ANNUAL PUBLICATIONS

2022



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

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Oral Pathology

Professor Tohru Ikeda

Junior Associate Professor Kei Sakamoto

Assistant Professor Kou Kayamori

Technical Staff Miwako Hamagaki

Graduate Students TEERAWONG CHANYANUCH NGUYEN PHAN THE HUY Fukawa Hironori HERDIANTOPUTRI RANNY RAHANINGRUM Youki Kamijyo

(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]

- Miyauchi M, Akashi T, Furukawa A, Uchida K, Tamura T, Ando N, Kirimura S, Shintaku H, Yamamoto K, Ito T, Miura K, Kayamori K, Ariizumi Y, Asakage T, Kudo A, Tanabe M, Fujii Y, Ishibashi H, Okubo K, Murakami M, Yamada T, Takemoto A, Bae Y, Eishi Y, Ohashi K. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocr Pathol. 2022.12; 33(4); 506-518
- Kugimoto T, Yamagata Y, Ohsako T, Hirai H, Nishii N, Kayamori K, Ikeda T, Harada H.. Massive low-grade myxoid liposarcoma of the floor of the mouth: A case report and review of literature. World J Clin Cases. 2022.12; 10(34); 12742-12749
- Yuki Fukawa, Kou Kayamori, Maiko Tsuchiya, Tohru Ikeda. IL-1 Generated by Oral Squamous Cell Carcinoma Stimulates Tumor-Induced and RANKL-Induced Osteoclastogenesis: A Possible Mechanism of Bone Resorption Induced by the Infiltration of Oral Squamous Cell Carcinoma. Int J Mol Sci. 2022.12; 24(1);
- 4. Hirai H, Kayamori K, Noji R, Kuroshima T, Ikeda T, Harada H. A rare case of solitary intraoral superficial angiomyxoma arising in the soft palate. J Oral Sci. 2022.11;
- 5. Takuya Komiyama, Takeshi Kuroshima, Takehito Sugasawa, Shin-Ichiro Fujita, Yuta Ikami, Hideaki Hirai, Fumihiko Tsushima, Yasuyuki Michi, Kou Kayamori, Fumihiro Higashino, Hiroyuki Harada. High expression of Sam68 contributes to metastasis by regulating vimentin expression and a motile phenotype in oral squamous cell carcinoma. Oncol Rep. 2022.10; 48(4); 183
- 6. Shinohara Shizu, Bychkov Andrey, Munkhdelger Jijgee, Kuroda Kishio, Yoon Han-Seung, Fujimura Shota, Tabata Kazuhiro, Furusato Bungo, Niino Daisuke, Morimoto Shinpei, Yao Takashi, Itoh Tomoo, Aoyama Hajime, Tsuyama Naoko, Mikami Yoshiki, Nagao Toshitaka, Ikeda Tohru, Fukushima Noriyoshi, Harada Oi, Kiyokawa Takako, Yoshimi Naoki, Aishima Shinichi, Maeda Ichiro, Mori Ichiro, Yamanegi Koji, Tsuneyama Koichi, Katoh Ryohei, Izumi Miki, Oda Yoshinao, Fukuoka Junya. Substantial improvement of histopathological diagnosis by whole-slide image-based remote consultation VIRCHOWS ARCHIV. 2022.08; 481(2); 295-305
- 7. Tsushima F, Sakurai J, Shimizu R, Kayamori K, Harada H. Oral lichenoid contact lesions related to dental metal allergy may resolve after allergen removal. J Dent Sci. 2022.07; 17(3); 1300-1306
- 8. Nguyen Phan-The-Huy, Sakamoto Kei, Ikeda Tohru. Deep-learning application for identifying histological features of epithelial dysplasia of tongue(タイトル和訳中) Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2022.07; 34(4); 514-522
- 9. Kuribayashi Ami, Kawashima Sakurako, Kayamori Kou, Sakamoto Junichiro, Tomisato Hiroshi, Watanabe Hiroshi, Kurabayashi Tohru. Magnetic resonance imaging of methotrexate-related lymphoproliferative disorder with a chief complaint of oral symptoms ORAL RADIOLOGY. 2022.06;
- Terauchi Masahiko, Uo Motohiro, Fukawa Yuki, Yoshitake Hiroyuki, Tajima Rina, Ikeda Tohru, Yoda Tetsuya. Chemical Diagnosis of Calcium Pyrophosphate Deposition Disease of the Temporomandibular Joint: A Case Report DIAGNOSTICS. 2022.03; 12(3); 651
- 11. Yasuyuki Michi, Hiroyuki Harada, Yu Oikawa, Kohei Okuyama, Takuma Kugimoto, Takeshi Kuroshima, Hideaki Hirai, Yumi Mochizuki, Hiroaki Shimamoto, Hirofumi Tomioka, Hirokazu Kachi, Jun-Ichiro Sakamoto, Kou Kayamori, Tetsuya Yoda. Clinical manifestations of diffuse large B-cell lymphoma that exhibits initial symptoms in the maxilla and mandible: a single-center retrospective study. BMC Oral Health. 2022.01; 22(1); 20
- 12. Mochizuki Y, Tsuchiya M, Oyama J, Wada A, Kugimoto T, Kuroshima T, Hirai H, Tomioka H, Harada H, Ikeda T, Akashi T. Left supraclavicular (Virchow's) node metastasis detected before primary infradiaphragmatic tumor: a case series. Journal of medical case reports. 2022.01; 16(1); 33
- Xie Cangyou, Satake-Ozawa Michiko, Rashed Fatma, Khan Masud, Ikeda Masaomi, Hayashi Shunya, Sawada Shinichi, Sasaki Yoshihiro, Ikeda Tohru, Mori Yoshiyuki, Akiyoshi Kazunari, Aoki Kazuhiro. Perforated Hydrogels Consisting of Cholesterol-Bearing Pullulan (CHP) Nanogels: A Newly Designed Scaffold for Bone Regeneration Induced by RANKL-Binding Peptides and BMP-2 INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES. 2022.07; 23(14); 7768 (1)-7768 (15)

