana K, Yamazaki H, Kosaka R, Maruyama O,. Development of real-time and quantitative monitoring of thrombus formation in a extracorporeal centrifugal blood pump. Photonic West 2018 2018.01.27 SanFrancisco, USA
2. Arai H. Multi-suction heart positioner “Tentacles” for OPCAB. The II All-Russian Scientific and Practical Conference 2018.04.16 Astrakhan, Russia
3. Arai H. Aortic scanning, epicardial scanning and TTFM. The II All-Russian Scientific and Practical Conference 2018.04.16 Astrakhan, Russia
4. Arai H. Subvalvular procedure for functional mitral regurgitation – Effectiveness of papillary muscle relocation. The II All-Russian Scientific and Practical Conference 2018.04.17 Astrakhan, Russia
5. Arai H. Current Japanese Coronary Artery Surgery. The II All-Russian Scientific and Practical Conference 2018.04.17 Astrakhan, Russia
6. Arai H. Arterial revascularization after ART trial in Japan. 4th Int’l Heart Symposium on The Beach 2018.04.21 Phuket, Thailand
7. Arai H. Intra-operative ultrasonic quality assessment and surgical guidance to improve CABG outcome. 4th Int’l Heart Symposium on The Beach 2018.04.21 Phuket, Thailand
8. Arai H. Subvalvular procedure for functional mitral regurgitation.. 2018 Annual meeting of Korean Society of Coronary Artery Surgery 2018.05.12 Busan Korea
9. Arai H. OPCAB Surgery in Japan & Current Trends/Perspectives of CV Surgery Development. Opening of the 1st in Russia Simulation Center for OPCAB surgery in Astrakhan Federal Center 2018.05.28 Astrakhan, Russia

10. Arai H. The Fuji Technique, Surgical Techniques: How I Repair.. MICS 2018 Mitral Conferences 2018.06.08 Rome, Italy
11. Tomohiro Mizuno, Tatsuki Fujiwara, Hidehito Kuroki, Hirokuni Arai. Development of a Heart Positioner for MICS CABG: Tentacles NEO. 2018 ISMICS Annual Meeting 2018.06.14 Vancouver, CANADA
12. Arai H. Cardiovascular Surgical Training and Quality Control in Japan.. RCST Annual Scientific Congress 2018.07.28 Pattaya, Bangkok
13. Arai H. How I Do My OPCAB 2. RCST Annual Scientific Congress 2018.07.28 Pattaya, Bangkok
14. Arai H. (Chair) Session 1: Indications for CABG in 2018.. 2018 International Coronary Congress 2018.08.02 Beijing, China
15. Arai H. (Chair) Session 10B (Simultaneous): Surgical Skill Training. 2018 International Coronary Congress 2018.08.04 Beijing, China
16. Arai H. CABG with Ischemic Mitral Regurgitation and/or Heart Failure. 2018 International Coronary Congress 2018.08.04 Beijing, China
17. Arai H. (Discussant) Special Session: East Meets West. 2018 International Coronary Congress 2018.08.04 Beijing, China
18. Arai H. Minimally Invasive Valve Surgery.. The 23rd ASEAN Federation of Cardiology Congress 2018.09.28 Bangkok, Thailand
19. Arai H. (moderator) Free Paper B: CVT. The 23rd ASEAN Federation of Cardiology Congress 2018.09.28 Bangkok, Thailand
20. Arai H. (moderator) Symposium 6: Current Advances in Valve Surgery. The 23rd ASEAN Federation of Cardiology Congress 2018.09.28 Bangkok, Thailand
21. Arai H. (moderator) Symposium 10: Advances in management of coronary artery disease: Surgical perspective. The 23rd ASEAN Federation of Cardiology Congress 2018.09.28 Bangkok, Thailand
22. Arai H. Current Strategy for Ischemic MR. The 23rd ASEAN Federation of Cardiology Congress 2018.09.29 Bangkok, Thailand
23. K Oi, A Izawa, T Mizuno, M Yashima, H Kuroki, T Fujiwara, M Takeshita, H Arai. Graft Selection in Coronary Artery Bypass Surgery for Restenosis after Percutaneous Coronary Intervention. 32nd EACTS Annual Meeting 2018.10.19
24. Arai H. Quality Assessment in CABG: Transit-time Flow Measurement and Epicardial Ultrasound. The 50th Annual Meeting of the Korean Society for Thoracic and Cardiovascular Surgery 2018.10.27 Korea
25. Tatsuki Fujiwara. Ventricular assist device therapy using MERA Monopivot Centrifugal Pumps for cardiogenic shock patients in INTERMACS profile-1. The 26th Annual Meeting of the International Society for Mechanical Circulatory Support (ISMCS2018) 2018.11.01 Tokyo
26. Arai H. Intraoperative Ultrasonic Quality Assessment and Surgical Guidance to Improve CABG Outcomes. ANZSCTS Annual Scientific Meeting 2018 2018.11.08 Noosa, Australia
27. Arai H. Ischaemic Mitral Valve Repair. ANZSCTS Annual Scientific Meeting 2018 2018.11.08 Noosa, Australia
28. Arai H. Surgical Strategy for Functional MR (Effectiveness of Papillary Muscle Relocation). ANZSCTS Annual Scientific Meeting 2018 2018.11.09 Noosa, Australia
29. Arai H. (Panelist) Aortic Surgery. ANZSCTS Annual Scientific Meeting 2018 2018.11.09 Noosa, Australia
30. Tomohiro Mizuno, Fujiwara T, Kuroki H, Oishi K, Takeshita M, Kubo T, Okumura H, Nabeshima A, Yashima M, Oi K, Arai H.. Hybrid Arch Repair for Extended Arch and Descending Aortic Disease.. American Heart Association 2018 Scientific Session 2018.11.10 Chicago, USA
31. Arai H. Intraoperative Ultrasonic Quality Assessment and Surgical Guidance to Improve CABG Outcomes. ANZSCTS Annual Scientific Meeting 2018 2018.11.10 Noosa, Australia

32. Arai H. New Guidline and Evidence Basis for CABG 2018. 7th RAMA OPCAB Meeting 2018.12.03 Bangkok, Thailand
33. Arai H. Intra operative ultrasonic quality assesment and surical guidance. 7th RAMA OPCAB Meeting 2018.12.03 Bangkok, Thailand
34. Arai H. Tentacles neo and new sternal fixation device "WAVE". 7th RAMA OPCAB Meeting 2018.12.03 Bangkok, Thailand
35. Arai H. MV Repair Posterior Leaflet Porlapse:. AATS Mitral Conclave Workshop 2018.12.15 Shanghai, China
36. Arai H. Dealing with Secondary Mitral Regurgitation. AATS Mitral Conclave Workshop 2018.12.16 Shanghai, China

Nephrology

Professor:

Shinichi UCHIDA

Tatemitsu RAI (Dept. of Nephrology and Regional Medicine (Ibaraki))

Associate Professor:

Tomokazu OKADO (Dept. of Blood Purification)

Eisei SOHARA

Junior Associate Professor:

Shotaro NAITO

Assistant Professor:

Naohiro NOMURA

Soichiro IIMORI (Dept. of Blood Purification)

Takayasu MORI (Dept. of Blood Purification)

Kiyoshi ISOBE (Dept. of Nephrology and Regional Medicine (Ibaraki))

Koichiro SUSA (Project Assistant Professor)

Fumiaki ANDO (Project Assistant Professor)

Graduate Student:

Sayaka YOSHIDA

Hiroaki KIKUCHI, Wakana SHODA, Hiroko HASHIMOTO

Takuya FUJIMARU, Taisuke FURUSHO, Yoshiaki MATSUURA

Naohiro TAKAHASHI, Tamami FUJIKI, Azuma NANAMATSU

Hospital Staff:

Haruna TANAKA (Project Assistant Professor)

Yuto TOMA, Saki KUBO, Yu HARA

(first half) Ken IKENOUCHI, Atsuhiko IMONO, Kaho YAMAZAKI

(second half) Reika IKEGAMI, Misato HARA, Nobuhisa MORIMOTO

Technician:

Chieko IJIMA, Motoko CHIGA

Secretary:

Asa MURANO, Yukiko ITO

(1) Outline

The policy of the Department of Nephrology is to accomplish trustworthy medicine and to educate excellent academic scientists and nephrologists. Our department is one of the pioneering institutes that introduced the hemodialysis therapy in Japan, and thus, has a long experience of clinical practice of kidney diseases.

We are now investigating pathophysiological mechanisms of various kidney diseases including genetic renal diseases. Furthermore, we are taking a proactive stance in developing innovative therapy. We hope new young scientists and physicians join us for future science and nephrology.

(2) Research

The theme of our study is "to investigate the mechanisms of maintaining blood pressure and body fluids homeostasis regulated by the kidney and to clear the pathophysiology caused by their failure, and to develop

novel strategies for their treatment.” This would lead to the development of kidney disease therapy itself and would also lead to studying for multiple organ failure caused by chronic kidney disease (CKD).

In 2018, our 13 presentations were adopted in the annual meeting of American Society of Nephrology (ASN KIDNEY WEEK). Moreover, our research manuscripts were published in several high impact journals such as Nature Communications (IF: 12.4), Kidney International (IF: 8.4), or Scientific Reports (IF: 4.3). We published 29 reports in English and six of them were presented in "press release".

In addition to them, a lot of our members have got prizes in various medical meetings regardless of whether they are in or out of the country. Further, comprehensive diagnosis of inherited kidney diseases using next generation sequencer (NGS) and clinical studies on genome information are now on track and is contributing to various genetic diagnosis of many patients. Genetic diagnosis was carried out for more than 200 cases a year. CKD-ROUTE study, which is the clinical cohort study with 1,000 subjects we take the initiative have been finished the observation period of 3 years, which enabled us to publish 9 clinical research papers (5 in Clin Exp Nephrol., 1 in Nephrology and others).

(3) Education

“Undergraduate education”

(Systematic lecture)

For third grade medical students, we are conducting lectures organized in a three-week ‘block form’ together with urology and pathology sections. Under the name of "Body Fluid Regulation and Urology" Block, the students can learn intensively about kidney and urologic diseases during a period of three weeks. In this lecture, we incorporate PBL (Problem-Based Learning) lectures and lectures held by actual patients, so that the students will be able to study independently and bi-directionally.

(Project semester)

We accept several students every year in the project semester, in which they are expected to participate in the forefront research with the assistance of graduate students.

(Clinical clerkship)

For the last three months of fourth grade following the systematic lectures and project semester, we provide the Pre-Clinical Clerkship (PCC) lectures for ten weeks (two weeks of large-class comprehensive lectures and eight weeks of small-class lectures), which are more practical and interactive than the previous lectures held in the classroom. After PCC, fifth grade students will undergo Clinical Clerkship (CC), in which they will actually take charge of patients in the hospital ward, and study about kidney diseases while developing their clinical skills. They will be in charge of one new inpatient each week, make a presentation about their patient at the regular ward conference, and are expected to learn about the pathophysiology of various kidney diseases in depth.

"Postgraduate education"

After the two-year initial training after graduation, postgraduate doctors will be engaged in clinical training as nephrologists either in the University Hospital or affiliated hospitals as senior trainees. During this period, we teach them so that they can be aware about unsolved clinical problems. We are planning to bring them up as “academic doctors”. Research activities in the graduate school are very active, and by carrying out the state-of-the-art research as described above, we are training doctors to be able to excel in both basic and clinical works.

(4) Clinical Services & Other Works

We are one of the first groups that introduced the hemodialysis therapy in Japan, and thus, have a long experience of clinical practice of kidney diseases. We have close coordination with our 19 affiliated hospitals, and are performing CKD-ROUTE clinical cohort study stated above in cooperation with 15 hospitals of the 19, which enabled us to publish 7 clinical research papers. We continue to make an effort to reveal the pathophysiology of CKD patients. We have been actively adopting the “educational admission” for CKD patients and it has been showing the significant inhibitory effect on progression of kidney disease. For end-stage renal disease patients, vascular access surgery, peritoneal dialysis-related surgery, and induction of dialysis are consistently carried out in our department. Our hemopurification center is one of the biggest institutions among 42 hospitals belonging to national universities. In 2018, the number of newly started dialysis patients and plasma exchange were in 1st place, the total number of blood purifications and the number of hemodialysis were in 2nd place. Furthermore, we developed diagnostic panel for comprehensive genetic diagnosis for hereditary kidney diseases like nephrogenic diabetes insipidus, pseudohypoaldosteronism type II, Liddle syndrome, and Polycystic kidney

diseases. Currently, we receive requests of genetic tests from all over the country. Genetic screening using next-generation sequencing technology enables definite diagnosis for rare hereditary diseases.

(5) Publications

[Original Articles]

1. Kikuchi H, Kanda E, Mori T, Sato H, Iimori S, Nomura N, Naito S, Sohara E, Okado T, Uchida S, Fushimi K, Rai T. Short-term prognosis of emergently hospitalized dialysis-independent chronic kidney disease patients: A nationwide retrospective cohort study in Japan. *PLoS ONE*. 2018; 13(11); e0208258
2. Soichiro Iimori, Shotaro Naito, Yumi Noda, Hidehiko Sato, Naohiro Nomura, Eisei Sohara, Tomokazu Okado, Sei Sasaki, Shinichi Uchida, Tatemitsu Rai. Prognosis of chronic kidney disease with normal-range proteinuria: The CKD-ROUTE study. *PLoS ONE*. 2018.01; 13(1); e0190493
3. Ishigami Junichi, Grams Morgan E., Naik Rakhi P., Caughey Melissa C., Loefer Laura R., Uchida Shinichi, Coresh Josef, Matsushita Kunihiro. Hemoglobin, Albuminuria, and Kidney Function in Cardiovascular Risk: The ARIC (Atherosclerosis Risk in Communities) Study *JOURNAL OF THE AMERICAN HEART ASSOCIATION*. 2018.01; 7(2);
4. Toriu N, Hoshino J, Kobori S, Watanabe S, Oguro M, Oshima Y, Hiramatsu R, Mizuno H, Ikuma D, Sekine A, Hayami N, Sumida K, Yamanouchi M, Hasegawa E, Sawa N, Takaichi K, Yanagita M, Fujimaru T, Sohara E, Uchida S, Ubara Y. Transcatheter Arterial Embolization Therapy for Huge Renal Cysts: Two Case Reports. *Case reports in nephrology and dialysis*. 2018.01; 8(1); 82-89
5. Nomura Naohiro, Shoda Wakana, Wang Yuanlong, Mandai Shintaro, Furusho Taisuke, Takahashi Daiei, Zeniya Moko, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi. Role of ClC-K and barttin in low potassium-induced sodium chloride cotransporter activation and hypertension in mouse kidney. *Biosci Rep*. 2018.02; 38(1);
6. Mori Takayasu, Yousefzadeh Matthew J, Faridounnia Maryam, Chong Jessica X, Hisama Fuki M, Hudgins Louanne, Mercado Gabriela, Wade Erin A, Barghouthy Amira S, Lee Lin, Martin George M, Nickerson Deborah A, Bamshad Michael J, Niedernhofer Laura J, Oshima Junko, University of Washington Center for Mendelian Genomics. ERCC4 variants identified in a cohort of patients with segmental progeroid syndromes. *Hum Mutat*. 2018.02; 39(2); 255-265
7. Ishikawa Seiko, Naito Shotaro, Iimori Soichiro, Takahashi Daiei, Zeniya Moko, Sato Hidehiko, Nomura Naohiro, Sohara Eisei, Okado Tomokazu, Uchida Shinichi, Rai Tatemitsu. Loop diuretics are associated with greater risk of sarcopenia in patients with non-dialysis-dependent chronic kidney disease. *PLoS One*. 2018.02; 13(2); e0192990
8. Ando F, Uchida S.. Activation of AQP2 water channels without vasopressin: therapeutic strategies for congenital nephrogenic diabetes insipidus. *Clin Exp Nephrol*. . 2018.02;
9. Hashimoto Hiroko, Nomura Naohiro, Shoda Wakana, Isobe Kiyoshi, Kikuchi Hiroaki, Yamamoto Kouhei, Fujimaru Takuya, Ando Fumiaki, Mori Takayasu, Okado Tomokazu, Rai Tatemitsu, Uchida Shinichi, Sohara Eisei. Metformin increases urinary sodium excretion by reducing phosphorylation of the sodium-chloride cotransporter. *Metabolism*. 2018.03;
10. Takada Daisuke, Sekine Akinari, Yabuuchi Junko, Kogure Yuta, Ueno Toshiharu, Yamanouchi Masayuki, Sumida Keiichi, Suwabe Tatsuya, Hayami Noriko, Hoshino Junichi, Takaichi Kenmei, Kinowaki Keiichi, Fujii Takeshi, Ohashi Kenichi, Mori Takayasu, Sohara Eisei, Uchida Shinichi, Ubara Yoshifumi. Renal histology and MRI in a 25-year-old Japanese man with nephronophthisis 4. *Clin Nephrol*. 2018.03; 89(3); 223-228
11. T Fujimaru, T Mori, A Sekine, S Mandai, M Chiga, H Kikuchi, F Ando, Y Mori, N Nomura, S Iimori, S Naito, T Okado, T Rai, J Hoshino, Y Ubara, S Uchida, E Sohara. Kidney enlargement and multiple liver cyst formation implicate mutations in PKD1/2 in adult sporadic polycystic kidney disease. *Clin. Genet.*. 2018.03;

12. Shintaro Mandai, Hidehiko Sato, Soichiro Iimori, Shotaro Naito, Takayasu Mori, Daiei Takahashi, Moko Zeniya, Naohiro Nomura, Eisei Sohara, Tomokazu Okado, Shinichi Uchida, Kiyohide Fushimi, Tatemitsu Rai. Dialysis Case Volume Associated With In-Hospital Mortality in Maintenance Dialysis Patients. *Kidney International Reports*. 2018.03; 3(2); 356-363
13. Wang Y, Nomura N, Zeniya M, Mori Y, Takahashi D, Naito S, Rai T, Uchida S, Sohara E.. High potassium concentration regulates the WNK3-SPAK-NKCC1 phosphorylation cascade via kelch-like protein 2 in mouse vascular smooth muscle cells *Journal of Medical and Dental Science*. 2018.03; 65(1); 35-44
14. Yohei Arai, Eiichiro Kanda, Soichiro Iimori, Shotaro Naito, Yumi Noda, Sei Sasaki, Eisei Sohara, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Low white blood cell count is independently associated with chronic kidney disease progression in the elderly: the CKD-ROUTE study. *Clin. Exp. Nephrol.*. 2018.04; 22(2); 291-298
15. Ando F, Mori S, Yui N, Morimoto T, Nomura N, Sohara E, Rai T, Sasaki S, Kondo Y, Kagechika H, Uchida S.. AKAPs-PKA disruptors increase AQP2 activity independently of vasopressin in a model of nephrogenic diabetes insipidus *Nature Communications*. 2018.04; 9(1); 1411
16. Tse-En J Wang, Hung-Ting Liu, Yu-Hua Lai, Tong-Rong Jan, Naohiro Nomura, Hui-Wen Chang, Chi-Chung Chou, Ya-Jane Lee, Pei-Shiue J Tsai. Honokiol, a Polyphenol Natural Compound, Attenuates Cisplatin-Induced Acute Cytotoxicity in Renal Epithelial Cells Through Cellular Oxidative Stress and Cytoskeleton Modulations. *Front Pharmacol*. 2018.04; 9; 357
17. Naoya Toriu, Hiroki Mizuno, Naoki Sawa, Keiichi Sumida, Tatsuya Suwabe, Noriko Hayami, Akinari Sekine, Masayuki Yamanouchi, Junichi Hoshino, Kenmei Takaichi, Motoko Yanagita, Takuya Fujimaru, Takayasu Mori, Eisei Sohara, Shinichi Uchida, Yoshifumi Ubara. Everolimus Reduces the Size of Tuberous Sclerosis Complex-Related Huge Renal Angiomyolipomas Exceeding 20 cm in the Longest Diameter. *Case Rep Oncol*. 2018.05; 11(2); 258-267
18. Gupta N, Susa K, Yoda Y, Bonventre JV, Valerius MT, Morizane R. CRISPR/Cas9-based Targeted Genome Editing for the Development of Monogenic Diseases Models with Human Pluripotent Stem Cells. *Current protocols in stem cell biology*. 2018.05; 45(1); e50
19. Shintaro Mandai, Takayasu Mori, Naohiro Nomura, Taisuke Furusho, Yohei Arai, Hiroaki Kikuchi, Emi Sasaki, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. WNK1 regulates skeletal muscle cell hypertrophy by modulating the nuclear localization and transcriptional activity of FOXO4. *Scientific Reports*. 2018.06; 8(1); 9101
20. Sayaka Yoshida, Yuya Araki, Takayasu Mori, Emi Sasaki, Yuri Kasagi, Kiyoshi Isobe, Koichiro Susa, Yuichi Inoue, Pascale Bomont, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Decreased KLHL3 expression is involved in the pathogenesis of pseudohypoaldosteronism type II caused by cullin 3 mutation in vivo. *Clin. Exp. Nephrol.*. 2018.06;
21. Satoko Miyamoto, Atsushi Ohkubo, Hiroshi Seshima, Hiroko Yamamoto, Ayako Itagaki, Takuma Maeda, Naoki Kurashima, Takayasu Mori, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida, Tomokazu Okado. Removal Dynamics of Autoantibodies, Immunoglobulins, and Coagulation Factors by Selective Plasma Exchange on Three Consecutive Days. *Ther Apher Dial*. 2018.06; 22(3); 255-260
22. Ando Fumiaki, Uchida Shinichi. Activation of AQP2 water channels without vasopressin: therapeutic strategies for congenital nephrogenic diabetes insipidus *CLINICAL AND EXPERIMENTAL NEPHROLOGY*. 2018.06; 22(3); 501-507
23. Miyamoto Satoko, Ohkubo Atsushi, Seshima Hiroshi, Yamamoto Hiroko, Itagaki Ayako, Maeda Takuma, Kurashima Naoki, Mori Takayasu, Iimori Soichiro, Naito Shotaro, Sohara Eisei, Rai Tatemitsu, Uchida Shinichi, Okado Tomokazu. Removal Dynamics of Autoantibodies, Immunoglobulins, and Coagulation Factors by Selective Plasma Exchange on Three Consecutive Days *Therapeutic Apheresis and Dialysis*. 2018.06; 22(3); 255-260
24. Lemos DR, McMurdo M, Karaca G, Wilflingseder J, Leaf IA, Gupta N, Miyoshi T, Susa K, Johnson BG, Soliman K, Wang G, Morizane R, Bonventre JV, Duffield JS. Interleukin-1 β Activates a MYC-Dependent Metabolic Switch in Kidney Stromal Cells Necessary for Progressive Tubulointerstitial Fibrosis. *Journal of the American Society of Nephrology : JASN*. 2018.06; 29(6); 1690-1705

25. Atsushi Ohkubo, Naoki Kurashima, Tomokazu Okado. Immunoabsorption With a Tryptophan-Immobilized Column Using Conventional and Selective Plasma Separators in the Treatment of Myasthenia Gravis. *Ther Apher Dial.* 2018.06; 22(3); 301-302
26. Katsuragawa F, Nagahama K, Naito S, Tsuura Y, Otani M, Koide T, Nishiyama S, Yanagi T, Nanamatsu A, Aki S, Aoyagi M, Tanaka H, Rai T, Uchida S. Ruptured infected aneurysm of the thoracic aorta associated with tunneled dialysis catheter-related methicillin-resistant *Staphylococcus aureus* bacteremia in a hemodialysis patient. *CEN case reports.* 2018.07;
27. Ayumi Matsumoto, Isao Matsui, Takayasu Mori, Yusuke Sakaguchi, Masayuki Mizui, Yoshiyasu Ueda, Atsushi Takahashi, Yohei Doi, Karin Shimada, Satoshi Yamaguchi, Keiichi Kubota, Nobuhiro Hashimoto, Tatsufumi Oka, Yoshitsugu Takabatake, Eisei Sohara, Takayuki Hamano, Shinichi Uchida, Yoshitaka Isaka. A Case of Severe Osteomalacia with Dent Disease Caused by a Novel Intronic Mutation of the *CLCN5* gene. *Intern. Med.* 2018.08;
28. Yamauchi Takahiro, Doi Shigehiro, Nakashima Ayumu, Doi Toshiki, Sohara Eisei, Uchida Shinichi, Masaki Takao. Na⁺-Cl⁻ cotransporter-mediated chloride uptake contributes to hypertension and renal damage in aldosterone-infused rats *AMERICAN JOURNAL OF PHYSIOLOGY-RENAL PHYSIOLOGY.* 2018.08; 315(2); F300-F312
29. Mochizuki Yumi, Harada Hiroyuki, Yokokawa Misaki, Kinoshita Naoya, Kubota Kazumasa, Okado Tomokazu, Fukayama Haruhisa. Oral and maxillofacial surgery in patients undergoing dialysis for advanced renal disease: report of five cases *BMC ORAL HEALTH.* 2018.10; 18(1); 166
30. Kikuchi H, Sasaki E, Nomura N, Mori T, Minamishima YA, Yoshizaki Y, Takahashi N, Furusho T, Arai Y, Mandai S, Yamashita T, Ando F, Maejima Y, Isobe K, Okado T, Rai T, Uchida S, Sohara E. Failure to sense energy depletion may be a novel therapeutic target in chronic kidney disease. *Kidney International.* 2018.11;
31. Yoshida Sayaka, Araki Yuya, Mori Takayasu, Sasaki Emi, Kasagi Yuri, Isobe Kiyoshi, Susa Koichiro, Inoue Yuichi, Bomont Pascale, Okado Tomokazu, Rai Tatsumitsu, Uchida Shinichi, Sohara Eisei. Decreased *KLHL3* expression is involved in the pathogenesis of pseudohypoaldosteronism type II caused by cullin 3 mutation in vivo *Clinical and Experimental Nephrology.* 2018.12; 22(6); 1251-1257

[Books etc]

1. Taisuke Furusho, Shinichi Uchida. Board Certified Endocrinologist Training Guidebook. *SHINDAN TO CHIRYO SHA*, 2018.05 (ISBN : 978-4787822925)
2. Takuya Fujimaru, Shuichi Ito. Nephrotis and Nephrotic Syndrome in Children. Tokyo Igakusha, 2018.11 (ISBN : 978-4-8856-3702-5)

[Misc]

1. Wakana Shoda, Eiichiro Kanda. Chloride ion Nutrition Care. 2018.07; 11(7); 32-33
2. Wakana Shoda, Eiichiro Kanda. Potassium ion Nutrition Care. 2018.07; 11(7); 40-41
3. Wakana Shoda, Eiichiro Kanda. Bicarbonate ion Nutrition Care. 2018.07; 11(7);
4. Taisuke Furusho, Eisei Sohara. Precision medicine in hypertension Kidney and Dialysis. 2018.08; 85(2); 326-331
5. Naohiro Nomura. Investigation of Regulatory Mechanism of Renal Water and Ion Transporters and Development of Novel Treatments 2018.11; 60(8); 1219-1223

[Conference Activities & Talks]

1. Naohiro Nomura, Wakana Shoda, Yuanlong Wang, Daiei Takahashi, Moko Zeniya, Eisei Sohara, Tatsumitsu Rai, Shinichi Uchida. Role of *ClC-K* and *Barttin* in Low-Potassium induced Sodium-Chloride Cotransporter Activation and Hypertension in Mouse Kidney. *ISN Frontiers Meetings 2018* 2018.02.23 Tokyo

2. Hiroaki Kikuchi, Eiichiro Kanda, Fumiaki Ando, Hidehiko Sato, Kiyoshi Isobe, Takayasu Mori, Soichiro Iimori, Naohiro Nomura, Shotaro Naito, Eisei Sohara, Tomokazu Okado, Shinichi Uchida, Kiyohide Fushimi and Tatemitsu Rai. Association between Body Mass Index and In-hospital Mortality in Emergently Hospitalized Dialysis-Independent CKD Patients; A Nationwide Retrospective Cohort Study in Japan. ISN Frontiers Meetings 2018 2018.02.23 Tokyo, Japan
3. Sayaka Yoshida, Yuya Araki, Takayasu Mori, Emi Sasaki, Yuri Kasagi, Kiyoshi Isobe, Koichiro Susa, Yuichi Inoue, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. . Decreased protein level of KLHL3 is involved in PHAII caused by CUL3 mutation. ISN Frontiers Meetings 2018 2018.02.23 Tokyo, Japan
4. Takuya Fujimaru, Takayasu Mori, Akinari Sekine, Shintaro Mandai, Motoko Chiga, Hiroaki Kikuchi, Fumiaki Ando, Yutaro Mori, Naohiro Nomura, Soichiro Iimori, Shotaro Naito, Tomokazu Okado, Tatemitsu Rai, Junichi Hoshino, Yoshifumi Ubara, Shinichi Uchida, Eisei Sohara. Genomic diagnosis of adult polycystic kidney disease with no family history. ISN Frontiers Meetings 2018 2018.02.24 Tokyo, Japan
5. Wakana Shoda . Potassium regulation in Kidney . The 12nd Caffé SSN meeting 2018.03.24
6. Tatemitsu Rai. Medical care of CKD in linkage with the community.. 2018.04.10
7. Furusho T, Sohara E, Mandai S, Kikuchi H, Zeniya M, Mori T, Nomura N, Rai T, Uchida S. WNK1-SPAK-NCC phosphorylation cascade is involved in salt sensitive hypertension in chronic kidney disease.. The 61st Annual Meeting of the Japanese Society of Nephrology 2018.06 Niigata
8. Naohiro Nomura. Investigation of Regulatory Mechanism of Renal Water and Ion Transporters and Development of Novel Treatments. 2018.06.04
9. Shoda W, Nomura N, Ando F, Isobe K, Mori T, Sohara E, Rai T, Uchida S.. Molecular mechanism of high-potassium induced Na-Cl cotransporter dephosphorylation.. The 61st Annual Meeting of Japanese Society of Nephrology. 2018.06.08
10. Mori T. Genome big data will open the way of the future in nephrology.. 5th Next Generation Kidney Research Meeting, Tokyo 2018.08.18
11. Kiyoshi Isobe. Systems-level identification of PKA-dependent signaling in epithelial cells. 2018.08.25
12. Hiroko Hashimoto, Naohiro Nomura, Wakana Shoda, Kiyoshi Isobe, Hiroaki Kikuchi, Kohei Yamamoto, Takuya Fujimaru, Fumiaki Ando, Takayasu Mori, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Metformin has natriuretic effects through reduction of the sodium-chloride cotransporter phosphorylation. The 52nd American Society of Nephrology, Kidney Week 2018 2018.10 San Diego
13. Ando F, Yui N, Nomura N, Sohara E, Rai T, Sasaki S, Uchida S. AKAPs-PKA Disruptors Robustly Increase AQP2 Activity Independently of Vasopressin. The 52nd American Society of Nephrology, Kidney Week 2018 2018.10 San Diego
14. Taisuke Furusho, Eisei Sohara, Shintaro Mandai, Hiroaki Kikuchi, Fumiaki Ando, Moko Zeniya, Takayasu Mori, Naohiro Nomura, Tatemitsu Rai, Shinichi Uchida. WNK1-SPAK-NCC signaling cascade is involved in salt sensitive hypertension induced by aristolochic acid nephropathy.. The 52nd American Society of Nephrology, KidneyWeek 2018 2018.10 San Diego
15. Naohiro Takahashi, Hiroaki Kikuchi, Tomoaki Ishihara, Makoto Arita, Taisuke Furusho, Fumiaki Ando, Takayasu Mori, Kiyoshi Isobe, Koichiro Susa, Naohiro Nomura, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Amelioration of Renal Fibrosis and Tubulointerstitial Damage in Fat-1 Transgenic CKD Mice by Compensation of Decreased Omega-3 Fatty Acids in the Kidney. The 52nd Annual Meeting of American Society of Nephrology, Kidney Week 2018 2018.10 San Diego
16. Tamami Fujiki, Fumiaki Ando, Kiyoshi Isobe, Takayasu Mori, Koichiro Susa, Naohiro Nomura, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Tolvaptan activates Nrf2/HO-1 pathway through PERK phosphorylation. The 52nd Annual Meeting of American Society of Nephrology, Kidney Week 2018 2018.10.26 San Diego
17. Fujimaru T, Mori T, Mandai S, Chiga M, Kikuchi H, Ando F, Mori Y, Susa K, Isobe K, Iimori S, Nomura N, Naito S, Okado T, Rai T, Nagatsuji K, Nagahama K, Mishima E, Mochizuki T, Sekine A, Hoshino J, Ubara Y, Uchida S, Sohara E.. Genomic Background of Adults with Suspected Ciliopathy on Renal Biopsy.. The 52nd Annual Meeting of American Society of Nephrology, Kidney Week 2018 2018.10.26 San Diego

18. Shoda W, Nomura N, Ando F, Isobe K, Mori T, Susa K, Sohara E, Rai T, Uchida S.. Molecular mechanism of high-potassium induced Na-Cl cotransporter dephosphorylation.. The 52nd Annual Meeting of American Society of Nephrology. 2018.10.27
19. Hiroaki Kikuchi, Eisei Sohara etc. Failure to sense energy depletion may be a novel therapeutic target in chronic kidney diseases. 2018.12.08 Tokyo

[Awards & Honors]

1. Hiroaki Kikuchi. ISN Frontiers Young Investigators Travel Grants, ISN Frontiers Meetings 2018, 2018.02
2. Takuya Fujimaru. Top 10% Ranked Poster Award, International Society of Nephrology, 2018.02
3. Kiyoshi Isobe. Young Investigator Award (YIA) of Japan Society of Nephrology, 2018.08

[Others]

1. Press release: Hiroaki Kikuchi, Eisei Sohara, Shinichi Uchida. Faulty sensing: cellular energy sensor linked to the progression of chronic kidney disease, 2018.12
Kidney International

Comprehensive Reproductive Medicine

Professor : Naoyuki MIYASAKA

Associate Professor : Satoshi OBAYASHI

Project Professor : Masakazu TERAUCHI

Junior Associate Professor : Naoyuki YOSHIKI, Kimio WAKANA

Project Junior Associate Professor: Tomonori ISHIKAWA, Makiko EGAWA

Assistant Professor : Yuki IWAHARA, Noriko OSHIMA- SUDO, Shiro HIRAMITSU, Nobuyuki KIDERA, Takashi NAKASUJI, kotoi TSURANE, Asuka HIROSE, Reiko NAKAMURA

Project Assistant Professor : Ayako FUDONO, kazuki SAITO

Hospital Staff :hiroshi YOMOGITA, Noriko KUROSAKA, Kiyoko ISHIZUKA

Graduate Student :Reiko SHIRAI, Kiyotaka KAWAI, Kazuki SAITO, Akiko FURUSAWA, Takuto MATSUURA, Rie OI, Takayuki TATSUMI, Masaki SEKIGUCHI, Tamami ODAI, Kenta TAKAHASHI, Mayumi KOBAYASHI, AsamiHIRATA, Shiho YAUCHI, Misako IWATA, Nobuyuki KIDERA, Ayako FUDONO, Misaki MASUYAMA

(1) Research

Research divisions :

- 1) Research in physiology, endocrinology and metabolism in the reproductive medicine
- 2) Research of female physical and mental change with aging
- 3) Pathophysiological examination of gynecological malignant tumor
- 4) Clinical research and basic research in perinatal medicine

Available scientific procedures :

- 1, Cell culture technique of ovarian granulosa cells, endometrial cells, malignant cells, osteoblast and so on.
- 2, Determination of intracellular calcium (by Fura 2 method and patch clamp)
- 3, Measurement of intra-cellular IP3
- 4, Hormonal assay in plasma, urine, follicular fluid (RIA & EIA)
- 5, Immunohistochemistry with ABC method
- 6, Analysis of micro-structure with electrical microscopy
- 7, Determination with molecular biological technique.
- 8, Physiological determination with isometric tension change
- 9, Determination of cerebral blood flow with MRI in cerebral infarction
- 10, Analysis of protein expression with flow cytometry

(2) Education

CRM (OB/GY) department has an obligation to offer medical services, education, research as one of the clinical departments in national graduate school, and has duty on making a mutual cooperation with local gynecological institutions.

Our main objectives are

- 1, Investigation for a new progress in treatment technique
- 2, Acquisition of medical knowledge and procedure
- 3, Providing systemic lecture about women's physiological and pathological change during adolescence through senescence.

Aims of research works are focusing on reproductive medicine, perinatal medicine and oncology.

Educational intention in medical doctor course and nursing course includes systemic lectures, clinical conferences and special lecture by many extramural speakers. During Bed-Side Learning period, students should be treated as one of medical stuffs, attend all of deliveries and be present at gynecological procedure. Several OB/GY institutions will be provided as an extramural drills.

(3) Clinical Performances

For intractable sterilization, satisfactory results are obtained with endoscopic examinations and IVF-ET methods. Health care unit for menopausal women was established, where inspections for atherosclerosis, osteoporosis (DEXA), autonomic nervous system are performed, and postmenopausal managements are provided including HRT, mental care and counseling.

After construction of LDR(labor, delivery, recovery) unit, cure for complicated pregnancies is now carried out, and cases of deliveries are rising now.

Malignant gynecological tumor is also an important aim of this department, for which surgery, chemotherapy and radiotherapy with complete cure are applied to patients. For benign tumor and endometriosis, laparoscopic operations are aggressively performed, whose number is now increasing.

(4) Publications

[Original Articles]

1. Oi R, Miyasaka N, Yamashita T, Adachi T. Associations of temporal changes in cervical length and the lower uterine segment length with spontaneous preterm delivery risk: A prospective study of 727 Japanese women *Journal of Medical Ultrasonics*. 2018;
2. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Mikako Masuda, Reiko Tsunoda, Hiroaki Fushiki, Naoyuki Miyasaka. Dizziness in peri- and postmenopausal women is associated with anxiety: a cross-sectional study. *Biopsychosoc Med*. 2018; 12; 21
3. Sayuri Udagawa, Sayaka Katagiri, Shogo Maekawa, Yasuo Takeuchi, Rina Komazaki, Anri Ohtsu, Naoki Sasaki, Takahiko Shiba, Kazuki Watanabe, Kazuyuki Ishihara, Noriko Sato, Naoyuki Miyasaka, Yuichi Izumi. Effect of *Porphyromonas gingivalis* infection in the placenta and umbilical cord in pregnant mice with low birth weight. *Acta Odontol. Scand.* 2018.01; 1-9
4. Hirose A, Terauchi M, Osaka Y, Akiyoshi M, Kato K, Miyasaka N. Effect of soy lecithin on fatigue and menopausal symptoms in middle-aged women: a randomized, double-blind, placebo-controlled study. *Nutrition Journal*. 2018.01; 17(4);
5. Tajirika-Shirai R, Takimoto H, Yokoyama T, Kaneko H, Kubota T, Miyasaka N. Effect of individualised dietary education at medical check-ups on maternal and fetal outcomes in pregnant Japanese women *Asia Pac J Clin Nutr*. 2018.01; 27(3); 607-616
6. Yuri Sukenobe, Masakazu Terauchi, Asuka Hirose, Miho Hirano, Mihoko Akiyoshi, Kiyoko Kato, and Naoyuki Miyasaka. Normal/high-fat milk consumption is associated with higher lean body and muscle mass in Japanese women aged between 40 and 60 years: a cross-sectional study *BMC Women's Health*. 2018.02; 18; 32
7. Takayuki Tatsumi, Kaori Takayama, Shunsuke Ishii, Atsushi Yamamoto, Taichi Hara, Naojiro Minami, Naoyuki Miyasaka, Toshiro Kubota, Akira Matsuura, Eisuke Itakura, Satoshi Tsukamoto. Forced lipophagy reveals that lipid droplets are required for early embryonic development in mouse. *Development*. 2018.02; 145(4);

8. Yamada Ichiro, Sakamoto Junichiro, Kobayashi Daisuke, Miyasaka Naoyuki, Wakana Kimio, Oshima Noriko, Wakabayashi Akira, Saida Yukihisa, Tateishi Ukihide, Eishi Yoshinobu. 子宮及び子宮内膜癌の Diffusion Kurtosis Imaging による評価 病理組織学的所見との対比 (Diffusion Kurtosis Imaging of the Uterus and Endometrial Carcinoma: Correlation with Histopathologic Findings) 日本医学放射線学会学術集会抄録集. 2018.02; 77 回; S296
9. Yamada Ichiro, Wakana Kimio, Kobayashi Daisuke, Miyasaka Naoyuki, Oshima Noriko, Wakabayashi Akira, Saida Yukihisa, Tateishi Ukihide, Eishi Yoshinobu. 子宮及び子宮内膜癌の Diffusion-Tensor Imaging による評価 免疫組織化学的所見との比較 (Diffusion-Tensor Imaging of the Uterus and Endometrial Carcinoma: Comparison with Immunohistochemical Findings) 日本医学放射線学会学術集会抄録集. 2018.02; 77 回; S193
10. Odai Tamami, Terauchi Masakazu, Hirose Asuka, Miyasaka Naoyuki. Bone mineral density in premenopausal women is associated with antioxidant nutrient intake(和訳中) 日本産科婦人科学会雑誌. 2018.02; 70(2); 513-514
11. Kawai K, Harada T, Ishikawa T, Sugiyama R, Kawamura T, Yoshida A, Tsutsumi O, Ishino F, Kubota T, Kohda T. . Parental age and gene expression profiles in individual human blastocysts. Scientific Reports. 2018.02;
12. Yamada I, Hikishima K, Yoshino N, Sakamoto J, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using q-space imaging; correlation with histopathologic findings. J Magn Reson Imaging. 2018.03; 48(4); 1059-1068
13. Rina Komazaki, Sayaka Katagiri, Hirokazu Takahashi, Shogo Maekawa, Takahiko Shiba, Yasuo Takeuchi, Yoichiro Kitajima, Anri Ohtsu, Sayuri Udagawa, Naoki Sasaki, Kazuki Watanabe, Noriko Sato, Naoyuki Miyasaka, Yuichiro Eguchi, Keizo Anzai, Yuichi Izumi. Author Correction: Periodontal pathogenic bacteria, *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. Sci Rep. 2018.03; 8(1); 4620
14. Rei Haruyama, Stuart Gilmour, Erika Ota, Sarah K Abe, Md Mizanur Rahman, Shuhei Nomura, Naoyuki Miyasaka, Kenji Shibuya. Causes and risk factors for singleton stillbirth in Japan: Analysis of a nationwide perinatal database, 2013-2014. Sci Rep. 2018.03; 8(1); 4117
15. Makiko Egawa, Hirokazu Kanegane, Kohsuke Imai, Tomohiro Morio, Naoyuki Miyasaka. Intravenous immunoglobulin (IVIG) efficiency in women with common variable immunodeficiency (CVID) decreases significantly during pregnancy. J. Matern. Fetal. Neonatal. Med.. 2018.04; 1-5
16. Mitsuhiro Kishino, Shuichiro Nakaminato, Yoshio Kitazume, Naoyuki Miyasaka, Toshifumi Kudo, Yukihisa Saida, Ukihide Tateishi. Balloon-Occluded Carbon Dioxide Gas Angiography for Internal Iliac Arteriography and Intervention. Cardiovasc Intervent Radiol. 2018.04;
17. Akiko Furusawa, Morikazu Miyamoto, Masashi Takano, Hitoshi Tsuda, Yong Sang Song, Daisuke Aoki, Naoyuki Miyasaka, Johji Inazawa, Jun Inoue. Ovarian cancer therapeutic potential of glutamine depletion based on GS expression. Carcinogenesis. 2018.04;
18. Mami Miyado, Koji Muroya, Momori Katsumi, Kazuki Saito, Masafumi Kon, Maki Fukami. Somatic Acquired Isodicentric Y and Mosaic Loss of Chromosome Y in a Boy with Hypospadias. Cytogenet. Genome Res.. 2018.04; 154(3); 122-125
19. Gulinisha Aihemaiti, Morito Kurata, Daichi Nogawa, Akiko Yamamoto, Tatsunori Mineo, Iichiroh Onishi, Yuko Kinowaki, Xiao-Hai Jin, Anna Tatsuzawa, Naoyuki Miyasaka, Masanobu Kitagawa, Kouhei Yamamoto. Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma. Oncotarget. 2018.06; 9(46); 28213-28225
20. Shigeru Nakamura, Yoshitomo Kobori, Yoshihiko Ueda, Yoko Tanaka, Hiromichi Ishikawa, Atsumi Yoshida, Momori Katsumi, Kazuki Saito, Akie Nakamura, Tsutomu Ogata, Hiroshi Okada, Hideo Nakai, Mami Miyado, Maki Fukami. STX2 is a causative gene for nonobstructive azoospermia. Hum. Mutat.. 2018.06; 39(6); 830-833
21. Kawai K, Ishikawa T, Ohuchi K, Kidera K. Kawahara M, Hiraoka K, Ogawa O, Masuzawa M, Harada T, Miyasaka N. WHO Group1 ovulation disorder successfully treated with recombinant follicle stimulating hormone: A revisit to the role of luteinizing hormone and estradiol Journal of Medical and Dental Sciences. 2018.06;

22. Tsukamoto S, Tatsumi T. Degradation of maternal factors during preimplantation embryonic development. *The Journal of reproduction and development*. 2018.06; 64(3); 217-222
23. Toba M, Moriwaki M, Oshima N, Aiso Y, Shima M, Nukui Y, Obayashi S, Fushimi K. Prevention of surgical site infection via antibiotic administration according to guidelines after gynecological surgery. *The journal of obstetrics and gynaecology research*. 2018.07;
24. Tomoko Yoshida, Toshiya Matsuzaki, Mami Miyado, Kazuki Saito, Takeshi Iwasa, Yoichi Matsubara, Tsutomu Ogata, Minoru Irahara, Maki Fukami. 11-oxygenated C19 steroids as circulating androgens in women with polycystic ovary syndrome. *Endocr. J.*. 2018.07;
25. Hiramitsu S, Ishikawa T, Lee WR, Khan T, Crumbley C, Khwaja N, Zamanian F, Asghari A, Sen M, Zhang Y, Hawse JR, Minna JD, Umetani M.. Estrogen Receptor Beta-Mediated Modulation of Lung Cancer Cell Proliferation by 27-Hydroxycholesterol. *Frontier Endocrinology*. 2018.08;
26. Shiro Hiramitsu, Tomonori Ishikawa, Wan-Ru Lee, Tamor Khan, Christine Crumbley, Nimra Khwaja, Faezeh Zamanian, Arvand Asghari, Mehmet Sen, Yang Zhang, John R Hawse, John D Minna, Michihisa Umetani. Estrogen Receptor Beta-Mediated Modulation of Lung Cancer Cell Proliferation by 27-Hydroxycholesterol. *Front Endocrinol (Lausanne)*. 2018.08; 9; 470
27. Woojin Kang, Eri Ishida, Kenji Yamatoya, Akihiro Nakamura, Mami Miyado, Yoshitaka Miyamoto, Maki Iwai, Kuniko Tatsumi, Takakazu Saito, Kazuki Saito, Natsuko Kawano, Toshio Hamatani, Akihiro Umezawa, Kenji Miyado, Hidekazu Saito. Autophagy-disrupted LC3 abundance leads to death of supporting cells of human oocytes. *Biochem Biophys Rep*. 2018.09; 15; 107-114
28. Hiraoka K, Kitamura S, Otsuka Y, Kawai K, Harada T, Ishikawa T. Effects of sperm direction in Piezo-ICSI on oocyte survival, fertilization, embryo development and implantation ability in humans: A preliminary study. *Journal of Obstetrics and Gynaecology Research*. 2018.10;
29. Sasaki N, Katagiri S, Komazaki R, Watanabe K, Maekawa S, Shiba T, Udagawa S, Takeuchi Y, Ohtsu A, Kohda T, Tohara H, Miyasaka N, Hirota T, Tamari M, Izumi Y. Endotoxemia by *Porphyromonas gingivalis* Injection Aggravates Non-alcoholic Fatty Liver Disease, Disrupts Glucose/Lipid Metabolism, and Alters Gut Microbiota in Mice *Frontiers in Microbiology*. 2018.10; 9; 2470
30. Tatsumi T, Ishida E, Tatsumi K, Okada Y, Saito T, Kubota T, Saito H. Advanced paternal age alone does not adversely affect pregnancy or live-birth rates or sperm parameters following intrauterine insemination. *Reproductive medicine and biology*. 2018.10; 17(4); 459-465
31. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Muscle and joint pains in middle-aged women are associated with insomnia and low grip strength: a cross-sectional study *Journal of Psychosomatic Obstetrics & Gynecology*. 2018.11;
32. Ichiro Yamada, Kimio Wakana, Daisuke Kobayashi, Naoyuki Miyasaka, Noriko Oshima, Akira Wakabayashi, Yukihisa Saida, Ukihide Tateishi, Yoshinobu Eishi. Endometrial carcinoma: Evaluation using diffusion-tensor imaging and its correlation with histopathologic findings. *J Magn Reson Imaging*. 2018.11;
33. Masakazu Terauchi, Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Mikako Masuda, Reiko Tsunoda, Hiroaki Fushiki, Naoyuki Miyasaka. Dizziness in peri- and postmenopausal women is associated with anxiety: a cross-sectional study *BioPsychoSocial Medicine*. 2018.12; 12; 21
34. Ichiro Yamada, Junichiro Sakamoto, Daisuke Kobayashi, Naoyuki Miyasaka, Kimio Wakana, Noriko Oshima, Akira Wakabayashi, Yukihisa Saida, Ukihide Tateishi, Yoshinobu Eishi. Diffusion kurtosis imaging of endometrial carcinoma: Correlation with histopathological findings. *Magn Reson Imaging*. 2018.12;
35. Masaki Sekiguchi, Masashi Mikami, Chie Nakagawa, Mika Ozaki, Shinji Tanigaki, Tohru Kobayashi, Naoyuki Miyasaka, Haruhiko Sago. An ultrasonographic estimated fetal weight reference for Japanese twin pregnancies. *J Med Ultrason (2001)*. 2018.12;

[Misc]

1. Masakazu Terauchi. Irisin, a promising but immature myokine linking between physical activity and its positive health effects *Menopause Live*. 2018.04; (4/6);

[Conference Activities & Talks]

1. Takashi Nakasuji, Kiyotaka Kawai, Nobuyuki Kidera, Kumi Ouchi, Yuki Iwahara, Tatsuya Harada, Tomonori Ishikawa. Efficacy of random-start ovarian stimulation and Duostim of breast cancer patients for fertility preservation. The 63rd Annual Meeting of Japan Society for Reproductive Medicine 2018
2. Y. Kitazume, Y. Ogihara, N. Oshima, K. Wakana, A. Takemoto, N. Miyasaka, U. Tateishi. Endometrial cancer: volumetric histogram analysis of apparent diffusion coefficient map for predicting the histological grade. European Congress of Radiology 2018 2018.02.28 Vienna, Austria
3. Takashi Nakasuji, Hiroshi Asahara, Nobuyuki Kidera, Atsushi Yamamoto, Yuki Iwahara, Tomonori Ishikawa, Naoyuki Miyasaka. Critical functions of Zfy1 and Zfy2 in spermatogenesis. The 8th Congress of the Asia Pacific Initiative on Reproduction 2018.04 TAIWAN
4. Miyuki Nonaka, Tomonori Ishikawa, Sachi Murakata, Kenichiro Hiraoka, Takashi Nakasuji, Yuki Iwahara, Naoyuki Miyasaka. Clinical efficiency of hyaluronic acid bound spermatozoa selection combined with Piezo-ICSI. The 8th Congress of the Asia Pacific Initiative on Reproduction 2018.04.14 Taipei
5. Takashi Nakasuji, Tomonori Ishikawa, Nobuyuki Kidera, Yuki Iwahara, Naoyuki Miyasaka. Validity of assisted reproductive technology after laparoscopic myomectomy. 70th Annual Congress of the Japan Society of Obstetrics and Gynecology 2018.05 日本
6. Tamami Odai, Masakazu Terauchi, Asuka Hirose, Kiyoko Kato, Naoyuki Miyasaka. Bone mineral density in premenopausal women is associated with the dietary intake of α -tocopherol. 第70回日本産婦人科学会学術講演会 2018.05.12
7. Rie OI. Shortening rate of cervical length in the second trimester can be the risk factor of preterm delivery. 2018.05.12
8. Tamami Odai, Masakazu Terauchi, Asuka Hirose, Kiyoko Kato, Naoyuki Miyasaka. Bone mineral density in premenopausal women is associated with the dietary intake of α -tocopherol. International Menopause Society 16th World Congress on Menopause 2018.06.06
9. Noriko Oshima, Reiko Nakamura, Akiko Furusawa, Mikayo Toba, Kimio Wakana, Masakazu Terauchi, Satoshi Obayashi, Naoyuki Miyasaka. Analysis of radical radiotherapy for endometrial cancer as the initial treatment. The 16th World Congress On Menopause 2018.06.06 Vancouver
10. Masakazu Terauchi. Chilliness in Japanese peri- and post-menopausal women is associated with reduced heart rate and resting energy expenditure. 16th World Congress on the Menopause 2018.06.07 Vancouver, Canada
11. Asuka Hirose. Postpartum depression is associated with antioxidant activity within a few days after delivery.. IMS 2018, the 16th World Congress on the Menopause 2018.06.07 Vancouver
12. Kazuki Saito, Akira Kuwahara, Tomonori Ishikawa, Takashi Nakasuji, Mami Miyado, Kenji Miyado, Maki Fukami, Naoyuki Miyasaka, Minoru Irahara, Hidekazu Saito. Pregnancy after frozen-thawed embryo transfer during hormonal replacement cycle is associated with hypertensive disorders of pregnancy and placenta accreta.. 2018.07.04 Barcelona
13. Oi R, Yamashita T, Izumi N, Yuzawa N, Samejima T, Miyagami S, Shuri E, Akamata N, Yasumizu N, Yabe S, Kawana Y, Takeda Y, Sakamoto H, Adachi T, Nakabayashi M. Accuracy of diagnosis of partial mole. 2018.07.08 Tokyo
14. Takashi Nakasuji, Tomonori Ishikawa, Kazuki Saito, Shiro Hiramitsu, Yuki Iwahara, Naoyuki Miyasaka. Efficacy of LM-ART hybrid therapy. The 58th Japan Society of Gynecologic and Obstetric Endoscopy and Minimally Invasive Therapy 2018.08 Japan
15. Masakazu Terauchi. Menopause and the Workplace. The 18th Congress of the Asian College of Psychosomatic Medicine 2018.08.24 Seoul
16. Noriko Oshima, Ken-ichi Nakahama, Naoyuki Miyasaka, Ikuo Morita. Tissue engineered lymphatic microvessels using cell-printing technology. 17th Biennial Meeting of the International Gynecologic Cancer Society 2018.09.14 Kyoto

17. Kenta Takahashi, Noriko Oshima, Reiko Nakamura, Kimio Wakana, Satoshi Miyake, Naoyuki Miyasaka, Sadakatu Ikeda. Ovarian mixed Brenner-mucinous borderline tumor with BRAF V600E mutation.. 17th Biennial Meeting of the International Gynecologic Cancer Society 2018.09.14 Kyoto
18. Kenta Takahashi, Noriko Oshima, Reiko Nakamura, Ichiroh Onishi, Kimio Wakana, Satoshi Miyake, Naoyuki Miyasaka, Sadakatu Ikeda. Ovarian mixed Brenner-mucinous borderline tumor with BRAF V600E mutation.. 17th Biennial meeting of the International Gynecologic Cancer Society 2018.09.16
19. Shiho Takeuchi, Makiko Egawa, Nobuyuki Kidera, Ayako Fudono, Asuka Hirose, Takashi Nakasuji, Naoyuki Miyasaka. Five Cases of Cesarean Scar Pregnancy.. IFPA Meeting 2018: Japan Placenta Association (JPA) 2018.09.21
20. Rie Oi. Ultrasound may help accurate diagnosis of partial hydatidiform mole in very early pregnancy. International Society of Ultrasound in Obstetrics and Gynecology 2018.10 Singapore
21. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Mikako Masuda, Reiko Tsunoda, Hiroaki Fushiki, Naoyuki Miyasaka. Dizziness in Peri- and Postmenopausal Women is Associated with Anxiety. North American Menopause Society Annual Meeting 2018.10.04 San Diego, CA
22. Tamami Odai, Masakazu Terauchi, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Hot flushes in middle-aged women are inversely associated with dietary intake of vitamin B. The North American Menopause Society 2018 Annual Meeting 2018.10.04
23. S. Jwa, A. Nakashima, A. Kuwahara, K. Saito, M. Irahara, T. Sakumoto, O. Ishihara, H. Saito. Ovarian stimulation using clomiphene citrate and adverse perinatal outcomes in pregnancies following fresh single-embryo transfers. 2018.10.10 Colorado
24. Masaki Sekiguchi, Chie Nakagawa, Mika Ozaki, Kohei Ogawa, Katsusuke Ozawa, Haruhiko Sago. A reference for the ultrasonographic estimated fetal weight in Japanese twin pregnancies. 28th World Congress on Ultrasound in Obstetrics and Gynecology, 2018.10.22 Singapore
25. Masakazu Terauchi. Special Session KSPOG-JSPOG: Introduction of JSPOG and cooperation with KSPOG. Annual Scientific Meeting of the Korean Society of Psychosomatic Obstetrics and Gynecology 2018.12.23 Seoul

Urology

Professor and Chairman: Yasuhisa Fujii

Associate Professor: Kazutaka Saito

Junior Associate Professor: Yoh Matsuoka,

Junichiro Ishioka (Department of Insured Medical Care Management), Minato Yokoyama

Assistant Professor: Soichiro Yoshida, Toshiki Kijima, Yosuke Yasuda, Sho Uehara

Project Assistant Professor: Shingo Moriyama (April -), Yuma Waseda (April - June),
Shohei Fukuda (April -)

Hospital Staff: Yuma Waseda (- March), Hiroshi Fukushima (July -), Shohei Fukuda (- March),
Masahiro Toide, Yuichi Fukuda (- June), Kasumi Kaneko (April -), Kenji Tanabe (April -)

Graduate Student: Saori Araki, Yosuke Yasuda (- March), Sho Uehara (- March), Yuma Waseda,
Hiroshi Fukushima,

Shingo Moriyama, Shohei Fukuda (April -), Yusuke Uchida (April -),
Masahiro Toide (April -)

Project Professor: Kazunori Kihara

(1) Outline

Urology is the branch of medicine that focuses on surgical and medical diseases of the male and female urinary-tract system and the male reproductive organs. Our mission is to establish and provide the best urological care to all patients in the super aging society which all over the world is facing. Besides offering urological practices of the international standard, we are making a continuous effort to improve daily practices based on the evidences of the clinical and translational research which we commit under the concept of “Bed to Bench, Feedback to Bed” .

(2) Research

Clinical Research

1. A minimally invasive surgery, minimum-incision endoscopic urological surgery
2. Optimal MRI-ultrasonography fusion prostate needle biopsy
3. Curative and minimally invasive bladder preservation using transurethral resection of bladder tumor, low-dose chemoradiotherapy and partial cystectomy
4. Minimum-incision endoscopic clampless partial nephrectomy against kidney cancer
5. Focal brachytherapy against localized prostate cancer
6. Diffusion-weighted MRI to diagnosis, assessment of therapeutic effects and monitoring of relapse in urological cancer
7. Whole body MRI using DWIBS technique
8. Imaging diagnosis for prostate and kidney cancers using deep learning
9. Serum C-reactive protein as a prognostic biomarker of urological malignancies
10. Prognostic prediction model for non-muscle-invasive bladder cancer
11. Renal function after kidney cancer surgery
12. Prevention of postoperative inguinal hernia after robot assisted radical prostatectomy

Translational Research

1. Biomarker in bladder preservation therapy using chemoradiotherapy

2. Overcoming therapeutic resistance to immune-check point inhibitors for urological cancers
3. Mechanisms of abscopal effect of immune-check point inhibitors and radiation in urothelial cancer

(3) Lectures & Courses

Our top priority is to establish the best urological practice in the super aging society which all over the world is facing. We are committed to offering educational programs to facilitate the development of outstanding academic urologists of the next generation. We believe that one of our missions is to educate students, residents and fellows in the art and science of urology and thereby to train the future leaders in the field. The continuous commitment to clinical and translational research is reflected to publications in international journals, presentations at international meetings and awards.

(4) Clinical Performances

Our mission is to provide the best urological care to all patients. Besides offering urological practices of the international standard including robot-assisted surgery and laparoscopic sacrocolpopexy, we are making a continuous effort to improve daily practices. To realize the mission, we have been developing various procedures with high quality and affordable cost.

1. Minimum-incision endoscopic urological surgery which can be applied to most of patients with urological tumors
2. Tetra-modal bladder sparing treatment consisting of transurethral resection of bladder tumor, low-dose chemoradiotherapy and partial cystectomy with pelvic lymph node dissection
3. Clampless partial nephrectomy
4. Focal brachytherapy
5. Prediction model of non-muscle invasive bladder cancer
6. Diagnostic model for small renal masses
7. Clinical implication of diffusion-weighted MRI

(5) Publications

[Original Articles]

1. Sho Uehara, Soichiro Yoshida, Hiroshi Tanaka, Yosuke Yasuda, Hajime Tanaka, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii. Prediction of Intraoperative Urinary Collecting System Entry in Patients with Peripheral Renal Tumors Undergoing Partial Nephrectomy: Usefulness of Tumor-Centered Multiplanar Reconstruction. *Urol. Int.*. 2018.01; 100(1); 85-91
2. Fujii Yasuhisa. Prediction models for progression of non-muscle-invasive bladder cancer: A review(和訳中) *International Journal of Urology*. 2018.03; 25(3); 212-218
3. Umakoshi Hironobu, Tsuiki Mika, Takeda Yoshiyu, Kurihara Isao, Itoh Hiroshi, Katabami Takuyuki, Ichijo Takamasa, Wada Norio, Yoshimoto Takanobu, Ogawa Yoshihiro, Kawashima Junji, Sone Masakatsu, Inagaki Nobuya, Takahashi Katsutoshi, Watanabe Minemori, Matsuda Yuichi, Kobayashi Hiroki, Shibata Hirotaka, Kamemura Kohei, Otsuki Michio, Fujii Yuichi, Yamamoto Koichi, Ogo Atsushi, Yanase Toshiko, Suzuki Tomoko, Naruse Mitsuhide. Significance of Computed Tomography and Serum Potassium in Predicting Subtype Diagnosis of Primary Aldosteronism *JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM*. 2018.03; 103(3); 900-908
4. Yujiro Nakano, Takanobu Yoshimoto, Tatsuya Fukuda, Masanori Murakami, Ryotaro Bouchi, Isao Minami, Koshi Hashimoto, Yasuhisa Fujii, Kazunori Kihara, Yoshihiro Ogawa. Effect of Eplerenone on the Glomerular Filtration Rate (GFR) in Primary Aldosteronism: Sequential Changes in the GFR During Preoperative Eplerenone Treatment to Subsequent Adrenalectomy. *Intern. Med.*. 2018.04;
5. Takuya Adachi, Minato Yokoyama, Yasuhisa Fujii, Yuko Kinowaki, Susumu Kirimura, Kazunori Kubota, Yukihiro Saida, Ukihide Tateishi. Neuroblastic tumors in young adults as a sequela of malignant neuroblastoma: report of two cases. *Abdom Radiol (NY)*. 2018.04;

6. Yosuke Yasuda, Kazutaka Saito, Takahiko Soma, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazunori Kihara, Yasuhisa Fujii . PD07-05 THE OUTCOME OF GASLESS LAPAROSCOPIC SINGLE-PORT CLAMPLESS SUTURELESS PARTIAL NEPHRECTOMY USING THREE-DIMENSIONAL HEAD-MOUNTED DISPLAY 2018.04;
7. shugo yajima, Soichiro Yoshida, Taro Takahara Minato Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii . MP08-03 ABSENCE OF INCHWORM SIGN ON DWI: A PREDICTIVE MARKER FOR PROGRESSION IN PT1 BLADDER CANCER the journal of UROLOGY. 2018.04;
8. Takahiko Soma, Junichiro Ishioka, Hajime Tanaka, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. MP36-08 A CONVOLUTIONAL NEURAL NETWORKS ALGORITHM FOR DIFFERENTIAL DIAGNOSIS OF FAT-POOR ANGIOMYOLIPOMA AND RENAL CELL CARCINOMA IN ENHANCED CT AND T2-WEIGHTED MAGNETIC RESONANCE IMAGING the journal of UROLOGY. 2018.04;
9. Yoh Matsuoka, Junichiro Ishioka, Hiroshi Tanaka, Tomo Kimura, Yuma Waseda, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, and others. MP20-09 MRI-BASED RISK ASSESSMENT FOR POSTOPERATIVE BIOCHEMICAL RECURRENCE USING THE PROSTATE IMAGING REPORTING AND DATA SYSTEM (PI-RADS) SCORES AND CAPSULAR CONTACT LENGTH 2018.04;
10. Kenji Tanabe, Kazutaka Saito, Kazuaki Nakagomi, Chizuru Arisawa, Tetsuro Tsukamoto, Tetsuo Okuno, Katsushi Nagahama, Akira Noro, and others. MP36-05 CHANGES IN PATTERN OF RECURRENCE OVER TIME AFTER RADICAL NEPHRECTOMY IN PATIENTS WITH LOCALIZED CLEAR CELL RENAL CELL CARCINOMA the journal of UROLOGY. 2018.04;
11. Minato Yokoyama, Naoko Kawamura, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Junichiro Ishioka, Yoh Matsuoka, and others. MP42-05 ACUTE KIDNEY INJURY AND INTERMEDIATE-TERM RENAL FUNCTION AFTER CLAMPLESS PARTIAL NEPHRECTOMY the journal of UROLOGY. 2018.04;
12. Yoh Matsuoka, Hiroshi Tanaka, Tomo Kimura, Yuma Waseda, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, and others. PD47-11 THE ROLE OF MRI-TARGETED BIOPSY IN PREDICTION OF ADVERSE PATHOLOGICAL AND ONCOLOGICAL OUTCOME AFTER RADICAL PROSTATECTOMY the journal of UROLOGY. 2018.04;
13. Yosuke Yasuda, Kazutaka Saito, Takahiko Soma, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, and others. PD07-05 THE OUTCOME OF GASLESS LAPAROSCOPIC SINGLE-PORT CLAMPLESS SUTURELESS PARTIAL NEPHRECTOMY USING THREE-DIMENSIONAL HEAD-MOUNTED DISPLAY the journal of UROLOGY. 2018.04;
14. Yoh Matsuoka, Junichiro Ishioka, Hiroshi Tanaka, Tomo Kimura, Yuma Waseda, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, and others. MP20-09 MRI-BASED RISK ASSESSMENT FOR POSTOPERATIVE BIOCHEMICAL RECURRENCE USING THE PROSTATE IMAGING REPORTING AND DATA SYSTEM (PI-RADS) SCORES AND CAPSULAR CONTACT LENGTH the journal of UROLOGY. 2018.04;
15. Junichiro Ishioka, Yoh Matsuoka, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Kazutaka Saito, and others. MP20-10 DEEP LEARNING WITH A CONVOLUTIONAL NEURAL NETWORK ALGORITHM FOR FULLY AUTOMATED DETECTION OF PROSTATE CANCER USING PRE-BIOPSY MRI the journal of UROLOGY. 2018.04;
16. Kasumi Kaneko, Soichiro Yoshida, Taro Takahara, Shugo Yajima, Tsuyoshi Sakamoto, Thomas Kwee, Yuki Arita, Minato Yokoyama, and others. MP20-18 SEMI-AUTOMATIC SEGMENTATION ANALYSIS OF DIFFUSION-WEIGHTED MRI AS AN IMAGING BIOMARKER FOR HISTOLOGICAL GRADE OF BLADDER CANCER the journal of UROLOGY. 2018.04;
17. Toshiki Kijima, Thomas Prince, Katsuo Mori, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, and others. MP64-14 TARGETING HEAT SHOCK FACTOR 1 SENSITIZES CASTRATION-RESISTANT PROSTATE CANCER CELLS TO HSP90 INHIBITION IN PART BY DESTABILIZING ANDROGEN RECEPTOR SPLICE VARIANTS the journal of UROLOGY. 2018.04;

18. Yosuke Yasuda, Kazutaka Saito, Takahiko Soma, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, and others. PD07-05 THE OUTCOME OF GASLESS LAPAROSCOPIC SINGLE-PORT CLAMPLESS SUTURELESS PARTIAL NEPHRECTOMY USING THREE-DIMENSIONAL HEAD-MOUNTED DISPLAY the journal of UROLOGY. 2018.04;
19. Yoh Matsuoka, Junichiro Ishioka, Hiroshi Tanaka, Tomo Kimura, Yuma Waseda, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, and others. MP20-09 MRI-BASED RISK ASSESSMENT FOR POSTOPERATIVE BIOCHEMICAL RECURRENCE USING THE PROSTATE IMAGING REPORTING AND DATA SYSTEM (PI-RADS) SCORES AND CAPSULAR CONTACT LENGTH the journal of UROLOGY. 2018.04;
20. Hiroshi Fukushima, Masaki Kobayashi, Keizo Kawano, Shinji Morimoto. Prognostic Value of Albumin/Globulin Ratio in Patients with Upper Tract Urothelial Carcinoma Patients Treated with Radical Nephroureterectomy. *Anticancer Res.* 2018.04; 38(4); 2329-2334
21. Matsuoka Yoh, Tanaka Hiroshi, Kimura Tomo, Waseda Yuma, Uehara Sho, Yasuda Yosuke, Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Clinical significance of MRI-targeted biopsy for the risk stratification of oncological outcome after radical prostatectomy(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; AOP-070
22. Yasuda Yosuke, Saito Kazutaka, Soma Takahiko, Tanaka Hajime, Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Kihara Kazunori, Fujii Yasuhisa. Gasless laparoscopic single-port clampless sutureless partial nephrectomy: Perioperative outcomes(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; IS-68
23. Uehara Sho, Yoshida Soichiro, Matsuoka Yoh, Yasuda Yosuke, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Head-mounted display assisted MRI-US elastic fusion prostate biopsy system(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; AVP-06
24. 齋藤 一隆, 松岡 陽, 吉田 宗一郎, 藤井 靖久. MRI/US fusion biopsy の現在と未来 MRI-超音波弾性融合画像生検の前立腺部分治療への適用 日本泌尿器科学会総会. 2018.04; 106 回; SY11-1
25. Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Novel therapy targeting androgen receptor splice variants by inhibiting heat shock factor 1(HSF1) for the treatment of castration-resistant prostate cancer(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; AOP-065
26. Yajima Shugo, Yoshida Soichiro, Tanaka Hiroshi, Tanaka Hajime, Inoue Masaharu, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Predictive significance of absence of inchworm sign on diffusion-weighted MRI for progression of the pT1 bladder cancer(和訳中) 日本泌尿器科学会総会. 2018.04; 106 回; IS-75
27. Junichiro Ishioka, Yoh Matsuoka, Sho Uehara, Yosuke Yasuda, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Kazutaka Saito, Kazunori Kihara, Noboru Numao, Tomo Kimura, Kosei Kudo, Itsuo Kumazawa, Yasuhisa Fujii. Computer-aided diagnosis of prostate cancer on magnetic resonance imaging using a convolutional neural network algorithm. *BJU Int.* 2018.05;
28. Shingo Moriyama, Soichiro Yoshida, Hajime Tanaka, Hiroshi Tanaka, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Intensity ratio curve analysis of small renal masses on T2-weighted magnetic resonance imaging: Differentiation of fat-poor angiomyolipoma from renal cell carcinoma. *Int. J. Urol.* 2018.06; 25(6); 554-560
29. Hajime Tanaka, Soichiro Yoshida, Fumitaka Koga, Kazuma Toda, Ryoichi Yoshimura, Yutaka Nakajima, Emiko Sugawara, Takumi Akashi, Yuma Waseda, Masaharu Inoue, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Impact of Immunohistochemistry-Based Subtypes in Muscle-Invasive Bladder Cancer on Response to Chemoradiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2018.06;
30. Moriyama Shingo, Yoshida Soichiro, Tanaka Hajime, Tanaka Hiroshi, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Intensity ratio curve analysis of small renal masses on T2-weighted magnetic resonance imaging: Differentiation of fat-poor angiomyolipoma from renal cell carcinoma(和訳中) *International Journal of Urology*. 2018.06; 25(6); 554-560

31. Fukushima Hiroshi, Kobayashi Masaki, Kawano Keizo, Morimoto Shinji.. Performance of Quick Sequential (Sepsis Related) and Sequential (Sepsis Related) Organ Failure Assessment to Predict Mortality in Patients with Acute Pyelonephritis Associated with Upper Urinary Tract Calculi. J Urol. 2018.06; 199(6); 1526-1533
32. Takahiko Soma, Junichiro Ishioka, Hajime Tanaka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii. Potential for computer-aided diagnosis using a convolutional neural network algorithm to diagnose fat-poor angiomyolipoma in enhanced computed tomography and T2-weighted magnetic resonance imaging. Int. J. Urol.. 2018.08;
33. Nakayama T, Saito K, Kumagai J, Nakajima Y, Kijima T, Yoshida S, Kihara K, Fujii Y. Higher Serum C-reactive Protein Level Represents the Immunosuppressive Tumor Microenvironment in Patients With Clear Cell Renal Cell Carcinoma. Clinical genitourinary cancer. 2018.08;
34. Kawamura N, Yokoyama M, Tanaka H, Nakayama T, Yasuda Y, Kijima T, Yoshida S, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Acute kidney injury and intermediate-term renal function after clampless partial nephrectomy. International journal of urology . 2018.09;
35. Nakano Yujiro, Yoshimoto Takanobu, Fukuda Tatsuya, Murakami Masanori, Bouchi Ryotaro, Minami Isao, Hashimoto Koshi, Fujii Yasuhisa, Kihara Kazunori, Ogawa Yoshihiro. Effect of Eplerenone on the Glomerular Filtration Rate(GFR) in Primary Aldosteronism: Sequential Changes in the GFR During Preoperative Eplerenone Treatment to Subsequent Adrenalectomy(和訳中) Internal Medicine. 2018.09; 57(17); 2459-2466
36. Kawamura N, Saito K, Inoue M, Ito M, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Kihara K, Fujii Y. Adherent Perinephric Fat in Asian Patients: Predictors and Impact on Perioperative Outcomes of Partial Nephrectomy. Urologia internationalis. 2018.10; 1-6
37. Waseda Y, Saito K, Ishikawa Y, Kawano K, Yokoyama M, Ishioka J, Matsuoka Y, Morimoto S, Kihara K, Fujii Y. Predictive ability of renal cortex enhancement in dynamic computed tomography for residual renal function after nephroureterectomy: Comparison with ^{99m}Tc-diethylenetriaminopentacetic acid renography and validation study. International journal of urology : official journal of the Japanese Urological Association. 2018.10;
38. Yajima Shugo, Yoshida Soichiro, Tanaka Hiroshi, Tanaka Hajime, Inoue Masaharu, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Predictive significance of absence of inchworm sign on diffusion-weighted MRI for progression of the pT1 bladder cancer INTERNATIONAL JOURNAL OF UROLOGY. 2018.10; 25; 234
39. Rie Kato, Hiroshi Fukushima, Masaki Kobayashi, Keizo Kawano, Shinji Morimoto.. A young female case of primary renal carcinoid tumor mimicking fat-poor angiomyolipoma Int Canc Conf J. 2018.10; 7(4); 156-158
40. Araki S, Kijima T, Waseda Y, Komai Y, Nakanishi Y, Uehara S, Yasuda Y, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Nakano Y, Yoshimoto T, Uchida T, Fujii Y. Incidence and predictive factors of hypoglycemia after pheochromocytoma resection. International journal of urology : official journal of the Japanese Urological Association. 2018.11;
41. Soma Takahiko, Ishioka Junichiro, Tanaka Hajime, Matsuoka Yoh, Saito Kazutaka, Fujii Yasuhisa. (和訳中) International Journal of Urology. 2018.11; 25(11); 978-979

[Misc]

1. Koga Fumitaka, Takemura Kosuke, Fukushima Hiroshi.. Biomarkers for Predicting Clinical Outcomes of Chemoradiation-Based Bladder Preservation Therapy for Muscle-Invasive Bladder Cancer. Int J Mol Sci. 2018.09; 19(9);
2. Fukushima Hiroshi, Takemura Kosuke, Suzuki Hiroaki, Koga Fumitaka.. Impact of Sarcopenia as a Prognostic Biomarker of Bladder Cancer. Int J Mol Sci. 2018.10; 19(10);

[Conference Activities & Talks]

1. Ishioka J, Matsuoka Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Matsuoka Y, Saito K, Kihara K, Kimura T, Kudo K, Kumazawa I, Fujii Y. Computer-aided diagnosis with a convolutional neural network algorithm for fully automated detection of prostate cancer using pre-biopsy MRI. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.16 Denmark
2. Soma T, Ihioka J, Tanaka H, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Matsuoka Y, Saito K, Kihara K, Fujii Y. Computer-aided differential diagnosis of fat-poor angiomyolipoma using a deep neural networks algorithm in enhanced CT and T2-weighted magnetic resonance imaging. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.17 Denmark
3. Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Favorable locoregional control in patients with histologic variants of urothelial carcinoma treated with tetra-modality bladder-sparing protocol incorporating consolidative partial cystectomy with lymph node dissection. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.18 Denmark
4. Fukushima H, Kobayashi M, Kwano K, Morimoto S. SOFA and quick SOFA are more clinically useful scoring systems than SIRS in predicting mortality of patients with acute pyelonephritis associated with upper urinary tract calculi. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.18 Copenhagen, Denmark
5. Fukushima H, Kobayashi M, Kwano K, Morimoto S.. Lower performance status is a risk factor for sepsis of patients with acute pyelonephritis associated with upper urinary tract calculi in the Sepsis-3 era. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.18 Copenhagen, Denmark
6. Yoshida S., Takahara T., Ishii C., Arita Y., Kijima T., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Kihara K., Fujii Y. 935 METastasis Reporting And Data System for Prostate cancer (MET-RADS-P) score of whole-body DWI as a prognostic biomarker for castration-resistant prostate cancer. The 33th Annual Congress of the European Association of Urology 2018.03.19 Copenhagen, Denmark
7. Yajima S, Yoshida S, Takahara T, Arita Y, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Absence of inchworm sign on DWI as a predictive marker for progression in pT1 bladder cancer. The 18th annual meeting of the European Association of Urology 2018.03.19 Copenhagen, Denmark
8. Yajima S, Yoshida S, Arita Y, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Absence of inchworm sign on DWI as a predictive marker for progression in pT1 bladder cancer. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
9. Soma T, Yoshida S, Tanaka H, Uehara S, Yasuda Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . The usefulness of diffusion-weighted MRI in the differential diagnosis of urachal disorders. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
10. Kaneko K, Yoshida S, Takahara T, Sakamoto T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . Diffusion-weighted MRI as an imaging biomarker for histological grade of bladder cancer: Semi-automatic segmentation analysis. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
11. Kaneko K, Yoshida S, Takahara T, Sakamoto T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Diffusion-weighted MRI as an imaging biomarker for histological grade of bladder cancer: Semi-automatic segmentation analysis. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
12. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Characteristics of global Gleason grading for MRI-targeted biopsy in comparison with systematic biopsy and prostatectomy grades.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark

13. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Clinical significance of MRI-targeted biopsy in prediction of adverse pathological and oncological outcome after radical prostatectomy.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
14. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Clinical significance of MRI-targeted biopsy in prediction of adverse pathological and oncological outcome after radical prostatectomy.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
15. Yoshida S, Takahara T, Ishii C, Arita Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . METastasis reporting and data system for prostate cancer score of whole-body DWI as a prognostic biomarker for castration-resistant prostate cancer. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
16. Uehara S, Matsuoka Y, Tanaka H, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y.. Do the Prostate Imaging Reporting and Data System scores reflect oncological outcome? Potential usefulness of scoring criteria-based assessment. . 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
17. Uehara S, Yoshida S, Tanaka H, Yasuda Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. . Prediction of intraoperative urinary collecting system entry in patients with peripheral renal tumors undergoing partial nephrectomy: Usefulness of tumor-centered multiplanar reconstruction.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
18. Uehara S, Yoshida S, Matsuoka Y, Yasuda Y, Kijima T, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y. . Head-mounted display assisted magnetic resonance/ultrasound fusion prostate biopsy system.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
19. Waseda Y, Yoshida S, Takahara T, Arita Y, Sakamoto T, Yajima S, Uehara S, Yasuda Y, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Feasibility of perfusion MRI to predict renal function after nephroureterectomy in upper tract urothelial carcinoma patients.. 欧州泌尿器科学会 (The 33th European Association of Urology annual congress, Copenhagen, Denmark) 2018.03.19 Copenhagen, Denmark
20. Waseda Y, Yoshida S, Takahara T, Arita Y, Sakamoto T, Yajima S, Uehara S, Yasuda Y, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Feasibility of perfusion MRI to predict renal function after nephroureterectomy in upper tract urothelial carcinoma patients. The 33th European Association of Urology annual congress 2018.03.26 Copenhagen, Denmark
21. 吉田 宗一郎. 全身拡散強調画像の歴史と発展. 第 77 回日本医学放射線学会総会、シンポジウム 12 2018.04.15 横浜
22. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y. Clinical significance of MRI-targeted biopsy for the risk stratification of oncological outcome after radical prostatectomy. 第 106 回日本泌尿器科学会総会 2018.04.19 京都
23. Matsuoka Y, Ishioka J, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Saito K, Kihara K, Fujii Y. MRI-based risk assessment for postoperative biochemical recurrence using the Prostate Imaging Reporting and Data System (PI-RADS) scores and capsular contact length. The 114th annual meeting of the American Urological Association 2018.05.18 San Francisco
24. 1 Yasuda Y, Saito K, Soma T, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Kihara K, Fujii Y. The outcome of gasless laparoscopic single-port clampless sutureless partial nephrectomy using three-dimensional head-mounted display. The outcome of gasless laparoscopic single-port clampless sutureless partial nephrectomy using three-dimensional head-mounted display. The 112th annual meeting of the American Urological Association 2018.05.18 San Francisco, USA
25. Yokoyama M, Kawamura N, Uehara S, Yasuda Y, Kijima T, Yoshida S, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y.. Acute kidney injury and intermediate-term renal function after clampless partial nephrectomy.. The 113rd annual meeting of the American Urological Association 2018.05.19 San Francisco, USA

26. Matsuoka Y, Tanaka H, Kimura T, Waseda Y, Uehara S, Yasuda Y, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Saito K, Kihara K, Fujii Y. The role of MRI-targeted biopsy in prediction of adverse pathological and oncological outcome after radical prostatectomy. The 114th annual meeting of the American Urological Association 2018.05.20 San Francisco

[Awards & Honors]

1. Best Poster Presentation, The 33rd Annual Congress of the European Association of Urology, European Association of Urology, 2018.03

Gastrointestinal Surgery

Professor

Yusuke KINUGASA

Associate Professor

Masamichi YASUNO, Mikito INOKUCHI, Yasuaki NAKAJIMA

Junior Associate Professor

Kenro KAWADA, Takuya OKADA

Assistant Professor

Yutaka TOKAIRIN, Takatoshi MATSUYAMA, Akifumi KIKUCHI,
Akihiro HOSHINO, Shinichi YAMAUCHI, Masatoshi NAKAGAWA,
Hironobu BABA

Project Assistant Professor

Tairo RYOTOKUJI, Kenta KOBAYASHI, Yuichiro KUME

Hospital Staff

Ryota SEKI, Fumi SHIGEYARA

Graduate Student

Yasunori SOMENO, Masafumi OKUNO, Yutaka NAKAJIMA,
Taichi OGO, Michiyo TOKURA, Marie HANAOKA,
Toshiro TANIOKA, Tomoki ABURATANI, Chiharu TOMII,
Toshihiro MATSUI, Keisuke OKUNO, Kentaro GOKITA,
Yuriko MATSUMIYA, Fukuichiro ORITA, Yudai KAWAMURA,
Megumi SASAKI, Tomiyuki MIURA, Kazuya YAMAGUCHI,
Emi KANEMOTO, Ayumi TAKAOKA, Yasuko AOYAGI,
Yuya UMEBAYASHI, Toshifumi SAITO, Ryosuke FUKUYO,
Yudai YAMAMOTO, Andres MORA

(1) Research

- 1) Development of esophageal surgery.
- 2) Development of gastric surgery.
- 3) Development of colorectal surgery.

(2) Education

The history of the department started as both the Department of Esophageal and General Surgery and the Department of Surgical Oncology of TMDU, and many surgeons and researchers in various specialties have gathered and have been keeping a high level of activities. Our main purposes of education are to make the post-graduate physicians grown up to excellent surgeons and to contribute in development of medical/surgical sciences. Surgeons with high-level medical knowledge and techniques are expected to grow up in this department. Moreover, making surgeons with matured humanity is one of the purposes. The department has a peaceful atmosphere and stands for active work in solving difficult problems.

(3) Clinical Performances

Main clinical services are diagnosis and treatment for esophageal, gastric and colorectal diseases. Post-graduate students learn and study general surgery and sub-specialty, e.g. esophageal surgery, gastric surgery and colorectal surgery. The territory of clinics is wide and the department provides a full spectrum of standard and special technologies such as minimally invasive surgery and extended radical surgery for malignancies.

(4) Publications

[Original Articles]

1. Tomohiro Yamaguchi, Yusuke Kinugasa. Safety and feasibility of robotic-assisted laparoscopic lateral lymph node dissection *Annals of Laparoscopic and Endoscopic Surgery*. 2018.01; 3(5);
2. Hamaguchi T, Shimada Y, Mizusawa J, Kinugasa Y, Kanemitsu Y, Ohue M, Fujii S, Takiguchi N, Yatsuoka T, Takii Y, Ojima H, Masuko H, Kubo Y, Mishima H, Yamaguchi T, Bando H, Sato T, Kato T, Nakamura K, Fukuda H, Moriya Y. Capecitabine versus S-1 as adjuvant chemotherapy for patients with stage III colorectal cancer (JCOG0910): an open-label, non-inferiority, randomised, phase 3, multicentre trial. *Lancet Gastroenterol Hepatol*. 2018.01; 3(1); 47-56
3. Numata M, Yamaguchi T, Kinugasa Y, Shiomi A, Kagawa H, Yamakawa Y, Furuatni A, Manabe S, Yamaoka Y, Torii K, Kato S. Safety and feasibility of laparoscopic reoperation for treatment of anastomotic leakage after laparoscopic colorectal cancer surgery. *Asian J Endosc Surg*. 2018.01; [Epub ahead of print]
4. Mora A. · Nakajima Y. · Okada T. · Tokairin Y. · Kawada K. · Kawano T. . Comparative Study of Predictive Mortality Scores in Esophagectomy with Three-Field Lymph Node Dissection in Patients with Esophageal Cancer *Digestive Surgery*. 2018.01; Epub ahead;
5. Yamauchi S., Takaoka A., Seki R., Matsumiya Y., Orita F., Sasaki M., Miura T., Kikuchi A., Matsuyama T., Ishiguro M., Ishikawa T., Uetake H., Yasuno M., Kinugasa Y., Sugihara K.. Indication of Extended Lateral Lymph Node Dissection for Patients with Lower Rectal Cancer *ANNALS OF SURGICAL ONCOLOGY*. 2018.02; 25; S164
6. Yamada I, Hikishima K, Yoshino N, Sakamoto J, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using q-space imaging; correlation with histopathologic findings. *J Magn Reson Imaging*. 2018.03; 48(4); 1059-1068
7. Yuya Sato, Kazuyuki Kojima, Mikito Inokuchi, Keiji Kato, Hirofumi Sugita, Sho Otsuki, Kenichi Sugihara. Intraoperative Pancreatic Injury Gives Rise to Severe Postoperative Pancreatic Fistula: Results of a Review of Unedited Videos of the Laparoscopic Surgical Procedures *International Surgery*. 2018.03; Published online ;
8. Kenro Kawada, Taro Sugimoto, Ryuhei Okada, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuuichiro Kume, Andres Mora, Tairo Ryotokuji, Takuta Okada, Akihiro Hoshino, Yutaka Tokairin, Yausaki Nakajima, Yusuke Kiyokawa, Fuminori Nomura, Yosuke Ariizumi, Shohei Tomii, Takashi Ito, Takahiro Asakage, Yusuke Kinugasa, Tatsuyuki Kawano. A case of simultaneous triple primary cancers of the hypopharynx, esophagus and stomach which were dissected by endoscopic laryngo-pharyngeal surgery combined with endoscopic submucosal dissection *Open Journal of Gastroenterology*. 2018.03; 8(3); 94-102
9. Ling Chang, Akihiro Hoshino, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Takuya Okada, Tatsuyuki Kawano, Yusuke Kinugasa. Flexible spectral imaging color enhancement markedly reduces the iodine concentration required for the endoscopic diagnosis of superficial esophageal cancer *Journal of Medical and Dental Sciences*. 2018.03; 65(1); 27-33
10. Yuichiro Kume, Yasuaki Nakajima, Takuya Okada, Akihiro Hoshino, Yutaka Tokairin, Kenro Kawada, Yusuke Kinugasa. A comparative analysis between pegfilgrastim and lenograstim administered to patients receiving cytotoxic chemotherapy for squamous cell carcinoma of the esophagus. *Journal of Medical and Dental Sciences*. 2018.04; 65(1); 19-26
11. Yuichiro Kume, Kenro Kawada, Takuya Okada, Akihiro Hoshino, Yutaka Tokairin, Yasuaki Nakajima, Takashi Ito, Yusuke Kinugasa, Tatsuyuki Kawano. The macroscopic and histological effects of argon plasma coagulation followed by subepithelial ablation on early esophageal squamous cell carcinoma using

- magnifying endoscopy with blue laser imaging *Journal of Medical and Dental Sciences*. 2018.04; 65(1); 1-8
12. Keisuke Okuno, Masatoshi Nakagawa, Kazuyuki Kojima, Emi Kanemoto, Kentaro Gokita, Toshiro Tanioaka, Mikito Inokuchi. Long-term functional outcomes of Roux-en-Y versus Billroth I reconstructions after laparoscopic distal gastrectomy for gastric cancer: a propensity-score matching analysis. *Surg Endosc*. 2018.04;
13. Tomoki Yamano, Shinichi Yamauchi, Kiyoshi Tsukamoto, Masafumi Noda, Masayoshi Kobayashi, Michiko Hamanaka, Akihito Babaya, Kei Kimura, Chihyon Son, Ayako Imada, Shino Tanaka, Masataka Ikeda, Naohiro Tomita, Kenichi Sugihara, . Evaluation of appropriate follow-up after curative surgery for patients with colorectal cancer using time to recurrence and survival after recurrence: a retrospective multicenter study. *Oncotarget*. 2018.05; 9(39); 25474-25490
14. Tomohiro Yamaguchi, Yusuke Kinugasa, Akio Shiomi, Hiroyasu Kagawa, Yushi Yamakawa, Akinobu Furutani, Shoichi Manabe, Yusuke Yamaoka, Hitoshi Hino. Oncological outcomes of robotic-assisted laparoscopic versus open lateral lymph node dissection for locally advanced low rectal cancer *Surgical Endoscopy*. 2018.05; published online;
15. Takuya Okada, Kenro Kawada, Taro Sugimoto, Takashi Ito, Kazuya Yamaguchi, Yudai Kawamura, Masafumi Okuda, Yuichiro Kume, Tairo Ryotokuji, Akihiro Hoshino, Yutaka Tokairin & Yasuaki Nakajima. Asymptomatic marginal zone lymphoma of mucosa-associated lymphoid tissue in the hypopharynx, detected with esophagogastroduodenoscopy *Acta Oto-Laryngologica Case Reports*. 2018.05; 3(1); 19-23
16. Tokairin Y, Nakajima Y, Kawada K, Hoshino A, Okada T, Ryotokuji T, Okuda M, Kume Y, Kawamura Y, Yamaguchi K, Nagai K, Akita K, Kinugasa Y. Histological study of the thin membranous structure made of dense connective tissue around the esophagus in the upper mediastinum. *Esophagus : official journal of the Japan Esophageal Society*. 2018.06; 15(4); 272-280
17. Chu Matsuda, Megumi Ishiguro, Satoshi Teramukai, Yoshiki Kajiwar, Shoichi Fujiie, Yusuke Kinugasa, Yoshihiko Nakamoto, Masanori Kotake, Yoshiyuki Sakamoto, Kiyotaka Kurachi, Atsuyuki Maeda, Koji Komori, Naohiro Tomita, Yasuhiro Shimada, Keiichi Takahashi, Kenjiro Kotake, Masahiko Watanabe, Hidetaka Mochizuki, Yoko Nakagawa, Kenichi Sugihara on behalf of the SAKURA Study Group. A randomised-controlled trial of 1-year adjuvant chemotherapy with oral tegafur-uracil versus surgery alone in stage II colon cancer: SACURA trial *Eur J Cancer*. 2018.06; 96; 54-63
18. Maki Kobayashi; Hiroshi Kawachi; Samara Pasternak; Carlos Delgado; Pablo Pinto; Takashi Ito; Stanko Karelovic; Hernan Carrasco; Koji Tanaka; Takuya Okada; Tomoyuki Odagaki; Alejandro J. Zárate; Alejandra Ponce; Udo Kronberg; Francisco López-Köstner; Masahiro Tsubaki; Tatsuyuki Kawano; Yoshinobu Eishi. Histopathologic study from a colorectal cancer screening in Chile *European Journal of Cancer Prevention*. 2018.06; Epub ahead;
19. Yusuke Yamaoka, Tomohiro Yamaguchi, Yusuke Kinugasa, Akio Shiomi, Hiroyasu Kagawa, Yushi Yamakawa, Akinobu Furutani, Shoichi Manabe, Kakeru Torii, Kohei Koido, Keita Mori. Mesorectal fat area as a useful predictor of the difficulty of robotic-assisted laparoscopic total mesorectal excision for rectal cancer *Surgical Endoscopy*. 2018.07; published online;
20. Yohei Yabuuchi, Kenichiro Imai, Kinichi Hotta, Sayo Ito, Yoshihiro Kishida, Tomohiro Yamaguchi, Akio Shiomi, Yusuke Kinugasa, Masao Yoshida, Masaki Tanaka, Noboru Kawata, Naomi Kakushima, Kohei Takizawa, Hirotoshi Ishiwatari, Hiroyuki Matsubayashi, Hiroyuki Ono. Higher incidence of metachronous advanced neoplasia in patients with synchronous advanced neoplasia and left-sided colorectal resection for colorectal cancer *Gastrointestinal Endoscopy*. 2018.08; 88(2); 348-359
21. Kobayashi M, Kawachi H, Hurtado C, Wielandt AM, Ponce A, Karelovic S, Pasternak S, Delgado C, Pinto P, Carrasco H, Ito T, Okada T, Tanaka K, Odagaki T, Zárate AJ, Kronberg U, López-Köstner F, Tsubaki M, Kawano T, Eishi Y.. A Pilot Trial to Quantify Plasma Exosomes in Colorectal Cancer Screening from the International Collaborative Study between Chile and Japan *Digestion*. 2018.08; 98(4); 270-274
22. Toshihiro Matsui, Takuya Okada, Kenro Kawada, Masahumi Okuda, Taichi Ogo, Yutaka Nakajima, Yuichiro Kume, Tairo Ryotokuji, Akihiro Hoshino, Yutaka Tokairin, Yasuyuki Michi, Hiroyuki Harada, Yasuaki Nakajima, Tatsuyuki Kawano. Detection of second primary malignancies of the esophagus and hypopharynx in oral squamous cell carcinoma patients *Laryngoscope Investigative Otolaryngology*. 2018.08; Epub ahead;

23. Masatoshi Takeuchi, Hirofumi Kawakubo, Yuta Abe, Akishige Kanazawa, Kazuhisa Ehara, Yusuke Kinugasa, Takahiro Kinoshita, Akinari Nomura, Yuko Kitagawa. Assessment of the Safety of the New Hybrid Pencil Type Energy (NP) Device Used Close to the Recurrent Laryngeal Nerve in a Porcine Model: Comparison With a Conventional Electrosurgical Knife. *Surgical Innovation (SRI)*. 2018.12; Epub ahead;
24. Tomohiro Yamaguchi, Yusuke Kinugasa, Akio Shiomi, Hiroyasu Kagawa, Yushi Yamakawa, Akinobu Furuatni, Shoichi Manabe, Yusuke Yamaoka, Hitoshi Hino. Short- and long-term outcomes of robotic-assisted laparoscopic surgery for rectal cancer: results of a single high-volume center in Japan *International Journal of Colorectal Disease*. 2018.12; 33(12); 1755-1762
25. Inokuhi M,Otsuki S,Ogawa N,Tanioka T,Okuno K,Gokita K,Kawano T,Kojima K. Postoperative Complications of Laparoscopic Total Gastrectomy versus Open Total Gastrectomy for Gastric Cancer in a Meta-Analysis of High-Quality Case-Control Studies. *Gastroenterology Res Pract*.
26. Nishikawaji t,Akiyama Y,Shimada s,Kojima K,Kawano T,Eishi Y,Yusa Y,Tanaka S. Onco-genic roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget*.
27. Higuchi K,Inokuchi M,Takagi Y,Ishikawa T,Otsuki S,Uetake H,Kojima K,Kawano T. Cadherin 5 expression correlates with poor survival in human gastric cancer. *J Clin Pathol*.
28. Nakagawa M, Kojima K,Inokuchi M,Kato K,Sugita H,Otsuki S,Sugihara K. Identification of frequency, severity and risk factors of complications after open gastrectomy: Retrospective analysis prospectively collected database using the Clavien-Dindo classification. *J Med Dent Sci*.
29. Inokuchi M, Otsuki S, Murase H, Kojima K, Kawano T. Feasibility of laparoscopy-assisted gastrectomy for patients with poor physical status: A propensity-score matching study. *Int J Surg*.
30. Akiyama Y, Koda Y, Byeon SJ, Shimada S, Nishikawaji T, Sakamoto A, Chen Y, Kojima K, Kawano T, Eishi Y, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget*.
31. Kobayashi k,Inokuchi M, Takagi Y,Otsuki S,Fujimori Y,Sato Y,Yanaka Y,Higuchi K,Aburatani T,Tomii C,Uketake H,Kojima K,Kawano T. Prognostic significance of PAK4 expression in gastric cancer. *J Clin Pathol*.

[Books etc]

1. Hiroyasu Kagawa, Yusuke Kinugasa. *Surgical Treatment of Colorectal Cancer*. Springer, Singapore, 2018.05 (ISBN : 978-981-10-5142-5)

[Conference Activities & Talks]

1. Yusuke Ogi,Tomohiro Yamaguchi, Yusuke Kinugasa, Akio Shiomi, Hiroyasu Kagawa, Yushi Yamakawa, Akinobu Furutani, Yusuke Yamaoka, Shoichi Manabe, Hitoshi Hino, Yoshinobu Nagasawa, Takuya Suzuki, Kakeru Torii, Shunichiro Kato, Kohei Koido, Shigeyuki Murayama. Effect and safety of proton beam therapy for locally recurrent rectal cancer.. 2018 Gastrointestinal Cancers Symposium (ASCO) 2018.01.20 San Francisco(USA)
2. Akinobu Furutani, Tomohiro Yamaguchi, Yusuke Kinugasa, Akio Shiomi, Hiroyasu Kagawa, Yushi Yamakawa, Shoichi Manabe, Yusuke Yamaoka, Yoshinobu Nagasawa, Hitoshi Hino, Shunichiro Kato, Takuya Suzuki, Kakeru Torii, Kohei Koido. Prognostic factors in patients who received surgery for colorectal cancer with peritoneal metastasis.. 2018 Gastrointestinal Cancers Symposium (ASCO) 2018.01.20 San Francisco(USA)
3. Masatoshi Nakagawa, Emi kanemoto, Kentaro Gokita, Keisuke Okuno, Toshiro Tanioka, Mikito Inokuchi, Kazuyuki Kojima. Double tract reconstruction for laparoscopic proximal gastrectomy in our institute - procedure and short- and middle-term results-. 13th Japan-China-Korea Laparoscopic Gastrectomy Joint Seminar 2018.02.10 Beppu
4. Toshiro Tanioka, Emi kanemoto, Keisuke Okuno, Kentaro Gokita, Masatoshi Nakagawa, Mikito Inokuchi, Kazuyuki Kojima. Intracorporeal esophagojejunostomy using circular stapler after laparoscopic total gastrectomy. 90th Annual Meeting of the Japanese Gastric Cancer Association 2018.03.08 Yokohama

5. Masatoshi Nakagawa, Kazuyuki Kojima, Mikito Inokuchi, Toshiro Tanioka, Kentaro Gokita, Keisuke Okuno. Short-term and long-term outcomes after gastrectomy for elderly patients. 90th Annual Meeting of the Japanese Gastric Cancer Association 2018.03.08 Yokohama
6. Mikito Inokuchi, Toshiro Tanioka, Masatoshi Nakagawa, Keisuke Okuno, Kentaro Gokita, Emi kanemoto, Kazuyuki Kojima. Long- and short-term outcomes of laparoscopic gastrectomy in clinical advanced gastric cancer. 90th Annual Meeting of the Japanese Gastric Cancer Association 2018.03.09 Yokohama
7. Shinichi Yamauchi, Ayumi Takaoka, Yuriko Matsumiya, Ryota Seki, Fukuichiro Orita, Megumi Sasaki, Tomiyuki Miura, Akifumi Kikuchi, Takatoshi Matsuyama, Megumi Ishiguro, Toshiaki Ishikawa, Masamichi Yasuno, Hiroyuki Uetake, Yusuke Kinugasa, Kenichi Sugihara. Indication of Extended Lateral Lymph Node Dissection for Patients with Lower Rectal Cancer. SSO 2018 Annual Cancer Symposium 2018.03.23 Chicago, US
8. Yusuke Kinugasa. The surgical technique and outcome of robotic rectal cancer surgery. International Association of Surgeons, Gastroenterologists and Oncologists (IASGO2018) 2018.04.04 Tokyo
9. Tomiyuki Miura, Shinichi Yamauchi, Takatoshi Matsuyama, Megumi Ishiguro, Toshiaki Ishikawa, Yasuaki Nakajima, Kazuyuki Kojima, Masamichi Yasuno, Hiroyuki Uetake, Yusuke Kinugasa. A case of Incarcerated Internal Hernia through a Defect of the Falciform Ligament. International Association of Surgeons, Gastroenterologists and Oncologists (IASGO2018) 2018.04.04 Tokyo
10. Shinichi Yamauchi, Takatoshi Matsuyama, Ayumi Takaoka, Yuriko Matsumiya, Ryota Seki, Fukuichiro Orita, Megumi Sasaki, Tomiyuki Miura, Akifumi Kikuchi, Megumi Ishiguro, Toshiaki Ishikawa, Hiroyuki Uetake, Masamichi Yasuno, Yasuaki Nakajima, Kazuyuki Kojima, Yusuke Kinugasa. Laparoscopic and open surgery for ulcerative colitis. International Association of Surgeons, Gastroenterologists and Oncologists (IASGO2018) 2018.04.12 Tokyo
11. Takatoshi Matsuyama, Shinichi Yamauchi, Akifumi Kikuchi, Kazuyuki Kojima, Yasuaki Nakajima, Masamichi Yasuno, Yusuke Kinugasa. Initial experience of laparoscopic total colectomy with transanal minimally invasive proctectomy for ulcerative colitis. 16th World Congress of Endoscopic Surgery 2018.04.12 Seattle
12. Yusuke Kinugasa. Robotic Lateral Pelvic Lymph Node Dissection : How To Do It Robotically. 16th World Congress of Endoscopic Surgery (SAGES & CAGS 2018) 2018.04.13 Seattle (USA)
13. Takatoshi Matsuyama, Raju Kandimalla, Xuan Wang, Toshiaki Ishikawa, Naoki Uetake, Yasuhide Yamada, Masamichi Yasuno, Yusuke Kinugasa, Hiroyuki Uetake, Ajay Goel. A mesenchymal-associated transcriptomic signature has a prognostic and predictive potential in stage II and III colorectal cancer patients. American Association for Cancer Research (AACR 2018) 2018.04.16 Chicago (USA)
14. Yasuaki Nakajima. Kenro Kawada, Yutaka Tokairin, Akihiro Hoshino, Takuya Okada, Tairo Ryotokuji, Masafumi Okuda, Yuichiro Kume, Yudai Kawamura, Kazuya Yamaguchi, Kazuyuki Kojima, Yusuke Kinugasa. Flexible Gastric Tube: A Noble Method of Gastric Tube Reconstruction without Anastomotic Leakage. ISDE 2018(The International Society for Diseases of the Esophagus) 2018.09.17 Vienna, Austria
15. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Akihiro Hoshino, Takuya Okada, Tairo Ryotokuji, Masafumi Okuda, Yuichiro Kume, Yudai Kawamura, Kazuya Yamaguchi, Kagami Nagai, Keiichi Akita, Yusuke Kinugasa. The Method and the Short Outcome of Mediastinal Lymph Nodes Dissection for Esophageal Cancer Using a Trans-Bicervical and Transhiatal Approach under the Pneumomediastinum. ISDE2018 (The International Society for Diseases of the Esophagus) 2018.09.17 Vienna, Austria
16. Akihiro Hoshino, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Takuya Okada, Tairo Ryotokuji, Yuichiro Kume, Kazuya Yamaguchi, Yusuke Kinugasa. A Method for Totally Mediastinoscopic Transhiatal Middle and Lower Mediastinal Lymph Node Dissection for Esophageal Cancer. ISDE2018 (The International Society for Diseases of the Esophagus) 2018.09.17 Vienna, Austria
17. Ymaguchi K., Kawada K., Nakajima Y., Tokairin T., Hoshino A., Okada T., Ryotokuji T., Kume Y., Ito T.. Planned semi-circular endoscopic submucosal dissection for widespread superficial esophageal cancer. UEG Week 2018(United European Gastroenterology) 2018.10.24 Vienna, Austria
18. Kawada K., Nakajima Y., Tokairin Y., Hoshino A., Okada T., Ryotokuji T., Kume Y., Mora A., Yamaguchi K., Ito T.. The mid-term outcomes of endoscopic treatment for superficial cervical esophageal cancer. UEG Week 2018(United European Gastroenterology) 2018.10.24 Vienna, Austria

19. Yusuke Kinugasa, Takatoshi Matsuyama, Shinichi Ymauchi. Robotic surgery for low rectal cancer. JDDW2018 (Japan Digestive Disease Week) 2018.11.02 Kobe
20. Yusuke Kinugasa, Takatoshi Matsuyama, Akifumi Kikuchi, Shinichi Ymauchi, Hironobu Baba, Ayumi Takaoka. The surgical technique and outcome of robotic rectal cancer surgery. The 73rd Annual Meeting of Japan Society of Coloproctology 2018.11.09 Tokyo
21. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairou Ryoutokuji, Takuya Okada, Yutaka Miyawaki, Youichi Kumagai, Kagami Nagai, Tatsuyuki Kawano. . Efficacy of endoscopy for evaluating esophago-gastric anastomosis on post-esophagectomy day 1. . 14th World Congress of the International Society for Diseases of the Esophagus

Thoracic Surgery

Professor Kenichi Okubo
Junior Associate Professor Hironori Ishibashi
Assistant Professor Masashi Kobayashi
Hospital assistant professor Chihiro Takasaki
Hospital assistant professor Sachiko Imai
Graduate Student Akiko Sugawara
Graduate Student Ken Takahashi
Graduate Student Katsutoshi Seto
Graduate Student Ryo Wakejima
Graduate Student Syunichi Baba
Graduate Student Yasuhiro Nakashima
Graduate Student Ayaka Asakawa
Graduate Student Yuya Ishikawa

(1) Outline

Department of Thoracic Surgery deal with clinical management, basic and clinical research, and education of thoracic surgery, which includes surgical diagnosis and treatment of respiratory diseases.

(2) Research

- Minimally invasive surgery for lung cancer
- Multimodal treatments for thoracic malignancies
- Surgery for metastatic lung tumors
- Clinico-pathological studies on lung cancer

(3) Education

Department of Thoracic Surgery has a mission to educate medical post-graduates for expert thoracic surgeons. Thoracic surgeon requires the Board of Surgery and the Board of Thoracic Surgery to perform clinical cares as a specialist. We provide clinical specialty course for thoracic surgery and graduate course for thoracic surgery, and support to obtain the boards.

(4) Clinical Services & Other Works

Out-patient Clinic: Tuesday, Thursday, Friday
Operative Day: Monday, Wednesday, Thursday, Friday
Clinical Conference: Monday
Chest Conference : Monday
Clinico-pathological Conference: Wednesday
Medical Round: every morning
Professor's Round: Tuesday
Journal Club: Tuesday (every other week)

Mortality & Morbidity Conference: Tuesday (every other week)

Lab Meeting: Tuesday (monthly)

Scientific Meeting: Japan Surgical Society, Japanese Association for Chest Surgery, Japanese Association for Thoracic Surgery, Japan Lung Cancer Society, Japan Society for Respiratory Endoscopy

(5) Clinical Performances

Thoracic Surgery deal with surgical treatment for lung, mediastinum, pleura and chest wall. We provide high-grade medical care as a university hospital. We offer less invasive surgery for early-stage lung cancers or benign diseases, and multimodality treatment for locally advanced thoracic malignancies.

(6) Publications

[Original Articles]

1. Sachiko Imai, Masashi Kobayashi, Chihiro Takasaki, Hironori Ishibashi, Kenichi Okubo. High expression of P-cadherin is significantly associated with poor prognosis in patients with non-small-cell lung cancer LUNGANCER. 2018.04; 118; 13-19
2. Kentaro Inamura, Yasuyuki Shigematsu, Hironori Ninomiya, Yasuhiro Nakashima, Maki Kobayashi, Haruyuki Saito, Katsuhiro Takahashi, Etsuko Futaya, Sakae Okumura, Yuichi Ishikawa and Hiroaki Kanda. CSF1R-Expressing Tumor-Associated Macrophages, Smoking and Survival in Lung Adenocarcinoma: Analyses Using Quantitative Phosphor-Integrated Dot Staining Cancers. 2018.08; 10(8); 252
3. Honda T, Sakashita H, Masai K, Totsuka H, Motoi N, Kobayashi M, Akashi T, Mimaki S, Tsuchihara K, Chiku S, Shiraishi K, Shimada Y, Otsuka A, Kanai Y, Okubo K, Watanabe S, Tsuta K, Inase N, Kohno T. Deleterious Pulmonary Surfactant System Gene Mutations in Lung Adenocarcinomas Associated With Usual Interstitial Pneumonia JCO Precision Oncology [published online August 17, 2018] . 2018.08;
4. Katsutoshi Seto, Hiroaki Kuroda, Tatsuya Yoshida, Shozo Sakata, Tetsuya Mizuno, Noriaki Sakakura, Toyooki Hida, Yasushi Yatabe, Yukinori Sakao. Higher frequency of occult lymph node metastasis in clinical N0 pulmonary adenocarcinoma with ALK rearrangement Cancer Management and Research. 2018.12; 10; 2117-2124

[Others]

1. Excision of thoracic vertebral chondrosarcoma after spinal decompression, 2018.04
Asian Cardiovascular & Thoracic Annals 2018, Vol. 26(4) 311-313
Ayaka Asakawa, Hironori Ishibashi, Masashi Kobayashi, Tsuyoshi Hachimaru, Hirokuni Arai, Kenichi Okubo
2. Endobronchial Granular Tumor Excision With Bronchial Resection Inclusive of Second Carinoplasty, 2018.05
The Annals of Thoracic Surgery 2018 May, Vol. 105(5)193-194
Hironori Ishibashi, Syunichi Baba, Yasuhiro Nakashima, Chihiro Takasaki, Masashi Kobayashi, Kenichi Okubo
3. Chylothorax post thoracoscopic surgery for an anterior mediastinal tumor, 2018.06
General Thoracic and Cardiovascular Surgery, 2018, Vol. 66(6)372-375
Hironori Ishibashi, Yuya Ishikawa, Ayaka Asakawa, Sachiko Imai, Masashi Kobayashi, Kenichi Okubo
4. Successful Excision of Endobronchial Cellular Schwannoma With Right Lower Sleeve Lobectomy, 2018.09
The Annals of Thoracic Surgery (2018 E-pub)
Hironori Ishibashi, Ryo Wakejima, Chihiro Takasaki, Kenichi Okubo
5. Epithelial-myoepithelial carcinoma of the lung: a case report, 2018.12
Surg Case Rep. 2018 ;4:74
Yasuhiro Nakashima, Riichiro Morita, Akiko Ui, Kuniko Iihara, Takuya Yazawa

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara

Visiting Professor Makoto Arai

Visiting Professor Masato Hasegawa

Visiting Professor Haruo Okado

Graduate Student Riichi Okuda, Yuna Takahashi, Maki Nakasone, Takahiro Mitsui, Harumi Tabata, Takuya Yagi (April~), Eiji Katada (April~), Yuki Mizuoka (April~).

(1) Research

[Takahiko Hara] We attempt to elucidate how tissue stem cells (hematopoietic stem cells, skeletal muscle stem cells, etc.) are developed in embryos and maintained in adults by utilizing *in vitro* differentiation systems of ES/iPS cells and conditional KO mouse strains. In addition, we advance the molecular biology of CXCL14, which is involved in obesity-induced diabetes, carcinogenesis, feeding behavior, etc.

[Makoto Arai] Our research focuses on unraveling the pathophysiology of mental illnesses using molecular biology tools. Our ultimate goal is to identify new disease mechanisms, leading to the development of novel and more efficacious therapies. We perform genetic association studies, as well as metabolomics studies using samples from patients with mental disorders. Any abnormalities identified from patient samples are investigated further, using *in vitro* and *in vivo* systems, such as, cell culture assays to highlight functional alterations and behavioral studies in gene knockout mouse models.

[Masato Hasegawa] We investigate the molecular pathogenesis and progression of neurodegenerative diseases including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. We use biochemistry, immunohistochemistry and molecular biology in all our work of *in vitro*, cellular and animal models to find effective ways for clinical therapy.

[Haruo Okado] To discover the fundamental cause of various nervous diseases, e.g., brain tumors, brain malformations, and neurodevelopmental disorders, we will study the molecular mechanisms for the regulation of neural development in the cerebral cortex using gene-targeted mice, primary cultures, viral vectors, *in-utero*

electroporation, real-time imaging of slice culture, immunohistochemistry, and transcription analysis.

(2) Education

We will educate students for the purpose that they could investigate molecular mechanisms of life-threatening diseases such as cancer, diabetes, schizophrenia, amyotrophic lateral sclerosis, and brain malformations. Trained students will eventually help us to develop novel therapeutic strategies against them. In addition, they must learn the importance of good animal models (including genetically engineered mice), which faithfully reproduce symptom and progression of the diseases.

(3) Publications

[Original Articles]

1. K. Kitajima, M. Kanokoda, M. Nakajima, and T. Hara. Domain-specific biological functions of the transcription factor Gata2 on hematopoietic differentiation of mouse embryonic stem cells. *Genes Cells*, 23: 753-766, 2018.
2. K. Tanaka, N. Ikeda, K. Miyashita, H. Nuriya, and T. Hara. DEAD box protein DDX1 promotes colorectal tumorigenesis through transcriptional activation of the *LGR5* gene. *Cancer Sci.*, 109: 2479-2489, 2018.
3. K. Miyashita, K. Kitajima, S. Goyama, T. Kitamura, and T. Hara. Overexpression of Lhx2 suppresses proliferation of human T cell acute lymphoblastic leukemia-derived cells, partly by reducing LMO2 protein levels. *Biochem. Biophys. Res. Commun.*, 495: 2310-2316, 2018.
4. S. Yamasaki, S. Ando, M. Richards, S. L. Hatch, S. Koike, S. Fujikawa, S. Kanata, K. Endo, Y. Morimoto, M. Arai, H. Okado, S. Usami, T. A. Furukawa, M. Hiraiwa-Hasegawa, K. Kasai, and A. Nishida. Maternal diabetes in early pregnancy, and psychotic experiences and depressive symptoms in 10-year-old offspring: A population-based birth cohort study. *Schizophr. Res.*, S0920-9964(18): 30704-30707, 2018.
5. M. Itokawa, M. Miyashita, M. Arai, T. Dan, K. Takahashi, T. Tokunaga, K. Ishimoto, K. Toriumi, T. Ichikawa, Y. Horiuchi, A. Kobori, S. Usami, T. Yoshikawa, N. Amano, S. Washizuka, Y. Okazaki, and T. Miyata. Pyridoxamine, a novel treatment for schizophrenia with enhanced carbonyl stress. *Psychiatry Clin. Neurosci.*, 72(1): 35-44, 2018.

6. T. Nonaka, M. Masuda-Suzukake, M. Hosokawa, A. Shimozaawa, S. Hirai, H. Okado, and M. Hasegawa. C9ORF72 dipeptide repeat poly-GA inclusions promote intracellular aggregation of phosphorylated TDP-43. *Hum. Mol. Genet.*, 27(15), 2658-2670, 2018.
7. T. Terada, G. Suzuki, T. Nonaka, F. Kametani, A. Tamaoka, and M. Hasegawa. The effect of truncation on prion-like properties of α -synuclein. *J. Biol. Chem.*, 293: 13910-13920, 2018.
8. A. Tarutani, T. Arai, S. Murayama, S.I. Hisanaga, M. Hasegawa. Potent prion-like behaviors of pathogenic α -synuclein and evaluation of inactivation methods. *Acta Neuropathol. Commun.*, 6: 29, 2018.
9. S. Hirai, K. Hotta, and H. Okado. Developmental roles and evolutionary significance of AMPA-type glutamate receptors. *BioEssays*, 40: e1800028, 2018.
10. H. Okado H. Regulation of brain development and brain function by the transcriptional repressor RP58. *Brain Res.*, doi: 10.1016/j.brainres.2018.02.042., 2018.
11. K. Inoue, S. Miyachi, K. Nishi, H. Okado, Y. Nagai, T. Minamimoto, A. Nambu, and M. Takada. Recruitment of calbindin into nigral dopamine neurons protects against drug-induced parkinsonism. *Movement Disorders*, doi: 10.1002/mds.107., 2018.
12. H. Toda, K. Kawasaki, S. Sato, M. Horie, K. Nakahara, A. K. Bepari, H. Sawahata, T. Suzuki, H. Okado, H. Takebayashi, and I. Hasegawa. Locally induced neuronal synchrony precisely propagates to specific cortical areas without rhythm distortion. *Sci. Rep.*, 8: 7678, 2018.

[Review Articles]

1. R. Mizutani, R. Saiga, A. Takeuchi, K. Uesugi, Y. Terada, Y. Suzuki, V. D. Andrade, F. D. Carlo, S. Takekoshi, C. Inomoto, N. Nakamura, I. Kushima, S. Iritani, N. Ozaki, S. Ide, K. Ikeda, K. Oshima, M. Itokawa, and M. Arai. Three-dimensional alteration of neurons in schizophrenia. *Neurons and Cognition (q-bio.NC); Biological Physics (physics.bio-ph)*, arXiv:1804.00404 [q-bio.NC], 2018.
2. F. Kametani and M. Hasegawa. Reconsideration of Amyloid Hypothesis and Tau Hypothesis in Alzheimer's Disease. *Front. Neurosci.*, 12: 25, 2018.
3. T. Nonaka, M. Masuda-Suzukake, and M. Hasegawa. Molecular mechanisms of the co-deposition of multiple pathological proteins in neurodegenerative diseases. *Neuropathology*, 38(1): 64-71, 2018.

[Books]

[Conference Activities & Talks]

1. K. Suzuki, K. Toriumi, Y. Horiuchi, M. Miyashita, M. Itokawa, and M. Arai. Behavioral phenotype of glyoxalase 1 knockout mice. Society for Neuroscience 2018 Annual Meeting, 2018.11.6, San Diego.
2. M. Arai, M. Miyashita, K. Toriumi, Y. Horiuchi, A. Kobori, and M. Itokawa. Pyridoxamine, a novel treatment for negative symptoms of schizophrenia. Society for Neuroscience 2018 Annual Meeting, 2018.11.5, San Diego.
3. M. Arai, M. Miyashita, T. Dan, K. Toriumi, Y. Horiuchi, K. Suzuki, T. Miyata, and M. Itokawa. Pyridoxamine, a novel treatment for negative symptoms of schizophrenia. 13th International Symposium on The Maillard reaction, 2018.9.11, Montreal.
4. K. Toriumi, M. Miyashita, Y. Horiuchi, A. Kobori, I. Nohara, Y. Shimada, M. Hama, N. Obata, M. Itokawa, and M. Arai. Effect of vitamin B6 deficiency on mouse behavior and monoaminergic system. 13th International Symposium on The Maillard reaction, 2018.9.11, Montreal.
5. M. Hasegawa. Prion-like propagation of pathological tau in neurodegenerative diseases. ICN2018 Symposium 12, Protein Propagation in Neurodegeneration, 2018. 9.24, Tokyo.
6. M. Hasegawa. α -Synuclein Propagation in Parkinson's Disease and Multiple System Atrophy. Basic Science Summer School MDS/Education/Conferences & Courses. 2018. 8. 3. Osaka.
7. M. Hasegawa. α Synuclein in Parkinson's disease and related disorders. WCP2018 KYOTO (18th World Congress of Basic and Clinical Pharmacology), 2018. 7. 5. Kyoto.

Clinical Anatomy

Professor : Keiichi AKITA

Associate Professor : Akimoto NIMURA (Department of Functional Joint Anatomy)

Junior Associate Professor : Kumiko YAMAGUCHI (Department of Professional Development in Health Science)

Assistant Professor : Masayo HARADA, Hisayo NASU, Shirou SUZUKI (Department of Functional Joint Anatomy)

Parttime Lecturer : Kenji IBUKURO, Itsuko OKUDA, Sachiya TSUKADA, Masataka NAKAZAWA, Kaoru KITSUKAWA

Graduate Student : Kazuhito SEKIZAWA, Eiichirou KAGAWA, Kohtaro EGUCHI, Saya HORIUCHI, Kentaro AMAHA, Yusuke UEDA, Yasunori TATARA, Shota HOSHIKA, Phichaya BARAMEE, Atsuhiko OCHI, Souichi HATTORI, Koh MIWA, Satoru MURO, Suriyut JANARUK, Syuusaku HOSONO, Haruka EISHI, Masahiro TSUTSUMI, Wachirawit SIRIRAT, Shouko MOUE(April~), Ming Yan HE(April~), Areeya JIAMJUNYASIRI(Sept~),

Pawaree NONTHASAEN(~March), Natnicha KAMPAN(~March), Motoki TANAKA(~March)

Research Student : Mamiko SUZUKI

(1) Outline

Department of Clinical Anatomy supports clinical medicine through formulation of human anatomical and developmental biological bases of diagnoses and surgical procedures. We handle the whole body in human anatomical researches. We think it is classic but important to represent human morphology for exactly what they are based on meticulous observations of human body structures regardless of diagnostic technics and surgical procedures. Our researches are aimed to share languages among all clinicians based on clinical anatomy by describing the results of observations in an accessible way for clinicians. In addition, we perform analyses using experimental embryological approaches and developmental biological approaches, because we think it is important to consider how human structures are constructed.

(2) Research

- 1) Clinical anatomic study of the shoulder joint and rotator cuff.
- 2) Clinical anatomic study of the anal region for the rectoanal surgery.
- 3) Cadaveric study of the female pelvis for the gynecologic oncology and colposcopy.
- 4) Analyses of the lamination in the masticatory muscles with special reference of nerve supply.
- 5) Embryological study of the differentiation of cloaca and surrounding muscles.

(3) Education

Clinical anatomy is generally considered as the practical application of anatomical knowledge to diagnosis and treatment, however we think that this course is a part of pure anatomical science based on the findings of the morphological observations of the human bodies. Main objective of Clinical anatomy in the graduate course is to make detailed anatomical data to answer the questions developed from clinical fields especially by surgeons and radiologists. We collaborate with many clinicians: ENT, orthopedics, gynecology, thoracic surgery, radiology and so on, and our projects have been broad areas. Students are expected to get fine dissection techniques of human bodies and also learn techniques of histology and embryological experiments. By using these techniques,

we study the spatial relationships of organs, vessels nerves, and also try to examine their developmental processes in various projects.

(4) Lectures & Courses

Theories and hypotheses of morphogenesis derived from descriptive anatomy and descriptive biology have been confirmed and modified by experimental biology. Furthermore, progresses of developmental biology identified molecules and signaling pathways involved in the morphogenesis. Progresses in the developmental biology also verified morphological hypotheses, and added revisions to the morphological models. The postulates of the morphological models which are currently investigated were built and completed by Anatomy. However, we find Anatomy is still not completed and has many obscure issues through careful dissection of human body. It might be thought that everything was done and there could be no new finding in the human anatomical field anymore because the anatomy employs the classic procedures such as the gross anatomy. However, there are still a lot of unclear anatomical topics, because they had not been focused and not investigated with their clinical significances.

(5) Publications

[Original Articles]

1. Hiroyuki Ogawa, Seiichirou Hasegawa, Sachi-yuki Tsukada, Masaaki Matsubara. A Pilot Study of Augmented Reality Technology Applied to the Acetabular Cup Placement During Total Hip Arthroplasty. *J Arthroplasty*. 2018.01; 33(6); 1833-1837
2. Yano T, Akita K, Yamaguchi K, Sawaizumi M. A Cadaver Study to Assess the Feasibility of a Cross-Nerve Transfer of the Infraorbital Nerve for Patients With Peripheral Infraorbital Nerve Injury. *Annals of plastic surgery*. 2018.02; 80(2); 141-144
3. A Sakata, K Abe, K Mizukoshi, T Gomi, I Okuda. Relationship between the retinacula cutis and sagging facial skin. *Skin Res Technol*. 2018.02; 24(1); 93-98
4. Nakajima Y, Tokairin Y, Nakajima Y, Kawada K, Nagai K, Yamaguchi K, Akita K, Kawano T. Anatomical study of the left superior mediastinal lymphatics for tracheal branches of left recurrent laryngeal nerve-preserving mediastinoscope-assisted surgery in esophageal cancer. *Surgery today*. 2018.03; 48(3); 333-337
5. Motoki Tanaka, Akimoto Nimura, Norimasa Takahashi, Tomoyuki Mochizuki, Ryuichi Kato, Hiroyuki Sugaya, Keiichi Akita. Location and thickness of delaminated rotator cuff tears: cross-sectional analysis with surgery record review. *JSES Open Access*. 2018.03; 2(1); 84-90
6. Sachi-yuki Tsukada, Sadao Niga, Tadahiro Nihei, Shoichiro Imamura, Masayoshi Saito, Jindo Hatanaka. Iliopsoas Disorder in Athletes with Groin Pain: Prevalence in 638 Consecutive Patients Assessed with MRI and Clinical Results in 134 Patients with Signal Intensity Changes in the Iliopsoas. *JB JS Open Access*. 2018.03; 3(1); e0049
7. Sachi-yuki Tsukada, Motohiro Wakui. Continuing versus discontinuing antiplatelet drugs, vasodilators, and/or cerebral ameliorators on perioperative total blood loss in total knee arthroplasty without pneumatic tourniquet. *Arthroplast Today*. 2018.03; 4(1); 89-93
8. Yugo Miura, Koji Fujita, Akimoto Nimura, Takashi Miyamoto, Yoshiaki Wakabayashi, Atsushi Okawa. Successful Reconstruction of a Traumatic Complete Femoral Nerve Rupture with a Sural Nerve Cable Graft: A Case Report. *JBJS Case Connect*. 2018.04; 8(2); e24
9. Okada R, Muro S, Eguchi K, Yagi K, Nasu H, Yamaguchi K, Miwa K, Akita K. The extended bundle of the tensor veli palatini: Anatomic consideration of the dilating mechanism of the Eustachian tube. *Auris, nasus, larynx*. 2018.04; 45(2); 265-272
10. Kotaro Yoshida, Osamu Matsui, Shiro Miyayama, Kenji Ibukuro, Norihide Yoneda, Dai Inoue, Kazuto Kozaka, Tetsuya Minami, Wataru Koda, Toshifumi Gabata. Isolated Arteries Originating from the Intrahepatic Arteries: Anatomy, Function, and Importance in Intervention. *J Vasc Interv Radiol*. 2018.04; 29(4); 531-537.e1

11. Nonthasaen P, Nasu H, Kagawa E, Akita K. A morphological comparison of the extraforaminal ligament between the cervical and thoracic regions. *Surgical and radiologic anatomy* : SRA. 2018.05; 40(5); 571-580
12. Kohtaro Eguchi, Masami Suzuki, Shota Ida, Keita Mori, Hisao Imai, Shigehiro Kudo, Ken Ando, Keiko Higuchi, Takeshi Ebara. Association Between Laryngopharyngeal Reflux and Radiation-induced Mucositis in Head and Neck Cancer. *Anticancer Res.*. 2018.06; 38(1); 477-480
13. Haruhiko Shimura, Akimoto Nimura, Koji Fujita, Takashi Miyamoto. Mid-Term Functional Outcome after Volar Locking Plate Fixation of Distal Radius Fractures in Elderly Patients. *J Hand Surg Asian Pac Vol.* 2018.06; 23(2); 238-242
14. Momma D, Nimura A, Muro S, Fujishiro H, Miyamoto T, Funakoshi T, Mochizuki T, Iwasaki N, Akita K. Anatomic analysis of the whole articular capsule of the shoulder joint, with reference to the capsular attachment and thickness. *Journal of experimental orthopaedics.* 2018.06; 5(1); 16
15. Tokairin Y, Nakajima Y, Kawada K, Hoshino A, Okada T, Ryotokuji T, Okuda M, Kume Y, Kawamura Y, Yamaguchi K, Nagai K, Akita K, Kinugasa Y. Histological study of the thin membranous structure made of dense connective tissue around the esophagus in the upper mediastinum. *Esophagus : official journal of the Japan Esophageal Society.* 2018.06; 15(4); 272-280
16. Kampan N, Tsutsumi M, Okuda I, Nasu H, Hur MS, Yamaguchi K, Akita K. The malaris muscle: its morphological significance for sustaining the intraorbital structures. *Anatomical science international.* 2018.06; 93(3); 364-371
17. Tetsuya Sato, Akimoto Nimura, Reiko Yamaguchi, Koji Fujita, Atsushi Okawa, Keiichi Akita. Intramuscular Tendon of the Adductor Pollicis and Underlying Capsule of the Metacarpophalangeal Joint: An Anatomical Study With Possible Implications for the Stener Lesion. *J Hand Surg Am.* 2018.07; 43(7); 682.e1-682.e8
18. Yamaguchi R, Nimura A, Amaha K, Yamaguchi K, Segawa Y, Okawa A, Akita K. Anatomy of the Tarsal Canal and Sinus in Relation to the Subtalar Joint Capsule. *Foot & ankle international.* 2018.07; 39(11); 1360-1369
19. Higashino T, Okazaki M, Mori H, Yamaguchi K, Akita K. Microanatomy of Sensory Nerves in the Upper Eyelid: A Cadaveric Anatomical Study. *Plastic and reconstructive surgery.* 2018.08; 142(2); 345-353
20. Yoshinori Sato, Hiroyasu Tsukaguchi, Hiroyuki Morita, Koichiro Higasa, Mai Thi Nhu Tran, Michito Hamada, Toshiaki Usui, Naoki Morito, Shoichiro Horita, Takao Hayashi, Junko Takagi, Izumi Yamaguchi, Huan Thanh Nguyen, Masayo Harada, Kiyoko Inui, Yuichi Maruta, Yoshihiko Inoue, Fumihiko Koiwa, Hiroshi Sato, Fumihiko Matsuda, Shinya Ayabe, Seiya Mizuno, Fumihiko Sugiyama, Satoru Takahashi, Ashio Yoshimura. A mutation in transcription factor MAFB causes Focal Segmental Glomerulosclerosis with Duane Retraction Syndrome. *Kidney Int.*. 2018.08; 94(2); 396-407
21. Naoyuki Hirasawa, Kenji Kurosaka, Masahiro Nishino, Tsutomu Nakayama, Masaaki Matsubara, Sachi-yuki Tsukada. No Clinically Important Difference in Pain Scores After THA Between Periarticular Analgesic Injection and Placebo: A Randomized Trial. *Clin. Orthop. Relat. Res.*. 2018.09; 476(9); 1837-1845
22. Keiichi Akita, Tomomi Sakaguchi-Kuma, Keiko Fukino, Takashi Ono. Masticatory Muscles and Branches of Mandibular Nerve: Positional Relationships between Various Muscle Bundles and Their Innervating Branches. *Anat Rec (Hoboken).* 2018.10; 302(4); 609-619
23. Sachi-yuki Tsukada, Kenji Kurosaka, Masahiro Nishino, Naoyuki Hirasawa. Cutaneous Hypesthesia and Kneeling Ability After Total Knee Arthroplasty: A Randomized Controlled Trial Comparing Anterolateral and Anteromedial Skin Incision. *J Arthroplasty.* 2018.10; 33(10); 3174-3180
24. Takuya Iseki, Sachi-yuki Tsukada, Motohiro Wakui, Shinichi Yoshiya. Intravenous tranexamic acid only versus combined intravenous and intra-articular tranexamic acid for perioperative blood loss in patients undergoing total knee arthroplasty. *Eur J Orthop Surg Traumatol.* 2018.10; 28(7); 1397-1402
25. Muro S, Tsukada Y, Harada M, Ito M, Akita K. Spatial distribution of smooth muscle tissue in the male pelvic floor with special reference to the lateral extent of the rectourethralis muscle: Application to prostatectomy. *Clinical anatomy (New York, N.Y.).* 2018.11; 31(8); 1167-1176

26. Fukino K, Tsutsumi M, Sanudo J, Ono T, Akita K. Anatomical Significance of the Spatial Distribution of the Palatopharyngeus With Regard to Velopharyngeal Closure. *The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association*. 2018.11; 1055665618813082
27. Tomoyuki Kuroiwa, Koji Fujita, Akimoto Nimura, Takashi Miyamoto, Toru Sasaki, Atsushi Okawa. A new method of measuring the thumb pronation and palmar abduction angles during opposition movement using a three-axis gyroscope. *J Orthop Surg Res*. 2018.11; 13(1); 288
28. H Fujiwara, J Kanamori, Y Nakajima, T Kawano, A Miura, T Fujita, K Akita, H Daiko. An anatomical hypothesis: a "concentric-structured model" for the theoretical understanding of the surgical anatomy in the upper mediastinum required for esophagectomy with radical mediastinal lymph node dissection. *Dis. Esophagus*. 2018.12; in press

[Conference Activities & Talks]

1. Akimoto Nimura, Shota Hoshika, Rerika Yamaguchi, Hiroyuki Sugaya, Keiichi Akita. Reconsideration of the anatomy regarding the ulnar collateral ligament of the elbow in terms of the tendinous fascia. The 2018 Annual Meeting of the American Academy of Orthopaedic Surgeons 2018.03.07 New Orleans, USA
2. Hisayo Nasu, Akimoto Nimura, Sara Sugiura, Hitomi Fujishiro, Hideyuki Koga, Keiichi Akita. An anatomic study on the attachment of the joint capsule to the tibia in the lateral side of the knee. 18th European Society of Sports Traumatology and Arthroscopy Congress 2018.05.09 Glasgow, UK
3. Soichi Hattori. The effectiveness and reproducibility of ultrasound in evaluation of the calcaneofibular ligament. 18th European Society of Sports Traumatology and Arthroscopy Congress 2018.05.09 Glasgow, UK
4. Kenji Ibukuro. The Hepatic Capsular Arteries: Anatomical and Clinical significance. The Japanese Society of Interventional Radiology 2018 2018.05.31 Tokyo, Japan
5. Kenji Ibukuro, Gou Ogasawara, Hozumi Fukuda, Kimiko Tobe, Mitsuhiro Kishino. The relationship between the location of the portal vein thrombus, the patency of the portal veins, and the coexisting disease. ESGAR2018 2018.06.04 Dublin, Ireland
6. Masayo Harada, Keiich Akita. The N143T mutation in mouse Fibroblast growth factor 9 leads to wider long bones. Joint Annual Meeting of JSDB 51st and JSCB 70th 2018 2018.06.08 Tokyo, Japan
7. Mochizuki Tomoyuki, Akita Keiichi. ACL anatomy and tunnel placement (ACL anatomy and tunnel placement Anatomic and histologic analysis of the mid-substance and fan-like extension fibres of the anterior cruciate ligament during knee motion, with special reference to the femoral attachment). 10th JOSKAS 2018.06.15 Fukuoka, Japan
8. Tomonori Yabuuchi, Satoru Muro, Keiichi Akita. Origins of the levator ani with special reference to the tendinous arch. 35th Annual meeting of American Association of Clinical Anatomy 2018.07.10 Atlanta, USA
9. Satoru Muro, Yuichiro Tsukada, Masayo Harada, Masaaki Ito, Keiichi Akita. Muscle layer structure in anterior wall of anorectal canal in females. 35th Annual meeting of American Association of Clinical Anatomy 2018.07.10 Atlanta, USA
10. Masahiro Tsutsumi, Akimoto Nimura, Keiichi Akita. Morphological analysis of gluteus medius tendon and its insertion sites. 35th Annual meeting of American Association of Clinical Anatomy 2018.07.11 Atlanta, USA
11. Shoko Nakata, Koichi Ogawa, Osamu Shimomura, Yusuke Ohara, Kazuhiro Takahashi, Yoshimasa Akashi, Katsuji Hisakura, Tsuyoshi Enomoto, Masanao Kurata, Tatsuya Oda, Nobuhiro Ohkohchi. To increase female surgeons. The 73rd General Meeting of the Japanese Society of Gastroenterological Surgery 2018.07.13 Kagoshima, Japan
12. Yusuke Ueda, Akimoto Nimura, Hiroyuki Sugaya, Norimasa Takahashi, Keisuke Matsuki, Morihito Tokai, Shouta Hoshika, Hiroshige Hamada. Difference in the Site of Rotator Cuff lesions between Shoulders with Recurrent Anterior Instability and Throwing Injuries. The 44th Annual Meeting of the Japanese Orthopaedic Society for Sports Medicine. 2018.09.08 Tokushima, Japan

13. Baramée Phichaya, Satoru Muro, Masahiro Tsutsumi, Keiichi Akita. Composition of the anterior wall of the external anal sphincter in female: Supporting system by two muscle slings. 10th Meeting of International Symposium of Clinical and Applied Anatomy 2018.09.14 Moscow, Russia
14. Keiko Fukino, Masahiro Tsutsumi, Jose Sanudo, Takashi Ono, Keiichi Akita. Anatomical significance of the spatial distribution of the palatopharyngeus with regard to closure of the nasopharynx. 10th Meeting of International Symposium of Clinical and Applied Anatomy 2018.09.15 Moscow, Russia
15. Suriyut Janyaruk, Satoru Muro, Masahiro Tsutsumi, Keiichi Akita. An anatomical interpretation of outer and inner muscle bundle groups in male pelvic floor muscles. 10th Meeting of International Symposium of Clinical and Applied Anatomy 2018.09.15 Moscow, Russia
16. Kaoru Kitsukawa, Yusuke Kimura, Yasuo Nakajima, Koji Kawakami, Hisateru Niki. MRI evaluation of cervical neural foraminal stenosis using 3D T2TFE sequence. The 33rd Annual Research Meeting of the Japanese Orthopaedic Association 2018.10.11 Nara, Japan
17. Nimura Akimoto, Akita Keiichi. Anatomy based on the common pathologies around the elbow joint. 4th Asian Association of Clinical Anatomists 2018.10.28 Busan, Korea
18. Masahiro Tsutsumi, Akimoto Nimura, Keiichi Akita. Morphological significance of the thickness distribution in the gluteus medius tendon with regard to the gluteus medius tendon tears. 8th Asia Pacific International Congress of Anatomists 2018.10.29 Busan, Korea
19. Satoru Muro, Yuichiro Tsukada, Masayo Harada, Masaaki Ito, Keiichi Akita. Anatomy of the smooth muscle structure in the female anorectal anterior wall. Annual joint academic meetings (surgical research society meeting) of Royal Australasian college of surgeons 2018.11.09 Sydney, Australia

Systems BioMedicine

Professor Hiroshi ASAHARA

Junior Associate Professor Masahiro SHINOHARA

Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA, Ryouta KURIMOTO

Graduate Students

Kensuke KATAOKA, Yuki YANO, Hiroto YAMAMOTO,

Takahiro MITSUMURA, Hiroki TSUTSUMI, Hitomi OMAKI, Takayuki MIYAZAKI, Kihou TAKADA,

Ken KUROIWA, Yusuke MOCHIZUKI, Yutaro Uchida

Kaduki ICHIKAWA, Natsuko SADAHIRO, Haruka HOSOGAI

(1) Research

Screening with an RNA binding protein library identified new regulators of microRNA.

We identified novel regulators of tumor suppressor microRNAs.

The function of the epigenome on bone morphogenesis was analyzed using micro-CT.

We have been shown that the tendons/ligaments specific transcription factor Mohawk is essential for the development and homeostasis processes in tendons and ligaments.

We have been developed completely automated ChIP system using LabDroid “Maholo”.

Search for novel regulator of microRNA by high throughput screening.

Established novel strategies for the osteoporosis by targeting molecules critical for the bone homeostasis.

Revealed the molecular mechanism by which osteocytes regulate bone homeostasis.

Analyzed the bone phenotype of spaceflight mice.

Analyzed molecular mechanisms by which the bone tissue regulates the energy metabolism.

The Screening of novel Damage-associated molecular patterns proteins

Protein localization analysis by High-throughput microscope system

MiRNA which regulates cartilage homeostasis was identified.

We developed screening system for miRNA target genes using reporter vector library.

MicroRNA KO mice were generated using CRISPR/Cas9 system, and its function in skeletal pattern formation was analyzed.

Molecular mechanisms and in vivo roles of RNA-binding proteins and long non-coding RNAs in the context of inflammatory response

(2) Education

Under Graduate:

Conducting “Molecular Genetics”, which is a series of lectures to understand the gene expression machinery and human genetics and their application to current medicine and biology. Under graduate students can join the lab works to learn the skills for molecular biology and pathology.

Graduate School:

Organizing “Development and Regeneration” lecture series to understand the basis for regenerative medicine and reproduction at the level of molecular genetics.

Students can join the Lab to perform researches using various experimental techniques, such as microarray, cell-based high throughput screening etc. Using these techniques, core molecular network for tissue development

and inflammatory diseases will be examined, which forms the basis of systems biomedicine.

(3) Publications

[Original Articles]

1. Kataoka K, Matsushima T, Ito Y, Sato T, Yokoyama S, Asahara H. Bhlha9 regulates apical ectodermal ridge formation during limb development. *JBMM*. 2018.01; 36(1); 64-72
2. Matsuzaki T, Alvarez-Garcia O, Mokuda S, Nagira K, Olmer M, Gamini R, Miyata K, Akasaki Y, Su AI, Asahara H, Lotz MK. FoxO transcription factors modulate autophagy and proteoglycan 4 in cartilage homeostasis and osteoarthritis. *Science translational medicine*. 2018.02; 10(428);
3. Inui M, Mokuda S, Sato T, Tamano M, Takada S, Asahara H. Dissecting the roles of miR-140 and its host gene. *Nature cell biology*. 2018.05; 20(5); 516-518
4. Saito T, Hara S, Kato T, Tamano M, Muramatsu A, Asahara H, Takada S. A tandem repeat array in IG-DMR is essential for imprinting of paternal allele at the Dlk1-Dio3 domain during embryonic development. *Human molecular genetics*. 2018.06;
5. Alvarez-Garcia O, Matsuzaki T, Olmer M, Miyata K, Mokuda S, Sakai D, Masuda K, Asahara H, Lotz MK. FOXO are required for intervertebral disk homeostasis during aging and their deficiency promotes disk degeneration. *Aging cell*. 2018.07; e12800
6. Yusuke Mochizuki, Tomoki Chiba, Kensuke Kataoka, Satoshi Yamashita, Tempei Sato, Tomomi Kato, Kenji Takahashi, Takeshi Miyamoto, Masashi Kitazawa, Tomohisa Hatta, Tohru Natsume, Shinro Takai, Hiroshi Asahara. Combinatorial CRISPR/Cas9 Approach to Elucidate a Far-Upstream Enhancer Complex for Tissue-Specific Sox9 Expression. *Dev. Cell*. 2018.08; 46(6); 794-806.e6
7. Mitsumura T, Ito Y, Chiba T, Matsushima T, Kurimoto R, Tanaka Y, Kato T, Uchida K, Ito T, Yamamoto K, Eishi Y, Kitagawa M, Miyazaki Y, Inase N, Asahara H. Ablation of miR-146b in mice causes hematopoietic malignancy. *Blood advances*. 2018.12; 2(23); 3483-3491

[Misc]

1. Masahiro Shinohara. Effects of Spaceflight on Bone Metabolism 2018.04;
2. Nakamichi R, Kataoka K, Asahara H. Essential role of Mohawk for tenogenic tissue homeostasis including spinal disc and periodontal ligament. *Modern rheumatology*. 2018.05; 1-8

[Conference Activities & Talks]

1. Hiroshi Asahara. The completely automated ChIP system performed by LabDroid " Maholo" . Robotics and Semantic Systems for Biology (RSSB) 2 2018.01.27
2. Hiroshi Asahara. Transcriptional and translational regulation of musculoskeletal development and arthritis pathogenesis.. Marc Montminy's 62nd Birthday Symposium 2018.08.31
3. Hiroshi Asahara. miRNAs in arthritis pathogenesis and therapy. JAJ RNA 2018.11.05
4. Hiroshi Asahara. Mechano-signal pathway regulating tendon and ligament via Mxk. ORS Tendon Section 2018 Conference 2018.11.16

Comprehensive Pathology

Professor
 Masanobu KITAGAWA
 Junior associate Professor
 Morito KURATA
 Assistant Professor
 Kouhei YAMAMOTO, Iichiro ONISHI
 Laboratory Technician
 Miori INOUE
 Technical Assistant
 Sachiko ISHIBASHI, Masumi IKEDA,
 Graduate Students
 Masae Yanai, Mariko Muto, Ryoko KATO, Naoko OZAWA, Risa Fusa,
 Sumito Shingaki, Masanori Matsuda, Tan Wang, Akiko YAMAMOTO,
 Miyaka Umemori, Jyunichiro SATO, Masahiro KAWADA,
 Noriaki FUKUHARA, Tomohiro YOKOUCHI, Shigeo TODA,
 Jyunnosuke HAYASAKA, Vilayvong Sulideyh,
 Luangxay Thitsamay,

(1) Outline

Main objective of comprehensive pathology in the graduate course is to acquire the technique of clinical and basic pathology. This course provides students opportunity to study clinical pathology (for example, histological and cytological diagnosis, autopsy, clinico-pathologic conference) and also basic pathology (molecular pathology and molecular biology).

(2) Research

- 1) Clinico-pathological study by morphological findings, immunohistochemistry, and electron microscope, etc.
- 2) Molecular analysis of leukomogenesis induced by Friend leukemia virus (FLV)
- 3) Enhancement of apoptosis by virus-derived protein and development of apoptosis-induction cancer therapy
- 4) Molecular pathology of the myelodysplastic syndromes (MDS)
- 5) Clarification of drug resistance mechanism for hematopoietic malignancies
- 6) Comprehensive research for aging focus on the decreased immune competence
- 7) Molecular biology of the cancer progression and metastasis

(3) Education

Main objective of comprehensive pathology in the graduate course is to acquire the techniques of clinical and basic pathology. This course provides students opportunities to study clinical pathology (for example, histological and cytological diagnosis, autopsy, clinico-pathologic conference) and also basic pathology (molecular pathology and molecular biology).

(4) Publications

[Original Articles]

1. Kinowaki Yuko, Yamamoto Kohei, Kurata Morito, Onishi Iichiroh, Kitagawa Masanobu. Clinico-pathological analysis of GPX4 expression in Diffuse large B cell lymphoma *CANCER SCIENCE*. 2018.01; 109; 683
2. Tatsuzawa Anna, Yamamoto Kouhei, Ohata Yae, Ohya Yashio, Mochizuki Yumi, Komatsu Hiroyoshi, Kitagawa Masanobu. Clinicopathologic and gene mutation analysis of oral diffuse large B-cell lymphoma *CANCER SCIENCE*. 2018.01; 109; 684
3. Kurata Morito, Yamamoto Kouhei, Kitagawa Masanobu, Noble-Orcutt Klara, Hillesheim Alexandra, Qarni Zain, Sachs Zohar, Largaespada David. Controllable oncogene; new aspects of signaling with controlling oncogene expression *CANCER SCIENCE*. 2018.01; 109; 457
4. Kinowaki Yuko, Yamamoto Kohei, Kurata Morito, Onishi Iichiroh, Kitagawa Masanobu. Clinico-pathological analysis of GPX4 expression in Diffuse large B cell lymphoma *CANCER SCIENCE*. 2018.01; 109; 683
5. Junichi Maruyama, Kazutoshi Inami, Fumiyoshi Michishita, Xinliang Jiang, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Norio Miyamura, Jun Hirayama, Hiroshi Nishina, Daichi Nogawa, Kouhei Yamamoto, Yutaka Hata. Novel YAP1 Activator, Identified by Transcription-Based Functional Screen, Limits Multiple Myeloma Growth. *Mol. Cancer Res.*. 2018.02; 16(2); 197-211
6. Yuko Kinowaki, Morito Kurata, Sachiko Ishibashi, Masumi Ikeda, Anna Tatsuzawa, Masahide Yamamoto, Osamu Miura, Masanobu Kitagawa, Kouhei Yamamoto. Glutathione peroxidase 4 overexpression inhibits ROS-induced cell death in diffuse large B-cell lymphoma. *Lab. Invest.*. 2018.02;
7. Kurata Morito, Yamamoto Kouhei, Moriarity Branden S., Kitagawa Masanobu, Largaespada David A.. CRISPR/Cas9 library screening for drug target discovery *Journal of Human Genetics*. 2018.02; 63(2); 179-186
8. Hashimoto Hiroko, Nomura Naohiro, Shoda Wakana, Isobe Kiyoshi, Kikuchi Hiroaki, Yamamoto Kouhei, Fujimaru Takuya, Ando Fumiaki, Mori Takayasu, Okado Tomokazu, Rai Tatsumitsu, Uchida Shinichi, Sohara Eisei. Metformin increases urinary sodium excretion by reducing phosphorylation of the sodium-chloride cotransporter. *Metabolism*. 2018.03;
9. Hiroki Yamada, Takahiro Takeda, Toshiki Uchihara, Shizuko Sato, Susumu Kirimura, Yuka Hirota, Makoto Kodama, Masanobu Kitagawa, Katsui Hirokawa, Takanori Yokota, Shuta Toru. Macroscopic Localized Subicular Thinning as a Potential Indicator of Amyotrophic Lateral Sclerosis. *Eur. Neurol.*. 2018.03; 79(3-4); 200-205
10. Maria Razzoli, Kewir Nyuyki-Dufe, Allison Gurney, Connor Erickson, Jacob McCallum, Nicholas Spielman, Marta Marzullo, Jessica Patricelli, Morito Kurata, Emily A Pope, Chadi Touma, Rupert Palme, David A Largaespada, David B Allison, Alessandro Bartolomucci. Social stress shortens lifespan in mice. *Aging Cell*. 2018.05; e12778
11. Gulinisha Aihemaiti, Morito Kurata, Daichi Nogawa, Akiko Yamamoto, Tatsunori Mineo, Iichiroh Onishi, Yuko Kinowaki, Xiao-Hai Jin, Anna Tatsuzawa, Naoyuki Miyasaka, Masanobu Kitagawa, Kouhei Yamamoto. Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma. *Oncotarget*. 2018.06; 9(46); 28213-28225
12. Takamori Takeda, Yoshiyuki Kawashima, Chiaki Hirai, Ayane Makabe, Taku Ito, Taro Fujikawa, Katsura Yamamoto, Ayako Maruyama, Takeshi Tsutsumi. Vestibular Dysfunction in Patients With Superficial Siderosis of the Central Nervous System. *Otol. Neurotol.*. 2018.07; 39(6); e468-e474
13. Morito Kurata, Natalie K Wolf, Walker S Lahr, Madison T Weg, Mitchell G Kluesner, Samantha Lee, Kai Hui, Masano Shiraiwa, Beau R Webber, Branden S Moriarity. Highly multiplexed genome engineering using CRISPR/Cas9 gRNA arrays. *PLoS ONE*. 2018.09; 13(9); e0198714

15. Sano Tatsuhiko, Kobayashi Zen, Takaoka Ken, Ota Kiyobumi, Onishi Iichiroh, Iizuka Mihoko, Tomimitsu Hiroyuki, Shintani Shuzo. Retrobulbar optic neuropathy associated with sphenoid sinus mucormycosis(和訳中) *Neurology and Clinical Neuroscience*. 2018.09; 6(5); 146-147
16. Sano T, Kobayashi Z, Takaoka K, Ota K, Onishi I, Iizuka M, Tomimitsu H, Shintani S. Retrobulbar optic neuropathy associated with sphenoid sinus mucormycosis. *Neurology and clinical neuroscience*. 2018.09; 6(5); 146-147
17. Nagatsuma M, Takasawa K, Yamauchi T, Nakagawa R, Mizuno T, Tanaka E, Yamamoto K, Uemura N, Kashimada K, Morio T. A postzygotic KRAS mutation in a patient with Schimmelpenning syndrome presenting with lipomatosis, renovascular hypertension, and diabetes mellitus. *Journal of human genetics*. 2018.11;
18. Mitsumura T, Ito Y, Chiba T, Matsushima T, Kurimoto R, Tanaka Y, Kato T, Uchida K, Ito T, Yamamoto K, Eishi Y, Kitagawa M, Miyazaki Y, Inase N, Asahara H. Ablation of miR-146b in mice causes hematopoietic malignancy. *Blood advances*. 2018.12; 2(23); 3483-3491
19. Kurata Morito, Yamamoto Kohei, Kitagawa Masanobu. Controllable NRAS expression system and analysis of different signals *CANCER SCIENCE*. 2018.12; 109; 895
20. Yamamoto Kohei, Abe Shinya, Kurata Morito, Honda Ayaka, Yamamoto Masahide, Kitagawa Masanobu. Ranolazine is a potential anti-tumor reagent against refractory cases in malignant lymphoma *CANCER SCIENCE*. 2018.12; 109; 494
21. Nogawa Daichi, Gulinisha Aihemaiti, Yamamoto Akiko, Onishi Iichiroh, Kurata Morito, Miyasaka Naoyuki, Yamamoto Kohei, Kitagawa Masanobu. Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma *CANCER SCIENCE*. 2018.12; 109; 503
22. Nogawa Daichi, Gulinisha Aihemaiti, Yamamoto Akiko, Onishi Iichiroh, Kurata Morito, Miyasaka Naoyuki, Yamamoto Kohei, Kitagawa Masanobu. Subcellular localization of MCM2 correlates with the prognosis of ovarian clear cell carcinoma *CANCER SCIENCE*. 2018.12; 109; 503

[Misc]

1. Morito Kurata, Kouhei Yamamoto, Branden S Moriarity, Masanobu Kitagawa, David A Largaespada. CRISPR/Cas9 library screening for drug target discovery. *J. Hum. Genet.*. 2018.02; 63(2); 179-186

Molecular Oncology

Professor: Shinji TANAKA
Associate Professor: Yoshimitsu AKIYAMA
Associate Professor: Hiroshi FUKAMACHI
Assistant Professor: Shu SHIMADA
Laboratory Technician: Hiromi NAGASAKI
Graduate Student: Misaki SERIZAWA

(1) Outline

To understand the molecular mechanisms underlying carcinogenesis and malignant progression for clinical application of cancer prevention, diagnosis and treatment.

(2) Research

1. Molecular analysis of refractory malignancies including liver, pancreatic and scirrhus gastric cancers
2. Development of molecularly targeted therapy for refractory malignancies
3. Cancer epigenetics/epigenomics and clinical application in refractory malignancies
4. Research of cancer stem cells and targeted therapy
5. Development of regenerative medicine using stem cell research

(3) Education

Hygiene is our charge. The undergraduate curriculum of hygiene includes lectures, and laboratory studies. Topics of lectures consist of environmental pollution and human health, world-wide environmental problems, carcinogen and occupational cancer, smoking-related diseases, infectious diseases including AIDS and hepatitis, food poisoning, anoxia and heat-related diseases.

(4) Lectures & Courses

The graduate students pursue their own projects associated with one of researches being in progress in the division. Every student can learn the basic scientific techniques, such as genetic engineering, cell culture and biochemical procedures. There are also many special lectures on cancer, gene, cell biology and biochemistry for the graduate students. On weekly seminars, the students present their own research data and introduce important papers from newly-arrived journals. Once the students get new findings, they are encouraged to present them at the domestic or international meeting and write manuscripts.

(5) Publications

[Original Articles]

1. Mizuno Y, Shimada S, Akiyama Y, Watanabe S, Aida T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Arii S, Yamaoka S, Tanabe M, Tanaka S. DEPDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma. *Scientific Reports*. 2018.01; 8(1);

2. Yoshiya Ishikawa, Daisuke Ban, Shuichi Watanabe, Keiichi Akahoshi, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Splenic artery as a simple landmark indicating difficulty during laparoscopic distal pancreatectomy Asian Journal of Endoscopic Surgery. 2018.02; 1-7
3. Ueda H, Akiyama Y, Shimada S, Mogushi K, Serizawa M, Matsumura S, Mitsunori Y, Aihara A, Ban D, Ochiai T, Kudo A, Tanabe M, Tanaka S. Tumor suppressor functions of DAXX through histone H3.3/H3K9me3 pathway in pancreatic NETs. Endocrine-Related Cancer. 2018.03; 25(6); 619-631
4. Yuki Mizuno, Atsushi Kudo, Takumi Akashi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Ukihide Tateishi, Minoru Tanabe. Sunitinib shrinks NET-G3 pancreatic neuroendocrine neoplasms Journal of Cancer Research and Clinical Oncology. 2018.03; 144; 1155-1163
5. Shu Shimada, Yoshimitsu Akiyama, Kaoru Mogushi, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiromi Nagasaki, Hiroshi Fukamachi, Yasuhito Yuasa, Shinji Tanaka. Identification of selective inhibitors for diffuse-type gastric cancer cells by screening of annotated compounds in preclinical models. Br. J. Cancer. 2018.04; 118(7); 972-984
6. Norimichi Chiyonobu, Shu Shimada, Yoshimitsu Akiyama, Kaoru Mogushi, Michiko Itoh, Keiichi Akahoshi, Satoshi Matsumura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shigeki Arai, Takayoshi Suganami, Shoji Yamaoka, Yoshihiro Ogawa, Minoru Tanabe, Shinji Tanaka. Fatty acid binding protein 4 (FABP4) overexpression in intratumoral hepatic stellate cells within hepatocellular carcinoma with metabolic risk factors The American Journal of Pathology. 2018.05; 188(5);
7. Kudo A, Akahoshi K, Ito S, Akashi T, Shimada S, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tateishi U, Tanaka S, Tanabe M. Downregulated Pancreatic Beta Cell Genes Indicate Poor Prognosis in Patients With Pancreatic Neuroendocrine Neoplasms. Annals of Surgery. 2018.07;
8. Keiichi Akahoshi, Daisuke Ban, Ryo Kuboki, Atsushi Oba, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka and Minoru Tanabe. Orotate phosphoribosyltransferase as a predictor of benefit from S-1 adjuvant chemotherapy for cholangiocarcinoma patients Journal of Gastroenterology and Hepatology. 2018.09;
9. Keiichi Akahoshi, Hiroaki Ono, Masafumi Akasu, Daisuke Ban, Atsushi Kudo, Atsuko Konta, Shinji Tanaka, Minoru Tanabe. Rapid growth speed of cysts can predict malignant intraductal mucinous papillary neoplasms Journal of Surgical Research. 2018.11; 231; 195-200

[Conference Activities & Talks]

1. Shinji Tanaka. Precision medicine for HCC and pancreatic cancer . The 7th International Forum of The Japanese Society of Gastroenterology Jointly with the 12th International Symposium on ALPD and Cirrhosis 2018.04.19 Tokyo
2. Minoru Tanabe, Toshiro Ogura, Atsushi Kudo, Daisuke Ban, Shinji Tanaka. Surgery for Obese Patients with HCC. APASL2018 2018.05.12 Yokohama
3. Tomotaka Kato, Atsushi Kudo, Hiroaki Ono, Masahumi Akasu, Jun Yoshino, Kosuke Ogawa, Toshiro Ogura, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. A Surgical Case of Spontaneous and Asymptomatic Intrahepatic Hemorrhage with HCC. APASL2018 2018.05.12 Yokohama
4. Jun Yoshino, Toshiro Ogura, Keiichi Akahoshi, Kosuke Ogawa, Yusuke Mitsunori, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Long-term outcomes and prognostic factors of patients with gallbladder cancer resection. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.08 Yokohama
5. Toshiro Ogura, Tomotaka Kato, Masafumi Akasu, Jun Yoshino, Shuichi Watanabe, Norimichi Chiyonobu, Yuki Mizuno, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The implication of lymph node metastasis on survival in cases with distal pancreatic cancer. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama
6. Shuichi Watanabe, Atsushi Kudo, Masafumi Akasu, Tomotaka Kato, Jun Yoshino, Norimichi Chiyonobu, Yuki Mizuno, Keiichi Akahoshi, Kosuke Ogawa, Toshiro Ogura, Yusuke Mitsunori, Hiroaki Ono, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. The efficacy of liver SASI test for the advanced functional

PNET patients. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama

7. Yusuke Mitsunori, Masafumi Akasu, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Norimichi Chiyonobu, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. What is predictive factor of postoperative diabetes mellitus in patients with distal pancreatectomy?. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama
8. Shuichi Watanabe, Shu Shimada, Yoshimitsu Akiyama, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Minoru Tanabe, Shinji Tanaka. Precision medicine for the poorest prognosis subtype of pancreatic cancer. The 73rd General Meeting of the Japanese Society of Gastroenterological Surgery 2018.07.12 Kagoshima
9. Tomotaka Kato, Daisuke Ban, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Treatment strategies of resectable pancreatic cancer with hazy density around major artery. The 73rd General Meeting of the Japanese Society of Gastroenterological Surgery 2018.07.12 Kagoshima
10. Shinji Tanaka, Atsushi Oba, Shu Shimada, Yoshimitsu Akiyama, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shigeki Arii, Minoru Tanabe. Precision immunotherapy for hypermutator and immunogenic subtypes of hepatocellular carcinoma. 73rd General Meeting of the Japanese Society of Gastroenterological Surgery 2018.07.12 Kagoshima
11. Shu Shimada, Norimichi Chiyonobu, Yoshimitsu Akiyama, Shinji Tanaka. FABP4 overexpression in intratumoral hepatic stellate cells within hepatocellular carcinoma with metabolic risk factors.. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.28 Osaka
12. Yuki Mizuno, Shu Shimada, Yoshimitsu Akiyama, Shuichi Watanabe, Tomomi Aida, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shoji Yamaoka, Shinji Tanaka, Minoru Tanabe. DE-PDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma. 2018.09.28
13. Shinji Tanaka. Molecular target therapy under precision medicine. 77th Annual Meeting of Japanese Cancer Association 2018.09.28 Osaka
14. Yoshimitsu Akiyama, Shu Shimada, Minoru Tanabe, Shinji Tanaka. DAXX acts as a tumor suppressor through histone H3.3/H3K9me3 pathway in pancreatic neuroendocrine tumors. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.29 Osaka
15. Hiroshi Fukamachi, Taketo Nishikawaji, Shu Shimada, Yoshimitsu Akiyama, Yasuhito Yuasa, Kiichiro Tsuchiya, Shinji Tanaka. Diffuse-type gastric cancers are classified into two clusters, which may be formed via different carcinogenic pathways. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.29 Osaka

[Patents]

1. Dominant negative mutants of IRS-1 and uses there of (Tanaka S, Wands JR), Patent Number : United States Patent 6,528,479
2. Compositions and methods for detection and treatment of hepatocellular carcinoma (Tanaka S, MacDonald G), Application Number : US 61/811,360

Surgical Pathology

Professor : Masanobu KITAGAWA
Associate Professor : Takumi AKASHI
Assistant Professor : Susumu KIRIMURA, Shohei TOMII,
Atsuko KONTA, Yuko Kinowaki
Hospital Staff Doctor : Keiko MIURA
Secretary : Ayako UENO

(1) Outline

Missions of diagnostic pathology are summarized to following 4 items. 1) participation to the medical treatment of the patients through anatomical diagnosis 2) assessment of medical treatment through autopsy examination 3) training of diagnostic pathologists 4) development of diagnostic methods by anatomical, immunohistochemical, microbiological and molecular technologies.

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides 1. diagnostic pathology services for the clinicians of the affiliated hospital 2. education of medical students and post-graduate students through both lectures and medical practice 3. development of new methods in diagnostic pathology.

(2) Research

- 1) Analysis of the pathophysiology of the disease, especially invasion mechanism of lung and gastrointestinal cancers by molecular biological technology.
- 2) Identification of epithelial neoplasms with chromosome translocation
- 3) Carcinogenesis of prostatic cancer in view of microbiology

(3) Education

Main object of surgical pathology in the course of graduate school is to provide medical students opportunity to study pathophysiology and diagnosis of core diseases, both neoplastic and non-neoplastic, through biopsy, surgical and autopsy cases. Another important mission is a training of pathology specialist in the post-graduate school through diagnostic services of surgical pathology, cytopathology and autopsy.

(4) Lectures & Courses

The initial purpose of this program is to acquire how to morphologically diagnose both neoplastic and non-neoplastic diseases. In addition, it is also very important to recognize the limitations and problems of morphological diagnosis and to learn the morphological and molecular methods which are necessary for the resolution of the problems. The ultimate purpose is to develop a new diagnostic method which can resolve the problems of morphological diagnosis.

(5) Clinical Services & Other Works

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides autopsy services (38 case in a year), cytopathology services (9,957 cases in a year) and surgical pathology (11,574 cases in a year) for the clinicians of the affiliated hospital. Diagnosis is mostly done by the organ-subspecialized staffs. Clinico-pathological conferences have been held about two hundred times in 2014.

(6) Clinical Performances

Department of diagnostic pathology participates in the medical treatment of the patients through anatomical diagnosis. In the era of molecule-targeted therapy, specialized information has been requested in the field of pathological diagnosis. In order to appropriately respond to a latest request of clinicians, we practice pathological diagnosis in cooperation with departments of human pathology and comprehensive pathology with latest techniques, such as immunohistochemistry, electron microscopy, and FISH.

(7) Publications

[Original Articles]

1. Yae Ohata, Maiko Tsuchiya, Hideaki Hirai, Satoshi Yamaguchi, Takumi Akashi, Kei Sakamoto, Akira Yamaguchi, Tohru Ikeda, Kou Kayamori. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. *PLoS ONE*. 2018.02; 13(2); e0191865
2. Yurie Soejima, Miho Takeuchi, Takumi Akashi, Motoji Sawabe, Toshio Fukusato. β 4 and β 6 Integrin Expression Is Associated with the Subclassification and Clinicopathological Features of Intrahepatic Cholangiocarcinoma. *Int J Mol Sci*. 2018.03; 19(4);
3. Keiko Miura, Takumi Akashi, Noboru Ando, Shinya Ayabe, Kou Kayamori, Takeshi Namiki, Yoshinobu Eishi. Homeobox transcriptional factor engrailed homeobox 1 is expressed specifically in normal and neoplastic sweat gland cells. *Histopathology*. 2018.06; 72(7); 1199-1208
4. G Amodini Rajakaruna, Mariko Negi, Keisuke Uchida, Masaki Sekine, Asuka Furukawa, Takashi Ito, Daisuke Kobayashi, Yoshimi Suzuki, Takumi Akashi, Makoto Umeda, Walter Meinzer, Yuichi Izumi, Yoshinobu Eishi. Localization and density of *Porphyromonas gingivalis* and *Tannerella forsythia* in gingival and subgingival granulation tissues affected by chronic or aggressive periodontitis. *Sci Rep*. 2018.06; 8(1); 9507
5. Yuki Mizuno, Atsushi Kudo, Takumi Akashi, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Ukihide Tateishi, Minoru Tanabe. Sunitinib shrinks NET-G3 pancreatic neuroendocrine neoplasms. *J. Cancer Res. Clin. Oncol.*. 2018.06; 144(6); 1155-1163
6. Ozaki K, Ohkubo T, Yamada T, Yoshioka K, Ichijo M, Majima T, Kudo S, Akashi T, Honda K, Ito E, Watanabe M, Sekine M, Hamagaki M, Eishi Y, Sanjo N, Ishibashi S, Mizusawa H, Yokota T. Progressive Encephalomyelitis with Rigidity and Myoclonus Resolving after Thymectomy with Subsequent Anasarca: An Autopsy Case. *Internal medicine (Tokyo, Japan)*. 2018.07;
7. Atsushi Kudo, Keiichi Akahoshi, Sakiko Ito, Takumi Akashi, Shu Shimada, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Ukihide Tateishi, Shinji Tanaka, Minoru Tanabe. Downregulated Pancreatic Beta Cell Genes Indicate Poor Prognosis in Patients With Pancreatic Neuroendocrine Neoplasms. *Ann. Surg.*. 2018.07;

Experimental Animal Model for Human Disease

Professor
Junior Associate Professor
Assistant Professor

Masami Kanai-Azuma
Yoshikazu Hirate
Hikaru Ito

(1) Research

- 1)Molecular biological analysis of organ formation using knockout mice and knockout ES cells.
- 2)Application of Sox17 mutant mice as the animal model for human disease.
- 3)Analysis of molecular mechanisms using mice with implantaion defects.
- 4)Effect of maternal stress during pregnancy.

(2) Publications

[Original Articles]

1. Takase MH, Kanai-Azuma M, Kanai Y. Differentiation of ovaries. Reference Module in Biomedical Sciences. 2018;
2. Higashiyama H, Uemura M, Igarashi H, Kurohmaru M, Kanai-Azuma M and Kanai Y. Anatomy and development of the extrahepatic biliary system in mouse and rat: a perspective on the evolutionary loss of the gallbladder. J. Anat. 2018.01; 232(1); 134-145
3. Yoshimura T, Watanabe T, Kuramochi-Miyagawa S, Takemoto N, Shiromoto Y, Kudo A, Kanai-Azuma M, Tashiro F, Miyazaki S, Katanaya A, Chuma S, Miyazaki J. Mouse GTSF1 is an essential factor for secondary piRNA biogenesis. EMBO Rep. 2018.04; 19(4); e42054
4. Saito K, Nobuhisa I, Harada K, Takahashi S, Anani M, Lickert H, Kanai-Azuma M, Kanai Y, and Taga T . Maintenance of hematopoietic stem and progenitor cells in fetal intra-aortic hematopoietic clusters by the Sox17-Notch1-Hes1 axis Exp Cell Res. 2018.04; 365(1); 145-155
5. Igarashi H, Uemura M, Hiramatsu R, Hiramatsu R, Segami S, Pattarapanawan M, Hirate Y, Yoshimura Y, Hashimoto H, Higashiyama H, Sumitomo H, Kurohmaru M, Saijoh Y, Suemizu H, Kanai-Azuma M, Kanai Y. Sox17 is essential for proper formation of the marginal zone of extraembryonic endoderm adjacent to a developing mouse placental disk. Biol. Reprod. 2018.09; 99(3); 578-589

[Misc]

1. Kanai-Azuma M. Basic research and analysis of the cause of implantation disorders due to environmental factors. J Soc Wom Health Sci Res. 2018.02; 7(1); 3-6
2. Hirate Y. Technological innovation in mouse developmental engineering Biomedical gerontology. 2018.09; 42(3); 31-36

[Conference Activities & Talks]

1. Pattarapanawan M, Uemura M, Higashiyama H, Hiramatsu R, Tsunekawa N, Kurohmaru M, Kanai-Azuma M, Kanai Y. Phenotypes of Adult Sox17+/- Hepatobiliary System in a Mouse Model of Biliary Atresia. The joint Symposium of the 9th Veterinary Research among Universities of Veterinary Medicine in East Asia 2018.02.22 Korea
2. Nomura R, Suzuki H, Liang Z, Hosokawa-Tsuji A, Kanai Y, Yagita H, Josephine B, Peter K, Morio T, Kanai-Azuma M, Kashimada K. The suppression of NR5A1/Ad4BP/SF1 during fetal period is essential for optimizing the ovarian development through Notch signaling in mice. The 100th Endocrine Society Annual Meeting and Expo 2018.03.17 Chicago
3. Hirate Y, Kanai Y, Kanai-Azuma M. Molecular pathways downstream of Sox17 in uterine epithelia during mouse implantation processes. Eighth International Symposium on Vertebrate Sex Determination 2018.04.16 Kona, Hawaii
4. Kashimada K, Nomura R, Suzuki H, Liang Z, Tsuji-Hosokawa A, Kanai Y, Yagita H, Josephine B, Peter K, Kanai-Azuma M, Morio T. Enforced expression of NA5A1 in mouse fetal ovaries causes premature ovarian insufficiency by dysregulating notch signalling. Eighth International Symposium on Vertebrate Sex Determination 2018.04.16 Kona, Hawaii
5. Hirate Y, Hayakawa K, Nakano Y, Uemura M, Miura K, Kanai Y, Kanai-Azuma M. Identification of downstream genes of the uterine SOX17 around the receptive period. The 65th Annual Meeting of Japanese Association for Laboratory Animal Science 2018.05.17 Toyama Prefectural Civic Center
6. Okano T, Cho K, Kawamura S, Onai N, Fujii W, Kakuta S, Kanai-Azuma M, Ohteki T, Imai K, Kanegane H, Otsu M, Ariga T and Morio T. Infantile onset pulmonary alveolar proteinosis with hypogammaglobulinemia caused by heterozygous mutations of 2'-5'-oligoadenylate synthase 1 (OAS1). The 18th Biennial Meeting 2018.10.24 Lisbon, Portugal
7. Kanai-Auzma M. Interaction between embryo and endometrium during implantation process. The 41st Annual Meeting of the Molecular Biology Society of Japan, Workshops[New perspectives on mammalian embryonic development] 2018.11.28 Pacifico Yokohama

Signal Gene Regulation

Professor (Molecular Pathogenesis) KIMURA Akinori
Associate Professor FUNATO Noriko

(1) Research

1. Genetic regulators of craniofacial and bone development.
2. Molecular control of cleft lip and/or palate.
3. Study of wound healing and tissue regeneration.

(2) Education

Lecture

Goals/Outline:

Students will learn the basics in life sciences by understanding the regulation of signal transduction involved in cell proliferation, differentiation, and death.

Practice

Goals/Outline:

Students will learn to handle recombinant DNA molecules and analyze the data obtained from experiments.

Lab

Goals/Outline:

Students will learn basic molecular biology and genetic engineering techniques by observing and/or performing biochemical experiments using cultured cells and gene-engineered mice.

(3) Lectures & Courses

The aim of Research Core is to provide laboratory equipments, and information for researches in advanced molecular and cellular biology. In educational objectives in the Graduate School, our Center gives lecture, seminar, training course and individual assistance in research fields of molecular genetics and histology.

(4) Publications

[Original Articles]

1. Yuki Taga, Masashi Kusubata, Kiyoko Ogawa-Goto, Shunji Hattori, and Noriko Funato. Collagen-derived X-Hyp-Gly-type tripeptides promote differentiation of MC3T3-E1 pre-osteoblasts Journal of Functional Foods. 2018.07; 46; 456-462
2. *Noriko Funato, Hiromi Yanagisawa. Deletion of the T-box transcription factor gene, Tbx1, in mice induces differential expression of genes associated with cleft palate in humans. Archives of Oral Biology. 2018.08; 95; 149-155

[Conference Activities & Talks]

1. Yuki Taga, Masashi Kusubata, Kiyoko Ogawa-Goto, Shunji Hattori, and Noriko Funato. Collagen-derived X-Hyp-Gly-type tripeptides promote osteoblast differentiation.. The 2018 Annual Meeting of the Japan Society for Bioscience, Biotechnology and Agrochemistry 2018.03.16 Meijo University, Japan
2. Noriko Funato. Tbx1 knockout mice exhibit dysregulated expression of genes associated with cleft palate in humans. The 60th Annual Meeting of Japanese Association for Oral Biology 2018.09.06 Kyusyu University, Japan
3. Noriko Funato. The transcription factor TBX1 Regulates Craniofacial Development. The 49 the Meeting of Astellas Foundation for Research on Metabolic Disorders 2018.10.20 The Industry Club of Japan, Japan

Material Biofunctions

Keiji Itaka (Professor)

Akiko Nagai (Associate Professor)

Kosuke Nozaki (Assistant Professor)

(1) Outline

The mission of this lab is to develop innovative medical technologies based on the science of biomaterials, DDS, and molecular biology. We aim at regulating biofunctions of host cells and the biomaterials, obtaining proof-of-concept of the therapeutic strategies by animal studies, and pursuing their clinical applications in collaboration with hospitals and companies.

1.mRNA-based therapeutics: a new paradigm of gene therapy

Gene therapy is defined as introducing genetic information for therapeutic purposes. Besides the conventional strategy of protein replacement for congenital gene defects, gene therapy may have wide application, including vaccination against cancer and infectious diseases, regenerative medicine by in situ cell regulation by introducing “therapeutic” gene(s), and the ultimate goal of “gene” therapy by the technology of gene editing. In addition, cell therapy combined with ex vivo gene introduction is also a promising field. Messenger RNA (mRNA) is a new tool for introducing the genetic information. Direct delivery of mRNA into cells is highlighted as a safe and effective method without concerning the risk of random integration into the genome. Despite the fact that mRNA delivered in the body would be susceptible to highly active RNases that are ubiquitous in the extracellular space, we have established a drug delivery system (DDS) based on synthesized polymers, polyplex nanomicelle, to transport mRNA into target cells by preventing its degradation. We have already achieved in vivo mRNA administration for therapeutic purposes of various organs and tissues including brain, spinal cord, bone, articular cartilage, skeletal muscle, and liver. The mRNA-based therapy is indicated for treatment of various diseases including the fields of gene therapy, cell therapy, and regenerative medicine.

2. Generally-modified spheroid cell culture system for cell transplantation

Cell transplantation therapy is an attractive strategy for various medical fields. One serious problem is that the therapeutic effects may be limited by the death of transplanted cells or the decrease in cell activity due to unfavorable microenvironments such as ischemia, hypoxia, or inflammation. We established an injectable spheroid system for cell transplantation therapy, based on three-dimensional (3D) spheroid cell culture system for preserving cell-to-cell interaction using micropatterned plates coated with a thermosensitive polymer. In addition, the genetic modification of the cells using a biocompatible non-viral gene carrier, polyplex nanomicelle, was integrated for augmenting the therapeutic effects of cell transplantation. This system can be used for many applications of cell transplantation therapy.

3. Development of functional dental implants

Although dental implant treatment has already been clinically applied and excellent clinical progress has been reported, some cases demonstrate the unexpected disorder. Because natural teeth integrate the bone via periodontal ligament to exert their functions, the osseointegration, which is a healing form of current dental implant, is thought to be one of the causes. In this department, we are working on the development of periodontal ligament-bonded dental implant material, and we are trying to elucidate the mechanism of periodontal tissue homeostasis.

4. Interaction between biomaterials and the host tissues

To develop a new biomaterial for clinical applications, the material is requested to enhance biocompatibility and to decrease possible side effects in addition to its functionality. Biomaterials meet and interact with the living tissues at their interfaces. We evaluate phenomena of material-tissue interfaces and try to clarify the mechanism through material science and biological methods. These findings based on surface science contribute to develop new biomaterial designs.

(2) Education

The objective and principle of this graduate course is to educate students with materials knowledge demanded to medical and dental doctors who are leading medical professionals and bioscientists who are capable of carrying out their own research at an international level in the area of their special fields of science, respectively.

(3) Publications

[Original Articles]

1. Kazuhisa Fujita, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Hiroyuki Miura, Akiko Nagai. Regulation of periodontal ligament-derived cells by type III collagen-coated hydroxyapatite. *Biomed Mater Eng.* 2018.01; 29(1); 15-27
2. Naohiro Horiuchi, Kazuki Madokoro, Kosuke Nozaki, Miho Nakamura, Keiichi Katayama, Akiko Nagai, Kimihiro Yamashita.. Electrical conductivity of polycrystalline hydroxyapatite and its application to electret formation. *Solid State Ionics.* 2018.02; 315; 19-25
3. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Yoshihara K, Nagaoka N, Zhang F, Vleugels J, Van Meerbeek B, Minakuchi S. Crystallographic and morphological analysis of sandblasted highly translucent dental zirconia. *Dent Mater.* 2018.03; 34(3); 508-518
4. Samuel T Crowley, Kazunori Kataoka, Keiji Itaka. Combined CatWalk Index: an improved method to measure mouse motor function using the automated gait analysis system. *BMC Res Notes.* 2018.04; 11(1); 263
5. Kayoko Yanagihara, Satoshi Uchida, Shinsuke Ohba, Kazunori Kataoka, Keiji Itaka. Treatment of Bone Defects by Transplantation of Genetically Modified Mesenchymal Stem Cell Spheroids. *Mol Ther Methods Clin Dev.* 2018.06; 9; 358-366
6. Naohiro Horiuchi, Kotaro Shibata, Hironori Saito, Yuki Iwabuchi, Norio Wada, Kosuke Nozaki, Kazuaki Hashimoto, Yumi Tanaka, Akiko Nagai, Kimihiro Yamashita. Size control synthesis of hydroxyapatite plates and their application in the preparation of highly oriented films *Crystal Growth & Design.* 2018.08;
7. Akitsugu Matsui, Satoshi Uchida, Akimasa Hayashi, Kazunori Kataoka, Keiji Itaka. Prolonged engraftment of transplanted hepatocytes in the liver by transient pro-survival factor supplementation using ex vivo mRNA transfection. *J Control Release.* 2018.09; 285; 1-11

[Conference Activities & Talks]

1. Samuel Crowley, Kazunori Kataoka, Keiji Itaka. Enhancement of motor function recovery in mice by delivery of mRNA nanomicelles encoding brain derived neurotrophic factor.. 3rd Japan-US Technical Information Exchange Forum on Blast Injury (JUFBI 2018) 2018.05.09
2. Keiji Itaka. mRNA-based therapy for intractable diseases and regenerative medicine. The 6th Japan-China Symposium on Nanomedicine 2018.05.26
3. Inokoshi M, Shimizubata M, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Minakuchi S. Sandblasting increases the flexural strength of highly translucent zirconia. 96th General Session and Exhibition of the IADR 2018.07.25 London
4. S OTAKE, K HAYASHI, K NOZAKI, W KOMADA, K YOSHIDA, H MIURA. Bond strengths of cements to a newly developed pressable ceramics. 2018.07.27

5. Kosuke Nozaki, Kazuhisa Fujita, Naohiro Horiuchi, Kimihiro Yamashita, Kazuaki Hashimoto, Hiroyuki Miura, Akiko Nagai. Calcium deficiency regulates surface charges of β -tricalcium phosphate. 96th General Session and Exhibition of the IADR 2018.07.28
6. Keiji Itaka, Shinsuke Ohba, Satoshi Uchida, Ung-il Chung, Kazunori Kataoka. mRNA-based therapy for cartilage degeneration diseases. 5th TERMIS World Congress – 2018 Kyoto, Japan 2018.09.04
7. Kano C, Kobayashi H, Nozaki K, Tsumanuma Y, Sudo T, Khemwong T, Izumi Y. The effective scaling strokes for root planing. The 32nd IADR-SEA Division Annual Scientific Meeting 2018.09.14 Da Nang, Vietnam
8. Kenichiro Hayashi, Kosuke Nozaki, Zhenquan Tan, Naohiro Horiuchi, Kimihiro Yamashita, Hiroyuki Miura, Keiji Itaka and Satoshi Ohara. Antibacterial property of titania nanosheet synthesized by organic ligand-assisted hydrothermal reaction. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25
9. Inokoshi M, Nozaki K, Shimizu H, Minakuchi S. Influence of yttria content on translucency and flexural strength of highly translucent dental zirconia. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.06 Sapporo
10. Matsumura M, Nozaki K, Yamashita K, Matsumura M, Miura H. Optimization of surface roughness of composite resin block by controlling milling condition. 2018.10.07 Hokkaido
11. Keiji Itaka. mRNA-based therapy for intractable diseases and regenerative medicine. 3rd International Symposium on Biomedical Engineering 2018.11.08 広島大学、広島
12. Keiji Itaka. mRNA medicine as a new paradigm of gene therapy for intractable diseases and regenerative medicine. 6th International mRNA Health Conference 2018.11.13 Boston, USA

Genetic Regulation

Professor Akinori KIMURA
Associate Professor Takeharu HAYASHI
Assistant Professor Jianbo AN
Research Associate Taeko K. NARUSE

(1) Outline

Research and Education in the Department of Genetic Regulation are carried out by staff members of the Department of Molecular Pathogenesis, Medical Research institute.

The main purpose of this Department is to decipher the genetic regulation involved in the pathogenesis of intractable diseases, including hereditary cardiovascular diseases such as hypertrophic cardiomyopathy, dilated cardiomyopathy and hereditary arrhythmia, autoimmune diseases such as rheumatoid arthritis, type I diabetes mellitus, autoimmune thyroid diseases (Graves disease and Hashimoto thyroiditis), inflammatory bowel diseases (Crohn disease and ulcerative colitis) and SLE, as well as infectious diseases including HIV/AIDS. We also investigate molecular pathogenesis of coronary heart disease (atherosclerosis) and intractable vascular diseases (Takayasu arteritis and Buerger disease).

(2) Research

- 1) Identification and functional analysis of disease-related genes for cardiovascular diseases including hereditary cardiomyopathy and arrhythmia
- 2) Identification and functional analysis of disease-related genes for autoimmune diseases including autoimmune thyroiditis and inflammatory bowel disease
- 3) Identification and functional analysis of disease-related genes for infectious diseases including HIV-1 infection
- 4) Structural, functional and evolutionary analyses of MHC and immune-related genes
- 5) Evolutionary medicine for human diseases

(3) Education

Structural and functional diversity of human genome, are involved in the etiology and pathogenesis of human diseases. Main objective of Genetic Regulation is to identify the gene mutations or polymorphisms and to decipher the molecular mechanisms involved in the etiology and pathogenesis of intractable diseases, in order to develop new strategies for diagnosis, treatment and/or prevention of the diseases. Current research is focused on the intractable cardiovascular diseases (e.g. idiopathic cardiomyopathy, idiopathic arrhythmia, and coronary heart disease), autoimmune diseases (e.g. Burger disease, Graves disease, and rheumatoid arthritis) and infectious diseases (e.g. HIV/AIDS). In addition, genome diversity in immune-related genes is investigated from the view-point of primate evolution.

(4) Lectures & Courses

Main purpose is to understand the molecular pathogenesis of various intractable diseases by methodologies in the fields of Human Genetics, Genome Medicine, Biochemistry and Cell Biology.

(5) Publications

[Original Articles]

1. Naruse TK, Akari H, Matano T, Kimura A. Diversity of ULBP5 in Old-World monkeys (Cercopithecidae) and divergence of the ULBP gene family in primates. *Proceedings of the Japan Academy. Series B, Physical and biological sciences.* 2018; 94(10); 441-453
2. Haruhito Harada, Takeharu Hayashi, Hirofumi Nishi, Ken Kusaba, Yoshinori Koga, Yasutoshi Koga, Ikuya Nonaka, Akinori Kimura. Phenotypic expression of a novel desmin gene mutation: hypertrophic cardiomyopathy followed by systemic myopathy. *J. Hum. Genet..* 2018.02; 63(2); 249-254
3. Takuro Arimura, Antoine Muchir, Masayoshi Kuwahara, Sachio Morimoto, Taisuke Ishikawa, Cheng-Kun Du, Dong-Yun Zhan, Shu Nakao, Noboru Machida, Ryo Tanaka, Yoshihisa Yamane, Takeharu Hayashi, Akinori Kimura. Overexpression of heart-specific small subunit of myosin light chain phosphatase results in heart failure and conduction disturbance. *Am. J. Physiol. Heart Circ. Physiol..* 2018.02;
4. Tomokazu Yamaguchi, Takashi Suzuki, Teruki Sato, Akinori Takahashi, Hiroyuki Watanabe, Ayumi Kadowaki, Miyuki Natsui, Hideaki Inagaki, Satoko Arakawa, Shinji Nakaoka, Yukio Koizumi, Shinsuke Seki, Shungo Adachi, Akira Fukao, Toshinobu Fujiwara, Tohru Natsume, Akinori Kimura, Masaaki Komatsu, Shigeomi Shimizu, Hiroshi Ito, Yutaka Suzuki, Josef M Penninger, Tadashi Yamamoto, Yumiko Imai, Keiji Kuba. The CCR4-NOT deadenylase complex controls Atg7-dependent cell death and heart function. *Sci Signal.* 2018.02; 11(516);
5. Harada Haruhito, Hayashi Takeharu, Nishi Hirofumi, Kusaba Ken, Koga Yoshinori, Koga Yasutoshi, Nonaka Ikuya, Kimura Akinori. Phenotypic expression of a novel desmin gene mutation: hypertrophic cardiomyopathy followed by systemic myopathy *Journal of Human Genetics.* 2018.02; 63(2); 249-254
6. Nobuyuki Tsujii, Takeharu Hayashi, Tamaki Hayashi, Akinori Kimura, Toshiya Nishikubo. Barth syndrome associated with triple mutation. *Pediatr Int.* 2018.03;
7. Tsujii Nobuyuki, Hayashi Takeharu, Hayashi Tamaki, Kimura Akinori, Nishikubo Toshiya. Barth syndrome associated with triple mutation(和訳中) *Pediatrics International.* 2018.04; 60(4); 385-387
8. Rie Murayama, Mariko Kimura-Asami, Marina Togo-Ohno, Yumiko Yamasaki-Kato, Taeko K Naruse, Takeshi Yamamoto, Takeharu Hayashi, Tomohiko Ai, Katherine G Spoonamore, Richard J Kovacs, Matteo Vatta, Mai Izuka, Masumi Saito, Shotaro Wani, Yuichi Hiraoka, Akinori Kimura, Hidehito Kuroyanagi. Phosphorylation of the RSRP stretch is critical for splicing regulation by RNA-Binding Motif Protein 20 (RBM20) through nuclear localization. *Sci Rep.* 2018.06; 8(1); 8970
9. Takeharu Hayashi, Kousuke Tanimoto, Kayoko Hirayama-Yamada, Etsuko Tsuda, Mamoru Ayusawa, Shinichi Nunoda, Akira Hosaki, Akinori Kimura. Genetic background of Japanese patients with pediatric hypertrophic and restrictive cardiomyopathy. *J. Hum. Genet..* 2018.06;
10. Natsuko Inagaki, Takeharu Hayashi, Yasuyoshi Takei, Kousuke Tanimoto, Taishiro Chikamori, Akinori Kimura. Clinical and genetic backgrounds of hypertrophic cardiomyopathy with mid-ventricular obstruction. *J. Hum. Genet..* 2018.09;
11. Hayashi Takeharu, Tanimoto Kousuke, Hirayama-Yamada Kayoko, Tsuda Etsuko, Ayusawa Mamoru, Nunoda Shinichi, Hosaki Akira, Kimura Akinori. Genetic background of Japanese patients with pediatric hypertrophic and restrictive cardiomyopathy *Journal of Human Genetics.* 2018.09; 63(9); 989-996
12. Takahashi N, Matsuoka S, Thi Minh TT, Ba HP, Naruse TK, Kimura A, Shiino T, Kawana-Tachikawa A, Ishikawa K, Matano T, Nguyen Thi LA. Human leukocyte antigen-associated gag and nef polymorphisms in HIV-1 subtype A/E-infected individuals in Vietnam. *Microbes and infection.* 2018.10;
13. Chikashi Terao, Hajime Yoshifuji, Takayoshi Matsumura, Taeko K Naruse, Tomonori Ishii, Yoshikazu Nakaoka, Yohei Kirino, Keitaro Matsuo, Tomoki Origuchi, Masakazu Shimizu, Yasuhiro Maejima, Eisuke Amiya, Natsuko Tamura, Takahisa Kawaguchi, Meiko Takahashi, Kazuya Setoh, Koichiro Ohmura, Ryu Watanabe, Tetsuya Horita, Tatsuya Atsumi, Mitsuru Matsukura, Tetsuro Miyata, Yuta Kochi, Toshio Suda, Kazuo Tanemoto, Akira Meguro, Yukinori Okada, Akiyoshi Ogimoto, Motohisa Yamamoto, Hiroki Takahashi, Shingo Nakayamada, Kazuyoshi Saito, Masataka Kuwana, Nobuhisa Mizuki, Yasuharu Tabara, Atsuhisa Ueda, Issei Komuro, Akinori Kimura, Mitsuaki Isobe, Tsuneyo Mimori, Fumihiko Matsuda.