- 1. Ami Kuribayashi, Junichiro Sakamoto, Kou Kayamori, Sakurako Kawashima, Hiroyuki Harada, Tohru Kurabayashi. A case of liposarcoma of the floor of the mouth. The 13th Asian Congress of Oral and Maxillo-Facial Radiology 2022.06.03
- Sakurako Kawashima, Ami Kuribayashi, Junichiro Sakamoto, Yoshikazu Nomura, Yuuki Fukawa ,Tohru Kurabayashi. Imaging findings of odontogenic myxofibroma in two cases. The 13th Asian Congress of Oral and Maxillo-Facial Radiology 2022.06.03
- 3. Pissacha Daroonpan, 加島義久, 濱垣美和子, 西井直人, 津島文彦, 原田浩之, 池田 通, 東みゆき. 肉眼分 類とがん浸潤様式からみた舌扁平上皮癌の免疫プロファイルの多様性. 第 76 回日本口腔科学会学術集会 2022.04.21

Bacterial Pathogenesis, Infection and Host Response

Professor SUZUKI Toshihiko Associate Professor ASHIDA Hiroshi Assistant Professor OKANO Tokuju Graduate Student BOONYALEKA Kotchakorn Graduate Student HSU Chen Wei Graduate Student **ONSOI** Poramed Graduate Student **TAKAHASHI** Yuto Graduate Student TAKINO Hisataka Technical Assistant Staff IIDA Tamako Administration Assistant Staff SAKURAGI Risa

(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. Mahazu S, Prah I, Ota Y, Hayashi T, Nukui Y, Suzuki M, Hoshino Y, Akeda Y, Suzuki T, Ishino T, Ablordey A, Saito R. Klebsiella Species and Enterobacter cloacae Isolates Harboring bla(OXA-181) and

bla
(OXA-48): Resistome, Fitness Cost, and Plasmid Stability. Microbiology spectrum. 2022.12; 10
(6); e0332022 $\,$

2. Samiratu Mahazu, Wakana Sato, Alafate Ayibieke, Isaac Prah, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Insights and genetic features of extended-spectrum beta-lactamase producing Escherichia coli isolates from two hospitals in Ghana. Sci Rep. 2022.02; 12(1); 1843

[Misc]

- 1. Hiroshi Ashida, Toshihiko Suzuki. The regulation mechanism of host cell death by Shigella Saibou. 2022.10; 54(10); 4-7
- 2. Marie Iwasawa, Hiroshi Ashida, Toshihiko Suzuki, Chihiro Sasakawa. The regulation mechanism of inflammasome by Shigella Inflammation and Immunity. 2022.02; 30; 123-127