Genetic determinants and an epistasis of LILRA3 and HLA-B*52 in Takayasu arteritis Proc. Natl. Acad. Sci. U.S.A.. 2018.11;

14. Inagaki Natsuko, Hayashi Takeharu, Takei Yasuyoshi, Tanimoto Kousuke, Chikamori Taishiro, Kimura Akinori. Clinical and genetic backgrounds of hypertrophic cardiomyopathy with mid-ventricular obstruction Journal of Human Genetics. 2018.12; 63(12); 1273-1276
15. Naruse Taeko K., Akari Hirofumi, Matano Tetsuro, Kimura Akinori. Diversity of ULBP5 in Old-World monkeys(Cercopithecidae) and divergence of the ULBP gene family in primates Proceedings of the Japan Academy Series B, Physical and Biological Sciences. 2018.12; 94(10); 441-453

[Misc]

1. Watanabe T, Kimura A, Kuroyanagi H. Alternative Splicing Regulator RBM20 and Cardiomyopathy. Frontiers in molecular biosciences. 2018.11; 5; 105

Applied Gene Medicine

Professor Yoshio MIKI
 Associate Professor Akira NAKANISHI
 Assistant professor Shigeaki Sunada
 Graduate Student Yu Deng,
 Gerelmaa Enkhbat,
 Zeyu Xu,
 Dou Dou Zhang,
 Ying Zhao,
 QianQian Guo,
 Yo Tojo,

(1) Outline

Since 1981, cancer has been a top leading cause of death in our country and a novel action is an urgent social challenge. In Department of Molecular Genetics, we aim to study a basic biology underlying cancer and establish novel diagnostic and therapeutic modalities based on findings from the fundamental researches. We have largely focused on three major research directions to understand the molecular mechanisms of breast cancer development: 1) Uncovering DNA damage repair function and genome stabilization mechanism, 2) Uncovering hormone-dependent cellular proliferation, and 3) Determining how the tumor microenvironment contributes to cancer development and progression. Utilizing a wide variety of approaches in genomics, molecular biology, biochemistry and informatics, we are addressing an integrative understanding of multidisciplinary analyses.

(2) Research

1. Molecular Mechanisms of Breast Cancer Progression
 - ◆ Understanding Molecular Mechanisms of Metastasis, Invasion, Recurrence in Cancer
 - ◆ Uncovering Molecular functions of hereditary breast cancer genes, BRCA1 and BRCA2
2. Cancer Genomics Research
 - ◆ Cancer Genomics Research with Next-Generation Sequencing
 - ◆ Identification of Genes Involved in Human Cancer Using Genome-Wide Association Studies
3. Cell Death Signaling in Cancer
4. DNA Damage Repair and Genome Instability in Cancer
5. Hormone-Dependent Breast Cancer Cell Growth
6. Cancer Microenvironment

(3) Education

Our research is directed at understanding the molecular mechanism of carcinogenesis, based on basic molecular cell biology and molecular genetics. We have applied new findings and information obtained by basic research to develop the new diagnosis, treatment, and prevention of cancer. Our objective in the graduate course is to provide students opportunity to study basic science and applied genome science for cancer research.

(4) Publications

[Original Articles]

1. Takahashi Yasuko, Matsushita Yosuke, Komatsu Masato, Yoshimaru Tetsuro, Honda Junko, Osumi Syozo, Miki Yoshio, Imoto Issei, Miyoshi Yasuo, Sasa Mitsunori, Katagiri Toyomasa. Identification of novel susceptibility genes in Japanese hereditary breast cancer families by whole exome sequencing *CANCER SCIENCE*. 2018.01; 109; 997
2. Takaoka Miho, Nakanishi Akira, Miki Yoshio. FKBP51 regulates cell motility and invasion via RhoA signaling *CANCER SCIENCE*. 2018.01; 109; 866
3. Yamada Shota, Takaoka Miho, Nakanishi Akira, Miki Yoshio. Microtubule stabilization by the loss of BRCA2 is attributed to MAP4 assembly *CANCER SCIENCE*. 2018.01; 109; 998
4. Hiroki Osumi, Eiji Shinozaki, Tetsuo Mashima, Takeru Wakatsuki, Mitsukuni Suenaga, Takashi Ichimura, Mariko Ogura, Yumiko Ota, Izuma Nakayama, Daisuke Takahari, Keisho Chin, Yoshio Miki, Kensei Yamaguchi. Phase II trial of biweekly cetuximab and irinotecan as third-line therapy for pretreated KRAS exon 2 wild-type colorectal cancer. *Cancer Sci.* 2018.06;
5. Moritoki Egi, Jun Kataoka, Takashi Ito, Osamu Nishida, Hideto Yasuda, Hiroshi Okamoto, Akira Shimoyama, Masayo Izawa, Shinsaku Matsumoto, Nana Furushima, Shigeki Yamashita, Koji Takada, Masahide Ohtsuka, Noritomo Fujisaki, Nobuaki Shime, Nobuhiro Inagaki, Yasuhiko Taira, Tomoaki Yatabe, Kenichi Nitta, Takeshi Yokoyama, Shigeki Kushimoto, Kentaro Tokunaga, Matsuyuki Doi, Takahiro Masuda, Yasuo Miki, Kenichi Matsuda, Takehiko Asaga, Keita Hazama, Hiroki Matsuyama, Masaji Nishimura, Satoshi Mizobuchi, . Oxygen management in mechanically ventilated patients: A multicenter prospective observational study. *J Crit Care*. 2018.08; 46; 1-5
6. Momozawa Y, Iwasaki Y, Parsons MT, Kamatani Y, Takahashi A, Tamura C, Katagiri T, Yoshida T, Nakamura S, Sugano K, Miki Y, Hirata M, Matsuda K, Spurdle AB, Kubo M. Germline pathogenic variants of 11 breast cancer genes in 7,051 Japanese patients and 11,241 controls. *Nature communications*. 2018.10; 9(1); 4083
7. Miki Yoshio, Tomita Naohiro. An update on hereditary tumors *CANCER SCIENCE*. 2018.12; 109; 777
8. Deng Yu, Nakanishi Akira, Miki Yoshio. Analysis of disruption mechanism of the breast duct and basement membrane by estradiol *CANCER SCIENCE*. 2018.12; 109; 1161
9. Tojo Yo, Sato Ami, Saito Hiroko, Nakanishi Akira, Miki Yoshio. Analysis of the function of estrogen-mediated BRCA2 *CANCER SCIENCE*. 2018.12; 109; 1136
10. Sunada Shigeaki, Miki Yoshio. DNA-PK inhibition releases PARP inhibitor-induced DNA replication stress *CANCER SCIENCE*. 2018.12; 109; 833

[Misc]

1. Shigeaki Sunada, Akira Nakanishi, Yoshio Miki. Crosstalk of DNA double-strand break repair pathways in poly(ADP-ribose) polymerase inhibitor treatment of breast cancer susceptibility gene 1/2-mutated cancer. *Cancer Sci.* 2018.02;
2. Miho Takaoka, Yoshio Miki. BRCA1 gene: function and deficiency. *Int. J. Clin. Oncol.* 2018.02; 23(1); 36-44
3. Takaoka Miho, Miki Yoshio. BRCA1 遺伝子 機能および欠損 (BRCA1 gene: function and deficiency) *International Journal of Clinical Oncology*. 2018.02; 23(1); 36-44
4. Sunada S, Nakanishi A, Miki Y. Crosstalk of DNA double-strand break repair pathways in poly(ADP-ribose) polymerase inhibitor treatment of breast cancer susceptibility gene 1/2-mutated cancer. *Cancer Science*. 2018.04; 109(4); 893-899

[Conference Activities & Talks]

1. Sunada Shigeaki, Nakanishi Akira, Miki Yoshio. 乳癌感受性遺伝子 1/2 変異癌のポリ (ADP-リボース) ポリメラーゼ阻害薬治療における DNA 二重鎖切断修復経路のクロストーク (Crosstalk of DNA double-strand break repair pathways in poly(ADP-ribose) polymerase inhibitor treatment of breast cancer susceptibility gene 1/2-mutated cancer). *Cancer Science* 2018.04.01
2. Osumi Hiroki, Shinozaki Eiji, Mashima Tetsuo, Wakatsuki Takeru, Suenaga Mitsukuni, Ichimura Takashi, Ogura Mariko, Ota Yumiko, Nakayama Izuma, Takahari Daisuke, Chin Keisho, Miki Yoshio, Yamaguchi Kensei. Phase II trial of biweekly cetuximab and irinotecan as third-line therapy for pretreated KRAS exon 2 wild-type colorectal cancer(和訳中). *Cancer Science* 2018.08.01
3. 砂田 成章, 三木 義男. DNA-PK 阻害は PARP 阻害剤誘発の DNA 複製ストレスを回避させる (DNA-PK inhibition releases PARP inhibitor-induced DNA replication stress). *日本癌学会総会記事* 2018.09.01
4. Deng Yu, 中西 啓, 三木 義男. エストロゲンによる乳管及び基底膜崩壊機構の解析 (Analysis of disruption mechanism of the breast duct and basement membrane by estradiol). *日本癌学会総会記事* 2018.09.01
5. 東條 陽, 佐藤 亜美, 斉藤 広子, 中西 啓, 三木 義男. エストロゲン誘導性 BRCA2 の機能解析 (Analysis of the function of estrogen-mediated BRCA2). *日本癌学会総会記事* 2018.09.01
6. 東條 陽「他」. Analysis of the function of estrogen-mediated BRCA2. 第 77 回日本癌学会学術総会 2018.09.29
7. Deng Yu「他」. Analysis of disruption mechanism of the breast duct and basement membrane by estradiol. 第 77 回日本癌学会学術総会 2018.09.29
8. 三木 義男. HBOC(遺伝性乳癌卵巣癌症候群) 遺伝子パネルによる乳がん発症危険度の遺伝学的検査 有効性・課題・展望. *日本癌治療学会学術集会抄録集* 2018.10.01
9. Gerelmaa Enkhbat, Yoshio Miki, Hiroyuki Uetake, Akira Nakanishi. Elucidation of the regulation mechanism of BRCA2 protein levels in cell cycle. 第 41 回日本分子生物学会 2018.11.29
10. 東條陽、中西啓、三木義男. BRCA2 とエストロゲン受容体相互作用による生理的役割の解明. 第 41 回日本分子生物学会 2018.11.29
11. Deng Yu、中西啓、三木義男. エストロゲンによる乳管構造および基底膜崩壊機構の解明. 第 41 回日本分子生物学会 2018.11.30

Molecular Cytogenetics

Professor Johji Inazawa M.D., Ph.D.

Lecturer Jun Inoue Ph.D.

Assistant Professor Tomoki Muramatsu Ph.D.

Assistant Professor Kosuke Tanimoto Ph.D.

(1) Research

1. Identification of genes responsible for intractable diseases including cancer and genomic disorders through integrative genomics and epigenomics.
2. Discovery of molecular mechanisms of cancer-related genes, including microRNAs, in the multistep processes of carcinogenesis and cancer progression, such as cancer stem cell, epithelial-mesenchymal transition (EMT), invasion and metastasis using systems biology.
3. Establishment of autophagy-based diagnosis and therapy in human cancers by understanding cellular context-dependent role of autophagy.
4. Multiple genomic analyses of genetic disorders of unknown etiology, e.g. mental retardation or epilepsy, to detect causative genes and clarify the etiology. Also, an array chip for diagnosis of known congenital disorders, 'Genome Disorder Array', was developed and released for a practical use at 2009.
5. Development of innovative techniques for genomics and epigenomics in medical science.
6. Development of practically useful tools for molecular diagnosis of intractable diseases.

(2) Lectures & Courses

The principal aim of the Department of Molecular Cytogenetics(MCG) is to understand the molecular mechanism underlying intractable diseases, such as cancer and uncharacterized genetic diseases. Main objective of MCG in the graduate course is to provide students opportunity to study molecular cytogenetic approach for intractable diseases, identify genes responsible for those diseases, and develop innovative techniques/ practically useful tools for detection of genomic and epigenomic aberrations in those diseases. It is our goal to bridge the gap between basic and clinical research for the benefit of each of the patients.

(3) Publications

[Original Articles]

1. Kevin Y Urayama, Masatoshi Takagi, Takahisa Kawaguchi, Keitaro Matsuo, Yoichi Tanaka, Yoko Ayukawa, Yuki Arakawa, Daisuke Hasegawa, Yuki Yuza, Takashi Kaneko, Yasushi Noguchi, Yuichi Taneyama, Setsuo Ota, Takeshi Inukai, Masakatsu Yanagimachi, Dai Keino, Kazutoshi Koike, Daisuke Toyama, Yozo Nakazawa, Hidemitsu Kurosawa, Kozue Nakamura, Koichi Moriwaki, Hiroaki Goto, Yujin Sekinaka, Daisuke Morita, Motohiro Kato, Junko Takita, Toshihiro Tanaka, Johji Inazawa, Katsuyoshi Koh, Yasushi Ishida, Akira Ohara, Shuki Mizutani, Fumihiko Matsuda, Atsushi Manabe. Regional evaluation of childhood acute lymphoblastic leukemia genetic susceptibility loci among Japanese. Sci Rep. 2018.01; 8(1); 789

2. Inazawa Johji. Basics of cancer genomics for the clinical implementation of precision cancer medicine CANCER SCIENCE. 2018.01; 109; 935
3. Furusawa Akiko, Inoue Jun, Tsuda Hitoshi, Miyasaka Naoyuki, Inazawa Johji. Differential requirement of amino acids on cell survival of ovarian cancer cells CANCER SCIENCE. 2018.01; 109; 128
4. Tonouchi Erina, Muramatsu Tomoki, Gen Yasuyuki, Hiramoto Hidekazu, Inazawa Johji. Function-based microRNA library screening identified a novel tumor suppressive miRNA regulating BRD4, a BET family gene CANCER SCIENCE. 2018.01; 109; 597
5. Akdemir Burak, Nakajima Yasuaki, Inazawa Johji, Inoue Jun. High expression of miR-432-3p is involved in NRF2 stabilization by directly targeting KEAP1 CANCER SCIENCE. 2018.01; 109; 466
6. Hiramoto Hidekazu, Muramatsu Tomoki, Ichikawa Daisuke, Otsuji Eigo, Inazawa Johji. miR-509-5p and miR-1243 inhibit epithelial-mesenchymal transition in pancreatic cancer. CANCER SCIENCE. 2018.01; 109; 601
7. Inoue Jun, Inazawa Johji. Molecular basis for autophagy-based cancer therapy CANCER SCIENCE. 2018.01; 109; 73
8. Gen Yasuyuki, Inoue Jun, Inazawa Johji. The exploration of miRNAs that induce cell death in p53-inactive cancer cells using functional-miRNA screening CANCER SCIENCE. 2018.01; 109; 598
9. Kanai Y, Nishihara H, Miyagi Y, Tsuruyama T, Taguchi K, Katoh H, Takeuchi T, Gotoh M, Kuramoto J, Arai E, Ojima H, Shibuya A, Yoshida T, Akahane T, Kasajima R, Morita K, Inazawa J, Sasaki T, Fukayama M, Oda Y. The Japanese Society of Pathology Guidelines on the handling of pathological tissue samples for genomic research: Standard operating procedures based on empirical analyses Pathology International. 2018.02; 68(2); 63-90
10. Chinen Y, Nakamura S, Ganaha A, Hayashi S, Inazawa J, Yanagi K, Nakanishi K, Kaname T, Naritomi K. Mild prominence of the Sylvian fissure in a Bainbridge-Ropers syndrome patient with a novel frameshift variant in *ASXL3*. Clinical case reports. 2018.02; 6(2); 330-336
11. Tonouchi E, Gen Y, Muramatsu T, Hiramoto H, Tanimoto K, Inoue J, Inazawa J. miR-3140 suppresses tumor cell growth by targeting BRD4 via its coding sequence and downregulates the BRD4-NUT fusion oncoprotein. Scientific reports. 2018.03; 8(1); 4482
12. Akiko Furusawa, Morikazu Miyamoto, Masashi Takano, Hitoshi Tsuda, Yong Sang Song, Daisuke Aoki, Naoyuki Miyasaka, Johji Inazawa, Jun Inoue. Ovarian cancer therapeutic potential of glutamine depletion based on GS expression. Carcinogenesis. 2018.04;
13. Erina Tonouchi, Yasuyuki Gen, Tomoki Muramatsu, Hidekazu Hiramoto, Kousuke Tanimoto, Jun Inoue, Johji Inazawa. miR-3140 suppresses tumor cell growth by targeting BRD4 via its coding sequence and downregulates the BRD4-NUT fusion oncoprotein. Sci Rep. 2018.04; 8(1); 6769
14. Tanikawa C, Kamatani Y, Takahashi A, Momozawa Y, Leveque K, Nagayama S, Mimori K, Mori M, Ishii H, Inazawa J, Yasuda J, Tsuboi A, Shimizu A, Sasaki M, Yamaji T, Sawada N, Iwasaki M, Tsugane S, Naito M, Wakai K, Koyama T, Takezaki T, Yuji K, Murakami Y, Nakamura Y, Kubo M, Matsuda K. GWAS identifies two novel colorectal cancer loci at 16q24.1 and 20q13.12. Carcinogenesis. 2018.05; 39(5); 652-660
15. Sato T, Muramatsu T, Tanabe M, Inazawa J. Identification and characterization of TGFBI in circulating tumor cell subline from pancreatic cancer cell line. Cancer science. 2018.08;
16. Takagawa Yuki, Gen Yasuyuki, Muramatsu Tomoki, Harada Hiroyuki, Inazawa Johji. Exploring novel tumor suppressive microRNAs in OSCC CANCER SCIENCE. 2018.12; 109; 1083
17. Inazawa Johji. From genomic alterations to target genes for cancer therapy; miRNA therapeutics has emerged as a promising strategy CANCER SCIENCE. 2018.12; 109; 1079
18. Tanikawa C, Kamatani Y, Toyoshima O, Sakamoto H, Ito H, Takahashi A, Momozawa Y, Hirata M, Fuse N, Takai-Igarashi T, Shimizu A, Sasaki M, Yamaji T, Sawada N, Iwasaki M, Tsugane S, Naito M, Hishida A, Wakai K, Furusyo N, Murakami Y, Nakamura Y, Imoto I, Inazawa J, Oze I, Sato N, Tanioka F, Sugimura H, Hirose H, Yoshida T, Matsuo K, Kubo M, Matsuda K. Genome-wide association study identifies gastric cancer susceptibility loci at 12q24.11-12 and 20q11.21. Cancer science. 2018.12; 109(12); 4015-4024

19. Takata Ryo, Akamatsu Shusuke, Nakagawa Hidewaki, Takahashi Atsushi, Terada Naoki, Kato Yoichiro, Kanehira Mitsugu, Sugimura Jun, Inazawa Johji, Ogawa Osamu, Obara Wataru. Identification of fourteen new susceptibility loci for prostate cancer in the Japanese population CANCER SCIENCE. 2018.12; 109; 1142
20. Inoue Jun, Furusawa Akiko, Miyamoto Morikazu, Takano Masashi, Tsuda Hitoshi, Song Yong Sang, Aoki Daisuke, Miyasaka Naoyuki, Inazawa Johji. Ovarian cancer therapeutic potential of glutamine depletion based on GS expression CANCER SCIENCE. 2018.12; 109; 330
21. Gen Yasuyuki, Inoue Jun, Inazawa Johji. The exploration of miRNAs that induce cell death in p53-inactive cancer cells using functional-miRNA screening CANCER SCIENCE. 2018.12; 109; 395
22. Gokita Kentaro, Inoue Jun, Ishihara Hiroshi, Kojima Kazuyuki, Inazawa Johji. Therapeutic potential of LNP-mediated delivery of miR-634 for cancer therapy CANCER SCIENCE. 2018.12; 109; 253
23. Kishikawa Masahiro, Inoue Jun, Hamamoto Hidetoshi, Kobayashi Katsunori, Fujiwara Kyoko, Asakage Takahiro, Inazawa Johji. Therapeutic potential of the topical treatment of miR-634 ointment for skin cancer CANCER SCIENCE. 2018.12; 109; 1012

[Conference Activities & Talks]

1. Kanai Yae, Nishihara Hiroshi, Miyagi Yohei, Tsuruyama Tatsuhiro, Taguchi Kenichi, Katoh Hiroto, Takeuchi Tomoyo, Gotoh Masahiro, Kuramoto Junko, Arai Eri, Ojima Hidenori, Shibuya Ayako, Yoshida Teruhiko, Akahane Toshiaki, Kasajima Rika, Morita Kei-ichi, Inazawa Johji, Sasaki Takeshi, Fukayama Masashi, Oda Yoshinao. ゲノム研究への病理組織検体取扱いに関する日本病理学会のガイドライン 実証分析に基づく標準実施要領 (The Japanese Society of Pathology Guidelines on the handling of pathological tissue samples for genomic research: Standard operating procedures based on empirical analyses). Pathology International 2018.02.01
2. Furusawa Akiko, Inoue Jun, Tsuda Hitoshi, Miyasaka Naoyuki, Inazawa Johji. 卵巣癌細胞の細胞生存におけるアミノ酸の異なる需要 (Differential requirement of amino acids on cell survival of ovarian cancer cells). 日本産科婦人科学会雑誌 2018.02.01
3. Inazawa J. Exploring novel cancer-related microRNAs and their diagnostic and therapeutic potentials in Precision Cancer Medicine (PCM). The 2nd International Symposium of International Society of Precision Cancer Medicine 2018.03.16 Busan, Korea
4. Inazawa J. Exploring novel cancer-related microRNAs and their diagnostic and therapeutic potentials in Precision Cancer Medicine (PCM). TMU-TMDU Joint Symposium 2018 2018.03.24 Tokyo, Japan
5. Takata Ryo, Akamatsu Shusuke, Nakagawa Hidewaki, Terada Naoki, Kato Yoichiro, Kanehira Mitsugu, Sugimura Jun, Omori So, Abe Takaya, Inazawa Johji, Ogawa Osamu, Obara Wataru. 日本人集団における前立腺癌に対する 14 の新たな感受性遺伝子座の同定 (Identification of fourteen new susceptibility loci for prostate cancer in the Japanese population). 日本泌尿器科学会総会 2018.04.01
6. Muramatsu T, Tonouchi E, Gen Y, Hiramoto H, Tanimoto K, Inoue J, Inazawa J. miR-3140 suppresses tumor cell growth by targeting BRD4 via its coding sequence and downregulates the BRD4-NUT fusion oncoprotein. AACR Annual Meeting 2018 2018.04.18 Chicago, USA
7. Inazawa J. Exploring novel cancer-related microRNAs and their diagnostic and therapeutic potentials in Personalized Cancer Medicine (PCM). IUBMB Seoul 2018 2018.06.04 Seoul, Korea
8. 高橋 和樹, 井上 ポディマ カタジナ アンナ, 高尾 千紘, 吉松 康裕, 村松 智輝, 稲澤 譲治, 渡部 徹郎. 口腔扁平上皮がん細胞 HOC313-LM の運動能と腫瘍形成能の制御におけるトランスフォーミング増殖因子 β シグナルの役割 (Regulatory Role of Transforming Growth Factor- β Signals in the Migration and Tumor Formation of HOC313-LM cells, an Oral Squamous Cell Carcinoma). 口腔病学会雑誌 2018.07.01
9. 五木田 憲太郎, 井上 純, 石原 比呂之, 小嶋 一幸, 稲澤 譲治. LNP を介した miR-634 の送達による抗腫瘍効果 (Therapeutic potential of LNP-mediated delivery of miR-634 for cancer therapy). 日本癌学会総会記事 2018.09.01
10. 井上 純, 古澤 啓子, 宮本 守員, 高野 政志, 津田 均, ソン・ヨンサン, 青木 大輔, 宮坂 尚幸, 稲澤 譲治. グルタミン合成酵素の発現に基づいた細胞外グルタミン枯渇による卵巣がん治療戦略の開発 (Ovarian cancer therapeutic potential of glutamine depletion based on GS expression). 日本癌学会総会記事 2018.09.01

11. 稲澤 譲治. ゲノム・エピゲノム異常解析による治療標的探索から浮上した癌抑制マイクロ RNA 治療戦略 (From genomic alterations to target genes for cancer therapy: miRNA therapeutics has emerged as a promising strategy). 日本癌学会総会記事 2018.09.01
12. 高川 祐希, 玄 泰行, 村松 智輝, 原田 浩之, 稲澤 譲治. 口腔扁平上皮癌における新規のがん抑制型マイクロ RNA の探索 (Exploring novel tumor suppressive microRNAs in OSCC). 日本癌学会総会記事 2018.09.01
13. 高田 亮, 赤松 秀輔, 中川 英刀, 高橋 篤, 寺田 直樹, 加藤 陽一郎, 兼平 貢, 杉村 淳, 稲澤 譲治, 小川 修, 小原 航. 日本人における前立腺癌の発症に関連する 14 遺伝子領域の同定 (Identification of fourteen new susceptibility loci for prostate cancer in the Japanese population). 日本癌学会総会記事 2018.09.01
14. 玄 泰行, 井上 純, 稲澤 譲治. 機能的 miRNA スクリーニングを用いた、p53 不活性型癌に細胞死を誘導する miRNA の探索 (The exploration of miRNAs that induce cell death in p53-inactive cancer cells using functional-miRNA screening). 日本癌学会総会記事 2018.09.01
15. 岸川 正大, 井上 純, 濱本 英利, 小林 勝則, 藤原 恭子, 朝蔭 孝宏, 稲澤 譲治. 皮膚癌に対する miR-634 軟膏の塗布による抗腫瘍効果 (Therapeutic potential of the topical treatment of miR-634 ointment for skin cancer). 日本癌学会総会記事 2018.09.01
16. Uehara DT, Tanimoto K, Inazawa J. Targeted next-generation resequencing analysis in 105 subjects with undiagnosed intellectual disability and multiple congenital anomalies. The 68th Annual Meeting of The American Society of Human Genetics 2018.10.17 San Diego, USA
17. Sato Taku, Muramatsu Tomoki, Tanabe Minoru, Inazawa Johji. Identification and characterization of transforming growth factor beta-induced in circulating tumor cell subline from pancreatic cancer cell line(和訳中). Cancer Science 2018.11.01
18. Tanikawa Chizu, Kamatani Yoichiro, Toyoshima Osamu, Sakamoto Hiromi, Ito Hidemi, Takahashi Atsushi, Momozawa Yukihide, Hirata Makoto, Fuse Nobuo, Takai-Igarashi Takako, Shimizu Atsushi, Sasaki Makoto, Yamaji Taiki, Sawada Norie, Iwasaki Motoki, Tsugane Shoichiro, Naito Mariko, Hishida Asahi, Wakai Kenji, Furusyo Norihiro, Murakami Yoshinori, Nakamura Yusuke, Imoto Issei, Inazawa Johji, Oze Isao, Sato Naomi, Tanioka Fumihiko, Sugimura Haruhiko, Hirose Hiroshi, Yoshida Teruhiko, Matsuo Keitaro, Kubo Michiaki, Matsuda Koichi. Genome-wide association study identifies gastric cancer susceptibility loci at 12q24.11-12 and 20q11.21(和訳中). Cancer Science 2018.12.01

Hematology

Professor Osamu Miura

Professor(Immunotherapy for Hematopoietic Disorders) Norihiko Kawamata

Junior Associate Professor Masahide Yamamoto

Assistant Professor Toshikage Nagao, Ken Watanabe, Yoshihiro Umezawa

Project Assistant Professor Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory) Ayako Nogami

Senior Resident Yuma Noguchi, Kosuke Arai, Atsushi Hamamura, Hiroki Akiyama

Graduate Student Daisuke Watanabe, Sunichiro Yasuda, Satoru Aoyama

(1) Outline

The Department of Hematology is responsible for clinical services at our University Hospital with treatment of patients with various hematological disorders including leukemias, lymphomas, anemia, and hemorrhagic diseases by chemotherapies, immunotherapies, molecularly-targeted therapies, and hematopoietic cell transplantation. Our department is also responsible for teaching undergraduate students with the lecture course in hematology as well as the clinical clerkship and for training junior and senior residents. Our department is also actively involved, with doctoral course students, in basic and clinical researches aiming to elucidate the molecular and cellular mechanisms involved in pathogenesis of hematological malignancies as well as in acquisition of therapy resistance to develop novel efficient therapies against these diseases.

(2) Research

1. Elucidation of the molecular mechanisms involved in acquisition of resistance against chemotherapies and molecularly-targeted therapies by leukemic cells from chronic myeloid leukemia, acute myeloid leukemia, and various myeloproliferative neoplasms expressing aberrant tyrosine kinases, including BCR/ABL, FLT3-ITD, and Jak2-V617F, aiming to develop novel therapeutic strategies to overcome the resistance.
2. Research focusing on Myeloproliferative Neoplasms (MPN): Tumorigenesis, Chemo-resistance, new drugs.
3. Signal transduction mechanisms from cytokine/growth factor receptors regulating proliferation, survival, and adhesion of hematopoietic cells including leukemia and lymphoma cells.
4. Molecular analysis of Chronic Myeloid Leukemia (CML): rare variants, chemo-resistance, target therapy.
5. Development of novel CAR-T technology: Chimeric Antigen Receptor T-cell targeting leukemia.

The Department is also actively involved in a variety of clinical studies for treatment of various leukemias, lymphomas, and multiple myeloma.

(3) Education

The Department of hematology is responsible for teaching basic and clinical hematology to the 3rd and 4th grade students in the integrated hematology course and the hematology and oncology united block course. The Department is also responsible for teaching the 5th and 6th grade students in clinical clerkship to obtain basic knowledge and problem-solving abilities in hematology as well as general internal medicine. The Department is also actively involved in training about 24 junior residents every year to acquire clinical skills in hematology and internal medicine and about 4 senior residents to practice diagnosis and treatment of various hematological disorders and to obtain the certificate for hematology specialist. As a division in the Graduate School of Medical and Dental Sciences, the Department is actively involved in education of 6 to 8 graduate students, who participate in the research projects listed above, to obtain the Ph. D. degree in medicine.

(4) Lectures & Courses

The major objective of the course is to understand the pathophysiology of blood cells, blood cell-forming organs, and hemostasis to provide a basis for rational diagnosis and treatment of their disorders.

(5) Clinical Services & Other Works

The Department of Hematology provides diagnosis and treatment for hematological diseases, such as leukemia, malignant lymphoma, anemia, and thrombocythemia, with chemotherapeutics, molecularly-targeted drugs, immunosuppressive agents, and hematopoietic cell trans-plantation.

(6) Clinical Performances

We provide the highest quality of patient care for a wide spectrum of blood diseases and cancers.

(7) Publications**[Original Articles]**

1. Yuko Kinowaki, Morito Kurata, Sachiko Ishibashi, Masumi Ikeda, Anna Tatsuzawa, Masahide Yamamoto, Osamu Miura, Masanobu Kitagawa, Kouhei Yamamoto. Glutathione peroxidase 4 overexpression inhibits ROS-induced cell death in diffuse large B-cell lymphoma. *Lab. Invest.* 2018.02;
2. Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Ayako Nogami, Gaku Oshikawa, Toshikage Nagao, Osamu Miura. Mechanisms for mTORC1 activation and synergistic induction of apoptosis by ruxolitinib and BH3 mimetics or autophagy inhibitors in JAK2-V617F-expressing leukemic cells including newly established PVT-2. *Oncotarget*. 2018.06; 9(42); 26834-26851
3. Erika Onozawa, Haruna Shibayama, Honami Takada, Ken-Ichi Imadome, Sho Aoki, Mayumi Yoshimori, Norio Shimizu, Shigeyoshi Fujiwara, Takatoshi Koyama, Osamu Miura, Ayako Arai. STAT3 is constitutively activated in chronic active Epstein-Barr virus infection and can be a therapeutic target. *Oncotarget*. 2018.07; 9(57); 31077-31089
4. Tomoko Yamashita, Yoshihiro Umezawa, Ken Watanabe, Tetsuya Fukuda, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Busulfan-based conditioning regimen for autologous stem-cell transplantation in patients with central nervous system lymphoma *Journal of Hematopoietic Cell Transplantation*. 2018.10; 7(4); 145-151
5. Makoto Nakagawa, Shuhei Fujita, Takuo Katsumoto, Kazutsune Yamagata, Yoko Ogawara, Ayuna Hattori, Yuki Kagiya, Daisuke Honma, Kazushi Araki, Tatsuya Inoue, Ayako Kato, Koichiro Inaki, Chisa Wada, Yoshimasa Ono, Masahide Yamamoto, Osamu Miura, Yasuhiro Nakashima, Issay Kitabayashi. Dual inhibition of EZH1/2 over-activates WNT signaling to deplete cancer stem cells in multiple myeloma. *Cancer Sci.* 2018.10; 110(1); 194-208
6. Yonese I, Takase H, Yoshimori M, Onozawa E, Tsuzura A, Miki T, Mochizuki M, Miura O, Arai A. CD79B mutations in primary vitreoretinal lymphoma: Diagnostic and prognostic potential. *European journal of haematology*. 2018.11;

7. Ayako Nogami, Keigo Okada, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Osamu Miura. Inhibition of the STAT5/Pim Kinase Axis Enhances Cytotoxic Effects of Proteasome Inhibitors on FLT3-ITD-Positive AML Cells by Cooperatively Inhibiting the mTORC1/4EBP1/S6K/Mcl-1 Pathway. *Transl Oncol.* 2018.11; 12(2); 336-349
8. Ken Watanabe, Kota Yoshifuji, Ryunosuke Ohkawa, Minoru Tozuka, Osamu Miura, Ayako Arai. Successful readministration of L-asparaginase after development of severe hypertriglyceridemia in a young adult with T-cell acute lymphoblastic leukemia *Rinsho Ketsueki.* 2018.12; 59(12); 2555-2560

[Conference Activities & Talks]

1. Satoru Aoyama, Hiroki Tsushumi, Tatsuya Saito, Masahide Yamamoto, Ken Watanabe, Toshikage Nagao, Tetsuya Fukuda, Norihiko Kawamata, Osamu Miura. Outcome of allogeneic transplantation with FLU/BU4/TBI conditioning regimen for myeloid malignancies. The 40th Annual Meeting of the Japan Society for Hematopoietic Cell Transplantation 2018.02.02 Sapporo
2. Shunichiro Yasuda, Satoru Aoyama, Daisuke Watanabe, Marito Araki, Norio Komatsu, Osamu Miura, Norihiko Kawamata. Introduction of CALR and JAK2 V617F mutations to a human leukemia cell lines, UT-7/Epo and K562, by CRISPR/Cas9 systems. American association for cancer research annual meeting 2018 2018.04.17 Chicago, USA
3. Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Daisuke Watanabe, Shinya Ishida, Ayako Nogami, Osamu Miura. Deubiquitinase Inhibitor WP1130 Exerts Anti-leukemic Effect by Causing Aggresomal Translocation of FLT3-ITD and Oxidative Stress to Induce Apoptosis. The 9th JSH International Symposium 2018 2018.07.27 Kyoto
4. Shunichiro Yasuda, Satoru Aoyama, Daisuke Watanabe, Marito Araki, Norio Komatsu, Osamu Miura, and Norihiko Kawamata . CALR and JAK2 V617F mutations in UT7-Epo and K562 . The 9th JSH international symposium 2018.07.27 Kyoto
5. Ayako Nogami, Keigo Okada, Daisuke Watanabe, Hiroki Akiyama, Yoshihiro Umezawa, Shinya Ishida, Gaku Oshikawa, Shuji Tohda, Osamu Miura . Proteasome Inhibitors Downregulate the mTORC1/4EBP1/S6K/Mcl-1 Pathway Cooperatively with Inhibitors for The STAT5/Pim Kinase Pathway to Induce Apoptosis in FLT3-ITD-positive AML Cells. The 9th JSH International Symposium 2018 2018.07.28 Kyoto
6. Yoshihiro Umezawa, ken Watanabe, Toshikage Nagao, Chizuko Sakashita, Ayako Nogami, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Achieving deep molecular response after first-line TKI therapy for CML. The 80th annual meeting of the japanese society of hematology 2018.10.12 Osaka
7. Gaku Oshikawa, Yoshihiro Umezawa, Aiko Igarashi, Kazuhiko Kakihana, Kazuteru Ohashi, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Impact of azacitidine for oligoblastic AML ineligible for stem cell transplantation. The 80th annual meeting of Japanese society of hematology 2018.10.12 Osaka
8. Ryoto Yoshimoto, Ken Watanabe, Emi Uchida, Shihoko Suwa, Shuji Tohda, Masahiko Hatano, Osamu Miura, Tetsuya Fukuda. IVNS1ABP/Nd1 is highly expressed in refractory lymphoma and implicated in resistance to chemotherapy. The 80th annual meeting of the Japanese society of hematology 2018.10.12 Osaka
9. Ayako Kukimoto, Tomoko Yamashita, Satoru Aoyama, Ken Watanabe, Sai Nagasaki, Kentaro Kobayashi, Satoshi Matsuda, Akiko Iwasaki, Yasuro Miura, Haruyuki Ishii, Ken Suzuki. An autopsy case of secondary pulmonary alveolar proteinosis 21 years after myelodysplastic syndrome. The 80th annual meeting of the Japanese society of hematology 2018.10.12 Osaka
10. Shunichiro Yasuda, Satoru Aoyama, Daisuke Watanabe, Marito Araki, Norio Komatsu, Osamu Miura, Norihiko Kawamata. MPL Overexpression Is a Mechanism of JAK2 Inhibitor Resistance in a CALR mutant Cell Line. The 80th annual meeting of Japanese society of hematology 2018.10.12 Osaka

Molecular Endocrinology and Metabolism

Professor: Tetsuya Yamada

Associate Professor: Takanobu Yoshimoto, Hajime Izumiyama

Assistant Professor: Chikara Komiya, Kazutaka Tsujimoto, Kumiko Shiba

Clinical Fellow: Takeshi Kakei, Akira Takeuchi, Emi Katayama, Yuko Adachi, Sayo Koseki, Nana Komatsu

Resident: Minami Kanai, Hiroko Seki, Fumiko Okamoto

Project Associate Professor: Koshi Hashimoto¹, Michiko Ito²

Project Assistant Professor: Xunmei Yuan, Ibuki Shirakawa², Mitsuyuki Numasawa

Graduate Students (Doctor's course): Maki Kawasaki, Toshihiro Goto, Takuya Ohmura, Megumi Hatano, Yujiro Nakano, Takato Takeuchi, Tatsuya Fukuda, Nozomi Hanzawa, Masahiro Asakawa

¹Department of Preemptive Medicine and Metabolism,

²Department of Organ Network and Metabolism

(1) Outline

1. Purpose of Education

Our training program enables postdoctoral trainees to prepare for the future academic careers and the clinical practice in the broad discipline of endocrinology and metabolism. The research program provides mentor-based training in experimental design, laboratory and clinical research techniques and methodology, and interpretation and analysis of the results obtained from cellular and molecular biology, physiology, clinical physiology, clinical therapeutics, and health sciences. This training program is designed to educate and establish 'physician-scientist' in the field of endocrinology and metabolism.

2. Research Subjects

- 1) Role of adipose tissue inflammation in the metabolic syndrome
- 2) Molecular mechanisms of saturated fatty acid-induced chronic inflammation
- 3) Molecular mechanism of vascular injury in diabetes, endocrine and metabolic diseases
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors
- 6) Development of novel diagnostic and therapeutic tools in endocrine and metabolic diseases

3. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including:

- 1) diseases of the thyroid, pituitary and adrenal glands.
- 2) diabetes mellitus, diabetic complications, metabolic syndrome, and obesity
- 3) primary and secondary hypertension
- 4) disorders of calcium metabolism

(2) Publications**[Original Articles]**

1. Hashimoto Koshi, Ogawa Yoshihiro. Epigenetic Switching and Neonatal Nutritional Environment DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE (DOHAD): FROM BIOLOGICAL BASIS TO CLINICAL SIGNIFICANCE. 2018; 1012; 19-25
2. Wada Michiko, Kita Makoto, Kawasaki Kaoru, Kusakabe Toru, Tagami Tetsuya, Satoh-Asahara Noriko, Shimatsu Akira, Hashimoto Koshi. False-positive TSH receptor antibody-a pitfall of third-generation TSH receptor antibody measurements in neonates- ENDOCRINE JOURNAL. 2018; 65(5); 587-592
3. Munakata Yuichiro, Yamada Tetsuya, Imai Junta, Takahashi Kei, Tsukita Sohei, Shirai Yuta, Kodama Shinjiro, Asai Yoichiro, Sugisawa Takashi, Chiba Yumiko, Kaneko Keizo, Uno Kenji, Sawada Shojiro, Hatakeyama Hiroyasu, Kanzaki Makoto, Miyazaki Jun-ichi, Oka Yoshitomo, Katagiri Hideki. Olfactory receptors are expressed in pancreatic beta-cells and promote glucose-stimulated insulin secretion SCIENTIFIC REPORTS. 2018.01; 8(1); 1499
4. Hashimoto Koshi, Nishihara Eijun, Matsumoto Masako, Matsumoto Shunichi, Nakajima Yasuyo, Tsujimoto Kazutaka, Yamakage Hajime, Satoh-Asahara Noriko, Noh Jaeduk Yoshimura, Ito Koichi, Miyauchi Akira, Mori Masatomo, Yamada Masanobu, Ogawa Yoshihiro. Sialic Acid-Binding Immunoglobulin-Like Lectin1 as a Novel Predictive Biomarker for Relapse in Graves' Disease: A Multicenter Study THYROID. 2018.01; 28(1); 50-59
5. Kumiko Shiba, Kyoichiro Tsuchiya, Chikara Komiya, Yasutaka Miyachi, Kentaro Mori, Noriko Shimazu, Shinobu Yamaguchi, Naomi Ogasawara, Makoto Katoh, Michiko Itoh, Takayoshi Suganami, Yoshihiro Ogawa. Canagliflozin, an SGLT2 inhibitor, attenuates the development of hepatocellular carcinoma in a mouse model of human NASH. Sci Rep. 2018.02; 8(1); 2362
6. Bouchi R, Fukuda T, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y. Dipeptidyl peptidase 4 inhibitors attenuates the decline of skeletal muscle mass in patients with type 2 diabetes. Diabetes/metabolism research and reviews. 2018.02; 34(2);
7. Yuan Xunmei, Tsujimoto Kazutaka, Hashimoto Koshi, Kawahori Kenichi, Hanzawa Nozomi, Hamaguchi Miho, Seki Takami, Nawa Makiko, Ehara Tatsuya, Kitamura Yohei, Hatada Izuho, Konishi Morichika, Itoh Nobuyuki, Nakagawa Yoshimi, Shimano Hitoshi, Takai-Igarashi Takako, Kamei Yasutomi, Ogawa Yoshihiro. Epigenetic modulation of Fgf21 in the perinatal mouse liver ameliorates diet-induced obesity in adulthood NATURE COMMUNICATIONS. 2018.02; 9(1); 636
8. Okamura T, Nakajima Y, Shibusawa N, Horiguchi K, Matsumoto S, Yamada E, Tomaru T, Ishii S, Ozawa A, Ishizuka T, Hashimoto K, Okada S, Satoh T, Yamada M. Pituitary NR4A1 is negatively regulated by thyroid hormone without direct binding of thyroid hormone receptors on the gene. Molecular and cellular endocrinology. 2018.02; 461; 32-42
9. Kawahori K, Hashimoto K, Yuan X, Tsujimoto K, Hanzawa N, Hamaguchi M, Kase S, Fujita K, Tagawa K, Okazawa H, Nakajima Y, Shibusawa N, Yamada M, Ogawa Y. Mild Maternal Hypothyroxinemia During Pregnancy Induces Persistent DNA Hypermethylation in the Hippocampal Brain-Derived Neurotrophic Factor Gene in Mouse Offspring. Thyroid : official journal of the American Thyroid Association. 2018.03; 28(3); 395-406
10. Umakoshi Hironobu, Tsuiki Mika, Takeda Yoshiyu, Kurihara Isao, Itoh Hiroshi, Katabami Takuyuki, Ichijo Takamasa, Wada Norio, Yoshimoto Takanobu, Ogawa Yoshihiro, Kawashima Junji, Sone Masakatsu, Inagaki Nobuya, Takahashi Katsutoshi, Watanabe Minemori, Matsuda Yuichi, Kobayashi Hiroki, Shibata Hirotaka, Kamemura Kohei, Otsuki Michio, Fujii Yuichi, Yamamoto Koichi, Ogo Atsushi, Yanase Toshiko, Suzuki Tomoko, Naruse Mitsuhide. Significance of Computed Tomography and Serum Potassium in Predicting Subtype Diagnosis of Primary Aldosteronism JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM. 2018.03; 103(3); 900-908
11. Fukuda T, Bouchi R, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y. Ratio of visceral-to-subcutaneous fat area predicts cardiovascular events in patients with type 2 diabetes. Journal of diabetes investigation. 2018.03; 9(2); 396-402

12. Ohno Y, Sone M, Inagaki N, Yamasaki T, Ogawa O, Takeda Y, Kurihara I, Itoh H, Umakoshi H, Tsuiki M, Ichijo T, Katabami T, Tanaka Y, Wada N, Shibayama Y, Yoshimoto T, Ogawa Y, Kawashima J, Takahashi K, Fujita M, Watanabe M, Matsuda Y, Kobayashi H, Shibata H, Kamemura K, Otsuki M, Fujii Y, Yamamoto K, Ogo A, Okamura S, Miyauchi S, Fukuoka T, Izawa S, Yoneda T, Hashimoto S, Yanase T, Suzuki T, Kawamura T, Tabara Y, Matsuda F, Naruse M, Nagahama Study., JPAS Study Group.. Prevalence of Cardiovascular Disease and Its Risk Factors in Primary Aldosteronism: A Multicenter Study in Japan. *Hypertension* (Dallas, Tex. : 1979). 2018.03; 71(3); 530-537
13. Masuda S, Murakami M, Bouchi R, Minami I, Hashimoto K, Yoshimoto T, Ogawa Y. Repeated Hypoglycemic Episodes with Postprandial Hyperinsulinemia after the Recovery from Acute Weight Loss Revealed by Continuous Glucose Monitoring and the Oral Glucose Tolerance Test. *Internal medicine* (Tokyo, Japan). 2018.03; 57(5); 697-700
14. Yujiro Nakano, Takanobu Yoshimoto, Tatsuya Fukuda, Masanori Murakami, Ryotaro Bouchi, Isao Minami, Koshi Hashimoto, Yasuhisa Fujii, Kazunori Kihara, Yoshihiro Ogawa. Effect of Eplerenone on the Glomerular Filtration Rate (GFR) in Primary Aldosteronism: Sequential Changes in the GFR During Preoperative Eplerenone Treatment to Subsequent Adrenalectomy. *Intern. Med.*. 2018.04;
15. Yasumoto Y, Miyazaki H, Ogata M, Kagawa Y, Yamamoto Y, Islam A, Yamada T, Katagiri H, Owada Y.. Glial Fatty Acid-Binding Protein 7 (FABP7) Regulates Neuronal Leptin Sensitivity in the Hypothalamic Arcuate Nucleus. *Mol Neurobiol.* . 2018.04;
16. Fukuda T, Bouchi R, Takeuchi T, Tsujimoto K, Minami I, Yoshimoto T, Ogawa Y. Sarcopenic obesity assessed using dual energy X-ray absorptiometry (DXA) can predict cardiovascular disease in patients with type 2 diabetes: a retrospective observational study. *Cardiovascular diabetology*. 2018.04; 17(1); 55
17. Honma M, Sawada S, Ueno Y, Murakami K, Yamada T, Gao J, Kodama S, Izumi T, Takahashi K, Tsukita S, Uno K, Imai J, Kakazu E, Kondo Y, Mizuno K, Kawagishi N, Shimosegawa T, Katagiri H. Selective insulin resistance with differential expressions of IRS-1 and IRS-2 in human NAFLD livers. *International journal of obesity* (2005). 2018.05;
18. Kaneko R, Sawada S, Tokita A, Honkura R, Tamura N, Kodama S, Izumi T, Takahashi K, Uno K, Imai J, Yamada T, Miyachi Y, Hasegawa H, Kanai H, Ishigaki Y, Katagiri H. Serum cystatin C level is associated with carotid arterial wall elasticity in subjects with type 2 diabetes mellitus: A potential marker of early-stage atherosclerosis. *Diabetes research and clinical practice*. 2018.05; 139; 43-51
19. Goto Toshihiro, Itoh Michiko, Suganami Takayoshi, Kanai Sayaka, Shirakawa Ibuki, Sakai Takeru, Asakawa Masahiro, Yoneyama Toshihiro, Kai Toshihiro, Ogawa Yoshihiro. Obeticholic acid protects against hepatocyte death and liver fibrosis in a murine model of nonalcoholic steatohepatitis *SCIENTIFIC REPORTS*. 2018.05; 8(1); 8157
20. Umakoshi H, Ogasawara T, Takeda Y, Kurihara I, Itoh H, Katabami T, Ichijo T, Wada N, Shibayama Y, Yoshimoto T, Ogawa Y, Kawashima J, Sone M, Inagaki N, Takahashi K, Watanabe M, Matsuda Y, Kobayashi H, Shibata H, Kamemura K, Otsuki M, Fujii Y, Yamamoto K, Ogo A, Yanase T, Okamura S, Miyauchi S, Suzuki T, Tsuiki M, Naruse M. Accuracy of adrenal computed tomography in predicting the unilateral subtype in young patients with hypokalaemia and elevation of aldosterone in primary aldosteronism. *Clinical endocrinology*. 2018.05; 88(5); 645-651
21. Shibayama Y, Wada N, Naruse M, Kurihara I, Ito H, Yoneda T, Takeda Y, Umakoshi H, Tsuiki M, Ichijo T, Fukuda H, Katabami T, Yoshimoto T, Ogawa Y, Kawashima J, Ohno Y, Sone M, Fujita M, Takahashi K, Shibata H, Kamemura K, Fujii Y, Yamamoto K, Suzuki T. The Occurrence of Apparent Bilateral Aldosterone Suppression in Adrenal Vein Sampling for Primary Aldosteronism. *Journal of the Endocrine Society*. 2018.05; 2(5); 398-407
22. Watanabe T, Ozawa A, Ishii S, Tomaru T, Shibusawa N, Saito T, Yamada E, Horiguchi K, Nakajima Y, Matsumoto S, Yoshino S, Katano-Toki A, Hashimoto K, Mori M, Okada S, Satoh T, Yamada M. Usage of continuous glucose monitoring (CGM) for detecting an unrecognized hypoglycemia and management of glucocorticoid replacement therapy in adult patients with central hypoadrenalism. *Endocrine journal*. 2018.05; 65(5); 547-556
23. Okuma H, Hashimoto K, Ohashi T, Mihara M, Minami I, Izumiyama H, Sasaki S, Inoshita N, Nishioka H, Yamada S, Yoshimoto T. A case of TSH-secreting pituitary adenoma with cyclic fluctuations in serum TSH levels. *Endocrine journal*. 2018.07; 65(7); 737-746

24. Okuma Hideyuki, Hashimoto Koshi, Ohashi Takuya, Mihara Masatomo, Minami Isao, Izumiyama Hajime, Sasaki Shigekazu, Inoshita Naoko, Nishioka Hiroshi, Yamada Shozo, Yoshimoto Takanobu. 血清 TSH 値が周期的に変動する TSH 産生下垂体腺腫の 1 例 (A case of TSH-secreting pituitary adenoma with cyclic fluctuations in serum TSH levels) *Endocrine Journal*. 2018.07; 65(7); 737-746
25. Mori Kentaro, Tsuchiya Kyoichiro, Nakamura Suguru, Miyachi Yasutaka, Shiba Kumiko, Ogawa Yoshihiro, Kitamura Kenichiro. Deficiency of Melanocortin 4 Receptor Promotes Vascular Vulnerability in Mice DIABETES. 2018.07; 67;
26. Inamori KI, Ito H, Tamura Y, Nitta T, Yang X, Nihei W, Shishido F, Imazu S, Tsukita S, Yamada T, Katagiri H, Inokuchi JI. Deficient ganglioside synthesis restores responsiveness to leptin and melanocortin signaling in obese KKAY mice. *Journal of lipid research*. 2018.08; 59(8); 1472-1481
27. Umakoshi H, Tsuiki M, Yokomoto-Umakoshi M, Takeda Y, Takashi Y, Kurihara I, Itoh H, Katabami T, Ichijo T, Wada N, Shibayama Y, Yoshimoto T, Ashida K, Ogawa Y, Kawashima J, Sone M, Inagaki N, Takahashi K, Watanabe M, Matsuda Y, Kobayashi H, Shibata H, Kamemura K, Otsuki M, Fujii Y, Yamamoto K, Ogo A, Okamura S, Miyauchi S, Fukuoka T, Izawa S, Yanase T, Hashimoto S, Yamada M, Yoshikawa Y, Kai T, Suzuki T, Kawamura T, Naruse M. Correlation Between Lateralization Index of Adrenal Venous Sampling and Standardized Outcome in Primary Aldosteronism. *Journal of the Endocrine Society*. 2018.08; 2(8); 893-902
28. Miyachi Yasutaka, Tsuchiya Kyoichiro, Shiba Kumiko, Mori Kentaro, Komiya Chikara, Ogasawara Naomi, Ogawa Yoshihiro. A reduced M1-like/M2-like ratio of macrophages in healthy adipose tissue expansion during SGLT2 inhibition *SCIENTIFIC REPORTS*. 2018.10; 8(1); 16113
29. Takeda M, Yamamoto K, Akasaka H, Rakugi H, Naruse M, Takeda Y, Kurihara I, Itoh H, Umakoshi H, Tsuiki M, Ichijo T, Katabami T, Wada N, Shibayama Y, Yoshimoto T, Ogawa Y, Kawashima J, Sone M, Inagaki N, Takahashi K, Fujita M, Watanabe M, Matsuda Y, Kobayashi H, Shibata H, Kamemura K, Otsuki M, Fujii Y, Ogo A, Okamura S, Miyauchi S, Yanase T, Suzuki T, Kawamura T, JPAS Study Group.. Clinical Characteristics and Postoperative Outcomes of Primary Aldosteronism in the Elderly. *The Journal of clinical endocrinology and metabolism*. 2018.10; 103(10); 3620-3629
30. Araki S, Kijima T, Waseda Y, Komai Y, Nakanishi Y, Uehara S, Yasuda Y, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Nakano Y, Yoshimoto T, Uchida T, Fujii Y. Incidence and predictive factors of hypoglycemia after pheochromocytoma resection. *International journal of urology : official journal of the Japanese Urological Association*. 2018.11;
31. Kobayashi H, Abe M, Soma M, Takeda Y, Kurihara I, Itoh H, Umakoshi H, Tsuiki M, Katabami T, Ichijo T, Wada N, Yoshimoto T, Ogawa Y, Kawashima J, Sone M, Inagaki N, Takahashi K, Watanabe M, Matsuda Y, Shibata H, Kamemura K, Yanase T, Otsuki M, Fujii Y, Yamamoto K, Ogo A, Nanba K, Tanabe A, Suzuki T, Naruse M, JPAS Study Group.. Development and validation of subtype prediction scores for the workup of primary aldosteronism. *Journal of hypertension*. 2018.11; 36(11); 2269-2276
32. Yuki Yasumoto, Hirofumi Miyazaki, Masaki Ogata, Yoshiteru Kagawa, Yui Yamamoto, Ariful Islam, Tetsuya Yamada, Hideki Katagiri, Yuji Owada. Glial Fatty Acid-Binding Protein 7 (FABP7) Regulates Neuronal Leptin Sensitivity in the Hypothalamic Arcuate Nucleus. *Mol. Neurobiol.*. 2018.12; 55(12); 9016-9028
33. Ohno Y, Sone M, Inagaki N, Yamasaki T, Ogawa O, Takeda Y, Kurihara I, Umakoshi H, Ichijo T, Katabami T, Wada N, Ogawa Y, Yoshimoto T, Kawashima J, Watanabe M, Matsuda Y, Kobayashi H, Shibata H, Miyauchi S, Kamemura K, Fukuoka T, Yamamoto K, Otsuki M, Suzuki T, Naruse M, JPAS Study Group.. Obesity as a Key Factor Underlying Idiopathic Hyperaldosteronism. *The Journal of clinical endocrinology and metabolism*. 2018.12; 103(12); 4456-4464
34. Izumi Tomohito, Imai Junta, Yamamoto Junpei, Kawana Yohei, Endo Akira, Sugawara Hiroto, Kohata Masato, Asai Yoichiro, Takahashi Kei, Kodama Shinjiro, Kaneko Keizo, Gao Junhong, Uno Kenji, Sawada Shojiro, Kalinichenko Vladimir V., Ishigaki Yasushi, Yamada Tetsuya, Katagiri Hideki. Vagus-macrophage-hepatocyte link promotes post-injury liver regeneration and whole-body survival through hepatic FoxM1 activation *NATURE COMMUNICATIONS*. 2018.12; 9(1); 5300

[Books etc]

1. Hashimoto K, Ogawa Y. Advances in Experimental Medicine and Biology 1012. Ed. . Springer Nature Media Singapore Pte Ltd., 2018

[Misc]

1. Chiba Y, Yamada T, Katagiri H. A Sodium-Glucose Co-transporter-2 Inhibitor Acutely Reduces Energy Expenditure in Brown Adipose Tissue via Neural Signals in Mice 2018.07; 138(7); 945-954

[Conference Activities & Talks]

1. 山田 哲也, 片桐 秀樹. 膵島再生研究のアップデート (Recent progress of research toward pancreatic islet regeneration MicroRNAs improve hyperglycemia in a mouse model of insulin-deficient diabetes via pancreatic β -cell proliferation). 第 61 回日本糖尿病学会年次学術集会 2018.05.24
2. Yamada Tetsuya, Katagiri Hideki. Role of the inter-organ neural network from the liver in systemic energy metabolism(和訳中). Experimental Animals 2018.07.01

Hepatobiliary and Pancreatic Surgery

Director & Professor

Minoru Tanabe MD, PhD

Lecturer

Atsushi Kudo MD, PhD

Daisuke Ban MD, PhD

Assistant Professor

Yusuke Mitsunori MD, PhD

Hiroaki Ono MD, PhD

Kosuke Ogawa MD, PhD

Toshiro Ogura MD, PhD

Keiichi Akahoshi MD, PhD (until March)

Graduate School Students

Norimichi Chiyonobu MD (until March)

Yuki Mizuno MD (until March)

Haku Liu MD

Shuichi Watanabe MD

Jun Yoshino MD

Daisuke Asano MD (joining April)

Masafumi Akasu MD

Tomotaka Kato MD

Toshitaka Sugawara MD (joining April)

Takeshi Ishii MD (joining April)

Satoshi Matsui MD (joining April)

Yoshiki Murase MD (joining October)

(1) Outline

The department of Hepato-Biliary-Pancreatic Surgery at Tokyo Medical and Dental University focus on the liver, biliary tract and pancreas with benign and malignant disorders. We constantly strive to provide the highest level of complex and innovative surgical care, comprehensive surgical training for tomorrow's leaders as well as groundbreaking basic science and clinical research.

(2) Research

We conduct medical research in both clinical and laboratory settings and develop novel ideas in research which impact patient outcomes, teaching, and clinical care.

Our research programs encompass:

- Biomolecular mechanisms of carcinogenesis, cancer growth, invasion and metastasis
- Molecular target therapy for malignant diseases
- Cancer stem cell
- Extended indication for hepatectomy
- The system of liver microcirculation
- Laparoscopic surgery for hepatobiliary pancreatic diseases

- Liver transplantation and organ preservation
- Treatments for neuroendocrine tumor
- Innovation of imaging modality for hepatobiliary pancreatic diseases

(3) Education

Medical students program:

We conduct the various experiences of hepatobiliary pancreatic diseases, diagnosis and management, through lectures, pre-clinical clerkship and clinical clerkship. Clinical clerkship exposes students to the surgical patients and basic surgical techniques. It also provides opportunities to participate in peri-operative care as well as operative procedures. Students learn interpersonal and communication skills that result in the effective exchange of information and teaming with patients, their families, and professional associates.

Surgical training program:

The aim of our surgical training program cultivates not only training for certified board surgeons, but also the future surgical leaders, through experiences from the academic, the operative, and the outpatient aspects of management in university hospital and affiliated hospitals. Clinically, the trainees receive training and experience in the preoperative, operative, and post-operative care of patients and basic science and clinical research in our training programs strive to help young surgeons develop both technical and cognitive expertise.

(4) Clinical Performances

Our highly experienced surgeons offer state-of-the-art diagnosis and treatment, such as the multidisciplinary treatments (based on radical surgery) for advanced malignant diseases, minimally invasive procedures (including reduced port surgery).

Annually, 235 operations (hepatectomy: 73 cases, pancreatectomy: 71 cases) were performed in 2018, placing one of the top high volume medical centers in the country for hepatobiliary pancreatic surgery.

The more than 450 patients with neuroendocrine tumors were treated in 2018. We have treated the largest number of the patients with NENs in Japan.

(5) Publications

[Original Articles]

1. Mizuno Y, Shimada S, Akiyama Y, Watanabe S, Aida T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Ariei S, Yamaoka S, Tanabe M, Tanaka S. DEPDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma. *Scientific Reports*. 2018.01; 8(1);
2. Yoshiya Ishikawa, Daisuke Ban, Shuichi Watanabe, Keiichi Akahoshi, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Splenic artery as a simple landmark indicating difficulty during laparoscopic distal pancreatectomy *Asian Journal of Endoscopic Surgery*. 2018.02; 1-7
3. Ueda H, Akiyama Y, Shimada S, Mogushi K, Serizawa M, Matsumura S, Mitsunori Y, Aihara A, Ban D, Ochiai T, Kudo A, Tanabe M, Tanaka S. Tumor suppressor functions of DAXX through histone H3.3/H3K9me3 pathway in pancreatic NETs. *Endocrine-Related Cancer*. 2018.03; 25(6); 619-631
4. Yuki Mizuno, Atsushi Kudo, Takumi Akashi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Ukihide Tateishi, Minoru Tanabe. Sunitinib shrinks NET-G3 pancreatic neuroendocrine neoplasms *Journal of Cancer Research and Clinical Oncology*. 2018.03; 144; 1155-1163
5. Ogihara Y, Kitazume Y, Iwasa Y, Taura S, Himeno Y, Kimura T, Sawano S, Terada S, Tanabe M, Saida Y, Tateishi U. Prediction of histological grade of hepatocellular carcinoma using quantitative diffusion-weighted MRI: a retrospective multivendor study. *The British Journal of Radiology*. 2018.04;
6. Norimichi Chiyonobu, Shu Shimada, Yoshimitsu Akiyama, Kaoru Mogushi, Michiko Itoh, Keiichi Akahoshi, Satoshi Matsumura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shigeki Ariei, Takayoshi Suganami, Shoji Yamaoka, Yoshihiro Ogawa, Minoru Tanabe, Shinji Tanaka.

- Fatty acid binding protein 4 (FABP4) overexpression in intratumoral hepatic stellate cells within hepatocellular carcinoma with metabolic risk factors *The American Journal of Pathology*. 2018.05; 188(5);
7. Nakata K, Shikata S, Ohtsuka T, Ukai T, Miyasaka Y, Mori Y, Velasquez VVDM, Gotoh Y, Ban D, Nakamura Y, Nagakawa Y, Tanabe M, Sahara Y, Takaori K, Honda G, Misawa T, Kawai M, Yamaue H, Morikawa T, Kuroki T, Mou Y, Lee WJ, Shrikhande SV, Tang CN, Conrad C, Han HS, Chinnusamy P, Asbun HJ, Kooby DA, Wakabayashi G, Takada T, Yamamoto M, Nakamura M. Minimally invasive spleen preservation versus splenectomy during distal pancreatectomy: A systematic review and meta-analysis. *Journal of Hepato-Biliary-Pancreatic Sciences*. 2018.06;
 8. Ban D, Ogura T, Akahoshi K, Tanabe M. Current topics in the surgical treatments for hepatocellular carcinoma. *Annals of Gastroenterological Surgery*. 2018.06; 2(2); 137-146
 9. Ishikawa Y, Ehara K, Yamada T, Matsuzawa N, Arai S, Ban D, Kudo A, Tanabe M, Kawashima Y, Sakamoto H. Three-dimensional computed tomography analysis of the vascular anatomy of the splenic hilum for gastric cancer surgery. *Surgery Today*. 2018.06;
 10. Kudo A, Akahoshi K, Ito S, Akashi T, Shimada S, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Tateishi U, Tanaka S, Tanabe M. Downregulated Pancreatic Beta Cell Genes Indicate Poor Prognosis in Patients With Pancreatic Neuroendocrine Neoplasms. *Annals of Surgery*. 2018.07;
 11. Sakai K, Mizuno T, Watanabe T, Nagaoka E, Oi K, Yashima M, Hachimaru T, Kuroki H, Fujiwara T, Takeshita M, Tanabe M, Arai H. Management of Right Gastroepiploic Arterial Coronary Grafts in Subsequent Abdominal Surgeries. *The Annals of Thoracic Surgery*. 2018.07; 106(1); 52-57
 12. Keiichi Akahoshi, Daisuke Ban, Ryo Kuboki, Atsushi Oba, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka and Minoru Tanabe. Orotate phosphoribosyltransferase as a predictor of benefit from S-1 adjuvant chemotherapy for cholangiocarcinoma patients *Journal of Gastroenterology and Hepatology*. 2018.09;
 13. Keiichi Akahoshi, Hiroaki Ono, Masafumi Akasu, Daisuke Ban, Atsushi Kudo, Atsuko Konta, Shinji Tanaka, Minoru Tanabe. Rapid growth speed of cysts can predict malignant intraductal mucinous papillary neoplasms *Journal of Surgical Research*. 2018.11; 231; 195-200

[Conference Activities & Talks]

1. Minoru Tanabe. Current progress in laparoscopic liver resection in Japan. TMU-TMDU Joint Symposium 2018 2018.03.24 Tokyo
2. Minoru Tanabe. Technical analysis of laparoscopic liver resection for safe and stable procedure. HBP Surgery Week 2018 2018.03.31 Busan
3. Toshiro Ogura, Keiichi Akahoshi, Kousuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Minoru Tanabe. The significance of lymph node dissection in distal pancreatic cancer. International Association of Surgeons, Gastroenterologists and Oncologists 2018.04.04 Tokyo
4. Tomotaka Kato, Daisuke Ban, Masahumi Akasu, Jun Yoshino, Kosuke Ogawa, Toshiro Ogura, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Minoru Tanabe. Tips and technics in laparoscopic liver resection of segment 7 and 8. International Association of Surgeons, Gastroenterologists and Oncologists 2018.04.04 Tokyo
5. Masafumi Akasu, Kosuke Ogawa, Atsushi Kudo, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Norimichi Chiyonobu, Yuki Mizuno, Keiichi Akahoshi, Toshiro Ogura, Yusuke Mitsunori, Hiroaki Ono, Daisuke Ban, Minoru Tanabe. A Case Report of Spontaneous Regression of HCC after Angiography. APASL2018 2018.05.11 Yokohama
6. Minoru Tanabe, Toshiro Ogura, Atsushi Kudo, Daisuke Ban, Shinji Tanaka. Surgery for Obese Patients with HCC. APASL2018 2018.05.12 Yokohama
7. Tomotaka Kato, Atsushi Kudo, Hiroaki Ono, Masahumi Akasu, Jun Yoshino, Kosuke Ogawa, Toshiro Ogura, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. A Surgical Case of Spontaneous and Asymptomatic Intrahepatic Hemorrhage with HCC. APASL2018 2018.05.12 Yokohama

8. Jun Yoshino, Toshiro Ogura, Akahoshi Keiichi, Ogawa Kosuke, Mitsunori Yusuke, Ono Hiroaki, Ban Daisuke, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Long-term outcomes and prognostic factors of patients with gallbladder cancer resection. Third Triangle Scientific Meeting of the Japan-Hungary-Poland Surgical Society 2018.06.03 Budapest
9. Toshiro Ogura, Daisuke Ban, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Minoru Tanabe. Laparoscopic surgery for obese patients with hepatocellular carcinoma. 2018.06.04 Budapest
10. Daisuke Ban, Jun Yoshino, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Minoru Tanabe. Simple criteria for decision making of drain removal after distal pancreatectomy. 2018.06.04 Budapest
11. Daisuke Ban, Tomotaka Kato, Masafumi Akasu, Jun Yoshino, Daisuke Asano, Shuichi Watanabe, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Step-up program and introduction of OSATS for laparoscopic liver resection. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.07 Yokohama
12. Daisuke Ban. Open Liver Resection by Lap. Liver Surgeon ~Techniques learned from Lap. Surgery~ . The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.07 Yokohama
13. Tomotaka Kato, Daisuke Ban, Masafumi Akasu, Jun Yoshino, Shuichi Watanabe, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Tips for the safe approach in laparoscopic liver resection of segment 7 and 8. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.08 Yokohama
14. Jun Yoshino, Toshiro Ogura, Keiichi Akahoshi, Kosuke Ogawa, Yusuke Mitsunori, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Long-term outcomes and prognostic factors of patients with gallbladder cancer resection. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.08 Yokohama
15. Atsushi Kudo, Keiichi Akahoshi, Toshiro Ogura, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Kosuke Ogawa, Minoru Tanabe. Educational outcome accompanying introduction of advanced skill specialist system of hepato-biliary-pancreatic surgery . The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.08 Yokohama
16. Atsushi Kudo. Surgical treatment starting from WHO 2017 classification ~Toward the dawn of NET therapy~. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.08 Yokohama
17. Masafumi Akasu, Atsushi Kudo, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Norimichi Chiyonobu, Yuki Mizuno, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. The results of molecular targeted drugs to P-NET. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.08 Yokohama
18. Toshiro Ogura, Tomotaka Kato, Masafumi Akasu, Jun Yoshino, Shuichi Watanabe, Norimichi Chiyonobu, Yuki Mizuno, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The implication of lymph node metastasis on survival in cases with distal pancreatic cancer. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama
19. Hiroaki Ono, Keiichi Akahoshi, Masafumi Akasu, Tomotaka Kato, Yuki Mizuno, Norimichi Chiyonobu, Toshiro Ogura, Kosuke Ogawa, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Appropriateness and evaluation for preoperative surgical indications of IPMN. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama
20. Shuichi Watanabe, Atsushi Kudo, Masafumi Akasu, Tomotaka Kato, Jun Yoshino, Norimichi Chiyonobu, Yuki Mizuno, Keiichi Akahoshi, Kosuke Ogawa, Toshiro Ogura, Yusuke Mitsunori, Hiroaki Ono, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. The efficacy of liver SASI test for the advanced functional PNET patients. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama

21. Yusuke Mitsunori, Masafumi Akasu, Tomotaka Kato, Jun Yoshino, Shuichi Watanabe, Norimichi Chiyonobu, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. What is predictive factor of postoperative diabetes mellitus in patients with distal pancreatectomy?. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama
22. Kosuke Ogawa, Atsushi Kudo, Keiichi Akahoshi, Toshiro Ogura, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Minoru Tanabe. Analysis of contrast-enhanced CT images in pancreatic neuroendocrine tumor. The 30th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2018.06.09 Yokohama
23. Daisuke Ban, Tomotaka Kato, Jun Yoshino, Atsushi Kudo, Minoru Tanabe. The implication of induction chemotherapy followed by chemoradiotherapy for locally advanced pancreatic cancer, intended conversion surgery. 50thEPC the jubilee meeting of the European Pancreatic Club 2018.06.14 Berlin
24. Tomotaka Kato, Daisuke Ban, Jun Yoshino, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Minoru Tanabe. Treatment strategies of resectable pancreatic cancer with hazy density around major artery. 50thEPC the jubilee meeting of the European Pancreatic Club 2018.06.15 Berlin
25. Jun Yoshino, Daisuke Ban, Tomotaka Kato, Atsushi Kudo, Minoru Tanabe. Two types of peripancreatic fluid collection after distal pancreatectomy. 50thEPC the jubilee meeting of the European Pancreatic Club 2018.06.15 Berlin
26. M.TANABE. SILS Laparoscopic cholecystectomy. ASIA IRCAD-TAIWAN ADVANCED COURSE IN HEPATOBILIARY AND PANCREATIC SURGERY 2018.06.28 TAIWAN
27. M.TANABE. Prerecorded LIVE case : Single Port laparoscopic cholecystectomy. ASIA IRCAD-TAIWAN ADVANCED COURSE IN HEPATOBILIARY AND PANCREATIC SURGERY 2018.06.28 TAIWAN
28. M.TANABE. State of the Art in radiofrequency, micro-wave and cryoablation. ASIA IRCAD-TAIWAN ADVANCED COURSE IN HEPATOBILIARY AND PANCREATIC SURGERY 2018.06.30 TAIWAN
29. Shuichi Watanabe, Shu Shimada, Yoshimitsu Akiyama, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Minoru Tanabe, Shinji Tanaka. Precision medicine for the poorest prognosis subtype of pancreatic cancer. The 73rd General Meeting of the Japanese Society of Gastroenterological Surgery 2018.07.12 Kagoshima
30. Tomotaka Kato, Daisuke Ban, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Treatment strategies of resectable pancreatic cancer with hazy density around major artery. The 73rd General Meeting of the Japanese Society of Gastroenterological Surgery 2018.07.12 Kagoshima
31. Ban Daisuke. The Surgical Anatomy Useful for Pancreatoduodenectomy, Including Vessels and Nerves Systems. The 16th Chinese Pancreatic Surgery Congress 2018.09.08 Xi'an
32. Yuichiro Watanabe, Shinya Honda, Akimitsu Konishi, Minoru Tanabe, Shinji Tanaka, Shigeomi Shimizu. Autophagy controls centrosome number by degrading Ceps63. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.27
33. Yuki Mizuno, Shu Shimada, Yoshimitsu Akiyama, Shuichi Watanabe, Tomomi Aida, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shoji Yamaoka, Shinji Tanaka, Minoru Tanabe. DE-PDC5 deficiency contributes to resistance to leucine starvation via p62 accumulation in hepatocellular carcinoma. 2018.09.28
34. Yoshimitsu Akiyama, Shu Shimada, Minoru Tanabe, Shinji Tanaka. DAXX acts as a tumor suppressor through histone H3.3/H3K9me3 pathway in pancreatic neuroendocrine tumors. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.29 Osaka
35. Minoru Tanabe. Live Demonstration2 Laparoscopic vs. Robotic Major Liver Resection. ISLS 2018 International Society of Liver Surgeons 2018.10.05 Seoul
36. Minoru Tanabe. How to be an academic surgeon?. Joint Meeting 2018 ICS Thailand section and IASGO-TH Post Graduated Course 2018.12.15 Thailand
37. Minoru Tanabe. Technical analysis of laparoscopic liver resection for safe and stable procedure. Joint Meeting 2018 ICS Thailand section and IASGO-TH Post Graduated Course 2018.12.15 Thailand

[Patents]

1. ORGAN FUNCTION MAINTAINING AND AMELIORATING SOLUTION, Patent Number:PCT/JP2006/304269

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa
Associate Professor: Toshitaka Yoshii
Junior Associate Professor: Hiroyuki Inose
Assistant Professor: Yuko Segawa, Hirotaka Koyanagi,
Koji Fujita, Takashi Hirai, Masato Yuasa
Specially Appointed Assistant Professor: Atsuhiro Tano,
Masanobu Hirao,
Shuta Ushio

「Department of Orthopaedic and Trauma Research」
Associate Professor: Shinichi Sotome, Yoshinori Asou
Junior Associate Professor: Yoto Oh

「Joint Research Department of Advanced Medical Technology」
Specially Appointed Professor: Shigenori Kawabata

(1) Outline

Members of our section and Orthopaedic Joint Sugery section work together in a clinic and OR. Through these practices we train to make the clinical diagnosis and to plan the adequate surgery. We study findings of clinical problem of the locomotorium lesion such as joints, spine and spinal cord, peripheral nerve disorders, aging, injury, tumorigenesis mechanism, and image findings. To solve a lot of clinical question and develop new methodology to treat patients having severe orthopaedic problems, we especcially research spinal cord function, bone regeneration, and pain perception mechanism at dorsal root ganglion.

(2) Research

Research themes:
Bone and cartilage metabolism
Development and evaluation of biomaterials for clinical application
Mechanism of spinal ligament ossification
Development of measuring device for spinal cord magnetic signals
Research of bone and spinal metastatic tumors

We collaborate with other sections in our university such as the Clinical Anatomy, the Neurology, and the Physiology and Cell Biology.

(3) Education

Our department has several regular program such as "Bedside Professor Round" at Monday 14:30-16:30, "Clinical Conference" at Monday 7:30-9:00, and "Journal Clubs or Research Progress meeting" at 7:30-8:00 of Tuesday, Thursday, and Friday.

Graduate students in our department can acquire the basic techniques of orthopaedic research and can learn

up-dated knowledge of clinical medicine through regularly-held journal clubs and research meetings.

(4) Lectures & Courses

Japanese orthopaedic research is characterized by the fact that orthopaedic surgeon himself participates in experiments while he is working as a clinician. A lot of new knowledge concerning bone, cartilage and nerve were discovered by this so-called "surgeon scientist".

We have already taken a new artificial bone developed in our section to the market and have been preparing a revolutionary measuring device for spinal magnetic signals. We think it very important that research by a surgeon should be based on clinical problems even when methodology of molecular biology is used.

Our graduate students learn basic technique of orthopaedic research and also acquire the ability of life-continuing attitude for clinical studies.

(5) Clinical Services & Other Works

Our orthopaedic department consists of two graduate school sections, the Orthopaedic and Spinal Surgery and the Joint Surgery and Sports Medicine. We deal with all kinds of orthopaedic diseases such as spine, hand, hip, knee, and musculo-skeletal tumor. More than twenty registered orthopaedic surgeons belong to our department.

Our anterior cervical operation for OPLL results in a good clinical outcome. We also organize many spinal surgeons who are members of a nation-wide research organization for spinal ligament ossification supported by the Ministry of Health, Labour and Welfare.

(6) Clinical Performances

We aim to provide safer surgery to the patients with intractable spinal disease using many kinds of modality as navigation, microscopic surgery, spinal cord monitoring, and intraoperative CAT scan. Treatments of adult spinal deformity and osteoporotic vertebral fracture are our other interest. We have also developed an original artificial bone composed of hydroxyapatite and collagen, now promoting to use aggressively to fill large bone defect.

(7) Publications

[Original Articles]

1. Hiroyuki Inose, Tsuyoshi Yamada, Mieradili Mulati, Takashi Hirai, Shuta Ushio, Toshitaka Yoshii, Tsuyoshi Kato, Shigenori Kawabata, Atsushi Okawa. Bone Turnover Markers as a New Predicting Factor for Nonunion After Spinal Fusion Surgery. *Spine*. 2018.01; 43(1); E29-E34
2. Kimura Atsushi, Takeshita Katsushi, Inoue Hirokazu, Seichi Atsushi, Kawasaki Yosuke, Yoshii Toshitaka, Inose Hiroyuki, Furuya Takeo, Takeuchi Kazuhiro, Matsunaga Shunji, Seki Shoji, Tsushima Mikito, Imagama Shiro, Koda Masao, Yamazaki Masashi, Mori Kanji, Nishimura Hirosuke, Endo Kenji, Yamada Kei, Sato Kimiaki, Okawa Atsushi. The 25-question Geriatric Locomotive Function Scale predicts the risk of recurrent falls in postoperative patients with cervical myelopathy. *J Orthop Sci*. 2018.01; 23(1); 185-189
3. Hirai Takashi, Yoshii Toshitaka, Sakai Kenichiro, Inose Hiroyuki, Yamada Tsuyoshi, Kato Tsuyoshi, Kawabata Shigenori, Arai Yoshiyasu, Shinomiya Kenichi, Okawa Atsushi. Long-term results of a prospective study of anterior decompression with fusion and posterior decompression with laminoplasty for treatment of cervical spondylotic myelopathy. *J Orthop Sci*. 2018.01; 23(1); 32-38
4. Wei Xuetao, Egawa Satoru, Matsumoto Renpei, Yasuda Hiroaki, Hirai Keigo, Yoshii Toshitaka, Okawa Atsushi, Nakajima Takehiko, Sotome Shinichi. Augmentation of fracture healing by hydroxyapatite/collagen paste and bone morphogenetic protein-2 evaluated using a rat femur osteotomy model. *J Orthop Res*. 2018.01; 36(1); 129-137
5. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates

- injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep*. 2018.01; 8(1); 1288
6. G. Jin, A. Aobulikasimu, J. Piao, Z. Aibibula, D. Koga, H. Ochi, K. Ishiyama, T. Kanno, Yoshimi Niwano, Atsushi Okawa, Yoshinori Asou. Proanthocyanidin-rich grape seed extract prevent estrogen deficiency-induced metabolic disorders *Journal of medical and dental sciences*. 2018.01; 65(2); 45-50
 7. Kyoko Hashimoto, Hiroki Ochi, Satoko Sunamura, Nobuyoshi Kosaka, Yo Mabuchi, Toru Fukuda, Kenta Yao, Hiroaki Kanda, Keisuke Ae, Atsushi Okawa, Chihiro Akazawa, Takahiro Ochiya, Mitsuru Futakuchi, Shu Takeda, Shingo Sato. Cancer-secreted hsa-miR-940 induces an osteoblastic phenotype in the bone metastatic microenvironment via targeting ARHGAP1 and FAM134A. *Proc. Natl. Acad. Sci. U.S.A.*. 2018.02; 115(9); 2204-2209
 8. Guangwen Jin, Alkebaier Aobulikasimu, Jinying Piao, Zulpiya Aibibula, Daisuke Koga, Shingo Sato, Hiroki Ochi, Kunikazu Tsuji, Tetsuo Nakabayashi, Toshio Miyata, Atsushi Okawa, Yoshinori Asou. A small-molecule PAI-1 inhibitor prevents bone loss by stimulating bone formation in a murine estrogen deficiency-induced osteoporosis model. *FEBS Open Bio*. 2018.02; 8(4); 523-532
 9. Yamada Tsuyoshi, Yoshii Toshitaka, Yamamoto Naoki, Hirai Takashi, Inose Hiroyuki, Kato Tsuyoshi, Kawabata Shigenori, Okawa Atsushi. Clinical Outcomes of Cervical Spinal Surgery for Cervical Myelopathic Patients With Coexisting Lumbar Spinal Canal Stenosis (Tandem Spinal Stenosis): A Retrospective Analysis of 297 Cases. *Spine (Phila Pa 1976)*. 2018.02; 43(4); E234-E241
 10. Yamada Tsuyoshi, Yoshii Toshitaka, Yamamoto Naoki, Hirai Takashi, Inose Hiroyuki, Okawa Atsushi. Surgical outcomes for lumbar spinal canal stenosis with coexisting cervical stenosis (tandem spinal stenosis): a retrospective analysis of 565 cases. *J Orthop Surg Res*. 2018.03; 13(1); 60
 11. Amano Eiichiro, Ozaki Kokoro, Egawa Satoru, Suzuki Motohiro, Hirai Takashi, Ishibashi Satoru, Ohkubo Takuya, Yoshii Toshitaka, Okawa Atsushi, Yokota Takanori. Dynamic spinal compression revealed by computed tomography myelography in overshunting-associated myelopathy: A case report. *Medicine (Baltimore)*. 2018.03; 97(10); e0082
 12. Wakasugi T, Shirasaka R, Kawauchi T, Fujita K, Okawa A. Complications of Intramedullary Fixation for Distal Radius Fractures in Elderly Patients: A Retrospective Analysis Using McKay's Complication Checklist. *The journal of hand surgery Asian-Pacific volume*. 2018.03; 23(1); 71-75
 13. Inose H, Yamada T, Hirai T, Yoshii T, Abe Y, Okawa A.. The impact of sarcopenia on the results of lumbar spinal surgery. *Osteoporosis and Sarcopenia*. 2018.03; 4(1); 33-36
 14. Yugo Miura, Koji Fujita, Akimoto Nimura, Takashi Miyamoto, Yoshiaki Wakabayashi, Atsushi Okawa. Successful Reconstruction of a Traumatic Complete Femoral Nerve Rupture with a Sural Nerve Cable Graft: A Case Report. *JBJS Case Connect*. 2018.04; 8(2); e24
 15. Guangwen Jin, Yoshinori Asou, Kirika Ishiyama, Atsushi Okawa, Taro Kanno, Yoshimi Niwano. Proanthocyanidin-Rich Grape Seed Extract Modulates Intestinal Microbiota in Ovariectomized Mice. *J. Food Sci.*. 2018.04; 83(4); 1149-1152
 16. Takashi Hirai, Toshitaka Yoshii, Narihito Nagoshi, Kazuhiro Takeuchi, Kanji Mori, Shuta Ushio, Akio Iwanami, Tsuyoshi Yamada, Shoji Seki, Takashi Tsuji, Kanehiro Fujiyoshi, Mitsuru Furukawa, Soraya Nishimura, Kanichiro Wada, Takeo Furuya, Yukihiro Matsuyama, Tomohiko Hasegawa, Katsushi Takeshita, Atsushi Kimura, Masahiko Abematsu, Hirotaka Haro, Tetsuro Ohba, Masahiko Watanabe, Hiroyuki Kato, Kei Watanabe, Hiroshi Ozawa, Haruo Kanno, Shiro Imagama, Kei Ando, Shunsuke Fujibayashi, Masao Koda, Masashi Yamazaki, Morio Matsumoto, Masaya Nakamura, Atsushi Okawa, Yoshiharu Kawaguchi. Distribution of ossified spinal lesions in patients with severe ossification of the posterior longitudinal ligament and prediction of ossification at each segment based on the cervical OP index classification: a multicenter study (JOSL CT study). *BMC Musculoskelet Disord*. 2018.04; 19(1); 107
 17. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Yuki Yamauchi, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Longitudinal morphological change of acetabular subchondral bone cyst after total hip arthroplasty in developmental dysplasia of the hip. *Eur J Orthop Surg Traumatol*. 2018.05; 28(4); 621-625

18. Masato Yuasa, Masanori Saito, Cesar Molina, Stephanie N Moore-Lotridge, Michael A Benvenuti, Nicholas A Mignemi, Atsushi Okawa, Toshitaka Yoshii, Herbert S Schwartz, Jeffrey S Nyman, Jonathan G Schoenecker. Unexpected timely fracture union in matrix metalloproteinase 9 deficient mice. *PLoS ONE*. 2018.05; 13(5); e0198088
19. Toru Sasaki, Shigenori Kawabata, Shuta Ushio, Koji Fujita, Yuko Hoshino, Kensuke Sekihara, Miho Akaza, Isamu Ozaki, Yoshiaki Adachi, Taishi Watanabe, Yuki Hasegawa, Takumi Yamaga, Atsushi Okawa. T112. Visualization of electrical activities in the carpal tunnel area by magnetoneurography of median nerve *Clinical Neurophysiology*. 2018.05; 129; e45-e46
20. Haruhiko Shimura, Akimoto Nimura, Koji Fujita, Takashi Miyamoto. Mid-Term Functional Outcome after Volar Locking Plate Fixation of Distal Radius Fractures in Elderly Patients. *J Hand Surg Asian Pac Vol*. 2018.06; 23(2); 238-242
21. Shuta Ushio, Shigenori Kawabata, Satoshi Sumiya, Tsuyoshi Kato, Toshitaka Yoshii, Tsuyoshi Yamada, Mitsuhiro Enomoto, Atsushi Okawa. A multi-train electrical stimulation protocol facilitates transcranial electrical motor evoked potentials and increases induction rate and reproducibility even in patients with preoperative neurological deficits. *J Clin Monit Comput*. 2018.06; 32(3); 549-558
22. Wakasugi T, Shirasaka R, Fujita K. Insufficiency Fracture of the Radial Diaphysis Following a Sauve-Kapandji Procedure for Osteoarthritis of the Distal Radioulnar Joint: A Case Report. *The journal of hand surgery Asian-Pacific volume*. 2018.06; 23(2); 270-273
23. Koji Makino, Nobutaka Sato, Koji Fujita, Takaiki Kanagawa, Masaya Miyamamoto, Toru Sasaki, Hirotaka Haro, Yasuo Kondo, Hidetsugu Terada. Development of a Dynamometer to Measure Grip Strength of Each Finger 2018 IEEE 27th International Symposium on Industrial Electronics (ISIE). 2018.06; 1100-1105
24. Tetsuya Sato, Akimoto Nimura, Reiko Yamaguchi, Koji Fujita, Atsushi Okawa, Keiichi Akita. Intramuscular Tendon of the Adductor Pollicis and Underlying Capsule of the Metacarpophalangeal Joint: An Anatomical Study With Possible Implications for the Stener Lesion. *J Hand Surg Am*. 2018.07; 43(7); 682.e1-682.e8
25. Yamaguchi R, Nimura A, Amaha K, Yamaguchi K, Segawa Y, Okawa A, Akita K. Anatomy of the Tarsal Canal and Sinus in Relation to the Subtalar Joint Capsule. *Foot & ankle international*. 2018.07; 39(11); 1360-1369
26. Shingo Morishita, Yoshiyasu Arai, Toshitaka Yoshii, Kenichiro Sakai, Takashi Hirai, Atsushi Okawa. Lumbar epidural lipomatosis is associated with visceral fat and metabolic disorders. *Eur Spine J*. 2018.07; 27(7); 1653-1661
27. Hirai T, Yoshii T, Inose H, Yamada T, Yuasa M, Ushio S, Egawa S, Hirai K, Okawa A.. Revision Surgery for Short Segment Fusion Influences Postoperative Low Back Pain and Lower Extremity Pain: A Retrospective Single-Center Study of Patient-Based Evaluation. *Spine. Surg. Related Res.*. 2018.07; 2(3); 215-220
28. Kiyotaka Horiuchi, Tsuyoshi Yamada, Kenichiro Sakai, Atsushi Okawa, Yoshiyasu Arai. Hemorrhagic Sudden Onset of Spinal Epidural Angiolipoma. *Case Rep Orthop*. 2018.07; 2018; 5231931
29. Makoto Kamegaya, Mitsuaki Morita, Takashi Saisu, Jun Kakizaki, Yasuhiro Oikawa, Yuko Segawa. Single Versus Combined Procedures for Severely Involved Legg-Calvé-Perthes Disease. *J Pediatr Orthop*. 2018.07; 38(6); 312-319
30. Takashi Hirai, Takashi Taniyama, Toshitaka Yoshii, Koichi Mizuno, Mikio Okamoto, Hiroyuki Inose, Masato Yuasa, Kazuyuki Otani, Shigeo Shindo, Osamu Nakai, Atsushi Okawa. Clinical Outcomes of Surgical Treatment for Arachnoid Web: A Case Series *Spine Surgery and Related Research*. 2018.07; 3(1); 43-48
31. Hiroyuki Inose, Tsuyoshi Kato, Masato Yuasa, Tsuyoshi Yamada, Hidetsugu Maehara, Takashi Hirai, Toshitaka Yoshii, Shigenori Kawabata, Atsushi Okawa. Comparison of Decompression, Decompression Plus Fusion, and Decompression Plus Stabilization for Degenerative Spondylolisthesis: A Prospective, Randomized Study. *Clin Spine Surg*. 2018.08; 31(7); E347-E352

32. Toshitaka Yoshii, Takashi Hirai, Tsuyoshi Yamada, Kenichiro Sakai, Shuta Ushio, Satoru Egawa, Masato Yuasa, Tsuyoshi Kato, Hiroyuki Inose, Shigenori Kawabata, Atsushi Okawa. A Prospective Comparative Study in Skin Antiseptic Solutions for Posterior Spine Surgeries: Chlorhexidine-Gluconate Ethanol Versus Povidone-Iodine. *Clin Spine Surg.* 2018.08; 31(7); E353-E356
33. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Akimasa Kimura, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Direct anterior versus anterolateral approach in one-stage supine total hip arthroplasty. Focused on nerve injury: A prospective, randomized, controlled trial. *J Orthop Sci.* 2018.09; 23(5); 783-787
34. Takuma Hashimoto, Suzanne Low, Koji Fujita, Risa Usumi, Hiroshi Yanagihara, Chihiro Takahashi, Maki Sugimoto, Yuta Sugiura. TongueInput: Input Method by Tongue Gestures Using Optical Sensors Embedded in Mouthpiece 2018 57th Annual Conference of the Society of Instrument and Control Engineers of Japan (SICE). 2018.09; 1219-1224
35. Go Yoshida, Muneharu Ando, Shiro Imagama, Shigenori Kawabata, Kei Yamada, Tsukasa Kanchiku, Yasushi Fujiwara, Nobuaki Tadokoro, Masahito Takahashi, Kanichiro Wada, Naoya Yamamoto, Sho Kobayashi, Hiroki Ushirozako, Kazuyoshi Kobayashi, Akimasa Yasuda, Kenichi Shinomiya, Toshikazu Tani, Yukihiro Matsuyama. Alert Timing and Corresponding Intervention with Intraoperative Spinal Cord Monitoring for High Risk Spinal Surgery. *Spine.* 2018.10;
36. Koji Makino, Nobutaka Sato, Koji Fujita, Masaya Miyamamoto, Toru Sasaki, Hirotaka Haro, Kazuki Yamada, Hidetsugu Terada. Development of a Finger Force Distribution Measurement System for Hand Dexterity IECON 2018-44th Annual Conference of the IEEE Industrial Electronics Society. 2018.10; 4270-4275
37. Tomoyuki Kuroiwa, Koji Fujita, Akimoto Nimura, Takashi Miyamoto, Toru Sasaki, Atsushi Okawa. A new method of measuring the thumb pronation and palmar abduction angles during opposition movement using a three-axis gyroscope. *J Orthop Surg Res.* 2018.11; 13(1); 288
38. Soraya Nishimura, Narihito Nagoshi, Akio Iwanami, Ayano Takeuchi, Takashi Hirai, Toshitaka Yoshii, Kazuhiro Takeuchi, Kanji Mori, Tsuyoshi Yamada, Shoji Seki, Takashi Tsuji, Kanehiro Fujiyoshi, Mitsuru Furukawa, Kanichiro Wada, Masao Koda, Takeo Furuya, Yukihiro Matsuyama, Tomohiko Hasegawa, Katsushi Takeshita, Atsushi Kimura, Masahiko Abematsu, Hirotaka Haro, Tetsuro Ohba, Masahiko Watanabe, Hiroyuki Katoh, Kei Watanabe, Hiroshi Ozawa, Haruo Kanno, Shiro Imagama, Kei Ando, Shunsuke Fujibayashi, Masashi Yamazaki, Kota Watanabe, Morio Matsumoto, Masaya Nakamura, Atsushi Okawa, Yoshiharu Kawaguchi, . Prevalence and Distribution of Diffuse Idiopathic Skeletal Hyperostosis on Whole-spine Computed Tomography in Patients With Cervical Ossification of the Posterior Longitudinal Ligament: A Multicenter Study. *Clin Spine Surg.* 2018.11; 31(9); E460-E465
39. Hiroaki Onuma, Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Masato Yuasa, Shigenori Kawabata, Atsushi Okawa. Clinical and radiologic outcomes of bone grafted and non-bone grafted double-door laminoplasty, the modified Kirita-Miyazaki method, for treatment of cervical spondylotic myelopathy: Five-year follow-up. *J Orthop Sci.* 2018.11; 23(6); 923-928
40. Akira Takahashi, Mieradili Mulati, Masanori Saito, Hoashi Numata, Yutaka Kobayashi, Hiroki Ochi, Shingo Sato, Philipp Kaldis, Atsushi Okawa, Hiroyuki Inose. Loss of cyclin-dependent kinase 1 impairs bone formation, but does not affect the bone-anabolic effects of parathyroid hormone. *J. Biol. Chem.* 2018.12; 293(50); 19387-19399
41. Shiro Imagama, Kei Ando, Kazuhiro Takeuchi, Satoshi Kato, Hideki Murakami, Toshimi Aizawa, Hiroshi Ozawa, Tomohiko Hasegawa, Yukihiro Matsuyama, Masao Koda, Masashi Yamazaki, Hirotaka Chikuda, Shigeo Shindo, Yukihiro Nakagawa, Atsushi Kimura, Katsushi Takeshita, Kanichiro Wada, Hiroyuki Katoh, Masahiko Watanabe, Kei Yamada, Takeo Furuya, Takashi Tsuji, Shunsuke Fujibayashi, Kanji Mori, Yoshiharu Kawaguchi, Kota Watanabe, Morio Matsumoto, Toshitaka Yoshii, Atsushi Okawa. Perioperative Complications After Surgery for Thoracic Ossification of Posterior Longitudinal Ligament: A Nationwide Multicenter Prospective Study. *Spine.* 2018.12; 43(23); E1389-E1397
42. Madoka Toriumi, Takuro Watanabe, Koji Fujita, Akimoto Nimura, Yuta Sugiura. Rehabilitation support system for patients with carpal tunnel syndrome using smartphone Proceedings of the 30th Australian Conference on Computer-Human Interaction. 2018.12; 532-534

[Conference Activities & Talks]

1. Tomoyuki Kuroiwa, Koji Fujita, Megumi Matsumoto, Ryuji Kato, Takashi Miyamoto, Akimoto Nimura, Toshitaka Yoshii, Atsushi Okawa. Diabetes Mellitus Affects the MAPK Signaling and Pathways in Cancer in Isolated Mature Human Osteoblasts. Orthopaedic Research Society 2018.03.10 New Orleans, USA
2. Tomoyuki Kuroiwa, Koji Fujita, Akimoto Nimura, Takashi Miyamoto, Atsushi Okawa. Dynamic Real-time Measurement of thumb Pronation during Opposition Movement with a Gyroscope: A New Evaluation Method for Impairment of Opposition due to Median Nerve Palsy . Orthopaedic Research Society 2018.03.10 New Orleans, USA
3. Masato Yuasa, Masanori Saito, Alexander Hysong, Deke Blum, Sasidhar Uppunganti, Adam Gailani, David Haynes, Toshitaka Yoshii, Jeffry Nyman, Atsushi Okawa, Herbert Schwartz, Jonathan Schoenecker. Rigidity of Fixation Affects Vascularization in Fracture Healing in the Murine Model . Orthopaedic Research Society 2018.03.10 New Orleans, USA
4. Rempei Matsumoto, Satoru Egawa, Toshitaka Yoshii, Keigo Hirai, Atsushi Okawa, Shinichi Sotome. Local control experiment by paclitaxel impregnated HAP/Col for the metastasis to breast cancer bone model rat . Orthopaedic Research Society 2018.03.10 New Orleans, USA
5. Satoshi Egawa, et.al. The Hydroxyapatite/collagen (HAP/Col) Composite With Antibiotics Prevents Growth Of Bacteria For A Week And Has No Adverse Effect On Bone Regeneration In Rats. . Orthopaedic Research Society 2018.03.10 New Orleans, USA
6. Takashi Hirai, Toshitaka Yoshii, Akio Iwanami, Kazuhiro Takeuchi, Kanji Mori, Soraya Nishimura, Masaya Nakamura, Morio Matsumoto, Atsushi Okawa and Yoshiharu Kawaguchi.. Distribution of ossified lesion in patients with severe ossification posterior longitudinal ligament and prevalence of each segment– A Multicenter Study. 9th Annual Meeting of Cervical Spine Research Society Asia Pacific Section 2018.03.22 Delhi, India
7. Onuma H, Hirai T, Yoshii T, Inose H, Yuasa M, Kawabata A, Okawa A. Clinical and Radiologic Outcomes of Bone Grafted and Non-bone grafted Double-door Laminoplasty for Treatment of Cervical Spondylotic Myelopathy: Five-year Follow-up . 9th Annual Meeting of Cervical Spine Research Society Asia Pacific Section 2018.03.22 New Delhi, India
8. Ushio Shuta, Toshitaka Yoshii, Takashi Hirai, Hiroyuki Inose, Masato Yuasa, Shigenori Kawabata, Atsushi Okawa. Investigation on factors related to outcomes in of surgical procedures for cervical spondylotic amyotrophy. 9th Annual Meeting of Cervical Spine Research Society Asia Pacific Section 2018.03.22 New Delhi, India
9. Takashi H, Yatendra M, Spigelman I.. Novel molecular target therapy for neuropathic pain.. 14th UCLA translational frontier reseach note 2018.03.26 Los Angeles, USA
10. Y. Oh, K. Fujita, Y. Wakabayashi, Y. Kurosa, A. Okawa. Validation of locational classification for atypical femoral fractures. 44th annual meeting of the Korean Fracture Society 2018.04.27 Gwangju, Korea
11. Yoto Oh . Staged internal plate fixation of lower extremity fractures that uses a temporary external fixator for initial treatment as an intraoperative reduction tool . AOTrauma Symposium - External fixator - an important tool in trauma care 2018.04.28 Gwangju, Korea
12. Toru Sasaki, Shigenori Kawabata, Koji Fujita, Shuta Ushio, Yuko Hoshino, Kensuke Sekihara, Miho Akaza, Isamu Ozaki, Yoshiaki Adachi, Taishi Watanabe, Yuki Hasegawa, Takumi Yamaga, Atsushi Okawa. Visualization of electrical activities in the carpal tunnel area by magnetoneurography of median nerve. 31st International Congress of Clinical Neurophysiology 2018.05.01 Washington, DC.
13. Taishi Watanabe, Shigenori Kawabata, Yuki Hasegawa, Toru Sasaki, Shuta Ushio, Miho Akaza, Yoshiaki Adachi, Isamu Ozaki, Kensuke Sekihara, Atsushi Okawa . Visualization of nerve impulse traveling along the brachial plexus after ulnar nerve stimulation using magnetoneurography system. 31st International Congress of Clinical Neurophysiology 2018.05.01 Washington, DC.
14. Miho Akaza, Shigenori Kawabata, Isamu Ozaki, Yuki Hasegawa, Taishi watanabe, Hiroshi Deguchi, Yoshiaki Adachi, Kensuke Sekihara, Atsushi Okawa, Yuki Sumi, Takanori Yokota. Magnetic recordings of sensory action currents in the cervical cord. 31st International Congress of Clinical Neurophysiology 2018.05.01 Washington, DC.

15. Ushio S. Kawabata S., Watanabe T., Hasegawa Y., Adachi Y., Yamaga T., Okawa A. Visualization of electrical activities of lumbar nerve root and cauda equina by a magnetospinograph system. 31st International Congress of Clinical Neurophysiology 2018.05.01 Washington, DC.
16. Yoto Oh, A. Tano, T. kaku, Y. Kurosa, A. Okawa. Temporary external fixator for the initial treatment of severe lower extremity fractures can be safely used in the operative field for definitive internal plate fixation in terms of postoperative infection . 19th European Congress of Trauma & Emergency Surgery 2018.05.06 Valencia, Spain
17. Hiroyuki Inose, Masato Yuasa, Takashi Hirai, Toshitaka Yoshii, Shigenori Kawabata, Atsushi Okawa. The prevalence of sarcopenia among urban dwelling populations and its impact on the results of lumbar spinal surgery . 91st. Annual Meeting of the Japanese Orthopaedic Association 2018.05.24 Kobe, Japan
18. Tsuyoshi Kato, Hiroyuki Inose, Toshitaka Yoshii, Atsushi Okawa. Treatment of OVF without neurological deficit in Japan: Development of a guide for initial conservative treatment for OVF. 91st Annual Meeting of the Japanese Orthopaedic Association 2018.05.26 Kobe, Japan
19. Koji Fujita . Fragility fracture prevention for patients with wrist fracture. Mayo Clinic Release Collaboration Meeting 2018.05.27 Rochester, USA
20. Akira Takahashi, Tetsuya Jinno, Kazumasa Miyatake, Ryohei Takada, Masanobu Hirano, Atsushi Okawa. Association Between Intraoperative Injury And Postoperative Change In TFL After Total Hip Arthroplasty Using Direct Anterior Approach. EFORT Barcelona, Spain 2018.05.30 Barcelona, Spain
21. Hiroyuki Inose, Tshuyoshi Kato, Atsushi Okawa. Comparison of decompression, decompression plus fusion, and decompression plus stabilization for degenerative spondylolisthesis: a prospective, randomized study. Asia Pacific Spine Society 2018.06.07 Taipei
22. Koji Fujita, Takuro Watanabe, Yuta Sugiura, Akimoto Nimura, Atsushi Okawa. Developing a tablet-based application for postoperative rehabilitation of patients with carpal tunnel syndrome . Euro hand 2018 2018.06.14 Copenhagen, Denmark
23. Naoki Yamamoto, Takuya Oyaizu, Toshiyuki Ohara, Mikio Shioda, Mitsuhiro Enomoto, Yasushi Kojima, Kazuyoshi Yagishita, Atsushi Okawa. Hyperbaric and high-oxygen environments accelerate muscle strength recovery in contused rat skeletal muscle. . Undersea and Hyperbaric Medical society 2018 Annual Scientific Meeting 2018.06.28 Orlando, USA
24. Koji Fujita Hidetoshi Kaburagi, Akimoto Nimura, Ryuichi. Kato, Atsushi Okawa. Decreased grip strength and dynamic body balancing in women with distal radial fractures . 7th Fragility Fracture Network Global Congress 2018.07.06 Dublin, Ireland
25. Hiroyuki Inose, Tsuyoshi Kato, Toshitaka Yoshii. Comparison of Decompression, Decompression Plus Fusion, and Decompression Plus Stabilization for Degenerative Spondylolisthesis:A Prospective, Randomized Study. Spine Across The Sea 2018 2018.07.29 Kauai, Hawai'i
26. Toshitaka Yoshii. Anterior or Posterior Approach. Spine Across The Sea 2018 2018.07.29 Kauai, Hawaii
27. Shuta Ushio, Shigenori Kawabata, Toru Sasaki, Satoshi Sumiya, Atsushi Okawa. Visualization of muscle electrical activity after electrical stimulation of the ulnar nerve using superconducting quantum interference device sensors . 21st International Conference on Biomagnetism (BIOMAG2018) 2018.08.26 Philadelphia, USA
28. Toru Sasaki, Shigenori Kawabata, Yuko Hoshino, Kensuke Sekihara, Miho Akaza, Isamu Ozaki, Yoshiaki Adachi, Taishi Watanabe, Yuki Hasegawa, Atsushi Okawa . Visualization of electrophysiological activity at the carpal tunnel area in response to stimulation of the digital nerve using magnetoneurography. 21st International Conference on Biomagnetism (BIOMAG2018) 2018.08.26 Philadelphia
29. Toru Sasaki, Shigenori Kawabata, Shuta Ushio, Yuko Hoshino, Kensuke Sekihara, Yoshiaki Adachi, Taishi Watanabe, Yuki Hasegawa, Takumi Yamaga, Atsushi Okawa. Magnetospinography visualizes electrophysiological activity in the lumbar radiculopathy. 21st International Conference on Biomagnetism (BIOMAG2018) 2018.08.26 Philadelphia

30. Shigenori Kawabata, Toru Sasaki, Shuta Ushio, Satoshi Sumiya, Taishi Watanabe, Yuki Hasegawa, Takumi Yamaga, Yoshiaki Adachi, Kensuke Sekihara, Atsushi Okawa. Diagnosis of conduction block in myelopathy patients by magnetospinography. 21st International Conference on Biomagnetism (BIOMAG2018) 2018.08.26 Philadelphia
31. Satoshi Sumiya, Shigenori Kawabata, Shuta Ushio, Toru Sasaki, Yuko Hoshino, Kensuke Sekihara, Taishi Watanabe, Takumi Yamaga, Yoshiaki Adachi, Hiromichi Komori, Kenichi Shinomiya, Atsushi Okawa. Magnetospinography visualizes electrophysiological activity in the cervical spine after peripheral nerve stimulation. 21st International Conference on Biomagnetism (BIOMAG2018) 2018.08.26 Philadelphia
32. Taishi Watanabe, Shigenori Kawabata, Yuki Hasegawa, Toru Sasaki, Shuta Ushio, Miho Akaza, Yoshiaki Adachi, Isamu Ozaki, Kensuke Sekihara, Atsushi Okawa. Visualization of neural activity in the brachial plexus after ulnar nerve stimuli using magnetoneurography system. 21st International Conference on Biomagnetism (BIOMAG2018) 2018.08.26 Philadelphia, USA
33. Koji Fujita, Hidetoshi Kaburagi, Akimoto Nimura, Ryuichi Kato, Atsushi Okawa. Decreased Grip Strength and Dynamic Body Balancing in Women with Distal Radial Fractures. ASSH 2018 2018.09.13 Boston, USA
34. Hiroyuki Inose, Tsuyoshi Kato, Atsushi Okawa. A prospective randomized study of surgical treatment for degenerative spondylolisthesis. EUROSPINE2018 2018.09.19 Barcelona, Spain
35. Alkebaier Aobulikasimu, Zulipiya Aibibula, Jinying Piao, Shingo Sato, Hiroki Ochi, Kunikazu Tsuji, Atsushi Okawa, Yoshinori Asou. Osteocyte Sirt6 has crucial roles in bone and phosphate metabolism . 40th Annual meeting for American society for bone and mineral research 2018.09.28 Montreal Canada
36. Yoto Oh. CT/FEA is not difficult to approach. 13th Fall Research Workshop of Korean Society for Bone and Mineral Research 2018.11.16
37. Yoto Oh. Biomechanics is essential to understand atypical femoral fractures in East Asia: Mechanical analysis by the CT-based finite element method. 30th Fall Scientific Congress of Korean Society for Bone and Mineral Research 2018.11.17 Seoul, Korea
38. T. Kaku, K. Miyatake, Y. Oh, A. Tano, T. Jinno, A. Okawa. Clinical experience with total hip arthroplasty for displaced femoral neck fracture in the elderly. 16th Biennial Conference of the International Society for Fracture Repair 2018.11.28 Kyoto, Japan
39. Y. Oh, K. Fujita, Y. Wakabayashi, Y. Kurosa, A. Tano, A. Okawa. Locational characteristics of atypical femoral fractures in Japan. 16th Biennial Conference of the International Society for Fracture Repair 2018.11.29 Kyoto, Japan

[Awards & Honors]

1. Korean Fracture Society and Japanese Society for Fracture Repair travelling fellowship program, The Japanese Society for Fracture Repair(Yoto Oh), 2018.04
2. Asia Pacific Spine Society [Best clinical paper award] (Hiroyuki Inose), Asia Pacific Spine Society, 2018.06
3. The 7th Fragility Fracture Network Global Congress [Top 6 Abstracts] (Koji Fujita), Fragility Fracture Network, 2018.07

Diagnostic Radiology and Nuclear Medicine

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Lecturers Mitsuhiro Kishino, Yoshio Kitazume,

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Kouichiro Kimura (Apr.~), Yuka Yashima (~Mar.),

Resident Takahiro Sato (~Mar.), Momo Wakui (~Mar.),

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(1) Outline

While diagnostic radiology and nuclear medicine demand high-level capabilities and therefore extensive training to acquire those capabilities, keeping a watch on developments in medical knowledge and maintaining those skills is also an issue for these disciplines. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Contributing to the community is a basic responsibility of diagnostic radiology so it remains the university's mission to unflinchingly fulfill its responsibility to provide high-level, advanced medical care, working toward resolution of community problems through education, research and medical activities, as well as to develop the diagnostic radiology professionals who will bear the responsibility for providing community medical care, and to develop professionals who have a global outlook and can flourish in this age of globalization. More than ever, advancing the fundamental medical concepts of "patient-oriented medical care" and "thorough medical safety management" are core principles in the field of diagnostic radiology and nuclear medicine, so continuing to maintain capabilities from this perspective is essential in daily practice. Under the new radiologist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiologist examination (sixth year after graduation). After passing that examination, it is then possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

Diagnostic radiology and nuclear medicine was divided off the specialist field responsible for diagnostic radiology in July 2013. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide it without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 15 external affiliated hospitals approved by JRS as training hospitals. When commencing specialist training, students are allocated to their specialist fields. After the two years of

specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. In addition, many also obtain certification as a senior (first class) radiation protection supervisor. In recent times, diagnostic radiology has been experiencing an increasing load in terms of image processing, the number of image readings, and server storage, owing to improvements in instrument performance. As hybrid imaging such as PET/CT, SPECT/CT, PET/MRI become more prevalent, the diversification of diagnostic methods is accelerating. This trend is expected to continue, so there is a need for work on adequate personnel responses, including infrastructure improvement. And because the combined use of functional images to monitor metabolism and blood flow from morphologic images alone will be fundamental, it is essential that the university goes on enhancing education for radiologists so that they acquire the capabilities to extract and analyze clinically useful information from the complex data gathered.

Remote diagnostic imaging is a good example of this. In regard to its responsibility to contribute to the community, there have been changes in the way diagnostic radiology today has been active in society. The community gives special privileges to the diagnosing doctor, including the exclusive or primary responsibility to provide specified medical services. The university must unwaveringly fulfill its mission as such by providing advanced medical care through medical practice, as well as developing the doctors who will provide healthcare to communities. Although it could not be claimed that the environment surrounding diagnostic radiology in community healthcare has fully matured, as specialists, it is necessary to contribute to the development of local communities and to exercise the privileges granted as specialists: we should carry out our responsibilities while firmly holding to this approach.

(2) Research

Diagnostic specialists must keep up with the latest research in their fields, applying medical research findings to clinical practice, and making use of continuing education, continuing professional development programs, medical journals, society activities and the internet to maintain their skills. Along with the importance of maintaining awareness of how to interpret and apply research findings to the patient, it is also necessary to go on formulating broad education programs from a specialist perspective, in order to stay well informed about the fundamentals of research methods and to practice appropriate medicine. By managing the faculty effectively, it will go on clarifying radiological perspectives designed to effect inter-disciplinary research activities, taking a whole-university outlook that crosses over the limits of individual departments or graduate schools. The faculty ensures the education and research activities at graduate schools are reflected in the departments while also energetically tackling strategies to secure external funding and strengthen industry collaborations, with the aim of further improving research results. The faculty continues to actively advance international cooperative networks with the Radiological Society of North America (RSNA), the European Congress of Radiology (ECR), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), etc. from the standpoint of diagnostic radiology and nuclear medicine, and continues to advance research based on a thorough awareness of the impacts emerging in the field and the potentialities developing in related practical application fields.

Diagnostic radiology provides diagnoses by extracting information about the morphology of organs and tissues, three-dimensional structures. It is important in terms of learning to systematically organize that information for comparison of imaging study analyses with the reference pathological tissue. Within that, using CT or MRI for tissue characterization that reflects the macro-pathology is important for identifying diseases.

Diagnostic radiology is a discipline in which it is possible to zero in on understanding of a pathological condition by collecting and analyzing blood flow and metabolic data over time. The faculty is continuing research into a minimally invasive method of extracting in vivo blood flow data to enable the use of in vivo dynamic analysis as a biomarker with formulation of dynamic scan protocols that obtain images over time with bolus contrast injection before high-resolution, multi-slice CT or high magnetic field MRI. Texture analysis and AI imaging are applied to both of anatomic and functional imaging modalities. We investigate from first order (kurtosis) to high order (NGLCM, NGTDM, GLSZM). The faculty is also formulating scan protocols that obtain images over time with 3D PET/CT, as a minimally invasive technique of extracting in vivo metabolic data. Known tracers include 18F-FDG (glucose metabolism), 11C-choline (lipid metabolism), 11C-acetate (lipid metabolism), 18F-FAZA (hypoxia), 18F-FACBC (amino acid metabolism), 62/64Cu-ATSM (redox), 18F-FLT (DNA synthesis), 18F-NaF (bone metabolism), 68Ga-DOTATATE (somatostatin receptor), and 18F-Fluorobetapir (Amyloid), 18F-Flutemetamol (Amyloid). The usefulness of multiple tracers in the discipline of oncology has been observed in numerous carcinomas. 177Lu-DOTATATE PRRT started as the first domestic Phase I study. Given the need for examination with standardized imaging and assessment techniques, by conducting a multi-center joint study using PET/CT, the faculty is working to realize and to formulate methodologies for standardization to facilitate

participation in global clinical trials in Japan.

(3) Education

In order to meet the expectations of both the patient and diagnostic radiologist, it is important to know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care, and to continue to independently demonstrate them. Diagnostic radiology demands high-level capabilities, so extensive training is required to acquire those capabilities, while keeping a watch on developments in medical knowledge and maintaining those capabilities is also an issue for the discipline. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global viewpoint, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective. An essential aspect of postgraduate school education is the ongoing maintenance of capabilities from that perspective.

Under the new radiology specialist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiology specialist examination (sixth year after graduation). After passing that examination, it is possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

In July 2013, radiation oncology was divided into diagnostic radiology and nuclear medicine responsible for diagnostic radiology and radiotherapeutic oncology, in turn responsible for radiotherapy. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide the training without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 11 external affiliated hospitals (five in Tokyo and six in the Kanto region) approved by the Society as training hospitals. When students commence specialist training, they will be allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all students then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. From the standpoint of managing sealed and unsealed sources in nuclear medicine, many students also obtain certification as a senior (first class) radiation protection supervisor before engaging in clinical and research work.

(4) Lectures & Courses

The department delivers education based on the university's fundamental policy aimed at realization of its mission: to contribute to the development of society, with a specific mission to bear the responsibility for the basic functions of education, research and medical care. As a department at the core of medical care, it develops professionals who can engage in practice across different fields, taking the approach that the standards of behavior demonstrated by diagnostic radiologists in clinical practice have far more impact than the formal curriculum in ethics.

The department develops professionals who can continue to work to resolve the issues faced by the university hospital, professionals who know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care to meet the expectations of both the patient and student, can independently demonstrate them, and can flourish while maintaining a global outlook. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those

groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global perspective, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective.

(5) Clinical Services & Other Works

Diagnostic Radiology

- CT: A total of three CT scanners are involved in diagnostic radiology: two in the radiology department (64-slice MDCT) and one in the ER center (16-slice MDCT). Not only has the number of examinations using MDCT increased, but it has been possible to obtain improved diagnostic performance by reading MPR (multi-planar reconstruction) images and 1-mm thick images.
- MRI: A total of four MRI scanners are involved in diagnostic radiology: two 1.5-tesla scanners and two 3-tesla scanners. This has allowed for an increase in examinations.
- Ultrasound: The main examinations carried out by diagnostic radiologists are breast and abdominal examinations.
- Angiography and Interventional Radiology (IVR): In the vascular area: TACE for hepatic carcinoma, PTA and stent placement for occlusive arterial disease, intraarterial injection for pelvic tumor, and emergency hemostasis for ER center patients. In the non-vascular area: mainly CT-guided chest biopsy, breast mass biopsy and lymph node biopsy.
- Breast: The department is responsible for breast diagnostic radiology and collaborates with the breast surgery department in team medical care. The department endeavors to diagnose breast cancer at an early stage, provide accurate pre-surgery diagnoses, and formulate treatment plans by providing high-quality diagnostic radiology services combining mammography reading, ultrasound examination, as well as MRI and FDG-PET/CT, in addition to providing image-guided biopsy and surgical marking.
- Conferences: The department holds inter-disciplinary conferences with all departments on a daily basis. The department holds its internal conference every Friday and participates in externally conducted conferences, as appropriate. The department also takes a lead role in organizing conferences aimed at external attendees (Shoheizaka Radiology: twice a year), and the three-university joint conferences (three times a year).

Nuclear Medicine

- Since the department began operating its second PET/CT scanner in November 2006, it has been conducting 17 PET examinations per day, mainly for malignant tumor, as well as eight to 10 general radioisotope examinations per day, mainly brain and myocardial SPECT. PET/CT for radiation planning and C-11 acetate PET/CT F-18 FLT PET/CT for malignancies were introduced in 2016.

(6) Clinical Performances

Being a core diagnosis and treatment department, diagnostic radiology and nuclear medicine is a department that engages in inter-disciplinary clinical practice forming strong partnerships to meet the needs of its internal client departments and works to resolve issues faced by the university hospital, bearing its responsibility to unswervingly fulfill its mission from a global perspective. Diagnostic radiology and nuclear medicine is equipped with the capabilities to process large volumes of imaging information, it develops problem presentation, technical skill acquisition, and collaboration with all departments, and possesses the characteristics to go on conscientiously tackling new modalities, probes and contrasts as well as clinical trials.

(7) Publications

[Original Articles]

1. Amano E, Komatsuzaki T, Ishido H, Ishihara T, Otsu S, Yamada I, Machida A. Pitfalls in the diagnosis of pupil-sparing oculomotor nerve palsy without limb ataxia: a case report of a variant of Claude's syndrome and neuroanatomical analysis using diffusion-tensor imaging. *J Clin Neurosci*. 2018.01; 47(1); 120-123
2. Sasaki M, Tozaki M, Kubota K, Murakami W, Yotsumoto D, Sagara Y, Ohi Y, Oosako S, Sagara Y.. Simultaneous whole-body and breast 18F-FDG PET/MRI examinations in patients with breast cancer: a

- comparison of apparent diffusion coefficients and maximum standardized uptake values. *Japanese Journal of Radiology*. 2018.02; 36(2); 122-133
3. Yoshikawa S, Shiraishi A, Kishino M, Honda M, Urushibata N, Sekiya K, Shoko T, Otomo Y. Predictive ability and interobserver reliability of computed tomography findings for angioembolization in patients with pelvic fracture. *The journal of trauma and acute care surgery*. 2018.02; 84(2); 319-324
 4. Yamada I, Hikishima K, Yoshino N, Sakamoto J, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using q-space imaging; correlation with histopathologic findings. *J Magn Reson Imaging*. 2018.03; 48(4); 1059-1068
 5. Mitsuhiro Kishino, Shuichiro Nakaminato, Yoshio Kitazume, Naoyuki Miyasaka, Toshifumi Kudo, Yukihisa Saida, Ukihide Tateishi. Balloon-Occluded Carbon Dioxide Gas Angiography for Internal Iliac Arteriography and Intervention. *Cardiovasc Intervent Radiol*. 2018.04;
 6. Yamada I, Yoshino N, Hikishima K, Sakamoto J, Yokokawa M, Oikawa Y, Harada H, Kurabayashi T, Saida Y, Tateishi U, Yukimori A, Izumo T, Asahina S. Oral carcinoma: clinical evaluation using diffusion kurtosis imaging and its correlation with histopathologic findings. *Magn Reson Imaging*. 2018.09; 51; 69-78
 7. Fujioka T, Kubota K, Kikuchi Y, Tsuchiya J, Tateishi U, Kasaharak M, Oda G, Ishiba T, Nakagawa T. The feasibility of using 18F-FDG-PET/CT in patients with mucinous breast carcinoma. *Nuclear medicine communications*. 2018.09;
 8. Ichiro Yamada, Kimio Wakana, Daisuke Kobayashi, Naoyuki Miyasaka, Noriko Oshima, Akira Wakabayashi, Yukihisa Saida, Ukihide Tateishi, Yoshinobu Eishi. Endometrial carcinoma: Evaluation using diffusion-tensor imaging and its correlation with histopathologic findings. *J Magn Reson Imaging*. 2018.11;
 9. Ichiro Yamada, Junichiro Sakamoto, Daisuke Kobayashi, Naoyuki Miyasaka, Kimio Wakana, Noriko Oshima, Akira Wakabayashi, Yukihisa Saida, Ukihide Tateishi, Yoshinobu Eishi. Diffusion kurtosis imaging of endometrial carcinoma: Correlation with histopathological findings. *Magn Reson Imaging*. 2018.12;
 10. Masashi Nakadate, Norikazu Miyamoto, Jay Starkey, Akira Toriihara, Ukihide Tateishi. Anterograde degeneration of the nigrostriatal pathway visualized by 123I-FP-CIT SPECT in patient with artery of Percheron infarction. *Clin Nucl Med*. 41; 483-484
 11. Yojiro Umezaki, Anna Miura, Motoko Watanabe, Miho Takenoshita, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Oral ceneosthopathy Biopsychosoc Med. 10; 20

[Conference Activities & Talks]

1. T. Fujioka, K. Kubota, H. Okuma, Y. Shirakawa, Y. Yashima, Y. Saida, U. Tateishi. Added value of US elastography for breast masses: comparison between shear- wave and strain elastography by several assessment. *European Congress of Radiology* 2018.02.28 Vienna, Austria
2. K. Kubota, M. Sasaki, M. Tozaki, Y. Sagara. Hybrid PET/MR Imaging of Breast Cancer: Advantages and Pitfalls. *ECR 2018* 2018.03.01 Vienna
3. T. Fujioka, K. Kubota, H. Okuma, Y. Shirakawa, Y. Yashima, Y. Saida, U. Tateishi. Added value of US elastography for breast masses: comparison between shear- wave and strain elastography by several assessment . *The 77th Annual Meeting of the Japan Radiological Society* 2018.04.12
4. Kishino Mitsuhiro, Fukuda Hozumi, Tobe Kimiko, Ogasawara Gou, Ibukuro Kenji. Analysis of aortic arch motion and segmental curvature change using four-dimensional computed tomography angiography: Consideration for the pathogenesis of aortic dissection.. *The 77th Annual Meeting of the Japan Radiological Society* 2018.04.12 Yokohama Japan
5. Kishino Mitsuhiro, Fukuda Hozumi, Tobe Kimiko, Ogasawara Gou, Ibukuro Kenji. A simple experimental model of air embolization associated with percutaneous lung biopsy. *JSIR&ISIR* 2018.05.31 Tokyo Daiba

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka
Project Assistant Professor, Ryo Watanabe

(1) Research

- 1) Elucidation of genetic architecture of human metabolic diseases using genome and meta-genome information
- 2) Identification of biomarkers for personalized medicine
- 3) Pharmacogenomics
- 4) Functional genomics
- 5) Statistical genetics and genome drug discovery

(2) Lectures & Courses

As we say “Every human is different” , human genetic diversity has essential impacts on clinical fields, e.g. disease risk, clinical efficacy, and drug responses. Our laboratory aims to elucidate the diversity of human being through comprehensive research activities including genome and epi-genome analyses of human diseases, methodological development of statistical genetics, and human resources cultivation to achieve personalized medicine.

(3) Publications

[Original Articles]

1. Kevin Y Urayama, Masatoshi Takagi, Takahisa Kawaguchi, Keitaro Matsuo, Yoichi Tanaka, Yoko Ayukawa, Yuki Arakawa, Daisuke Hasegawa, Yuki Yuza, Takashi Kaneko, Yasushi Noguchi, Yuichi Taneyama, Setsuo Ota, Takeshi Inukai, Masakatsu Yanagimachi, Dai Keino, Kazutoshi Koike, Daisuke Toyama, Yozo Nakazawa, Hidemitsu Kurosawa, Kozue Nakamura, Koichi Moriwaki, Hiroaki Goto, Yujin Sekinaka, Daisuke Morita, Motohiro Kato, Junko Takita, Toshihiro Tanaka, Johji Inazawa, Katsuyoshi Koh, Yasushi Ishida, Akira Ohara, Shuki Mizutani, Fumihiko Matsuda, Atsushi Manabe. Regional evaluation of childhood acute lymphoblastic leukemia genetic susceptibility loci among Japanese. *Sci Rep.* 2018.01; 8(1); 789
2. McCormack M, Gui H, Ingason A, Speed D, Wright GEB, Zhang EJ, Secolin R, Yasuda C, Kwok M, Wolking S, Becker F, Rau S, Avbersek A, Heggeli K, Leu C, Depondt C, Sills GJ, Marson AG, Auce P, Brodie MJ, Francis B, Johnson MR, Koeleman BPC, Striano P, Coppola A, Zara F, Kunz WS, Sander JW, Lerche H, Klein KM, Weckhuysen S, Krenn M, Gudmundsson LJ, Stefánsson K, Krause R, Shear N, Ross CJD, Delanty N; EPIGEN Consortium; Pirmohamed M, Carleton BC; Canadian Pharmacogenomics Network for Drug Safety; Cendes F, Lopes-Cendes I, Liao WP, O'Brien TJ, Sisodiya SM; EpiPGX Consortium; Cherny S, Kwan P, Baum L; International League Against Epilepsy Consortium on Complex Epilepsies; Cavalleri GL. Genetic variation in CFH predicts phenytoin-induced maculopapular exanthema in European-descent patients. *Neurology.* . 2018.01; 90(4); e332-e341

3. Hirata J, Hirota T, Ozeki T, Kanai M, Sudo T, Tanaka T, Hizawa N, Nakagawa H, Sato S, Mushiroda T, Saeki H, Tamari M, Okada Y.. Variants at HLA-A, HLA-C, and HLA-DQB1 Confer Risk of Psoriasis Vulgaris in Japanese. *J Invest Dermatol.* 2018.03; 138(3); 542-548
4. El Rouby N, McDonough CW, Gong Y, McClure LA, Mitchell BD, Horenstein RB, Talbert RL, Crawford DC; eMERGE network, Gitzendanner MA, Takahashi A, Tanaka T, Kubo M, Pepine CJ, Cooper-DeHoff RM, Benavente OR, Shuldiner AR, Johnson JA.. Genome-wide association analysis of common genetic variants of resistant hypertension. *Pharmacogenomics J.* 2018.09;
5. Roselli C, Chaffin MD, Weng LC, Aeschbacher S, Ahlberg G, Albert CM, Almgren P, Alonso A, Anderson CD, Aragam KG, Arking DE, Barnard J, Bartz TM, Benjamin EJ, Bihlmeyer NA, Bis JC, Bloom HL, Boerwinkle E, Bottinger EB, Brody JA, Calkins H, Campbell A, Cappola TP, Carlquist J, Chasman DI, Chen LY, Chen YI, Choi EK, Choi SH, Christophersen IE, Chung MK, Cole JW, Conen D, Cook J, Crijns HJ, Cutler MJ, Damrauer SM, Daniels BR, Darbar D, Delgado G, Denny JC, Dichgans M, Dörr M, Dudink EA, Dudley SC, Esa N, Esko T, Eskola M, Fatkin D, Felix SB, Ford I, Franco OH, Geelhoed B, Grewal RP, Gudnason V, Guo X, Gupta N, Gustafsson S, Gutmann R, Hamsten A, Harris TB, Hayward C, Heckbert SR, Hernesniemi J, Hocking LJ, Hofman A, Horimoto ARVR, Huang J, Huang PL, Huffman J, Ingelsson E, Ipek EG, Ito K, Jimenez-Conde J, Johnson R, Jukema JW, Kääb S, Kähönen M, Kamatani Y, Kane JP, Kastrati A, Kathiresan S, Katschnig-Winter P, Kavousi M, Kessler T, Kietselaer BL, Kirchhof P, Kleber ME, Knight S, Krieger JE, Kubo M, Launer LJ, Laurikka J, Lehtimäki T, Leineweber K, Lemaitre RN, Li M, Lim HE, Lin HJ, Lin H, Lind L, Lindgren CM, Lokki ML, London B, Loos RJJ, Low SK, Lu Y, Lyytikäinen LP, Macfarlane PW, Magnusson PK, Mahajan A, Malik R, Mansur AJ, Marcus GM, Margolin L, Margulies KB, März W, McManus DD5, Melander O, Mohanty S, Montgomery JA, Morley MP, Morris AP, Müller-Nurasyid M, Natale A, Nazarian S, Neumann B, Newton-Cheh C, Niemeijer MN, Nikus K, Nilsson P, Noordam R, Oellers H, Olesen MS, Orho-Melander M, Padmanabhan S, Pak HN, Paré G, Pedersen NL, Pera J, Pereira A, Porteous D, Psaty BM, Pulit SL, Pullinger CR, Rader DJ, Refsgaard L, Ribasés M, Ridker PM, Rienstra M, Risch L, Roden DM, Rosand J, Rosenberg MA, Rost N, Rotter JJ, Saba S, Sandhu RK, Schnabel RB, Schramm K, Schunkert H, Schurman C, Scott SA, Seppälä I, Shaffer C, Shah S, Shalaby AA, Shim J, Shoemaker MB, Siland JE, Sinisalo J, Sinner MF, Slowik A, Smith AV, Smith BH, Smith JG, Smith JD, Smith NL, Soliman EZ, Sotoodehnia N, Stricker BH, Sun A, Sun H, Svendsen JH, Tanaka T, Tanriverdi K, Taylor KD, Teder-Laving M, Teumer A, Thériault S, Trompet S, Tucker NR, Tveit A, Uitterlinden AG, Van Der Harst P, Van Gelder IC, Van Wagener DR, Verweij N, Vlachopoulou E, Völker U, Wang B, Weeke PE, Weijs B, Weiss R, Weiss S, Wells QS, Wiggins KL, Wong JA, Woo D, Worrall BB, Yang PS, Yao J, Yoneda ZT, Zeller T, Zeng L, Lubitz SA, Lunetta KL, Ellinor PT.. Multi-ethnic genome-wide association study for atrial fibrillation. *Nat Genet.* 2018.09; 50(9); 1225-1233

[Books etc]

1. Precision Medicine & Drug Development. 2018.09

[Conference Activities & Talks]

1. Ryo Watanabe, Naomasa Makita, Toshihiro Tanaka. Next-generation sequencing unveils novel mutations for long QT syndrome in Japanese patients. The 1st JCS Council Forum on Basic CardioVascular Research 2018.01.06 Tokyo
2. Identification of biomarkers for sarcoidosis by expression analysis of circulating exosomal microRNAs. 2018.10.11

Applied Regenerative Medicine

Professor: Ichiro SEKIYA

Assistant Professor: Koji OTABE, Hisako KATANO

Project Assistant Professor: Nobutake OZEKI, Mitsuru MIZUNO,
Keiichiro KOMORI, Yuji KONO

Graduate Student: Naoto WATANABE, Yoshihisa KUSHIDA, So SUZUKI,
Akinobu HYODO, Hayato AOKI, Mana NARITOMI,
Rei KUBOTA, Kiyotaka HORIUCHI, Ryota FUJISAWA

Technical Staff : Shizuka FUJII, Mika WATANABE, Kimiko TAKANASHI,
Emi KODA, Atsuko TAKEBE, Youko HATANO, Kaoru KOMORIYA

Assistant Clerk: Hitomi SEKI

(1) Outline

Our purpose is to support and advance stem cell research and regenerative medicine for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury.

(2) Research

- 1) Development of regenerative medicine with stem cells.
- 2) Realization and industrialization of the cell and regenerative therapy.
- 3) Establishment of safety test for regenerative medicine.
- 4) Translational research.
- 5) Development of software for 3D analysis of knee MRI.

(3) Clinical Services & Other Works

Our purpose is to establish a new treatment for osteoarthritis of the knee. We have demonstrated that synovial mesenchymal stem cells (MSCs) have a high differentiation potential for cartilage and meniscus and that transplantation of synovial MSCs promotes the natural healing process in the knee joints. We have also developed the operative procedures for transplantation of synovial MSCs into cartilage and meniscus by minimally invasive arthroscopic surgery. Based on the results of these fundamental studies, we conducted two clinical studies to confirm the safety and efficacy. Furthermore, to obtain applications for the manufacture and sales approval as cellular and tissue-based products, we started the doctor-led clinical trial targeting meniscal injury with autologous synovial MSCs in August 2017. Besides, to develop a new approach for transplantation of synovial MSCs, we started the clinical study “intraarticular injection of synovial MSCs for osteoarthritis” in December 2017 with the support of AMED regenerative medicine research project (leader: Ichiro Sekiya).

Katano Hisako wrote one chapter "Collection of tissues and cells" in the official textbook "Regenerative Medicine -Creating, Conducting, Supporting- 1st Edition" published by Japan Society for Regenerative Medicine.

(4) Publications**[Original Articles]**

1. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep.* 2018.01; 8(1); 1288
2. Hideyuki Koga, Atsuo Nakamae, Yosuke Shima, Roald Bahr, Tron Krosshaug. Hip and Ankle Kinematics in Noncontact Anterior Cruciate Ligament Injury Situations: Video Analysis Using Model-Based Image Matching. *Am J Sports Med.* 2018.02; 46(2); 333-340
3. Kana Ishii, Hidetoshi Sakurai, Nobuharu Suzuki, Yo Mabuchi, Ichiro Sekiya, Kiyotoshi Sekiguchi, Chihiro Akazawa. Recapitulation of Extracellular LAMININ Environment Maintains Stemness of Satellite Cells In Vitro. *Stem Cell Reports.* 2018.02; 10(2); 568-582
4. Yuji Kohno, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Koji Otabe, Hideyuki Koga, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Ichiro Sekiya. Comparison of mesenchymal stem cells obtained by suspended culture of synovium from patients with rheumatoid arthritis and osteoarthritis. *BMC Musculoskelet Disord.* 2018.03; 19(1); 78
5. Ken Watanabe, Koji Otabe, Norio Shimizu, Keiichirou Komori, Mitsuru Mizuno, Hisako Katano, Hideyuki Koga, Ichiro Sekiya. High-sensitivity virus and mycoplasma screening test reveals high prevalence of parvovirus B19 infection in human synovial tissues and bone marrow. *Stem Cell Res Ther.* 2018.03; 9(1); 80
6. Kanehiro Hiyama, Yusuke Nakagawa, Toshiyuki Ohara, Takeshi Muneta, Toshifumi Watanabe, Masafumi Horie, Koji Otabe, Hiroki Katagiri, Kenta Katagiri, Mai Katakura, Takashi Hoshino, Hiroko Ueki, Kei Inomata, Naoko Araya, Ichiro Sekiya, Hideyuki Koga. Anterior cruciate ligament injuries result in a larger functional deficit in fighting sport athletes: comparison of functional status among different sport types. *Journal of ISAKOS.* 2018.03; (3); 128-133
7. Takao Minami, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Takeshi Muneta. Posteriorly inserted anterior cruciate ligament in knees with discoid lateral meniscus corresponding to bony morphological characteristics of femoral lateral condyle. *J Orthop Sci.* 2018.03; 23(2); 350-355
8. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Shizuka Fujii, Koji Otabe, Keiichiro Komori, Nobutake Ozeki, Hideyuki Koga, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Specific markers and properties of synovial mesenchymal stem cells in the surface, stromal, and perivascular regions. *Stem Cell Research & Therapy.* 2018.05; 9(1); 123
9. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Nobutake Ozeki, Koji Otabe, Keiichiro Komori, Shizuka Fujii, Shizuko Ichinose, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Petaloid recombinant peptide enhances in vitro cartilage formation by synovial mesenchymal stem cells. *Journal of Orthopaedic Research.* 2018.05;
10. Mari Uomizu, Takeshi Muneta, Miyoko Ojima, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. PDGF-induced proliferation and differentiation of synovial mesenchymal stem cells is mediated by the PI3K-PKB/Akt pathway. *J Med Dent Sci.* 2018.06; 65(2); 73-82
11. Ogata Yusuke, Mabuchi Yo, Shinoda Kosuke, Horiike Yuta, Mizuno Mitsuru, Otabe Koji, Suto Eriko Grace, Suzuki Nobuharu, Sekiya Ichiro, Akazawa Chihiro. Anterior cruciate ligament-derived mesenchymal stromal cells have a propensity to differentiate into the ligament lineage *Regenerative Medicine.* 2018.06; 8; 20-28
12. Kaori Nakamura, Kunikazu Tsuji, Mitsuru Mizuno, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Initial cell plating density affects properties of human primary synovial mesenchymal stem cells. *J. Orthop. Res..* 2018.07;
13. Hisako Katano, Hideyuki Koga, Nobutake Ozeki, Koji Otabe, Mitsuru Mizuno, Makoto Tomita, Takeshi Muneta, Ichiro Sekiya. Trends in isolated meniscus repair and meniscectomy in Japan, 2011-2016 *PLoS ONE.* 2018.07; 23(4); 676-681

14. Akari Sasaki, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Manabu Mochizuki, Ichiro Sekiya. Canine mesenchymal stem cells from synovium have a higher chondrogenic potential than those from infrapatellar fat pad, adipose tissue, and bone marrow. *PLoS ONE*. 2018.08; 13(8); e0202922
15. Yoichi Murata, Soshi Uchida, Hajime Utsunomiya, Akihisa Hatakeyama, Hirotaka Nakashima, Angela Chang, Ichiro Sekiya, Akinori Sakai. Synovial mesenchymal stem cells derived from the cotyloid fossa synovium have higher self-renewal and differentiation potential than those from the paralabral synovium in the hip joint. *American Journal of Sports Medicine*. 2018.10; 46(12); 2942-2953
16. Hiroko Ueki, Yusuke Nakagawa, Toshiyuki Ohara, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Kenta Katagiri, Kanehiro Hiyama, Mai Katakura, Takashi Hoshino, Kei Inomata, Naoko Araya, Ichiro Sekiya. Risk factors for residual pivot shift after anterior cruciate ligament reconstruction: data from the MAKS group. *Knee Surg Sports Traumatol Arthrosc*. 2018.12; 26(12); 3724-3730

[Conference Activities & Talks]

1. Yuji Kohno, Nobutake Ozeki, Akinobu Hyodo, So Suzuki, Hayato Aoki, Yoshihisa Kushida, Naoto Watanabe, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Validations for cartilage thickness, cartilage area ratio and meniscus volume in the knee by 3D MRI analysis. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
2. Yuji Kohno, Hideyuki Koga, Nobutake Ozeki, Junpei Matsuda, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Ichiro Sekiya. Biomechanical analysis of meniscus centralization for extruded meniscus after meniscectomy. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
3. Koji Otabe, Kenta Katagiri, Toshiyuki Ohara, Hiroki Katagiri, Masafumi Horie, Toshifumi Watanabe, Hideyuki Koga, Ichiro Sekiya. Wide Oval Gantry 3.0T MRI Analysis Revealed Dynamic Knee Neurovascular Transposition During Flexion of the Knee. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
4. So Suzuki, Nobutake Ozeki, Akinobu Hyodo, Hayato Aoki, Yoshihisa Kushida, Naoto Watanabe, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. "Cartilage Area Ratio" by MRI 3D Analysis Reveals Subtle Change of Cartilage Volume in Middle Aged Patients with Medial Meniscus Degenerative Tear. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
5. Nobutake Ozeki, Yuji Kohno, Yoshihisa Kushida, Naoto Watanabe, Kenta Katagiri, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Tomoyuki Saito, Ichiro Sekiya. Three-Dimensional MRI, T2 Mapping and Histological Analyses of Meniscus Repair After Transplantation of Synovial Mesenchymal Stem Cells in a Novel Degenerative Meniscus Injury Model in Pig. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
6. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichi Komori, Shizuka Fujii, Shizuko Ichinose, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Petaloid Recombinant Peptide Constructs the Framework of Cartilage Pellet and Promotes In Vitro Cartilage Formation. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
7. Akari Sasaki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Manabu Mochizuki, Ichiro Sekiya. Comparison Of Canine Mesenchymal Stem Cells Derived From Synovium, Infrapatellar Fat Pad, Subcutaneous Adipose Tissue And Bone Marrow. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
8. Ryota Fujisawa, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichi Komori, Shizuka Fujii, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Investigation of Freezing Medium for Synovial Mesenchymal Stem Cells. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*
9. Miharuru Ochi, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Effects of synovial stem cells and BMP-2 on cartilage formation of tendon. *Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA*

10. Naoto Watanabe, Mitsuru Mizuno, Jumpei Matsuda, Naoko Nakamura, Koji Otabe, Hisako Katano, Nobutake Ozeki, Yuji Kono, Tsuyoshi Kimura, Kunikazu Tsuji, Hideyuki Koga, Akio Kishida, Ichiro Sekiya. Can Decellularized Meniscus by High Hydrostatic Pressure be an Alternative to Meniscus Allograft? - Compared with Deep Frozen Meniscus. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
11. Mitsuru Mizuno, Hisako Katano, Yuri Shimozaeki, Sho Sanami, Keiichiro Komori, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Koga Hideyuki, Ichiro Sekiya. Image Analysis Method to Predict Cell Proliferation at Early Phase for Autologous Synovial Stem Cell Transplantation. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
12. Hayato Aoki, Nobutake Ozeki, Kohno yuji, Kushida Yoshihisa, Naoto Watanabe, Akinobu Hyodo, So Suzuki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Mri 3d Analysis For Discoid Lateral Meniscus Of The Knee. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
13. Yoshihisa Kushida, Koichiro Kishima Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Pseudo Color Images and Volume Measurement of Cartilage by Optical Coherence Tomography in a Rat Meniscectomized Model. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
14. Ichiro Sekiya. Transplantation of synovial mesenchymal stem cells onto repaired meniscus with degenerative tear. 5th TERMIS World Congress-2018 2018.09.05 Kyoto, Japan
15. Ichiro Sekiya. Transplantation of synovial mesenchymal stem cells onto repaired menisci with degenerative tears: a 2-year follow-up study. ICRS Focus Meeting 2018.12.13 Milano, Italy

JFCR Cancer Biology

Professor Takuro NAKAMURA

Professor Noriko Saitoh

Professor Kiyotaka SHIBA

Professor Kengo TAKEUCHI

Professor Akihiro TOMIDA

Professor Toru HIROTA

Graduate Student Yoshiharu Kusama, Yasuyo
Teramura

(1) Research

Understanding the mechanisms of carcinogenesis and cancer progression. Studying the basics of personalized medicine for innovative cancer therapy.

(2) Education

We are committed to training talented and motivated graduate students, helping launch careers in basic and translational cancer research.

1. Molecular mechanisms of carcinogenesis and identification of cell-of-origin of cancer (Nakamura)
2. Understanding of molecular mechanisms for epigenetic regulation in breast cancer (Saitoh)
3. Application of nanobiotechnology in cancer diagnostics (Shiba)
4. Pathological and genetic analysis of human cancer such as malignant lymphoma and lung cancer (Takeuchi)
5. Strategy for innovative drug therapy based on cancer biology (Tomida)
6. To understand how chromosomes are assembled and segregated in mitosis, and to elucidate the pathology underlying chromosomal instability in cancers (Hirota)

(3) Publications

[Original Articles]

1. Owa T, Taya S, Miyashita S, Yamashita M, Adachi T, Yamada K, Yokoyama M, Aida S, Nishioka T, Inoue U, Goitsuka R, Nakamura T, Inoue T, Kaibuchi K, Hoshino M. Meis1 coordinates cerebellar granule cell development by regulating Pax6 transcription, BMP signaling and Atoh1 degradation. *J Neurosci*, 38:1277-1294, 2017.

2. Shimizu R, Tanaka M, Tsutsumi S, Aburatani H, Yamazaki Y, Homme M, Kitagawa Y, Nakamura T. EWS-FLI1 regulates a transcriptional program in cooperation with Foxq1 in mouse Ewing sarcoma. *Cancer Sci*, 109:2907-2918, 2018.
3. Namatame N, Tamaki N, Yoshizawa Y, Okamura M, Nishimura Y, Yamazaki K, Tanaka M, Nakamura T, Semba K, Yamori T, Yaguchi S, Dan S. Antitumor profile of the PI3K inhibitor ZSTK474 in human sarcoma cell lines. *Oncotarget*, 9:35141-35161, 2018.
4. Yamamoto, T., Sakamoto, C., Tachiwara, H., Kumabe, M., Matsui, T., Yamashita, T., Shinagawa, M., Ochiai, K., Saitoh, N.* Nakao, M.* Endocrine therapy-resistant breast cancer model cells are inhibited by soybean glyceollin I through Eleanor non-coding RNA. *Sci. Rep*, *Sci. Rep* 8:15202, 2018, doi: 10.1038/s41598-018-33227-y
5. Ichikawa, Y., Saitoh, N., Kaufman, P.D.* An asymmetric centromeric nucleosome. *eLife*, 7, 2018. pii: e37911, doi: 10.7554/eLife.37911
6. Takagi, M., Ono, Y., Natsume, T., Sakamoto, C., Nakao, M., Saitoh, N., Kanemaki, M.T., Hirano, T. and Imamoto, N. Ki-67 and condensins support the integrity of mitotic chromosomes through distinct mechanisms. *J. Cell Sci*, 131:6, 2018. doi: 10.1242/jcs.212092.
7. Thery, C. et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. *J Extracell Vesicles* 7, 1535750 (2018).
8. Nitta, N., et al. Intelligent Image-Activated Cell Sorting. *Cell* 175, 266-276 e13 (2018).
9. Ito, K., Ogawa, Y., Yokota, K., Matsumura, S., Minamisawa, T., Suga, K., Shiba, K., Kimura, Y., Hirano-Iwata, A., Takamura, Y. & Ogino, T. Host cell prediction of exosomes using morphological features on solid surfaces analyzed by machine learning. *J Phys Chem B* 122, 6224-6235 (2018).
10. Tara Bahadur, K., C., Suga, K., Isoshima, T., Aigaki, T., Ito, Y., Shiba, K. & Uzawa, T. Wash-free and selective imaging of epithelial cell adhesion molecule (EpCAM) expressing cells with fluorogenic peptide ligands. *Biochem Biophys Res Commun* 500, 283-287 (2018).
11. Kokubun, K., Matsumura, S., Yudasaka, M., Iijima, S. & Shiba, K. Immobilization of a carbon nanomaterial-based localized drug-release system using a bispecific material-binding peptide. *Int J Nanomedicine* 13, 1643-1652 (2018). Yoshida, M., Hibino, K., Yamamoto, S., Matsumura, S., Yajima, Y. & Shiba, K. Preferential capture of EpCAM-expressing extracellular vesicles on solid surfaces coated with an aptamer-conjugated zwitterionic polymer. *Biotechnol Bioeng* 115, 536-544 (2018).
12. Kato, Y., Kunimasa, K., Sugimoto, Y., Tomida, A. BCR-ABL tyrosine kinase inhibition induces metabolic vulnerability by preventing the integrated stress response in K562 cells. *Biochem. Biophys. Res. Commun.*, 504:721-726, 2018.

13. Koido, M., Tani, Y., Tsukahara, S., Okamoto, Y., Tomida, A. InDePTH: detection of hub genes for developing gene expression networks under anticancer drug treatment. *Oncotarget*.9:29097-29111, 2018.
14. Kuroda N, Sugawara E, Kusano H, Yuba Y, Yorita K, Takeuchi K. A review of ALK-rearranged renal cell carcinomas with a focus on clinical and pathobiological aspects. *Pol J Pathol*.69:109-113, 2018.
15. Wang RC, Sakata S, Chen BJ, Chang ST, Hsieh PP, Yang CS, Baba S, Takeuchi K, Chuang SS. Mycosis fungoides in Taiwan shows a relatively high frequency of large cell transformation and CD56 expression. *Pathology*.50:718-724, 2018.
16. Tamura S, Kawamoto K, Miyoshi H, Suzuki T, Katagiri T, Kasami T, Nemoto H, Miyakoshi S, Kobayashi H, Shibasaki Y, Masuko M, Takeuchi K, Ohshima K, Sone H, Takizawa J. Cladribine treatment for Erdheim-Chester disease involving the central nervous system and concomitant polycythemia vera: A case report. *J Clin Exp Hematop*.58:161-165, 2018.
17. Ukaji T, Takemoto A, Katayama R, Takeuchi K, Fujita N. A safety study of newly generated anti-podoplanin-neutralizing antibody in cynomolgus monkey (*Macaca fascicularis*). *Oncotarget*.9:33322-33336, 2018.
18. Abe Y, Narita K, Kobayashi H, Kitadate A, Takeuchi M, Kikuchi Y, Ouchi T, Takeuchi K, Matsue K. Clinical value of abnormal findings on brain magnetic resonance imaging in patients with intravascular large B-cell lymphoma. *Ann Hematol*.97:2345-2352, 2018.
19. Saiki M, Kitazono S, Yoshizawa T, Dotsu Y, Ariyasu R, Koyama J, Sonoda T, Uchibori K, Nishikawa S, Yanagitani N, Horiike A, Ohyanagi F, Oikado K, Ninomiya H, Takeuchi K, Ishikawa Y, Nishio M. Characterization of Computed Tomography Imaging of Rearranged During Transfection-rearranged Lung Cancer. *Clin Lung Cancer*.19:435-440 e431, 2018.
20. Sakamoto K, Katayama R, Asaka R, Sakata S, Baba S, Nakasone H, Koike S, Tsuyama N, Dobashi A, Sasaki M, Ichinohasama R, Takakuwa E, Yamazaki R, Takizawa J, Maeda T, Narita M, Izutsu K, Kanda Y, Ohshima K, Takeuchi K. Recurrent 8q24 rearrangement in blastic plasmacytoid dendritic cell neoplasm: association with immunoblastoid cytomorphology, MYC expression, and drug response. *Leukemia*.32:2590-2603, 2018.
21. Nakayama R, Togashi Y, Baba S, Kaku Y, Teramoto Y, Sakurai T, Haga H, Takeuchi K. Epithelioid cell histiocytoma with SQSTM1-ALK fusion: a case report. *Diagn Pathol*.13:28, 2018.
22. Dobashi A, Togashi Y, Tanaka N, Yokoyama M, Tsuyama N, Baba S, Mori S, Hatake K, Yamaguchi T, Noda T, Takeuchi K. TP53 and OSBPL10 alterations in diffuse large B-cell lymphoma: prognostic markers identified via exome analysis of cases with extreme prognosis. *Oncotarget*.9:19555-19568, 2018.

23. Fujimoto M, Togashi Y, Matsuzaki I, Baba S, Takeuchi K, Inaba Y, Jinnin M, Murata SI. A case report of atypical Spitz tumor harboring a novel MLPH-ALK gene fusion with discordant ALK immunohistochemistry results. *Hum Pathol*.80:99-103, 2018.
24. Takamatsu M, Sato Y, Muto M, Nagano H, Ninomiya H, Sakakibara R, Baba S, Sakata S, Takeuchi K, Okumura S, Ishikawa Y. Hyalinizing clear cell carcinoma of the bronchial glands: presentation of three cases and pathological comparisons with salivary gland counterparts and bronchial mucoepidermoid carcinomas. *Mod Pathol*.31:923-933, 2018.
25. Togashi Y, Dobashi A, Sakata S, Sato Y, Baba S, Seto A, Mitani H, Kawabata K, Takeuchi K. MYB and MYBL1 in adenoid cystic carcinoma: diversity in the mode of genomic rearrangement and transcripts. *Mod Pathol*.31:934-946, 2018.
26. Kuroda N, Ohara M, Wada Y, Yasuoka K, Mizuno K, Yorita K, Obayashi C, Takeuchi K. Cytological features in eight patients with ALK-rearranged lung cancer. *Diagn Cytopathol*.46:516-519, 2018.
27. Kusano Y, Yokoyama M, Inoue N, Yamauchi H, Takahashi A, Tsuyama N, Mishima Y, Nishimura N, Takeuchi K, Terui Y, Hatake K. Delayed recovery of serum immunoglobulin G is a poor prognostic marker in patients with follicular lymphoma treated with rituximab maintenance. *Ann Hematol*.97:289-297, 2018.
28. Nagasaki A, Ogawa I, Sato Y, Takeuchi K, Kitagawa M, Ando T, Sakamoto S, Shrestha M, Uchisako K, Koizumi K, Toratani S, Konishi M, Takata T. Central mucoepidermoid carcinoma arising from glandular odontogenic cyst confirmed by analysis of MAML2 rearrangement: A case report. *Pathol Int*.68:31-35, 2018.
29. Kuroda N, Tamiya H, Nakatani K, Ide H, Wada Y, Yasuoka K, Ohara M, Mizuno K, Yorita K, Takeuchi K. Cytological findings of ROS1-rearranged lung adenocarcinoma. *Diagn Cytopathol*.46:336-339, 2018.
30. Mishima Y, Terui Y, Yokoyama M, Nishimura N, Ueda K, Kusano Y, Yamauchi H, Inoue N, Takahashi A, Tsuyama N, Mishima Y, Takeuchi K, Hatake K. Bearing 19q13 aberration predicts poor prognosis in non-germinal centre type of CD5(+) DLBCL. *Br J Haematol*.183:661-664, 2018.
31. Maehara R, Fujikura K, Takeuchi K, Akita M, Abe-Suzuki S, Karbanova J, Corbeil D, Itoh T, Kakeji Y, Zen Y. SOX2-silenced squamous cell carcinoma: a highly malignant form of esophageal cancer with SOX2 promoter hypermethylation. *Mod Pathol*.31:83-92, 2018.
32. Fujisawa M, Sakata-Yanagimoto M, Nishizawa S, Komori D, Gershon P, Kiryu M, Tanzima S, Fukumoto K, Enami T, Muratani M, Yoshida K, Ogawa S, Matsue K, Nakamura N, Takeuchi K, Izutsu K, Fujimoto K, Teshima T, Miyoshi H, Gaulard P, Ohshima K, Chiba S. Activation of RHOA-VAV1 signaling in angioimmunoblastic T-cell lymphoma. *Leukemia*.32:694-702, 2018

33. Tsuyama N, Asaka R, Dobashi A, Baba S, Mishima Y, Ueda K, Oguchi M, Tsuji H, Hatake K, Takeuchi K. Epstein-Barr virus-negative extranodal "true" natural killer-cell lymphoma harbouring a KDM6A mutation. *Hematol Oncol*.36:328-335, 2018.
34. Tomita N, Yokoyama M, Yamamoto W, Watanabe R, Shimazu Y, Masaki Y, Tsunoda S, Hashimoto C, Murayama K, Yano T, Okamoto R, Kikuchi A, Tamura K, Sato K, Sunami K, Shibayama H, Takimoto R, Ohshima R, Takahashi H, Moriuchi Y, Kinoshita T, Yamamoto M, Numata A, Nakajima H, Miura I, Takeuchi K. The standard international prognostic index for predicting the risk of CNS involvement in DLBCL without specific prophylaxis. *Leuk Lymphoma*.59:97-104, 2018.
35. Abe, Y., Sako, K., Takagaki, K., Hirayama, Y., Uchida, KSK., Herman, J., DeLuca, J., Hirota, T. HP1-assisted Aurora B kinase activity prevents chromosome segregation errors. *Dev. Cell* 36: 487-497, 2016.
36. Takahashi, M., Tanaka, K., Wakai, T., Hirota, T. Phosphoproteomic analysis of human mitotic chromosomes identified a chromokinesin KIF4A. *Biomed. Res.* 37: 161-165, 2016.
37. Nagasaka, K., Hirota, T. Clarifying the role of condensins in shaping chromosomes. *Nature Cell Biol.* 17: 711-713, 2015.
38. Minamino, M., Ishibashi, M., Nakato, R., Akiyama, K., Tanaka, H., Kato, Y., Negishi, L., Hirota, T., Sutani, T., Bando, M., Shirahige, K. Escol acetylates cohesin via a mechanism different from that of Escol2. *Curr. Biol.* 25: 1694-1706, 2015.
39. Kataoka K, Nagata Y, Kitanaka A, Shiraishi Y, Shimamura T, Yasunaga J, Totoki Y, Chiba K, Sato-Otsubo A, Nagae G, Ishii R, Muto S, Kotani S, Watatani Y, Takeda J, Sanada M, Tanaka H, Suzuki H, Sato Y, Shiozawa Y, Yoshizato T, Yoshida K, Makishima H, Iwanaga M, Ma G, Nosaka K, Hishizawa M, Itonaga H, Imaizumi Y, Munakata W, Ogasawara H, Sato T, Sasai K, Muramoto K, Penova M, Kawaguchi T, Nakamura H, Hama N, Shide K, Kubuki Y, Hidaka T, Kameda T, Nakamaki T, Ishiyama K, Miyawaki S, Yoon SS, Tobinai K, Miyazaki Y, Takaori-Kondo A, Matsuda F, Takeuchi K, Nureki O, Aburatani H, Watanabe T, Shibata T, Matsuoka M, Miyano S, Shimoda K, Ogawa S. Integrated molecular analysis of adult T cell leukemia/lymphoma. *Nat Genet.* 2015;47:1304-1315.
40. Aoki T, Suzuki R, Kuwatsuka Y, Kako S, Fujimoto K, Taguchi J, Kondo T, Ohata K, Ito T, Kamoda Y, Fukuda T, Ichinohe T, Takeuchi K, Izutsu K, Suzumiya J. Long-term survival following autologous and allogeneic stem cell transplantation for blastic plasmacytoid dendritic cell neoplasm. *Blood.* 2015;125:3559-3562.
41. Lin SY, Chuang SS, Jhuang JY, Sakamoto K, Takeuchi K, Bahrami A, Tsai CC. ALK positive large B-cell lymphoma with a massive neutrophilic infiltrate: report of a case mimicking epithelioid inflammatory myofibroblastic tumour. *J Clin Pathol.* 2015;68:496-498.

42. Nitta H, Terui Y, Yokoyama M, Mishima Y, Nishimura N, Ueda K, Kusano Y, Tsuyama N, Takeuchi K, Kanda Y, Hatake K. Absolute peripheral monocyte count at diagnosis predicts central nervous system relapse in diffuse large B-cell lymphoma. *Haematologica*. 2015;100:87-90.
43. Nakada T, Okumura S, Kuroda H, Uehara H, Mun M, Takeuchi K, Nakagawa K. Imaging Characteristics in ALK Fusion-Positive Lung Adenocarcinomas by Using HRCT. *Ann Thorac Cardiovasc Surg*. 2015;21:102-108.
44. Sakurai H, Sugimoto KJ, Shimada A, Imai H, Wakabayashi M, Sekiguchi Y, Ota Y, Izutsu K, Takeuchi K, Komatsu N, Noguchi M. Primary CNS CCND1/MYC-Positive Double-Hit B-Cell Lymphoma: A Case Report and Review of the Literature. *J Clin Oncol*. 2015;33:e79-83.
45. Tomita N, Kodama F, Tsuyama N, Sakata S, Takeuchi K, Ishibashi D, Koyama S, Ishii Y, Yamamoto W, Takasaki H, Hagihara M, Kuwabara H, Tanaka M, Hashimoto C, Yamazaki E, Koharazawa H, Fujimaki K, Sakai R, Fujisawa S, Ishigatsubo Y. Biweekly THP-COP therapy for newly diagnosed peripheral T-cell lymphoma patients. *Hematol Oncol*. 2015;33:9-14.
46. Nishimura, K., Johmura, Y., Deguchi, K., Jiang, Z., Uchida, KSK., Suzuki, N., Shimada, M., Chiba, Y., Hirota, T., Yoshimura, SH., Kono, K., Nakanish, M (2019) Cdk1-mediated DIAPH1 phosphorylation maintains metaphase cortical tension and inactivates the spindle assembly checkpoint at anaphase. *Nat Comm*. in-press.
47. Nakayama, I., Shinozaki, E., Sakata, S., Yamamoto, N., Fujisaki, J., Muramatsu, Y., Hirota, T., Takeuchi, K., Takahashi, S., Yamaguchi, K., Noda, T. (2019) Enrichment of CLDN18-ARHGAP fusion gene in gastric cancers in young adults. *Cancer Sci*. in-press.
48. Hayashi, Y., Fujimura, A., Kato, K., Udagawa, R., Hirota, T., and Kimura, K. (2018) Nucleolar integrity during interphase supports faithful Cdk1 activation and mitotic entry. *Sci Adv*. 4: eaap7777.
49. Konishi, M., Shindo, N., Komiya, M., Tanaka, K., Itoh, T. and Hirota, T. (2018) Quantitative analyses of the metaphase-to-anaphase transition reveal differential kinetic regulation for securin and cyclin B1. *Biomed Res*. 39: 75-85.

[Review Articles]

1. Nozawa, R. and Saitoh, N. RNA and interphase chromatin structure. *Yodosha Jikken Igaku* 36: 2941-2948, 2018.
2. Takahashi, M., and *Hirota, T. (2019) Folding the genome into mitotic chromosomes. *Curr. Opin Cell Biol*. In-press.

3. Takahashi, M., and *Hirota, T. (2018) Dynamics of sister chromatids through the cell cycle: Together and apart. Spotlight. *J Cell Biol.* 217: 1887-1889.
4. Uchida, K., and *Hirota, T. (2018) Chromosome segregation: Stepwise dissociation of sister chromatid cohesion. *Jikken Igaku* 36 (17): 135-141.

[Conference Activities & Talks]

1. Saitoh, N. *Eleanor* long non-coding RNAs in the active TAD of breast cancer. The 41st Annual Meeting of the Molecular Biology Society of Japan, Workshop 2PW2-16 (organizer) “Regulation of the nuclear events by long non-coding RNAs” November 29, 2018. Pacifico Yokohama, Kanagawa.
2. Saitoh, N. Nuclear non-coding RNAs *Eleanors*, define the active *ESR1* chromatin domain in breast cancer cells. Cold Spring Harbor Conferences Asia, RNA Biology. October 30, 2018. Dashu Lake Conference Hotel, Suzhou, China.
3. Saitoh, N. Chromatin regulation by nuclear non-coding RNA in breast cancer cells. 10th HiHA international workshop: Understanding chromosomal dynamics, segregation and function. October 10, 2018, Hiroshima Univ, Higashi Hiroshima.
4. Saitoh, N. Nuclear non-coding RNAs Eleanors, define the active ESR1 chromatin domain in breast cancer cells. The 77th Annual Meeting of the Japanese Cancer Association. September 29, Osaka International convention Center, Osaka
5. Saitoh, N. Non-coding RNA and 3D genome organization involved in breast cancer. (16th seminar for chromatin metabolism. August 7, 2018. Chiba Univ, Chiba.
6. Saitoh, N. *Eleanor* long non-coding RNAs in the active chromosomal domain in breast cancer. 2nd Toyama RNA workshop and seminar for graduate school of innovative life science. March 7, 2018. Toyama Univ, Toyama.
7. Saitoh, N. Breast cancer and the cell nucleus. Public symposium by Grant-in-Aid for Scientific Research on Innovative Areas, MEXT, Japan “Chromatin Structure, Dynamics, and Function”. January 8, 2018. Waseda Univ, Tokyo.
8. Nakamura T. Animal models for bone and soft tissue sarcoma by fusion gene expression. The 65th Annual Meeting of Japanese Association for Laboratory Animal Science April, 2018, Toyama
9. Nakamura T. Modeling bone and soft tissue sarcoma to clarify fusion gene and epigenome interaction. The 77th Annual Meeting of the Japanese Cancer Association October, 2018, Osaka
10. Nakamura T. ex vivo Mouse models to understand developmental mechanisms of leukemia and bone and soft tissue sarcoma. The 60th Congress of the Japanese Society of Paediatric Oncology. November, 2018, Kyoto.
11. Nakamura T. Novel insights into fusion gene-dependent sarcoma development. The 2nd Meeting of Japanese Association of Sarcoma Treatment and Research. February, 2019, Tokyo.

12. Nakamura T. Developmental mechanisms of fusion gene associated sarcoma. Asia-Pacific Scientific Workshop. March, 2019, Singapore.
13. Toru Hirota: A robust transition from metaphase to anaphase prevents chromosome missegregation. Symposium. The 77th Annual meeting of JCA. Osaka, Sept 27, 2018.
14. Motoko Takahashi and Toru Hirota: Single stranded DNA in interphase is a key chromatin structure for mitotic chromosome organization. The 3R+3C Symposium. Kanazawa, Nov 12-16, 2018.
15. Toru Hirota: Troubles of the brake and engine driving chromosome segregation in cancer. Symposium. Genoproteomic signature of human diseases. Ajou Univ Suwon, Nov 26, 2018.
16. Toru Hirota: A robust control of metaphase-to-anaphase transition ensures stable chromosome segregation. Symposium. The 41st Annual meeting of the MBSJ. Yokohama, Nov 29, 2018.
17. Toru Hirota: Fast-in, Fast-out: a safe driving through mitotic transitions. Seminar. Okinawa Institute of Science and Technology, Mar 6, 2019.

Medical Science Mathematics

Professor: Tatsuhiko Tsunoda, Junior Associate Professor: Fuyuki Miya,
Assistant Professor: Jo Nishino, Assistant Professor: Takashi Kamatani

(1) Outline

Medical application of rapidly progressing omic profiling technologies and, in particular, the promotion of personalized/precision/preventive medicine have been keenly desired. Our department overcomes such medical science issues by using a combination of mathematics and computational sciences: (1) Integrative analysis of clinical and omic data for exploring etiologies of intractable diseases, (2) Molecular classification of and systems approach to understanding disease based on omic profiling, and (3) Prediction for personalized/precision/preventive medicine - we apply mathematical methods, e.g, machine learning techniques, to optimum therapy prediction for each patient when she/he visits to a hospital/medical institute, and we can also apply these methods to disease prevention based on an individual's health check records.

(2) Publications

[Original Articles]

1. Mochimaru T., Fukunaga K., Kuwae M., Watanabe R., Okuzumi S., Baba R., Kamatani T., Tanosaki T., Matsusaka M., Ueda S., Betsuyaku T.. Neutrophil to Lymphocyte Ratio Is a Novel Predictor of Severe Exacerbation in Asthma Patients AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2018; 197;
2. Florence Demenais, Michiaki Kubo, Atsushi Takahashi, Tatsuhiko Tsunoda, et al.. Multiancestry association study identifies new asthma risk loci that colocalize with immune-cell enhancer marks. Nat. Genet.. 2018.01; 50(1); 42-53
3. Yosvany López, Alok Sharma, Abdollah Dehzangi, Sunil Pranit Lal, Ghazaleh Taherzadeh, Abdul Sattar, Tatsuhiko Tsunoda. Success: evolutionary and structural properties of amino acids prove effective for succinylation site prediction. BMC Genomics. 2018.01; 19(Suppl 1); 923
4. Abdollah Dehzangi, Yosvany López, Sunil Pranit Lal, Ghazaleh Taherzadeh, Abdul Sattar, Tatsuhiko Tsunoda, Alok Sharma. Improving succinylation prediction accuracy by incorporating the secondary structure via helix, strand and coil, and evolutionary information from profile bigrams. PLoS ONE. 2018.02; 13(2); e0191900
5. Yasuhiro Ikeda, Koji M Nishiguchi, Fuyuki Miya, Nobuhiro Shimozaawa, Jun Funatsu, Shunji Nakatake, Kohta Fujiwara, Takashi Tachibana, Yusuke Murakami, Toshio Hisatomi, Shigeo Yoshida, Yasuhiro Yasutomi, Tatsuhiko Tsunoda, Toru Nakazawa, Tatsuro Ishibashi, Koh-Hei Sonoda. Discovery of a Cynomolgus Monkey Family With Retinitis Pigmentosa. Invest. Ophthalmol. Vis. Sci.. 2018.02; 59(2); 826-830
6. Tamai K, Tada K, Takeuchi A, Nakamura M, Marunaka H, Washio Y, Tanaka H, Miya F, Okamoto N, Kageyama M. Fetal ultrasonographic findings including cerebral hyperechogenicity in a patient with non-lethal form of Raine syndrome AMERICAN JOURNAL OF MEDICAL GENETICS PART A. 2018.03; 176(3); 682-686

7. Daichi Shigemizu, Fuyuki Miya, Shintaro Akiyama, Shujiro Okuda, Keith A Boroevich, Akihiro Fujimoto, Hidewaki Nakagawa, Kouichi Ozaki, Shumpei Niida, Yonehiro Kanemura, Nobuhiko Okamoto, Shinji Saitoh, Mitsuhiro Kato, Mami Yamasaki, Tatsuo Matsunaga, Hideki Mutai, Kenjiro Kosaki, Tatsuhiko Tsunoda. IMSindel: An accurate intermediate-size indel detection tool incorporating de novo assembly and gapped global-local alignment with split read analysis. *Sci Rep.* 2018.04; 8(1); 5608
8. Jo Nishino, Yuta Kochi, Daichi Shigemizu, Mamoru Kato, Katsunori Ikari, Hidenori Ochi, Hisashi Noma, Kota Matsui, Takashi Morizono, Keith A Boroevich, Tatsuhiko Tsunoda, Shigeyuki Matsui. Empirical Bayes Estimation of Semi-parametric Hierarchical Mixture Models for Unbiased Characterization of Polygenic Disease Architectures. *Front Genet.* 2018.04; 9; 115
9. Noriomi Suzuki, Hideki Mutai, Fuyuki Miya, Tatsuhiko Tsunoda, Hiroshi Terashima, Noriko Morimoto, Tatsuo Matsunaga. A case report of reversible generalized seizures in a patient with Waardenburg syndrome associated with a novel nonsense mutation in the penultimate exon of SOX10. *BMC Pediatr.* 2018.05; 18(1); 171
10. Sakurai Kaori, Chubachi Shotaro, Irie Hidehiro, Tsutsumi Akihiro, Kameyama Naofumi, Kamatani Takashi, Koh Hidefumi, Terashima Takeshi, Nakamura Hidetoshi, Asano Koichiro, Betsuyaku Tomoko. Clinical utility of blood neutrophil-lymphocyte ratio in Japanese COPD patients *BMC PULMONARY MEDICINE.* 2018.05; 18(1); 65
11. Ronesh Sharma, Gaurav Raicar, Tatsuhiko Tsunoda, Ashwini Patil, Alok Sharma. OPAL: prediction of MoRF regions in intrinsically disordered protein sequences. *Bioinformatics.* 2018.06; 34(11); 1850-1858
12. Ikumi Hori, Fuyuki Miya, Yutaka Negishi, Ayako Hattori, Naoki Ando, Keith A Boroevich, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. A novel homozygous missense mutation in the SH3-binding motif of STAMBP causing microcephaly-capillary malformation syndrome. *J. Hum. Genet..* 2018.06; 63; 957-963
13. Jo Nishino, Hidenori Ochi, Yuta Kochi, Tatsuhiko Tsunoda, Shigeyuki Matsui. Sample Size for Successful Genome-Wide Association Study of Major Depressive Disorder. *Front Genet.* 2018.06; 9; 227
14. Yumi Yamaguchi-Kabata, Takashi Morihara, Tomoyuki Ohara, Toshiharu Ninomiya, Atsushi Takahashi, Hiroyasu Akatsu, Yoshio Hashizume, Noriyuki Hayashi, Daichi Shigemizu, Keith A Boroevich, Manabu Ikeda, Michiaki Kubo, Masatoshi Takeda, Tatsuhiko Tsunoda. Integrated analysis of human genetic association study and mouse transcriptome suggests LBH and SHF genes as novel susceptible genes for amyloid- β accumulation in Alzheimer's disease. *Hum. Genet..* 2018.07; 137(6-7); 521-533
15. Otani T, Noma H, Nishino J, Matsui S. Re-assessment of multiple testing strategies for more efficient genome-wide association studies. *European journal of human genetics : EJHG.* 2018.07; 26(7); 1038-1048
16. Daichi Shigemizu, Fuyuki Miya, Shintaro Akiyama, Shujiro Okuda, Keith A Boroevich, Akihiro Fujimoto, Hidewaki Nakagawa, Kouichi Ozaki, Shumpei Niida, Yonehiro Kanemura, Nobuhiko Okamoto, Shinji Saitoh, Mitsuhiro Kato, Mami Yamasaki, Tatsuo Matsunaga, Hideki Mutai, Kenjiro Kosaki, Tatsuhiko Tsunoda. Publisher Correction: IMSindel: An accurate intermediate-size indel detection tool incorporating de novo assembly and gapped global-local alignment with split read analysis. *Sci Rep.* 2018.07; 8(1); 10367
17. Matsuhisa T, Takahashi N, Aomatsu M, Takahashi K, Nishino J, Ban N, Mercer SW. How many patients are required to provide a high level of reliability in the Japanese version of the CARE Measure? A secondary analysis. *BMC family practice.* 2018.08; 19(1); 138
18. Takahiro Otani, Hisashi Noma, Shonosuke Sugawara, Aya Kuchiba, Atsushi Goto, Taiki Yamaji, Yuta Kochi, Motoki Iwasaki, Shigeyuki Matsui, Tatsuhiko Tsunoda. Exploring predictive biomarkers from clinical genome-wide association studies via multidimensional hierarchical mixture models. *Eur. J. Hum. Genet..* 2018.09;
19. Computational pipelines and workflows in Bioinformatics. 2018.09;
20. Nguyen Dang Ton, Hidewaki Nakagawa, Nguyen Hai Ha, Nguyen Thuy Duong, Vu Phuong Nhung, Le Thi Thu Hien, Huynh Thi Thu Hue, Nguyen Huy Hoang, Jing Hao Wong, Kaoru Nakano, Kazuhiro Maejima, Aya Sasaki-Oku, Tatsuhiko Tsunoda, Akihiro Fujimoto, Nong Van Hai. Whole genome sequencing and mutation rate analysis of trios with paternal dioxin exposure. *Hum. Mutat..* 2018.10; 39(10); 1384-1392

21. Masato Akiyama, Atsushi Takahashi, Yukihide Momozawa, Satoshi Arakawa, Fuyuki Miya, Tatsuhiko Tsunoda, Kyota Ashikawa, Yuji Oshima, Miho Yasuda, Shigeo Yoshida, Hiroshi Enaida, Xue Tan, Yasuo Yanagi, Tsutomu Yasukawa, Yuichiro Ogura, Yoshimi Nagai, Kanji Takahashi, Kimihiko Fujisawa, Maiko Inoue, Akira Arakawa, Koji Tanaka, Mitsuko Yuzawa, Kazuaki Kadonosono, Koh-Hei Sonoda, Tatsuro Ishibashi, Michiaki Kubo. Genome-wide association study suggests four variants influencing outcomes with ranibizumab therapy in exudative age-related macular degeneration. *J. Hum. Genet.*. 2018.10; 63(10); 1083-1091
22. Ronesh Sharma, Alok Sharma, Gaurav Raicar, Tatsuhiko Tsunoda, Ashwini Patil. OPAL+: Length-Specific MoRF Prediction in Intrinsically Disordered Protein Sequences. *Proteomics*. 2018.10; e1800058
23. Hideki Mutai, Fuyuki Miya, Hiroaki Shibata, Yasuhiro Yasutomi, Tatsuhiko Tsunoda, Tatsuo Matsunaga. Gene expression dataset for whole cochlea of *Macaca fascicularis*. *Sci Rep*. 2018.10; 8(1); 15554
24. Dang Ton Nguyen, Hai Ha Nguyen, Thuy Duong Nguyen, Thi Thanh Hoa Nguyen, Kaoru Nakano, Kazuhiro Maejima, Aya Sasaki-Oku, Van Ba Nguyen, Duy Bac Nguyen, Bach Quang Le, Jing Hao Wong, Tatsuhiko Tsunoda, Hidewaki Nakagawa, Akihiro Fujimoto, Van Hai Nong. Whole Genome Sequencing of a Vietnamese Family from a Dioxin Contamination Hotspot Reveals Novel Variants in the Son with Undiagnosed Intellectual Disability. *Int J Environ Res Public Health*. 2018.11; 15(12);
25. Artem Lysenko, Alok Sharma, Keith A Boroevich, Tatsuhiko Tsunoda. An integrative machine learning approach for prediction of toxicity-related drug safety. *Life Sci Alliance*. 2018.12; 1(6); e201800098
26. Abdollah Dehzangi, Yosvany López, Ghazaleh Taherzadeh, Alok Sharma, Tatsuhiko Tsunoda. SumSec: Accurate Prediction of Sumoylation Sites Using Predicted Secondary Structure. *Molecules*. 2018.12; 23(12); 3260
27. Abel Chandra, Alok Sharma, Abdollah Dehzangi, Shoba Ranganathan, Anjeela Jokhan, Kuo-Chen Chou, Tatsuhiko Tsunoda. PhoglyStruct: Prediction of phosphoglycerylated lysine residues using structural properties of amino acids. *Sci Rep*. 2018.12; 8(1); 17923
28. Kohji Kato, Fuyuki Miya, Nanako Hamada, Yutaka Negishi, Yoko Narumi-Kishimoto, Hiroshi Ozawa, Hidenori Ito, Ikumi Hori, Ayako Hattori, Nobuhiko Okamoto, Mitsuhiko Kato, Tatsuhiko Tsunoda, Yonehiro Kanemura, Kenjiro Kosaki, Yoshiyuki Takahashi, Koh-Ichi Nagata, Shinji Saitoh. de novo gain-of-function mutation in a patient with a novel megalencephaly syndrome. *J. Med. Genet.*. 2018.12;

[Misc]

1. Mansoor Saqi, Artem Lysenko, Yi-Ke Guo, Tatsuhiko Tsunoda, Charles Auffray. Navigating the disease landscape: knowledge representations for contextualizing molecular signatures. *Brief. Bioinformatics*. 2018.04;
2. Katsuyuki Yugi, Tatsuhiko Tsunoda, Shinya Kuroda. Decipher GWAS with Trans-Omics Gene & Medicine MOOK. 2018.04; 33; 127-136
3. Tatsuhiko Tsunoda. Machine learning enables T2D onset prediction for precision medicine *Medical Science Digest*. 2018.06; 44(6); 306-309

[Conference Activities & Talks]

1. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST Big Data Fields Joint Meeting 2018.01.16 Tokyo, Japan
2. Tatsuhiko Tsunoda. Development and applications of next-generation human whole-omic analysis methodology. Group Meeting of Grant-in-Aid for Scientific Research on Innovative Areas 2018.06.11 Tokyo
3. Tatsuhiko Tsunoda. Fully Utilize Big Data for Clinical Research. Clinical Research Statistics Course 2018.08.31 Tokyo
4. Tatsuhiko Tsunoda. Omic analysis with AI drives precision medicine. The 5th RIKEN-KI/SciLifeLab Joint Symposium 2018.09.20 Stockholm, Sweden

5. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST International Symposium on Big Data Application 2018.09.30 Tokyo, Japan
6. Tatsuhiko Tsunoda. Public Big Data Accelerate Medical Science Research. Symposium “Public database and application for medicine in Japan and Asia” , The 63rd Annual Meeting of the Japan Society of Human Genetics 2018.10.13
7. Tatsuhiko Tsunoda. Omic Big Data Analysis Drives Precision Medicine. The 8th Annual Translational Bioinformatics Conference/2018 Annual Conference of Korean Society for Bioinformatics 2018.11.01
8. Tatsuhiko Tsunoda. Trans-omic Analysis Strategy for Precision Medicine. The 2nd International Symposium for Trans-Omics 2018.11.14
9. Tatsuhiko Tsunoda. Trans-omic and Trans-species Analysis Drives Precision Medicine. The 41st Annual Meeting of the Molecular Biology Society of Japan 2018.11.30 Yokohama, Japan
10. Tatsuhiko Tsunoda. Progress of Genomic Medicine and Promotion of Precision Medicine. Tohoku Medical Megabuck the 16th Genome and Omics Collaboration Promoting Seminar 2018.12.04

[Patents]

1. METHOD FOR SELECTING IPS CELL CLONE, AND METHOD FOR SELECTING GENE USED IN METHOD FOR SELECTING SAME, Announcement Number : WO 2012/115270

[Works]

1. IMSIndel: An accurate intermediate-size indel detection tool incorporating de novo assembly and gapped global-local alignment with split read analysis., Software, 2018.04

[Others]

1. Development of Accurate Method for Identifying Middle-size DNA Sequence Insertions and Deletions in Genome, 2018.04
Appeared in newspaper Nikkei Sangyo Shimbun
2. Alzheimer disease associated genes were identified by RIKEN-TMDU, 2018.08
Appeared in newspaper Kagaku-Kougyou-Nippou
3. RIKEN, TMDU, and Tohoku U discovered new Alzheimer disease causing genes, 2018.08
Appeared in newspaper NIKKEI inc.
4. Alzheimer disease associated genes were identified, 2018.08
Appeared in newspaper NIKKEI-biotech
5. Two new Alzheimer disease causing genes were identified, 2018.08
Appeared in newspaper Medical News QLifePro
6. RIKEN et al identified new Alzheimer disease associated genes, 2018.08
Appeared in newspaper Nikkan Kougyou Shimbun
7. New Alzheimer disease causing genes were identified with an integrative analysis method, 2018.08
Appeared in newspaper YAKUJINIPPO

Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi
 Junior Associate Professor: Takahiro Arakawa
 Assistant Professor: Koji Toma
 Lecturer (part-time): Kazuyoshi Yano

(1) Outline

Our research is based on a broad range of areas such as electrochemistry, mechanical engineering, electrical engineering, material science and biochemistry. The group aims to pursue interdisciplinary research in bio-MEMS, bio-optics, bio-electronics or bioinformatics by combining biotechnology and information technology.

(2) Research

1. Detachable “Cavitas sensors” as bioinformation monitoring systems in body cavities
 “Cavitas sensors” such as a soft contact-lens biosensor and a mouth guard biosensor have been developed for novel biomonitoring methods by using advanced polymer microelectromechanical systems (MEMS) techniques.
2. Biochemical gas sensor “Bio-sniffers” and spatiotemporal gas visualization system “Sniff-camera” for volatile organic compounds from human body
 Highly selective gas sensors “Bio-sniffers” and gas visualization systems “Sniff-camera” for acquiring spatiotemporal information of distribution of volatile chemicals have been developed by exploiting metabolizing enzymes in human liver. Potential applications of these gas sensors include halitosis analysis, breath alcohol and aldehyde measurement, medical screening or dental health, etc.
3. Immunosensors for medical treatment and environmental medicine
 Development of optical or surface acoustic wave immunosensors have been pursued for semi-continuous (rapid and repeated) measurement of antigens in body and airborne allergens in living environment.
4. “Organic engine” and “Air bio-battery” based on chemo-mechanical energy conversion
 Novel chemo-mechanical energy conversion systems (Organic engine and Air bio-battery) that utilize enzyme reactions and active transport of chemicals has been constructed. Biomedical applications (chemical pumps, drug release systems, etc.) are also investigated.

(3) Education

In advanced medicine, technologies enabling to accurately measure biological information are highly demanded. The development of “human-friendly” non-invasive measurement methods could release patients from the pain and the risks of sampling. The students will learn the basic knowledge and skills of biological information measurement through the lectures (e.g., “Biomedical Device Science and Engineering”, “Practice in Global Linkage between University and Industry” and “Nanobiotechnology”), seminars and practical training. Especially research including biochemical measurement, the development of biosensing devices and their applications to medicine will be carried out based on “sensor and biomedical engineering.”

(4) Lectures & Courses

The students will learn the basic technology related to advanced medicine and biological information measurement. Through practical training, they will also engage in research activities for biochemical measurement, the development of biosensing devices and their applications to medicine based on “sensor and biomedical engineering”. The objective of this course is to help the students be able to think about and conduct a research by themselves throughout the activities with academic researches.

(5) Publications**[Original Articles]**

1. Koji Toma, Keisuke Tomoto, Kumi Yokota, Nao Yasuda, Tatsuya Ishikawa, Takahiro Arakawa, and Kohji Mitsubayashi. Mouthguard controller for unconstrained controlling of external devices *Sensors and Materials*. 2018; 30(12); 3053-3060
2. Kenta Iitani, Toshiyuki Sato, Munire Naisierding, Yuuki Hayakawa, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Fluorometric sniff-cam (gas-imaging system) utilizing alcohol dehydrogenase for imaging concentration distribution of acetaldehyde in breath and transdermal vapor after drinking *Analytical Chemistry*. 2018.01; 90(4); 2678-2685
3. Kenta Iitani, Po-Jen Chien, Takuma Suzuki, Koji Toma, Takahiro Arakawa, Yasuhiko Iwasaki, Kohji Mitsubayashi. Fiber-optic bio-sniffer (biochemical gas sensor) using ADH reverse reaction for exhaled acetaldehyde *ACS Sensors*. 2018.01; 3(2); 425-431
4. Takahiro Arakawa, Rui Xie, Fumiya Seshima, Koji Toma, Kohji Mitsubayashi. Air bio-battery with a gas/liquid porous diaphragm cell for medical and health care devices *Biosensors and Bioelectronics*. 2018.04; 103; 171-175

[Books etc]

1. Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Reusable surface acoustic wave immunosensor for monitoring of mite allergens, *Modern Sensing Technologies*. Springer, 2018.10 (ISBN : 978-3-319-99540-3)

[Conference Activities & Talks]

1. Toma K, Arakawa T, Mitsubayashi K. Continuous antigen sensors "Immunowatchers" for prevention of bioaerosol-associated and acute diseases. The 4th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2018.01.12 Bangkok, Thailand
2. Mitsubayashi K. Gas-imaging system (SNIFF-CAM) of dermal volatiles for skin condition and aging analysis. The 9th International Conference of Skin Ageing & Challenges 2018.02.25 Porto, Portugal
3. Iitani K, Sato T, Toma K, Arakawa T, Mitsubayashi K. Biofluorometric gas-imaging system "Sniff-cam" for ethanol and acetaldehyde from body after drinking. EUROPT(R)ODE 2018 2018.03.25 Naples, Italy
4. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Gas-imaging system (sniff-cam) using NADH-dependent alcohol dehydrogenase for assessment of alcohol metabolism. 22nd Topical Meeting of the International Society of Electrochemistry 2018.04.15 Tokyo, Japan
5. Mitsubayashi K. Non-invasive biosensing devices for preemptive medicine. 2018 International Conference in Electronics Packaging and iMAPS All Asia Conference (ICEP-IAAC 2018) 2018.04.17 Mie, Japan
6. Arakawa T, Mitsubayashi K. Non-invasive biosensing for preemptive medicine. Nano/Micro Engineered and Molecular Systems (NEMS) 2018 2018.04.25 Singapore
7. Toma K, Seshima F, Maruyama A, Arakawa T, Yano K, Mitsubayashi K. Advanced glucose-driven „ Air bio-battery” with closely-placed electrodes for medical and healthcare devices. *Biosensors* 2018 2018.06.12 Miami, USA
8. Toma K, Yoshimura N, Arakawa T, Yatsuda H, Mitsubayashi K. A reusable surface acoustic wave (SAW) immunosensor for monitoring of airborne mite allergens. *Biosensors* 2018 2018.06.12 Miami, USA

9. Arakawa T, Suzuki T, Tujii M, Chien P-J, Ye M, Toma K, Iwasaki Y, Mitsubayashi K. Direct skin gas monitoring system using high-sensitive ethanol bio-sniffer (gas-phase biosensor) by detecting NADH consumption on enzymatic reaction. Biosensors 2018 2018.06.12 Miami, USA
10. Iitani K, Hayakawa Y, Toma K, Arakawa T, Mitsubayashi K. Switchable sniff-cam (Gas-imaging system) based on pH-dependent redox reactions of alcohol dehydrogenase (ADH) between gaseous ethanol and acetaldehyde after drinking. Biosensors 2018 2018.06.12 Miami, USA
11. Toma K, Oishi K, Kodaira K, Yoshimura N, Arakawa T, Yatsuda H, Kanamori K, Mitsubayashi K. Precipitate-assisted signal amplification of surface acoustic wave immunosensor for mite allergen. 17th International Meeting on Chemical Sensors (IMCS2018) 2018.07.15 Vienna, Austria
12. Mitsubayashi K. Cavity biosensors for IoT health care & preventive medicine. A Joint Taiwan-Japan Research Grant 2018, “Secure IoT-Based Information Platform with Privacy-Preserving Data Mining on Big Data for M-Healthcare” 2018.07.16 Meiji Univ., Chiyoda-ku, Tokyo.
13. Mitsubayashi K. Non-invasive biomedical devices for the future of medicine. SDM-18 (Sustainable Design and Manufacturing 2018) 2018.07.25 Gold Coast, Australia
14. Arakawa T, Ye M, Toma K, Mitsubayashi K. Soft contact lens type biosensor for continuous monitoring of tear glucose. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.05 Tokyo, Japan
15. Xing M, Toma K, Arakawa T, Mitsubayashi K. Soft contact lens type biosensor for continuous monitoring of tear glucose. International Conference on Innovative Technologies, IN-TECH 2018 2018.09.06 Zagreb, Croatia
16. Arakawa T, Ye M, Toma K, Mitsubayashi K. Acetone bio-sniffer (biochemical gas sensor) for breath acetone as a volatile organic compound of lipid metabolism. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
17. Mitsubayashi K. Sniff-cam for real-time imaging of volatile chemicals. DOS (Digital Olfaction Society) Annual Meeting 2018 2018.12.04 Tokyo, Japan
18. Toma K, Arakawa T, Mitsubayashi K. Acetone bio-sniffer (biochemical gas sensor) for breath acetone as a volatile organic compound of lipid metabolism. ICCTS 2018 (2018 7th International Conference on Computer Technology and Science) 2018.12.07 Ho Chi Minh, Vietnam

Biomedical Information

Professor Yoshikazu NAGAJIMA
Research Assistant Teruyo MORI
Graduate Student Yoshihiro SUGIO

(1) Research

1. Surgical Scene Recognition with Artificial Intelligence
2. Deep-Learning Segmentation and Annotation of Brain MRI volumes
3. Probabilistic Approach of Error-distribution Estimation in 2D Projection Measurement
4. Pneumatic Stiffness-Tunable Mechanism and its Application for Laparoscopic Surgeries

(2) Publications

[Original Articles]

1. Hayashi T, Tokihiro T, Kurihara H, Nomura F, Yasuda K. Integrate and Fire Model with Refractory Period for Synchronization of Two Cardiomyocytes J. Theor. Biol.. 2018.01; 437; 141-148
2. Kaneko T, Toriumi H, Shimada J, Nomura F. Extracellular field potential recording of single cardiomyocytes in agarose microchambers using microelectrode array Japanese Journal of Applied Physics. 2018.01; 57(3S2); 03EB03
3. Fujii K, Nomura F, Kaneko T. Dependences of the geometrical parameters of cell community on stimulation voltage and frequency in chick embryonic cardiomyocytes Jpn. J. Appl. Phys.. 2018.02; 57(3S2); 03EB04

[Conference Activities & Talks]

1. Nakajima Y. Computer integrated analysis of pre-and intra-operative surgical data. The 4th Joint Symposium between IBB/TMDU and Chulalongkorn University on Biomedical Materials and Engineering 2018.01.12 Bangkok, Thailand
2. Yoshikazu Nakajima. Autonomous Networking of Small and Weak-AI Computers and Its Applications for Medical Assistance. The 21st East Asia Round Table Meeting of Academies of Engineering (EA-RTM) 2018.10.25 Hangzhou, China
3. Yoshikazu Nakajima. Knowledge sharing among small AI computers in medicine. IKCEST International Symposium 2018 2018.10.26 Hangzhou, China
4. Yoshikazu Nakajima. Strong-AI data analysis in medicine by using autonomous networking of small and weak AIs. The 6th International Symposium of " Dialogue for Global Innovation" on Technology and Humanity-part 2 2018.11.02 Cambridge, UK

5. Joonhwan Kim, Yoshikazu Nakajima, Hiroshi Tsukihara, Hidemichi Kiyomatsu, Sakura Uto, Ichiro Sakuma. Effectiveness and invasiveness evaluation of the organ manipulation finger in in-vivo trial. The 14th Asian Conference on Computer Aided Surgery (ACCAS2018) 2018.11.18 Shanghai, China
6. Yoshikazu Nakajima. Computerization of Medicine and Biology. International Symposium on Frontier of Science, Technology and Engineering (FOSTE) 2018.11.23 Chiang Mai, Thailand

Bioelectronics

Staff

Yuji Miyahara (Professor)
Akira Matsumoto (Associate Professor)
Tatsuro goda (Assistant Professor)
Miyuki Tabata (tenure track Assistant Professor)
Yukichi Horiguchi (Assistant Professor)
Toshihiro Yoshizumi (Specially Appointed Assistant Professor)
Siyuan Chen (Collaborative Researcher)
Taiki Miyazawa (Project Assistant Professor)
Hiroko Matsumoto (Technical Assistant)
Yuki Morooka (Technical Assistant)
Chiharu Mizoi (Technical Assistant)
Sayo Kotaki (Technical Assistant)
Kayoko Nakagawa (Staff Assistant)
Ulala Minamibata (Staff Assistant)

Graduate student

Chindanai RATANAPORNCHAROEN, Hideki Fujisaki, Dilinaer AINIWAER,
Hiroaki Hatano, Chattarika KHAMHANGLIT, Maki Shikatani, Ayumu Tsuchiya

(1) Outline

Bioelectronics group is engaged in developing methodologies to determine and analyze functions of biomolecules and their relationships to diseases based on solid-state biosensor technology. Our interests include design & understanding of physicochemical properties of the interface between biomolecules and the device materials, signal-transduction mechanism as well as the pursuit of improved sensitivity and selectivity. These technologies involve many different disciplines of science and engineering, through which we propose new solutions to future medicine.