- 1. Kotchakorn Boonyaleka, Tokuju Okano, Toshihiko Suzuki. Fusobacterium nucleatum infection activates the non-canonical inflammasome pathway to exacerbate inflammatory response in acute colitis mice.. The 51st Annual Meeting of the Japanese Society for Immunology 2022.12.08 Kumamoto-Jo Hall
- 2. Tokuju Okano, Toshihiko Suzuki. Porphyromnas gingivalis infection triggers enhancement of severity for EAE following inflammasome activation in macrophages. The 51st Annual Meeting of the Japanese Society for Immunology 2022.12.07 Kumamoto-Jo Hall
- 3. Boonyaleka KOTCHAKORN, Tokuju OKANO, Toshihiko SUZUKI. Fusobacterium nucleatum infection induces non-canonical inflammasome activation to exacerbate inflammation in acute colitis mice.. The 87th Annual Meeting of Stomatological Society, Japan 2022.12.03 Tokyo Medical and Dental University
- 4. Toshihiko Suzuki. Advanced collaborative research in infectious diseases in Ghana. Africa Symposium 2022 2022.12.02 Kisumu, Kenya
- 5. Mahazu Samiratu, Prah Isaac, Ota Yusuke, Hayashi Takaya, Nukui Yoko, Suzuki Masato, Hoshino Yoshihiko, Akeda Yukihiro, Suzuki Toshihiko, Ishino Tomoko, Ablordey Anthony, Saito Ryoichi. Genetic analysis of carbapenemase-producing Enterobacter cloacae and Klebsiella species. Annual meeting of the Japanese Society for Clinical Microbiology 2022.12.01
- 1. Hiroshi Ashida, Toshihiko Suzuki. Analysis of host cell death mechanism by enteric pathogens. The 34th Microorganism synposium 2022.08.31
- 2. Yoshihiko Hoshino, Mitsunori Yoshida, Yohei Nishikawa, Masato Suzuki, Hanako Fukano, Haruko Takeyama, Toshihiko Suzuki. Understanding microbial community structures and dynamics A distribution survey of environmental microbiome by single-cell genomics. Annual meeting of Japan Society for Bacteriology 2022.02.01
- 3. Marie Iwasawa, Toshihiko Suzuki. Analysis of type I IFN regulation by Pseudomonas aeruginosa. The 33rd Annual meeting of the Japanese Society for clinical microbiology 2022.01.29

Molecular Immunology

Professor Miyuki Azuma AssociateProfessor Shigenori Nagai AssistantProfessor Chenyang Zhang Specially Appointed Assistant Professor Eri Ikeda Adjunct instructor Emi Nishii Shigeru Okuhara (May.-) Graduate Students(Doctor) Amrita Widyagarini Subagyo (-Sep.) Pissacha Daroonpan Faruzana Sultana Ryo Ouchi (University of Toyama, Apr.-) Yi Lu (Oct.-) (Master) Yuto Nagatomo Honoka Aoshima **R**rsearch Student Jin Lu(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. Eri Ikeda, Daiki Tanaka, Michael Glogauer, Howard C Tenenbaum, Yuichi Ikeda. Healing effects of monomer and dimer resveratrol in a mouse periodontitis model. BMC Oral Health. 2022.11; 22(1); 460
- Widyagarini A, Nishii N, Kawano Y, Zhang C, Azuma M. VSIG4/CRIg directly regulates early CD8⁺ T cell activation through its counter-receptor in a narrow window. Biochemical and biophysical research communications. 2022.07; 614; 100-106
- 3. Kawada-H E, Kita S, Okita T, Nakamura Y, Nishida H, Honma Y, Fukuda S, Tsugawa-S Y, Kozawa J, Sakaue T, Kawachi Y, Fujishima Y, Nishizawa H, Azuma M, Maeda N, Shimomura I. Human adipose-derived mesenchymal stem cells prevent type 1 diabetes induced by immune checkpoint blockade. Diabetologia. 2022.07; 65(7); 1185-1197
- 4. Yuichi Ikeda, James Holcroft, Eri Ikeda, Bernhard Ganss. Amelotin Promotes Mineralization and Adhesion in Collagen-Based Systems. Cell Mol Bioeng. 2022.06; 15(3); 245-254
- 5. Takahashi F, Zhang C, Hohjoh H, Raveney B, Yamamura T, Hayashi N, Oki S. Immune-mediated neurodegenerative trait provoked by multimodal derepression of long-interspersed nuclear element-1. iScience. 2022.05; 25(5); 104278
- 6. Nakayama K, Nishijo T, Miyazawa M, Watabe T, Azuma M, Sakaguchi H. Hapten sensitization to vaginal mucosa induces less recruitment of dendritic cells accompanying TGF- β -expressing CD206⁺ cells compared with skin. Immunity, inflammation and disease. 2022.04; 10(4); e605
- Wongtim K, Ikeda E, Ohno T, Nagai S, Okuhara S, Kure K, Azuma M. Overexpression of PD-L1 in gingival basal keratinocytes reduces periodontal inflammation in a ligature-induced periodontitis model. J Periodontol. 2022.01; 93(1); 146-155

Advanced Biomaterials

Professor UO Motohiro Junior Associate Professor WADA Takahiro Assistant Professor MIYAYASU Anna Graduate Student Wang Liwei Graduate Student OKAJIMA Natsuki Graduate Student TSUKADA Saho 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. Masataka Watanabe, Manabu Kanazawa, Daisuke Sato, Yoko Uehara, Anna Miyayasu, Maiko Iwaki, Yuriko Komagamine, Sai Tun Naing, Awutsadaporn Katheng, Yuriko Kusumoto, Kazuyoshi Baba, Shunsuke Minakuchi. Oral function of implant-assisted removable partial dentures with magnetic attachments using short implants: A prospective study Tokyo Medical and Dental University. 2022.12;
- 2. Murata N, Suzuki T, Lin Y, Nitani H, Niwa Y, Wada T, Uo M, Asakura K. Structure of Atomically Dispersed Pt in a SnO₂ Thin Film under Reaction Conditions: Origin of Its High Performance in Micro Electromechanical System Gas Sensor Catalysis. ACS applied materials & interfaces. 2022.08; 14(34); 39507-39514
- Adel S, Hashimoto K, Kawashima N, Wada T, Uo M, Okiji T. Biocompatibility and pro-mineralization effect of tristrontium aluminate cement for endodontic use Journal of Dental Sciences. 2022.07; 17(3); 1193-1200

- 4. Sanon K, Tichy A, Hatayama T, Thanatvarakorn O, Prasansuttiporn T, Wada T, Shimada Y, Hosaka K, Nakajima M. Addition of metal chlorides to a HOCl conditioner can enhance bond strength to smear layer deproteinized dentin. Dental materials : official publication of the Academy of Dental Materials. 2022.06; 38(8); 1235-1247
- Masahiko Terauchi, Motohiro Uo, Yuki Fukawa, Hiroyuki Yoshitake, Rina Tajima, Tohru Ikeda, Tetsuya Yoda. Chemical Diagnosis of Calcium Pyrophosphate Deposition Disease of the Temporomandibular Joint: A Case Report Diagnostics. 2022.03; 12(651); 1-11
- 6. Hiroki Matsuda, Yoichi Nibe-Shirakihara, Akiko Tamura, Emi Aonuma, Satoko Arakawa, Kana Otsubo, Yasuhiro Nemoto, Takashi Nagaishi, Kiichiro Tsuchiya, Shigeomi Shimizu, Averil Ma, Mamoru Watanabe, Motohiro Uo, Ryuichi Okamoto, Shigeru Oshima. Nickel particles are present in Crohn's disease tissue and exacerbate intestinal inflammation in IBD susceptible mice. Biochem Biophys Res Commun. 2022.02; 592; 74-80
- 7. Ruman Uddin Chowdhury, Hiroshi Churei, Gen Tanabe, Yuriko Yoshida, Kairi Hayashi, Hidekazu Takahashi, Takahiro Wada, Motohiro Uo, Takahiro Mizobuchi, Nafees Uddin Chowdhury, Toshiaki Ueno. Useful design of custom-made mouthguard for athletes undergoing orthodontic treatment with brackets and wires. J Dent Sci. 2022.01; 17(1); 308-315
- Dumrongvute K., Adel S., Wada T, Kawashima N., Piyachon C., Watanabe H., Kurabayashi T., Okiji T., Uo M.. Distrontium Cerate as a Radiopaque Component of Hydraulic Endodontic Cement Materials. 2022.01; 15;
- Kittisak Sanon, Takashi Hatayama, Antonin Tichy, Ornnicha Thanatvarakorn, Taweesak Prasansuttiporn, Takahiro Wada, Masaomi Ikeda, Keiichi Hosaka, Masatoshi Nakajima. Smear layer deproteinization with NaOCl and HOCl: Do application/wash-out times affect dentin bonding of one-step self-etch adhesives? Dent Mater J. 2022.01;
- 10. Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 560-567
- Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes with immediate- loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 70-77
- 12. Sai Tun Naing, Kanazawa M, Hada T, Iwaki M, Komagamine Y, Miyayasu A, Uehara Y, Minakuchi S. In vitro study of the effect of implant position and attachment type on stress distribution of implant-assisted removable partial dentures Journal of Dental Sciences. 2022;
- 1. Uo Motohiro. Types and surface treatments of the fillers for resin composites The Journal of the Japanese Society for Dental Materials and Devices. 2022.05; 41(2); 125-129