(2) Research

1. Bioelectronics for Next-generation DNA Sequencing

Our research is focused on the development of nano-interfaces between biomolecules and semiconducting materials for label-free and highly sensitive electrical monitoring of nucleotide base sequences and their amplification processes. The goal of the project is to provide a smaller and cheaper alternative next-generation DNA sequencer to the traditional techniques that involve optical sensing using fluorescence and bioluminescence.

2. Devices for Early Cancer Diagnosis

For applications to early-stage diagnostics of cancers, we aim to establish the device technology enabling detection of small amount of cancer markers out of blood samples with remarkable quickness and sensitivity. The focus is on the design of nano-interfaces that involves chemical modification of biomolecular targets as well as solid/ liquid interfaces in order to achieve efficient biomolecular recognitions on the electrode surfaces. We also pursue optimized materials and the surface property of the electrode in order to obtain remarkably target-specific signals out of complicated electrical signals obtained from raw biological samples.

3. Discovering Intra/Extracellular Molecular Dynamics on Inflammatory Response

Molecular dynamics at inflammation and bacterial infection is investigated using biomimetic surfaces. The term “biomimetics” in this context represents mimicking the interplay between biomolecules and local changes of microenvironment that has evolved as a mechanism for inauguration of immune responses. Our new nano-bio-technology will reveal unidentified active molecular dynamics in pathophysiology.

4. “Artificial Pancreas” to Treat Diabetes

Development of self-regulated insulin delivery systems to treat diabetes is a long-standing challenge of biomedical engineering. We propose a synthetic gel based solution, which could offer a remarkably simple, “electronics-free” and thus significantly low-cost alternative to the ongoing efforts of artificial pancreas.

(3) Education

1. Engagement: we are engaged in teaching a part of Biomedical Engineering course and mentoring master & doctor students.
2. Course objective: Serum components play crucial roles in metabolic cycles and their concentration homeostasis reflects dynamic equilibrium of life. On occasion of abnormal metabolic pathway, it is manifested as a fluctuation of each specific serum component. Our lecture provides an overview of advanced materials and engineering aimed at determination of body fluids including serum components and mechanisms for their concentration homeostasis.
3. Deepen knowledge of theory, mechanisms, methodologies, application, and limitation of detection technology for biomolecules in various clinical samples. Learn integrative technology of advanced materials/devices and biology/medicine, present problems and future perspective in bioelectronics. Familiarize each student with other related techniques, lab skills including planning of experiments, presenting research results and preparing reports.

(4) Publications

[Original Articles]

1. Akira Matsumoto, Yuji Miyahara. 'Borono-lectin' based engineering as a versatile platform for biomedical applications. *Sci Technol Adv Mater.* 2018; 19(1); 18-30
2. Tatsuro Goda, Yuji Miyahara. Specific binding of human C-reactive protein towards supported monolayers of binary and engineered phospholipids *Colloids and Surfaces B: Biointerfaces.* 2018.01; 161; 662-669
3. Naito Mitsuru, Yoshinaga Naoto, Ishii Takehiko, Matsumoto Akira, Miyahara Yuji, Miyata Kanjiro, Kataoka Kazunori. Enhanced Intracellular Delivery of siRNA by Controlling ATP-Responsivity of Phenylboronic Acid-Functionalized Polyion Complex Micelles *MACROMOLECULAR BIOSCIENCE.* 2018.01; 18(1 SI); 1700357
4. Taiki Miyazawa, Kiyotaka Nakagawa, Sharon H Kim, Michael J Thomas, Ligi Paul, Jean-Marc Zingg, Gregory G Dolnikowski, Susan B Roberts, Fumiko Kimura, Teruo Miyazawa, Angelo Azzi, Mohsen Meydani. Curcumin and piperine supplementation of obese mice under caloric restriction modulates body fat and interleukin-1 β . *Nutr Metab (Lond).* 2018.02; 15; 12
5. Taiki Miyazawa, Reina Kamiyoshihara, Naoki Shimizu, Takahiro Harigae, Yurika Otoki, Junya Ito, Shunji Kato, Teruo Miyazawa, Kiyotaka Nakagawa. Amadori-glycated phosphatidylethanolamine enhances the physical stability and selective targeting ability of liposomes. *R Soc Open Sci.* 2018.02; 5(2); 171249
6. Enrico Tenaglia, Yuki Imaizumi, Yuji Miyahara, Carlotta Guiducci. Isothermal Multiple Displacement Amplification of DNA Templates in Minimally Buffered Conditions using Phi29 Polymerase *Chemical Communications.* 2018.02; 17(57); 2158-2161
7. Chindanai Ratanaporncharoen, Miyuki Tabata, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami, Yuji Miyahara. pH Mapping on Tooth Surfaces for Quantitative Caries Diagnosis Using Micro Ir/IrOx pH Sensor. *Anal. Chem..* 2018.03; 90(7); 4925-4931

8. Taiki Miyazawa, Reina Kamiyoshihara, Teruo Miyazawa, Kiyotaka Nakagawa. Potential usability of Amadori-glycated phosphatidylethanolamine as a glycoconjugated biomaterial (short review) IMARS Highlights. 2018.03;
9. Yukichi, Horiguchi, Tatsuro, Goda, Yuji, Miyahara. Simple functionalization method for single conical pores with a polydopamine layer. Applied Physics Express. 2018.04; 11(4); 047001
10. Wenfeng Hai, Tatsuro Goda, Hiroaki Takeuchi, Shoji Yamaoka, Yukichi Horiguchi, Akira Matsumoto, Yuji Miyahara. Human Influenza Virus Detection Using Sialyllactose-Functionalized Organic Electrochemical Transistors. Sensors and Actuators B: Chemical. 2018.05; 260; 635-641
11. Chindanai Ratanaporncharoen, Miyuki Tabata, Natthapol Watanagool, Tatsuro Goda. Characterization and Optimization of Thermally Grown Iridium Oxide and Its Application to pH Sensors Sensors and Materials. 2018.05; 30(5); 1175-1185
12. Toshihiro Yoshizumi, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Gas-sensitive field-effect transistor incorporating polymer layer and porous metal electrode in the gate structure Sensors and Materials. 2018.05; 30(5); 1001-1008
13. カーン・タホミナタレク, カブラル・オラシオ, 松元 亮, 片岡 一則. DEVELOPMENT OF 5-BORONOPICOLINIC ACID-INSTALLED POLYMERIC MICELLES FOR TARGETING SIALYLATED EPITOPES ON CANCER CELLS 日本 DDS 学会学術集会プログラム予稿集. 2018.05; 34 回; 202
14. Tatsuro Goda, Yuji Miyahara. Electrodeposition of Zwitterionic PEDOT Films for Conducting and Antifouling Surfaces Langmuir. 2018.07;
15. Takuya Miyagawa, Sadato Hongo, Naofumi Nakamura, Yukichi Horiguchi, Yuji Miyahara, Hideki Shibata. A Novel Diagnostic System for Infectious Diseases Using Solid-State Nanopore Devices Proceedings of 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). 2018.07; 2833-2836
16. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Gold Nanoparticles with Ligand/Zwitterion Hybrid Layer for Individual Counting of Influenza A H1N1 Subtype Using Resistive Pulse Sensing. Langmuir. 2018.08;
17. Naito Mitsuru, Yoshinaga Naoto, Ishii Takehiko, Matsumoto Akira, Miyahara Yuji, Miyata Kanjiro, Kataoka Kazunori. Fabrication of Intracellular ATP-responsive Polyion Complex Micelles for Smart Nucleotide Therapeutics Delivery(和訳中) 日本バイオマテリアル学会大会予稿集. 2018.11; 40 回; 489

[Misc]

1. Ratanaporncharoen Chindanai, Tabata Miyuki, Goda Tatsuro, Matsumoto Akira, Miyahara Yuji, Ishihara Noboru, Masu Kazuya, Sriyudthsak Mana. Ir/IrOx ワイヤレス pH センサーを用いた齧食部位の pH マッピング 生体医歯工学共同研究拠点成果報告書. 2018.04; 平成 29 年度; 171

[Conference Activities & Talks]

1. Yuji Miyahara. Medical and dental applications of solid-state electrochemical sensors. 3rd Japan-Thailand Joint Symposium on Advanced Nanomaterials and Devices for Electronics and Photonics (JT-AND 2018) 2018.01.22 Chulalongkorn University, Bangkok, Thailand
2. Akira Matsumoto, Miyako Tanaka, Hiroko Matsumoto, Kozue Ochi, Yuki Moro-oka, Hirohito Kuwata, Hironori Yamada, Ibuki Shirakawa, Taiki Miyazawa, Hitoshi Ishii, Kazunori Kataoka, Yoshihiro Ogawa, Yuji Miyahara, Takayoshi Suganami. Synthetic “smart-gel” based approach toward “electronics-free” artificial pancreas. The 11th international conference on advanced technologies and treatment for diabetes (ATTD 2018) 2018.02.14
3. Taiki Miyazawa, Akira Matsumoto, Taturu Goda, Yuji Miyahara. Determination of cellular uptake of oxidized vitamin c in erythrocyte and cancer cells. 2018 Annual Meeting of the Japan Society for Bioscience, Biotechnology, and Agrochemistry (JSBBA) 2018.03.16 meijo university, Nagoya, Japan
4. Taiki Miyazawa, Kiyotaka Nakagawa, Reina Kamiyoshihara, Teruo MIYAZAWA. Preparation and cellular uptake of Amadori-PE containing liposomes.. 日本化学会 第 98 春季年会 2018.03.20 日本大学 理工学部 船橋キャンパス

5. Taiki Miyazawa, Akira Matsumoto, Tatsuhiro Goda, Yuji Miyahara. Direct determination of vitamin C and oxidized vitamin C by UV-HPLC. 日本化学会 第 98 春季年会 2018.03.21 日本大学 理工学部 船橋キャンパス
6. Yukichi Horiguchi, Tatsuhiro Goda, Yuji Miyahara. Easy functionalization method and electrical characteristics of single conical pores with a polydopamine layer. International Symposium on Organic Molecular Electronics (ISOME 2018) 2018.05.31
7. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Cytodiagnosis of hypersialylated metastatic cancers by phenylboronic acid-installed PEGylated gold nanoparticle and their management by nitroxide radical-containing nanoparticles. The 19th biennial meeting for the Society for Free Radical Research International (SFRRI 2018) 2018.06.04 Lisbon, Portugal
8. Akira Matsumoto. "Borono-lectin" Engineering as a Versatile Platform for Intelligent Drug Delivery Systems. CIMTEC 2018 8th Forum on New Materials 2018.06.14
9. Tatsuhiro Goda, Wenfeng Hai, Yukichi Horiguchi, Akira Matsumoto, Yuji Miyahara. Sugar-Incorporated Conducting Polymers for Influenza Virus Diagnosis. Finland Japan Workshop: The next generation medical engineering in biomaterials 2018.06.17
10. Thahomina Khan, Akira Matsumoto, Horacio Cabral and Kazunori Kataoka. 5-Boronopicolinic acid-installed nano-carriers for targeting sialylated epitopes on cancer cells. 34th Japan Drug Delivery Society Conference 2018.06.21
11. Thahomina Khan, Akira Matsumoto, Horacio Cabral and Kazunori Kataoka. Development of 5-boronopicolinic acid-installed polymeric micells for targeting sialylated epitopes on cancer cells. Biomaterials International Conference 2018.06.22
12. Akira Matsumoto. Borono-lectin Based Engineering for Smart Drug Delivery Applications. The 35th International Conference of Photopolymer Science and Technology 2018.06.26
13. Tatsuhiro Goda, Wenfeng Hai, Yukichi Horiguchi, Akira Matsumoto, Yuji Miyahara. Incorporation of Sugar into Conducting Polymer Enables Specific Biosensing of Human Influenza Virus. 17th International Meeting on Chemical Sensors 2018.07.15
14. Takuya Miyagawa, Sadato Hongo, Naofumi Nakamura, Yukichi Horiguchi, Yuji Miyahara, Hideki Shibata. A Novel Diagnostic System for Infectious Diseases Using Solid-State Nanopore Devices. 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC2018) 2018.07.17
15. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Diagnosis and Management of Hypersialylated Metastatic Cancers by Surface-Enhanced Raman Spectroscopy and Nitroxide Radical-containing Nanoparticles. 第 47 回医用高分子シンポジウム 2018.07.21 江東区、東京
16. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Diagnosis and Management of Hypersialylated Metastatic Cancers by Phenylboronic Acid-installed PEGylated Gold Nanoparticles and Nitroxide Radical-containing Nanoparticles. 第 67 回高分子討論会 2018.09.12
17. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Cytodiagnosis of Hypersialylated Metastatic Breast Cancers by Phenylboronic acid-installed PEGylated Gold Nanoparticle. Tsukuba Global Science Week 2018 2018.09.12
18. Akira Matsumoto. "Borono-lectin" engineering as a versatile platform for biosensing and drug delivery applications. "Frontiers2018" - EPFL/TMDU/ UTokyo Symposium 2018.09.19
19. Yukichi Horiguchi, Tatsuhiro Goda, Yuji Miyahara. Investigation of Simple and Easy Functionalization method for Single Conical Pore with a Polydopamine Layer. 31st International Microprocesses and Nanotechnology Conference (MNC2018) 2018.11.13

Material-Based Medical Engineering

Prof. Akio Kishida
Assoc. Prof. Tsuyoshi Kimura
Assist. Prof. Yoshihide Hashimoto
Research Associate Yongwei Zhang
Secretary Naomi Hiwatari

Doctor Course Student
Masaki Watanabe
Takuya Konishi
MAko Kobayashi

(1) Outline

In our laboratory, we deal with many research topics from the fundamental study of biomaterials in terms of material engineering to the application study of the medical devices.

The key words of our policy are "contribution to medical care" and "exploration of basic scientific principles".

(2) Research

In order to develop technologies that contribute to the medical and dental care, there is a need for a system to build up the design concepts at the molecular level and to realize it. Based on polymer chemistry, organic chemistry, and physical chemistry, we proceed a research aimed at specific clinical applications using cell engineering, genetic engineering techniques. Target area are new medical material development, regenerative medicine, gene therapy, and the treatment engineering.

(1) Regenerative medicine using decellularized biological tissue

In order to remove the xenogeneic cells, the living tissue is decellularized using a new processing method, high-hydrostatic pressure (HHP) method has been developed. Using this process, complete removal of infectious bacteria, viruses, and cells was accomplished.

(2) Molecular aggregates formed by the high-hydrostatic pressure process. Hydrogen bond assembles molecular assembly under high pressure. Using the HHP processing of more than 6,000 atmospheres, we prepare the nucleic acid assembly and apply them as gene delivery system.

(3) Extracellular matrix remodeling

We are conducting research on tissue remodeling using artificially reconstructed extracellular matrix structure. Specifically, we are researching the application of as artificial skin and artificial cornea of precision design artificial extracellular matrix structure.

(4) Immune control system: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulates immune reactions, to be able to enhance the anti-tumor immune responses have been revealed. We are developing technologies to capture and recover Treg using interfacial science.

(3) Education

In the Graduate School of Medical and Dental Sciences, we provide the lectures entitled “medical materials engineering”, “applied biomaterials”, and “medical, dental and pharmaceutical industrial engineering”.

(4) Publications

[Original Articles]

1. Yongwei Zhang, Takuya Iwata, Kwangwoo Nam, Tsuyoshi Kimura, Pingli Wu, Naoko Nakamura, Yoshihide Hashimoto, Akio Kishida. Water absorption by decellularized dermis *Heliyon*. 2018.04; 4(4); 1-17
2. Kaori Taniguchi, Mariko Funasaki, Akio Kishida, Samir K. Sadhu, Firoj Ahmed, Masami Ishibashi, Ayumi Ohsaki. Two new coumarins and a new xanthone from the leaves of *Rhizophora mucronata* *Bioorganic & Medicinal Chemistry Letters*. 2018.04; 28(6); 1063-1066

[Misc]

1. Y. Sawa, G. Matsumiya, K. Matsuda, E. Tatsumi, T. Abe, K. Fukunaga, S. Ichiba, A. Kishida, 他. Journal of Artificial Organs 2017:the year in review *J. Artif Organs*. 2018.03; 21(1); 1-7
2. Yoshihide Hashimoto, Sada-atsu Mukai, Yoshihiro Sasaki, Kazunari Akiyoshi. Nanogel tectonics for tissue engineering: Protein delivery systems with nanogel chaperones *Advanced Healthcare Materials*. 2018.12; 7(23); e1800729

[Conference Activities & Talks]

1. Tsuyoshi Kimura, Naoko Nakamura, Yoshihide Hashimoto, Akio Kishida. Induction of immunogenic cell death of cancer cell by using chemical detergent treatment and its activation of immune system. Experimental Biology 2018 2018.04.21 San Diego, USA
2. Akio Kishida. Preparation, characterization and performance of decellularized cornea. CIMTEC2018 2018.06.04 Perugia, Italy
3. Akio Kishida, Mayuka Kondo, Yoshihide Hashimoto, Toshiya Fujisato, Naoko Nakamura, Tsuyoshi Kimura.. Topological study of basement membrane of decellularized aorta using its synthetic replica. Finland-Japan Workshop: The next generation medical engineering in biomaterials 2018.06.17 Oulu, Finland
4. Tsuyoshi Kimura, Naoko Nakamura, Shimon Sakaguchi, Shunsaku Kimura, Akio Kishida. Development of an antibody immobilizing device for label-free selective capture of target cells. Finland-Japan Workshop: The next generation medical engineering in biomaterials 2018.06.17 Oulu, Finland
5. Naoko Nakamura, Tsuyoshi Kimura, Masahiro Okada, Toshiya Fujisato, Akio Kishida. Surface Modification of Artificial Tooth Root for Periodontal Tissue Reconstruction. 5Th TERMIS World Congress 2018.09.04 Kyoto
6. Tsuyoshi Kimura, Mayuka Kondo, Yoshihide Hashimoto, Naoko Nakamura, Akio Kishida. Surface topology of decellularized aorta and its synthetic replica affected cell behavior. 5Th TERMIS World Congress 2018.09.05 Kyoto
7. Naoko Nakamura, Shunya Shiba, Satoshi Shinohara, Shogo Suzuki, Tsuyoshi Kimura, Akio Kishida. An adipose tissue extraction method from decellularized cancerous bone for exploring hematopoietic-related extracellular matrix. 5Th TERMIS World Congress 2018.09.05 Kyoto
8. Junpei Kadota, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Preparation and characterization of hydrogels derived from decellularized urinary bladder matrix (UBM) and small intestinal submucosa (SIS). 5Th TERMIS World Congress 2018.09.05 Kyoto

9. Naruki Kimura, Kei Oya, Yoshihide Hashimoto, Seiichi Funamoto, Yuki Suzuki, Yuichiro Nawa, Akio Kishida, Takeo Nakano. Fabrication of visible marker on decellularized tissue for non-invasive techniques via sputtering. 5Th TERMIS World Congress 2018.09.05 Kyoto
10. Tsuyoshi Kimura, Mayuka Kondo, Yoshihide Hashimoto, Naoko Nakamura, Akio Kishida. Basement membrane topology of decellularized aorta and its synthetic replica affected endothelial cell behavior. 5Th TERMIS World Congress 2018.09.05 Kyoto
11. Tsuyoshi Kimura. Development of a synthetic replica having surface morphology of aortic lumen. Polymer minisymposium in Tsukuba 2018.09.14
12. Tsuyoshi Kimura, Mayuka Kondo, Yoshihide Hashimoto, Toshiya Fujisato, Naoko Nakamura, Akio Kishida. Cellular behavior on decellularized tissue and its replica. Frontier 2018 2018.09.19 lausanne, Switzerland
13. Junpei Kadota, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. In vitro microvascular network formation in/on hydrogels derived from decellularized tissues. Frontier 2018 2018.09.19 lausanne, Switzerland
14. Tsuyoshi Kimura, Mayuka Kondo, Yoshihide Hashimoto, Toshiya Fujisato, Naoko Nakamura, Akio Kishida. Bio-surface replicated from decellularized tissue. 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo
15. Junpei Kadota, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Preparation and characterization of ECM hydrogels derived from acellular urinary bladder matrix (UBM) and small intestinal submucosa (SIS). 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo
16. Mako Kobayashi, Mayuka Kondo, Ayano Tamura, Yoshihide Hashimoto, Toshiya Fujisato, Tsuyoshi Kimura, Akio Kishida. Cell behavior on the decellularized aorta with various basement membrane structures. 1st G' L' owing Polymer Symposium in KANTO 2018.12.15 Tokyo
17. Junpei Kadota, Yoshihide Hashimoto, Toshiya Fujisato, Tsuyoshi Kimura, Akio Kishida. Characterization of ECM hydrogels prepared by different decellularization methods. 1st G' L' owing Polymer Symposium in KANTO 2018.12.15 Tokyo

Organic and Medicinal Chemistry

Professor Hiroyuki KAGECHIKA
Associate Professor Tomoya Hirano
Assistant Professor Syuichi MORI
Assistant Professor Mari YUASA
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Graduate Student
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Daiki Kato
Yusuke Dobashi
Noriaki Manaka
Tatsuki Morozumi
Erika Yamazaki
Aoi Takeshita
Kana Naito

(1) Outline

1) Medicinal Chemistry of Retinoids

Retinoids regulates various significant biological phenomena, such as cell differentiation, proliferation, morphogenesis, metabolism and homeostasis. We have developed novel synthetic retinoid, Am80 (tamibarotene) as drug for acute promyelocytic leukemia. Novel synthetic retinoids have been developed for clinical use in the field of autoimmune diseases, neurodegenerative diseases, metabolic syndromes.

2) Medicinal Chemistry of Nuclear Receptors

Small hydrophobic molecules such as steroid hormones and activated vitamins A/D control various biological phenomena, including growth, development, metabolism, and homeostasis, by binding to and activating specific nuclear receptors. Nuclear receptors have become one of the most significant molecular targets for drug discovery in the fields of cancer, metabolic syndrome, autoimmune diseases, and so on. In this project, novel ligands of various nuclear receptors have been developed.

3) Development of Novel Functional Fluorescent Molecules for Elucidation of Intracellular Signal Transduction Pathways

Functional fluorescent molecules useful in many fields of scientific research, including analytical chemistry or cell biology have been developed.

4) Aromatic Architecture Based on the Steric Properties of N-Methylated Amides

The amide bond structure of amide derivatives often plays a key role in functions such as molecular recognition events or biological activities. In contrast to the extended trans structures of most secondary amides, the corresponding N-methylated compounds exist in cis form in the crystals and predominantly in cis form in various solvents. The cis conformational preference is useful as a building block to construct aromatic molecules with unique crystal or solution structures.

(2) Lectures & Courses

Organic and Medicinal Chemistry covers several aspects of organic chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand the fundamental knowledge, recent topics, and experimental techniques related to these fields.

(3) Publications**[Original Articles]**

1. Junichi Maruyama, Kazutoshi Inami, Fumiyoshi Michishita, Xinliang Jiang, Hiroaki Iwasa, Kentaro Nakagawa, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Norio Miyamura, Jun Hirayama, Hiroshi Nishina, Daichi Nogawa, Kouhei Yamamoto, Yutaka Hata. Novel YAP1 Activator, Identified by Transcription-Based Functional Screen, Limits Multiple Myeloma Growth. *Mol. Cancer Res.* 2018.02; 16(2); 197-211
2. Yokoo, H.; Ohsaki, A.; Kagechika, H.; Hirano, T.. Unique properties of 1,5-naphthyridin-2(1H)-one derivatives as environmental-polarity-sensitive fluorescent dyes. *Eur. J. Org. Chem.* 2018.03; 679-687
3. Shu Shimada, Yoshimitsu Akiyama, Kaoru Mogushi, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Hiromi Nagasaki, Hiroshi Fukamachi, Yasuhito Yuasa, Shinji Tanaka. Identification of selective inhibitors for diffuse-type gastric cancer cells by screening of annotated compounds in preclinical models. *Br. J. Cancer.* 2018.04; 118(7); 972-984
4. Ando Fumiaki, Mori Shuichi, Yui Naofumi, Morimoto Tetsuji, Nomura Naohiro, Sohara Eisei, Rai Tatsumitsu, Sasaki Sei, Kondo Yoshiaki, Kagechika Hiroyuki, Uchida Shinichi. AKAPs-PKA disruptors increase AQP2 activity independently of vasopressin in a model of nephrogenic diabetes insipidus *NATURE COMMUNICATIONS*. 2018.04; 9(1); 1411
5. Park, S.; Uchida, J.; Urushibara, K.; Kagechika, H.; Kato, T.; Tanatani, A.. Self-assembly of Liquid-crystalline Squaramides. *Chem. Lett.* 2018.04; 47; 601-604
6. Tojo, Y.; Urushibara, K.; Yamamoto, S.; Mori, H.; Masu, H.; Kudo, M.; Hirano, T.; Azumaya, I.; Kagechika, H.; Tanatani, A.. Conformational Properties of Aromatic Oligoamides Bearing Pyrrole Rings. *J. Org. Chem.* 2018.04; 83(8); 4606-4617
7. Urushitani, H.; Katsu, Y.; Kagechika, H.; Sousa, A. C. A.; Barroso, C. M.; Ohta, Y.; Shiraishi, H.; Iguchi, T.; Horiguchi, T.. Characterization and comparison of transcriptional activities of the retinoid X receptors by various organotin compounds in three prosobranch gastropods; *Thais clavigera*, *Nucella lapillus* and *Babylonia japonica*. *Aquatic Toxicol.* 2018.04; 199; 103-115
8. Qin, X.-Y.; Suzuki, H.; Honda, M.; Okada, H.; Kaneko, S.; Inoue, I.; Ebisui, E.; Hashimoto, K.; Carninci, P.; Kanki, K.; Tatsukawa, H.; Ishibashi, N.; Masaki, T.; Matsuura, T.; Kagechika, H.; Toriguchi, K.; Hatano, E.; Shirakami, Y.; Shiota, G.; Shimizu, M.; Moriwaki, H.; Kojima, S. . Prevention of hepatocellular carcinoma by targeting MYCN-positive liver cancer stem cells with acyclic retinoid. *Proc. Nat. Acad. Sci. USA*. 2018.06; 115(19); 4969-4974
9. Takashi Murayama, Nagomi Kurebayashi, Mari Ishigami-Yuasa, Shuichi Mori, Yukina Suzuki, Ryunosuke Akima, Haruo Ogawa, Junji Suzuki, Kazunori Kanemaru, Hideto Oyamada, Yuji Kiuchi, Masamitsu Iino, Hiroyuki Kagechika, Takashi Sakurai. Efficient High-Throughput Screening by Endoplasmic Reticulum Ca²⁺ Measurement to Identify Inhibitors of Ryanodine Receptor Ca²⁺-Release Channels. *Mol. Pharmacol.* 2018.07; 94(1); 722-730
10. Shikshya Timalina, Kyoko Arimoto-Matsuzaki, Masami Kitamura, Xiaoyin Xu, Qiu Wenzhe, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Yutaka Hata. Chemical compounds that suppress hypoxia-induced stress granule formation enhance cancer drug sensitivity of human cervical cancer HeLa cells. *J. Biochem.* 2018.07;
11. Nishiyama Yuko, Mori Shuichi, Makishima Makoto, Fujii Shinya, Kagechika Hiroyuki, Hashimoto Yuichi, Ishikawa Minoru. Novel Nonsteroidal Progesterone Receptor (PR) Antagonists with a Phenanthridinone Skeleton *ACS MEDICINAL CHEMISTRY LETTERS*. 2018.07; 9(7); 641-645

12. Fujii Shinya, Mori Shuichi, Kagechika Hiroyuki, Parra Marco Antonio Mendoza, Gronemeyer Hinrich. Development of biotin-retinoid conjugates as chemical probes for analysis of retinoid function *BIOORGANIC & MEDICINAL CHEMISTRY LETTERS*. 2018.08; 28(14); 2442-2445
13. Hirano, T.; Fujiwara, T.; Niwa, H.; Hirano, M.; Ohira, K.; Okazaki, Y.; Sato, S.; Umehara, T.; Maemoto, Y.; Ito, A.; Yoshida, M.; Kagechika, H.. Development of novel inhibitors for histone methyltransferase SET7/9 based on cyproheptadine *ChemMedChem*. 2018.08; 13; 1530-1540
14. Loppi, S.; Kolosowska, N.; Kärkkäinen, O.; Korhonen, P.; Huuskonen, M.; Grubman, A.; Dhungana, H.; Wojciechowski, S.; Pomeshchik, Y.; Giordano, M.; Kagechika, H.; White, A.; Auriola, S.; Koistinaho, J.; Landreth, G.; Hanhineva, K.; Kanninen, K.; Malm, T.. HX600, a synthetic agonist for RXR-Nurr1 heterodimer complex, prevents ischemia-induced neuronal damage *Brain Behav. Immunol.* 2018.09; 73; 670-681
15. Li, M.; Qin, X.-Y.; Furutani, Y.; Inoue, I.; Sekihara, S.; Kagechika, H.; Kojima S.. Prevention of acute liver injury by suppressing plasma kallikrein-dependent activation of latent TGF- β *Biochem. Biophys. Res. Chem.* 2018.09; 504; 857-864
16. Kazui, Y.; Fujii, S.; Yamada, A.; Ishigami-Yuasa, M.; Kagechika, H.; Tanatani, A.. Structure-Activity Relationship of Novel Androgen Receptor Antagonists Bearing a (Benzoylaminophenoxy)phenol Pharmacophore. *Bioorg. Med. Chem.* 2018.10; 26; 5118-5127
17. Urushibara, K.; Masu, H.; Mori, H.; Azumaya, I.; Hirano, T.; Kagechika, H.; Tanatani, A.. Synthesis and Conformational Analysis of Alternately N-Alkylated Aromatic Amide Oligomers *J. Org. Chem.* 2018.11; 83(23); 14338-14349

[Conference Activities & Talks]

1. Tomoya Hirano, Michitake Hirano, Takashi Fujiwara, Takashi Umehara, Akihiro Ito, Minoru Yoshida, Hiroyuki Kagechika. Structural development of cyproheptadine as an inhibitor for histone methyltransferase Set7/9. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
2. Shuichi Mori, Ryohei Takagaki, Shinya Fujii, Aya Tanatani, Hiroyuki Kagechika. Development of novel progesterone receptor ligands bearing m-carborane as a hydrophobic pharmacophore. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
3. Mari Ishigami-Yuasa, Yuko Watanabe, Honoka Suzuyama, Hiroyuki Masuno, Shinya Fujii, Takayasu Mori, Eriko Kikuchi, Shinichi Uchida, Hiroyuki Kagechika. Development of WNK Signaling Inhibitors as a New Class of Antihypertensive Drugs. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
4. Yusuke Okazaki, Takashi Fujiwara, Asuka Takaguchi, Tomoya Hirano, Shuichi Mori, Hiroyuki Kagechika. Development of facile method to detect the activity of histone methyltransferase based on SNAr reaction. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
5. Nozomi Tsuemoto, Shuichi Mori, Emiko Kawachi, Hiroyuki Kagechika. Development of novel retinoids bearing pentafluorosulfanyl group. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
6. Tsuyoshi Oikawa, Shinya Fujii, Hiroyuki Masuno, Emiko Kawachi, Hiroyuki Kagechika. Development of Novel Silyl-containing Retinoids. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
7. Mai Negishi, Hitomi Koga, Shuichi Mori, Hiroyuki Kagechika, Aya Tanatani. Development of Nitrogen-Containing Heteroaromatic Compounds as Novel Progesterone Antagonists. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京

8. Haru Kawasaki, Harue Sasaki, Hiroyuki Masuno, Emiko Kawachi, Nobutoshi Ito, Hiroyuki Kagechika, Aya Tanatani. Development of Lithocholic Acid Derivatives with A 3-Hydroxyalkyl Group as Novel Nonsecosteroidal Vitamin D Analogs. Symposium on Frontier of Genomic Medicine ‘Retinoid (Am80, Tamibarotene) as therapeutics for intractable diseases’ 2018.01.29 東京
9. Hiroyuki Kagechika. Development of Novel Synthetic Retinoids with Unique Hydrophobic Pharmacophore. FASEB meeting on retinoid 2018.06.10 Steamboat Springs, Colorado, USA
10. Tomoya Hirano, Chihiro Komatsu, Yuki Noji, Hiroyuki Kagechika. Development of photofunctional compounds that function under specific range of pH with “OFF-ON-OFF” type of change. Gordon Research Conference, Bioanalytical Sensors 2018.06.22 Newport, RI, USA
11. Hidetomo Yokoo, Tomoya Hirano, Ayumi Ohsaki, Hiroyuki Kagechika. Development of novel environment-dependent fluorophore derived from fluorescent natural compounds. Gordon Research Conference, Bioanalytical Sensors 2018.06.22 Newport, RI, USA
12. Soyoung Park, Junya Uchida, Ko Urushibara, Hiroyuki Kagechika, Takashi Kato, Aya Tanatani. Self-assembly of Liquid-Crystalline Squaramides. 27th International Liquid Crystal Conference 2018.06.22 京都
13. Hiroyuki Kagechika, Shinya Fujii, Tomoya Hirano, Shinya Mori, Aya Tanatani. Development of Functional Molecules Based on Unique Scaffolds. EPFL/TMDU/UTokyo Joint Symposium 2018 2018.09.19 Lausanne, Switzerland
14. Ishigami-Yuasa, M., Ekimoto, H., Kagechika, H.. Synergistic inhibition of several human cancer cell proliferations by a synthetic retinoid tamibarotene (Am80) in combination with the epigenetic modulators. FASEB meeting on retinoid Florida, USA
15. Tsuemoto, N., Mori, S., Kawachi, E., Kagechika, H.. Design and synthesis of novel RAR ligands containing pentafluorosulfanyl group. FASEB meeting on retinoid Florida, USA

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru YOSHIDA
Assistant Professor	Yoshitake NISHIYAMA
Assistant Professor	Kazuya KANEMOTO
Technical Assistant	Yoshihiro MISAWA, Yuki HAZAMA, Tomoko KURIBARA
Graduate Students	Keisuke UCHIDA, Tomohiro MEGURO, Yu NAKAMURA, Harumi ITO, Tsubasa MATSUZAWA, Tsuneyuki KOBAYASHI, Keisuke ADACHI, Saki OZAWA, Shuhei KAMADA, Keita SHIMIZU, Norikazu TERASHIMA, Naoya TOKUNAGA, Yoshihiro MIYATA, Mai IKEDA TOKUNAGA, Daisuke KORI

(1) Outline

Development of new organic synthetic methods, new chemical methodologies, and new chemical tools, those are useful for biological and drug discovery researches.

(2) Research

- 1) Development of novel generation methods for benzyne species and their synthetic applications.
- 2) Development of new bioconjugation methods using strained alkynes.
- 3) Target identification of drugs or drug candidates by photoaffinity labeling based on diazido probe method..
- 4) Development of new molecular ligation methods based on new azido chemistry.
- 5) Design and synthesis of efficient substrates for bioluminescence reactions and fluorescent probes for bioimaging and diagnosis of diseases.
- 6) Design and synthesis of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

(3) Publications

[Original Articles]

1. Kanemoto K, Yoshida S, Hosoya T. Modified Conditions for Copper-Catalyzed *ipso*-Thiolation of Aryl-boronic Acid Esters with Thiosulfonates. Chem Lett. 2018.01; 47(1); 85-88
2. Yoshida S, Kanno K, Kii I, Misawa Y, Hagiwara M, Hosoya T. Convergent synthesis of trifunctional molecules by three sequential azido-type-selective cycloadditions. Chem Commun. 2018.04; 54(30); 3705-3708
3. Kii I, Hirahara-Owada S, Yamaguchi M, Niwa T, Koike Y, Sonamoto R, Ito H, Takahashi K, Yokoyama C, Hayashi T, Hosoya T, Watanabe Y. Quantification of receptor activation by oxytocin and vasopressin

- in endocytosis-coupled bioluminescence reduction assay using nanoKAZ. *Anal Biochem.* 2018.04; 549; 174-183
4. Ajiro M, Sakai H, Onogi H, Yamamoto M, Sumi E, Sawada T, Nomura T, Kabashima K, Hosoya T, Hagiwara M. CDK9 Inhibitor FIT-039 Suppresses Viral Oncogenes E6 and E7 and Has a Therapeutic Effect on HPV-Induced Neoplasia. *Clin Cancer Res.* 2018.04;
 5. Yoshida S, Kuribara T, Morita T, Matsuzawa T, Morimoto K, Kobayashi T, Hosoya T. Expanding the synthesizable multisubstituted benzo[*b*] thiophenes via 6,7-thienobenzynes generated from *o*-silylaryl triflate-type precursors. *RSC Adv.* 2018.06; 8(39); 21754-21758
 6. Meguro Tomohiro, Terashima Norikazu, Ito Harumi, Koike Yuka, Kii Isao, Yoshida Suguru, Hosoya Takamitsu. Staudinger reaction using 2,6-dichlorophenyl azide derivatives for robust aza-ylide formation applicable to bioconjugation in living cells *CHEMICAL COMMUNICATIONS.* 2018.07; 54(57); 7904-7907
 7. Matsuzawa Tsubasa, Uchida Keisuke, Yoshida Suguru, Hosoya Takamitsu. Synthesis of Diverse Phenothiazines by Direct Thioamination of Arynes with S-(*o*-Bromoaryl)-S-methylsulfilimines and Subsequent Intramolecular Buchwald-Hartwig Amination *CHEMISTRY LETTERS.* 2018.07; 47(7); 825-828
 8. Meguro Tomohiro, Yoshida Suguru, Igawa Kazunobu, Tomooka Katsuhiko, Hosoya Takamitsu. Transient Protection of Organic Azides from Click Reactions with Alkynes by Phosphazide Formation *ORGANIC LETTERS.* 2018.07; 20(13); 4126-4130
 9. Inouye S, Tomabechei Y, Hosoya T, Sekine S, Shirouzu M. Slow luminescence kinetics of semi-synthetic aequorin: expression, purification and structure determination of *cf3*-aequorin. *J Biochem.* 2018.09; 164(3); 247-255
 10. Nishiyama Y, Kamada S, Yoshida S, Hosoya T. Generation of Arynes by Selective Cleavage of a Carbon–Phosphorus Bond of *o*-(Diarylphosphinyl)aryl Triflates Using a Grignard Reagent. *Chem Lett.* 2018.09; 47(9); 1216-1219
 11. Yoshida S, Tanaka J, Nishiyama Y, Hazama Y, Matsushita T, Hosoya T. Further enhancement of the clickability of doubly sterically-hindered aryl azides by para-amino substitution. *Chemical communications (Cambridge, England).* 2018.10;
 12. Sumida Y, Harada R, Sumida T, Hashizume D, Hosoya T. Hydrosilyl Group-directed Iridium-catalyzed peri-Selective C–H Borylation of Ring-fused (Hetero)Arenes. *Chem Lett.* 2018.10; 47(10); 1251-1254
 13. Zhang Z, Niwa T, Watanabe Y, Hosoya T. Palladium(II)-mediated rapid ¹¹C-cyanation of (hetero)arylborons. *Org Biomol Chem.* 2018.11; 16(41); 7711-7716
 14. Takahashi K, Hosoya T, Onoe K, Takashima T, Tanaka M, Ishii A, Nakatomi Y, Tazawa S, Takahashi K, Doi H, Wada Y, Watanabe Y. Association between aromatase in human brains and personality traits. *Sci Rep.* 2018.11; 8(1); 16841

[Misc]

1. Matsuzawa T, Yoshida S, Hosoya T. Recent advances in reactions between arynes and organosulfur compounds. *Tetrahedron Lett.* 2018.10; 59(48); 4197-4208

[Conference Activities & Talks]

1. Kanemoto K, Sugimura Y, Shimizu S, Yoshida S, Hosoya T. Synthesis of Divergent Sulfur-Containing Heterocycles Using Thiosulfonates as Sulfur Surrogates. The 99th CSJ Annual Meeting 2018.03.21 Funabashi, Japan
2. Yoshida S, Hatakeyama Y, Kuribara T, Makio N, Karaki F, Johmoto K, Uekusa H, Hosoya T. Molecular Conjugations Based on Transient Protection of Strained Alkynes via Complexation with Copper. 28th International Conference on Organometallic Chemistry (ICOMC 2018) 2018.07.16 Florence, Italy
3. Uchida K, Yoshida S, Hosoya T. Generation of Arynes via Carbon-Carbon Bond Cleavage of Benzocyclobutenones Using an Organolithium Reagent. 28th International Conference on Organometallic Chemistry (ICOMC 2018) 2018.07.17 Florence, Italy

4. Nakamura Y, Yoshida S, Hosoya T. Facile Synthesis of Diverse Benzopyran Derivatives via Au-Catalyzed Cyclization and Generation of Arynes. 28th International Conference on Organometallic Chemistry (ICOMC 2018) 2018.07.19 Florence, Italy
5. Nakamura Y, Yoshida S, Uchida K, Hazama Y, Hosoya T. Aryne Relay Chemistry en Route to Aminoarenes: Synthesis of 3-Aminoaryne Precursors via Regioselective Silylation of 3-(Triflyloxy)arynes. International Symposium on Main Group Chemistry Directed towards Organic Synthesis (MACOS) 2018.08.25 Kyoto, Japan
6. Nishiyama Y, Hazama Y, Yoshida S, Hosoya T. Synthesis of Unsymmetrical Tertiary Phosphine Oxides via Sequential Substitution Reaction Using Stable Substrates with Thio Leaving Groups. International Symposium on Main Group Chemistry Directed towards Organic Synthesis (MACOS) 2018.08.25 Kyoto, Japan
7. Matsuzawa T, Uchida K, Yoshida S, Hosoya T. Synthesis of Diverse Aromatic Organosulfurs by Reactions of Arynes with Organosulfur(IV) Compounds. 28th International Symposium on the Organic Chemistry of Sulfur (ISOCs-28) 2018.08.27 Tokyo, Japan
8. Yoshida S, Uchida K, Karaki F, Nagai A, Tamura Y, Nishiyama Y, Hosoya T. Generation of Arynes and Cycloalkynes via Sulfoxide-Magnesium Exchange Reaction. 28th International Symposium on the Organic Chemistry of Sulfur (ISOCs-28) 2018.08.27 Tokyo, Japan
9. Kanemoto K, Yoshida S, Hosoya T. Rhodium-Catalyzed Odorless Thiolation of Organoboronic Acids Using Thiosulfonates. 28th International Symposium on the Organic Chemistry of Sulfur (ISOCs-28) 2018.08.27 Tokyo, Japan
10. Yoshida S. Controlled Click Chemistry Based on Transient Protection of Strained Alkynes via Complexation with Copper. 2018.09.01 Chiba, Japan
11. Nishiyama Y, Kamada S, Yoshida S, Hosoya T. Synthesis of Unsymmetrical Tertiary Phosphine Oxides via Sequential Substitution Reaction of Phosphonic Acid Dithioesters with Grignard Reagents. 22nd International Conference on Organic Synthesis (22-ICOS) 2018.09.17 Florence, Italy
12. Yoshida S, Meguro T, Igawa K, Tomooka T, Hosoya T. Transient Protection of Organic Azides from Click Reactions with Alkynes by Phosphazide Formation. Tateshina Conference on Organic Chemistry 2018 2018.11.09 Chino, Japan
13. Matsuzawa T, Uchida K, Yoshida S, Hosoya T. Synthesis of Multisubstituted Benzo[*b*] thiophenes via Reaction of Arynes with Alkynyl Sulfides. The 14th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-14) 2018.11.14 Kyoto, Japan
14. Nakamura Y, Yoshida S, Hosoya T. Facile Synthesis of Diverse Benzopyran Derivatives via Au-Catalyzed Cyclization and Generation of Arynes. The 14th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-14) 2018.11.14 Kyoto, Japan
15. Meguro T, Yoshida S, Igawa K, Tomooka K, Hosoya T. Protection of Azido Group from Click Reaction by Formation of Phosphazide. The 14th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-14) 2018.11.15 Kyoto, Japan
16. Nishiyama Y, Kamada S, Hazama Y, Yoshida S, Hosoya T. Selective Cleavage Reactions of Pentavalent Organophosphorus Electrophiles. The 14th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-14) 2018.11.15 Kyoto, Japan
17. Nishiyama Y, Misawa Y, Hazama Y, Oya K, Yoshida S, Hosoya T. Facile Synthesis of Diazido Compounds via Formal C–H Azidation and Functional Group-Selective Conversions. The 4th International Symposium of Middle Molecular Strategy (ISMMS-4) and The 7th Innovative Area Symposium on Middle Molecular Strategy: Creation of Higher Bio-Functional Molecules by Integrated Synthesis 2018.11.30 Sendai, Japan

[Patents]

1. COMPOUND AND PHARMACEUTICAL COMPOSITION FOR NEUROPSYCHOLOGICAL DISORDER OR MALIGNANT TUMOR, Patent Number : 2880487

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D.
Associate Professor Wataru NOMURA, Ph.D.
Assistant Professor Takuya KOBAYAKAWA, Ph.D.
Support Researcher Ami MASUDA
Technical Assistant Satoko KIKUCHI
Assistant Miho TANABE, Tomoe KAMEI

Graduate students

D3 Shohei TAKETOMI, Kiju KONNO, Yuzuna HONDA, Maxwell Mamfe Sakyamah,
Daisuke MATSUMOTO, Daisuke MIYAKI
D1 Kento EBIHARA, Kofi Baffour-Awuah Owusu
M2 Tsukasa HASHIMOTO, Tomoki KISHI, Shunsuke SAWAMURA, Kohei TAKAHASHI
M1 Takumi KAMIMURA, Masaki KURAKAMI, Yuki WATANABE, WANG RONGYI, LIU YISHAN

internal Collaborators

LIU YIJIE, YANG TINGTING

External Collaborators

Chika AZUMA

(1) Outline

Research in the lab is mainly focused to two topics; 1) development of artificial enzymes for regulation of gene functions and (2) exploration and analyses of cellular functions by methods based on peptide chemistry. Students will learn how to design research, experimental techniques, and analysis methods of research data. Research themes are related to multiple research fields such as molecular biology, chemistry, chemical biology, and synthetic biology.

(2) Research

1. Development of conformational-constrained templates for drug discovery.
Drug-discovery templates for conformational restriction, which enable pharmacophores of bioactive compounds (ex. peptides) to be suitably disposed in three-dimensional space, are being developed. Drug discovery for the chemotherapy of cancer, AIDS, Alzheimer's disease, rheumatoid arthritis, SARS, etc. is being performed based on targeting several receptors, enzymes, etc.
2. Development of bio-probes, bio-sensing, medicinal chemistry towards chemical biology.
Bio-probes that specifically recognize each receptor or enzyme are being developed for research on chemical biology involving imaging and sensing.
3. Structural analysis of the interactions between receptors/enzymes and their ligands.
Using X-ray crystal structural analysis, the mechanism of signal transduction operated by binding of ligands to receptors/enzymes is being analyzed.
4. Development of applications of zinc finger protein for gene therapy and nano technology.

Utilizing DNA sequence-specific recognition of zinc finger protein, technologies for DNA recombination, modifications, and DNA labeling are being developed.

(3) Education

Practice

Goals/Outline:

Presenter reports about the recent topics related to molecular biomedicine from Journals. The report must come with the backgrounds and motivations of research fields. Research designs, experimental methods, data analyses, and perspectives for future development will be discussed about the topics. Students are also encouraged to attend to lectures for the graduate course and discuss about the topics with lecturers.

Available programs:

Lectures for the graduate course: as occasion

Journal Club: Every Thursday from 15:00 to 16:30

Lab

Goals/Outline:

Research in the lab is mainly focused to two topics; 1) development of artificial enzymes for regulation of gene functions and (2) exploration and analyses of cellular functions by methods based on peptide chemistry. Students will learn how to design research, experimental techniques, and analysis methods of research data. Research themes are related to multiple research fields such as molecular biology, chemistry, chemical biology, and synthetic biology.

Available program:

Lab meeting (progress report): every week, about 1 hour per person (will be announced)

(4) Lectures & Courses

Format:

Small group

Venue:

Practice: Third laboratory room (603) at Institute of Biomaterials and Bioengineering

Lab: Laboratory of Medicinal Chemistry (602) at Institute of Biomaterials and Bioengineering

Grading:

Practice: Attendance and report

Lab: Progress of research and report

(5) Publications

[Original Articles]

1. Takuya Kobayakawa, Yudai Matsuzaki, Kentaro Hozumi, Wataru Nomura, Motoyoshi Nomizu, Hirokazu Tamamura. Synthesis of a Chloroalkene Dipeptide Isostere-Containing Peptidomimetic and Its Biological Application. *ACS Medicinal Chemistry Letters*. 2018.01; 9(1); 6-10
2. Kei Toyama, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Delivery of a Proapoptotic Peptide to EGFR-Positive Cancer Cells by a Cyclic Peptide Mimicking the Dimerization Arm Structure of EGFR. *Bioconjugate Chemistry*. 2018.06; 29(6); 2050-2057
3. Kei Toyama, Takuya Kobayakawa, Wataru Nomura, Hirokazu Tamamura. Inhibition of EGFR Activation by Bivalent Ligands Based on a Cyclic Peptide Mimicking the Dimerization Arm Structure of EGFR *Chemical and Pharmaceutical Bulletin*. 2018.11; 66(11); 1083-1089

4. Wataru Nomura, Daisuke Matsumoto, Taisuke Sugii, Takuya Kobayakawa, Hirokazu Tamamura. Efficient and Orthogonal Transcription Regulation by Chemically Inducible Artificial Transcription Factors. *Biochemistry*. 2018.11; 57(45); 6452-6459
5. Takuya Kobayakawa, Nami Ohashi, Yuki Hirota, Kohei Takahashi, Yuko Yamada, Tetsuo Narumi, Kazuhisa Yoshimura, Shuzo Matsushita, Shigeyoshi Harada, Hirokazu Tamamura. Flexibility of small molecular CD4 mimics as HIV entry inhibitors. *Bioorg. Med. Chem.*. 2018.11; 26(21); 5664-5671

[Books etc]

1. Hirokazu Tamamura, Takuya Kobayakawa, Nami Ohashi. Mid-size Drugs Based on Peptides and Peptidomimetics. Springer Singapore, 2018.01 (ISBN : 978-981-10-7691-6)
2. Synthesis Technology of Peptides, Nucleic Acids and Sugar Chains for Medium Molecule Drug Discovery. CMC Publishing Co.,Ltd., 2018.02 (ISBN : 978-4-7813-1320-7)

[Conference Activities & Talks]

1. Maxwell M. Sakyamah, Wataru Nomura, Hirokazu Tamamura. Development of a sensitive screening method to search potent ligands of CXCR4. 138th Annual Meeting of the Pharmaceutical Society of Japan 2018.03.26 Ishikawa, Japan
2. Wataru Nomura, Takumi Kamimura, Atsumi Mori, Takuya Kobayakawa, Hirokazu Tamamura. Peptide-based fluorescent imaging tools for observation of target protein dynamics. 138th Annual Meeting of the Pharmaceutical Society of Japan 2018.03.28 Ishikawa, Japan
3. Tsutomu Murakami, Masayuki Fujino, Masaru Yokoyama, Takuya Kobayakawa, Hiroaki Takeuchi, Takao Masuda, Osamu Kotani, Hirokazu Tamamura, Hironori Sato. Biological and molecular characterization of a novel anti-HIV-1 compound created by in silico design and de novo organic synthesis. Cold Spring Harbor Laboratory Meetings & Courses, Retrovirus Meeting 2018.05.23 Cold Spring Harbor, United States of America
4. Daisuke Matsumoto, Wataru Nomura, Hirokazu Tamamura. Development of genome editing systems with a FokI-based chemically inducible nuclease. The 13th Annual Meeting of Japanese Society for Chemical Biology 2018.06.12 Tokyo, Japan
5. Kento Ebihara, Yuzuna Honda, Takuya Kobayakawa, Wataru Nomura, Tsutomu Murakami, Hirokazu Tamamura. Development of HIV-1 fusion inhibitors based on the C34 dimers derived from gp41. The 13th Annual Meeting of Japanese Society for Chemical Biology 2018.06.13 Tokyo, Japan
6. Maxwell M. Sakyamah, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Development of NanoBRET assay system in living cells to search potent CXCR4 ligands. The 13th Annual Meeting of Japanese Society for Chemical Biology 2018.06.13 Tokyo, Japan
7. Kohei Takahashi, Ami Masuda, Shigeyoshi Harada, Takuya Kobayakawa, Yusuke Ishida, Yu Irahara, Tomoyuki Miura, Shuzo Matsushita, Kazuhisa Yoshimura, Hirokazu Tamamura. Development of novel small molecule CD4 mimics with anti-HIV activity. The 13th Annual Meeting of Japanese Society for Chemical Biology 2018.06.13
8. Tamamura H. HIV-1 fusion inhibitors based on the C34 dimers derived from gp41. 15th Chinese International Peptide Symposium 2018.07.04 Shenzhen, China
9. Tamamura H. Synthesis of Peptidomimetics Based on Chloroalkene Dipeptide Isosteres and Their Biological Application. The 17th Akabori Conference 2018: German- Japanese Symposium on Peptide Science 2018.09.04 Lindau, Germany
10. Maxwell Mamfe Sakyamah, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Development of NanoBRET assay system in living cells for structure-activity relationship studies of CXCR4 ligands. The 62nd Annual Meeting of the Pharmaceutical Society of Japan Kanto Branch 2018.09.15 Tokyo, Japan
11. Maxwell M. Sakyamah, Wataru Nomura, Takuya Kobayakawa, Hirokazu Tamamura. Development of a new NanoBRET assay system for CXCR4 ligands and their Structure-activity relationship studies. Frontiers 2018 Symposium (EPFL/TMDU/UTokyo Joint Symposium) 2018.09.21 Lausanne, Switzerland

12. Daisuke Matsumoto, Wataru Nomura, Hirokazu Tamamura. Split site-specific nucleases for controlled genome editing by chemicals. Frontiers 2018 Symposium (EPFL/TMDU/UTokyo Joint Symposium) 2018.09.21 Lausanne, Switzerland
13. Tamamura H. Peptidomimetic-based mid-size drugs: anti-cancer and anti-HIV agents. Frontiers 2018 Symposium (EPFL/TMDU/UTokyo Joint Symposium) 2018.09.21 Lausanne, Switzerland
14. Tsutomu Murakami, Kento Ebihara, Masayuki Fujino, Yuzuna Honda, Takuya Kobayakawa, Wataru Nomura, Hirokazu Tamamura. Development of new membrane fusion inhibitors against HIV-1 by “dimerization” strategy. The 66th Annual Meeting of the Japanese Society for Virology 2018.10.28 Kyoto, Japan
15. Takuya Kobayakawa, Hirokazu Tamamura. Development of peptidomimetics based on a chloroalkene structure. 44th Symposium on Progress in Organic Reactions and Syntheses 2018.11.05 Kumamoto, Japan
16. Takuya Kobayakawa, Kohei Takahashi, Ami Masuda, Shigeyoshi Harada, Tomoyuki Miura, Shuzo Matsushita, Kazuhisa Yoshimura, Hirokazu Tamamura. Structure - activity relationship studies of CD4 mimic molecules for targeting an envelope protein gp120 on HIV-1. 19th Kumamoto AIDS Seminar 2018.11.06 Kumamoto, Japan
17. Takuya Kobayakawa, Kohei Takahashi, Ami Masuda, Shigeyoshi Harada, Tomoyuki Miura, Shuzo Matsushita, Kazuhisa Yoshimura, Hirokazu Tamamura. Structure - activity relationship studies of CD4 mimic molecules for targeting an envelope protein gp120 on HIV-1. 19th Kumamoto AIDS Seminar 2018.11.06 Kumamoto, Japan
18. Kohei Takahashi, Ami Masuda, Shigeyoshi Harada, Takuya Kobayakawa, Yusuke Ishida, Yu Irahara, Tomoyuki Miura, Shuzo Matsushita, Kazuhisa Yoshimura, Hirokazu Tamamura. Novel CD4 mimics Increase the Activity of HIV Neutralizing Antibodies. 2018.11.28 Kyoto, Japan
19. Takuya Kobayakawa, Hirokazu Tamamura. Synthetic Strategy of Peptidomimetic Based on Chloroalkene Dipeptide Isoteres and Its Biological Application. 10th International Peptide Symposium 2018.12.03 Kyoto, Japan
20. Kento Ebihara, Yuzuna Honda, Takuya Kobayakawa, Tsutomu Murakami, Hirokazu Tamamura. HIV-1 Fusion Inhibitors Based on gp41-C34 dimers. 10th International Peptide Symposium 2018.12.03 Kyoto, Japan
21. Tamamura H. Peptidomimetic-based mid-size drugs: anti-cancer and anti-HIV agents. 10th International Peptide Symposium / 55th Japanese Peptide Symposium 2018.12.03 Kyoto, Japan
22. Wataru Nomura, Takumi Kamimura, Daisuke Matsumoto, Takuya Kobayakawa, Hirokazu Tamamura. Fluorogenic and genetically encodable tag-probe system for in-cell imaging of protein synthesis. 10th International Peptide Symposium 2018.12.05 Kyoto, Japan
23. Tamamura H. Peptide drug discovery. 25th Peptide Forum – International Forum on Peptides in Drug Discovery - /Satellite Symposium of 10th International Peptide Symposium 2018.12.10 Tokyo, Japan

Metallic Biomaterials

Takao HANAWA Prof
Yusuke TSUTSUMI Senior Assoc Prof
Maki ASHIDA Assist Prof
Peng CHEN Assist Prof
Hisashi DOI Assist Prof
Akira UMISE Assist Prof
Shukan OKANO Technical Support Staff
Noriko NAKAISHI Technical Support Staff
Tomoko SETOGUCHI Secretary

(1) Outline

1. Bio-functionilization of metals with surface modification

Bio-functionalization of metals is investigated with surface treatment techniques, such as molecule immobilization and anodic oxidation. These surface treatments make it possible to inhibit protein adsorption, platelet adhesion, and biofilm formation, and to enhance wear resistance and hard-tissue compatibility.

2. Development of novel alloys and porous composites for biomedical applications

Novel alloy systems for biomedical applications are designed from the viewpoints of mechanical properties and biocompatibility. Co-Cr-Mo alloys having high strength and ductility for dental applications are developed. The porous alloys having low Young's modulus are obtained with selective laser melting technique.

3. Development of Zr-based alloys for minimizing MRI artifacts

Zr-based alloys with low magnetic susceptibility, high strength and corrosion resistance are investigated for minimizing MRI artifact by controlling their microstructure and constituent phase for aneurysm clips, artificial joints, and dental implants, etc.

4. Effort to minimize metal allergy

Countermeasure techniques for metal ion release from metallic biomaterials which causes metal allergy are investigated. Novel reagents of patch testing for the detection of sensitization to metal ions are developed.

(2) Lectures & Courses

Metallic biomaterials play an important role as medical devices. Our laboratory mainly deals with effects of crystal structure, process, and thermal treatment on mechanical properties (e.g. strength or toughness). We also focus on structure and property of nanometer-scaled surface phenomena: Formation of living tissue on metals, especially, reactions between biomolecules or cells and metals, changes in surface oxide layers in living tissues, and electrochemical property of metallic biomaterials. The aim of the education is perfect understanding of metallic biomaterials, enabling students to select a proper material for medical treatments or researches.

(3) Publications

[Original Articles]

1. Akimoto T, Ueno T, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions J Biomed Mater Res B Appl Biomater. 2018.01; 106(1); 73-79

2. Watanabe K, Ashida M, Masuda T, Kral P, Takizawa Y, Yumoto M, Otagiri Y, Sklenicka V, Hanawa T, Horita Z. Production of superplastic Ti-6Al-7Nb alloy using high-pressure sliding process J Japan Instit Light Met. 2018.01; 68(1); 9-15
3. Kajima Y, Takaichi A, Nakamoto T, Kimura T, Kittikundecha N, Tsutsumi Y, Nomura N, Kawasaki A, Takahashi H, Hanawa T, Wakabayashi N. Effect of adding support structures for overhanging part on fatigue strength in selective laser melting J Mech Behav Biomed Mater. 2018.02; 78; 1-9
4. Ishimoto T, Yamada K, Takahashi H, Takahata M, Ito M, Hanawa T, Nakano T. Trabecular health of vertebrae based on anisotropy in trabecular architecture and collagen/apatite micro-arrangement after implantation of intervertebral fusion cages in the sheep spine Bone. 2018.03; 108; 25-33
5. Oishi M, Tsutsumi Y, Chen P, Ashida M, Doi H, Hanawa T. Surface changes of yttria-stabilized zirconia in water and Hanks solution characterized using XPS Surf Interface Anal. 2018.05; 50(5); 587-591
6. Kajima Y, Takaichi A, Kittikundecha N, Nakamoto T, Kimura T, Nomura N, Kawasaki A, Hanawa T, Takahashi H, Wakabayashi N. Effect of heat-treatment temperature on microstructures and mechanical properties of Co-Cr-Mo alloys fabricated by selective laser melting Mater Sci Eng A. 2018.05; 726; 21-31
7. Ashida M, Morita M, Tsutsumi Y, Nomura N, Doi H, Chen P, Hanawa T. Effects of cold swaging on mechanical properties and magnetic susceptibility of the Zr-1Mo alloy Metals. 2018.06; 8(6); 454
8. Takakusaki K, Fueki K, Tsutsumi C, Tsutsumi Y, Iwasaki N, Hanawa T, Takahashi H, Takakuda K, Wakabayashi N. Effect of incorporation of surface pre-reacted glass ionomer filler in tissue conditioner on the inhibition of Candida albicans adhesion Dent Mater J. 2018.06; 37(3); 453-459
9. Correa DRN, Rocha LA, Ribeiro AR, Gemini-Piperni S, Archanjo BS, Achete CA, Werckmann J, Afonso Shimabukuro M, Doi H, Tsutsumi Y, Hanawa T. Growth mechanisms of Ca- and P-rich MAO films in Ti-15Zr-xMo alloys for osseointegrative implants Surf Coat Technol. 2018.06; 344; 373-382
10. Yoshihara C, Ueno T, Chen P, Tsutsumi Y, Hanawa T, Wakabayashi N. Inverse response of osteoblasts and fibroblasts to growth on carbon-deposited titanium surfaces J Biomed Mater Res Part B-Appl Biomater. 2018.07; 106(5); 1869-1877
11. Ida H, Seiryu M, Takeshita N, Iwasaki M, Yokoyama Y, Tsutsumi Y, Ikeda E, Sasaki S, Miyashita S, Sasaki S, Fukunaga T, Deguchi T, Takano-Yamamoto T. Biosafety, stability, and osteogenic activity of novel implants made of Zr70Ni16Cu6Al8 bulk metallic glass for biomedical application Acta Biomater. 2018.07; 74(1); 505-517
12. Park JW, Han SH, Hanawa T. Effects of surface nanotopography and calcium chemistry of titanium bone implants on early blood platelet and macrophage cell function BioMed Res. Int.. 2018.07; 2018; 1-10
13. Nishijo M, Ebihara A, Tokita D, Doi H, Hanawa T, Okiji T. Evaluation of selected mechanical properties of NiTi rotary glide path files manufactured from controlled memory wires Dent Mater J. 2018.07; 37(4); 549-554
14. Washio K, Tsutsumi Y, Tsumanuma Y, Yano K, Srithanyarat SS, Takagi R, Ichinose S, Meinzer W, Yamato M, Okano, T, Hanawa T, Ishikawa I. In vivo periodontium formation around titanium implants using periodontal ligament cell sheet Tissue Eng Part A. 2018.08; 24(15-16); 1273-1282
15. Chen P, Aso T, Sasaki R, Ashida M, Tsutsumi Y, Doi H, Hanawa T. Adhesion and differentiation behaviors of mesenchymal stem cells on titanium with micrometer and nanometer-scale grid patterns produced by femtosecond laser irradiation J Biomed Mater Res A. 2018.10; 106(10); 2735-2743
16. Wei D, Koizumi Y, Chiba A, Ueki K, Ueda K, Narushima T, Tsutsumi Y, Hanawa T. Heterogeneous microstructures and corrosion resistance of biomedical Co-Cr-Mo alloy fabricated by electron beam melting (EBM) Addit Manuf. 2018.12; 24; 103-114

[Books etc]

1. Hanawa T. 2.1 Transition of surface modification of titanium for medical and dental use, In: Titanium in Medical and Dental Applications, Eds, F. H. Froes, M Qian. Woodhead Publishing, UK, 2018.05

[Misc]

1. Tsutsumi Y. II. Fundamental electrochemical measurement for corrosion study: Potentiostatic method Corros Eng. 2018.03; 67(3); 87-93

[Conference Activities & Talks]

1. Tsutsumi Y. Surface modification technique for metallic biomaterials to realize multibiofunctional properties. The 4th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2018.01.12 Chulalongkorn University, Bangkok, Thailand
2. Hanawa T. Next generation metallic implant materials and surfaces. Finland-Japan Workshop:The next generation medical engineering in biomaterials 2018.06.17 Oulu, Finland
3. Tsutsumi Y, Chen P, Ashida M, Doi H, Hanawa T. Long-term corrosion monitoring of metallic biomaterials. Finland-Japan Workshop:The next generation medical engineering in biomaterials 2018.06.17 Oulu, Finland
4. Umise A. Deformation behavior of biomedical Au28Cu22Al shape memory alloy. 4st International workshop for advanced materials 2018.06.18 Busan, Korea
5. Hanawa T. Next generation metallic implant materials and surfaces. THERMEC'2018 2018.07.09 Paris, France
6. Nomura N, Sun X, Zhou W, Kikuchi K, Kawasaki A, Doi H, Tsutsumi Y, Hanawa T. Microstructure and mechanical properties of a low magnetic Zr-Mo alloy for biomedical applications. THERMEC'2018 2018.07.09 Paris, France
7. Chen P, Aso T, Sasaki R, Ashida M, Doi H, Tsutsumi Y, Hanawa T. Adhesion and differentiation of mesenchymal stem cells response to Ti surface with multi-scaled topographies. Biomaterials International 2018 2018.07.23 Tokyo, Japan
8. Isoshima K, Ueno T, Arai Y, Saito H, Tan T, Chen P, Tsutsumi Y, Hanawa T, Wakabayashi N. Increased extracellular proteins adsorption on electropositive titanium surfaces. 96th General Session & Exhibition of the IADR (IADR/PER 2018) 2018.07.25 London, UK
9. Tan T, Ueno T, Arai Y, Saito H, Tsutsumi Y, Doi H, Hanawa T, Wakabayashi N. Surface characterization and bioactivity of Ti-Zr alloy with compositional change. 96th General Session & Exhibition of the IADR (IADR/PER 2018) 2018.07.25 London, UK
10. Tsutsumi Y. Evaluation of corrosion resistance of metallic biomaterials: Conventional and advanced techniques. The 13th International Workshop on Biomaterials in Interface Science 2018.08.02 Sendai, Miyagi, Japan
11. Tsutsumi Y, Shimabukuro M, Chen P, Ashida M, Doi H, Hanawa T. Development of surface treatment to realize novel biomaterial with both tissue compatibility and antibacterial property. 15th International Symposium on Functionally Graded Materials 2018.08.07 Kitakyushu, Fukuoka, Japan
12. Chen P, Aso T, Sasaki R, Ashida M, Doi H, Tsutsumi Y, Hanawa T. Multi-scaled hierarchical topography of titanium regulated adhesion and multi-differentiation of mesenchymal stem cells. Biointerfaces International 2018 2018.08.14 Zurich, Switzerland
13. Hanawa T. New alloys and surfaces for next generation implants. International Conference on Biomaterial 2018 2018.08.16 London, UK
14. Hanawa T. Durability and biofunction of metallic implant devises. International Workshop on Giant Straining Process for Advanced Materials in 2018(GSAM2018) 2018.09.03 Fukuoka, Japan
15. Ashida M, Kitamura Y, Chen P, Doi H, Tsutsumi Y, Takizawa Y, Yumoto M, Otagiri Y, Horita Z, Hanawa T. Strengthening of Ti-6Al-7Nb alloy by high-pressure sliding. International Workshop on Giant Straining Process for Advanced Materials in 2018(GSAM2018) 2018.09.03 Fukuoka, Japan
16. Hanawa T, Honma K, Ashida M, Tsutsumi Y, Nomura N, Doi H, Simojo M. New zirconium alloy to decrease MRI artifact. 29th Annual Meeting of the European Society for Biomaterials (ESB 2018) 2018.09.09 Maastricht, the Netherlands

17. Tsutsumi Y, Shimabukuro M, Yamada R, Nozaki K, Chen P, Ashida M, Doi H, Nagai A, Hanawa T. Antibacterial property of the surface oxide layer containing antibacterial elements on titanium formed by electrochemical treatment. 29th Annual Meeting of the European Society for Biomaterials (ESB 2018) 2018.09.09 Maastricht, the Netherlands
18. Chen P, Takenaka K, Tsukamoto M, Ashida M, Doi H, Tsutsumi Y, Hanawa T. Calcification of pre-osteoblast cultured on titanium surfaces with different patterned nano-topographies produced with femtosecond laser irradiation. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
19. Toriyabe A, Goto K, Umise A, Takahara M, Hanawa T, Kanetaka H, Hosoda H. Microstructure and mechanical properties of Au-Cu-Al biomedical shape memory alloys containing Ag. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
20. Shun N, Tsutsumi Y, Hanawa T, Ikoma T, Matsushita N. High corrosion resistance of Mg alloy surface modified by solution processes. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
21. Takenaka K, Tsukamoto M, Sato Y, Hanawa T, Chen P, Asai S. Femtosecond laser induced periodic nanostructures formation on PLA film surface with Ti plate. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
22. Arisaka Y, Tamura A, Tsutsumi Y, Hanawa T, Yui N. Immobilization of ethylated polyrotaxanes with amino groups at both terminals onto titanium surfaces using an electrodeposition method. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
23. Tsutsumi Y, Oishi M, Chen P, Ashida M, Doi H, Hanawa T. Change in surface of yttria-stabilized zirconia in water and Hanks' solution characterized by XPS analysis. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo, Japan
24. Tsutsumi Y. Corrosion behavior of metallic biomaterials used in living body environment. 18th Asian Pacific Corrosion Control Conference (APCCC18) 2018.11.06
25. Hanawa T. Titanium and its alloys in dentistry. Lecture and Seminar in School of Stomatology "New Technologies and Materials in Dentistry" 2018.11.08 Brno, Czech
26. Umise A, Yamaji K, Gunji H, Goto K, Tahara M, Hanawa T, Hosoda H. Ductility enhancement of AuCuAl biomedical shape memory alloys by introducing fcc α phase. 2018 MRS Fall Meeting 2018.11.25 Boston, USA
27. Hanawa T. Next generation metallic implant materials: Contribution of nanoscience and nanotechnology. 28th International Conference and Expo on Nanosciences and Nanotechnology 2018.11.26 Barcelona, Spain
28. Chen P. Nanotechnology for intelligent surface designing of metallic dental devices. 2nd International Symposium on Precision Medicine and Biomedical Technologies 2018.12.07 Quanzhou, China

Inorganic Biomaterials

Professor Kimihiro Yamashita
Associate Prof. Miho Nakamura
Assistant Prof. Naohiro Horiuchi
Research Associate Takako Takuma

(1) Outline

(1) Development of Electrovector ceramics

Some ceramics, such as a hydroxyapatite, are able to be ionically polarized by thermoelectrical treatments. Consequently, the polarized ceramics have large and time-durable induced electrostatic charges on their surfaces. The effects of the induced charges profoundly dominate the proximate few millimeter regions. We named the effects “Electrovector effects” and develop “Electrovector ceramics” defined as ceramics emitting the Electrovector Effects.

(2) Control of electrical space on Electrovector ceramic

To translate the Electrovector ceramics into practical applications for medical devices, electrical space on Electrovector ceramics should be suitably controlled under the poling process. We are evaluating the poling mechanisms of some bioceramics, based on the various disciplines. In particular, we are putting emphasis on the relationship between the origin of electrical space and the crystal structure on the surface of the polarized bio-ceramics. The crystal defect, crystal distortion and fine change of ion composition of Electrovector ceramics polarized under various conditions are systematically investigated.

(3) Manipulation of biological responses by Electrovector ceramics

The electrostatic energies of the Electrovector effects aforementioned dominate the limited proximate areas and can control reactions locally. Therefore, the Electrovector ceramics can manipulate biological responses in a target space by both of the surface character and the electrostatic energies of the Electrovector ceramics at ion and tissue levels. We have demonstrated that the Electrovector ceramics enhanced protein adsorption, proliferation, adhesion, and differentiation of cultured cells on the ceramics as well as osteoconductivities in vivo by molecular biological and immunological detections.

(4) Development of applicable devices by ceramic technologies

We apply the Electrovector ceramics aforementioned to implant systems, such as artificial bones, bone joints, tooth roots, and are developing implantable devices with autograft-like osteoconductivities. We are undergoing improvements of sol-gel method for hydroxyapatite thin film coating and materials for vascular regeneration. We are extending our researches based on ceramic technologies farther, such as a control of oral environment, an improvement of oral esthetics, more effective and precise diagnosis systems for clinical laboratory medicine.

(2) Publications

[Original Articles]

1. Kazuhisa Fujita, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Hiroyuki Miura, Akiko Nagai. Regulation of periodontal ligament-derived cells by type III collagen-coated hydroxyapatite. Biomed Mater Eng. 2018.01; 29(1); 15-27

2. Naohiro Horiuchi, Kazuki Madokoro, Kosuke Nozaki, Miho Nakamura, Keiichi Katayama, Akiko Nagai, Kimihiro Yamashita.. Electrical conductivity of polycrystalline hydroxyapatite and its application to electret formation. Solid State Ionics. 2018.02; 315; 19-25
3. Naohiro Horiuchi, Kotaro Shibata, Hironori Saito, Yuki Iwabuchi, Norio Wada, Kosuke Nozaki, Kazuaki Hashimoto, Yumi Tanaka, Akiko Nagai, Kimihiro Yamashita. Size control synthesis of hydroxyapatite plates and their application in the preparation of highly oriented films Crystal Growth & Design. 2018.08;

[Conference Activities & Talks]

1. Kosuke Nozaki, Kazuhisa Fujita, Naohiro Horiuchi, Kimihiro Yamashita, Kazuaki Hashimoto, Hiroyuki Miura, Akiko Nagai. Calcium deficiency regulates surface charges of β -tricalcium phosphate. 96th General Session and Exhibition of the IADR 2018.07.28
2. Naohiro Horiuchi, Hironori Saito, Kazuaki Hashimoto, Kimihiro Yamashita. Hydrothermal synthesis of hydroxyapatite plates using calcium dicarboxylates. 6th International Solvothermal and Hydrothermal Association Conference (ISHA2018) 2018.08.09
3. Kenichiro Hayashi, Kosuke Nozaki, Zhenquan Tan, Naohiro Horiuchi, Kimihiro Yamashita, Hiroyuki Miura, Keiji Itaka and Satoshi Ohara. Antibacterial property of titania nanosheet synthesized by organic ligand-assisted hydrothermal reaction. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25
4. Matsumura M, Nozaki K, Yamashita K, Matsumura M, Miura H. Optimization of surface roughness of composite resin block by controlling milling condition. 2018.10.07 Hokkaido
5. Naohiro Horiuchi, Hironori Saito, Kazuaki Hashimoto, Kimihiro Yamashita. Plate-shaped Hydroxyapatite Synthesis Using Sebacic Acid. Bioceramics30 2018.10.26
6. Naohiro Horiuchi. Electric properties of hydroxyapatite and their applications. The 3rd International Symposium on Biomedical Engineering 2018.11.08 Satake Memorial Hall, Hiroshima University

[Patents]

1. METHOD FOR CONTROLLING ORGANISMS AND MATERIAL THEREFORE, METHOD FOR SELECTIVE ADSORPTION OF PROTEINS AND MATERIAL THEREFORE, CEMENT MATERIAL AND BIOMATERIAL, Patent Number : US6777214B1
2. Material for controlling organisms and for selective adsorption of protein, cement and biomaterial, Patent Number : EU 00104225.8-2107

Organic Biomaterials

Professor: Nobuhiko YUI

Associate Professor: Atsushi TAMURA

Assistant Professor: Yoshinori ARISAKA

Part-time Lecturer : Satoshi YAMAGUCHI

Researcher: Masahiko TERAUCHI

Secretary: Nanae NISHI

(1) Research

1. Design of Polyrotaxane-based Surfaces and Three-dimensional Architectures

Biomaterials surfaces with dynamic properties are designed by utilizing a molecularly movable architecture of polyrotaxanes, and examined their effects on a variety of interactions with living body. In addition, Polyrotaxane-based three-dimensional architectures such as hydrogels, scaffolds, and resins are developed for biologically active supramolecular biomaterials. The mobility and stimuli-responsively dissociative character of polyrotaxanes are integrated to the three-dimensional architectures to demonstrate novel functions in the Biomaterials.

2. Stimuli-labile Polyrotaxanes as a Therapeutic Agent for Intractable Diseases

Stimuli-labile polyrotaxanes that release threaded cyclodextrins under intracellular environments are developed and evaluated their activity in the treatment of various intractable diseases including lysosomal storage disorders.

3. Supramolecular Complexes for Bioactive Molecules for Enhancing Biological Activities

Supramolecular polyelectrolyte complexes of biomolecules, such as nucleic acid and protein, with polyrotaxanes are designed to enhance stability and biological activities, and their therapeutic efficacies are evaluated in vitro and in vivo.

4. Detachable Dental Adhesives Based on Photo-degradable Supermolecular Cross-linkers

Photo-degradable polyrotaxanes are developed as a component of detachable dental adhesive, cement, and resin. By the irradiation of light, the mechanical strength of the polyrotaxane-containing dental materials are found to decrease. Therefore, the photo-degradable polyrotaxanes-containing dental materials would be applied as detachable dental materials.

(2) Publications

[Original Articles]

1. Atsushi Tamura, Nobuhiko Yui. Polyrotaxane-based systemic delivery of β -cyclodextrins for potentiating therapeutic efficacy in a mouse model of Niemann-Pick type C disease. *Journal of Controlled Release*. 2018.01; 269; 148-158
2. Takasuke Inada, Atsushi Tamura, Masahiko Terauchi, Satoshi Yamaguchi, Nobuhiko Yui. A silencing-mediated enhancement of osteogenic differentiation by supramolecular ternary siRNA polyplexes compris-

- ing biocleavable cationic polyrotaxanes and anionic fusogenic peptides. *Biomaterials Science*. 2018.02; 6(2); 440-450
3. Takasuke Inada, Atsushi Tamura, Masahiko Terauchi, Satoshi Yamaguchi, Nobuhiko Yui. A silencing-mediated enhancement of osteogenic differentiation by supramolecular ternary siRNA polyplexes comprising biocleavable cationic polyrotaxanes and anionic fusogenic peptides *Biomaterials Science*. 2018.02; 6(2); 440-550
 4. Yae Ohata, Maiko Tsuchiya, Hideaki Hirai, Satoshi Yamaguchi, Takumi Akashi, Kei Sakamoto, Akira Yamaguchi, Tohru Ikeda, Kou Kayamori. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. *PLoS ONE*. 2018.02; 13(2); e0191865
 5. Tomoki Kanemaru, Yoshio Ohyama, Kazuhiro Aoki, Atsushi Tamura, Nobuhiko Yui, Satoshi Yamaguchi, Yoshiyuki Mochida. Modulation of matrix mineralization by von Willebrand factor C domain containing 2 in vivo and in vitro. *Journal of Oral Tissue Engineering*. 2018.03; 15(3); 131-142
 6. Kei Nishida, Atsushi Tamura, Nobuhiko Yui. ER stress-mediated autophagic cell death induction through methylated β -cyclodextrins-threaded acid-labile polyrotaxanes. *Journal of Controlled Release*. 2018.04; 275; 20-31
 7. Jun Kobayashi, Yoshinori Arisaka, Nobuhiko Yui, Yoshikatsu Akiyama, Masayuki Yamat, Teruo Okano. Effect of temperature changes on serum protein adsorption on thermoresponsive cell-culture surfaces monitored by a quartz crystal microbalance with dissipation. *International Journal of Molecular Sciences*. 2018.05; 19(5); 1516
 8. Masahiko Terauchi, Atsushi Tamura, Satoshi Yamaguchi, Nobuhiko Yui. Enhanced cellular uptake and osteogenic differentiation efficiency of melatonin by inclusion complexation with 2-hydroxypropyl β -cyclodextrin. *International Journal of Pharmaceutics*. 2018.05; 547(1-2); 53-60
 9. Kei Nishida, Atsushi Tamura, Nobuhiko Yui. pH-responsive coacervate droplets formed from acid-labile methylated polyrotaxanes as an injectable protein carrier. *Biomacromolecules*. 2018.06; 19(6); 2238-2247
 10. Hideto Matsui, Atsushi Tamura, Mamoru Osawa, Asato Tonegawa, Yoshinori Arisaka, Mitsuaki Matsumura, Hiroyuki Miura, Nobuhiko Yui. Scavenger receptor A-mediated targeting of carboxylated polyrotaxanes to macrophages and the impacts of supramolecular structure. *Macromolecular Bioscience*. 2018.08; 18(8); 1800059
 11. Aimin Ge, Lin Qiao, Ji-Hun Seo, Nobuhiko Yui, Shen Ye. Surface-restructuring differences between polyrotaxanes and random copolymers in aqueous environment *Langmuir*. 2018.10; 34(41); 12463-12470

[Books etc]

1. Ji-Hun Seo, Nobuhiko Yui. "Functional Hydrogels as Biomaterials (Springer Series in Biomaterials Science and Engineering, vol 12)" Mobile properties of supramolecular polyrotaxane surfaces on modulation of cellular functions. Springer (Berlin, Heidelberg), 2018.07 (ISBN : 978-3662575093)

[Conference Activities & Talks]

1. Atsushi Tamura. Autophagic cell death induction in apoptosis-resistant cancer cells by methylated cyclodextrin-threaded polyrotaxanes. The 4th Joint Symposium between IBB/TMDU and Chulalongkorn University on "Biomedical Materials and Engineering" 2018.01.12 Chulalongkorn University, Bangkok, Thailand
2. Masahiko Terauchi, Takesuke Inada, Atsushi Tamura, Nobuhiko Yui, Satoshi Tamaguchi. Enhanced bone regeneration efficacy of bone morphogenetic protein-2 by the complexation with sulfonated polyrotaxanes. The 30th Annual Congress of Taiwanese Association of Oral and Maxillofacial Surgeons 2018.03.11 Kaohsiung, Taiwan
3. Masahiko Terauchi, Takesuke Inada, Atsushi Tamura, Nobuhiko Yui, Satoshi Tamaguchi. Enhanced bone regeneration efficacy of bone morphogenetic protein-2 by the complexation with sulfonated polyrotaxanes. The 30th Annual Congress of Taiwanese Association of Oral and Maxillofacial Surgeons 2018.03.11 Kaohsiung, Taiwan

4. Yoshinori Arisaka, Nobuhiko Yui. Surface design of sulfonated-supramolecular substrates for tethering bone morphogenetic protein 2. ACS National Meeting & Expo 2018.03.22 Louisiana, New Orleans, USA
5. Yoshinori Arisaka, Nobuhiko Yui. Surface design of sulfonated-supramolecular substrates for tethering bone morphogenetic protein 2. 255th ACS National Meeting & Exposition 2018.03.22
6. Yoshinori Arisaka, Nobuhiko Yui. Dynamic biointerfaces based on sulfonated polyrotaxanes for enhancing osteogenic differentiation. 2018 Society for Biomaterials Annual Meeting (2018 SFB) 2018.04.12 Hilton Atlanta, Georgia, Atlanta, USA
7. Yoshinori Arisaka, Nobuhiko Yui. Dynamic biointerfaces based on sulfonated polyrotaxanes for enhancing osteogenic differentiation. The Society For Biomaterials, 2018 Annual Meeting and Exposition 2018.04.13
8. Kentaro Morita, Taishi Higashi, Xia Song, Jing-ling Zhu, Jun Li, Atsushi Tamura, Nobuhiko Yui, Keiichi Motoyama, Hidetoshi Arima. One-pot synthesis and facile isolation of cyclodextrin-based polycatenanes. The 19th International Cyclodextrin Symposium 2018.04.27 Tokyo, Japan
9. Kentaro Morita, Taishi Higashi, Xia Song, Jing-ling Zhu, Jun Li, Atsushi Tamura, Nobuhiko Yui, Keiichi Motoyama, Hidetoshi Arima. One-pot synthesis and facile isolation of cyclodextrin-based polycatenanes. The 19th International Cyclodextrin Symposium 2018.04.28 Tokyo, Japan
10. Nobuhiko Yui, Ji Hun Seo, Atsushi Tamura, Yoshinori Arisaka. Cellular and tissue modulation via exploiting molecularly movable polyrotaxane surfaces. International Conferences on Modern Materials & Technologies 2018 (CIMTEC 2018), 8th Forum on New Materials 2018.06.11 Centro Congressi Hotel Quattrotorri, Perugia, Italy
11. Nobuhiko Yui, Ji Hun Seo, Atsushi Tamura, Yoshinori Arisaka. Cellular and tissue modulation via exploiting molecularly movable polyrotaxane surfaces. International Conferences on Modern Materials & Technologies 2018 (CIMTEC 2018), 8th Forum on New Materials 2018.06.11 Perugia, Italy
12. Atsushi Tamura, Nobuhiko Yui. Rational design of polyrotaxanes as a therapeutic agent to metabolic diseases. International Conferences on Modern Materials & Technologies 2018 (CIMTEC 2018), 8th Forum on New Materials 2018.06.12 Perugia, Italy
13. Atsushi Tamura, Nobuhiko Yui. Rational design of polyrotaxanes as a therapeutic agent to metabolic diseases . International Conferences on Modern Materials & Technologies 2018 (CIMTEC 2018), 8th Forum on New Materials 2018.06.12 Centro Congressi Hotel Quattrotorri, Perugia, Italy
14. Atsushi Tamura, Kei Nishida, Nobuhiko Yui. Emerging new biological functions of supramolecular polyrotaxanes in autophagy and autophagic cell death. 2018 Controlled Release Society Annual Meeting and Exposition (2018 CRS) 2018.07.23 New York Hilton Midtown Manhattan Hotel, New York, USA.
15. Atsushi Tamura, Kei Nishida, Nobuhiko Yui. Emerging new biological functions of supramolecular polyrotaxanes in autophagy and autophagic cell death. Controlled Release Society Annual Meeting and Exposition (CRS2018) 2018.07.23 New York, NY, USA
16. Yoshinori Arisaka, Nobuhiko Yui. Supermolecule-based culture substrates with tethered BMP-2 enhance osteogenic differentiation. 2018 TERMIS World Congress 2018.09.05
17. Katsuya Hyodo, Yoshinori Arisaka, Satoshi Yamaguchi, Nobuhiko Yui. Design of sulfonated polyrotaxane surfaces to activate vascular endothelial cells. 2018 TERMIS World Congress 2018.09.05
18. Yoshinori Arisaka, Nobuhiko Yui. Supermolecule-based culture substrates with tethered BMP-2 enhance osteogenic differentiation. 5th TERMIS World Congress 2018.09.05 Kyoto International Conference Center, Kyoto, Japan
19. Katsuya Hyodo, Yoshinori Arisaka, Satoshi Yamaguchi, Nobuhiko Yui. Design of sulfonated polyrotaxane surfaces to activate vascular endothelial cells. 5th TERMIS World Congress 2018.09.05 Kyoto International Conference Center, Kyoto, Japan
20. Asato Tonegawa, Atsushi Tamura, Nobuhiko Yui. Self-assembly of acetylated polyrotaxanes and their applications as drug carriers. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25

21. Yoshinori Arisaka, Atsushi Tamura, Yusuke Tsutsumi, Takao Hanawa, Nobuhiko Yui. Immobilization of ethylated polyrotaxanes with amino groups at both terminals onto titanium surfaces using an electrodeposition method. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo Garden Palace, Tokyo, Japan
22. Yoshinori Arisaka, Atsushi Tamura, Yusuke Tsutsumi, Takao Hanawa, Nobuhiko Yui. Immobilization of ethylated polyrotaxanes with amino groups at both terminals onto titanium surfaces using an electrodeposition method. 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25
23. Atsushi Tamura, Masahiko Terauchi, Nobuhiko Yui. Improving function of low molecular weight osteoinductive agents by an inclusion complex with cyclodextrins. 2018.10.06
24. Nobuhiko Yui. Emergence of supramolecular biomaterials using polyrotaxane frames. 2018 Fall Meeting of The Korean Society for Biomaterials 2018.10.18 Cha Bio Complex, Korea
25. Yoshinori Arisaka, Nobuhiko Yui. Molecularly mobile surfaces with heparin-binding proteins for improving functions of hepatocyte-derived cells. The 2018 MRS Fall Meeting & Exhibit 2018.11.27
26. Yoshinori Arisaka, Nobuhiko Yui. Molecularly mobile surfaces with heparin-binding proteins for improving functions of hepatocyte-derived cells. The 2018 MRS Fall Meeting & Exhibit 2018.11.27 Hynes Convention Center, Boston, Massachusetts, USA
27. Atsushi Tamura, Kei Nishida, Nobuhiko Yui. Acid-degradable coacervates formed from methylated cyclodextrins-threaded polyroaxanes for local protein delivery. The 12th SPSJ International Polymer Conference (IPC2018) 2018.12.05 International Conference Center Hiroshima, Hiroshima, Japan
28. Atsushi Tamura, Kei Nishida, Nobuhiko Yui. Acid-degradable coacervates formed from methylated cyclodextrins-threaded polyroaxanes for local protein delivery. The 12th SPSJ International Polymer Conference (IPC2018) 2018.12.05 International Conference Center Hiroshima, Hiroshima, Hiroshima, Japan

Biomechanics

Kenji Kawashima
Takahiro Kanno
Tetsuro Miyazaki
Toshihiro Kawase

(1) Outline

Kawashima Lab. mainly working on the development of medical devices and systems based on control engineering, robotics and fluid dynamics.

Key word is system integration such as hardware and software, electrical and pneumatics, human and machine.

(2) Research

- 1)Surgical robot system
- 2)Power assist devices using pneumatic actuators
- 3)Forceps manipulator for minimally invasive surgery
- 4)Development of soft robots
- 5)Haptic device using biological and visual information

(3) Education

Learn about mechanical design and control engineering for medical devices based on biomechanics. Master a basic skill to develop the devices from the researchers and engineers working on the medical devices and systems. Learn the basic control method of a surgical robot using a personal computer.

(4) Lectures & Courses

The object is to provide the ability to design and develop medical devices based on biomechanics, which studies the structure and function of biological systems, with mechanical dynamics, robotics and control engineering.

(5) Publications**[Original Articles]**

1. Hongbing Li, Lei Zhang, Kenji Kawashima. Operator Dynamics for Stability Condition in Haptic and Teleoperation System: A Survey The International Journal of Medical Robotics and Computer Assisted Surgery. 2018.01; 1-10
2. Hongbing Li, Weiwen Liu, Kundong Wang, Kenji Kawashima, Evgeni Magid. A cable-pulley transmission mechanism for surgical robot with backdrivable capability Robotics and Computer-Integrated Manufacturing. 2018.02; 49; 328-334
3. Takashi Takizawa, Takahiro Kanno, Ryoken Miyazaki, Kotaro Tadano, Kenji Kawashima. Grasping force estimation in robotic forceps using a soft pneumatic actuator with a built-in sensor Sensors and Actuators, A: Physical. 2018.03; 271; 124-130
4. Ryoken Miyazaki, Kohei Hirose, Yoshiya Ishikawa, Takahiro Kanno, Kenji Kawashima. A Master-Slave Integrated Surgical Robot with Active Motion Transformation using Wrist Axis IEEE/ASME Transactions on Mechatronics (TMECH). 2018.03; 23(3); 1215-1225
5. Sho Yoshida, Takahiro Kanno, Kenji Kawashima. Surgical Robot with Variable Remote Center of Motion Mechanism Using Flexible Structure Trans. ASME Journal of Mechanism and Robotics. 2018.04; 10(3);
6. Sato Y, Kawase T, Takano K, Spence C, Kansaku K. Body ownership and agency altered by an electromyographically controlled robotic arm. Royal Society open science. 2018.05; 5(5); 172170
7. Karponis D, Koya Y, Miyazaki R, Kanno T, Kawashima K. Evaluation of a pneumatic surgical robot with dynamic force feedback. Journal of robotic surgery. 2018.09;
8. Takahiro Kanno, Takashi Hasegawa, Tetsuro Miyazaki, Nobuyuki Yamamoto, Daisuke Haraguchi, Kenji Kawashima. Development of a Poppet-Type Pneumatic Servo Valve Applied Sciences. 2018.10; 8(11); 2094
9. 川嶋 健嗣, 宮崎 良兼, 菅野 貴皓, 只野 耕太郎. 異分野融合-産学連携による更なるがん治療の進歩を目指して 空気圧駆動を用いた低侵襲外科手術支援ロボット 日本癌治療学会学術集会抄録集. 2018.10; 56 回; SSY8-3

[Misc]

1. Kawashima Kenji. Robot surgical system using pneumatic actuators INTERNATIONAL JOURNAL OF UROLOGY. 2018.10; 25; 103

[Conference Activities & Talks]

1. Tetsuro Miyazaki. Power assist suits using pneumatic actuators. The 4th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2018.01.12 Chulalongkorn University
2. K. Aoyagi, T. Miyazaki, T. Kawase, T. Kanno, K. Kawashima. Pneumatically driven waist-attaching robot arm for holding endoscope. The 5th Multi-symposium on Control Systems: MSCS 2018 2018.03.08 Tokyo City University
3. Ryo Okabayashi, Kengo Watanabe, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. A Pneumatically Driven Forceps Manipulator with 5 DOFs inside Abdominal Cavity. The 5th Multi-symposium on Control Systems: MSCS 2018 2018.03.08 Tokyo City University
4. Tomonori Kawakami, Takahiro Kanno, Tetsuro Miyazaki, Kenji kawashima. Development of Supporting Device in Ophthalmic Surgical Operation Using Soft Actuator. The 5th Multi-symposium on Control Systems: MSCS 2018 2018.03.08 Tokyo City University
5. Kenji Kawashima. Robot surgical system using pneumatic actuators. 2018.04.20
6. Victor Barradas, Toshihiro Kawase, Yasuharu Koike, Nicolas Schweighofer. Savings in muscle activation patterns during a virtual surgery task. The 28th Annual Meeting of the Society for the Neural Control of Movement 2018.05.01 Santa Fe

7. Toshihiro Kawase, Yuki Sato, Kenji Kansaku. EMG-controlled robotic arm intended to be incorporated into body representation. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.27
8. Osamu Azami, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima . Robotic Forceps Driven by Extension Type Pneumatic Soft Actuator . IEEE ICMA2018 2018.08
9. Masahiko Minamoto, Masaki Saito, Takahiro Kanno, Kenji Kawashima . Tele-Operation of Robot by Image Processing of Markers Attached to Operator' s Head . IEEE ICMA2018 2018.08
10. Osamu Azami, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. Robotic Forceps Driven by Extension Type Pneumatic Soft Actuator. In Proceedings of the 2018 IEEE International Conference on Mechatronics and Automation (ICMA) 2018.08.05 Changchun, China
11. Osamu Azami, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. Robotic Forceps Driven by Extension Type Pneumatic Soft Actuator. 2018 IEEE International Conference on Mechatronics and Automation 2018.08.06
12. Masahiko Minamoto, Masaki Saito, Takahiro Kanno, Kenji Kawashima. Tele-Operation of Robot by Image Processing of Markers Attached to Operator' s Head. 2018 IEEE International Conference on Mechatronics and Automation 2018.08.08
13. Toshihiro Tagami, Toshihiro Kawase, Daisuke Morisaki, Ryoken Miyazaki, Tetsuro Miyazaki, Takahiro Kanno, Kenji Kawashima. Development of Master-slave Type Lower Limb Motion Teaching System. Proc. of the IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS2018) 2018.10.01
14. Toshihiro Tagami, Daisuke Morisaki, Tetsuro Miyazaki, Toshihiro Kawase, Takahiro Kanno, Kenji Kawashima. Gait Assistive Suit with Phase Detection Using Pneumatic Artificial Rubber Muscles. The Japan Fluid Power System Society Fall Conference 2018.10.25
15. Tomonori Kawakami, Norihiko Ito, Takahiro Kanno, Tetsuro Miyazaki, Toshihiro Kawase, Kenji Kawashima. Development of Supporting Device in Ophthalmic Surgical Operation Using Pneumatic Soft Actuator. The Japan Fluid Power System Society Fall Conference 2018.10.25
16. Tetsuro Miyazaki, Daisuke Morisaki, Toshihiro Tagami, Toshihiro Kawase, Takahiro Kanno, Kenji Kawashima. Soft Sensorless Gait Assistive Suit for Ground and Underwater Training. In Proceedings of the 3rd International Symposium on Biomedical Engineering (ISBE2018) 2018.11.08 Hiroshima Univ.
17. Toshihiro Kawase, Ryoken Miyazaki, Tetsuro Miyazaki, Takahiro Kanno, Kotaro Tadano, Kenji Kawashima. Hand-held Robotic Forceps Using a Force Sensing Input Device. In Proceedings of the 3rd International Symposium on Biomedical Engineering (ISBE2018) 2018.11.08 Hiroshima Univ.
18. Masahiko Minamoto, Takahiro Kanno, Tetsuro Miyazaki, Toshihiro Kawase, Kenji Kawashima. Operation of Laparoscope Holder by Tracking Image Markers. In Proceedings of the 3rd International Symposium on Biomedical Engineering (ISBE2018) 2018.11.08 Hiroshima Univ.
19. Toshihiro Kawase, Ryoken Miyazaki, Tetsuro Miyazaki, Takahiro Kanno, Kenji Kawashima. Development of a Hand-held Robotic Forceps Controlled by a User Interface Using a Force Sensor. The 27th Annual Congress of Japan Society of Computer Aided Surgery 2018.11.09
20. Hiroki Kaji, Takahiro Kanno, Tetsuro Miyazaki, Toshihiro Kawase, Kenji Kawashima. Extraction of major tasks in surgical by text analysis of videos. The 27th Annual Congress of Japan Society of Computer Aided Surgery 2018.11.09
21. Takuto MIKADA, Hiroki KAJI, Takuya IWAI, Takahiro KANNO, Toshihiro KAWASE, Tetsuro MIYAZAKI, Kenji KAWASHIMA. Posture Estimation of Robot Forceps using Endoscope with CNN. SICE 2018 Industrial Application Division Conference 2018.11.22
22. Tetsuro MIYAZAKI, Daisuke MORISAKI, Toshihiro TAGAMI, Takahiro KANNO, Toshihiro KAWASE, Kenji KAWASHIMA. Pressure Trajectory-Based Control of Pneumatic Driven Assistive Suit. SICE 2018 Industrial Application Division Conference 2018.11.22
23. Hiroki Kaji, Takahiro Kanno, Tetsuro Miyazaki, Toshihiro Kawase, Kenji Kawashima. External force estimation of forceps tip using machine learning. In Proceedings of the 8th International Conference on Position Technology (ICPT 2018) 2018.11.28

24. Tadatoshi Sato, Takahiro Kanno, Ryoken Miyazaki, Tetsuro Miyazaki, Kenji Kawashima. Variable Remote Center of Motion Mechanism Using Flexible Structure for Forceps Holder. In Proceedings of the 8th International Conference on Position Technology (ICPT 2018) 2018.11.28
25. Toshihiro Kawase, Ryoken Miyazaki, Tetsuro Miyazaki, Takahiro Kanno, Kenji Kawashima. Development of a Hand-held Robotic Forceps Using a Force Sensor as a User Interface. In Proceedings of the 8th International Conference on Position Technology (ICPT 2018) 2018.11.28

[Awards & Honors]

1. Advanced Robotics Best Paper Award, The Robotics Society of Japan, 2018.09

Molecular Cell Biology

Professor Hiroshi Shibuya
Associate Professor Toshiyasu Goto
Assistant Professor Atsushi Sato

(1) Lectures & Courses

Various signaling molecules inducing the cell-growth and differentiation regulate morphogenesis and organogenesis of the vertebrate. The failure of these signal molecules has also been caused with induction of the diseases. Therefore, the elucidation of signal transduction network regulating generation and differentiation is important upon clarifying the mechanism of morphogenesis, organogenesis and diseases. Our research aim is to clarify the signal transduction network regulating the mechanisms of morphogenesis and organogenesis in developmental process. We serve these research and following education to provide graduate students who will become senior scientists in life sciences.

(2) Publications

[Original Articles]

1. Sato A, Shibuya H.. Glycogen synthase kinase 3 β functions as a positive effector in the WNK signaling pathway. PLoS One. 2018.03; 13; e0193204
2. Sato, A and Shibuya, H. Glycogen synthase kinase 3 β functions as a positive effector in the WNK signaling pathway. PLoS One. 2018.03; 13; e0193204

[Conference Activities & Talks]

1. Atsushi Sato, Hiroshi Shibuya. GSK3 β functions as a positive effector in WNK signaling pathway. The 13rd Japanese Drosophila Research Conference 2018.09.10

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D.
 Lecturer Kengo Homma, Ph.D.
 Assistant Professor Erika Ishihara, Ph.D.
 Junior Assistant Professor Yukari Mori, Ph.D.
 Secretary Kazuko Tanaka

(1) Outline

Our goal is to define the molecular basis for the mechanism of organ formation and regeneration using knockout mice and mutant fishes. To accomplish this goal, we have focused on defining signaling molecules and pathways that regulate liver formation and stress responses. Moreover, we are trying to establish a cell therapy for intractable diseases such as liver failures using self-bone marrow cells. Our study will provide new insights into understanding the precise molecular mechanisms that underlie organ failures found in human disease and will lead to the development of new rational therapy for the diseases.

(2) Research

1. Studies on vertebrate early embryogenesis
2. Studies on vertebrate organogenesis
3. Studies on organ homeostasis
4. Studies on behavioral rhythm

(3) Publications

[Original Articles]

1. Hiroki Goto, Miki Nishio, Yoko To, Tatsuya Oishi, Yosuke Miyachi, Tomohiko Maehama, Hiroshi Nishina, Haruhiko Akiyama, Tak Wah Mak, Yuma Makii, Taku Saito, Akihiro Yasoda, Noriyuki Tsumaki, Akira Suzuki. in mice results in chondrodysplasia due to YAP1/TAZ-TEAD-dependent repression of SOX9. *Development*. 2018; 145(6);
2. Asami Kawasaki, Masayasu Okada, Atsushi Tamada, Shujiro Okuda, Motohiro Nozumi, Yasuyuki Ito, Daiki Kobayashi, Tokiwa Yamasaki, Ryo Yokoyama, Takeshi Shibata, Hiroshi Nishina, Yutaka Yoshida, Yukihiro Fujii, Kosei Takeuchi, Michihiro Igarashi. Growth Cone Phosphoproteomics Reveals that GAP-43 Phosphorylated by JNK Is a Marker of Axon Growth and Regeneration. *iScience*. 2018.06; 4; 190-203
3. Tsuburaya N, Homma K, Higuchi T, Balia A, Yamakoshi H, Shibata N, Nakamura S, Nakagawa H, Ikeda SI, Umezawa N, Kato N, Yokoshima S, Shibuya M, Shimonishi M, Kojima H, Okabe T, Nagano T, Naguro I, Imamura K, Inoue H, Fujisawa T, Ichijo H. A small-molecule inhibitor of SOD1-Derlin-1 interaction ameliorates pathology in an ALS mouse model. *Nature communications*. 2018.07; 9(1); 2668

[Misc]

1. Erika Ishihara, Hiroshi Nishina. The Hippo-YAP Pathway Regulates 3D Organ Formation and Homeostasis. *Cancers (Basel)*. 2018.04; 10(4);

Immunology

Professor: Takeshi TSUBATA, M.D., Ph.D.
 Associate Professor: Takahiro ADACHI, Ph.D.
 Assistant Professor: Chizuru AKATSU, Ph.D.
 Project Assistant Professor: Shuichi KINPARA, Ph.D.
 Lecturer: Ji-Yang WANG, Ph.D.
 Researcher: Nazim MEDZHIDOV, Ph.D.
 Technicians: Shiori OZEKI, Emi HAGIUDA
 Secretary: Chikako SAWADA
 Graduate Students: Yang-Yang FENG
 Graduate Students: Amin ALBORZIAN DE SHEIKH,
 Graduate Students: Yuki ANBE, Kyoko NISHIDA, Wang LONG
 Graduate Students: Hongrui YANG, Xuexin LI,
 Graduate Students: Moe ENDO, Yuming HUANG,
 Graduate Students: Akio KATO
 Graduate Research Students: Masato SUZUKI, Yang CUI

(1) Research

Immune responses to non-protein antigens play crucial roles in host defense against pathogens, and autoimmune diseases. The mechanisms for immune responses to non-protein antigens are distinct from those to protein antigens, but are largely unknown. The aims of our research are to elucidate the mechanisms for antibody responses to non-protein antigens, and to develop novel drugs for autoimmune diseases and cancer immunotherapy by regulating antibody responses. Followings are our research subjects.

- 1) Elucidation of the mechanisms for humoral immune responses to polysaccharide antigens.
- 2) Elucidation of the mechanisms for autoantibody production in lupus and immuno-neurological disorders.
- 3) Elucidation of the role of glycan signals in the regulation of humoral immune responses, and development of glycomimetics for therapy.
- 4) Elucidation of the Role of reactive oxygen species (ROS) and membrane traffic in B cell activation.
- 5) Development of novel drugs for autoimmune diseases by regulating regulatory B cells.
- 6) Development of therapeutic vaccines that substitute for therapeutic antibodies.

(2) Education

Our department is responsible for the education on immunology provided by the PhD Program in Biomedical Sciences and Engineering, and the Master's Program in Medical and Dental Science and Technology.

Research projects in both the Master's and PhD Programs aim at training the students to acquire basic research skills on immunology, molecular biology and biochemistry, and abilities to conduct cutting-edge research in the field of immunology by themselves under supervision.

Lecture course on immunology at the Master's Program aims at giving the students basic ideas how immune system recognizes and responds to the antigens, and how immune system efficiently removes pathogens without

responding to self-antigens or environmental antigens. In the lecture course on biomedical science and lecture course on molecular pathophysiology at the PhD Program, lectures on immune responses and pathophysiology of immunological diseases are given so that the students are introduced with the current topics in the field of humoral immune responses and immunological diseases.

(3) Publications

[Original Articles]

1. Tsubata, T. Negative regulation of B cell responses and self-tolerance to RNA-related lupus self-antigen. *Proc. Jpn. Acad. Ser. B Phys. Biol. Sci.* 2018.01; 94(1); 35-44
2. Amin Alborzian Deh Sheikh, Akatsu Chizuru, Imamura Akihiro, Abdu-Allah Hajjaj H. M., Takematsu Hiromu, Ando Hiromune, Ishida Hideharu, Tsubata Takeshi. Proximity labeling of cis-ligands of CD22/Siglec-2 reveals stepwise alpha 2,6 sialic acid-dependent and -independent interactions. *Biochemical and biophysical research communications.* 2018.01; 495(1); 854-859
3. Taro Watabe, Takashi Nagaishi, Naoya Tsugawa, Yudai Kojima, Nisha Jose, Akinori Hosoya, Michio Onizawa, Yasuhiro Nemoto, Shigeru Oshima, Tetsuya Nakamura, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. B cell activation in the cecal patches during the development of an experimental colitis model. *Biochem. Biophys. Res. Commun.* 2018.02; 496(2); 367-373
4. Liu, J., Zhu, H., Qian, J., Xiong, E., Zhang, L., Chu, Y., Kubagawa, H., Tsubata, T. and Wang, J.-Y. . Fc μ Receptor promotes the survival and activation of marginal zone B cells and protects mice against bacterial sepsis *Front. Immunol.* 2018.02; 9; 160-169
5. Naoko Matsubara, Akihiro Imamura, Tatsuya Yonemizu, Chizuru Akatsu, Hongrui Yang, Akiharu Ueki, Natsuki Watanabe, Hajjaj Abdu-Allah, Nobutaka Numoto, Hiromu Takematsu, Shinobu Kitazume, Thomas F Tedder, Jamey D Marth, Nobutoshi Ito, Hiromune Ando, Hideharu Ishida, Makoto Kiso, Takeshi Tsubata. CD22-Binding Synthetic Sialosides Regulate B Lymphocyte Proliferation Through CD22 Ligand-Dependent and Independent Pathways, and Enhance Antibody Production in Mice. *Front Immunol.* 2018.04; 9; 820
6. Lino, A. C., Dang, V. D., Lampropoulou, V., Welle, A., Joedicke, J., Pohar, J., Simon, Q., Thalmensi, J., Baures, A., Fluehler, V., Sakwa, I., Stervbo, U., Ries, S., Jouneau, L., Boudinot., P., Tsubata, T. Adachi, T., Hutloff, A., Doener, T., Zimmer-Strobl, U., de Vos, A. F., Dahlke, K., Loh, G., Komiotis, S., Goosmann, C., Weill, J.-C., Raynaud, C.-A., Kaufmann, S. H. E., Walter, J. and Fillatreau, S. . LAG-3 expression identifies immunosuppressive natural regulatory plasma cells. 2018.07; 49(1); 120-133
7. Li Shuyin, Liu Jun, Min Qing, Ikawa Tomokatsu, Yasuda Shoya, Yang Yang, Wang Yan-Qing, Tsubata Takeshi, Zhao Yaofeng, Wang Ji-Yang. Ketch-like protein 14 promotes B-1a but suppresses B-1b cell development. *International Immunology.* 2018.07; 30(7); 311-318
8. Fujii Y, Suzuki K, Hasegawa Y, Nanba F, Toda T, Adachi T, Taira S, Osakabe N. Single oral administration of flavan 3-ols induces stress responses monitored with stress hormone elevations in the plasma and paraventricular nucleus. *Neuroscience letters* . 2018.08; 682; 106-111
9. Tsubata Takeshi. Ligand Recognition Determines the Role of Inhibitory B Cell Co-receptors in the Regulation of B Cell Homeostasis and Autoimmunity. *Frontiers in Immunology.* 2018.10; 9; 2276
10. Jin K, Imada T, Nakamura S, Izuta Y, Oonishi E, Shibuya M, Sakaguchi H, Adachi T, Tsubota K. Intravital Two-photon Imaging of Ca²⁺ signaling in Secretory Organs of Yellow Cameleon Transgenic Mice. *Scientific reports.* 2018.10; 8(1); 15880
11. Kumazawa T, Nishimura A, Asai N, Adachi T. Isolation of immune-regulatory *Tetragenococcus halophilus* from miso. *PLOS ONE.* 2018.12; 13(12); e0208821

[Conference Activities & Talks]

1. Takahiro Adachi. Intravital imaging of cellular signaling in immune cells. The 3rd International Symposium on Stem Cell Traits and Developmental Systems. KEY Forum 2018 2018.01.11 Kumamoto
2. Takashi Nagaishi, Naoya Tsugawa, Taro Watabe, Akinori Hosoya, Nisha Jose, Yudai Kojima, Takahiro Adachi, Mamoru Watanabe. Verification of intestinal microflora-mediated mucosal homeostasis by immunoglobulin A. The 11th International Gastrointestinal Consensus Symposium 2018.02.10 Tokyo
3. Takeshi Tsubata. Inhibitory B cell co-receptors and autoimmune diseases. 45th IMSUT Founding Commemorative Symposium "A new era of medical researches created by disease models" 2018.06.01 Tokyo
4. Takeshi Tsubata. Endogenous ligands of inhibitory B lymphocyte co-receptors. 2018.06.14 Zürich, Switzerland
5. Takeshi Tsubata. Endogenous ligands of inhibitory B cell co-receptors. 2018.06.15 Berlin, Germany
6. Takeshi Tsubata. The Inhibitory B Cell Co-Receptor CD72 Regulates Tolerance to Self Nucleic Acids Crucial for Development of Systemic Lupus Erythematosus. Keystone Symposia, B cells: Mechanisms in Immunity and Autoimmunity 2018.06.21 Dresden, Germany
7. Amin Alborzian Deh Sheikh, Chizuru Akatsu, Hideharu Ishida and Takeshi Tsubata. The role of CD22 glycan cis-ligands in the regulation of B cell tonic signaling. The Regular Meeting of the Japanese Biochemical Society Kanto Branch 2018.06.23 Saitama
8. Yang-Yang Feng, Miao Tang, Mitsuhiro Suzuki, Jun Liu, Helmut Grasberger, Mamoru Ohkita, Yasuo Matsumura, Ji-Yang Wang, and Takeshi Tsubata. Role of NADPH oxidases in BCR signaling and B cell proliferation. The Regular Meeting of the Japanese Biochemical Society Kanto Branch 2018.06.23 Saitama
9. Takeshi Tsubata. Essential role of NADPH oxidase-dependent production of reactive oxygen species in maintenance of sustained B cell receptor signaling and B cell proliferation. 2018.06.25 Freiburg, Germany
10. Chizuru Akatsu, Xuexin Li, Susumu Kusunoki, Takeshi Tsubata. SHP-1-activating B lymphocyte co-receptors and autoimmune diseases. Workshop on Frontiers in Phosphatase Research and Drug Discovery (ICPP13) 2018.10.23 Tokyo
11. Moe Endo, Chizuru Akatsu, Quan-Zhen Li, Chengsong Zhu, Teizo Fujita, Hideharu Sekine, Takeshi Tsubata. Ligand recognition of the SHP-1-activating inhibitory B cell co-receptor CD72. Workshop on Frontiers in Phosphatase Research and Drug Discovery (ICPP13) 2018.10.23 Tokyo
12. Amin Alborzian Deh Sheikh, Chizuru Akatsu, Hideharu Ishida and Takeshi Tsubata. The role of ligand recognition of SHP-1 activating receptor CD22 in the regulation of B cell tonic signaling. Workshop on Frontiers in Phosphatase Research and Drug Discovery (ICPP13) 2018.10.23 Tokyo
13. Yang-Yang Feng, Miao Tang, Mitsuhiro Suzuki, Jun Liu, Helmut Grasberger, Ji-Yang Wang and Takeshi Tsubata. Essential role of NADPH oxidases in BCR signaling and B cell proliferation. Workshop on Frontiers in Phosphatase Research and Drug Discovery (ICPP13) 2018.10.23 Tokyo
14. Chinthika Gunasekara, Kozo Watanabe, Takeshi Tsubata. Reactive oxygen species play a role in endosomal B cell antigen receptor signaling. 7th Federation of Immunological Societies of Asia-Oceania (FIMSA) Congress 2018 2018.11.10 Bangkok, Thailand
15. Takeshi Tsubata. Ligand recognition determines functional properties of inhibitory B cell co-receptors. International Symposium on B cells 2018.12.07 Shanghai, China
16. Kyoko Nishida, Akihiro Kimura, Takeshi Tsubata, Harumi Suzuki. NQO1 regulates pathogenicity of Th17 cells by suppressing IL-10 production. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.10 Fukuoka
17. Yangyang Feng, Jun Liu, Helmut Grasberger, Ji-Yang Wang, Takeshi Tsubata. Essential role of NADPH oxidase-dependent production of reactive oxygen species in maintenance of sustained B cell receptor signaling and B cell proliferation. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.10 Fukuoka

18. Xuexin Li, Soha Gomaa Ramadan Abdel Salam, Matthew Routledge, Yuki Hitomi, Susumu Kusunoki, Takeshi Tsubata. Significant associations of human SIGLEC10 polymorphisms with susceptibility to Guillain-Barré syndrome. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.10 Fukuoka
19. Chizuru Akatsu, Quan-Zhen Li, and Takeshi Tsubata. Roles of CD72 in the regulation of autoantibody production and type 1 interferon production in autoimmune disease. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.10 Fukuoka
20. Chizuru Akatsu, Xuexin Li, Susumu Kusunoki, Takeshi Tsuabta. SHP-1-activating B lymphocyte co-receptors and autoimmune diseases. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.10 Fukuoka
21. Takahiro Adachi, Hajime Karasuhama, Sochiro Yoshikawa. Kinetics of Ca²⁺ signaling in immune cells predict predisposition and pre-pathological conditions of immune disease. The 47th Annual Meeting of the Japanese Society for Immunology 2018.12.11 Fukuoka

[Awards & Honors]

1. Best Presentation Award (Xuexin, Li), Japanese Society for Immunology, 2018.12

Epigenetics

Professor Fumitoshi Ishino
 Associate Professor Jiyoung Lee
 Assistant Professor Moe Kitazawa
 Project Assistant Professor Ayumi Matsuzawa
 Adjunct Lecturer Takashi Kohda
 Adjunct Lecturer Shin Kobayashi
 Adjunct Lecturer Hirosuke Shiura

(1) Outline

Epigenetics and Genetics are basics of biology that enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of the organisms including our human beings. Genomic imprinting is a mammalian-specific epigenetic mechanism that gives rise to functional differences between paternally- and maternally-derived genomes in development, behavior and growth. Somatic cloned animals give us unique chances to examine ‘genetically identical but epigenetically diverged animals’. Mammalian-specific LTR retrotransposon-derived genes are essential for mammalian development, such as placenta and brain functions. These studies show us how Epigenetics and Genetics are important in mammalian biology. We focus on these mammalian-specific genomic functions to elucidate how these genomic functions work and have been evolved as new genomic functions during evolution. Our final goal is to contribute to the human biology as well as medicine in the 21st century by novel understanding of genomic functions.

(2) Research

- 1) Genomic imprinting in human and mammalian development and diseases (Role of PEG11/RTL1 in Kagami-Ogata syndrome and Temple syndrome)
- 2) Function of Rtx lncRNA in X chromosome inactivation.
- 3) Domesticated genes from LTR retrotransposons/retroviruses and mammalian evolution
- 4) Assisted reproductive technology: its epigenetic effects and safer application.
- 5) Genomic imprinting memory in ES cells
- 6) EnIGMA method: a new method for simultaneous identification of methyl cytosine and hydroxymethylcytosine
- 7) Heart organoid generation from ES and iPS cells

(3) Education

Graduate School of Medical and Dental Science
 Biomedical Sciences and Engineering Track
 Biomedical Science
 Medical and Dental Science and Technology Track
 Molecular and Cellular Biology
 Developmental and Regenerative Bioscience
 Molecular Cell Biology
 Introduction to Human Molecular Genetics

(4) Lectures & Courses

Obtain basic and applicative knowledges and techniques by challenging cutting-edge themes.

(5) Clinical Services & Other Works

Research Center for Science Systems, Senior Researcher
Japan Society for Biological Sciences, Board member
Japan Society for Epigenetics, Board member

(6) Publications

[Original Articles]

1. Kawai K, Harada T, Ishikawa T, Sugiyama R, Kawamura T, Yoshida A, Tsutsumi O, Ishino F, Kubota T and Kohda T.. Parental age and gene expression profiles in individual human blastocysts. Scientific Reports. 2018.02; 8(1); 2380
2. Lee J, Matsuzawa A, Shiura H, Sutani A, Ishino F. Preferable in vitro condition for maintaining faithful DNA methylation imprinting in mouse embryonic stem cells. Genes to cells : devoted to molecular & cellular mechanisms. 2018.03; 23(3); 146-160
3. Hosoi Y, Soma M, Shiura H, Sado T, Hasuwa H, Abe K, Kohda T, Ishino F, Kobayashi S.. Female mice lacking Ftx lncRNA exhibit impaired X-chromosome inactivation and a microphthalmia-like phenotype. Nature Communications. 2018.09; 9(1); 3829

[Conference Activities & Talks]

1. Lee J. Epigenetic instability of imprinting regions in mouse embryonic stem cells caused by in vitro environments.. KEY Forum: The 3rd International Symposium on Stem Cell Traits and Developmental Systems 2018.01.12
2. Fumitoshi Ishino. Roles of LTR retrotransposon-derived genes in mammalian development and evolution.. International Symposium on Mammalian Reproduction & Evolutionary Genetics 2018.02.28 長野
3. Futmitoshi Ishino, Moe Kitazawa and Tomoko Kaneko-Ishino.. Evolution of skeletal muscle in mammals by domestication of an LTR retrotransposon.. 22nd Evolutionary Biology Meeting at Marseilles 2018.09.25 Marseilles, France
4. Futmitoshi Ishino and Tomoko Kaneko-Ishino.. Gene domestication from retrotransposons contributed to Mammalian evolution.. The 41st Annual Meeting of Molecular Biology Society of Japan 2018.11.26 横浜

Structural Biology

Professor Nobutoshi ITO
Associate Professor Teikichi IKURA
Assistant Professor Nobutaka NUMOTO

(1) Outline

The advance of genome science and proteomic analysis has produced a large amount of information about the primary structure of proteins and their spatial and temporal distributions. On the other hand, most of the proteins only function when they take certain three dimensional structures. As obviously seen in so-called prion diseases, proteins which are chemically correct but structurally incorrect not only fail to function properly but also can harm cells. Our laboratory aims to understand the function of biological macromolecules at atomic level through structure analysis and other methods of physical chemistry, in the hope that accumulation of such knowledge will eventually lead to development of drugs. We are also involved in providing database of such structural data to scientists through the activities of Protein Data Bank Japan.

(2) Research

Collaborating with groups within and outside of the university, we are engaged in various research projects including;

- 1) Structural analyses of B-cell coreceptors
- 2) Physicochemical analysis on the mechanism of the signal transduction for activation of T cells
- 3) Structural analyses of potential drug targets of nuclear receptors
- 4) Analysis of interactions between tau protein and Pin1
- 5) Molecular mechanism of the sero-specificity of dengue virus
- 6) Structural basis of giant hemoglobins
- 7) Molecular basis of suppression of HIV-1
- 8) Structure based drug design for protein kinases
- 9) Improvement in Protein Data Bank

(3) Lectures & Courses

The students learn theoretical basis of structure determination, mainly X-ray crystallography, of proteins and other biological macromolecules. Recent advance in structural biology is also discussed in seminar. Students learn lab techniques related to large-scale production, purification and crystallization of protein samples. They also learn computational methods to determine and refine crystal structures.

(4) Publications**[Original Articles]**

1. Naoko Matsubara, Akihiro Imamura, Tatsuya Yonemizu, Chizuru Akatsu, Hongrui Yang, Akiharu Ueki, Natsuki Watanabe, Hajjaj Abdu-Allah, Nobutaka Numoto, Hiromu Takematsu, Shinobu Kitazume, Thomas F Tedder, Jamey D Marth, Nobutoshi Ito, Hiromune Ando, Hideharu Ishida, Makoto Kiso, Takeshi Tsubata. CD22-Binding Synthetic Sialosides Regulate B Lymphocyte Proliferation Through CD22 Ligand-Dependent and Independent Pathways, and Enhance Antibody Production in Mice. *Front Immunol.* 2018.04; 9; 820
2. Naoki Miyamoto, Miho Yoshimura, Yuji Okubo, Kayo Suzuki-Nagata, Takeshi Tsumuraya, Nobutoshi Ito, Ikuo Fujii. Structural basis of the broad substrate tolerance of the antibody 7B9-catalyzed hydrolysis of p-nitrobenzyl esters. *Bioorg. Med. Chem.* 2018.05; 26(8); 1412-1417
3. Koki Makabe, Takashi Nakamura, Debanjan Dhar, Teikichi Ikura, Shohei Koide, Kunihiro Kuwajima. An Overlapping Region between the Two Terminal Folding Units of the Outer Surface Protein A (OspA) Controls Its Folding Behavior. *J. Mol. Biol.* 2018.06; 430(12); 1799-1813
4. Rocio Otero, Michiyasu Ishizawa, Nobutaka Numoto, Teikichi Ikura, Nobutoshi Ito, Hiroaki Tokiwa, Antonio Mouriño, Makoto Makishima, Sachiko Yamada. 25 S-Adamantyl-23-yne-26,27-dinor-1 α ,25-dihydroxyvitamin D₃: Synthesis, Tissue Selective Biological Activities, and X-ray Crystal Structural Analysis of Its Vitamin D Receptor Complex. *J. Med. Chem.* 2018.08; 61(15); 6658-6673
5. Numoto N, Kamiya N, Bekker GJ, Yamagami Y, Inaba S, Ishii K, Uchiyama S, Kawai F, Ito N, Oda M. Structural Dynamics of PET-degrading Cutinase-like Enzyme from *Saccharomonospora viridis* AHK190 in Substrate-bound States Elucidates Ca²⁺ Driven Catalytic Cycle. *Biochemistry.* 2018.09; 57(36); 5289-5300
6. Teikichi Ikura, Naoya Tochio, Ryosuke Kawasaki, Mizuki Matsuzaki, Akihiro Narita, Mahito Kikumoto, Naoko Utsunomiya-Tate, Shin-Ichi Tate, Nobutoshi Ito. The trans isomer of Tau peptide is prone to aggregate, and the WW domain of Pin1 drastically decreases its aggregation. *FEBS Lett.* 2018.09; 592(18); 3082-3091

[Conference Activities & Talks]

1. Kanade Shimizu, Yurina Miyashita, Naoya Matsuo, Shogo Nakano, Sohei Ito, Nobutaka Numoto, Teikichi Ikura, Nobutoshi Ito, Hiroki Kakuta, Hiroaki Tokiwa. What is the origin of partial agonist activity of CBt-PMN for hRXR α ?. 138th Annual Meeting of the Pharmaceutical Society of Japan 2018.03.27 Ishikawa
2. Yurina Miyashita, Yuta Yamamoto, Shogo Nakano, Sohei Ito, Nobutaka Numoto, Teikichi Ikura, Nobutoshi Ito, Motohiro Sekiya, Hitoshi Shimano, and Hiroaki Tokiwa. Molecular mechanism by a novel design of NADH-dependent proteins involved in lipid metabolism. 138th Annual Meeting of the Pharmaceutical Society of Japan 2018.03.27 Ishikawa
3. Kanade Shimizu, Yurina Miyashita, Yuta Yamamoto, Naoya Matsuo, Shogo Nakano, Sohei Ito, Nobutaka Numoto, Nobutoshi Ito, Hiroki Kakuta, Hiroaki Tokiwa. What is the origin of partial agonist activity of CBt-PMN for hRXR α ?. Experimental biology 2018 2018.04.24 USA
4. Yurina Miyashita, Naoya Matsuo, Yuta Yamamoto, Shogo Nakano, Sohei Ito, Nobutaka Numoto, Teikichi Ikura, Nobutoshi Ito, Motohiro Sekiya, Hitoshi Shimano, and Hiroaki Tokiwa. Computational design and molecular mechanism in oligomerization of C-terminal binding protein 2. Experimental biology 2018 2018.04.24 USA
5. Nobutaka Numoto. Molecular recognition mechanism of proteins revealed by X-ray crystallography. 2018.05.18 Okinawa Institute of Science and Technology Graduate University
6. Satomi Inaba, Nobutaka Numoto, Nobutoshi Ito, Masayuki Oda. Molecular interactions between signaling molecules, SH2 domains, and co-stimulatory receptors. The 18th Annual Meeting of the Protein Science Society of Japan 2018.06.26 Niigata

7. Nobutaka Numoto, Satomi Inaba, Yuri Yamagami, Fusako Kawai, Masayuki Oda, Nobutoshi Ito. Crystal structures of PET degrading enzyme Cut190 in complex with its substrates. The 18th Annual Meeting of the Protein Science Society of Japan 2018.06.27 Niigata
8. Teikichi Ikura, Yasushige Yonezawa and Nobutoshi Ito. Structural dynamics on the catalytic site of a protease derived from Pin1. The 18th Annual Meeting of the Protein Science Society of Japan 2018.06.27
9. Teikichi Ikura and Nobutoshi Ito. Mutational analysis on the catalytic site of a protease derived from Pin1. The 56th Annual Meeting of the Biophysical Society of Japan 2018.09.15
10. Yurina Miyashita, Nobutaka Numoto, Sundaram Arulmozhiraja, Shogo Nakano, Naoya Matsuo, Kanade Shimizu, Osamu Shibahara, Michiko Fujiwara, Hiroki Kakuta, Sohei Ito, Teikichi Ikura, Nobutoshi Ito, Hiroaki Tokiwa. Crystal structure of the tetrameric ligand binding domain of RXRalpha complexed with a novel synthetic partial agonist. The 56th Annual Meeting of the Biophysical Society of Japan 2018.09.15
11. Nobutaka Numoto, Chizuru Akatsu, Kenro Shinagawa, Takeshi Tsubata, Nobutoshi Ito. Prediction of the complex of B cell inhibitory receptor CD72 and Sm/RNP. The 91st Annual Meeting of the Japanese Biochemical Society 2018.09.24 Kyoto
12. Yuhi Hosoe, Satomi Inaba, Nobutaka Numoto, Nobutoshi Ito, Masayuki Oda. Evaluation of stability and function of SH2 domain swap dimer. The 91st Annual Meeting of the Japanese Biochemical Society 2018.09.24 Kyoto
13. Akane Senga, Satomi Inaba, Nobutaka Numoto, Yohei Miyanoiri, Yuri Yamagami, Nobutoshi Ito, Fusako Kawai, Masayuki Oda. Structural and thermal stability changes associated with Ca^{2+} binding of PET-degrading enzyme cutinase. The 91st Annual Meeting of the Japanese Biochemical Society 2018.09.24 Kyoto
14. Nobutaka Numoto, Narutoshi Kamiya, Gert-Jan Bekker, Yuri Yamagami, Satomi Inaba, Fusako Kawai, Masayuki Oda, Nobutoshi Ito. Substrate bound structure of PET-degrading enzyme cutinase. Annual Meeting 2018 and General Assembly of Crystallographic Society of Japan 2018.11.11 Tokyo
15. Nobutaka Numoto, Yuhi Hosoe, Satomi Inaba, Shuhei Ogawa, Hisayuki Morii, Ryo Abe, Masayuki Oda, Nobutoshi Ito. High Resolution Crystal Structure Analysis towards Visualization of Hydrogen Atom of Signaling Molecule Grb2 SH2 Domain and CD28 Derived Peptide Complex. The 36th Medicinal Chemistry Symposium 2018.11.29
16. Yurina Miyashita, Yuta Yamamoto, Shogo Nakano, Sohei Ito, Nobutaka Numoto, Teikichi Ikura, Nobutoshi Ito, Motohiro Sekiya, Hitoshi Shimano, Hiroaki Tokiwa. Molecular design, structure and physical properties evaluation based on amino acid sequence of novel metabolic sensor molecule CtBP2. The 36th Medicinal Chemistry Symposium 2018.11.29
17. Teikichi Ikura, Naoya Tochio, Ryosuke Kawasaki, Mizuki Matsuzaki, Akihiro Narita, Mahito Kikumoto, Naoko Utsunomiya-Tate, Shin-ichi Tate, Nobutoshi Ito. The trans isomer of Tau peptide is prone to aggregate, and WW domain of Pin1 drastically decreases its aggregation. The 41st Annual Meeting of the Molecular Biology Society of Japan 2018.11.29 Yokohama

Neuroscience

Professor Kohichi Tanaka
Associate Professor Tomomi Aida
Assistant Professor Saeko Ishida
Assistant Professor Yuichi Hiraoka

Graduate Student (doctor course)
Zhao Zhuoyang
Takehisa Handa

Graduate Student (master course)
Kurumi Hagiwara
Bi Haining
Haruna Aikawa
Yuuta Sawada
Zhao Di

Graduate International Research Student
Cheng Zhao

Technical Staff
Satomi Ohno

(1) Outline

The final goal of our research is to understand molecular, cellular, and neuronal ensemble mechanisms underlying higher order brain functions including learning and memory. For that purpose, we combine molecular genetics, physiological and behavioral methods. The laboratory also studies the mechanism that underlies neuronal cell death and regeneration.

(2) Research

1. Functions of glutamate transporters in the brain

Glutamate is a major excitatory neurotransmitter and plays an important role in neuronal plasticity and neurotoxicity in the central nervous system. Glutamate transport proteins provide the mechanism by which synaptically released glutamate is inactivated and kept below toxic levels in the extracellular space. By now, five subtypes of high-affinity glutamate transporters have been identified in the mammalian brain. Our lab studies the physiological and pathological roles of glutamate transporter subtypes using subtype-specific knockout mice.

Recent human genetic studies have suggested that de novo mutations in GLT1 (EAAT2) cause early-onset epilepsy with multiple seizure types. Consistent with these findings, global GLT1 null mice show lethal spontaneous seizures. The consequences of GLT1 dysfunction vary between different brain regions, suggesting that the role of GLT1 dysfunction in epilepsy may also vary with brain regions. In this study, we generated region-specific GLT1 knockout mice by crossing floxed-GLT1 mice with mice that express the Cre recombinase in a particular

domain of the ventricular zone. Selective deletion of GLT1 in the diencephalon, brainstem and spinal cord is sufficient to reproduce the phenotypes of the global GLT1 null mice. By contrast, dorsal forebrain-specific GLT1 knockout mice showed nonlethal complex seizures including myoclonic jerks, hyperkinetic running, spasm and tonic-clonic convulsion via the activation of NR2A-containing NMDA receptors during a limited period from P12 to P14 and selective neuronal death in cortical layer II/III and the hippocampus. Thus, GLT1 dysfunction in the dorsal forebrain is involved in the pathogenesis of infantile epilepsy and GLT1 in the diencephalon, brainstem and spinal cord may play a critical role in preventing seizure-induced sudden death.

Among glutamate signaling components, accumulating evidence suggests that the glial glutamate transporter GLT1 plays a critical role in neuropathic pain. Here, we generated periaqueductal gray (PAG)-specific and spinal cord-specific GLT1 knockout mice. Nerve injury-induced neuropathic pain was enhanced in spinal cord-specific GLT1 knockout mice but alleviated in PAG-specific GLT1 knockout mice. In addition, ceftriaxone upregulated GLT1 expression in the spinal cord, but not the PAG, of control mice and attenuated tactile hypersensitivity in nerve-injured control mice but not in nerve-injured spinal cord-specific GLT1 knockout mice. Based on these results, the anti-neuropathic pain effect of ceftriaxone is mediated by the upregulation of GLT1 expression in the spinal cord.

2. Role of DEPDC5 in the pathogenesis of epilepsy and psychiatric disorder

Epilepsy is one of the most frequent (1%) neurological disorders characterized by spontaneous and recurrent seizures. However, pharmacoresistance occurs in 30% of the patients. Recently, a role for genetic factors in idiopathic epilepsies, with no identified structural lesion or metabolic cause, is becoming clear. DEP (Dishevelled, Egl-10 and Pleckstrin) domain containing protein 5 (DEPDC5) is a newly identified causative gene for epilepsy (Ishida et al., 2013). DEPDC5 has no transmembrane domain and no homology with known epilepsy genes encode ion channel or transmitter receptor subunits. Its role in epileptogenesis likely differs from the mechanisms known so far. In addition, some individuals also have psychiatric disorder, like autistic features and schizophrenia. This suggests that DEPDC5 is a new key to clarify the common mechanism of refractory epilepsy and psychosis.

So far, we revealed that knockout *Depdc5* in rats or mice results in embryonic lethal (Marsan and Ishida et al., 2016), and knock down it in Zebrafish leads hyperactive behavior (de Calbiac et al., 2018). We also clarified that *Depdc5* heterozygous KO mice show abnormal behaviors. We strongly promote our research to understand the pathogenesis. Research of DEPDC5 is likely to give new insight into epilepsy and psychosis research.

(3) Education

Goals/Outline:

Students should generate genetically modified animals to comprehensively understand the cognitive mechanisms at the level of molecule to behavior. Then, students should analyze cognitive deficits of mutant animals and those molecular mechanisms.

Available programs:

Participation in the ongoing research project; as needed

Training for cell biology: five times a year 13:00 – 16:00

Experiment:

1. Gene cloning and generation of targeting vector.
2. Generation of genetically modified mice
3. Behavioral analysis of the mice
4. Morphological analysis of central nervous systems.

(4) Lectures & Courses

The aim of this practice is to learn molecular biological, anatomical, electrophysiological and psychological approaches to elucidate the mechanism of cognition. Moreover, based on previous case reports of cognitive deficits, students should plan and discuss what kinds of the researches are possible and meaningful to elucidate

the pathology of these diseases, leading to unveil the mechanism of cognition.

(5) Publications

[Original Articles]

1. Kaori Sugiyama, Kohichi Tanaka. Spinal cord-specific deletion of the glutamate transporter GLT1 causes motor neuron death in mice. *Biochem. Biophys. Res. Commun.*. 2018.03; 497(2); 689-693
2. Junya Sugimoto, Moeko Tanaka, Kaori Sugiyama, Yukiko Ito, Hidenori Aizawa, Miho Soma, Tomoko Shimizu, Akira Mitani, Kohichi Tanaka. Region-specific deletions of the glutamate transporter GLT1 differentially affect seizure activity and neurodegeneration in mice. *Glia*. 2018.04; 66(4); 777-788
3. Bettina Reichenbach, Johanna Classon, Tomomi Aida, Kohichi Tanaka, Maria Genander, Christian Göritz. Glutamate transporter Slc1a3 mediates inter-niche stem cell activation during skin growth. *EMBO J.*. 2018.05; 37(9); e98280
4. Zhuoyang Zhao, Yuichi Hiraoka, Hiroshi Ogawa, Kohichi Tanaka. Region-specific deletions of the glutamate transporter GLT1 differentially affect nerve injury-induced neuropathic pain in mice. *Glia*. 2018.05;
5. Emma M Perkins, Yvonne L Clarkson, Daumante Suminaite, Alastair R Lyndon, Kohichi Tanaka, Jeffrey D Rothstein, Paul Skehel, David J A Wyllie, Mandy Jackson. Loss of cerebellar glutamate transporters EAAT4 and GLAST differentially affects the spontaneous firing pattern and survival of Purkinje cells. *Hum. Mol. Genet.*. 2018.05;
6. Nakade S, Mochida K, Kunii A, Nakamae K, Aida T, Tanaka K, Sakamoto N, Sakuma T, Yamamoto T. Biased genome editing using the local accumulation of DSB repair molecules system. *Nature communications*. 2018.08; 9(1); 3270

[Conference Activities & Talks]

1. Ishida Saeko, Ogawa Hiroshi, Tanaka Kohichi. Glutamate-induced excitotoxicity in midbrain and cerebellum. *Experimental Animals* 2018.07.01

Epigenetic Epidemiology

Professor: Masaaki MURAMATSU
Associate Professor : Noriko SATO
Assistant Professor : Chihiro Imai

Adjunct Instructor : Tomio Arai

Graduate Student: Fujitani, Tadaaki Katsuta,
Shilpa Pavethynath, Maidina Abudushataer, Ake Ko Ko Minn, Zong Yuan, Naomi Hichiwa, Jin Xin, Arisa Nakata
Research Resident: Marina Uematsu

(1) Outline

Many common chronic diseases are multifactorial in that they are caused by multiple genetic and environmental factors. By applying the technology and information of human genome to epidemiological studies, we aim to clarify the role of genetic polymorphisms, epigenetic changes, as well as their interaction with environmental factors, which may contribute to the development of these diseases.

(2) Research

Our research subjects are as follows.

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Responder vs non-responder of prodrugs and polymorphisms of drug metabolizing enzymes.
4. Severe cutaneous adverse response (Stevens-Jhonson' s Syndrome) and HLA genotypes.
5. The role of epigenetic regulation and fetal programming in common diseases.
6. Likelihood ratio based integrated personal risk assessment of type 2 diabetes.

(3) Education

Noriko Sato, Masaaki Muramatsu: Bioscience I
Noriko Sato: Molecular and Cellular Biology
Noriko Sato: Bimomedical Science

(4) Lectures & Courses

We focus on common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis which are caused by multiple genetic and environmental factors, and aim to decipher these factors as well as their interactions by applying the technology and information of human genome to epidemiology. Our goal is

not only to identify disease genes and polymorphisms but also to elucidate gene-environment interactions that contribute to the onset and progression of the diseases. Epigenetic changes in common diseases are also in our scope. A new project has been started to study methods for educating genome-based health literacy by employing information generated from personal genome sequences

(5) Publications

[Original Articles]

1. Sayuri Udagawa, Sayaka Katagiri, Shogo Maekawa, Yasuo Takeuchi, Rina Komazaki, Anri Ohtsu, Naoki Sasaki, Takahiko Shiba, Kazuki Watanabe, Kazuyuki Ishihara, Noriko Sato, Naoyuki Miyasaka, Yuichi Izumi. Effect of *Porphyromonas gingivalis* infection in the placenta and umbilical cord in pregnant mice with low birth weight. *Acta Odontol. Scand.* 2018.01; 1-9

[Misc]

1. Noriko Sato. The Advent of a New Era for Understanding DOHaD: A New Perspective of the Link between Genome/Epigenome and Age-Related Chronic Disease 2018.09; 55(9); 613-620

[Conference Activities & Talks]

1. Noriko Sato. Perinatal Immunomethylomics towards DOHaD. 17 th Surugadai International Symposium & Joint Usage/Research Program of Medical Research Institute International Symposium 2018.11.19 Tokyo

RIKEN Molecular and Chemical Somatology

Visiting Professor	Soichi Kojima
Visiting Professor	Mikiko Sodeoka
Visiting Professor	Nobumoto Watanabe
Visiting Professor	Ichiro Taniuchi
Visiting Professor	Motomasa Tanaka
Visiting Lecturer	Nobuhiko Miyasaka
Visiting Lecturer	Ambara R. Pradipta
Visiting Lecturer	Takeshi Nakano
Visiting Lecturer	Kosuke Dodo
Visiting Lecturer	Ryo Endo
Visiting Lecturer	Akiko Tane
Visiting Lecturer	Yutaka Furutani
Visiting Lecturer	Qin Xian-Yang
Visiting Lecturer	Sanae Sekihara
Visiting Lecturer	Vivian Saitou
Visiting Lecturer	Kai-Wan Hui
Graduate Students	D3 Mengqian Li (~September)
	D2 Chih-Hao Shen
	D1 Ziyu Liu (October~)

(1) Research

Molecular and Chemical Somatology is an interdisciplinary field for understanding of the basis of Bioorganic Chemistry, Chemical Biology, Structural Biology and Molecular Immunology and Molecular Neuroscience as well as their applications to Medicine and Biology by dealing with a variety of molecules that regulate cellular functions including low molecular weight organic compounds, proteins, sugars, and hormones. Students will learn and discuss about the outlines and/or the latest topics on discovery, structure, synthesis, biology, and management of the key molecules/factors, and deepen their understanding of this new research field.

(2) Education

- 1) Synthetic Organic Chemistry
 - Design and synthesis of bioactive molecules based on synthetic organic chemistry and chemical biology research.
- 2) Chemical Biology
 - Discovery, target identification and analyses of mechanism of action of bioactive compounds that regulate biological function.
- 3) Molecular Cellular Pathology
 - Clarification of pathogenesis of diseases at molecular and cellular levels utilizing bioprobes.
- 4) Molecular Immunology
 - Regulatory mechanisms for lymphocyte development
- 5) Molecular Neuropathology
 - Molecular basis of neurodegenerative disorders and psychiatric diseases

(3) Publications

[Original Articles]

1. Li, M., Qin, X-Y., Furutani, Y., Inoue, I., Sekihara, S., Kagechika, H., Kojima, S. Prevention of acute liver injury by suppressing plasma kallikrein-dependent activation of latent TGF- β . *Biochemical and Biophysical Research Communications*, 504 (4), 857-864 (2018).
2. Sohtome, Y., Shimazu, T., Barjau, J., Fujishiro, S., Akakabe, M., Terayama, N., Dodo, K., Ito, A., Yoshida, M., Shinkai, Y., Sodeoka, M. Unveiling epidithiodiketopiperazine as a non-histone arginine methyltransferase inhibitor by chemical protein methylome analyses. *Chemical Communications*, 54 (66), 9202-9205 (2018).
3. Endo, R., Takashima, N., Nekooki-Machida, Y., Komi, Y., Hui, K.K., Takao, M., Akatsu, H., Murayama, S., Sawa, A., Tanaka, M. TDP-43 and DISC1 Co-Aggregation Disrupts Dendritic Local Translation and Mental Function in FTLT. *Biological Psychiatry*, 84 (7), 509-521 (2018).

4. Chen, C.W., Tanaka, M. Genome-Wide Translation Profiling by Ribosome-Bound tRNA Capture. *Cell Reports*, 23 (2), 608-621 (2018).
5. Ohhashi, Y., Yamaguchi, Y., Kurahashi, H., Kamatari, Y.O., Sugiyama, S., Uluca, B., Piechatzek, T., Komi, Y., Shida, T., Müller, H., Hanashima, S., Heise, H., Kuwata, K., Tanaka, M. Molecular basis for diversification of yeast prion strain conformation, *Proceedings of the National Academy of Sciences of the United States of America*, 115 (10), 2389-2394 (2018).

[Review Articles]

None

[Books]

None

[Conference Activities & Talks]

1. Li, M., Qin, X.Y., Furutani, Y., Inoue, I., Sekihara, S., Kagechika, H., Kojima, S. “Clarification of the pathogenesis of acute liver injury using protease inhibitors”. The 13th Annual Meeting of Japanese Society for Chemical Biology. June 11-13, 2018. Tokyo, Japan.
2. Kojima, S., “Molecular mechanism by which acyclic retinoid selectively kills MYCN-positive liver cancer stem cells”. FASEB the 4th International Conference on Retinoids. Jun 10-15, 2018. Steamboat Springs, Colorado, USA.
3. Taniuchi, I. “Unraveling pathogenesis of human primary immune deficiency by mouse models”. The 6th Kyoto Course on Bioinformatics for Genomic Medicine International Symposium on Disease Genomics. Oct 6, 2018. Kyoto, Japan.
4. Suvarna, K., Muroi, M., Osada, H., Watanabe, N. “A small-molecule ligand of VCP inhibits accelerated fibroblast migration by cancer cells”. The 77th Annual Meeting of the Japanese Cancer Association, Sep. 27-29, 2018 Osaka, Japan.
5. Shen, C.H., Nakagawa, Y., Yamaguchi, Y., Tanaka, M. “Structural basis of chaperone-mediated yeast prion propagation”. The 18th Annual Meeting of the Protein Science Society of Japan. Jun 26-28, 2018. Kobe, Japan.

6. Shen, C.H., Nakagawa, Y., Yamaguchi, Y., Tanaka, M. “Structural basis of chaperone-mediated yeast prion propagation”. Asian Pacific Prion Symposium 2018. Oct 4-5, 2018. Tokyo, Japan.

NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
Visiting Professor	Ryuji HAMAMOTO
Visiting Associate Professor	Masahiro YASUNAGA
Visiting Associate Professor	Satoshi FUJII
Visiting Lecturer	Tohru KIYONO
Visiting Lecturer	Kazunori AOKI
Visiting Lecturer	Takashi KOHNO
Visiting Lecturer	Michihiro MUTOH
Visiting Lecturer	Yasuhito UEZONO
Visiting Lecturer	Naoto TSUCHIYA
Graduate Students	D2 Tomoko WATANABE
	D1 Kazuma KOBAYASHI
	Takahiro SHIRAI
	M2 Yamato OGIWARA,
	Maiko TAKAHASHI,
	Naoki TSUKIMATA,
	Miyu YOSHIDA
	M1 Megumi KAMISHIMA
	Kurumi KISHIMOTO
	Yuma NOZUE

(1) Research

1. Carcinogenesis and molecular mechanism
2. Functions of cancer-associated genes and their alterations
3. Genomic, epigenomic and proteomic analysis of cancer and personalized medicine
4. Tumor microenvironment
5. Cancer stem cells/non-coding RNA/signaling pathway
6. Molecular target/drug delivery/diagnosis and therapy

(2) Education

To learn knowledge and skill for cancer research, students attend lectures and seminars,

and attend and/or practice research meeting, journal club, scientific meeting, etc. These practices will enable students to develop an ability to conduct their studies as an independent cancer researcher in the future. To obtain good skills to carry out experiments that are required for cancer research, students belong to one of our research groups, and conduct their own studies under the guidance of the instructor and/or staff. Students perform various experiments involved in genetics, gene technology, biochemistry, cellular biology, molecular biology, physiology, experimental animal, pathology, genomic/epigenomic/proteomic analysis, imaging, next generation sequencing, etc.

(3) Publications

[Original Articles]

1. Gaowa S, Futamura M, Tsuneki M, Kamino H, Tajima JY, Mori R, Arakawa H, Yoshida K. Possible role of p53/Micap-regulated mitochondrial quality control as a tumor suppressor in human breast cancer. *Cancer Sci.* 109: 3910-3920. 2018.
2. Maekawa T, Liu B, Nakai D, Yoshida K, Nakamura K, Yasukawa M, Koike M, Takubo K, Chatton B, Ishikawa F, Masutomi K, Ishii S. ATF7 mediates TNF- α -induced telomere shortening. *Nucleic Acids Res.* 46: 4487-4504. 2018.
3. Maida Y, Yasukawa M, Ghilotti M, Ando Y, Masutomi K. Semi-quantitative Detection of RNA-dependent RNA Polymerase Activity of Human Telomerase Reverse Transcriptase Protein *J Vis Exp* 136:e57021. 2018.
4. Shigekawa Y, Hayami S, Ueno M, Miyamoto A, Suzaki N, Kawai M, Hirono S, Okada KI, Hamamoto R, Yamaue H. Overexpression of KDM5B/JARID1B is associated with poor prognosis in hepatocellular carcinoma. *Oncotarget*, 9, 34320-34335. 2018.
5. Toyokawa G, Takada K, Tagawa T, Kinoshita F, Kozuma Y, Matsubara T, Haratake N, Takamori S, Akamine T, Hirai F, Yamada Y, Hamamoto R, Oda Y, Maehara Y: Prevalence of Enhancer of Zeste Homolog 2 in Patients with Resected Small Cell Lung Cancer. *Anticancer Research*, 38, 3707-3711. 2018.
6. Fuchigami H, Manabe S, Yasunaga M, Matsumura Y. Chemotherapy payload of anti-insoluble fibrin antibody-drug conjugate is released specifically upon binding to

fibrin. *Sci Rep.* 8:14211. 2018.

7. Yamazaki S, Higuchi Y, Ishibashi M, Hashimoto H, Yasunaga M, Matsumura Y, Tsuchihara K, Tsuboi M, Goto K, Ochiai A, Ishii G. Collagen type I induces EGFR-TKI resistance in EGFR-mutated cancer cells by mTOR activation through Akt-independent pathway. *Cancer Sci.* 2018 109: 2063-2073. 2018.
8. Sawada K, Nakamura Y, Yamanaka T, Kuboki Y, Yamaguchi D, Yuki S, Yoshino T, Komatsu Y, Sakamoto N, Okamoto W, Fujii S. Prognostic and Predictive Value of HER2 Amplification in Patients With Metastatic Colorectal Cancer. *Clin Colorectal Cancer.* 17: 198-205. 2018.
9. Kadota T, Hatogai K, Yano T, Fujita T, Kojima T, Daiko H, Fujii S. Pathological tumor regression grade of metastatic tumors in lymph node predicts prognosis in esophageal cancer patients. *Cancer Sci.* 109: 2046-2055. 2018.
10. Kudo-Saito C, Ishida A, Shouya Y, Teramoto K, Igarashi T, Kon R, Saito K, Awada C, Ogiwara Y, Toyoura M. Breaking the FSTL1-DIP2A axis improves anti-tumor immunity. *Cell Reports*, 24: 1790-180. 2018.

[Reviews Articles]

1. Yasunaga M, Manabe S, Furuta M, Ogata K, Koga Y, Takashima H, Nishida T, Matsumura Y. Mass spectrometry imaging for early discovery and development of cancer drugs. *AIMS Md Sci.* 5: 162-180. 2018.

[Conference Activities & Talks]

1. Hirofumi Arakawa. Non-canonical mitophagy induced by Mieap and its role in p53 tumor suppression via iron-dependent cell death. ASMRM (The 15th Conference of Asian Society for Mitochondrial Research and Medicine) 2018. Busan (Korea), November 2018.
2. Makoto Yamamoto, Yasuyuki Nakamura, Hirofumi Arakawa. Non-canonical mitophagy induced by Mieap and its role in tumor suppression via ferroptosis-like cell death. AACR Annual Meeting 2018, Chicago (USA), April 2018.
3. Ryuji Hamamoto. Utilization of AI in Oncology An Example at NCH of Japan. 6th US – Japan Clinical Trials in Oncology Workshop, Washington, D.C, June 2018.

4. Masahiro Yasunaga. Development of Antibody-Drug Conjugate Using DDS and Molecular Imaging. International Advanced Drug Delivery Symposium. (Hsinchu, Taiwan) April, 2018.
5. Masahiro Yasunaga, Shino Manabe and Yasuhiro Matsumura IL-7R targeting therapy for immunoregulation and overcoming steroid-resistance in cancer and autoimmune disease. AACR Annual Meeting 2018, Chicago (USA), April 2018.
6. Masahiro Yasunaga, Shino Manabe, Atsushi Tsuji , Masaru Furuta, Koretsugu Ogata, Hirobumi Fichigami, Yoshikatsu Koga and Yasuhiro Matsumura. DDS and Molecular Imaging for Antibody-Drug Conjugate (ADC) Development. 29th Antibody Engineering & Therapeutics, San Diego (USA), December 2018.
7. Fujii S, AM Magliocco, E Valtorta, et al. International harmonization of diagnostic criteria for HER2-amplified metastatic colorectal cancer and application of targeted next-generation sequencing panel as a diagnostic method. ASCO 2018, Chicago (USA), June 2018.
8. Chie Kudo-Saito, Takahiro Miyamoto, Yamato Ogiwara, Kazunori Aoki. Increase of senescent mesenchymal stromal/stem cells is predictive of unresponsiveness to the treatment with immune checkpoint inhibitors
AACR Annual Meeting 2018, Chicago (USA), April 2018.

Anatomy and Physiological Science

(1) Publications

[Original Articles]

1. Virachith S, Saito M, Watanabe Y, Inoue K, Hoshi O, Kubota T. Anti-beta2-glycoprotein I antibody with DNA binding activity enters monocytes via cell surface DNA and induces tissue factor expression Clinical and Experimental Immunology. 2018;
2. Osamu Hoshi, Ayana Sugizaki, Yuichiro Cho, Nobuyuki Takei. BDNF Reduces eEF2 Phosphorylation and Enhances Novel Protein Synthesis in the Growth Cones of Dorsal Root Ganglia Neurons. Neurochem. Res.. 2018.06; 43(6); 1242-1249

Biochemistry and Biophysics

(1) Publications

[Original Articles]

1. Kyoko Hashimoto, Hiroki Ochi, Satoko Sunamura, Nobuyoshi Kosaka, Yo Mabuchi, Toru Fukuda, Kenta Yao, Hiroaki Kanda, Keisuke Ae, Atsushi Okawa, Chihiro Akazawa, Takahiro Ochiya, Mitsuru Futakuchi, Shu Takeda, Shingo Sato. Cancer-secreted hsa-miR-940 induces an osteoblastic phenotype in the bone metastatic microenvironment via targeting ARHGAP1 and FAM134A. *Proc. Natl. Acad. Sci. U.S.A.*. 2018.02; 115(9); 2204-2209
2. Kana Ishii, Hidetoshi Sakurai, Nobuharu Suzuki, Yo Mabuchi, Ichiro Sekiya, Kiyotoshi Sekiguchi, Chihiro Akazawa. Recapitulation of Extracellular LAMININ Environment Maintains Stemness of Satellite Cells In Vitro. *Stem Cell Reports*. 2018.02; 10(2); 568-582
3. Lewis K, Takebe T. Tumoroid à la carte: Path for personalization. *Hepatology (Baltimore, Md.)*. 2018.02;
4. Zhang Ran-Ran, Koido Masaru, Tadokoro Tomomi, Ouchi Rie, Matsuno Tatsuya, Ueno Yasuharu, Sekine Keisuke, Takebe Takanori, Taniguchi Hideki. Human iPSC-Derived Posterior Gut Progenitors Are Expandable and Capable of Forming Gut and Liver Organoids *STEM CELL REPORTS*. 2018.03; 10(3); 780-793
5. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Shizuka Fujii, Koji Otabe, Keiichiro Komori, Nobutake Ozeki, Hideyuki Koga, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Specific markers and properties of synovial mesenchymal stem cells in the surface, stromal, and perivascular regions. *Stem Cell Res Ther*. 2018.05; 9(1); 123
6. Takahashi Y, Takebe T, Taniguchi H. Methods for Generating Vascularized Islet-Like Organoids Via Self-Condensation. *Current protocols in stem cell biology*. 2018.05; 45(1); e49
7. Takahashi Yoshinobu, Sekine Keisuke, Kin Tatsuya, Takebe Takanori, Taniguchi Hideki. Self-Condensation Culture Enables Vascularization of Tissue Fragments for Efficient Therapeutic Transplantation *CELL REPORTS*. 2018.05; 23(6); 1620-1629
8. Rao Mahendra S., Pei Ying, Garcia Thelma Y., Chew Shereen, Kasai Toshiharu, Hisai Tomoko, Taniguchi Hideki, Takebe Takanori, Lamba Deepak A., Zeng Xianmin. Illustrating the potency of current Good Manufacturing Practice-compliant induced pluripotent stem cell lines as a source of multiple cell lineages using standardized protocols *CYTOTHERAPY*. 2018.06; 20(6); 861-872
9. Takebe Takanori, Wells James M., Helmrath Michael A., Zorn Aaron M.. Organoid Center Strategies for Accelerating Clinical Translation *CELL STEM CELL*. 2018.06; 22(6); 806-809
10. Ogata Yusuke, Mabuchi Yo, Shinoda Kosuke, Horiike Yuta, Mizuno Mitsuru, Otabe Koji, Suto Eriko Grace, Suzuki Nobuharu, Sekiya Ichiro, Akazawa Chihiro. Anterior cruciate ligament-derived mesenchymal stromal cells have a propensity to differentiate into the ligament lineage *Regenerative Medicine*. 2018.06; 8; 20-28
11. Kimura, M., Azuma, M., Zhang, R. -R., Thompson, W., Mayhew, C. N., & Takebe, T.. Digitalized Human Organoid for Wireless Phenotyping. *iScience*. 2018.07; 4; 294-301

12. Ayabe H, Anada T, Kamoya T, Sato T, Kimura M, Yoshizawa E, Kikuchi S, Ueno Y, Sekine K, Camp JG, Treutlein B, Ferguson A, Suzuki O, Takebe T, Taniguchi H. Optimal Hypoxia Regulates Human iPSC-Derived Liver Bud Differentiation through Intercellular TGFB Signaling. *STEM CELL REPORTS*. 2018.08; 11(2); 306-316
13. Nie YZ, Zheng YW, Miyakawa K, Murata S, Zhang RR, Sekine K, Ueno Y, Takebe T, Wakita T, Ryo A, Taniguchi H. Recapitulation of hepatitis B virus-host interactions in liver organoids from human induced pluripotent stem cells. *EBioMedicine*. 2018.08;
14. Matsuzaki T, Matsumoto S, Kasai T, Yoshizawa E, Okamoto S, Yoshikawa HY, Taniguchi H, Takebe T. Defining Lineage-Specific Membrane Fluidity Signatures that Regulate Adhesion Kinetics. *Stem Cell Reports*. 2018.08; 11(4); 852-860
15. Yamamoto K, Tanimura K, Watanabe M, Sano H, Uwamori H, Mabuchi Y, Matsuzaki Y, Chung S, Kamm R, Tanishita K, Sudo R. Construction of continuous capillary networks stabilized by pericyte-like perivascular cells. *Tissue engineering. Part A*. 2018.09;
16. Tanaka J, Ogawa M, Hojo H, Kawashima Y, Mabuchi Y, Hata K, Nakamura S, Yasuhara R, Takamatsu K, Irié T, Fukada T, Sakai T, Inoue T, Nishimura R, Ohara O, Saito I, Ohba S, Tsuji T, Mishima K. Generation of orthotopically functional salivary gland from embryonic stem cells. *Nature communications*. 2018.10; 9(1); 4216

[Books etc]

1. Chikako Hayashi, Nobuharu Suzuki. *Myelin-Basic and Clinical Advances*. Springer, 2018

[Conference Activities & Talks]

1. Takebe T. The era of Organoid Medicine– Liver Organoid Based Approach. Southern California Stem Cell Seminar Series 2018.03.08
2. Nobuharu Suzuki, Kana Ishii, Yo Mabuchi, Chihiro Akazawa. Teneurin-4 Regulates Quiescence of Muscle Satellite Cells and Myelination in the Central Nervous System. The 17th Congress of the Japanese Society for Regenerative Medicine 2018.03.21 Pacifico Yokohama, Yokohama, Kanagawa
3. 武部貴則. ヒトオルガノイドを用いたホロミクス研究の可能性. 多次元生命システム研究戦略分子・細胞アトラスに関する意見交換会 2018.03.28 市ヶ谷
4. 武部貴則. オルガノイド 4.0—ヒト臓器創出への展望. JMSA NY Life Science Forum 2018.04.07 NYU Langone Medical Center Farkas Auditorium, NY, USA
5. 武部貴則. 一次世代オルガノイド医療の展望. 日本小児科学会学術集会・講演 2018.04.20 福岡
6. Takebe T. The Era of Organoid Medicine. Korea Organoid Symposioium 2018.05.16 Seoul
7. Takebe T. Modelling Steatosis and Fibrosis in Human Vascularized Organoids. Gordon Research Conference Lipoprotein Metabolism 2018.06.12 Waterville Valley, NH, US
8. Nobuharu Suzuki. The Molecular Mechanism of CNS Myelination by Teneurin-4. The 4th Annual Meeting of the Japanese Society for Myelin 2018.07.14 TKP Garden City PREMIUM, Yokohama, Kanagawa
9. Chikako Hayashi, Nobuharu Suzuki, Naomi Kikura, Yukina Hosoda, Yo Mabuchi, Chihiro Akazawa. Teneurin-4 Mediates Oligodendrocyte-Axon Interaction and Regulates Myelination. The 61st Annual Meeting of The Japanese Society for Neurochemistry 2018.09.07 Kobe International Conference Center, Kobe, Hyogo
10. Takebe T.. Modeling Early Hepatogenesis Using Human iPSC Towards Organoid Medicine. Cincinnati CuSTOM industrial Symposium 2018.10.19
11. Takebe T.. Promise of future health impact of liver organoids . NASPGHAN Balistreri Lecture 2018.10.26
12. Chikako Hayashi, Nobuharu Suzuki, Naomi Kikura, Yukina Hosoda, Yo Mabuchi, Chihiro Akazawa. Oligodendrocyte-Axon Interaction via Teneurin-4 Controls Cell Adhesion and Morphogenesis of Oligodendrocytes for Myelination. Neuroscience 2018 2018.11.03 San Diego Convention Center, San Diego, CA, USA

13. Nobuharu Suzuki, Yoshihiko Yamada. Teneurin-4 regulates oligodendrocyte process formation in CNS myelination. Neuroscience 2018 2018.11.03 San Diego Convention Center, San Diego, CA, USA
14. Takebe T.. The Era of Organoid Medicine-from screen to therapeutics-. Korean organoid symposium 2018.11.07
15. Takebe T.. Translational Embryology Towards Therapy -from human liver organoid experience. 分子生物学会 2018.11.29
16. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yuuko Kagihuku, Takashi Ono, Chihiro Akazawa, Takashi Asada, Shunsuke Minakuchi. Approaches of investigating oral function in Mild Cognitive Impairment (MCI) patients. The 6th Tri-University Consortium 2018.11.30 Tokyo

[Awards & Honors]

1. The Excellent Presentation Award at the 61st Annual Meeting of the Japanese Society for Neurochemistry, The Japanese Society for Neurochemistry, 2018.09

[Others]

1. 2018 Research grant from Hokuto Foundation for Bioscience, 2018.12
Research for elucidation of the molecular mechanism of neuronal activity-dependent myelination and its application

Department of Molecular and Cellular Biology

Nobuharu Suzuki, Associate Professor

(1) Outline

Our department has been started at FY2018. The members are Assoc. Prof. Suzuki and 4 graduate students. Regarding research, we have three projects: 1) the molecular mechanism of myelination in the central nervous system, 2) the maintenance system of the stemness of somatic stem cells, and 3) the pericellular microenvironment organized by extracellular matrix molecules. In terms of education, we teach graduate and undergraduate students at lectures and laboratory classes of molecular biology and biochemistry, particularly related to medical tests/technologies. In addition, Suzuki is a member of the administrative office of Lab Safety and contributes to their activities.

(2) Research

1) Molecular mechanism of myelination in the central nervous system

In the central nervous system, myelin is formed by oligodendrocytes and is essential for rapid propagation of neuronal signal. In our department, we investigate its cellular and molecular mechanism using the mutant mouse line that develops hypomyelination in the central nervous system and expand the results of our research to application studies. In 2018, we gave presentations of our recent data at international and domestic meetings. Also, we wrote a chapter of a book about myelination written in English.

2) Maintenance mechanism of the stemness of somatic stem cells

We particularly focus on skeletal muscle satellite cells and carry out collaborated works together with other groups. We published an article of the study in 2018.

3) Pericellular microenvironment organized by extracellular matrix molecules

In recent years, research of pericellular microenvironment by extracellular matrix molecules has become popular. In our department, we examine functions of extracellular matrix proteins in myelination in the central nervous system and in maintenance of skeletal muscle stem cells. In 2018, we published an article of our collaborated study that revealed a significance of the microenvironment in the maintenance of the stemness of muscle satellite cells.

(3) Education

For undergraduate students, we teach “Medical Genetics and Human Genome Science, Lecture” and “Biochemistry, Laboratory”, and parts of “Advanced Laboratory Sciences”, “Practice of Medical Science” and “General Medical Technology”.

For graduate students, we teach parts of “Medical Technology I” and “Study of Pathogenesis and Pathophysiology” (master course), and a part of “Development of Novel Technologies for Clinical Tests” (Ph.D. course).

(4) Lectures & Courses

At first, we well-explain the fundamental mechanism of phenomena in organisms to students at any classes, since we want them to have curiosity as much as possible. Based on that, we teach them more expertized

knowledge and techniques that are essential for medical technologists in order to let them to achieve at a high level of acquisition. In laboratory, we teach students from fundamental to advanced parts of our research field at lectures, journal clubs, and discussions to let them understand the history and our position in the current research field. Finally, we make efforts for students to have high motivation with their research and study and to enjoy new findings.

(5) Clinical Services & Other Works

Suzuki is Special Volunteer at National Institutes of Health (NIH) and a visiting fellow at National Center of Neurology and Psychiatry (NCNP) and contributes to relationships between the research institutes and universities, internationally and domestically. Also, Suzuki is a member of Society for Neuroscience (SfN), The American Society for Cell Biology (ASCB), The Molecular Biology Society of Japan (MBSJ), The Japan Neuroscience Society (JNS), The Japanese Society for Neurochemistry (JSN), and The Japanese Society for Matrix Biology and Medicine (JSMBM) and contributes to their activities.

(6) Publications

[Original Articles]

1. Kana Ishii, Hidetoshi Sakurai, Nobuharu Suzuki, Yo Mabuchi, Ichiro Sekiya, Kiyotoshi Sekiguchi, Chihiro Akazawa. Recapitulation of Extracellular LAMININ Environment Maintains Stemness of Satellite Cells In Vitro. *Stem Cell Reports*. 2018.02; 10(2); 568-582
2. Ogata Yusuke, Mabuchi Yo, Shinoda Kosuke, Horiike Yuta, Mizuno Mitsuru, Otabe Koji, Suto Eriko Grace, Suzuki Nobuharu, Sekiya Ichiro, Akazawa Chihiro. Anterior cruciate ligament-derived mesenchymal stromal cells have a propensity to differentiate into the ligament lineage *Regenerative Medicine*. 2018.06; 8; 20-28

[Books etc]

1. Chikako Hayashi, Nobuharu Suzuki. *Myelin-Basic and Clinical Advances*. Springer, 2018

[Conference Activities & Talks]

1. Nobuharu Suzuki, Kana Ishii, Yo Mabuchi, Chihiro Akazawa. Teneurin-4 Regulates Quiescence of Muscle Satellite Cells and Myelination in the Central Nervous System. The 17th Congress of the Japanese Society for Regenerative Medicine 2018.03.21 Pacifico Yokohama, Yokohama, Kanagawa
2. Nobuharu Suzuki. The Molecular Mechanism of CNS Myelination by Teneurin-4. The 4th Annual Meeting of the Japanese Society for Myelin 2018.07.14 TKP Garden City PREMIUM, Yokohama, Kanagawa
3. Chikako Hayashi, Nobuharu Suzuki, Naomi Kikura, Yukina Hosoda, Yo Mabuchi, Chihiro Akazawa. Teneurin-4 Mediates Oligodendrocyte-Axon Interaction and Regulates Myelination. The 61st Annual Meeting of The Japanese Society for Neurochemistry 2018.09.07 Kobe International Conference Center, Kobe, Hyogo
4. Chikako Hayashi, Nobuharu Suzuki, Naomi Kikura, Yukina Hosoda, Yo Mabuchi, Chihiro Akazawa. Oligodendrocyte-Axon Interaction via Teneurin-4 Controls Cell Adhesion and Morphogenesis of Oligodendrocytes for Myelination. Neuroscience 2018 2018.11.03 San Diego Convention Center, San Diego, CA, USA
5. Nobuharu Suzuki, Yoshihiko Yamada. Teneurin-4 regulates oligodendrocyte process formation in CNS myelination. Neuroscience 2018 2018.11.03 San Diego Convention Center, San Diego, CA, USA

[Awards & Honors]

1. The Excellent Presentation Award at the 61st Annual Meeting of the Japanese Society for Neurochemistry , The Japanese Society for Neurochemistry, 2018.09

[Others]

1. 2018 Research grant from Hokuto Foundation for Bioscience, 2018.12
Research for elucidation of the molecular mechanism of neuronal activity-dependent myelination and its application

Molecular Pathology

Professor: Motoji Sawabe

Assistant Professor: Yurie Soejima

Graduate student (Doctoral Program): Tamami Denda, Ayana Horiguchi, Nobuyuki Nakamura, Mayumi Kinoshita, Akiya Tatsumi, Kana Miyata, Yuichi Koyama, Mizuho Sato, Yoshifumi Morita

Graduate student (Master's Program): Yasuhiro Enoki, Masahiro Kato, Minami Kikuchi, Miho Takeuchi, Satsuki Yuba, Hatthakone Thavisouk

Graduate Research student: KO PO JUI

Clerical assistant: Shoko Matsubara

(1) Outline

Pathology is the basic science of medicine that involved both the basic and clinical stages to elucidate the essence of diseases.

Pathological techniques play a role in conducting to higher quality diagnosis by various examinations and methods such as histology, cytology, immunohistochemistry, electron microscopy and genetic analysis. We explore the essence of the diseases in both aspect of pathology and pathological techniques.

(2) Research

In our department, we research the following programs in order to investigate and elucidate the etiology and pathophysiology, and further to explore and develop the theoretics and methods of examination that can contribute to diagnosis.

1. Proteome analysis and immunohistochemical study of arterial and cardiac aging
2. Immunohistochemical analysis of human and mouse cardiac conduction system
3. Molecular epidemiologic and clinicopathological study of Lipoprotein(a)
4. Molecular pathological study of hepatic tumors
5. Histological and cytological analysis for early diagnosis of biliary tract cancer

(3) Education

In the undergraduate course, students learn the etiology and pathophysiology of basic disease in Pathological Technology, lecture and practice (Medical Technology), and Pathology (Nursing science).

In graduate school, we provide the education and conduct the research with the aim of exploring, developing, and systematizing the theoretics and methods of molecular pathological techniques with a higher level of pathological expertise and a broad international perspective.

(4) Lectures & Courses

In order to cultivate medical professionals with interdisciplinary and international perspectives, rich humanity and high ethical values, ability of self-problem raising and solution, life-long-thinking, the following education

is providing.

1) Undergraduate education

- In second grade of Medical Technology and Nursing science, students learn common changes in disease, the essence of pathogenesis and their origins systematically in the general theory of Pathology / Pathological technology.
- In second grade of Medical Technology, practical training of pathological examination is organized to contribute to the diagnosis of diseases and elucidation the pathogenesis, such as various special staining methods, immunohistochemistry, cytology and frozen section preparation methods, in addition to visual inspection of organs, basic preparation of specimens and observation.
- In second grade of Nursing science, we have pathological anatomical observation as a part of the Practice of Medical Sciences.
- In fourth grade of Medical Technology, we provide the education of basics of research, such as how to proceed the research and how to write the research paper as the Undergraduate Research, and pathological examination practice is carried out at the department of Pathology in hospital as Clinical Practice.

2) Graduate education

- In Master's Program, we discuss essentials of diseases, with investigation and understanding the origin, pathophysiology and pathological characteristics (macroscopical, histological, cytological and molecular pathological) of the disease. Furthermore, students learn the theory and method of pathological techniques (immunohistochemistry, electron microscopy, image analysis, etc.) which useful for elucidation the pathophysiology and diagnosis. In addition, students will acquire the skills of quality management and problem solving in the laboratory. We participate in various research meetings and academic societies, and learn about the current status and prospects of international and interdisciplinary research in the pathology / pathological techniques field. Through this course, students will complete their research as a Master's thesis and acquire basic research ability.
- In Doctoral Program, we provide higher education, research instruction and medical English learning to acquire the independent research skills that internationally applicable.

(5) Clinical Services & Other Works

- In the pathology department of the medical hospital, Sawabe participates in the pathological diagnosis of autopsy cases, Soejima participates in the cytological diagnosis.
- At the Ministry of Health, Labor and Welfare, medical technology international development promotion project 2018 "Human Resource and System Developments for Cervical Cancer Screening in Cambodia", Sawabe participated as an instructor of pathologists and medical technologists, Soejima participated as an instructor of medical technologists in the request of the National Center for Global Health and Medicine, Japan.

(6) Publications

[Original Articles]

1. [Department of Molecular Pathology : SAWABE Motoji] Matsuda Yoko, Tanaka Masashi, Sawabe Motoji, Mori Seijiro, Muramatsu Masaaki, Mieno Makiko Naka, Furukawa Toru, Arai Tomio. Relationship between pancreatic intraepithelial neoplasias, pancreatic ductal adenocarcinomas, and single nucleotide polymorphisms in autopsied elderly patients GENES CHROMOSOMES & CANCER. 2018.01; 57(1); 12-18
2. [Department of Molecular Pathology : SAWABE Motoji] Matsuda Yoko, Seki Atsuko, Nonaka Keisuke, Kakizaki Mototsune, Wang Tan, Aida Junko, Ishikawa Naoshi, Nakano Yuta, Kaneda Daita, Takata Tadayuki, Takahashi-Fujigasaki Junko, Murayama Shigeo, Takubo Kaiyo, Ishiwata Toshiyuki, Sawabe Motoji, Arai Tomio. Clinicopathological characteristics of distant metastases of adenocarcinoma, squamous cell carcinoma and urothelial carcinoma: An autopsy study of older Japanese patients GERIATRICS & GERONTOLOGY INTERNATIONAL. 2018.02; 18(2); 211-215
3. [Department of Molecular Pathology : SOEJIMA Yurie] Kinoshita M., Matsuda Y., Arai T., Soejima Y., Sawabe M., Honma N.. Cytological diagnostic clues in poorly differentiated squamous cell carcinomas

of the breast: Streaming arrangement, necrotic background, nucleolar enlargement and cannibalism of cancer cells CYTOPATHOLOGY. 2018.02; 29(1); 22-27

4. [Department of Molecular Pathology : SOEJIMA Yurie] Yurie Soejima, Miho Takeuchi, Takumi Akashi, Motoji Sawabe, Toshio Fukusato. β 4 and β 6 Integrin Expression Is Associated with the Subclassification and Clinicopathological Features of Intrahepatic Cholangiocarcinoma. Int J Mol Sci. 2018.03; 19(4);
5. [Department of Molecular Pathology : SOEJIMA Yurie] Hando K, Luangxay T, Vilayvong S, Vongdala C, Vongsonephet K, Xayaphet P, Soejima Y, Fukuda T, Xaysomphet P, Phengsavanh A, Arounlangsy P, Sawabe M. . Knowledge and attitude toward cervical cancer and its prevention among female workers in the Vientiane Capital, Lao PDR. J Med Dent Sci . 2018.03; 65(1); 9-18
6. [Department of Molecular Pathology : SAWABE Motoji] Yamada Yoshiji, Horibe Hideki, Oguri Mitsutoshi, Sakuma Jun, Takeuchi Ichiro, Yasukochi Yoshiki, Kato Kimihiko, Sawabe Motoji. Identification of novel hyper- or hypomethylated CpG sites and genes associated with atherosclerotic plaque using an epigenome-wide association study INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE. 2018.05; 41(5); 2724-2732
7. [Department of Molecular Pathology : SAWABE Motoji] Kitamura Kazutaka, Sato Kayoko, Sawabe Motoji, Yoshida Masayuki, Hagiwara Nobuhisa. P-Selectin Glycoprotein Ligand-1 (PSGL-1) Expressing CD4 T Cells Contribute Plaque Instability in Acute Coronary Syndrome CIRCULATION JOURNAL. 2018.08; 82(8); 2128-+
8. [Department of Molecular Pathology : SAWABE Motoji] Kato K., Horibe H., Oguri M., Sakuma J., Takeuchi I., Yasukochi Y., Murohara T., Sawabe M., Yamada Y.. Identification of novel hyper- or hypomethylated CpG sites and genes associated with atherosclerotic plaque by an epigenome-wide association study EUROPEAN HEART JOURNAL. 2018.08; 39; 1403
9. [Department of Molecular Pathology : SAWABE Motoji] Sugino Mire, Naitou Takeshi, Sawabe Motoji, Kanbara Masayuki, Sawabe Taishi, Yamazaki Yukiko, Mizohata Satoko. ネパールの農村における個別的な健康管理の改善 (Improving Personal Health Management in Nepalese Villages) 国際保健医療. 2018.09; 33(3); 234
10. [Department of Molecular Pathology : SAWABE Motoji] Prak Thavsothavin, Chankong Huy, Chhut Vathana, Cheng Sam Ang, Sophean Sahakcheat, Wakasa Tomoko, Kawai Toshiaki, Sawabe Motoji. 子宮広間膜の腹腔子宮内膜症 症例報告 (Peritoneal Endometriosis in the Broad Ligament: Case Report) 日本臨床細胞学会雑誌. 2018.10; 57(Suppl.2); 747

[Conference Activities & Talks]

1. [Department of Molecular Pathology : SOEJIMA Yurie] Yuri Miura, Hiroki Tsumoto, Machiko Iwamoto, Yuya Yamaguchi, Yurie Soejima, Tosifusa Toda, Tomio Arai, Akihiko Hamamatsu, Tamao Endo, Motoji Sawabe. Proteomic alterations in the human aortic media with aging: Deposition of MFGE8, elevation of oxidative damages, and imbalance of actin and actin-related proteins. 第 41 回日本基礎老化学会大会 2018.05.31
2. [Department of Molecular Pathology : SOEJIMA Yurie] 廣井禎之、小松京子、沢辺元司、副島友莉恵、片山博徳、河合俊明、若狭朋子. 子宮頸がん検診のための病理技術者育成と体制整備事業（カンボジア）における病理・細胞診標本の質向上. 第 107 回日本病理学会総会 2018.06.21
3. [Department of Molecular Pathology : SOEJIMA Yurie] 東海林琢男、近藤福雄、副島友莉恵、斉藤光次、笹島ゆう子、甲嶋洋平、吉留博之、安達章子、宇於崎宏、福里利夫. TERT promoter 領域遺伝子変異を認めた beta-catenin 遺伝子活性化型肝細胞腺腫の一例. 第 107 回日本病理学会総会 2018.06.21
4. [Department of Molecular Pathology : SOEJIMA Yurie] 斉藤光司、近藤福雄、福里利夫、東海林琢男、副島友莉恵、石田毅、増田芳雄、堀内啓、佐野圭二. グルタミンシンセターゼ（GS）びまん性陽性を示す良性肝細胞性結節の病理診断 -2 例-. 第 107 回日本病理学会総会 2018.06.21
5. [Department of Molecular Pathology : SOEJIMA Yurie] 沢辺元司、副島友莉恵、明石巧. ヒト悪性腫瘍における apolipoprotein (a) の免疫組織化学的検討. 第 107 回日本病理学会総会 2018.06.21

6. [Department of Molecular Pathology : SOEJIMA Yurie] Yurie Soejima, Yuya Yamaguchi, Yuri Miura, Hiroki Tsumoto, Machiko Iwamoto, Shoko Yoshida, Tomio Arai, Akihiko Hamamatsu, Tamao Endo, Motoji Sawabe. Proteomic analysis and immunohistochemical analysis of human aortic aging. The 107th of Annual Meeting of the Japanese Society of Pathology 2018.06.21
7. [Department of Molecular Pathology : SOEJIMA Yurie] Immunohistochemical analysis of TGF- β 1 and beta6 integrin in intrahepatic cholangiocarcinoma. 2018.06.28

Biophysical System Engineering

Professor ITO Minami
Assistant Professor
HONMA Satoru
Visiting Lecturer
IDE Eiko
Visiting Lecturer
AKAZAWA Kouhei
Visiting Lecturer
SHIGEO Ookubo
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FUNAKI Daito

(1) Outline

Biological measurements tell a lot about functions of the human bodies. Norbert Wiener, known as a founder of cybernetics, indicated that our body is a kind of control mechanism. Thus, our goal is to understand mechanisms underlying our complex biological systems and to control them for improving our life. Here, we have explored the visual information processing underlying contour integration and material perception, by combining behavioral studies indicating animals' percept, electro-physiological studies at the level of a single unit, and computational studies with mathematical models. On the other hand, we have developed a temperature control system in hypothermia based on a heat conduction model of the brain.

(2) Research

- 1) Mathematical models for context dependent visual information processing
- 2) Neural mechanisms underlying context dependent visual information processing

Our visual perception mechanism is well flexible to reveal stable recognition of the external information even under various environments. Furthermore, it realizes dynamics given by the surrounding situation, past experiences and learning processes. Our goal is to reveal the mechanism underlying such flexible visual information processing, by studying the process of integrating fragmentary information into the contour of objects or the process of material representation on an object surface, in middle stages of the cerebral visual cortex. Especially, by performing behavioral study with psychophysical methods and recording of electrophysiological activities mainly on single cell recording in an animal, we may reveal causal relationships between them.

So far, we have trained three Japanese monkeys to conduct our material discrimination tasks. We selected five materials (metal, fabric, gel sheet, wood bark, fur) as reference stimuli, which represent categories of material discrimination. We found that the animals were able to conduct such material discrimination into five categories. In parallel, the same task was applied to human subjects for comparison. In order to compare the results of material perception under different conditions using principal component analysis, we modified multidimensional scaling techniques. Our study was presented in the annual meeting of the Japanese Society of Neurosciences and the Society for Neuroscience (USA).

- 3) Developing methods to monitor vital information with aid of mathematical models

Our goal is to develop new devices of to control functions in living bodies, which can be introduced into the medical treatment or rehabilitation. Toward this end, we are studying comprehensive methods to understand the interactions among multiple biological functions and the mathematical methods to express the non-linearity,

individuality, temporal changes and their environmental conditions of biological phenomena, and an adaptive control system to overcome such complexity of human mechanisms. So, we have developed a brain temperature control system for the brain hypothermia. The heat conduction in the head tissue was reproduced using a physical model, and the validity of the temperature control system using different control methods was compared and verified by simulation. In addition, we are preparing a simulation head model that assumes the occurrence of local inflammation and circulatory disorders, and is preparing to use these to simulate more realistically.

(3) Education

1) Undergraduate school Clinical Laboratory Management; students learn about the basic management methods in the medical laboratory sciences. Medical Measurement, System and Information (1); students learn the frequency-filters and amplification systems of electrical signals, in order to understand the principle of the physiological measurements and to conduct them safely. Medical Measurement, System and Information (2); students learn about basic concepts of (1) informatics, (2) computer and network, information security, and (3) the hospital information systems. In practice, students learn some of logical ways to build up some programming rules and programming tools to achieve some calculation programs in C language. Principles and Practice of Medical Information Processing (1)&(2); students learn statistical tests to compare data with a spreadsheet software, the evidence based medicine (EBM), database, experimental designs for biological experiments, the regression analysis and some recent topics covering the multivariate analysis and the Bayesian inference.

2) Graduate school Students learn the way to collect necessary information and to solve their problems to advance their own research projects. Through intensive reading of original articles and text books in English, students learn basic ideas of the central nervous system, underlying mechanisms, and the way of logical thinking. Health care informatics; this is a joint course with Nursing Innovation Science Track. Invited lecturers give omnibus-style lectures on a wide range of topics, following group discussion.

(4) Lectures & Courses

Rapid progress of the medical technology change the role of a medical technologist. Introduction of the systematic management system, IT technology, auto measurement devices, new measurement methods, new statistical analysis, demand diverse knowledge across a wide range of fields from medicine/life sciences to engineering.

1) Undergraduate school Not only acquiring practical techniques necessary as a clinical laboratory technician, students learn the background, principle and mechanism of biological measurement. They also learn about the advantages and disadvantages of the current measurement technologies. Our purpose is to train new type laboratory technicians with a broad perspective suitable for the healthcare and medical field, a high degree of expertise and versatility, who can be a bridge between engineering and life sciences,

2) Graduate school Our purpose is to train autonomous researchers with a broad perspective suitable for the life science and medical science who are capable of working in an international and interdisciplinary environment. Students learn the way of preparing, organizing and conducting research projects. We also encourage students to use English, which is necessary for activities in international community.

(5) Publications

[Original Articles]

1. Satoru HONMA, Hidetoshi WAKAMATSU. Regular tetrahedral lattice coordinate system for an equivalent arrangement of bio-mathematical models reflecting objects' shape Electronics and Communications in Japan. 2018.04; 101(4); 42-54

[Conference Activities & Talks]

1. Satoru HONMA, Daito FUNAKI. Medical engineering practical training with external TA. Technical Meeting on Frontiers in Education 2018.03.02 Niigata
2. Satoru HONMA. Importance of basic education in medical engineering lecture. Technical Meeting on Frontiers in Education 2018.03.02 Niigata

3. Minami Ito, Hatta Chisaki, Yoshida Sakie. Behavioral study of haptic material perception in macaque monkeys. The 41st Annual Meeting of the Japan Neuroscience Society 2018.07.29 Kobe
4. Minami Ito, Chisaki Hatta, Sakie Yoshida, Kanoko Katsube, Yuka Morisue, Tensei Iwata. Surface materials are recognized by the visual and haptic ckues in non-human primate subjects. Society for Neuroscience 2018 Annual Meeting 2018.10.04 San Diego, USA

Department of Respiratory and Nervous System Science

Professor: Yuki Sumi, MD, PHD.

Assistant Professor: Miho Akaza, MD, PHD.

Part-time: Keiko Hara, MD, PHD. Katsuya Ota, MD, PHD.

Doctoral: Yuri Ichikawa, MT, Msc.

Master's: Fumika Koike MT. Takao Miyoshi MT. Yuri Yoshimura MT.

Students: Saori Kaminaka. Nozomi Sano. Miri Takahashi. Yuki Takemoto

(1) Outline

We research and educate on the respiratory and nerves systems. Our interests are looking at the living body as an integrated system from the molecular and cellular level to the organs and looking at the relationship between clinical medicine and physiological tests.

Until last year, research and education on respiratory, cardiovascular, and nerves were conducted by the name of “Biofunctional Informatics”. At the time of reorganization of Tokyo Medical and Dental University, cardiovascular division separated, and we moved from “Graduate School of Health Care Sciences” to “Graduate School of Medical and Dental Sciences” and was renamed to “Respiratory and Nervous System Science”.

(2) Research

The research is conducted independently in each field by specialists in the respiratory and nervous system.

In the respiratory field, we are studying the clinical significance of new lung function tests, mechanisms and endotype classification of bronchial asthma and COPD, gene therapy for lung diseases, and diagnostic imaging using AI.

In the central nervous system area, we are researching on electroencephalogram (EEG) and epilepsy, and in the peripheral nervous system area, we are developing a new imaging methods.

(3) Education

In education, we provide education in general clinical medicine and acquire theory and skills through lectures and practical training in physiological function tests (lung function, EEG, peripheral nerve tests, various sonography, etc.). Undergraduate and graduate research educations are conducted in each specialized field.

1) Undergraduate student education

In the 1st year, a lecture on “Respiratory and Nervous System Science” is given on Advanced Laboratory Sciences. Second-year students have Physiological Laboratory Science, Lecture(I). Here students learn the basics of EEG, lung function tests, and sonographies. Physiological Laboratory Science, Lecture(II) and Physiological Laboratory Science, Laboratory(II) will be conducted jointly with the cardiovascular field in the 3rd years (2nd and 3rd years in the new curriculum). The contents include neurophysiological examination, respiratory examination, circulatory examination, ultrasonic examination, image analysis, thermography, sense of equilibrium function examination, fundus examination, and other basic examinations such as blood sampling practice, sample collection, etc. We also provide education on clinical techniques in general, including taking vital signs and procedures for critical care. In the 4th graders, students undergo Undergraduate research. In the clinical training, practical training of respiratory tests including blood gas measurement, EEG, evoked potential test, and abdominal ultrasonography will be given during two weeks.

2) Graduate education

In the Master's course, we are in charge of Medical Technology I, Medical Technology II, Seminar of Respiratory and Nervous System Science, Practice of Respiratory and Nervous System Science, and Respiratory and Nervous System Analysis Research for Thesis. Medical Technology I deepens the understanding of the scientific knowledge that is the basis of clinical tests currently being conducted in the medical field from various levels of genes, molecules, cells, tissues, and individuals, and further toward the future. The purpose is to reinforce the foundation for studying research topics. The purpose of Medical Technology II is to deepen the understanding of clinical tests currently being conducted in the medical field and to develop the ability to consider future research issues. In each lecture of Respiratory and Nervous Systems Science, we educate new knowledge and techniques, clarify areas that have already been elucidated and areas that do not, and acquire scientific research attitudes to clarify areas that are still unknown.

In the Doctoral course, we are in charge of Clinical Reasoning and Respiratory and Nervous System Science. In the Clinical Reasoning, we aim to cultivate the clinical laboratory technologists who can discuss with physicians of inferring disease conditions from laboratory data. In the Respiratory and Nervous System Science, we aim to teach the theory and techniques to inspect the living body as an integrated system. In particular, students learn the cutting edge medical knowledge in the respiratory or nervous system, the methodology to analyze the relationship between the biological information obtained by the examination and the pathogenesis, and the theory and techniques to developed novel examination methods.

(4) Lectures & Courses

What is important in education is to motivate learning. In particular, in the lower grades of undergraduate students, many students do not understand how basic learning is useful, and are not motivated to study despite being important. For this reason, we have increased practical training, conducted early exposure to understand how it is needed in the clinical setting. We wish students to be eager to learn and to acquire competency as if the water is soaking into dry sand.

In particular, as the physiological function testing is a clinical front line that is conducted in direct contact with patients, we educate from the standpoint of clinical medicine. The goal is that students learn theories and techniques of clinical physiological examinations in nerves, respiration, cardiovascular, digestive organs, and diagnostic imaging, and be able to apply them to researches. Physiological function testing involves not only device operation, safety measures, recording of biological phenomena, data organization / analysis techniques and knowledge, but also testing directly in contact with humans, so medical knowledge about diseases, medical ethics and communication skills are also required. It is also important to cultivate the ability to quickly recognize and take appropriate measures for test results that require emergency treatment of patients. In addition to these, we are also educating students on how to respond to sudden changes in patients during testing.

(5) Clinical Services & Other Works

Dr. Sumi is a Respiratory specialist and Respiratory instructor, and Allergy specialist certified by the academic society. He treats patients at respiratory medicine department in the hospital. He also takes care of the study groups of doctors and takes part in as discussant. He gave lecture at Evening seminar for medical interns, at CC (Clinical Clerkship) in respiratory medicine for undergraduate 5th and 6th grade medical students, at PCC (Preparation for Clinical Clerkship) in respiratory internal medicine for 4th year undergraduate medical students, at Respiratory Internal medicine for 3rd year undergraduate medical students, at Respiratory physiology for 2nd year undergraduate medical students, and at MIC (Medical Introductory Course) for 1st year undergraduate medical students.

The neurologist, Dr. Akaza, is familiar with peripheral neuropathy in addition to neurological diseases in general, and plays a central role in performing peripheral nerve tests and evaluating results in medical hospitals.

Dr. Hara is the psychiatrist, Mental health designated physician, specialist / instructor of the Japan Epilepsy Society, certified by the Japanese Society of Clinical Neurophysiology (EEG), and Delegate of the Japanese Society of Clinical Neurophysiology, Councilor of the Japan Pharmac-EEG Society, Board secretary of the Japan Epilepsy Society. She examines many patients with epilepsy in the outpatient department including second opinions. In cooperation with the Department of Neurosurgery, she attends weekly EEG conferences, monthly EEG and epilepsy lectures, and analyzes high frequency EEG (HFO). She also performs intraoperative electroencephalogram measurements in many brain surgeries.

(6) Clinical Performances

Dr. Akaza is a specialist in peripheral nerve function testing and performs most tests for neurological patients. She is conducting clinical research on peripheral neuropathy in diabetic patients.

Dr. Hara treats many patients with epilepsy including second opinions. She specializes in the treatment of pregnant women with epilepsy. In cooperation with obstetrics and gynecology doctors, patients with epilepsy are referred to her consultant before pregnancy since 2013.

(7) Publications

[Original Articles]

1. Koike F., Otani Y., Oyama S., Furuie W., Endo J., Nakamura Y., Akaza M., Sasano T., Miyazaki Y., Inase N., Sumi Y.. The Role of Forced Oscillation Technique to Diagnose Patients with Cough Variant Asthma. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. 2018; 197;
2. A case of absence epilepsy in the 30s 2018.01; 36(1); 52-58
3. Miyoshi Takao, Furuie Wakaba, Otani Yoshio, Tani Chihiro, Waku Marika, Miyazaki Yasunari, Inase Naohiko, Akaza Miho, Sasano Tetsuo, Koike Fumika, Kubota Tetsuo, Sumi Yuki. Study on indoor cleaning effect by air purifier and the influence on asthma(和訳中) アレルギー. 2018.05; 67(4-5); 519
4. Koike Fumika, Otani Yoshio, Furuie Wakaba, Endo Junji, Nakamura Yoichi, Akaza Miho, Sasano Tetsuo, Tsuchiya Kimitake, Tamaoka Meiyo, Miyazaki Yasunari, Inase Naohiko, Sumi Yuki. The role of Most-Graph to diagnose patients with untreated Cough Variant Asthma(和訳中) アレルギー. 2018.05; 67(4-5); 498
5. Miho Akaza, Itaru Akaza, Tadashi Kanouchi, Tetsuo Sasano, Yuki Sumi, Takanori Yokota. Nerve conduction study of the association between glycemic variability and diabetes neuropathy. Diabetol Metab Syndr. 2018.09; 10; 69
6. Nagamori Chizuko, Hara Keiko, Hirose Yuka, Ohta Katsuya, Akaza Miho, Sumi Yuki.. Public awareness and experiences associated with epilepsy in Japan, 2013-2017 EPILEPSY & BEHAVIOR. 2018.09; 86; 138-144
7. Miyoshi Takao, Furuie Wakaba, Otani Yoshio, Tani Chihiro, Waku Marika, Koike Fumika, Miyazaki Yasunari, Inase Naohiko, Sasano Tetsuo, Akaza Miho, Kubota Tetsuo, Sumi Yuki. Can air purifier promote the indoor cleanliness and improve the patients with asthma? EUROPEAN RESPIRATORY JOURNAL. 2018.09; 52;
8. Koike Fumika, Otani Yoshio, Oyama Saki, Furuie Wakaba, Endo Junji, Nakamura Yoichi, Miyoshi Takao, Akaza Miho, Sasano Tetsuo, Miyazaki Yasunari, Inase Naohiko, Sumi Yuki. Cluster analysis of cough variant asthma using exhaled value of forced oscillation technique. EUROPEAN RESPIRATORY JOURNAL. 2018.09; 52;
9. Nagamori C, Hara K, Hirose Y, Ohta K, Akaza M, Sumi Y. Public awareness and experiences associated with epilepsy in Japan, 2013-2017. Epilepsy Behav. 2018.09; 86; 138-144
10. Akaza M, Akaza I, Kanouchi T, Sasano T, Sumi Y, Yokota T.. Nerve conduction study of the association between glycemic variability and diabetes neuropathy. Diabetology and Metabolic Syndrome. 2018.09; 12(10); 69

[Conference Activities & Talks]

1. Miho Akaza 他. Magnetic recordings of sensory action currents in the cervical cord.. 31st International Congress of Clinical Neurophysiology of the IFCN 2018.05.03
2. Fumika Koike, Yoshio Otani, Saki Oyama, Wakaba Furuie, Junji Endo, Yoichi Nakamura, Miho Akaza, Tetsuo Sasano, Yasunari Miyazaki, Naohiko Inase, Yuki Sumi.. The Role of Forced Oscillation Technique to Diagnose Patients with Cough Variant Asthma.. ATS 2018 International Conference 2018.05.20 San Diego

3. 赤座 実穂, 赤座 至, 叶内 匡, 笹野 哲郎, 角 勇樹, 横田 隆徳 . Study for association between glycemic variability and diabetic neuropathy assessed by NCS. 第 59 回神経学会総会 2018.05.24
4. Takao Miyoshi, Furuie wakaba, Yoshio Otani, Chihiro Tani, Waku Marika, Yasunari Miyazaki, Naohiko Inase, Miho Akaza, Tetsuo Sasano, Fumika Koike, Tetsuo Kubota, Yuki Sumi.. Study On Indoor Cleaning Effect By Air Purifier And The Influence On Asthma.. The 67th Annual Meeting of Japanese Society of Allergology. 2018.06.23
5. Fumika Koike, Yoshio Otani, Wakaba Furuie, Junji Endo, Yoichi Nakamura, Miho Akaza, Tetsuo Sasano, Kimitake Tsuchiya, Meiyo Tamaoka, Yasunari Miyazaki, Naohiko Inase, Yuki Sumi.. The role of Most-Graph to diagnose patients with untreated Cough Variant Asthma.. The 67th Annual Meeting of Japanese Society of Allergology. 2018.06.23
6. T. Miyoshi, W. Furuie, Y.Otani, C. Tani, M. Waku, F. Koike,Y. Miyazaki,N. Inase, T.Sasano, M. Akaza, T. Kubota, Y. Sumi. Can air purifier promote the indoor cleanliness and improve the patients with asthma?. ERS International Congress 2018 2018.09.01 Paris
7. F. Koike, Y. Otani, S. Oyama1, W. Furuie, J. Endo, Y. Nakamura, T. Miyoshi, M. Akaza, T. Sasano, Y. Miyazaki, N. Inase, Y. Sumi. Cluster analysis of cough variant asthma using exhaled value of forced oscillation technique. ERS International Congress 2018 2018.09.01 Paris
8. Diagnosis of C8 radiculopathy by magnetospinogram. 2018.11.09

Department of Cardiovascular Physiology

Associate Professor
Tetsuo Sasano
PhD course student
D3 Hiroko Iino
D2 Kayoko Takada
D1 Hiroaki Komuro
Master course student
M2 Anna Suzuki, Naomi Takahashi
M1 Kanae Sasaki, Risako Chiba, Ryota Mieda, Fuyuko Watanabe
Collaborator
Satomi Hamada
Technical assistant
Yuuka Nakagama

(1) Outline

Our department performs basic research focusing on the cardiovascular disease and clinical research regarding physiological assessment of cardiovascular system. Our another mission is to cultivate academic medical technologists who can design basic and clinical studies from clinical questions.

(2) Research

We perform basic research and clinical physiological research. The first topic of basic research is to elucidate the pathophysiological mechanisms focusing on the intercellular communication in cardiovascular diseases. The second topic is to clarify the functional contribution of genes identified by genome-wide association study in the field of cardiac diseases. The third topic is to develop a novel therapeutic strategy using novel gene transfer method and new biomaterials.

Regarding the clinical physiological research, we develop the novel frequency analysis of surface electrocardiogram (ECG), and application of artificial intelligence on the analysis of ECG. In addition, we are inventing the noninvasive monitoring of blood pressure using novel biosensors. Our another purpose is to establish biomarkers to assess cardiovascular diseases, focusing on the extracellular nucleotides and vesicles.

(3) Education

Our mission on the education is to acquire the technique of physiological examinations on the cardiovascular field like electrocardiogram, ultrasound echocardiogram, vascular ultrasonography, pulse wave velocity measurement, vascular endothelial function, and venous function assessment.

(4) Lectures & Courses

We aim to cultivate an academic technologist who can design the basic and clinical researches based on the clinical questions.

(5) Clinical Services & Other Works

Our clinical service includes outpatient clinic in medical hospital, and the supervision of ECG assessment in dental hospital. Dr. Sasano also works as several committee chairs in Japanese Heart Rhythm Society.

(6) Publications

[Original Articles]

1. Kawaguchi N, Okishige K, Yamauchi Y, Kurabayashi M, Nakamura T, Keida T, Sasano T, Hirao K, Valderrábano M. Clinical impact of ethanol infusion into the vein of Marshall on the mitral isthmus area evaluated by atrial electrograms recorded inside the coronary sinus. *Heart rhythm*. 2019.01;
2. Komuro Hiroaki, Sasano Tetsuo, Horiuchi Naohiro, Yamashita Kimihiro, Nagai Akiko. The effect of glucose modification of hydroxyapatite nanoparticles on gene delivery *JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A*. 2019.01; 107(1); 61-66
3. Shigeta Takatoshi, Okishige Kaoru, Aoyagi Hideshi, Nishimura Takuro, Nakamura Rena A., Ito Naruhiko, Tsuchiya Yusuke, Asano Mitsutoshi, Shimura Tsukasa, Suzuki Hidetoshi, Kurabayashi Manabu, Fukami Yuichi, Sakita Shinya, Keida Takehiko, Sasano Tetsuo, Hirao Kenzo, Yamauchi Yasuteru. Clinical investigation of esophageal injury from cryoballoon ablation of persistent atrial fibrillation *PACE-PACING AND CLINICAL ELECTROPHYSIOLOGY*. 2019.02; 42(2); 230-237
4. Nishimura T, Yamauchi Y, Aoyagi H, Tsuchiya Y, Shigeta T, Nakamura R, Yamashita M, Asano M, Nakamura T, Suzuki H, Shimura T, Kurabayashi M, Keida T, Sasano T, Hirao K, Okishige K. The clinical impact of the left atrial posterior wall lesion formation by the cryoballoon application for persistent atrial fibrillation: Feasibility and clinical implications. *Journal of cardiovascular electrophysiology*. 2019.02;
5. Suzuki Y, Miyajima M, Ohta K, Yoshida N, Watanabe T, Fujiwara M, Okumura M, Nakamura M, Sasano T, Kawara T, Matsuura M, Matsushima E. Changes in cardiac autonomic nervous system activity during a course of electroconvulsive therapy. *Neuropsychopharmacology reports*. 2019.03; 39(1); 2-9
6. Suzuki Yoko, Miyajima Miho, Ohta Katsuya, Yoshida Noriko, Watanabe Takafumi, Fujiwara Mayo, Okumura Masaki, Nakamura Mitsuru, Sasano Tetsuo, Kawara Tokuhiko, Matsuura Masato, Matsushima Eisuke. Changes in cardiac autonomic nervous system activity during a course of electroconvulsive therapy(和訳中) *Neuropsychopharmacology Reports*. 2019.03; 39(1); 2-9
7. Okishige K, Shigeta T, Nishimura T, Nakamura RA, Hirao T, Yoshida H, Yamauchi Y, Sasano T, Hirao K. Cryofreezing catheter ablation of adenosine triphosphate sensitive atrial tachycardia. *Journal of cardiovascular electrophysiology*. 2019.04; 30(4); 528-537
8. Nakamura R, Okishige K, Shigeta T, Nishimura T, Kurabayashi M, Yamauchi Y, Sasano T, Hirao K. Clinical comparative study regarding interrupted and uninterrupted dabigatran therapy during perioperative periods of cryoballoon ablation for paroxysmal atrial fibrillation. *Journal of cardiology*. 2019.04;

Analytical Laboratory Chemistry

Professor: Minoru Tozuka
 Assistant Professor: Ryunosuke Ohkawa
 Project Researcher: Naoko Sugiyama
 Graduate Student: Mayu Nambu, Yuka Yamagata
 Konomi Igarashi, Mai Sasaoka, Yuki Fujii
 Ayaka Nakamura, Azusa Yamazaki
 Yuna Horiuchi, Shao Jui Lai
 Under Graduate Student: Mutumi Gotanda, Yuri Sonoda
 Yuko Mishima, Tamaki Kobayasi

(1) Outline

The central mission of the Analytical Laboratory Chemistry is to educate and research through “Clinical Chemistry” in Clinical Laboratory Science. Our topic is “Development of a new biomarker to predict a risk for cardiovascular disease”. To achieve our goal, skill and ability to create new reliable method are required. Development of students who can give back to a society through active outreach like publishing a paper and presenting at a congress is most important. We also aim to develop a Biomedical Laboratory Scientist who not only plays a pivotal role in medical front but also be active in education or research institutes. For that reason, creation of a laboratory where students can throw themselves into their research with enjoyment is essential.

(2) Research

We analyze lipoproteins and its components; cholesterol, triglyceride, apolipoproteins and their metabolites. Through these studies, we are aiming toward developing a new biomarker to predict a risk for cardiovascular disease in an early stage. In detail, we are focusing on cholesterol efflux capacity (reverse cholesterol transport, RCT), antioxidant ability and anti-inflammatory effect for high-density lipoprotein and its main apolipoprotein, apolipoprotein A-I. Our hypothesis is that evaluation of these capacities would be available to make a specific diagnosis for coronary artery disease (CAD).

Many risk factors for CAD have been reported and testing these factors have been contributing to reduce the risk in some patients with CAD. However, despite many people are trying to keep their health to reduce their risk for heart disease, the actual number of heart event have not been decreased. We believe that investigating the mechanism of progression of atherosclerosis by analyzing RCT, antioxidant ability and anti-inflammatory effect in HDL would lead to find useful biomarker and establish new assay for diagnosis for cardiovascular disease.

Research Focus

- Development of a new biomarker to estimate residual risk for cardiovascular disease
- Study on the functions of chemically modified HDL and apolipoprotein A-I
- Study on the functions and clinical significance of apolipoprotein E containing HDL

(3) Lectures & Courses

Undergraduate education: Main topic is Analytical Laboratory Chemistry which includes Urinalysis & Body Fluid Tests and Clinical Chemistry. In addition, Associate Professor Masayuki Hara from General Isotope Research Division helps to educate radioisotope. We aim to educate student to become a leader of biomedical laboratory scientist in hospital or company. Our final goal is that student develop their creativities to think, solve a problem and improve by themselves.

Graduate education: Analytical skill is essential for research. There is no research achievement without analytical skill. Our first purpose is to understand an importance of reliable analytical skill and obtain the skill. Next, by using these skills, we aim to find new biomarker and develop a novel assay for the biomarker. Though these research process, students can obtain the analytical skill and cultivate capacity as researcher to make a research plan and choose the optimal way to proceed by themselves. Moreover, students can develop their outreach skill through presenting their research achievements at a congress and publishing their papers.

(4) Publications**[Original Articles]**

1. Ryunosuke Ohkawa, Makoto Kurano, Noboru Sakai, Tatsuya Kishimoto, Takahiro Nojiri, Koji Igarashi, Shigemi Hosogaya, Yukio Ozaki, Tomotaka Dohi, Katsumi Miyauchi, Hiroyuki Daida, Junken Aoki, Shigeo Okubo, Hitoshi Ikeda, Minoru Tozuka, Yutaka Yatomi. Measurement of plasma choline in acute coronary syndrome: importance of suitable sampling conditions for this assay. *Sci. Rep.*. 2018.03; 8(1); 4725
2. Kareinen I, Baumann M, Nguyen SD, Maaninka K, Anisimov A, Tozuka M, Jauhiainen M, Lee-Rueckert M, Kovanen PT.. Chymase released from hypoxia-activated cardiac mast cells cleaves human apolipoproteinA-I at Tyr192 and compromises its cardioprotective activity *J Lipid Res.* 2018.03;
3. Yuna Horiuchi, Shao-Jui Lai, Azusa Yamazaki, Ayaka Nakamura, Ryunosuke Ohkawa, Kouji Yano, Takahiro Kameda, Shigeo Okubo, Shitsuko Shimano, Michio Hagihara, Shuji Tohda, Minoru Tozuka. Validation and application of a novel cholesterol efflux assay using immobilized liposomes as a substitute for cultured cells. *Biosci. Rep.*. 2018.04; 38(2);
4. Hitoshi Ikeda, Mariko Kobayashi, Hiromitsu Kumada, Kenichiro Enooku, Kazuhiko Koike, Makoto Kurano, Masaya Sato, Takahiro Nojiri, Tamaki Kobayashi, Ryunosuke Ohkawa, Satoshi Shimamoto, Koji Igarashi, Junken Aoki, Yutaka Yatomi. Performance of autotaxin as a serum marker for liver fibrosis. *Ann. Clin. Biochem.*. 2018.07; 55(4); 469-477
5. Yuko Mishima, Makoto Kurano, Tamaki Kobayashi, Masako Nishikawa, Ryunosuke Ohkawa, Minoru Tozuka, Yutaka Yatomi. Dihydro-sphingosine 1-phosphate interacts with carrier proteins in a manner distinct from that of sphingosine 1-phosphate. *Biosci. Rep.*. 2018.10;
6. Megumi Sato, Ryunosuke Ohkawa, Hann Low, Madoka Nishimori, Shigeo Okubo, Akira Yoshimoto, Kouji Yano, Takahiro Kameda, Yutaka Yatomi, Minoru Tozuka. Serum amyloid A does not affect high-density lipoprotein cholesterol measurement by a homogeneous assay. *Clin. Biochem.*. 2018.10;

[Conference Activities & Talks]

1. Horiuchi Y., Lai SJ., Yamazaki A., Nakamura A., Ohkawa R., Yano K., Kameda T., Okubo S., Hagihara M., Tohda S., and Tozuka M. Validation and application of a novel cholesterol efflux assay using immobilized liposomes as a substitute for cultured cells. The XVIIIth International Symposium on Atherosclerosis 2018.07.09 Toronto
2. Lai SJ., Ohkawa R., Horiuchi Y., Yamazaki A., Nakamura A., Tozuka M. Possible Concern of Erythrocytes with Reverse Cholesterol Transport. 70th AACC Annual Scientific Meeting & Clinical Lab Expo 2018.08.02 Chicago
3. Ohkawa R.. Lost in translation: cholesterol metabolism in red blood cells. Immunometabolism meeting 2018.08.29 Victoria, Australia
4. Tozuka M., Horiuchi Y., Lai S.J., Ohkawa R.. Development of a novel method to estimate the cholesterol efflux capacity of high-density lipoprotein. 2018 TMU Medical Laboratory Forum 2018.10.29

Department of Laboratory Molecular Genetics of Hematology

Associate professor :
Ayako ARAI

Specially Appointed Assistant Professor :
Mayumi YOSHIMORI

Adjunct Lecturer :
Takatoshi KOYAMA, Ken-ichi IMADOME, Yoichi NAKAYAMA, Miwako NISHIO

Graduate Student :
Shiho HASHIMOTO, Ayaka OHASHI

Secretary :
Harumi OIKAWA

(1) Outline

For undergraduate education, we are in charge of Clinical Laboratory Hematology, Hematology, Clinical Practice, Clinical clerkship (School of Medicine), Clinical Hematology (Track of Nursing Science). We provide lectures on hematopoiesis, mechanisms of coagulation and fibrinolysis, pathology and clinical features of main hematological disorders as well as fundamental laboratory practices.

For graduate education, we focus on clarifying molecular mechanisms of development of hematological disorders. We apply the results to develop new diagnostic procedures and treatment strategies. Our current research subject is EB virus-positive T- and NK-cell neoplasms.

(2) Research

Our research goals:

1. Clarifying pathogenesis of hematopoietic malignancies and innovation of a new treatment strategies
2. Clarifying mechanisms of EB virus-positive T- and NK-cell neoplasms and developing new treatment strategies
3. Creating new methods for diagnosing hematopoietic tumors

We collaborate on several researches with doctors of Deps. Hematology, Pediatrics, Neurology, Molecular Virology, Center for Stem Cell and Regenerative Medicine, Ophthalmology, Dermatology, Department of Comprehensive Pathology, and Diagnostic Radiology on-campus in TMDU. We are also doing research with members of National Center for Child Health and Development, Osaka Women's and Children's Hospital, Biochemistry department at Justus-Liebig Universität (Gießen. We collaborate with several companies as well.

(3) Education

1.Undergraduate Education

We are in charge of Clinical Laboratory Hematology, Clinical Hematology, clinical clerkship (School of Medicine), Clinical Hematology (Track of Nursing Science). We provide lectures on hematopoiesis, hematological disorders, mechanism of coagulation and fibrinolysis, hematopoietic malignancies as well as fundamental laboratory practices.

Students are also involved in Undergraduate Research, which objective is to learn basis of research including how to plan and carry out research activities, how to write theses, and how to give an academic presentation. They also experience as trainees for Clinical Practice for hematological examination in cooperation with Clinical Laboratory at Medical Hospital. These lectures and practices are conducted in collaboration with the members of Departments of Hematology and Pediatrics.

2.Graduate Education

For graduate education, we focus on clarifying molecular mechanisms of development of hematological neoplasms. We apply the results to develop new diagnostic procedures and treatment strategies for these disorders. Our current research subject is EB virus-positive T- and NK-cell neoplasms. Now we are carrying on an investigator initiated clinical trial for chronic active Epstein-Barr virus infection. We instruct students to summarize what they investigated and complete English manuscripts for publication.

Detailed educational contents are shown below:

- 1)Investigating and understanding pathogenesis and pathology of hematopoietic disorders, especially neoplasms
- 2)Acquiring skills for cellular, molecular and genetic examination that play significant roles for diagnosing and clarifying cause and state of diseases. These molecular techniques are useful not only for clinical situation, but also for elucidating mechanisms of developing diseases
- 3)Acquiring current information for diagnosis and treatment of hematological diseases
- 4)Publishing papers on hematological laboratory testing and clinical hematology on main international academic journals and present them at international conferences

(4) Lectures & Courses

Cultivating interdisciplinary- and internationally-minded medical staffs with rich humanity, a strong sense of ethics, and ability to suggest and solve unmet medical issues

(5) Clinical Services & Other Works

Clinical: Provide medical care, educate and lead in Hematology and general internal medicine.

Research:

The associate professor Arai belongs to the Research group of Measures against Intractable Diseases by Ministry of Health, Labour and Welfare of Japan that plans the clinical guidelines of chronic active EBV infection and the associated diseases as well as establishes the disease registry.

Arai is also a principal investigator of Japan Agency for Medical Research and Development (AMED) study group ‘the Investigator-initiated clinical research of a JAK1/2 inhibitor ruxolitinib for chronic active Epstein-Barr virus infection’ .

We are supporting patients with chronic active Epstein-Barr virus infection (CAEBV) through CAEBV patient's association (SHAKE).
<http://caebv.com/>

(6) Clinical Performances

We are the only group that specialize EBV-positive T- or NK-cell neoplasms especially chronic active EBV infection. We accept referral patients with CAEBV from all over Japan and abroad.

(7) Publications

[Original Articles]

1. Erika Onozawa, Haruna Shibayama, Honami Takada, Ken-Ichi Imadome, Sho Aoki, Mayumi Yoshimori, Norio Shimizu, Shigeyoshi Fujiwara, Takatoshi Koyama, Osamu Miura, Ayako Arai. STAT3 is constitutively activated in chronic active Epstein-Barr virus infection and can be a therapeutic target. *Oncotarget*. 2018.07; 9(57); 31077-31089
2. Yonese I, Takase H, Yoshimori M, Onozawa E, Tsuzura A, Miki T, Mochizuki M, Miura O, Arai A. CD79B mutations in primary vitreoretinal lymphoma: Diagnostic and prognostic potential. *European journal of haematology*. 2018.11;

[Conference Activities & Talks]

1. Arai A, Yonese I, Sakashita C, Imadome KI, Kobayashi T, Sawada A, Itoh Y, Ohga S, Kimura H, Fujiwara S. Nationwide survey of chemotherapy for CAEBV in Japan. 2018 International Conference on EBV and KSHV 2018.07.29 Madison, U.S.A
2. A Arai, C Sakashita, A Sawada, H Kimura. Nationwide survey of chemotherapy for CAEBV in Japan. The 77th Annual Meeting of the Japanese Cancer Association 2018.09.28
3. Arai A, Yonese I, Takase H, Yoshimori M, Miki T, Mochizuki M, Miura O. CD79B Y196 mutations in primary vitreoretinal lymphoma: Diagnostic and prognostic potential. The 80th Annual Meeting of the Japanese Society of Hematology 2018.10.12 Osaka
4. Yoshimori M , Shinki H, Imadome KI, Wu S, Tateishi M , Koyama T, Arai A. EBV-NK-cells induce procoagulant activity of monocytic and vascular endothelial cells causing DIC. The 80th Annual Meeting of the Japanese Society of Hematology 2018.10.12 Osaka
5. Arai A, Yonese I, Sakashita C, Imadome KI, Kobayashi T, Sawada A, Itoh Y, Ohga S, Kimura H, Fujiwara S. Nationwide survey of chemotherapy for CAEBV in Japan. The 59th American Society of Hematology Annual Meeting & Exposition 2018.12.01 San Diego

Department of Immunopathology

Professor: Tetsuo Kubota

Associate Professor: Yuko Kato

Doctor Course Graduate Students: Naoko Hisasue, Kumi Inoue, Siriphone Virachith

Master Course Graduate Students: Yoshino Watanabe, Masumi Saito

Under Graduate Research Students: Tomomi Makino, Miku Ishizawa, Nobuyo Kondo

(1) Outline

Since the beginning of this school year, we have been transferred from Graduate School of Health Care Sciences to Graduate School of Medical and Dental Sciences, and the organization, curriculum, as well as the process of thesis defense have been changed drastically. Kubota have been involved in this dizzying year as a chairman of Faculty Council in Division of Biomedical Laboratory Sciences, and Director of School of Health Care Sciences. According to this, our laboratory have changed from Department of Microbiology and Immunology to Department of Immunopathology, separating a bacteriologist Associate Professor Saito. Fortunately, however, brilliant students contributed a lot to our research on the roles of autoantibodies in systemic autoimmune diseases, and some of the results was successfully published. Because of that progress, an international student Siriphone Virachith, came from Laos, got Ph D, and an undergraduate student Yumi Makino won the best presentation award in a scientific meeting.

(2) Research

1. Role of autoantibodies in pathogenesis of systemic autoimmune diseases.
2. Pathogenesis of autoinflammatory diseases.
3. Production of novel antibodies useful for immunological experiments or clinical diagnosis.

(3) Education

[Undergraduate Course] Clinical Immunology Lecture, Clinical Immunology Laboratory, Undergraduate Research, Clinical Practice, General Medical Technology, Clinical Medicine

[Master Course] Introductory Experiments for Medical Technologist Internship, Medical Technologist Internship I, Medical Technologist Internship II, Medical Technology II, Seminar of Medical Laboratory Science, Practice of Medical Laboratory Science, Research for Thesis

[Doctor Course] Introductory Experiments for Medical Technologist Advanced Internship, Medical Technologist Advanced Internship I, Medical Technologist Advanced Internship II, Medical Technology II, Clinical Reasoning, Immunopathology Practice, Immunopathology Laboratory

(4) Lectures & Courses

[Undergraduate]

In order to cultivate human resources capable of studying and developing novel methods of clinical laboratory tests, besides what we have already known, we teach how to think from a scientific point of view. To cultivate

application skills, therefore, the classes spend a lot of time for teaching basic immunology introducing how the findings were revealed.

[Graduate]

To cultivate professionals, we administer the internship program in TMDU hospital. In addition, we show students actual clinical data and discuss how we should interpret them. As for research, we encourage not only the doctor course students, but also the master course students to publish the results.

(5) Clinical Services & Other Works

In TMDU hospital, Kubota works for the Department of Rheumatology, and Kato for the clinical laboratory.

(6) Publications

[Original Articles]

1. Kato Y, Yokoyama U, Fujita T, Umemura M, Kubota T, Ishikawa Y. Epac1 deficiency inhibits basic fibroblast growth factor-mediated vascular smooth muscle cell migration. *Journal of Physiological Sciences*. 2018;
2. Virachith S, Saito M, Watanabe Y, Inoue K, Hoshi O, Kubota T. Anti-beta2-glycoprotein I antibody with DNA binding activity enters monocytes via cell surface DNA and induces tissue factor expression *Clinical and Experimental Immunology*. 2018;

[Conference Activities & Talks]

1. Yuko Kato, Utako Yokoyama, Takayuki Fujita, Tetsuo Kubota, Yoshihiro Ishikawa. Epac1 deficiency inhibits bFGF-induced neointimal formation via diminished phosphorylation of GSK3 β . The 95th Annual Meeting of the Physiological Society of Japan 2018.03.29
2. Siriphone Virachith, Kumi Inoue, Masumi Saito, Tetsuo Kubota. Some anti-CL-beta2-GPI antibodies induce a prothrombotic state by the dual reactivity with DNA and internalization into live cells. 第62回日本リウマチ学会 2018.04.28 東京

Department of Molecular Microbiology

Associate Professor : Ryoichi SAITO

Graduate Student: Miyuki MIZOGUCHI, Alafate AYIBIEKE,
Ayaka OTA, Yukino USUI, Wakana SATO

(1) Outline

Our department is engaged in both lecture and practical course for medical microbiology. These include education on prevention, diagnosis and treatment of infectious diseases for both undergraduate and graduate students. Regarding our research, we are interested in investigating molecular mechanisms of antibiotic resistance and virulence gene regulation in bacteria.

(2) Research

Research Interests:

1. Molecular mechanism of antibiotic resistance in bacteria
2. Mechanism of sporulation, spore germination and toxin production in *Clostridioides difficile* and *Clostridium perfringens*

(3) Education

Our course provides the conceptual basis for understanding pathogenic microorganisms including host response in infectious diseases, antimicrobial resistance, and epidemiologic surveillance. It also provides opportunities for undergraduate and graduate students to gain basic techniques, such as identification of microorganisms and antimicrobial susceptibility testing which are performed in the clinical laboratory at medical facilities.

(4) Publications

[Original Articles]

1. Shinji Ogihara, Ryoichi Saito, Etsuko Sawabe, Takahiro Kozakai, Mari Shima, Yoshibumi Aiso, Toshihide Fujie, Yoko Nukui, Ryuji Koike, Michio Hagihara, Shuji Tohda. Molecular typing of methicillin-resistant *Staphylococcus aureus*: Comparison of PCR-based open reading frame typing, multilocus sequence typing, and *Staphylococcus* protein A gene typing. *J. Infect. Chemother.* 2018.04; 24(4); 312-314
2. Ryoichi Saito, Prabhat K Talukdar, Saud S Alanazi, Mahfuzur R Sarker. RelA/DTD-mediated regulation of spore formation and toxin production by *Clostridium perfringens* type A strain SM101. *Microbiology (Reading, Engl.)*. 2018.05; 164(5); 835-847
3. Mahoko Ikeda, Miyuki Mizoguchi, Yukie Oshida, Keita Tatsuno, Ryoichi Saito, Mitsuhiro Okazaki, Shu Okugawa, Kyoji Moriya. Clinical and microbiological characteristics and occurrence of *Klebsiella pneumoniae* infection in Japan. *Int J Gen Med*. 2018.07; 11; 293-299
4. Saud Alanazi, Maryam Alnoman, Saeed Banawas, Ryoichi Saito, Mahfuzur R Sarker. The inhibitory effects of essential oil constituents against germination, outgrowth and vegetative growth of spores of

Clostridium perfringens type A in laboratory medium and chicken meat. *Food Microbiol.* 2018.08; 73; 311-318

5. Ayako Kasai, Ayaka Ohta, Yuina Maeda, Kageto Yamada, Kazuyuki Tao, Ryoichi Saito. Novel mechanism responsible for high-level macrolide resistance in *Moraxella catarrhalis*. *Infect Drug Resist.* 2018.11; 11; 2137-2140
6. Alafate Ayibieke, Wakana Sato, Samiratu Mahazu, Isaac Prah, John Addow-Thompson, Mitsuko Ohashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Molecular characterisation of the NDM-1-encoding plasmid p2189-NDM in an *Escherichia coli* ST410 clinical isolate from Ghana. *PLoS ONE.* 2018.12; 13(12); e0209623

[Misc]

1. Ryoichi Saito. Clinical laboratory procedures based on infection control and prevention in *Clostridioides difficile* *Clinical microbiology.* 2018.09; 45(5); 39-44

[Conference Activities & Talks]

1. Ryoichi Saito, Mahfuzur R. Sarker. Role of RelA and D-tyrosyl-tRNA(Tyr) deacylase for growth, sporulation and toxin production in *Clostridium perfringens* type A strain SM101. The 29th Annual Meeting of Japanese Society for Clinical Microbiology 2018.02.09 Gifu, Japan
2. Kageto Yamada, Saori Muto, Ryoichi Saito. Colistin susceptibility among *Enterobacteriaceae*. The 29th Annual Meeting of Japanese Society for Clinical Microbiology 2018.02.09 Gifu, Japan
3. Kageto Yamada, Saori Muto, Ryoichi Saito. Molecular mechanism of quinolone resistance in *Moraxella catarrhalis*. The 29th Annual Meeting of Japanese Society for Clinical Microbiology 2018.02.09 Gifu, Japan
4. Ayaka Ota, Ayako Kasai, Kageto Yamada, Ryoichi Saito. Molecular mechanism of macrolide resistance in *Moraxella catarrhalis*. The 29th Annual Meeting of Japanese Society for Clinical Microbiology 2018.02.09 Gifu, Japan
5. Alafate Ayibieke, Miyuki Mizoguchi, Kageto Yamada, Tomoaki Sato, Kyoji Moriya, Yoshibumi Aiso, Toshihide Fujie, Yoko Nukui, Ryuji Koike, Ryoichi Saito. Tolerance to antiseptics among *Staphylococcus epidermidis* isolates. The 33rd Annual Meeting of Japanese Society for Infection Prevention and Control 2018.02.23 Tokyo, Japan
6. Ryoichi Saito. Clinical microbiology procedures for *Clostridium difficile*. The 33rd Annual Meeting of Japanese Society for Infection Prevention and Control 2018.02.23 Tokyo, Japan
7. Takeshi Ohtsuka, Kenichi Shizuno, Ayaka Ohta, Ayako Kasai, Kageto Yamada, Ryoichi Saito. Case report: lower respiratory tract infection related to amoxicillin/clavulanic acid-nonsusceptible *Moraxella catarrhalis*. 67th JAMT CONGRESS 2018 2018.05.12 Shizuoka, Japan
8. Yoko Nukui, Tetushi Aiso, Ryoichi Saito, Chihiro Tani, Shuji Toda, Ryuji Koike. Molecular epidemiology of outbreak in *C. difficile*. The 92nd Annual Meeting of the Japanese association for infectious diseases 2018.06.01 Okayama, Japan
9. Y. Nukui, Y. Aiso, T. Chino, R. Saito, C. Tani, J. Nakajima, K. Sonobe, S. Tohda, R. Koike. Molecular epidemiological analysis of *Clostridium difficile* that caused an outbreak in a Japanese hospital . *ASM Microbe* 2018 2018.06.07 Atlanta, GA, USA
10. Ayaka Ohta, Ayako Kasai, Yuina Maeda, Kageto Yamada, Ryoichi Saito. Genetic profile in the development of macrolide resistance in *Moraxella catarrhalis*. *ASM Microbe* 2018 2018.06.07 Atlanta, GA, USA
11. Alafate Ayibieke, Miyuki Mizoguchi, Kageto Yamada, Tomoaki Sato, Chino Takashi, Yoshibumi Aiso, Toshihide Fujie, Yoko Nukui, Kyoji Moriya, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Dissemination of *qac* genes among *Staphylococcus epidermidis* isolates from a University teaching hospital in Tokyo. *ASM Microbe* 2018 2018.06.07 Atlanta, GA, USA

12. Alafate Ayibieke, Wakana Sato, Samiratu Mahazu, Isaac Prah, John Thompson, Chihiro Tani, Mitsuko Ohashi, Shiroh Iwanaga, Toshihiko Suzuki, Anthony Ablordey, Ryoichi Saito. First clinical isolation of NDM-1 carbapenemase-producing *Escherichia coli* in Ghana. ASM Microbe 2018 2018.06.07 Atlanta, GA, USA
13. Ryoichi Saito, Prabhat K. Talukdar, Saud S. Alanazi, Mahfuzur R. Sarker. RelA/DTD-mediated regulation of spore formation and toxin production by *Clostridium perfringens* type A strain SM101. ASM Microbe 2018 2018.06.07 Atlanta, GA, USA
14. Saud Alanazi, Maryam Alnoman, Saeed Banawas, Ryoichi Saito, Mahfuzur R. Sarker. The inhibitory effects of essential oil constituents against germination, outgrowth and vegetative growth of spores of *Clostridium perfringens* type A in laboratory medium and chicken meat. ASM Microbe 2018 2018.06.07 Atlanta, GA, USA
15. Ayaka Ota, Takeshi Ohtsuka, Eimi Hasegawa, Ayako Kasai, Kageto Yamada, Yoshihiro Yamaguchi, Wachino Jun-ichi, Koji Kimura, Ryoichi Saito. Molecular mechanism of amoxicillin-clavulanate resistance in *Moraxella catarrhalis*. The 55th JAMT CONGRESS at Kanto region, 2018 2018.10.28 Gunma, Japan
16. Yukino Usui, Yuko Kamiichi, Nozomi Uchida, Shu Okugawa, Kazunari Sonobe, Shuji Tohda, Ryoichi Saito. Role of bile acids for growth, toxin production and spore formation in *Clostridium difficile*. The 55th JAMT CONGRESS at Kanto region, 2018 2018.10.28 Gunma, Japan
17. Wakana Sato, Alafate Ayibieke, Ayumi Kobayashi, Chihiro Tani, Ryoichi Saito. Antimicrobial susceptibility in clinical isolates of bacteria in Ghana. The 55th JAMT CONGRESS at Kanto region, 2018 2018.10.28 Gunma, Japan
18. Takahito Nei, Ryoichi Saito. Case report: infectious endocarditis caused by *Cardiobacterium valvarum*. The 14th JAMT CONGRESS at Tokyo region, 2018 2018.12.02 Tokyo, Japan

Department of Liver Disease Control

Professor
Associate Professor

Yasuhiro ASAHINA
Sei KAKINUMA

Graduate Student
(collaboration with Department of Gastroenterology and Hepatology in TMDU)

Emi INOUE, Tomoyuki TSUNODA, Masato MIYOSHI, Ayako SATO
Jyun TUCHIYA

(1) Outline

Patients died of chronic liver diseases, including liver cancer, are about 40,000 persons per a year in Japan. Liver transplantation remains the only effective treatment available to patients with end-stage liver diseases. Because of a serious shortage of donors for allogeneic liver transplantation, an alternative therapy is needed. Prevention of hepatocarcinogenesis and hepatic fibrosis is also necessary for patients with chronic hepatitis, and the development of effective treatment for progressive liver diseases has been quite essential. We believe that the central role of clinical departments in the graduate school of TMDU is to establish basis for the innovative medical treatment in the next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel therapeutics established upon basic research are required.

Our section is a donation-funded department collaborating with the Department of Gastroenterology and Hepatology in TMDU. Most of basic research projects, education for students, and clinical contributions including multicenter studies are collaboration with the Department of Gastroenterology and Hepatology in TMDU. The goal of our education is to promote students to become a well-developed hepatologist, and also a leading expert in the field of Hepatology and Gastroenterology.

(2) Research

Our principle is to achieve a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice.

We focus on the basic studies of molecular mechanism regulating development, pathophysiology, progression, and therapeutic resistance of hepatocellular carcinoma (HCC). We also focus on the development of novel disease models using human induced pluripotent stem cells, the research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis, the study for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells, analysis of mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and factors for therapeutic resistance against antiviral agents.

Research projects

- Research for mechanism regulating development, pathophysiology, progression, and therapeutic resistance of HCC, based on molecular biology and genome informatics
- Development of novel disease models using human induced pluripotent stem cells to elucidate the pathophysiology of liver diseases
- Research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis
- Research for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells

· Analyses of molecular mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and clinical factors for therapeutic resistance against antiviral agents.

(3) Education

Primary goal for education in our section is to train highly educated and experienced clinician-researchers in the field of hepatology. Our goal for education of graduate students is to produce clinical researchers thinking from a wide perspective and to bring up leaders of the next generation in hepatology.

(4) Lectures & Courses

Our lectures and courses are collaboration with the Department of Gastroenterology and Hepatology in School of Medicine, TMDU. We also educate clinical residents in Medical Hospital of TMDU and graduate students of the Department of Gastroenterology and Hepatology, in TMDU in collaboration with such department.

(5) Clinical Services & Other Works

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. In the clinical section, we pursue development and application of highly advanced technologies, including novel procedures, for sophisticated diagnosis and treatment of diseases of liver, biliary duct, and pancreas. We also operate a lot of multicenter study collaborating with the Department of Gastroenterology and Hepatology in TMDU. We participate in four research projects for treatment and eradication of hepatitis virus funded by Japan Agency for Medical Research and Development (AMED). We published a lot of studies in peer-reviewed international journals and presented the recent works in a lot of international and domestic conferences as described below.

(6) Clinical Performances

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. We have recently established the outpatient department specialized for chronic hepatitis, cirrhosis, and HCC. We have operated a lot of multicenter study about efficacy of treatment against viral hepatitis, named as “Ochyanomizu Liver Conference”. More than 2000 patients with viral hepatitis were enrolled in such studies. We have clarified the clinical factors predicting accurately the therapeutic prognosis and risk for development of HCC. We are developing the screening programs for the early detection of HCC in patients with chronic hepatitis after eradication of viruses utilizing non-invasive elastography, novel serum markers, and dynamic contrast-enhanced ultrasonography. For the treatment of HCC, three-dimensional location and structure of tumors and vessels are evaluated by multilateral approaches using dynamic contrast-enhanced ultrasonography, Gd-EOB-DTPA enhanced MRI, and real-time virtual ultrasonography (RVS). We have reported the utility and safety of such therapeutic approaches. We are providing patients the appropriate therapeutic option based on collective multimodal therapeutic strategy in collaboration with departments of surgery and radiology.

(7) Publications

[Original Articles]

1. Yutaka Yasui, Kaoru Tsuchiya, Masayuki Kurosaki, Takaya Takeguchi, Yuko Takeguchi, Mao Okada, Wan Wang, Yohei Kubota, Tomoyuki Goto, Yasuyuki Komiyama, Mayu Higuchi, Kenta Takaura, Tsuguru Hayashi, Hitomi Takada, Nobuharu Tamaki, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Yasuhiro Asahina, Nobuyuki Enomoto, Yoshiro Himeno, Namiki Izumi. Up-to-seven criteria as a useful predictor for tumor downstaging to within Milan criteria and Child-Pugh grade deterioration after initial conventional transarterial chemoembolization. *Hepatol. Res.* 2018.05; 48(6); 442-450

2. Maekawa Shinya, Sato Mitsuaki, Kuratomi Natsuhiko, Inoue Taisuke, Suzuki Yuichiro, Tatsumi Akihisa, Miura Mika, Matsuda Shuya, Muraoka Masaru, Nakakuki Natsuko, Amemiya Fumitake, Takano Shinichi, Fukasawa Mitsuharu, Nakayama Yasuhiro, Yamaguchi Tatsuya, Sato Tadashi, Sakamoto Minoru, Murakawa Miyako, Nakagawa Mina, Asahina Yasuhiro, Enomoto Nobuyuki. Association between alanine aminotransferase elevation and UGT1A1*6 polymorphisms in daclatasvir and asunaprevir combination therapy for chronic hepatitis C J. Gastroenterol. 2018.06; 53(6); 780-786
3. Wai-Kay Seto, Yasuhiro Asahina, Todd T Brown, Cheng-Yuan Peng, Carol Stanciu, Dzhamal Abdurakhmanov, Fehmi Tabak, Tuan T Nguyen, Wan-Long Chuang, Tetsuro Inokuma, Fusao Ikeda, Teresa Antonia Santantonio, François Habersetzer, Alnoor Ramji, Audrey H Lau, Vithika Suri, John F Flaherty, Hongyuan Wang, Anuj Gaggar, G Mani Subramanian, Shrikant Mukewar, Maurizia R Brunetto, Scott Fung, Henry Lik-Yuen Chan. Improved Bone Safety of Tenofovir Alafenamide Compared to Tenofovir Disoproxil Fumarate Over 2 Years in Patients With Chronic HBV Infection.[Epub ahead of print] Clin. Gastroenterol. Hepatol. 2018.06;
4. Yasuhiro Asahina, Yoshito Itoh, Yoshiyuki Ueno, Yasushi Matsuzaki, Yasuhiro Takikawa, Hiroshi Yatsuhashi, Takuya Genda, Fusao Ikeda, Takuma Matsuda, Hadas Dvory-Sobol, Deyuan Jiang, Benedetta Massetto, Anu O Osinusi, Diana M Brainard, John G McHutchison, Norifumi Kawada, Nobuyuki Enomoto. Ledipasvir-sofosbuvir for treating Japanese patients with chronic hepatitis C virus genotype 2 infection. Liver Int. 2018.09; 38(9); 1552-1561

[Misc]

1. Hiroko Nagata, Mina Nakagawa, Yasuhiro Asahina. Reply to: "Imaging Basis of AFP and WFA+M2BP as Indicators of the risk of HCC after SVR". J. Hepatol. 2018.03; 68(3); 607-608

[Conference Activities & Talks]

1. Asahina Y. Host genome mutations and HBV integration in HCC patients with HBV infection. 36th US-Japan Hepatitis Panel Meeting 2018.01.10 Shenzhen (China)
2. Asahina Y, Liu CJ, Gane E, Itoh Y, Kawada N, Ueno Y, Wang CY, Llewellyn J, Osinusi A, Svarovskaia J, Mo H, Crans G, Chuang WL, Chen PJ, Enomoto N. Ledipasvir/Sofosbuvir All-oral Regimen for Patients with Chronic Hepatitis C Genotype 2 Infection: Integrated Analysis of Three Clinical Studies. 27th Annual Conference of the Asian Pacific Association for the Study of the Liver 2018.03.15 Dehli (India)
3. Asahina Y, Kakinuma S . HBV reactivation and changes in interferon-stimulated gene expression during treatment of direct-acting antivirals for HCV: Analyses in a novel in vitro model for HBV-HCV coinfection using human induced pluripotent stem cell-derived hepatic cells . EASL, The International Liver Congress 2018 2018.04.14 Paris (France)
4. Kitahata-kawai F, Asahina Y, KakinumaS, Murakawa M, Nitta S, Nagata H, Kaneko S, Inoue E, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N and Watanabe M. Difference of gene mutational profile among viral- and non-viral HCC with or without prior HBV infection: Results of comprehensive deep sequencing analyses of cancer genes and HBV/A AV integration. EASL, The International Liver Congress 2018 2018.04.14 Paris (France)
5. Nitta S, Kato T, Tuchiya J, Shinomiya-Inoue E, Sato A, Tsunoda T, Miyoshi M, Kitahata-Kawai F, Murakawa M, Istui Y, Azuma S, Nakagawa M, Kakinuma S, Asahina Y. The in vitro analysis of NS5A resistance-associated substitutions (RAS) observed in DAA treatment failure patients. 25th International Symposium on Hepatitis C Virus and Related Viruses 2018.10.09 Dublin (Ireland)
6. Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Nakagawa M, Kakinuma S, Watanabe M. Gene Mutational Profile and Viral Integration in Hepatocellular Carcinoma with or without HBV/HCV Suppression. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
7. Nakagawa M, Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tomita M, Watanabe M. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)

8. Nitta S, Kato T, Tuchiya J, Sato A, Tsunoda T, Miyoshi M, Inoue- Shinomiya E, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The Characteristic and the Anti-HCV Reagents Susceptibility Analysis of NS5A Resistance-Associated Substitutions (RAS) Detected after Daa Treatment Failure Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
9. Asahina Y. Increased risk of HCC following DAA: fact or fiction? / Follow up strategy after SVR in chronic hepatitis C. Asian Pacific Digestive Week 2018 2018.11.16 Seoul (Korea)

Department of Advanced Therapeutics for GI Diseases

Professor
Associate Professor
Associate Professor
Assistant Professor

Tetsuya NAKAMURA
Katsuyoshi MATSUOKA (-03/2018)
Takashi NAGAISHI
Michio ONIZAWA

(1) Outline

The goal of our department is to develop novel therapeutic strategies for inflammatory bowel diseases (IBD) in humans. With multiple layers of support of corporations who wish to contribute to our mission, we have been focusing on IBD research from the clinical and basic science perspectives, providing an exceptional education program for graduate students at TMDU.

(2) Research

Our research activities focus on the key areas listed below. We have a particular emphasis on translational (bench to clinic) research on IBD.

- Research on the intestinal epithelium to develop regenerative medicine approaches for IBD
- The study of mucosal immunology to develop novel approaches for the diagnosis and treatment of IBD

(3) Education

We share our expertise and teaching program in graduate course education with the Department of Gastroenterology and Hepatology at TMDU. We are also involved in many programs designed for undergraduates.

(4) Lectures & Courses

Our goal is to create future leaders who are able to reach the highest level of quality in IBD research through the training of fellows and graduate/undergraduate students.

(5) Clinical Services & Other Works

We focus on developing highly advanced technologies, including novel procedures, for diagnosis and treatment of IBD in collaboration with the Department of Gastroenterology and Hepatology at TMDU. In addition, we have been playing a major role in nation-wide survey and multi-center studies on IBD, which is funded by the Japanese Ministry of Health, Labor and Welfare.

(6) Clinical Performances

- Development of new treatment protocol for IBD patients with stem cell therapy or immunomodulators.
- Development of minimally-invasive diagnostic modalities for inflammatory bowel diseases (i.e. MRE).

- Diagnosis and treatment of small intestinal lesions of inflammatory bowel diseases by double-balloon enteroscopy.

(7) Publications

[Original Articles]

1. Dong Il Park, Tadakazu Hisamatsu, Minhu Chen, Siew Chien Ng, Choon Jin Ooi, Shu Chen Wei, Rupa Banerjee, Ida Normiha Hilmi, Yoon Tae Jeon, Dong Soo Han, Hyo Jong Kim, Zhihua Ran, Kaichun Wu, Jiaming Qian, Pin-Jin Hu, Katsuyoshi Matsuoka, Akira Andoh, Yasuo Suzuki, Kentaro Sugano, Mamoru Watanabe, Toshifumi Hibi, Amarendra S Puri, Suk-Kyun Yang. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 2: Management. *J. Gastroenterol. Hepatol.* 2018.01; 33(1); 30-36
2. Dong Ii Park, Tadakazu Hisamatsu, Minhu Chen, Siew Chien Ng, Choon Jin Ooi, Shu Chen Wei, Rupa Banerjee, Ida Normiha Hilmi, Yoon Tae Jeon, Dong Soo Han, Hyo Jong Kim, Zhihua Ran, Kaichun Wu, Jiaming Qian, Pin-Jin Hu, Katsuyoshi Matsuoka, Akira Andoh, Yasuo Suzuki, Kentaro Sugano, Mamoru Watanabe, Toshifumi Hibi, Amarendra S Puri, Suk-Kyun Yang. Asian Organization for Crohn's and Colitis and Asian Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 1: Risk assessment. *J. Gastroenterol. Hepatol.* 2018.01; 33(1); 20-29
3. Shiro Yui, Luca Azzolin, Martti Maimets, Marianne Terndrup Pedersen, Robert P Fordham, Stine L Hansen, Hjalte L Larsen, Jordi Guiu, Mariana R P Alves, Carsten F Rundsten, Jens V Johansen, Yuan Li, Chris D Madsen, Tetsuya Nakamura, Mamoru Watanabe, Ole H Nielsen, Pawel J Schweiger, Stefano Piccolo, Kim B Jensen. YAP/TAZ-Dependent Reprogramming of Colonic Epithelium Links ECM Remodeling to Tissue Regeneration. *Cell Stem Cell.* 2018.01; 22(1); 35-49.e7
4. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Katsuyoshi Matsuoka, Masakazu Nagahori, Toshimitsu Fujii, Eiko Saito, Maiko Kimura, Tomoyuki Fujioka, Mamoru Watanabe. Utility of Magnetic Resonance Enterography For Small Bowel Endoscopic Healing in Patients With Crohn's Disease *Am. J. Gastroenterol.* 2018.02; 113(2); 283-294
5. Shinya Sugimoto, Yuki Ohta, Masayuki Fujii, Mami Matano, Mariko Shimokawa, Kosaku Nanki, Shoichi Date, Shingo Nishikori, Yoshihiro Nakazato, Tetsuya Nakamura, Takanori Kanai, Toshiro Sato. Reconstruction of the Human Colon Epithelium In Vivo. *Cell Stem Cell.* 2018.02; 22(2); 171-176.e5
6. Taro Watabe, Takashi Nagaishi, Naoya Tsugawa, Yudai Kojima, Nisha Jose, Akinori Hosoya, Michio Onizawa, Yasuhiro Nemoto, Shigeru Oshima, Tetsuya Nakamura, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. B cell activation in the cecal patches during the development of an experimental colitis model. *Biochem. Biophys. Res. Commun.* 2018.02; 496(2); 367-373
7. Makoto Naganuma, Shinya Sugimoto, Keiichi Mitsuyama, Taku Kobayashi, Naoki Yoshimura, Hidehisa Ohi, Shinji Tanaka, Akira Andoh, Naoki Ohmiya, Keiichiro Saigusa, Takayuki Yamamoto, Yuichi Morohoshi, Hitoshi Ichikawa, Katsuyoshi Matsuoka, Tadakazu Hisamatsu, Kenji Watanabe, Shinta Mizuno, Wataru Suda, Masahira Hattori, Shinji Fukuda, Akiyoshi Hirayama, Takayuki Abe, Mamoru Watanabe, Toshifumi Hibi, Yasuo Suzuki, Takanori Kanai, . Efficacy of Indigo Naturalis in a Multicenter Randomized Controlled Trial of Patients With Ulcerative Colitis. *Gastroenterology.* 2018.03; 154(4); 935-947
8. Kohei Suzuki, Tatsuro Murano, Hiromichi Shimizu, Go Ito, Toru Nakata, Satoru Fujii, Fumiaki Ishibashi, Ami Kawamoto, Sho Anzai, Reiko Kuno, Konomi Kuwabara, Junichi Takahashi, Minami Hama, Sayaka Nagata, Yui Hiraguri, Kento Takenaka, Shiro Yui, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Mamoru Watanabe, Ryuichi Okamoto. Single cell analysis of Crohn's disease patient-derived small intestinal organoids reveals disease activity-dependent modification of stem cell properties. *J. Gastroenterol.* 2018.09; 53(9); 1035-1047
9. Ami Kawamoto, Sayaka Nagata, Sho Anzai, Junichi Takahashi, Mao Kawai, Minami Hama, Daichi Nogawa, Kohei Yamamoto, Reiko Kuno, Kohei Suzuki, Hiromichi Shimizu, Yui Hiraguri, Shiro Yui, Shigeru Ohshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Masanobu Kitagawa, Ryuichi Okamoto, Mamoru Watanabe. Ubiquitin D is up-regulated by synergy of Notch signalling and TNF- α in the inflamed intestinal epithelia of IBD patients. [Epub ahead of print] *J Crohns Colitis.* 2018.11;

[Misc]

1. Tetsuya Nakamura. Recent progress in organoid culture to model intestinal epithelial barrier functions. *Int. Immunol.* 2018.10;

[Conference Activities & Talks]

1. Nishimura R, Tsuchiya K, Shirasaki T, Watanabe S, Hibiya S, Okamoto R, Nakamura T, Watanabe M.. The identification of lesion-specific gene expression in intestinal epithelial cells of Ulcerative Colitis by comparing colonic organoids from lesion and non-lesion parts of same patients. The 13th Congress of ECCO 2018.02.16 Vienna (Austria)
2. Matsuoka K, Naganuma M, Tanida S, Kitamura K, Matsui T, Arai M, Fujiya M, Horiki N, Nebiki H, Kinjo F, Miyazaki T, Matsumoto T, Esaki M, Mitsuyama K, Saruta M, Ido A, Hojo S, Takenaka O, Oketani K, Imai T, Tsubouchi H, Hibi T, Kanai T. Efficacy and safety of anti-fraktalkine monoclonal antibody, E6011, for the patients with Crohn's disease who had lost response to anti-TNF α antibody : a multi-center, open-label, Phase 1/2 study. The 13th Congress of ECCO 2018.02.16 Vienna (Austria)
3. Hibiya S, Tsuchiya K, Watanabe S, Nishimura R, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Establishment of in vitro human model for Ulcerative Colitis by using human colon organoid culture. 13th Congress of ECCO 2018.02.16 Vienna (Austria)
4. Shiro Yui, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. Fetalization of colonic epithelium mediated by YAP/TAZ links ECM remodeling to tissue regeneration. GI Research Academy 2018 2018.05.25 Tokyo (Japan)
5. Suzuki K, Kuwabara K, Takahashi J, Anzai S, Kuno R, Kawamoto A, Ishibashi F, Nagata S, Hiraguri Y, Yui S, Tsuchiya K, Nakamura T, Ohtsuka K, Okamoto R, Watanabe M. Single-cell level analysis of organoids derived from CD patients reveals disease-status related modifications of small intestinal stem cells. DDW2018 2018.06.04 Washington D.C (USA)
6. Shirasaki T, Tsuchiya K, Nishimura R, Watanabe S, Hibiya S, Katsukura N, Okamoto R, Nakamura T, Watanabe M. Identification of lesion-specific epithelial function of ulcerative colitis by comparing colonic organoids from lesion and non-lesion parts of same patients. DDW2018 2018.06.05 Washington D.C (USA)
7. Hibiya S, Tsuchiya K, Watanabe S, Nishimura R, Shirasaki T, Oshima S, Okamoto R, Nakamura T, Watanabe M. Human colonic organoid treated with inflammatory factors might mimic the pathophysiology of epithelial cells in ulcerative colitis. DDW2018 2018.06.05 Washington D.C (USA)
8. Taro Watabe, Takashi Nagaishi, Naoya Tsugawa, Yudai Kojima, Nisha Jose, Akinori Hosoya, Takahiro Adachi, Mamoru Watanabe. Analysis of ileocecal immune response in an animal model of colitis using intra-vital imaging. DDW 2018 2018.06.05 Washington D.C (USA)
9. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Mice overexpressing MKL1 in macrophages are susceptible to the development of colitis. DDW 2018 2018.06.05 Washington D.C (USA)
10. Ishibashi F, Shimizu H, Kawamoto A, Suzuki K, Anzai S, Kuwabara K, Takahashi J, Nagata S, Oshima S, Tsuchiya K, Nakamura T, Watanabe M, Okamoto R. Mouse colonic secretory cells de-differentiate into intestinal stem cells and promote mucosal repair through activation of NF-KB signalin. ISSCR2018 2018.06.20 Melbourne (Australia)
11. Takashi Nagaishi, Taro Watabe, Tsugawa, Yudai Kojima, Nisha Jose, Daiki Yamada, Takahiro Adachi, Mamoru Watanabe. Analysis of cecal immune response in a murine model of colitis using intravital imaging. FOCIS 2018 2018.06.20 San Francisco (USA)
12. Saito E, Suzuki K, Shimizu H, Motobayashi M, Takenaka K, Onizawa M, Fujii T, Nagahori M, Ohtsuka K, Watanabe M. The clinical efficacy of switching cases between Infliximab(IFX) and Adalimumab(ADA) in patients with ulcerative colitis. AOCC2018 2018.06.22 Shanghai (China)
13. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Mice overexpressing MKL1 in macrophages are susceptible to DSS-induced colitis. FOCIS 2018 2018.06.22 San Francisco (USA)

14. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Overexpression of MKL1 in Macrophages leads to the development of murine colitis. MICS 2018 2018.07.19 Oxford (UK)
15. Yuka Matsumoto, Mamoru Watanabe, Tetsuya Nakamura. Development of a new mouse model of short bowel syndrome that may allow for the assessment of therapeutic efficacy of heterotopic transplantation of small intestinal organoids. 5th TERMIS World Congress 2018.09.04 Kyoto (JAPAN)
16. Suzuki K, Murano T, Hiraguri Y, Takahashi J, Shimizu H, Anzai S, Kuwabara K, Kawamoto A, Ishibashi F, Yui S, Tsuchiya K, Nakamura T, Ohtsuka K, Watanabe M, Okamoto R. Crohn' s disease patient-derived small intestinal organoids reveal disease-status related modification of stem cell properties. 5th TERMIS World Congress 2018 2018.09.06 Kyoto (JAPAN)
17. Suzuki K, Takahashi J, Hiraguri Y, Yui S, Shimizu H, Tsuchiya K, Nakamura T, Ohtsuka K, Okamoto R, Watanabe M. Crohn' s disease patient-derived small intestinal organoids reveal disease status related modification of stem cell properties. FALKsymposium 2018.09.08 Kyoto (JAPAN)
18. Yudai Kojima, Takashi Nagaishi, Taro Watabe, Naoya Tsugawa, Nisha Jose, Daiki Yamada, Akinori Hosoya, Takahiro Adachi, Mamoru Watanabe. B cell-mediated ileocecal immune response is activated in the early phase of colitis development. UEGW 2018 2018.10.22 Vienna (Austria)
19. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K. Naruse, Mamoru Watanabe, Akinori Kimura. Mice overexpressing MKL1 in macrophages experience fulminant colitis. UEGW 2018 2018.10.22 Vienna (Austria)
20. Hibiya S, Tsuchiya K, Nishimura R, Shirasaki T, Watanabe S, Katsukura N, Okamoto R, Nakamura T, Watanabe M. Lesion-specific gene expression in the Epithelial cells of Crohn' s disease by comparing Small intestinal organoids from active and inactive Lesion in the same patient. UEGW 2018 2018.10.22 Vienna (Austria)
21. Ishibashi F, Kuwabara K, Kawamoto A, Anzai S, Takahashi J, Nagata S, Shimizu H, Yui S, Oshima S, Tsuchiya K, Nakamura T, Watanabe M, Okamoto R. Ectopic expression of reg3a in the mice distal Colon is mediated by interactions between notch and Il-22 signaling pathways, and promotes tissue repair By the augmentation of EGFR signaling. UEGW 2018 2018.10.22 Vienna (Austria)
22. Kuwabara K, Ishibashi F, Kawamoto A, Anzai S, Takahashi J, Nagata S, Shimizu H, Yui S, Oshima S, Tsuchiya K, Nakamura T, Watanabe M, Okamoto R. Long-lived secretory cells residing in the mouse proximal colon serve as reserve stem cells under DNA damage-induced mucosal injury. UEGW 2018 2018.10.22 Vienna (Austria)

Department of Women's Health

Professor Masakazu Terauchi MD PhD; Assistant Professor Asuka Hirose MD PhD (concurrent)

(1) Outline

Japanese women boast world's #1 longevity, although the final stage of their lives is not necessarily of good health-related quality. To stay physically and psychologically sound in later life, women need to optimize their health starting from their midlife, especially through good diet and exercise. Tokyo Medical and Dental University (TMDU) Department of Obstetrics and Gynecology have promoted midlife women's health with our renowned Systemic Health and Nutrition Education Program (SHNEP) since 1995, which inspired Kikkoman Corporation to generously support to establish a new department in TMDU focusing on "Health Maintenance of Women through Food and Nutrition" in 2012. Dr. Masakazu Terauchi, Associate Professor and Chair of TMDU Department of Women's Health, is intensively studying with his colleagues about the changes in women's bodies and minds induced by aging, and the effects of bioactive food ingredients on them.

(2) Research

Department of Women's Health has dealt with a variety of topics listed below since its inception in 2012, mainly focusing our research on the effects of bioactive food ingredients on women's physical and psychological health.

- Effects of grape seed extract on middle-aged women's health-related quality of life
- Effects of hormone therapy and keishibukuryogan on blood pressure in perimenopausal and postmenopausal women
- Effects of nonbenzodiazepine, melatonin receptor agonist, and Kampo medication on sleep disturbances in perimenopausal and postmenopausal women
- Effects of selective serotonin reuptake inhibitors on subjective and objective sleep parameters in middle-aged women with depression
- Effects of oral contraceptive pills on sleep disturbances in young women with primary dysmenorrhea
- Effects of tomato juice on cardiovascular risk markers in middle-aged women
- Effects of soy isoflavone aglicone on middle-aged women's health-related quality of life
- Menopausal hormone therapy: route of administration and platelet-derived microparticles
- Effects of soy lecithin on middle-aged women's tiredness
- Effects of soy milk on middle-aged women's sleep
- Long-term effectiveness of eszopiclone on chronic insomnia disorder in middle-aged women
- Oxidative stress and postmenopausal osteoporosis: prevention of fragility fractures with healthy dietary habits
- Effects of grape seed proanthocyanidin extract on the endothelial function in patients with stage 1 hypertension

(3) Education

Cooperating with the Department of Obstetrics and Gynecology, we have shared responsibility in the education of Obstetrics and Gynecology, as well as in the training of medical students on clinical clerkship.

(4) Clinical Services & Other Works

Cooperating with the Department of Obstetrics and Gynecology, we have provided a comprehensive diagnosis, treatment, and disease management solution for women suffering from:

- menopausal symptoms
- premature ovarian insufficiency
- postmenopausal osteoporosis
- dyslipidemia
- hypertension
- pelvic organ prolapse
- lower urinary tract syndrome
- depression
- anxiety disorder
- insomnia
- dysmenorrhea
- premenstrual syndrome etc.

(5) Publications

[Original Articles]

1. Hirose A, Terauchi M, Osaka Y, Akiyoshi M, Kato K, Miyasaka N. Effect of soy lecithin on fatigue and menopausal symptoms in middle-aged women: a randomized, double-blind, placebo-controlled study. *Nutrition Journal*. 2018.01; 17(4);
2. Yuri Sukenobe, Masakazu Terauchi, Asuka Hirose, Miho Hirano, Mihoko Akiyoshi, Kiyoko Kato, and Naoyuki Miyasaka. Normal/high-fat milk consumption is associated with higher lean body and muscle mass in Japanese women aged between 40 and 60 years: a cross-sectional study *BMC Women's Health*. 2018.02; 18; 32
3. Odai Tamami, Terauchi Masakazu, Hirose Asuka, Miyasaka Naoyuki. Bone mineral density in premenopausal women is associated with antioxidant nutrient intake(和訳中) *日本産科婦人科学会雑誌*. 2018.02; 70(2); 513-514
4. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Muscle and joint pains in middle-aged women are associated with insomnia and low grip strength: a cross-sectional study *Journal of Psychosomatic Obstetrics & Gynecology*. 2018.11;
5. Masakazu Terauchi, Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Mikako Masuda, Reiko Tsunoda, Hiroaki Fushiki, Naoyuki Miyasaka. Dizziness in peri- and postmenopausal women is associated with anxiety: a cross-sectional study *BioPsychoSocial Medicine*. 2018.12; 12; 21

[Misc]

1. Masakazu Terauchi. Irisin, a promising but immature myokine linking between physical activity and its positive health effects *Menopause Live*. 2018.04; (4/6);

[Conference Activities & Talks]

1. Masakazu Terauchi. Chilliness in Japanese peri- and post-menopausal women is associated with reduced heart rate and resting energy expenditure. 16th World Congress on the Menopause 2018.06.07 Vancouver, Canada
2. Masakazu Terauchi. Menopause and the Workplace. The 18th Congress of the Asian College of Psychosomatic Medicine 2018.08.24 Seoul
3. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Mikako Masuda, Reiko Tsunoda, Hiroaki Fushiki, Naoyuki Miyasaka. Dizziness in Peri- and Postmenopausal Women is Associated with Anxiety. North American Menopause Society Annual Meeting 2018.10.04 San Diego, CA

4. Masakazu Terauchi. Special Session KSPOG-JSPOG: Introduction of JSPOG and cooperation with KS-POG. Annual Scientific Meeting of the Korean Society of Psychosomatic Obstetrics and Gynecology 2018.12.23 Seoul

Department of Lifetime Clinical Immunology

(1) Publications

[Original Articles]

1. Tomiita Minako, Kobayashi Ichiro, Inoue Yuzaburo, Nonaka Yukiko, Okamoto Nami, Iwata Naomi, Hara Ryoki, Umebayashi Hiroaki, Itoh Yasuhiko, Mori Masaaki. Usefulness of "Guidance for the diagnosis of Sjogren's syndrome in pediatric patients (2015)": new criteria for the diagnosis of Sjogren's syndrome in children and adolescents CLINICAL AND EXPERIMENTAL RHEUMATOLOGY. 2018; 36(3); S264-S265
2. Toshihiro Matsui, Takumi Matsumoto, Fumio Hirano, Fumika Tokunaga, Keisuke Okamoto, Shigeto Tohma, Tomohiro Morio, Hitoshi Kohsaka, Masaaki Mori. Survey of the awareness of adult rheumatologists regarding transitional care for patients with juvenile idiopathic arthritis in Japan Mod Rheumatol. 2018.01; 1-11
3. Kawasaki Aya, Yamashita Keita, Hirano Fumio, Sada Ken-Ei, Tsukui Daisuke, Kondo Yuya, Kimura Yoshitaka, Asako Kurumi, Kobayashi Shigeto, Yamada Hidehiro, Furukawa Hiroshi, Nagasaka Kenji, Sugihara Takahiko, Yamagata Kunihiro, Sumida Takayuki, Tohma Shigeto, Kono Hajime, Ozaki Shoichi, Matsuo Seiichi, Hashimoto Hiroshi, Makino Hirofumi, Arimura Yoshihiro, Harigai Masayoshi, Tsuchiya Naoyuki. Association of ETS1 polymorphism with granulomatosis with polyangiitis and proteinase 3-anti-neutrophil cytoplasmic antibody positive vasculitis in a Japanese population. J Hum Genet. 2018.01; 63(1); 55-62
4. Matsui T, Mori M. 他. Survey of the awareness of adult rheumatologists regarding transitional care for patients with juvenile idiopathic arthritis in Japan. Mod Rheumatol.. 2018.01;
5. Mori Masaaki, Sugiyama Naonobu, Morishima Yosuke, Sugiyama Noriko, Kokubo Takeshi, Takei Syuji, Yokota Shumpei. 若年性特発性関節炎に対するエタネルセプト投与の安全性と有効性 市販後調査の成績 (Safety and effectiveness of etanercept for treatment of juvenile idiopathic arthritis: Results from a postmarketing surveillance) Modern Rheumatology. 2018.01; 28(1); 101-107
6. Mori Masaaki, Hara Takuma, Kikuchi Masako, Shimizu Hiroyuki, Miyamoto Tomoyuki, Iwashima Satoru, Oonishi Tatsuya, Hashimoto Kunio, Kobayashi Norimoto, Waki Kenji, Suzuki Yasuo, Otsubo Yoshikazu, Yamada Hiroshi, Ishikawa Chikao, Kato Taichi, Fuse Shigeto. Infliximab versus intravenous immunoglobulin for refractory Kawasaki disease: a phase 3, randomized, open-label, active-controlled, parallel-group, multicenter trial SCIENTIFIC REPORTS. 2018.01; 8(1); 1994
7. Masaaki Mori, Naonobu Sugiyama, Yosuke Morishima, Noriko Sugiyama, Takeshi Kokubo, Syuji Takei, Shumpei Yokota. Safety and effectiveness of etanercept for treatment of juvenile idiopathic arthritis: Results from a postmarketing surveillance. Mod Rheumatol. 2018.01; 28(1); 101-107
8. Honda Suguru, Hirano Fumio, Mouri Mariko, Hasegawa Hisanori, Kohsaka Hitoshi. Aneurysm formation after stent grafting in vascular Behcet's disease. Arthritis Rheumatol. 2018.02; 70(2); 322
9. Mori Masaaki, Nakagawa Masao, Tsuchida Nao, Kawada Kou, Sato Junko, Sakiyama Michiyo, Hirano Shinya, Sato Katsuaki, Nakamura Hidefumi. 小児リウマチに対する生物製剤開発の提案 (Proposal for the development of biologics in pediatric rheumatology) Pediatrics International. 2018.02; 60(2); 108-114

10. Mori Masaaki, Nakagawa Masao, Tsuchida Nao, Kawada Kou, Sato Junko, Sakiyama Michiyo, Hirano Shinya, Sato Katsuaki, Nakamura Hidefumi. Proposal for the development of biologics in pediatric rheumatology PEDIATRICS INTERNATIONAL. 2018.02; 60(2); 108-114
11. Takahiro Kamiya, Desmond Wong, Yi Tian Png, Dario Campana. A novel method to generate T-cell receptor-deficient chimeric antigen receptor T cells. Blood Adv. 2018.03; 2(5); 517-528
12. Ryoko Sakai, Shoko Kasai, Fumio Hirano, Sayoko Harada, Mari Kihara, Waka Yokoyama, Michi Tsutsumino, Kenji Nagasaka, Ryuji Koike, Hisashi Yamanaka, Nobuyuki Miyasaka, Masayoshi Harigai. No increased risk of herpes zoster in TNF inhibitor and non-TNF inhibitor users with rheumatoid arthritis: epidemiological study using the Japanese health insurance database. Int J Rheum Dis. 2018.04;
13. Okumura Akihisa, Ida Shinobu, Mori Masaaki, Shimizu Toshiaki. Vitamin B1 Deficiency Related to Excessive Soft Drink Consumption in Japan JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION. 2018.05; 66(5); 838-842
14. Okumura Akihisa, Ida Shinobu, Mori Masaaki, Shimizu Toshiaki. Attitudes of pediatricians toward Children's consumption of ionic beverages BMC PEDIATRICS. 2018.05; 18(1); 176
15. Kawakami C, Sato A, Sumita H, Isozaki A, Shimizu H, Kanetaka T, Maehara K, Ao K, Nariai A, Takeshita F, Kizu R,*Mori M.. Fever Responses Are Enhanced with Advancing Age during RSV Infection among Children under 24 Months Old. Tohoku J.Exp.Med. . 2018.07; 245(3); 217-222
16. Kawakami Chiaki, Sato Atsuo, Sumita Hiroko, Isozaki Atsushi, Shimizu Hiroyuki, Kanetaka Taichi, Maehara Koji, Ao Kota, Nariai Akiyoshi, Takeshita Fumihiko, Kizu Rika, Mori Masaaki. Fever Responses Are Enhanced with Advancing Age during Respiratory Syncytial Virus Infection among Children under 24 Months Old TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE. 2018.07; 245(3); 217-222
17. Okumura A, Ida S, Ito S, Oguni T, Suzuki M, Mori M, Shimizu T, Committee on Pediatric Nutrition of The Japanese Pediatric Society.. Parental Awareness of Young Children's Pattern of Ionic Beverage Consumption. Pediatrics international : official journal of the Japan Pediatric Society. 2018.07;
18. Naoko Nakano, Masaaki Mori, Hiroaki Umebayashi, Naomi Iwata, Norimoto Kobayashi, Kenji Masunaga, Tomoyuki Imagawa, Takuji Murata, Noriko Kinjo, Kazushige Nagai, Mari Miyoshi, Syuji Takei, Shumpei Yokota, Eiichi Ishii. Characteristics and outcome of intractable vasculitis syndrome in children: Nationwide survey in Japan. Mod Rheumatol. 2018.07; 28(4); 697-702
19. Koji Yokoyama, Masaaki Mori, Akira Yoshida. Mycophenolate mofetil therapy for two cases of antiphospholipid antibody-associated chorea. Mod Rheumatol. 2018.07; 28(4); 709-711
20. Okamoto N, Mori M.. Clinical Practice Guidance for Juvenile Idiopathic Arthritis (JIA) 2018. Mod Rheumatol . 2018.08;
21. Shimizu H, Mori M.. Safety and efficacy of DTaP-IPV vaccine use in healthcare workers for prevention of pertussis. Vaccine. 2018.08;
22. Sakurai N, Hino-Shishikura A, Nozawa T, Kamide H, Ohara A, Nishimura K, Kikuchi M, Hara R, Mori M, Ito S.. Clinical significance of subcutaneous fat and fascial involvement in juvenile dermatomyositis. Mod Rheumatol . 2018.08;
23. Okumura A, Ida S, Ito S, Oguni, T, Suzuki M, Mori M, Shimizu T. . Parental Awareness of Young Children' s Pattern of Ionic Beverage Consumption. Pediatr Intern . 2018.08;
24. Tamura J, Mori M.. Hypercytokinemia with hemophagocytic syndrome due to human metapneumovirus. Pediatr Int. 2018.08;
25. Okamoto N, Yokota S, Takei S, Okura Y, Kubota T, Shimizu M, Nozawa T, Iwata N, Umebayashi H, Kinjo N, Kunishima T, Yasumura J, Mori M. Clinical Practice Guidance for Juvenile Idiopathic Arthritis (JIA) 2018. Modern rheumatology. 2018.08; 1-53
26. Sakurai N, Hino-Shishikura A, Nozawa T, Kamide H, Ohara A, Nishimura K, Kikuchi M, Hara R, Mori M, Ito S. Clinical significance of subcutaneous fat and fascial involvement in juvenile dermatomyositis. Modern rheumatology. 2018.08; 1-16

27. Fumio Hirano, Waka Yokoyama-Kokuryo, Hayato Yamazaki, Michi Tsutsumino, Ryoko Sakai, Shiro Satoh, Tomo Kimura, Naoko Tojo, Hitoshi Kohsaka, Masayoshi Harigai. Comparison of fluorescence optical imaging, ultrasonography and clinical examination with magnetic resonance imaging as a reference in active rheumatoid arthritis patients Immunological Medicine. 2018.09;
28. Mari Kubota-Tanaka, Tomoo Osumi, Shouko Miura, Hiroshi Tsujimoto, Toshihiko Imamura, Akira Nishimura, Kentaro Oki, Kozue Nakamura, Satoshi Miyamoto, Kento Inoue, Maiko Inoue, Takahiro Kamiya, Masakatsu Yanagimachi, Tsubasa Okano, Noriko Mitsuiki, Takeshi Isoda, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio, Shinji Kounami, Mikiya Endo, Motohiro Kato, Masatoshi Takagi. B-lymphoblastic lymphoma with the TCF3-PBX1 fusion gene. Haematologica. 2018.09;
29. Okamoto Nami, Shabana Kosuke, Nakagishi Yasuo, Nishimura Kenichi, Mizuta Mao, Okura Yuka, Shimizu Masaki, Wakiguchi Hiroyuki, Yasumura Junko, Mori Masaaki. Methotrexate Polyglutamates As an Evaluation Tool for Appropriate Dosage of Oral Methotrexate Administration in Pediatric Patients ARTHRITIS & RHEUMATOLOGY. 2018.09; 70;
30. Tamura Daisuke, Inoue Shun, Kawahara Yuta, Mori Masaaki, Yamagata Takanori. Hypercytokinemia with hemophagocytic syndrome due to human metapneumovirus PEDIATRICS INTERNATIONAL. 2018.10; 60(10); 974-976
31. Takumi Matsumoto, Toshihiro Matsui, Fumio Hirano, Shigeto Tohma, Masaaki Mori. Disease activity, treatment and long-term prognosis of adult juvenile idiopathic arthritis patients compared with rheumatoid arthritis patients. Mod Rheumatol. 2018.11; 1-15

[Conference Activities & Talks]

1. Mori Masaaki. Pediatric rheumatic diseases: a review regarding the improvement of long-term prognosis and the transition to adults(和訳中). Immunological Medicine 2018.04.01
2. Nakano Naoko, Mori Masaaki, Umebayashi Hiroaki, Iwata Naomi, Kobayashi Norimoto, Masunaga Kenji, Imagawa Tomoyuki, Murata Takuji, Kinjo Noriko, Nagai Kazushige, Miyoshi Mari, Takei Syuji, Yokota Shumpei, Ishii Eiichi. Characteristics and outcome of intractable vasculitis syndrome in children: Nationwide survey in Japan(和訳中). Modern Rheumatology 2018.07.01
3. Tamura Daisuke, Inoue Shun, Kawahara Yuta, Mori Masaaki, Yamagata Takanori. Hypercytokinemia with hemophagocytic syndrome due to human metapneumovirus(和訳中). Pediatrics International 2018.10.01
4. Okumura Akihisa, Ida Shinobu, Ito Setsuko, Oguni Tatsuya, Suzuki Mitsuyoshi, Mori Masaaki, Shimizu Toshiaki, the Committee on Pediatric Nutrition of the Japanese Pediatric Society. Parental awareness of young children's pattern of ionic beverage consumption(和訳中). Pediatrics International 2018.10.01
5. Hematopoietic stem cell transplantation for IPEX syndrome might be effective in preventing progression of β -cell death. 2018.10.04
6. Nakaseko H, Iwata N, Yasuoka R, Kohagura T, Abe N, Kawabe S, Mori M. Pharmacokinetics of mycophenolate mofetil in juvenile patients with autoimmune diseases.. Modern rheumatology 2018.10.05
7. Takahiro Kamiya, Desmond Wong, Yi Tian Png, Natasha Vinanica, Seow See Voon, Noriko Shiasaki, . Protein Expression Blockers (PEBLs) for safer and effective allogenic CAR-T cell therapy. 第80回日本血液学会学術集会 2018.10.14 大阪
8. Matsui Toshihiro, Matsumoto Takumi, Hirano Fumio, Tokunaga Fumika, Okamoto Keisuke, Tohma Shigeto, Morio Tomohiro, Kohsaka Hitoshi, Mori Masaaki. Survey of the awareness of adult rheumatologists regarding transitional care for patients with juvenile idiopathic arthritis in Japan(和訳中). Modern Rheumatology 2018.11.01
9. Matsumoto T, Matsui T, Hirano F, Tohma S, Mori M. Disease activity, treatment and long-term prognosis of adult juvenile idiopathic arthritis patients compared with rheumatoid arthritis patients.. Modern rheumatology 2018.11.30

Department of Collaborative Medicine for Gastroenterology and Hepatology (CMGH)

Associate Professor : Seishin Azuma
Assistant Professor : Kento Takenaka

(1) Outline

Our department was established for the aim to support the medical care at Tokyo Medical and Dental University (TMDU), and to foster experts in the field of gastroenterology and hepatology who engaged a community medicine such as Ibaraki prefecture. In collaboration with the Department of Gastroenterology and Hepatology in TMDU, we will strengthen an information sharing system and an education training support system that build up with Tsuchiura Kyodo General Hospital and other related facilities. We hope to develop the community medicine through the communication and personal exchanges between such hospitals and us.

(2) Research

- Clinical research on liver diseases related to lifestyle-related diseases
- Establishment of optimized therapy in hepatobiliary diseases
- Development of evaluation and treatment of small bowel lesions in Crohn's disease.
- Development of support technology for diagnosis of digestive and liver diseases by artificial intelligence (AI).

(3) Education

Primary goal for education in our department is to train highly educated and experienced clinicians in the field of gastroenterology and hepatology. Therefore, our goal for education of graduate students is to produce clinicians thinking from a wide perspective and to bring up leaders of the next generation in the field of gastroenterology and hepatology.

(4) Lectures & Courses

Our lectures and courses for medical students are collaboration with the Department of Gastroenterology and Hepatology in School of Medicine, TMDU. We also educate clinical residents in Medical Hospital of TMDU and graduate students of the Department of Gastroenterology and Hepatology, TMDU in collaboration with such department.

(5) Clinical Services & Other Works

In collaboration with the Department of Gastroenterology and Hepatology, we mainly provide outpatient and inpatient care of gastrointestinal and hepatobiliary diseases. In addition, we are managing a lot of multicenter studies including Tsuchiura Kyodo General Hospital. We are conducting industry-academic collaborative research in the field of AI research using the comprehensive collaboration program of TMDU.

(6) Clinical Performances

In collaboration with the Department of Gastroenterology and Hepatology, TMDU, we provide a medical care of liver and inflammatory bowel diseases. We have recently established special outpatient clinics for chronic hepatitis, liver cirrhosis, hepatocellular carcinoma and inflammatory bowel diseases.

We are operating a lot of multicenter studies. One of the multicenter studies evaluates the efficacy of treatment against viral hepatitis, named as “Ochanomizu Liver Conference”, in which more than 2,000 patients have been enrolled. We approach to improve the safety and reliance of treatment for hepatocellular carcinoma, the patients are treated using multilateral approaches by dynamic contrast-enhanced ultrasonography, Gd-EOB-DTPA enhanced MRI, and real-time virtual ultrasonography (RVS). We have reported the utility and safety of such therapeutic approaches. We have also performed balloon-assisted enteroscopy for the small intestine. The patients' number were top-class in the world.

(7) Publications

[Original Articles]

1. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Katsuyoshi Matsuoka, Masakazu Nagahori, Toshimitsu Fujii, Eiko Saito, Maiko Kimura, Tomoyuki Fujioka, Mamoru Watanabe. Utility of Magnetic Resonance Enterography For Small Bowel Endoscopic Healing in Patients With Crohn's Disease Am. J. Gastroenterol. 2018.02; 113(2); 283-294
2. Shintaro Akiyama, Masakazu Nagahori, Shinya Oooka, Mariko Negi, Takashi Ito, Kento Takenaka, Kazuo Ohtsuka, Mamoru Watanabe. Small intestinal obstruction due to the metastasis of intrahepatic cholangiocarcinoma: A case report. Medicine (Baltimore). 2018.03; 97(12); e0190
3. Fumihiko Iwamoto, Katsuyoshi Matsuoka, Maiko Motobayashi, Kento Takenaka, Toru Kuno, Keisuke Tanaka, Yuya Tsukui, Shoji Kobayashi, Takashi Yoshida, Toshimitsu Fujii, Eiko Saito, Tatsuya Yamaguchi, Masakazu Nagahori, Tadashi Sato, Kazuo Ohtsuka, Nobuyuki Enomoto, Mamoru Watanabe. Prediction of disease activity of Crohn's disease through fecal calprotectin evaluated by balloon-assisted endoscopy. J. Gastroenterol. Hepatol. 2018.06;
4. Kohei Suzuki, Tatsuro Murano, Hiromichi Shimizu, Go Ito, Toru Nakata, Satoru Fujii, Fumiaki Ishibashi, Ami Kawamoto, Sho Anzai, Reiko Kuno, Konomi Kuwabara, Junichi Takahashi, Minami Hama, Sayaka Nagata, Yui Hiraguri, Kento Takenaka, Shiro Yui, Kiichiro Tsuchiya, Tetsuya Nakamura, Kazuo Ohtsuka, Mamoru Watanabe, Ryuichi Okamoto. Single cell analysis of Crohn's disease patient-derived small intestinal organoids reveals disease activity-dependent modification of stem cell properties. J. Gastroenterol. 2018.09; 53(9); 1035-1047
5. Yamazaki K, Takenaka K, Ohtsuka K. Laterally Spreading Tumor-like Early Cancer in Ileum.[Epub ahead of print] Intern Med. 2018.10;

[Conference Activities & Talks]

1. Kitahata-kawai F, Asahina Y, Kakinuma S, Murakawa M, Nitta S, Nagata H, Kaneko S, Inoue E, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N and Watanabe M. Difference of gene mutational profile among viral- and non-viral HCC with or without prior HBV infection: Results of comprehensive deep sequencing analyses of cancer genes and HBV/A AV integration. EASL, The International Liver Congress 2018 2018.04.14 Paris (France)
2. Ohtsuka K, Takenaka K, Suzuki K, Fujii T, Nagahori M, Matsuoka K, Saito E, Katsukura N, Fukuda M, Araki A, Watanabe M. Usefulness of single-balloon enteroscopy: from a single center 990 experiences. DDW2018 2018.06.03 Washington D.C (USA)
3. Saito E, Suzuki K, Shimizu H, Motobayashi M, Takenaka K, Onizawa M, Fujii T, Nagahori M, Ohtsuka K, Watanabe M. The clinical efficacy of switching cases between Infliximab (IFX) and Adalimumab (ADA) in patients with ulcerative colitis. AOCC2018 2018.06.22 Shanghai (China)
4. Takenaka K, Ohtsuka K, Fujii T, Nagahori M, Saito E, Motobayashi M, Suzuki K, Watanabe M. Small bowel mucosal healing of Crohn's disease treated with anti-TNF antibodies. FALK Symposium 2018.09.07 Kyoto (JAPAN)

5. Nitta S, Kato T, Tuchiya J, Shinomiya-Inoue E, Sato A, Tsunoda T, Miyoshi M, Kitahata-Kawai F, Murakawa M, Istui Y, Azuma S, Nakagawa M, Kakinuma S, Asahina Y. The in vitro analysis of NS5A resistance-associated substitutions (RAS) observed in DAA treatment failure patients. 25th International Symposium on Hepatitis C Virus and Related Viruses 2018.10.09 Dublin (Ireland)
6. Nakagawa M, Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tomita M, Watanabe M. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)
7. Nitta S, Kato T, Tuchiya J, Sato A, Tsunoda T, Miyoshi M, Inoue- Shinomiya E, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The Characteristic and the Anti-HCV Reagents Susceptibility Analysis of NS5A Resistance-Associated Substitutions (RAS) Detected after Daa Treatment Failure Patients. AASLD, The Liver Meeting 2018 2018.11.10 San Francisco (USA)

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA
Junior Associate Professor Keiko KONDO
Assistant Professor Masayo YASUDA
Specially Appointed Assistant Professor Masayuki TOI, Chizuko SUGIMOTO
Graduate Student Anongwee LEEWANANTHAWET, Yuko INOUE
Resident Anri OTSU

(1) Outline

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care. Regarding research, the effects of the functional waters to organism and clinical application of them were investigated.

(2) Research

- 1) Clinical and basic studies on Ozone ultrafine bubble water (OUFBW) :antimicrobial activity and effects to eukaryotic cells (induction of anti-oxidant capacities and wound healing activities etc.)
- 2) Study on virulence factors of periodontopathic bacteria
- 3) Development of education system for dental (oral) hygienists to prevent oral diseases
- 4) Development of assessment program in technical education for dental (oral) hygienists

(3) Education

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care.

(4) Lectures & Courses

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care

(5) Clinical Services & Other Works

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

(6) Clinical Performances

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

(7) Publications**[Original Articles]**

1. Leewananthawet Anongwee, Arakawa Shinichi, Okano Tokuju, Ashida Hiroshi, Izumi Yuichi, Suzuki Toshihiko. in vitro におけるオゾン微細泡の生物学的影響の評価 (Evaluation the biological effects of Ozone Ultrafine-Bubble Water in vitro) 日本歯周病学会会誌. 2018.05; 60(春季特別); 135
2. Akiyama Masato, Takahashi Atsushi, Momozawa Yukihide, Arakawa Satoshi, Miya Fuyuki, Oshima Yuji, Yasuda Miho, Yoshida Shigeo, Yanagi Yasuo, Tanaka Koji, Ogura Yuichiro, Takahashi Kanji, Fujisawa Kimihiko, Kadonosono Kazuaki, Ishibashi Tatsuro, Sonoda Koh-hei. Genome-wide association study for response to ranibizumab therapy in 919 individuals with age-related macular degeneration INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE. 2018.07; 59(9);
3. Atsushi Oishi, Hitoyata Shimokawa,2 Eri Sakaniwa, Masayoshi Takahashi, Michiyo Miyashin, Shinichi Arakawa. Oxygen and air nanobubbles in water inhibit proliferation of dental follicle stem cells in vitro Journal of Dental Health Oral Disorders & Therapy. 2018.11; 9(6); 460-462

[Misc]

1. Shinichi Arakawa. Ozone antiseptic shows potential for treating severe gum infections Asia Research News 2015.

[Conference Activities & Talks]

1. Shinichi Arakawa. Relationship between oral health and systemic condition. International Conference On Dentistry and Integrated Medicine 2018.05.08 Tokyo, Japan
2. Arakawa S.. The clinical utilization of Ozone Ultrafine Bubble Water to get symbiosis. 2018.05.08
3. Anongwee Leewananthawet, Shinichi Arakawa, Tokuju Okano, Yuichi Izumi, Toshihiko Suzuki. Evaluation of the biological effects of Ozone Ultrafine-Bubble Water in vitro. 第 61 回春季日本歯周病学会学術大会 2018.06.01 東京
4. Kanako NORITAKE,Jun TSURUTA,Koji MIZUTANI,Keiko KONDO,Shinich ARAKAWA,Kouji ARAKI. Study on educational effect measurement of the IPW program in practical clinical training.. The 50th Annual Meeting of the Japan Society for Medical Education 2018.08.04 Tokyo
5. Shinichi Arakawa. Ozone Ultrafine Bubble Water (OUFBW) Basic characteristic and Clinical application. 上海市医学会第 11 回物理医学及び健康回復研究学術活動 2018 年度委員会会議 2018.10.17 上海市第一人民医院
6. Shinichi Arakawa. Basic characters and clinical application of Ozone Ultrafine bubble water. 上海市医学会第 11 回物理医学及び健康回復研究学術活動 2018.10.17 上海市第一人民医院
7. Shinichi Arakawa. Ozone Ultrafine Bubble Water Clinical utilization and biological effects. Nanobubble 2018, 2018.10.18 Suzhou, CHINA,
8. Clinical investigation of perioperative oral management in the oral health care clinic. 2018.12.01

Oral Care for Systemic Health Support

Professor Yuhji Kabasawa
Assistant Professor Kanade Ito

(1) Outline

(1) Education

We teach the knowledge and skills necessary for oral health activities through classes in charge. Specifically, we will teach about the relationship between oral health and general health such as perioperative oral function management and periodontal disease and diabetes. In addition to teaching health assessment of the oral and maxillofacial area, we will acquire basic knowledge and skills through vital signs measurement practice, emergency life-saving activity practice, which is one of general health evaluation indicators.

Furthermore, we lecture on the pathology, diagnosis and treatment related to mandibular oral cavity disease, and teach necessary knowledge on oral health education, prevention of oral diseases of people with basic diseases in the medical field.

(2) Research

We will conduct research to support maintenance and promotion of health by oral health. Especially contribute to people's health and well-being through research on perioperative oral cavity function management, research on oral care of people with underlying diseases, research on regeneration of jawbone with FGF-2, etc.

We also working about the Research on social inequalities in oral health.

(3) Clinical

In order to maintain and promote general health through oral health, we cooperate with each outpatient at the dentistry hospital and do dental prophylactic treatment of the patient and oral health education at oral care outpatient. In addition to oral care for inpatients at dental and medical hospital while working in cooperation with nurses, nutritionists, pharmacists and others, they practice oral care according to the condition of patients as a member of team medicine.

(2) Research

1. Oral health care of patients with oral cancer, cleft lip and palate and other oral diseases
2. Research for safety in supplements in oral functions
3. Research on social inequalities in oral health.
4. Basic research for bone regeneration using FGF-2.

(3) Education

Team medical practice, clinical practice, clinical practice, oral surgery and dental anesthesiology, clinical medicine, graduation research, health care services, biomaterials science, oral disease prevention basics and practical training, clinical oral health practice, Dental practice support theory,etc

(4) Lectures & Courses

The purpose is to develop dental hygienist who can contribute to oral and general health. Train student who can contribute to the health and welfare of people based on the knowledge and skills for oral health activities,

understanding oral medicine and social environmental factors that affect health.

(5) Clinical Services & Other Works

Oral care department, in cooperation with each outpatient in the dental school attached hospital, in order to maintain and improve the general health through oral health, do patients' dental preventive measures and oral health education in oral care outpatient. In addition, we do oral care for hospitalized patients in the dentistry department and medical hospital affiliated hospitals, we receive consultation about patient oral care from ward nurses, and instruct oral care methods according to patient condition.

In oral surgery unit, we are engaged in diagnosis, treatment, oral health guidance etc of various oral disease patients.

(6) Clinical Performances

Based on knowledge of oral medicine through oral care department, we are conducting perioperative oral function management with more specialized expertise.

(7) Publications

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA
Assistant Professor Hiromi OTSUKA(-March), Naoko ADACHI(April-)
Part-time lecturer Atsushi OHYAMA,
Hiromi OTSUKA (April-)
Graduate Students Master Course
Shin Yujeong,
Liao Shin Ru,
Sakura Hayashi(April-),
Liu Zhenyan(April-)

(1) Outline

In order to cultivate students' abilities to prevent and detect oral diseases at an early stage, which are important to maintain and improve the nation's health, we help students acquire deep academic knowledge and high standard skills in preventive oral health care such as skills to check over the condition of oral cavities. Additionally, we help students develop skills to provide oral health counseling and oral health promotion, and nurture human resources who can actively contribute the development of oral health promotion.

(2) Research

- 1) Preventive Oral Health Care Sciences
 - ① Incident factors and preventive methods on dental caries
 - ② Incident factors and preventive methods on periodontal disease
 - ③ Incident factors and preventive methods on oral malodor
 - ④ Incident factors and preventive methods on other oral diseases
- 2) Development of education system for the patients to prevent oral diseases and for dental hygiene students.
- 3) Development of new assessment programs in technical education for dental hygienist students.

(3) Clinical Services & Other Works

In our Oral Health Care Clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases, for the patients to maintain their oral health for the entire lifetime.

(4) Publications

[Original Articles]

1. Doki S, Harano S, Shinada K, Ohyama A, Kojimahara N. Return-to-work support programs for workers on sick leave: a systematic review and meta-analysis Sangyo eiseigaku zasshi = Journal of occupational health. 2018.11; 60(6); 169-179

[Conference Activities & Talks]

1. S. LIAO, Y. SHIN, N. ADACHI, K. SHINADA. A study of the relationship between schoolchildren's life habits and oral conditions on Taiwan. Japanese Association for Dental Research 66th annual meeting 2018.11.18 北海道札幌市
2. Y. SHIN, N. ADACHI, K. SHINADA. In vitro study of demineralization on porcine in infant formula milk and juice with *Streptococcus mutans*. Japanese Association for Dental Research 66th annual meeting 2018.11.18 北海道札幌市
3. Clinical investigation of perioperative oral management in the oral health care clinic. 2018.12.01

[Social Contribution]

1. Preventive Dentistry Seminar in Thailand, Dental Training Center , Radisson Blu Plaza Bangkok, 2018.12.15

Oral Health Sciences for Community Welfare

Professor Junichi FURUYA
Junior Associate Professor Rena NAKAYAMA
Graduate Student Akane BENIYA
Graduate Research Student Junji TOKUNAGA
Graduate Student (Gerodontology and Oral rehabilitation) Chiaki MATSUBARA
Graduate Student (Gerodontology and Oral rehabilitation) Michiyo OBANA

(1) Outline

The role of Department of Oral Health Sciences for Community Welfare is to develop education, practice, research for turning out dental profession who can play an important role as profession of oral function and eating in medical care and welfare of super-aging society. All of our research and education is based on daily medical and dental care so that we can produce medical and dental professions who can work globally and locally.

The department is particularly focusing on improving oral health such as mastication, swallowing, dentures and oral hygiene through dysphagia rehabilitation, diet modification support, multi-disciplinary team approach so that the department contributes to prevent and improve aspiration pneumonia, malnutrition, and quality of life. Recently, we're also focusing on oral function of stroke patients and community cooperation, oral function of dementia and MCI patients and dental care, and dentures and swallowing in team approach.

All educational and research activities are based on clinical practice and experiences so that knowledge and skills of oral function will be acquired. Concretely, oral functional rehabilitation and oral hygiene care are performed as oral health management for hospitalized and institutionalized patients, and out patient in clinic. In addition, we supply multi-disciplinary team approach as a member of NST (Nutrition Support Team), PCT (Palliative Care Team), Oral hygiene care team in medical hospital of TMDU, and Visiting Dysphagia Rehabilitation Team.

(2) Research

1. Oral function, mastication, swallowing and dentures for dysphagia rehabilitation of older people
2. Oral health management for multidisciplinary team approach (NST and palliative care team) in medical care and community welfare
3. Frailty, malnutrition and oral frailty of older people
4. Oral function of patients with stroke and dementia
5. Home care dentistry and team approach for enjoyment of oral intake in community welfare

(3) Education

Gerodontology
Welfare for older people
Nursing-care for older people
Prosthodontics
Home visiting dentistry
Community dental care

Social work
etc

(4) Publications

[Original Articles]

1. Takuya Kobayashi, Masafumi Kubota, Toshiyuki Takahashi, Ayaka Nakasato, Taro Nomura, Junichi Furuya, Hisatomo Kondo. Effects of tooth loss on brain structure: a voxel-based morphometry study. *J Prosthodont Res.* 2018.02;
2. Rena Nakayama, Akira Nishiyama, Masahiko Shimada. Bruxism-Related Signs and Periodontal Disease: A Preliminary Study *The Open Dentistry Journal.* 2018.05; 12; 400-405
3. Shunsuke Minakuchi, Kazuhiro Tsuga, Kazunori Ikebe, Takayuki Ueda, Fumiyo Tamura, Kan Nagao, Junichi Furuya, Koichiro Matsuo, Ken Yamamoto, Manabu Kanazawa, Yutaka Watanabe, Hirohiko Hirano, Takeshi Kikutani, Kaoru Sakurai. Oral hypofunction in the older population: Position paper of the Japanese Society of Gerodontology in 2016. *Gerodontology.* 2018.06; 35(4); 317-324
4. Mikami Y, Watanabe Y, Eda Hiro A, Motokawa K, Shirobe M, Yasuda J, Murakami M, Murakami K, Taniguchi Y, Furuya J, Hirano H. Relationship between mortality and Council of Nutrition Appetite Questionnaire scores in Japanese nursing home residents. *Nutrition (Burbank, Los Angeles County, Calif.).* 2018.08; 57; 40-45

[Conference Activities & Talks]

1. Yuki Ohara, Junichi Furuya, Adrienne Lapidos, Danielle Furgeson. Dental hygiene students' perceptions of social welfare education in a bachelor's degree program in Japan. *The 2018 ADEA Annual Session & Exhibition* 2018.03.18 Orlando, Florida
2. Chiaki Matsubara, Junichi Furuya, Rena Nakayama, Michiyo Obana, Shunsuke Minakuchi. Collaborative transdisciplinary team approach for oral health care of acute stroke patients. *Japan-Korea joint symposium The 24th Dysphagia Rehabilitation Society in Japan* 2018.09.07 仙台
3. Shohei Onodera, Junichi Furuya, Yasushi Tamada, Shigeharu Joh, Hisatomo Kondo. Differences of oral and pharyngeal movements during mastication and swallowing in edentulous elderly individuals by wearing complete dentures. . *Japan-Korea joint symposium The 24th Dysphagia Rehabilitation Society in Japan* 2018.09.07 仙台
4. Junichi Furuya. Functional occlusal scheme for complete dentures.. *Complete denture restoration techniques under different concepts.* 2018.10.27 Nanjing
5. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yuuko Kagihuku, Takashi Ono, Chihiro Akazawa, Takashi Asada, Shunsuke Minakuchi. Approaches of investigating oral function in Mild Cognitive Impairment (MCI) patients. *The 6th Tri-University Consortium* 2018.11.30 Tokyo
6. Clinical investigation of perioperative oral management in the oral health care clinic. 2018.12.01

Oral Health Care Education

Professor Naomi Yoshida
Junior Associate Professor Yuki Ohara

(1) Research

- 1) Research on oral health behavior
- 2) Research on oral health management
- 3) Research on frailty and oral frailty
- 4) Research and development of education methods in dental hygienists education

(2) Education

Oral health care education is special field of study which deals with establishment of theoretic and skill for health promotion to contribute to the development of the health. Educational objects of Oral health care education in the graduate course is to foster human resources who will be able to implement health promotion program in collaboration with other career or residents in many fields.

(3) Clinical Services & Other Works

In oral health care clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases for the patients to maintain their oral and general health in the entire lifetime.

(4) Publications

[Original Articles]

1. Watanabe Y, Arai H, Hirano H, Morishita S, Ohara Y, Eda Hiro A, Murakami M, Shimada H, Kikutani T, Suzuki T. Oral function as an indexing parameter for mild cognitive impairment in older adults Geriatr Gerontol Int. . 2018.01;
2. N Yoshida, K Sugimoto, S Suzuki, H Kudo. Change in oral health status associated with menopause in Japanese dental hygienists. Int J Dent Hyg. 2018.02; 16(1); 157-164
3. Undergraduate education in perioperative oral management for dental hygienists 2018.02; 12(2); 36-45
4. Ohara Y, Yoshida N, Kawai H, Obuchi S, Mataka S, Hirano H, Watanabe Y.. Response to comments on: Development of an oral health-related self-efficacy scale for use with older adults. Geriatr Gerontol Int. . 2018.03; 18(3); 514-515
5. Yuki Ohara, Naomi Yoshida, Hisashi Kawai, Shuichi Obuchi, Shiro Mataka, Hirohiko Hirano, Yutaka Watanabe. Response to comments on: Development of an oral health-related self-efficacy scale for use with older adults. Geriatr Gerontol Int. . 2018.05; 18(3); 514-515

6. Murakami Masaharu, Yutaka Watanabe, Edahiro Ayako, Yuki Ohara, Obuchi Shuichi, Kawai Hisashi, Hunkyung Kim, Yoshinori Fujiwara, Ihara Kazushige, Murakami Masato, Hirohiko Hirano. Factors related to dissociation between objective and subjective masticatory function in Japanese community-dwelling elderly adults. *J Oral Rehabil.* 2018.05;
7. Kento Umeki, Yutaka Watanabe, Hirohiko Hirano, Ayako Edahiro, Yuki Ohara, Hideyo Yoshida, Shuichi Obuchi, Hisashi Kawai, Masaharu Murakami, Daisuke Takagi, Kazushige Ihara,. The relationship between masseter muscle thickness and appendicular skeletal muscle mass in Japanese community-dwelling elders: A cross-sectional study *Archives of Gerontology and Geriatrics.* 2018.09; 78; 18-22

[Conference Activities & Talks]

1. Yuki Ohara, Junichi Furuya, Adrienne Lapidos, Danielle Furgeson. Dental hygiene students' perceptions of social welfare education in a bachelor' s degree program in Japan. The 2018 ADEA Annual Session & Exhibition 2018.03.18 Orlando, Florida

Basic Sciences of Oral Health Care

Junior Associate Professor Yujiro Sakamoto

(1) Outline

Graduate School of Medical and Dental Sciences has been reorganized in April 2012, and the section of Basic Sciences of Oral Health Care was established in Medical and Dental Science and Technology master' s program course.

(2) Research

- 1) Basic medical and dental studies for oral health care
- 2) Basic study on clinical application of oral health care
- 3) Gross anatomical study of head and neck region

(3) Education

Purpose of Education

Basic sciences of oral health care is a branch of morphological sciences, developmental biology, pathology and the neurosciences to understand the structure and function of human body and its pathological conditions. Students are taught in more detail about the normal tooth anatomy and occlusal function as well as the anatomy of the head and neck with specific attention to the skull, muscles, nerves, and arteries associated with the mouth and teeth. In addition, students are also taught the oral pathology and dental pharmacology and pharmaceuticals.

Subjects and contents.

- Structure and function of human body I and II: anatomy, histology, physiology, embryology, oral anatomy, oral histology, oral physiology.
- Mechanism of disease and promotion of recovery process: pathology, oral pathology, microbiology, immunology, pharmacology.
- Dental pharmacology and pharmaceuticals.
- Graduation thesis:

Other education.

- Human anatomy (in School of Medicine, Faculty of Medicine).
- Head and neck basic medical sciences (in School of Medicine, Faculty of Medicine and School of Dentistry, Faculty of Dentistry).
- Structure and function of human body (in Course for Oral Health Engineering, School of Oral Health Care Sciences, Faculty of Dentistry).
- Oral health generic care sciences (in Health Sciences and Biomedical Engineering, Graduate School of Medical and Dental Sciences).

(4) Publications

[Original Articles]

1. Paglio Audrey E., Bradley Aaron P., Tubbs R. Shane, Loukas Marios, Kozlowski Piotr B., Dilandro Anthony C., Sakamoto Yujiro, Iwanaga Joe, Schmidt Cameron, D'Antoni Anthony V.. Morphometric analysis of temporomandibular joint elements. JOURNAL OF CRANIO-MAXILLOFACIAL SURGERY. 2018.01; 46(1); 63-66
2. Sakamoto Y. Morphological Features of the Branching Pattern of the Hypoglossal Nerve. Anatomical record (Hoboken, N.J. : 2007). 2018.04; Published online;
3. Sakamoto Yujiro. Structural arrangement of the intrinsic muscles of the tongue and their relationships with the extrinsic muscles. SURGICAL AND RADIOLOGIC ANATOMY. 2018.06; 40(6); 681-688
4. Sakamoto Y. Morphological features of the glossopharyngeal nerve in the peripharyngeal space, the oropharynx and the tongue. Anatomical Record. 2018.11; Published online;

[Conference Activities & Talks]

1. Sakamoto Y. Structural Relationships between the Extrinsic and Intrinsic Muscles of the Tongue. The 35th annual meeting American Association of Clinical Anatomists 2018.07.09 Atlanta, USA.

Basic Oral Health Engineering

Professor Kazuhiro Aoki
Associate Professor Meiko Oki
Assistant Professor Shingo Kamijo

(1) Outline

Basic Oral Health Engineering is a department assigned to basic science field of oral health in three master course departments which were reorganized from the departments of Oral Health Engineering Course in 2015. The department is originated in Basic Oral Health Sciences.

The department of Basic Oral Health Engineering aims to create a scientific foundation for the clinical applications based on interdisciplinary research between engineering and biology and/or interface studies between basic and clinical sciences. We believe that these research activities, which are focused on the region of the oral cavity, can contribute to attaining healthy and happy living conditions. We have the responsibility to train our students to be medical personnel who are eager to contribute to people's happiness through a broad range of educational courses from basic level courses to professional level courses, which integrate areas of study such as the structure and function of the human body, stomatognathic region, pharmacology and the research process.

(2) Research

Research Subjects

- 1) The development of non-invasive methods of bone mass augmentation (Interdisciplinary research)
- 2) Research related to the connection between oral bacteria and systemic diseases
- 3) The development of surface coating materials for the prevention of plaque growth (International collaboration)
- 4) The fabrication of facial prostheses using a three-dimensional rapid manufacturing method
- 5) Clinical studies of treatments for patients with maxillofacial defects
- 6) The development of materials for facial prostheses
- 7) The education of dental technicians using computer simulation training

(3) Lectures & Courses

Basic Oral Health Engineering is a department of oral health engineering which deals with the basic oral health sciences to perform evidence-based oral health care and prosthetic treatments to support people to promote oral health and improve quality of life. Main objective of Basic Oral Health Engineering in the undergraduate course is to provide students opportunity to study the structure and function of the human body, pharmacology, fabrication of dental and maxillofacial prostheses, dental CAD/CAM technology and research process.

(4) Clinical Services & Other Works

Clinical activities

- Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects
- Making dental and maxillofacial prostheses

(5) Publications**[Original Articles]**

1. Yasuhiro Shimizu, Masud Khan, Genki Kato, Kazuhiro Aoki & Takashi Ono. Occlusal disharmony-induced stress causes osteopenia of the lumbar vertebrae and long bones in mice. *Scientific Reports*. 2018.01; 8(173); 1-9
2. Hideaki Inagawa, Natsuki Suzuki, Kazuhiro Aoki, Noriyuki Wakabayashi. Potential for estimation of Young's modulus based on computed tomography numbers in bone: A validation study using a nano-indentation test on murine maxilla *Dental, Oral and Craniofacial Research*. 2018.01; 4(4); 1-7
3. Yesiboli Yeerken, Takafumi Otomaru, Mohamed Said, Meiko Oki, Hisashi Taniguchi. Non-contact eye surface impression and fabrication of radiotherapy prosthesis for eyelid tumor with CAD/CAM technique. *Materials Today Communications*. 2018.06; 15; 322-324
4. Cui Xinnan, Murakami Tatsuya, Tamura Yukihiro, Aoki Kazuhiro, Hoshino Yu, Miura Yoshiko. Bacterial Inhibition and Osteoblast Adhesion on Ti Alloy Surfaces Modified by Poly(PEGMA-r-Phosmer) Coating *ACS APPLIED MATERIALS & INTERFACES*. 2018.07; 10(28); 23674-23681
5. Urata Mariko, Kokabu Shoichiro, Matsubara Takuma, Sugiyama Goro, Nakatomi Chihito, Takeuchi Hiroshi, Hirata-Tsuchiya Shizu, Aoki Kazuhiro, Tamura Yukihiro, Moriyama Yasuko, Ayukawa Yasunori, Matsuda Miho, Zhang Min, Koyano Kiyoshi, Kitamura Chiaki, Jimi Eijiro. A peptide that blocks the interaction of NF- κ B p65 subunit with Smad4 enhances BMP2-induced osteogenesis *JOURNAL OF CELLULAR PHYSIOLOGY*. 2018.09; 233(9); 7356-7366
6. Ikebuchi Yuki, Aoki Shigeki, Honma Masashi, Hayashi Madoka, Sugamori Yasutaka, Khan Masud, Kariya Yoshiaki, Kato Genki, Tabata Yasuhiko, Penninger Josef M., Udagawa Nobuyuki, Aoki Kazuhiro, Suzuki Hiroshi. Coupling of bone resorption and formation by RANKL reverse signalling *NATURE*. 2018.09; 561(7722); 195-200
7. Kamijo Shingo, Sugimoto Kumiko, Oki Meiko, Tsuchida Yumi, Suzuki Tetsuya. Trends in domiciliary dental care including the need for oral appliances and dental technicians in Japan *JOURNAL OF ORAL SCIENCE*. 2018.12; 60(4); 626-633

[Conference Activities & Talks]

1. N. Wakabayashi, H. Inagawa, N. Suzuki, K. Aoki, T. Yamazaki, C. Watanabe, N. Murakami.. Validity of Young's Modulus Estimated Based on Computed Tomography. 96th General Session & Exhibition of the IADR 2018.07.28 London, England
2. Van Anh Nguyen Vu, Maho Shiozawa, Meiko Oki, Tetsuya Suzuki. Analysis of three-dimensional shape of mandibular complete dentures. 1st Meeting of International Oral Health Engineering Consortium 2018.09.24 Tokyo, Japan
3. Ayaka Urakawa, Masud Khan, Yosuke Sasaki, Michiko Ozawa, Kazunari Akiyoshi, and Kazuhiro Aoki. An investigation of scaffold materials suitable for new bone anabolic agents. 1st Meeting of the International Oral Engineering Consortium 2018.09.24 Tokyo, Japan

[Awards & Honors]

1. The 2nd prize of the student competition at the 1st Meeting of International Oral Health Engineering Consortium (Ayaka Urakawa) , 2018.09

[Social Contribution]

1. Science Dialog (Dr. Masud Khan and Prof Kazuhiro Aoki), JSPS, Public school of Sagamihara juniro high school in Kanagawa prefecture, 2018.01.20

Oral Biomaterials Development Engineering

Professor
Junior Associate Professor
Assistant Professor

Hidekazu TAKAHASHI
Tohru YASUE
Naohiko IWASAKI

Graduate student (Master course)
Graduate student (Master course)
Graduate student (Doctor course)

Yuko NAKAJIMA (until March)
Yusuke YAMAMOTO (from April)
Patcharanun CHAIAMORNSUP (Advanced Biomaterials)

(1) Outline

Basic knowledge of dental materials and devices for oral health engineering are provided for student. Basic exercise for dental materials and prosthetic training are also provided. Development and evaluation of new dental materials are performed.

(2) Research

1. Evaluation of various factors on mechanical properties of teeth substance.
2. Evaluation of fatigue properties of dentin and dental materials using miniature testing pieces
3. Measurement of characteristics of dental ceramic materials and establishment of new testing methods for dental ceramics
4. Measurement of precise deformation using non-contact methods
5. Development of new composite resin with similar machinability of dentin
6. Study on dental root fracture mechanism
7. Application of various types of fiberglass for dentistry
8. Evaluation of composite resin mechanical properties and improvement their bonding efficiency to various materials.
9. Evaluation of impact force absorption of mouthguard and face protect materials

(3) Education

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices. The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible.

(4) Lectures & Courses

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices

used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices.

The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible. Presentation not only domestic but also international meeting is strongly encouraged.

(5) Clinical Services & Other Works

Participation in various congresses are strongly recommended. Assistance for standard publication is also cooperated. Especially, Prof. Takahashi, head of Oral Biomaterials Engineering acts as the chairperson of ISO TC106 Dentistry/SC9 Dental CAD/CAM systems for publishing ISO standards.

(6) Publications

[Original Articles]

1. Hubban Nasution, Krid Kamonkhantikul, Mansuang Arksornnukit, Hidekazu Takahashi. Pressure transmission area and maximum pressure transmission of different thermoplastic resin denture base materials under impact load. *J Prosthodont Res.* 2018.01; 62(1); 44-49
2. Pisaisit Chaijareenont, Sasiprapha Prakhamchai, Patcharawan Silthampitag, Hidekazu Takahashi, Mansuang Arksornnukit. Effects of different sulfuric acid etching concentrations on PEEK surface bonding to resin composite. *Dent Mater J.* 2018.01; 37;
3. 岩崎 直彦, 山本 宥佑, 高橋 英和. 改良した被削性評価試験機による CAD/CAM 用材料の評価 日本医歯科機器学会誌. 2018.04; 23(1); 31-33
4. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takahashi, Motohiro Uo. Improvement of the Shock Absorption Ability of a Face Guard by Incorporating a Glass-Fiber-Reinforced Thermoplastic and Buffering Space *BioMed Research International.* 2018.05; 2018; 1-8
5. Yuka Kajima, Atsushi Takaichi, Nuttaphon Kittikundecha, Takayuki Nakamoto, Takahiro Kimura, Naoyuki Nomura, Akira Kawasaki, Takao Hanawa, Hidekazu Takahashi, Noriyuki Wakabayashi. Effect of heat-treatment temperature on microstructures and mechanical properties of Co–Cr–Mo alloys fabricated by selective laser melting. *Materials Science and Engineering: A.* 2018.05; 726(30); 21-31
6. Kensuke Takakusaki, Kenji Fueki, Chiaki Tsutsumi, Yusuke Tsutsumi, Naohiko Iwasaki, Takao Hanawa, Hidekazu Takahashi, Kazuo Takakuda, Noriyuki Wakabayashi. Effect of incorporation of surface pre-reacted glass ionomer filler in tissue conditioner on the inhibition of *Candida albicans* adhesion. *Dent Mater J.* 2018.06; 37(3); 453-459
7. Pornpot Jiangkongkho, Mansuang Arksornnukit, Hidekazu Takahashi. The synthesis, modification, and application of nanosilica in polymethyl methacrylate denture base. *Dent Mater J.* 2018.07; 37(4); 582-591

[Books etc]

1. The newest series of textbooks for dental technologist, Dental Materials Science. 2018.01 (ISBN : 976-968-368-220-2)

[Conference Activities & Talks]

1. Hidekazu TAKAHASHI. Characteristics of composite resin blocks for CAD/CAM. The winter seminar of Japan Academy of Digital Dentistry 2018.02.18
2. Kajima Y, Takaichi A, Kittikundecha N, Nomura N, Takahashi H, Hanawa T, Wakabayashi N and Kawasaki A. Investigation of the effective heat treatment condition for controlling the anisotropy of selective laser melted Co-Cr alloy.. The Japan Institute of metals and materials 2018 Spring Annual Meeting 2018.03.20 Chiba

3. Maho Shiozawa, Tetsuya Suzuki, Naohiko Iwasaki, Hidekazu Takahashi. Discoloration of CAD/CAM resin materials for removable denture frameworks. 2018.04.14
4. Chaiamornsup P, Uo M, Yamamoto Y, Yasue T, Iwasaki N, Takahashi H. Effect of build direction and exposure time on edge reproducibility of prism specimens using DLP. 第71回日本歯科理工学会学術講演会 2018.04.14
5. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Yoshida Yuriko, Tanabe Gen, Uo Motohiro, Takahashi Hidekazu, Ueno Toshiaki. The behavior of pressure sensor with a built-in mouth guard material. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
6. Kittikundecha Nuttaphon, Kajima Yuka, Takaichi Atsushi, Nakamoto Takayuki, Doi Hisashi Tsutsumi Yusuke, Nomura Naoyuki, Kawasaki Akira, Takahashi Hidekazu, Hanawa Takao, Wakabayashi Noriyuki. Effect of heat treatment on the microstructure and fatigue strength of the Co-Cr-Mo alloy prepared by selective laser melting. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka
7. T. Yamazaki, N. Murakami, S. Suzuki, M. Yatabe, H. Takahashi, N. Wakabayashi.. Influence of block-out area on retentive force of non-metal clasp denture. The 127th Annual Meeting of the Japan Prosthodontic Society 2018.06.17 Okayama
8. Kajima Y, Takaichi A, Takahashi H, Wakabayashi N. Evaluation of effectiveness of heat treatment on Co-Cr-Mo alloy fabricated by selective laser melting. The 127th annual meeting of the Japan Prosthodontic society 2018.06.17
9. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The evaluation of a force sensor for the development of the mouth guard type wearable sensor. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
10. Maho Shiozawa, Hidekazu Takahashi. Discoloration of resin materials for CAD/CAM. 2018.07.22
11. N. Murakami, T. Yamazaki, S. Suzuki, M. Yatabe, H. Takahashi, N. Wakabayashi. Influence of block-out on retention of thermoplastic non-metal resin clasps. 96th General Session & Exhibition of the IADR IADR/PAN European regional congress 2018.07.28 London, England
12. Kittikundecha N, Kajima Y, Takaichi A, Doi H, Nomura N, Hanawa T, Wakabayashi N, Kawasaki A. Effect of heat treatment temperature on microstructures and fatigue strength of Co-Cr-Mo alloy clasps prepared by selective laser melting. Annual meeting of the Japanese Society for Biomaterials Tohoku Block 2018.08.24 Miyagi
13. Kittikundecha Nuttaphon, Kajima Yuka, Takaichi Atsushi, Nakamoto Takayuki, Doi Hisashi, Tsutsumi Yusuke, Nomura Naoyuki, Kawasaki Akira, Takahashi Hidekazu, Hanawa Takao, Wakabayashi Noriyuki. Relationship between microstructures and fatigue strengths in selective laser melted Co-Cr-Mo alloy subjected to heat treatments(和訳中). 日本歯科理工学会誌 2018.09.01
14. Yamamoto, Iwasaki N, Yasue T, Takahashi H. Color change of color modified CAD/CAM composite resin blocks after toothbrush wear. The 1st Meeting of International Oral Health Engineering Consortium Organizing Committee 2018.09.24 Tokyo Medical and Dental University
15. Chaiamornsup P, Iwasaki N, Yasue T, Wada T, Uo M, Takahashi H. Effects of glycerin immersion during post-curing process on mechanical property of polymers fabricated using digital light process. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo Garden Place Hotel
16. Kinjo R, Wada T, Churei H, Takahashi H, Ueno T, Uo M. Evaluating the use of a force sensor for the development of a mouth guard-type wearable sensor. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo Garden Place Hotel
17. Kittikundecha N, Kajima Y, Takaichi A, Nakamoto T, Doi H, Tsutsumi Y, Nomura N, Kawasaki A, Takahashi H, Hanawa T, Wakabayashi N. Relationship between microstructures and fatigue strengths in selective laser melted CoCrMo alloy subjected to heat treatment. The 72th General Session of the Japanese Society for Dental Materials and Devices 2018.10.07 Hokkaido

Oral Prosthetic Engineering

Professor Tetsuya SUZUKI

Junior Associate Professor Masaomi IKEDA

Research Associate Maho SHIOZAWA

(1) Outline

Oral Health Information Technology educates deepen understanding of the production of the dental prosthesis using the latest computer science and cultivate basics power to new technology development. This course cultivates the ability to offer high quality medical technology taking advantage of expertise or knowledge. And the purpose of this section is to educate professional dental technologists who has ability to apply newly developed materials and technologies and who is able to contribute in not only clinical situation but also research institution or educational organization at international levels. Presently, the latest technologies such as dental implant and dental CAD/CAM etc became popular by the development of materials and the progress in technologies among dental treatment. Therefore, it is necessary to understand and lean knowledge about newly developed materials and technologies for properly control the dental laboratory works. Furthermore, It is necessary that the communication skill for report information about the materials and technologies to dentists and dental hygienists. Based on these evidences, it is an education in which specialists are raised to not be bound by classification as technologist and have ambition.

(2) Research

- 1) The advanced technology which utilized a CAD/CAM system.
- 2) The education of dental technician which utilized computer simulation training.
- 3) Relation of "medical care to support life" and the dental technician.
- 4) Evaluation of newly developed materials.

(3) Education

Introduction of Oral Health Engineering, Introduction of Clinical Dental Technology, Formative Arts Practice, Basic Technology of Manufacturing, Teeth Morphological Curving, Advanced Teeth Morphological Curving, Conservative Dentistry, Science of Occlusion, Clinical Science of Occlusion, Communication Theory, Dental Technologist and law, Health Promotion, Basic Fixed Prosthodontics, Advanced Fixed Prosthodontics, Complete Denture Prosthodontics, Removable Partial Prosthodontics, Oral Rehabilitation Engineering, Laws for Dental Technologists, CAD/CAM System Technology, CAD/CAM System Technology Practice, Advanced Technology for Oral Health, Digital Image Processing Practice, Oral Appliances, Comprehensive Oral Rehabilitation Engineering Practice, Graduation Research, Graduation Product

(4) Publications

[Original Articles]

1. Sato T, Takagaki T, Ikeda M, Nikaido T, Burrow MF, Tagami J. Effects of Selective Phosphoric Acid Etching on Enamel Using "No-wait" Self-etching Adhesives. The journal of adhesive dentistry. 2018; 20(5); 407-415

2. Yusuke Kakiuchi, Tomohiro Takagaki, Masaomi Ikeda, Takaaki Sato, Naoko Matsui, Toru Nikaido, Michael F Burrow, Junji Tagami. Evaluation of MDP and NaF in Two-step Self-etch Adhesives on Enamel Microshear Bond Strength and Morphology of the Adhesive-Enamel Interface. *J Adhes Dent.* 2018; 20(6); 527-534
3. Arakida T, Kanazawa M, Iwaki M, Suzuki T, Minakuchi S.. Evaluating the influence of ambient light on scanning trueness, precision, and time of intra oral scanner. *J Prosthodont Res.* . 2018.02; 62(3); 324-329
4. Chindanai Ratanaporncharoen, Miyuki Tabata, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami, Yuji Miyahara. pH Mapping on Tooth Surfaces for Quantitative Caries Diagnosis Using Micro Ir/IrOx pH Sensor. *Anal. Chem.*. 2018.03; 90(7); 4925-4931
5. Sai Kham Lyann, Tomohiro Takagaki, Toru Nikaido, Motohiro Uo, Masaomi Ikeda, Alireza Sadr, Junji Tagami. Effect of Different Surface Treatments on the Tensile Bond Strength to Lithium Disilicate Glass Ceramics. *J Adhes Dent.* 2018.05; 20(3); 261-268
6. Yuichi Kitasako, Alireza Sadr, Yasushi Shimada, Masaomi Ikeda, Yasunori Sumi, Junji Tagami. Remineralization capacity of carious and non-carious white spot lesions: clinical evaluation using ICDAS and SS-OCT. *Clin Oral Investig.* 2018.06;
7. Keita Taguchi, Keiichi Hosaka, Masaomi Ikeda, Ryuzo Kishikawa, Richard Foxton, Masatoshi Nakajima, Junji Tagami. The effect of warm air-blowing on the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *J Prosthodont Res.* 2018.07; 62(3); 330-336
8. Lyann SK, Takagaki T, Nikaido T, Uo M, Ikeda M, Sadr A, Tagami J.. Effect of Different Surface Treatments on the Tensile Bond Strength to Lithium Disilicate Glass Ceramics. *J Adhes Dent.* . 2018.07; 20(3); 261-268
9. Nagano D, Nakajima M, Takahashi M, Ikeda M, Hosaka K, Sato K, Prasansuttiorn T, Foxton RM, Tagami J. Effect of Water Aging of Adherend Composite on Repair Bond Strength of Nanofilled Composites. *The journal of adhesive dentistry.* 2018.10; 1-9
10. Naruse Yuki, Takagaki Tomohiro, Matsui Naoko, Sato Takaaki, Ali Alghamdi, Ikeda Masaomi, Nikaido Toru, Tagami Junji. Effect of alumina-blasting pressure on adhesion of CAD/CAM resin block to dentin. *Dental Materials Journal.* 2018.10; 37(5); 805-811
11. Alqarni D, Nakajima M, Hosaka K, Ide K, Nagano D, Wada T, Ikeda M, Mamanee T, Thanatvarakorn O, Prasansuttiorn T, Foxton R, Tagami J. The repair bond strength to resin matrix in cured resin composites after water aging. *Dental materials journal.* 2018.11;
12. Kamijo Shingo, Sugimoto Kumiko, Oki Meiko, Tsuchida Yumi, Suzuki Tetsuya. Trends in domiciliary dental care including the need for oral appliances and dental technicians in Japan *JOURNAL OF ORAL SCIENCE.* 2018.12; 60(4); 626-633
13. Nakamoto Ayako, Ikeda Masaomi, Hiraishi Noriko, Nikaido Toru, Uo Motohiro, Tagami Junji. Effect of fluoride mouthrinse on adhesion to bovine root dentin *Dental Materials Journal.* 2018.12; 37(6); 919-927

[Conference Activities & Talks]

1. Maho Shiozawa, Tetsuya Suzuki, Naohiko Iwasaki, Hidekazu Takahashi. Discoloration of CAD/CAM resin materials for removable denture frameworks. 2018.04.14
2. Arakida T, Kanazawa M, Iwaki M, Soeda Y, Hada T, Suzuki T, Minakuchi S . The effect of artificial landmark to the precision of digital impression for edentulous jaw . 2018.04.14
3. ナシリ・ハンラー・レイラ , 高垣 智博, 猪越 正直, 池田 正臣, 二階堂 徹, 田上 順次. ジルコニアセラミックス接着前処理におけるカルボン酸系モノマーの効果. 日本歯科保存学会 148 回学術大会 2018.06.14
4. Arakida T, Kanazawa M, Iwaki M, Soeda Y, Hada T, Suzuki T, Minakuchi S . The effect of artificial landmark to the precision of digital impression to edentulous jaw . 2018.06.16
5. Maho Shiozawa, Hidekazu Takahashi. Discoloration of resin materials for CAD/CAM. 2018.07.22

6. Keiichi Hosaka, Juri Hayashi, Daisuke Araoka, Masatoshi Nakajima, Richard Foxton, Masaomi Ikeda, Wurihan, Yo Shibata, Takashi Miyazaki, Junji Tagami. Eight-year Durability of Resin-dentin Interfaces of a 1-SEA. IADR/PER General Session 2018.07.25 London, England
7. Van Anh Nguyen Vu, Maho Shiozawa, Meiko Oki, Tetsuya Suzuki. Analysis of three-dimensional shape of mandibular complete dentures. 1st Meeting of International Oral Health Engineering Consortium 2018.09.24 Tokyo, Japan
8. Nagano M., Ogata Y., Ikeda M., Tsukada K., Tokunaga K., Iida S.. RISK FACTORS LIVING WITH AN OSTOMY FROM RECTAL CANCER BASED ON PERISTOMAL EROSION. WOUND REPAIR AND REGENERATION 2018.10
9. ミン・カン・コ・コ, 高垣 智博, 高橋 彬文, 宇尾 基弘, 池田 正臣, 二階堂 徹, 田上 順次. セラミックス前処理剤の成分比が接着性能に及ぼす影響について. 日本歯科保存学会 149 回学術大会 2018.10
10. UEDA Nanako, TAKAGAKI Tomohiro, SATO Takaaki, Matsui Naoko, IKEDA Masaomi, NIKAIDO Toru, TAGAMI Junji. Effect of different surface treatment agents on the micro-shear bond strength to lithium disilicate ceramics. The 149th Meeting of the Japanese Society of Conservative Dentistry 2018.11.01
11. VICHEVA Martina, SATO Takaaki, TAKAGAKI Tomohiro, BABA Yuuta, IKEDA Masaomi, NIKAIDO Toru, TAGAMI Junji. Effect of Repair Systems on Dentin Bonding Performance. 日本歯科保存学会 平成 30 年度春季大会 (第 149 回) 2018.11.02

[Awards & Honors]

1. Best oral presentaion award, International Oral Health Engineering Consortium, 2018.09

Clinical Laboratory

General Manager

-Professor : Shuji Tohda

Associate Manager

-Junior Associate Professor : Tadashi Kanouchi

Assistant Professor : Miyako Murakawa

Assistant Professor : Ayako Nogami

Assistant Professor : Hideki Arima

Medical Staff : Shintaro Iida

(1) Outline

The Clinical Laboratory is a central clinical department that conducts laboratory tests in order to obtain information about the diagnosis, treatment, and prevention of diseases. Physiological tests such as electrocardiogram, echocardiography, pulmonary function tests, and electroencephalogram are also performed at our facility.

(2) Research

Our research subjects are

- 1) New genetic tests for hematological disorders,
- 2) Development of tests for molecular pathology and drug sensitivity of hematological malignancies,
- 3) Genotypic analysis of bacteria for monitoring those transmission in the hospital,
- 4) Development of electrophysiological diagnostic tests for peripheral neuropathies,
- 5) Clinical and electrophysiological study for amyotrophic lateral sclerosis,
- 6) Quality control of nerve conduction study,
- 7) Molecular mechanisms of treatment for hepatitis C.
- 8) Novel methods to analyze cardiac function using echocardiography.

(3) Education

We lecture on clinical laboratory medicine and give technical training on clinical laboratory tests and physiological function tests to not only the medical students and medical technologist students in the faculty of medicine of the university but also those in the other vocational school for medical technologists. We give a labo tour and practice to master course graduate students, too. We gave a general training for clinical laboratory medicine to ten junior residents of university hospital in 2018. We also held hands-on seminars of Gram staining, urinary sediment, cardiac and abdominal ultrasonography for the residents.

(4) Clinical Services & Other Works

Clinical laboratory bears an important responsibility for advanced and high quality medical care. Our clinical laboratory is based on the principle of providing the speedy and high quality tests. The highest level of advanced tests, such as qualitative and quantitative analysis of various viral DNA by the PCR method, are also introduced here. In the night time and holidays, the clinical laboratory provides blood products for transfusion in cooperation with the blood transfusion service of the hospital. The updated information on antibiotic sensitivity of the pathogens in each ward is also provided online regularly. Together with the division of infection control and prevention, we monitor the nosocomial transmission of bacteria such as MRSA by genotypic analysis of those. Our clinical laboratory and blood transfusion service have received accreditation of ISO15189 (Medical laboratories - Particular requirements for quality and competence) in June 2014, and renewed it with the latest version in June 2018. It means that the clinical laboratory is an international standard on quality and that our hospital is allowed to conduct the international clinical trials. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

(5) Clinical Performances

We are developing new diagnostic methods collaborating with various clinical departments. We are also supporting them in their diagnostic procedure.

(6) Publications

[Original Articles]

1. Yuna Horiuchi, Shao-Jui Lai, Azusa Yamazaki, Ayaka Nakamura, Ryunosuke Ohkawa, Kouji Yano, Takahiro Kameda, Shigeo Okubo, Shitsuko Shimano, Michio Hagihara, Shuji Tohda, Minoru Tozuka. Validation and application of a novel cholesterol efflux assay using immobilized liposomes as a substitute for cultured cells. *Biosci. Rep.* 2018.04; 38(2);
2. Shinji Ogihara, Ryoichi Saito, Etsuko Sawabe, Takahiro Kozakai, Mari Shima, Yoshibumi Aiso, Toshihide Fujie, Yoko Nukui, Ryuji Koike, Michio Hagihara, Shuji Tohda. Molecular typing of methicillin-resistant *Staphylococcus aureus*: Comparison of PCR-based open reading frame typing, multilocus sequence typing, and *Staphylococcus* protein A gene typing. *J. Infect. Chemother.* 2018.04; 24(4); 312-314
3. Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Ayako Nogami, Gaku Oshikawa, Toshikage Nagao, Osamu Miura. Mechanisms for mTORC1 activation and synergistic induction of apoptosis by ruxolitinib and BH3 mimetics or autophagy inhibitors in JAK2-V617F-expressing leukemic cells including newly established PVT-2. *Oncotarget*. 2018.06; 9(42); 26834-26851
4. Horiuchi Yuna, Lai Shao-Jui, Yamazaki Azusa, Nakamura Ayaka, Ohkawa Ryunosuke, Yano Kouji, Kameda Takahiro, Okubo Shigeo, Shimano Shitsuko, Hagihara Michio, Tohda Shuji, Tozuka Minoru. VALIDATION AND APPLICATION OF A NOVEL CHOLESTEROL EFFLUX ASSAY USING IMMOBILIZED LIPOSOMES AS A SUBSTITUTE FOR CULTURED CELLS ATHEROSCLEROSIS SUPPLEMENTS. 2018.06; 32; 59
5. Yonekura S, Itoh M, Shiratori E, Ohtaka M, Tohda S. FOXP3 knockdown inhibits the proliferation and reduces NOTCH1 expression of T cell acute lymphoblastic leukemia cells. *BMC research notes*. 2018.08; 11(1); 582
6. Wang S, Itoh M, Shiratori E, Ohtaka M, Tohda S. NOTCH activation promotes glycosyltransferase expression in human myeloid leukemia cells. *Hematology reports*. 2018.09; 10(3); 7576
7. Hamada Satomi, Hasegawa Yuki, Oono Ai, Suzuki Anna, Takahashi Naomi, Nishimura Takuro, Koyama Takatoshi, Hagihara Michio, Tohda Shuji, Furukawa Tetsushi, Hirao Kenzo, Sasano Tetsuo. Differential Assessment of Factor Xa Activity and Global Blood Coagulability Utilizing Novel Dielectric Coagulometry SCIENTIFIC REPORTS. 2018.10; 8(1); 16129
8. Nakagawa Mina, Asahina Yasuhiro, Kawai-Kitahata Fukiko, Murakawa Miyako, Nitta Sayuri, Itsui Yasuhiro, Azuma Seishin, Kakinuma Sei, Tomita Makoto, Watanabe Mamoru. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients HEPATOLOGY. 2018.10; 68; 398A

9. Ayako Nogami, Keigo Okada, Shinya Ishida, Hiroki Akiyama, Yoshihiro Umezawa, Osamu Miura. Inhibition of the STAT5/Pim Kinase Axis Enhances Cytotoxic Effects of Proteasome Inhibitors on FLT3-ITD-Positive AML Cells by Cooperatively Inhibiting the mTORC1/4EBP1/S6K/Mcl-1 Pathway. *Transl Oncol.* 2018.11; 12(2); 336-349
10. Okuhashi Yuki, Itoh Mai, Tohda Shuji. GLI1 and CTNNB1 Knockdown Activates NOTCH and mTOR Signalling in NB4 Myeloid Leukaemia Cells *ANTICANCER RESEARCH.* 2018.11; 38(11); 6329-6332

[Conference Activities & Talks]

1. Kitahata-kawai F, Asahina Y, Kakinuma S, Murakawa M, Nitta S, Nagata H, Kaneko S, Inoue E, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N and Watanabe M. Difference of gene mutational profile among viral- and non-viral HCC with or without prior HBV infection: Results of comprehensive deep sequencing analyses of cancer genes and HBV/A AV integration. *EASL, The International Liver Congress 2018* 2018.04.14 Paris (France)
2. Miyako Murakawa, Yasuhiro Asahina, Mamoru Watanabe. The analysis of viral kinetics and the predictive factors for HBsAg loss during long term observation of patients with chronic HBV infection.. *The 54th Annual Meeting of Japan Society of Hepatology* 2018.06.14 Osaka
3. Ayako Nogami, Keigo Okada, Daisuke Watanabe, Hiroki Akiyama, Yoshihiro Umezawa, Shinya Ishida, Gaku Oshikawa, Shuji Tohda, Osamu Miura . Proteasome Inhibitors Downregulate the mTORC1/4EBP1/S6K/Mcl-1 Pathway Cooperatively with Inhibitors for The STAT5/Pim Kinase Pathway to Induce Apoptosis in FLT3-ITD-positive AML Cells. *The 9th JSH International Symposium 2018* 2018.07.28 Kyoto
4. Kazuaki Yamamoto, Yumi Iwasaki, Michio Hagihara, Shuji Tohda. Multiplex strip PCR test for rapid and simultaneous detection of twelve kinds of virus DNA in patients' samples. *15th congress of the Asian society of clinical pathology and laboratory medicine* 2018.09.07
5. Nitta S, Kato T, Tuchiya J, Shinomiya-Inoue E, Sato A, Tsunoda T, Miyoshi M, Kitahata-Kawai F, Murakawa M, Istui Y, Azuma S, Nakagawa M, Kakinuma S, Asahina Y. The in vitro analysis of NS5A resistance-associated substitutions (RAS) observed in DAA treatment failure patients. *25th International Symposium on Hepatitis C Virus and Related Viruses* 2018.10.09 Dublin (Ireland)
6. Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Nakagawa M, Kakinuma S, Watanabe M. Gene Mutational Profile and Viral Integration in Hepatocellular Carcinoma with or without HBV/HCV Suppression. *AASLD, The Liver Meeting 2018* 2018.11.10 San Francisco (USA)
7. Nakagawa M, Asahina Y, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tomita M, Watanabe M. Post-Treatment M2BPGi Level Is Useful for Predicting HCC Occurrence and Recurrence after Viral Eradication in Chronic Hepatitis C Patients. *AASLD, The Liver Meeting 2018* 2018.11.10 San Francisco (USA)
8. Nitta S, Kato T, Tuchiya J, Sato A, Tsunoda T, Miyoshi M, Inoue- Shinomiya E, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The Characteristic and the Anti-HCV Reagents Susceptibility Analysis of NS5A Resistance-Associated Substitutions (RAS) Detected after Daa Treatment Failure Patients. *AASLD, The Liver Meeting 2018* 2018.11.10 San Francisco (USA)

Center for Transfusion Medicine and Cell Therapy

Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine/Professor)
 Vice Director: Michiko Kajiwara (Center for Transfusion Medicine and Cell Therapy/Junior Associate Professor)
 Vice Director: Hisako Katano (Center for Stem Cell and Regenerative Medicine/Assistant Professor)
 Quality control manager: Norio Shimizu (Center for Stem Cell and Regenerative Medicine/Associate Professor)
 Product manager: Mitsuru Mizuno (Center for Stem Cell and Regenerative Medicine/Project Assistant Professor)
 Specially Appointed Assistant Professor: Shihoko Suwa (Center for Transfusion Medicine and Cell Therapy)
 Project Researcher: Kei-ichiro Komori (Center for Stem Cell and Regenerative Medicine)
 Head Medical Technologist: Naoki Ohtomo
 Section Chief Medical Technologist: Keiko Baba
 Assisitant Section Chief Medical Technologist: Yukiko Ohishi
 Medical Technologist: Yukari Usui, Kaoru Okuyama, Chihiro Toyama, Miho Yamasaki, Misaki Chiba
 Technician: Yuri Kohno, Ayako Tsuji
 Clerical Assistant: Jun Kusano, Saki Nishimura

(1) Outline

Center for Transfusion Medicine and Cell Therapy provides “Blood Transfusion”, “Cell Therapy” and “Regenerative Medicine” to assist and regenerate dysfunctional tissues and organs.

In the Blood Transfusion group, Japan Society of Blood Transfusion and Cell Therapy Association certified doctors, certified blood transfusion laboratory stuffs, and cell therapy certified administrators enroll. We cover blood transfusion testing, blood product management, safety measures up to the implementation of blood transfusion including blood transfusion certification, and blood transfusion history management. We perform safe and appropriate blood transfusion therapy and hematopoietic stem cell transplantation.

In the Cell Therapy group, we set up a cell processing facility with the aim of putting the world’s top level of regenerative medicine and cell therapy into practical use. Japan Society of Regenerative Medicine certified doctors and clinical culture specialists process cells for clinical research and trials there. We support the practical application of useful regenerative medicine procedures inside and outside our university.

(2) Research

· Blood Transfusion group

- 1) The practice of safe and appropriate transfusion therapy
(including prevention of medical accident related transfusion)
- 2) Basic and clinical research of hematopoietic stem cell transplantation

· Cell Therapy group

- 1) Development of innovative techniques for quality assurance of cell products
- 2) Development of a novel measure for rapid and sensitive detection of multiple pathogens
- 3) Development of multi-virus specific T lymphocytes for adoptive immunotherapy
(Department of Pediatrics and Developmental Biology)
- 4) Research on a regeneration system of the cartilage from the synovial membrane
(Department of Orthopedic Surgery)
- 5) Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia

(Department of Immunotherapeutics/ Department of Hematology)

(3) Education

· Blood Transfusion group

Transfusion therapy is supplementation of the blood component, but it also has aspects of cell therapy and transplantation. So, it is important to practice safe and appropriate transfusion therapy. Clinical tests of transfusion, such as blood type test, are the most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of the medical treatment. From this point of view, we educate the students of the school of medicine, school of allied health sciences, a graduate school of medical and dental sciences, medical doctors, and co-medicals.

· Cell Therapy group

Center of Cell Therapy assist to prepare standard operation procedure (SOP) and offer on-the-job training for cell processing/ manipulating procedures and that for quality assurance at the center. Facility for the education and training were recently installed at the CPC annex.

(4) Clinical Services & Other Works

Clinical Services (The result of 2018)

1)The number of blood products used

Red cell component products 12,148 Units (6,169 bags)

Platelet concentration 30,940 Units (2,560 bags)

Fresh frozen plasma 9,462 Units (4,372 bags)

2)Autologous blood collection and transfusion

Autologous blood collection 236 cases (314 times, 614 Units)

Autologous blood transfusion 204 cases (495 Units)

3)The number of clinical tests of transfusion

Blood typing 11,340

Anti-red blood cell antibody test 5,367

Crossmatch 11,726

4)Hematopoietic stem cell harvest

Autologous peripheral blood stem cell harvest 11cases 12times

Allogenic peripheral blood stem cell harvest 4cases 5times

Allogenic bone marrow harvest 11cases 11times

(Including Japan Marrow Donor Program donors)

5)Hematopoietic stem cell transplantation

(The evaluation and preservation of the stem cells were done in our department)

Autologous peripheral blood stem cell transplantation 13cases 13times

Allogenic peripheral blood stem cell transplantation 4cases 4times

Allogenic bone marrow transplantation 12 cases 12times

Allogenic umbilical cord blood transplantation 3cases 3times

The cell products currently prepared in our center include

#1 Synovium-derived mesenchymal stem cells

#2 Processed peripheral blood stem cells

(5) Clinical Performances

· Blood Transfusion group

We provide safe and wide of variation transfusion therapy. We cope with highly urgent blood transfusion of critical care center and blood transfusion with a high specialty such as NICU. In the area of hematopoietic stem cell transplantation, we closely cooperate with the clinical department. Transfusion medicine staffs mainly conduct collection, evaluation, processing, and storage of cells.

· Cell Therapy group

Our center in TMDU Medical Hospital was renovated and re-started operation as of March 2015. We have five Central Clinical Facilities independent cell processing rooms (class 10,000 clean rooms). All the rooms are equipped with a bio-safety cabinet. The hardware, as well as software used in our center, fulfills all the guidelines that are required for the preparation of cell products of clinical grade.

(6) Publications

[Original Articles]

1. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep.* 2018.01; 8(1); 1288
2. Kana Ishii, Hidetoshi Sakurai, Nobuharu Suzuki, Yo Mabuchi, Ichiro Sekiya, Kiyotoshi Sekiguchi, Chihiro Akazawa. Recapitulation of Extracellular LAMININ Environment Maintains Stemness of Satellite Cells In Vitro. *Stem Cell Reports.* 2018.02; 10(2); 568-582
3. Takasawa Kei, Nakagawa Ryuichi, Takishima Shigeru, Moriyama Kengo, Watanabe Ken, Kiyohara Koji, Hasegawa Takeshi, Shimohira Masahiro, Kashimada Kenichi, Shimizu Norio, Morio Tomohiro. Cause of acute encephalitis/encephalopathy in Japanese children diagnosed by a rapid and comprehensive virological detection system and differences in their clinical presentations *Brain & Development.* 2018.02; 40(2); 107-115
4. Yuji Kohno, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Koji Otabe, Hideyuki Koga, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Ichiro Sekiya. Comparison of mesenchymal stem cells obtained by suspended culture of synovium from patients with rheumatoid arthritis and osteoarthritis. *BMC Musculoskelet Disord.* 2018.03; 19(1); 78
5. Ken Watanabe, Koji Otabe, Norio Shimizu, Keiichirou Komori, Mitsuru Mizuno, Hisako Katano, Hideyuki Koga, Ichiro Sekiya. High-sensitivity virus and mycoplasma screening test reveals high prevalence of parvovirus B19 infection in human synovial tissues and bone marrow. *Stem Cell Res Ther.* 2018.03; 9(1); 80
6. Kanehiro Hiyama, Yusuke Nakagawa, Toshiyuki Ohara, Takeshi Muneta, Toshifumi Watanabe, Masafumi Horie, Koji Otabe, Hiroki Katagiri, Kenta Katagiri, Mai Katakura, Takashi Hoshino, Hiroko Ueki, Kei Inomata, Naoko Araya, Ichiro Sekiya, Hideyuki Koga. Anterior cruciate ligament injuries result in a larger functional deficit in fighting sport athletes: comparison of functional status among different sport types. *Journal of ISAKOS.* 2018.03; (3); 128-133
7. Setsuko Shioda, Fumio Kasai, Ken Watanabe, Kohei Kawakami, Azusa Ohtani, Masashi Iemura, Midori Ozawa, Akemi Arakawa, Noriko Hirayama, Eiko Kawaguchi, Tomoko Tano, Sayaka Miyata, Motonobu Satoh, Norio Shimizu, Arihiro Kohara. human cells by viral infection. *R Soc Open Sci.* 2018.05; 5(5); 172472
8. Mitsuru Mizuno, Hisako Katano, Yo Mabuchi, Yusuke Ogata, Shizuko Ichinose, Shizuka Fujii, Koji Otabe, Keiichiro Komori, Nobutake Ozeki, Hideyuki Koga, Kunikazu Tsuji, Chihiro Akazawa, Takeshi Muneta, Ichiro Sekiya. Specific markers and properties of synovial mesenchymal stem cells in the surface, stromal, and perivascular regions. *Stem Cell Research & Therapy.* 2018.05; 9(1); 123
9. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Nobutake Ozeki, Koji Otabe, Keiichiro Komori, Shizuka Fujii, Shizuko Ichinose, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Petaloid recombinant peptide enhances in vitro cartilage formation by synovial mesenchymal stem cells. *Journal of Orthopaedic Research.* 2018.05;
10. Noguchi Y, Tomizawa D, Hiroki H, Miyamoto S, Tezuka M, Miyawaki R, Tanaka-Kubota M, Okano T, Kobayashi C, Mitsuiki N, Aoki Y, Imai K, Kajiwara M, Kanegane H, Morio T, Takagi M.. Hematopoietic cell transplantation for myeloid/NK cell precursor acute leukemia in second remission. *Clin Case Rep.* 2018.06; 6(6); 1023-1028

11. Mari Uomizu, Takeshi Muneta, Miyoko Ojima, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. PDGF-induced proliferation and differentiation of synovial mesenchymal stem cells is mediated by the PI3K-PKB/Akt pathway. *J Med Dent Sci.* 2018.06; 65(2); 73-82
12. Ogata Yusuke, Mabuchi Yo, Shinoda Kosuke, Horiike Yuta, Mizuno Mitsuru, Otabe Koji, Suto Eriko Grace, Suzuki Nobuharu, Sekiya Ichiro, Akazawa Chihiro. Anterior cruciate ligament-derived mesenchymal stromal cells have a propensity to differentiate into the ligament lineage *Regenerative Medicine.* 2018.06; 8; 20-28
13. Masaaki Yoshida, Takehiro Hariya, Shunji Yokokura, Kazuichi Maruyama, Kota Sato, Sunao Sugita, Yasuhiro Tomaru, Norio Shimizu, Toru Nakazawa. Diagnosing superinfection keratitis with multiplex polymerase chain reaction. *J. Infect. Chemother..* 2018.07;
14. Erika Onozawa, Haruna Shibayama, Honami Takada, Ken-Ichi Imadome, Sho Aoki, Mayumi Yoshimori, Norio Shimizu, Shigeyoshi Fujiwara, Takatoshi Koyama, Osamu Miura, Ayako Arai. STAT3 is constitutively activated in chronic active Epstein-Barr virus infection and can be a therapeutic target. *Oncotarget.* 2018.07; 9(57); 31077-31089
15. Hiroyuki Takahashi, Ryosuke Kajiwara, Motohiro Kato, Daisuke Hasegawa, Daisuke Tomizawa, Yasushi Noguchi, Kazutoshi Koike, Daisuke Toyama, Hiromasa Yabe, Michiko Kajiwara, Junya Fujimura, Manabu Sotomatsu, Setsuo Ota, Miho Maeda, Hiroaki Goto, Yoko Kato, Tetsuya Mori, Takeshi Inukai, Hiroyuki Shimada, Keitaro Fukushima, Chitose Ogawa, Atsushi Makimoto, Takashi Fukushima, Kentaro Ohki, Katsuyoshi Koh, Nobutaka Kiyokawa, Atsushi Manabe, Akira Ohara. Treatment outcome of children with acute lymphoblastic leukemia: the Tokyo Children's Cancer Study Group (TCCSG) Study L04-16. *Int. J. Hematol..* 2018.07; 108(1); 98-108
16. Nakano Satoko, Tomaru Yasuhiro, Takase Hiroshi, Kubota Toshiaki, Mochizuki Manabu, Shimizu Norio, Sugita Sunao. Evaluation of a multiplex Strip PCR examination for infectious uveitis and endophthalmitis: A prospective multi-center study *INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE.* 2018.07; 59(9);
17. Kaori Nakamura, Kunikazu Tsuji, Mitsuru Mizuno, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Initial cell plating density affects properties of human primary synovial mesenchymal stem cells. *J. Orthop. Res..* 2018.07;
18. Hisako Katano, Hideyuki Koga, Nobutake Ozeki, Koji Otabe, Mitsuru Mizuno, Makoto Tomita, Takeshi Muneta, Ichiro Sekiya. Trends in isolated meniscus repair and meniscectomy in Japan, 2011-2016 *PLoS ONE.* 2018.07; 23(4); 676-681
19. Shiori Kinoshita, Takashi Ishida, Asahi Ito, Tomoko Narita, Ayako Masaki, Susumu Suzuki, Takashi Yoshida, Masaki Ri, Shigeru Kusumoto, Hirokazu Komatsu, Norio Shimizu, Hiroshi Inagaki, Taruho Kuroda, Arne Scholz, Ryuzo Ueda, Takaomi Sanda, Shinsuke Iida. Cyclin-dependent kinase 9 as a potential specific molecular target in NK cell leukemia/lymphoma. *Haematologica.* 2018.08;
20. Akari Sasaki, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Manabu Mochizuki, Ichiro Sekiya. Canine mesenchymal stem cells from synovium have a higher chondrogenic potential than those from infrapatellar fat pad, adipose tissue, and bone marrow. *PLoS ONE.* 2018.08; 13(8); e0202922
21. Okuno Y, Murata T, Sato Y, Muramatsu H, Ito Y, Watanabe T, Okuno T, Murakami N, Yoshida K, Sawada A, Inoue M, Kawa K, Seto M, Ohshima K, Shiraishi Y, Chiba K, Tanaka H, Miyano S, Narita Y, Yoshida M, Goshima F, Kawada JI, Nishida T, Kiyoi H, Kato S, Nakamura S, Morishima S, Yoshikawa T, Fujiwara S, Shimizu N, Isobe Y, Noguchi M, Kikuta A, Iwatsuki K, Takahashi Y, Kojima S, Ogawa S, Kimura H.. defective epstein-barr virus in chronic active infection and haematological malignancy. *Clinical blood.* 2018.09; 59(9); 1484
22. Yoichi Murata, Soshi Uchida, Hajime Utsunomiya, Akihisa Hatakeyama, Hirotaka Nakashima, Angela Chang, Ichiro Sekiya, Akinori Sakai. Synovial mesenchymal stem cells derived from the cotyloid fossa synovium have higher self-renewal and differentiation potential than those from the paralabral synovium in the hip joint. *American Journal of Sports Medicine.* 2018.10; 46(12); 2942-2953

23. Okuno Yusuke, Murata Takayuki, Sato Yoshitaka, Muramatsu Hideki, Ito Yoshinori, Watanabe Takahiro, Okuno Tatsuya, Murakami Norihiro, Yoshida Kenichi, Sawada Akihisa, Inoue Masami, Kawa Keisei, Seto Masao, Ohshima Koichi, Shiraishi Yuichi, Chiba Kenichi, Tanaka Hiroko, Miyano Satoru, Narita Yohei, Yoshida Masahiro, Goshima Fumi, Kawada Junichi, Nishida Tetsuya, Kiyoi Hitoshi, Kato Seiichi, Nakamura Shigeo, Morishima Satoko, Fujiwara Shigeyoshi, Shimizu Norio, Isobe Yasushi, Noguchi Masaaki, Kikuta Atsushi, Iwatsuki Keiji, Takahashi Yoshiyuki, Kojima Seiji, Ogawa Seishi, Kimura Hiroshi. The Presence of Defective Epstein-Barr Virus (EBV) Infection in Patients with EBV-Associated Hematological Malignancy BLOOD. 2018.11; 132;
24. Yoshida Masaaki, Hariya Takehiro, Yokokura Shunji, Maruyama Kazuichi, Sato Kota, Sugita Sunao, Tomaru Yasuhiro, Shimizu Norio, Nakazawa Toru. Diagnosing superinfection keratitis with multiplex polymerase chain reaction(和訳中) Journal of Infection and Chemotherapy. 2018.12; 24(11-12); 1004-1008
25. Hiroko Ueki, Yusuke Nakagawa, Toshiyuki Ohara, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Kenta Katagiri, Kanehiro Hiyama, Mai Katakura, Takashi Hoshino, Kei Inomata, Naoko Araya, Ichiro Sekiya. Risk factors for residual pivot shift after anterior cruciate ligament reconstruction: data from the MAKS group. Knee Surg Sports Traumatol Arthrosc. 2018.12; 26(12); 3724-3730

[Conference Activities & Talks]

1. Yuji Kohno, Nobutake Ozeki, Akinobu Hyodo, So Suzuki, Hayato Aoki, Yoshihisa Kushida, Naoto Watanabe, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Validations for cartilage thickness, cartilage area ratio and meniscus volume in the knee by 3D MRI analysis. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
2. Yuji Kohno, Hideyuki Koga, Nobutake Ozeki, Junpei Matsuda, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Ichiro Sekiya. Biomechanical analysis of meniscus centralization for extruded meniscus after meniscectomy. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
3. Koji Otabe, Kenta Katagiri, Toshiyuki Ohara, Hiroki Katagiri, Masafumi Horie, Toshifumi Watanabe, Hideyuki Koga, Ichiro Sekiya. Wide Oval Gantry 3.0T MRI Analysis Revealed Dynamic Knee Neurovascular Transposition During Flexion of the Knee. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
4. So Suzuki, Nobutake Ozeki, Akinobu Hyodo, Hayato Aoki, Yoshihisa Kushida, Naoto Watanabe, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. "Cartilage Area Ratio" by MRI 3D Analysis Reveals Subtle Change of Cartilage Volume in Middle Aged Patients with Medial Meniscus Degenerative Tear. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
5. Nobutake Ozeki, Yuji Kohno, Yoshihisa Kushida, Naoto Watanabe, Kenta Katagiri, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Tomoyuki Saito, Ichiro Sekiya. Three-Dimensional MRI, T2 Mapping and Histological Analyses of Meniscus Repair After Transplantation of Synovial Mesenchymal Stem Cells in a Novel Degenerative Meniscus Injury Model in Pig. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
6. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichi Komori, Shizuka Fujii, Shizuko Ichinose, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Petaloid Recombinant Peptide Constructs the Framework of Cartilage Pellet and Promotes In Vitro Cartilage Formation. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
7. Akari Sasaki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Manabu Mochizuki, Ichiro Sekiya. Comparison Of Canine Mesenchymal Stem Cells Derived From Synovium, Infrapatellar Fat Pad, Subcutaneous Adipose Tissue And Bone Marrow. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
8. Ryota Fujisawa, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichi Komori, Shizuka Fujii, Nobutake Ozeki, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Investigation of Freezing Medium for Synovial Mesenchymal Stem Cells. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA

9. Miharuru Ochi, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Effects of synovial stem cells and BMP-2 on cartilage formation of tendon. Orthopaedic Research Society 2018 Annual Meeting 2018.03.11 New Orleans, USA
10. Naoto Watanabe, Mitsuru Mizuno, Jumpei Matsuda, Naoko Nakamura, Koji Otabe, Hisako Katano, Nobutake Ozeki, Yuji Kono, Tsuyoshi Kimura, Kunikazu Tsuji, Hideyuki Koga, Akio Kishida, Ichiro Sekiya. Can Decellularized Meniscus by High Hydrostatic Pressure be an Alternative to Meniscus Allograft? - Compared with Deep Frozen Meniscus. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
11. Mitsuru Mizuno, Hisako Katano, Yuri Shimozaeki, Sho Sanami, Keiichiro Komori, Koji Otabe, Nobutake Ozeki, Kunikazu Tsuji, Koga Hideyuki, Ichiro Sekiya. Image Analysis Method to Predict Cell Proliferation at Early Phase for Autologous Synovial Stem Cell Transplantation. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
12. Hayato Aoki, Nobutake Ozeki, Kohno yuji, Kushida Yoshihisa, Naoto Watanabe, Akinobu Hyodo, So Suzuki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Yoshinori Itai, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Mri 3d Analysis For Discoid Lateral Meniscus Of The Knee. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
13. Yoshihisa Kushida, Koichiro Kishima Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Pseudo Color Images and Volume Measurement of Cartilage by Optical Coherence Tomography in a Rat Meniscectomized Model. Orthopaedic Research Society 2018 Annual Meeting 2018.03.12 New Orleans, USA
14. Watanabe k, Shimada H, Yunomae Y, Shimizu N, Sekiya I. . Ensuring microbiol safety in regenerative medicine: Development of rapid detection method for live or dead bacteria selection.. 17th The Japanese Society for Regenerative Medicine 2018.03.21 Yokohama, Japan.
15. Ichiro Sekiya. Transplantation of synovial mesenchymal stem cells onto repaired meniscus with degenerative tear. 5th TERMIS World Congress-2018 2018.09.05 Kyoto, Japan
16. Sugita N, Takase H, Nakako S, Takarano A, Tomaru Y, Shimizu N, Mochizuki M.. PCR diagnostic of uveitis.. 2th Annual Congress of Japan Clinical Ophthalmology. 2018.10.11 Tokyo Japan.
17. Ohki Kentaro, Kiyokawa Nobutaka, Takahashi Hiroyuki, Kajiwaru Ryosuke, Kato Motohiro, Hasegawa Daisuke, Tomizawa Daisuke, Noguchi Yasushi, Koike Kazutoshi, Toyama Daisuke, Yabe Hiromasa, Kajiwaru Michiko, Fujimura Junya, Sotomatsu Manabu, Ota Setsuo, Maeda Miho, Goto Hiroaki, Kato Yoko, Mori Tetsuya, Inukai Takeshi, Shimada Hiroyuki, Fukushima Keitaro, Ogawa Chitose, Fukushima Takashi, Koh Katsuyoshi, Manabe Atsushi, Ohara Akira, Tokyo Children's Cancer Study Group. Treatment outcome of children with acute lymphoblastic leukemia harbouring newly identified genetic abnormalities: Results from TCCSG Study L04-16. 2018.11.14
18. Ichiro Sekiya. Transplantation of synovial mesenchymal stem cells onto repaired menisci with degenerative tears: a 2-year follow-up study. ICRS Focus Meeting 2018.12.13 Milano, Italy

Hyperbaric Medical Center

Senior Director and Associate Professor; Kazuyoshi YAGISHITA

Assistant Professor ; Toshiyuki OHHARA

Specially Appointed Assistant Professor ; Ryouhei TAKADA(~2018/03) Mikio SHIODA(2018/04~)

Senior Resident; Naoki YAMAMOTO

Adjunct Lecturer; Yasushi KOJIMA, Masaharu SHIBAYAMA, Yumi NIIZEKI

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(1) Outline

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in population to atomic pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute anterior disturbance, and peripheral ischemic disease. The mechanism of HBO can be described as hyperoxygenation in ischemic soft tissues, reduction of edema, stimulation of fibroblast proliferation and differentiation, increased collagen formation and cross-linking, angiogenesis, and improved preservation of energy metabolism.

This curious treatment has clinically many kinds of efficacy, however, the mechanism of the effect has not been fully understood, and many researchers in the world still attempt to reveal the mechanism of the effect of HBO. This HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

(2) Research

Research Subjects

- 1) Soft tissue injuries related with sports activities
- 2) HBO for conditioning in sports activities
- 3) Diving medicine
- 4) Hyperbaric oxygen therapy

(3) Education

HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

(4) Clinical Services & Other Works

In 2018, 682 times hyperbaric oxygen therapy (HBO) in 6,423 patients were performed in the university hospital.

(5) Clinical Performances

HBO is applied for several conditions, including decompression illness, carbon monoxide poisoning, infection, wound healing, delayed radiation injury, acute arterial disturbance, and peripheral ischemic disease. Recently, for the purpose of rapid recovery from injury, we perform HBO aggressively for soft tissue injury related with sports activities including compartment syndrome, ankle sprain, knee ligament injury, and muscle contusion.

(6) Publications

[Original Articles]

1. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep.* 2018.01; 8(1); 1288
2. Naoko Suzuki, Kazuyoshi Yagishita, Mitsuhiro Enomoto, Yasushi Kojima, Takuya Oyaizu, Masaharu Shibayama, Kazuo Yamamoto. A case-control questionnaire survey of decompression sickness risk in Okinawa divers. *Undersea Hyperb Med.* 2018.01; 45(1); 41-48
3. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Limb-dominance and gender differences in the ground reaction force during single-leg lateral jump-landings. *Journal of Physical Therapy Science.* 2018.03; 30(3); 387-392
4. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Yuki Yamauchi, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Longitudinal morphological change of acetabular subchondral bone cyst after total hip arthroplasty in developmental dysplasia of the hip. *Eur J Orthop Surg Traumatol.* 2018.05; 28(4); 621-625
5. Oyaizu Takuya, Yamamoto Naoki, Yagishita Kazuyoshi. ラット下腿筋圧挫損傷において高気圧酸素治療は炎症を抑制し、マクロファージを介して筋衛星細胞を活性化し骨格筋再生を促進する (Hyperbaric-oxygen reduces inflammation and regenerates skeletal muscle via macrophage and satellite cell activation in rats) *JOSKAS.* 2018.05; 43(4); 447
6. Oyaizu Takuya, 榎本 光裕, 堀江 正樹, 山本 尚輝, 柳下 和慶. Hyperbaric oxygen treatment accelerates skeletal muscle regeneration via activation of the IL-6/STAT3 pathway and suppression of NF κ B in rat contused muscle(和訳中) *日本整形外科スポーツ医学会雑誌.* 2018.08; 38(4); 562
7. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Akimasa Kimura, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Direct anterior versus anterolateral approach in one-stage supine total hip arthroplasty. Focused on nerve injury: A prospective, randomized, controlled trial. *J Orthop Sci.* 2018.09; 23(5); 783-787
8. Nakamura T, Koga H, Otabe K, Horie M, Watanabe T, Yagishita K, Sekiya I, Muneta T. Comparison of three approaches for femoral tunnel during double-bundle anterior cruciate ligament reconstruction: A case controlled study. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association.* 2018.09;

[Conference Activities & Talks]

1. Shunsuke Ohji, Jyunya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlation Between Kinesiophobia and Vastus Medialis Activation Prior to Landing During Single-Leg Jump Landing in Athletes After Anterior Cruciate Ligament Reconstruction.. AOA & APKASS Combined Meeting 2018.05.31 Sidney
2. Y Kojima, S Suzuki, Y Niizeki, A Kojima, H Kawaguchi, K Yagishita. Recreational diving related injuries among insured Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014.. 51th Undersea & Hyperbaric Medical Society Annual Scientific Meeting 2018.06.29 Orlando, USA
3. Initiatives of International Divers Alert Network (IDAN) for creation of guideline for pre-hospital management of decompression illness.. 2018.07.22

4. 小柳津 卓哉, 榎本 光裕, 堀江 正樹, 山本 尚輝, 柳下 和慶. Hyperbaric oxygen treatment accelerates skeletal muscle regeneration via activation of the IL-6/STAT3 pathway and suppression of NF κ B in rat contused muscle. 第 44 回日本整形外科スポーツ医学会学術集会 2018.09.07 徳島市

Sports Medicine Center

Director and Associate Professor; Kazuyoshi YAGISHITA
Head Physical Therapist ; Jyunya AIZAWA
Assistant Professor ; Toshiyuki OHHARA
Specially Appointed Assistant Professor ; Ryouhei TAKADA
Specially Appointed Assistant Professor ; Mikio SHIOTA
Physical Therapist ; Kenji HIROHATA, Takehiro OHMI,
Shunsuke OHJI
Adjunct Lecturer ; Tomohiko TATEISHI
Staff Assistant; Kiyomi ITOH

(1) Publications

[Original Articles]

1. Development of the Japanese Version of the Lumbar Stiffness Disability Index Following Lumbar Spinal Surgery 2018;
2. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep*. 2018.01; 8(1); 1288
3. Naoko Suzuki, Kazuyoshi Yagishita, Mitsuhiro Enomoto, Yasushi Kojima, Takuya Oyaizu, Masaharu Shibayama, Kazuo Yamamoto. A case-control questionnaire survey of decompression sickness risk in Okinawa divers. *Undersea Hyperb Med*. 2018.01; 45(1); 41-48
4. Hideyuki Koga, Atsuo Nakamae, Yosuke Shima, Roald Bahr, Tron Krosshaug. Hip and Ankle Kinematics in Noncontact Anterior Cruciate Ligament Injury Situations: Video Analysis Using Model-Based Image Matching. *Am J Sports Med*. 2018.02; 46(2); 333-340
5. Kanehiro Hiyama, Yusuke Nakagawa, Toshiyuki Ohara, Takeshi Muneta, Toshifumi Watanabe, Masafumi Horie, Koji Otabe, Hiroki Katagiri, Kenta Katagiri, Mai Katakura, Takashi Hoshino, Hiroko Ueki, Kei Inomata, Naoko Araya, Ichiro Sekiya, Hideyuki Koga. Anterior cruciate ligament injuries result in a larger functional deficit in fighting sport athletes: comparison of functional status among different sport types. *Journal of ISAKOS*. 2018.03; (3); 128-133
6. Takao Minami, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Takeshi Muneta. Posteriorly inserted anterior cruciate ligament in knees with discoid lateral meniscus corresponding to bony morphological characteristics of femoral lateral condyle. *J Orthop Sci*. 2018.03; 23(2); 350-355
7. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Limb-dominance and gender differences in the ground reaction force during single-leg lateral jump-landings. *Journal of Physical Therapy Science*. 2018.03; 30(3); 387-392
8. Watanabe Toshifumi, Aoki Akino, Hoshi Kenji, Gamada Kazuyoshi, Muneta Takeshi, Horie Masafumi, Katagiri Hiroki, Otabe Koji, Ohara Toshiyuki, Sekiya Ichiro, Koga Hideyuki. 後方安定化補綴物における階段上り中の前方脛骨ポストでのインピンジメント (Anterior tibial post impingement in posterior-stabilized prosthesis during stair climbing) *日本整形外科学会雑誌*. 2018.03; 92(2); S422

9. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Yuki Yamauchi, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Longitudinal morphological change of acetabular subchondral bone cyst after total hip arthroplasty in developmental dysplasia of the hip. *Eur J Orthop Surg Traumatol*. 2018.05; 28(4); 621-625
10. Horie Masafumi, Katagiri Hiroki, Watanabe Toshifumi, Otabe Koji, Ohara Toshiyuki, Katagiri Kenta, Sekiya Ichiro, Muneta Takeshi, Koga Hideyuki. Early intervention on early knee osteoarthritis focusing on the medial meniscus posterior root tear 内側半月板逸脱を伴う変形性膝関節症に対する鏡視下半月板セントラリゼーションを併用した高位脛骨骨切り術の臨床成績 (Early intervention on early knee osteoarthritis focusing on the medial meniscus posterior root tear Clinical outcomes after medial open-wedge high tibial osteotomy combined with arthroscopic medial meniscus centralization for medial compartment OA with meniscal extrusion) *JOSKAS*. 2018.05; 43(4); 164
11. Koga Hideyuki, Katakura Mai, Watanabe Toshifumi, Horie Masafumi, Katagiri Hiroki, Otabe Koji, Ohara Toshiyuki, Sekiya Ichiro, Muneta Takeshi. How to eliminate residual instability in ACLR ACL 再建術後の残存不安定性の制動 回旋不安定性と半月板 (How to eliminate residual instability in ACLR How to eliminate residual instability in ACLR: Rotational instability and Meniscus) *JOSKAS*. 2018.05; 43(4); 415
12. Watanabe Toshifumi, Muneta Takeshi, Sekiya Ichiro, Horie Masafumi, Katagiri Hiroki, Otabe Koji, Ohara Toshiyuki, Katagiri Kenta, Koga Hideyuki. Knee Prostheses from Asia ACTIYAS: Implant design, surgical tips, and clinical outcomes(和訳中) *JOSKAS*. 2018.05; 43(4); 473
13. Koga Hideyuki, Watanabe Toshifumi, Horie Masafumi, Katagiri Hiroki, Otabe Koji, Ohara Toshiyuki, Sekiya Ichiro, Muneta Takeshi. Meniscal Repair up to date 逸脱半月板に対する治療戦略 (Meniscal Repair up to date Meniscus repair up to date: Treatment strategy for meniscus extrusion) *JOSKAS*. 2018.05; 43(4); 160
14. Otabe Koji, Katagiri Kenta, Ohara Toshiyuki, Katagiri Hiroki, Horie Masafumi, Watanabe Toshifumi, Sekiya Ichiro, Muneta Takeshi, Koga Hideyuki. オーバル型ワイドガントリー MRI を用いた膝関節屈曲位における若年者および高齢者の膝窩動脈走行解析 (Wide Oval Gantry 3.0T MRI Analysis Revealed Smaller Knee Neurovascular Transposition during Flexion of the Knee among Elderly Patients) *JOSKAS*. 2018.05; 43(4); 466
15. Kusunoki Yusuke, Horie Masafumi, Watanabe Toshifumi, Katagiri Hiroki, Otabe Koji, Ohara Toshiyuki, Katagiri Kenta, Sekiya Ichiro, Koga Hideyuki. 後内側ポータルを用いた膝関節遊離体摘出術後に生じた伏在神経障害に対して伏在神経剥離術を施行した 1 例 (A case of saphenous neuralgia following arthroscopic removal of loose bodies through posteromedial portal) *JOSKAS*. 2018.05; 43(4); 728
16. Hasegawa Shoichi, Horie Masafumi, Watanabe Toshifumi, Katagiri Hiroki, Otabe Koji, Ohara Toshiyuki, Katakura Mai, Sekiya Ichiro, Muneta Takeshi, Koga Hideyuki. 脛骨軟骨面と一部癒合した両側半月板低形成の一例 (A case of bilateral hypoplastic menisci partially fused to cartilage surface of the tibia) *JOSKAS*. 2018.05; 43(4); 706
17. Oyaizu Takuya, Yamamoto Naoki, Yagishita Kazuyoshi. ラット下腿筋圧挫損傷において高気圧酸素治療は炎症を抑制し、マクロファージを介して筋衛星細胞を活性化し骨格筋再生を促進する (Hyperbaric-oxygen reduces inflammation and regenerates skeletal muscle via macrophage and satellite cell activation in rats) *JOSKAS*. 2018.05; 43(4); 447
18. Mindae Kim, Watanabe Toshifumi, Muneta Takeshi, Ohara Toshiyuki, Sekiya Ichiro, Koga Hideyuki. Coronal Instability after Total Knee Arthroplasty using Bi-Surface type 3: An Averaged 10 Year Follow-up Study(和訳中) *Journal of Medical and Dental Sciences*. 2018.06; 65(2); 51-58
19. Yumi Yamaguchi-Kabata, Takashi Morihara, Tomoyuki Ohara, Toshiharu Ninomiya, Atsushi Takahashi, Hiroyasu Akatsu, Yoshio Hashizume, Noriyuki Hayashi, Daichi Shigemizu, Keith A Boroevich, Manabu Ikeda, Michiaki Kubo, Masatoshi Takeda, Tatsuhiko Tsunoda. Integrated analysis of human genetic association study and mouse transcriptome suggests LBH and SHF genes as novel susceptible genes for amyloid- β accumulation in Alzheimer's disease. *Hum. Genet.* 2018.07; 137(6-7); 521-533
20. Oyaizu Takuya, 榎本 光裕, 堀江 正樹, 山本 尚輝, 柳下 和慶. Hyperbaric oxygen treatment accelerates skeletal muscle regeneration via activation of the IL-6/STAT3 pathway and suppression of NF κ B in rat contused muscle(和訳中) *日本整形外科スポーツ医学会雑誌*. 2018.08; 38(4); 562

21. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Akimasa Kimura, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Direct anterior versus anterolateral approach in one-stage supine total hip arthroplasty. Focused on nerve injury: A prospective, randomized, controlled trial. *J Orthop Sci.* 2018.09; 23(5); 783-787
22. Nakamura T, Koga H, Otabe K, Horie M, Watanabe T, Yagishita K, Sekiya I, Muneta T. Comparison of three approaches for femoral tunnel during double-bundle anterior cruciate ligament reconstruction: A case controlled study. *Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association.* 2018.09;
23. Suzuki M, Koyama S, Kimura Y, Ishiyama D, Otobe Y, Nishio N, Ichikawa T, Kunieda Y, Ohji S, Ito D, Yamada M. Relationship between characteristics of skeletal muscle and oral function in community-dwelling older women. *Archives of gerontology and geriatrics.* 2018.11; 79; 171-175
24. Ueki H, Nakagawa Y, Ohara T, Watanabe T, Horie M, Katagiri H, Otabe K, Katagiri K, Hiyama K, Katakura M, Hoshino T, Inomata K, Araya N, Sekiya I, Muneta T, Koga H. Risk factors for residual pivot shift after anterior cruciate ligament reconstruction: data from the MAKS group. *Knee Surg Sports Traumatol Arthrosc.* 2018.12; 26(12); 3724-3730
25. Takehiro Omi, Takumi YAMADA. Reduction of Knee Adduction Moment And Lateral Joint Reaction Force by Simulation Analysis for Knee Osteoarthritis Patients 2018.12; 33(6); 883-886

[Conference Activities & Talks]

1. The Gait Analysis of the patients after Rotating Hinge Knee TKA. 2018.02.24
2. Kenji Hirohata, Junya Aizawa, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Asymmetry in the reactive strength index during single-leg vertical hopping in anterior cruciate ligament-reconstructed athletes. Australian Orthopaedic Association (AOA) Continuing Orthopaedic Education Conference (COE) and the 2018 Asia-Pacific Knee, Arthroscopy and Sports Medicine Society (APKASS) Congress 2018.05.31 Sidney
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4. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Kazuyoshi Yagishita. Correlation Between Kinesiophobia and Vastus Medialis Activation Prior to Landing During Single-Leg Jump Landing in Athletes After Anterior Cruciate Ligament Reconstruction.. AOA & APKASS Combined Meeting 2018.05.31 Sidney
5. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Asymmetry Of Knee Extension Strength And Single-leg Landing Impact In ACL reconstructed Athletes. American College of Sports Medicine 65th Annual Meeting 2018.06.01 Orlando
6. Y Kojima, S Suzuki, Y Niizeki, A Kojima, H Kawaguchi, K Yagishita. Recreational diving related injuries among insured Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014.. 51th Undersea & Hyperbaric Medical Society Annual Scientific Meeting 2018.06.29 Orlando, USA
7. Initiatives of International Divers Alert Network (IDAN) for creation of guideline for pre-hospital management of decompression illness.. 2018.07.22
8. 小柳津 卓哉, 榎本 光裕, 堀江 正樹, 山本 尚輝, 柳下 和慶. Hyperbaric oxygen treatment accelerates skeletal muscle regeneration via activation of the IL-6/STAT3 pathway and suppression of NF κ B in rat contused muscle. 第 44 回日本整形外科スポーツ医学会学術集会 2018.09.07 徳島市

Cleanroom

Associate Professor SUNAKAWA Mitsuhiro
Assistant Professor MATSUMOTO Hiroyuki

(1) Research

- 1) The development of disposable hygienic materials for dental use.
- 2) The survey for the oral diseases in patients with HIV.
- 3) The survey for the relationship between the consciousness of the staff and students and the needle stick accident in the hospital.

(2) Education

The improvement of the nosocomial infection control system in the University Hospital, Faculty of Dentistry, Tokyo Medical and Dental University and the education of the actual infection control method to all staff and clinical course students.

(3) Publications

[Original Articles]

1. Rashed B, Iino Y, Komatsu K, Nishijo M, Hanada T, Ebihara A, Sunakawa M, Sumi Y, Okiji T. Evaluation of root canal anatomy of maxillary premolars using swept-source optical coherence tomography in comparison with dental operating microscope and cone beam computed tomography Photomedicine and Laser Surgery. 2018.08; 36(9); 487-492

[Misc]

1. Iino Y, Ebihara A, Sunakawa M, Okiji T. Application of optical coherence tomography in endodontics. The Journal of Japan Society for Laser Surgery and Medicine. 2018.08; 39(1); 50-58

Clinical Center for Sports Medicine and Sports Dentistry

Clinical Center of Sports Medicine

Center Chief and Junior Associate Professor ; Kazuyoshi YAGISHITA

Assistant Professor ; Toshoyuki OHHARA

Specially Appointed Assistant Professor ; Mikio SHIODA

Physical therapy operator chief ; Junya AIZAWA

Physiotherapist; Kenji HIROHATA, Takehiro OHMI, Shunsuke OHJI

Staff Assistant; Kiyomi ITOH

Sports Medicine/Dentistry

Associate Professor; Toshiaki UENO

Assistant Professor; Hiroshi CHUREI

Specially Appointed Assistant Professor ; Kairi HAYASHI

(1) Outline

Center of Sports Medicine and Sports Dentistry was established as a bridgehead for sports medical science and sports dental science which deals the clinical management of trauma and disorder for athletes and sports-active people, and the safety measures and prevention of sports-related traumatic injuries and disorders. Center of Sports Medicine and Sports Dentistry is consisted of Clinical Center of Sports Medicine in University Hospital of Medicine and Sports Medicine/Dentistry and Sports dentistry clinic in University Hospital of Dentistry.

(2) Research

○ Clinical Center of Sports Medicine

- 1) Athletic rehabilitation for rapid recovery from injury and high performance in athletes.
- 1)-a Intervention of core strength in patients with anterior cruciate ligament reconstruction.
- 1)-b Treatment from the aspect of core function in patients with overuse and fatigue fracture.
- 2) Evaluation methods for core function.
- 3) Development of dynamic stability.
- 4) Hyperbaric oxygen treatment
- 4)-a Soft tissue injuries related with sports activities.
- 4)-b Conditioning in sports activities

○ Sports Medicine/Dentistry

- 1) Oral health promotion of athletes and sports-active people
- 1)-a Field survey of oral health conditions in athletes and sports-active people
- 1)-b Changes of oral environment associated with physical and sporting activities
- 1)-c Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
- 2)-a Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
- 2)-b Development and innovation of sports mouthguard
- 2)-c Development and innovation of sports faceguard
- 2)-d Development and innovation of scuba diving mouthpiece
- 3) Correlations between occlusion and general motor functions

- 3)-a Biomechanical assessment of motor performance associated with occlusion
- 3)-b Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

(3) Clinical Services & Other Works

Center of Sports Medicine and Sports Dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered traumatic injuries, overuse disorders, disorders related with internal medicine, and dental diseases.

○ Clinical Center of Sports Medicine

Number of patients (From January 2017 to December 2017)

Section of out-patient clinic: 4,650

Section of athletic rehabilitation: 4,100

○ Sports Medicine/Dentistry, Sports dentistry clinic

Sports dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and face-guard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art.

(4) Publications

[Original Articles]

1. Development of the Japanese Version of the Lumbar Stiffness Disability Index Following Lumbar Spinal Surgery 2018;
2. Takuya Oyaizu, Mitsuhiro Enomoto, Naoki Yamamoto, Kunikazu Tsuji, Masaki Horie, Takeshi Muneta, Ichiro Sekiya, Atsushi Okawa, Kazuyoshi Yagishita. Hyperbaric oxygen reduces inflammation, oxygenates injured muscle, and regenerates skeletal muscle via macrophage and satellite cell activation. *Sci Rep.* 2018.01; 8(1); 1288
3. Naoko Suzuki, Kazuyoshi Yagishita, Mitsuhiro Enomoto, Yasushi Kojima, Takuya Oyaizu, Masaharu Shibayama, Kazuo Yamamoto. A case-control questionnaire survey of decompression sickness risk in Okinawa divers. *Undersea Hyperb Med.* 2018.01; 45(1); 41-48
4. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Limb-dominance and gender differences in the ground reaction force during single-leg lateral jump-landings. *Journal of Physical Therapy Science.* 2018.03; 30(3); 387-392
5. Takahiro Wada, Hiroshi Churei, Haruka Takayanagi, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takahashi, Motohiro Uo. Improvement of the Shock Absorption Ability of a Face Guard by Incorporating a Glass-Fiber-Reinforced Thermoplastic and Buffering Space *BioMed Research International.* 2018.05; 2018; 1-8
6. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Yuki Yamauchi, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Longitudinal morphological change of acetabular subchondral bone cyst after total hip arthroplasty in developmental dysplasia of the hip. *Eur J Orthop Surg Traumatol.* 2018.05; 28(4); 621-625
7. Oyaizu Takuya, Yamamoto Naoki, Yagishita Kazuyoshi. ラット下腿筋圧挫損傷において高気圧酸素治療は炎症を抑制し、マクロファージを介して筋衛星細胞を活性化し骨格筋再生を促進する (Hyperbaric-oxygen reduces inflammation and regenerates skeletal muscle via macrophage and satellite cell activation in rats) *JOSKAS.* 2018.05; 43(4); 447
8. Yoshida Yuriko, Churei Hiroshi, Takeuchi Yasuo, Wada Takahiro, Uo Motohiro, Izumi Yuichi, Ueno Toshiaki. Novel antibacterial mouthguard material manufactured using silver-nanoparticle-embedded ethylene-vinyl acetate copolymer masterbatch *DENTAL MATERIALS JOURNAL.* 2018.06; 37(3); 437-444

9. Shuta Ushio, Shigenori Kawabata, Satoshi Sumiya, Tsuyoshi Kato, Toshitaka Yoshii, Tsuyoshi Yamada, Mitsuhiro Enomoto, Atsushi Okawa. A multi-train electrical stimulation protocol facilitates transcranial electrical motor evoked potentials and increases induction rate and reproducibility even in patients with preoperative neurological deficits. *J Clin Monit Comput.* 2018.06; 32(3); 549-558
10. Tanabe-Ikegawa M, Takahashi T, Churei H, Mitsuyama A, Ueno T. Interactive effect of rehydration with diluted sports drink and water gargling on salivary flow, pH, and buffering capacity during ergometer exercise in young adult volunteers *Journal of Oral Science.* 2018.06; 60(2); 269-277
11. Oyaizu Takuya, 榎本 光裕, 堀江 正樹, 山本 尚輝, 柳下 和慶. Hyperbaric oxygen treatment accelerates skeletal muscle regeneration via activation of the IL-6/STAT3 pathway and suppression of NF κ B in rat contused muscle(和訳中) *日本整形外科スポーツ医学会雑誌.* 2018.08; 38(4); 562
12. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Akimasa Kimura, Daisuke Koga, Kazuyoshi Yagishita, Atsushi Okawa. Direct anterior versus anterolateral approach in one-stage supine total hip arthroplasty. Focused on nerve injury: A prospective, randomized, controlled trial. *J Orthop Sci.* 2018.09; 23(5); 783-787
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14. Tanabe-Ikegawa M, Hayashi K, Churei H, Takahashi T, Shimoyama K, Yagishita K, Ueno T. Interactive effect of toothbrush abrasion and enamel erosion caused by a sports drink: An in vitro analysis *Int J Sports Dent.* 2018.11; 11(1); 16-24
15. Suzuki M, Koyama S, Kimura Y, Ishiyama D, Otobe Y, Nishio N, Ichikawa T, Kunieda Y, Ohji S, Ito D, Yamada M. Relationship between characteristics of skeletal muscle and oral function in community-dwelling older women. *Archives of gerontology and geriatrics.* 2018.11; 79; 171-175
16. Takehiro Omi, Takumi YAMADA. Reduction of Knee Adduction Moment And Lateral Joint Reaction Force by Simulation Analysis for Knee Osteoarthritis Patients 2018.12; 33(6); 883-886

[Conference Activities & Talks]

1. The Gait Analysis of the patients after Rotating Hinge Knee TKA. 2018.02.24
2. Wada Takahiro, Churei Hiroshi, Ueno Toshiaki, Uo Motohiro. Application of a carbon-fiber reinforced thermoplastic to face guard. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
3. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Yoshida Yuriko, Tanabe Gen, Uo Motohiro, Takahashi Hidekazu, Ueno Toshiaki. The behavior of pressure sensor with a built-in mouth guard material. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
4. Kenji Hirohata, Junya Aizawa, Shunsuke Ohji, Takehiro Ohmi, Kazuyoshi Yagishita. Asymmetry in the reactive strength index during single-leg vertical hopping in anterior cruciate ligament-reconstructed athletes. Australian Orthopaedic Association (AOA) Continuing Orthopaedic Education Conference (COE) and the 2018 Asia-Pacific Knee, Arthroscopy and Sports Medicine Society (APKASS) Congress 2018.05.31 Sydney
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8. Wada Takahiro, Churei Hiroshi, Tanabe Gen, Kinjo Rio, Ueno Toshiaki, Uo Motohiro. Shock absorption analysis of face guards made of carbon fiber reinforced thermoplastics using high-speed camera. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
9. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The evaluation of a force sensor for the development of the mouth guard type wearable sensor. The 29th Annual Meeting of Japanese Academy of Sports Dentistry 2018.06.24 Sendai, Miyagi, Japan
10. Y Kojima, S Suzuki, Y Niizeki, A Kojima, H Kawaguchi, K Yagishita. Recreational diving related injuries among insured Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014.. 51th Undersea & Hyperbaric Medical Society Annual Scientific Meeting 2018.06.29 Orlando, USA
11. Aung W, Shwe H, Tun PS, Aung TK, Tanabe G, Kinjo R, Takahashi Y, Hayashi K, Yoshiada Y, Yano A, Churei H, Ueno T. Effectiveness of mouthguard for Myanmar Lethwei player and coach. 9th Mandalay Dental Conference 2018.07.14 Mandalay, Myanmar
12. Initiatives of International Divers Alert Network (IDAN) for creation of guideline for pre-hospital management of decompression illness.. 2018.07.22
13. 小柳津 卓哉, 榎本 光裕, 堀江 正樹, 山本 尚輝, 柳下 和慶. Hyperbaric oxygen treatment accelerates skeletal muscle regeneration via activation of the IL-6/STAT3 pathway and suppression of NF κ B in rat contused muscle. 第 44 回日本整形外科スポーツ医学会学術集会 2018.09.07 徳島市
14. Kinjo R, Wada T, Churei H, Takahashi H, Ueno T, Uo M. Evaluating the use of a force sensor for the development of a mouth guard-type wearable sensor. The 3rd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-3) 2018.09.25 Tokyo Garden Place Hotel

Sports Dentistry

(1) Publications

[Conference Activities & Talks]

1. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Yoshida Yuriko, Tanabe Gen, Uo Motohiro, Takahashi Hidekazu, Ueno Toshiaki. The behavior of pressure sensor with a built-in mouth guard material. The 71th General Session of the Japanese Society for Dental Materials and Devices 2018.04.15 Osaka, Japan
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