[Misc]

1. Uo Motohiro. Features of the polymer materials applied for the orthodontic appliances 2022.01; 217; 31-34

- Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Mechanical evaluation of face guards fabricated by stereolithographic three- dimensional printing. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 (IDMC2022) 2022.11.04 Taipei, Taiwan
- 2. Tamaki HADA, Manabu KANAZAWA, Maiko IWAKI, Anna MIYAYASU, Motohiro UO, Shunsuke MINAKUCHI. Evaluation of mechanical properties of custom blocks for digital dentures fabricated using a new polymerization method. International Dental Materials Congress 2022 (IDMC2022) 2022.11.04 Taipei

- 3. Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Ayumu Murata, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Evaluation of core and cushion materials of face guards made by stereolithography additive manufacturing. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA) 2022.10.25 Osaka, Japan
- 4. K. Asakura, Y. Wakisaka, D. Kido, B. Hu, F. E. Feiten, T. Wada, H. Uehara, S. Takakusagi, Y. Uemura, N. Todoroki, T. Wadayama, T. Uruga, Y. Iwasawa. Abnormal Au-Au bond length contraction in PtAu alloy nanocluster on HOPG. XAFS2022 18th International Conference on X-Ray Absorption and Fine Structure HYBRID 2022.07.10 Sydney, Australia
- 5. Tonprasong W, Inokoshi M, Tamura M, Yoshihara K, Takahashi R, Wada T, Nozaki K, Minakuchi S. Porphyromonas gingivalis adhesion on highly polished tooth-colored materials. 2022 IADR/APR General Session & Exhibition 2022.06.24 web
- 6. Uo M.. Application of synchrotron radiation for the analyses of biological specimens. International Symposium for Interface Oral Health Science 2022 2022.01.16 ZOOM

Oral and Maxillofacial Surgical Oncology

Professor: Hiroyuki HARADA Associate Professor: Yasuyuki MICHI Junior Associate Professor: Fumihiko TSUSHIMA, Hirofumi TOMIOKA Assistant Professor: Hideaki HIRAI, Takeshi KUROSHIMA, Takuma KUGIMOTO, Yu OIKAWA Specially Appointed Assistant Professor: Yuriko SATO, Toshimitsu OHSAKO, Naoto NISHII, Rikuka SHIMIZU Graduate Student: Misako TANAKA, Takuya KOMIYAMA, Phung TRAN XUAN, Rika NOJI, Shiori TOKIZAKI, Haruka IBI, Takahiro NAITO, Makiko YATOMI, Tatsuhiro YOKOYAMA

(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) Development of multidisciplinary treatment of oral mucosal diseases.

Clinical Services

The Oral and Maxillofacial Surgery Clinic examines yearly more than 4,000 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 and oral mucosal 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]

 Hitomi Nojima, Atsushi Kaida, Hiroyuki Harada, Masako Akiyama, Masahiko Miuraa. Effect of Ablative Dose Irradiation on Redistribution and Radioresponse in a Mouse Xenograft Model. Radiat Res. 2022.12; 198(6); 632-638

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Dental Radiology and Radiation Oncology

Professor Associate Professor Lecturer Assistant Professor	Masahiko MIURA (~June, Dept Oral Radiat Oncol, ORO) HiroshiI WATANABE (~June, Dept Oral Maxillofac Radiol, OMFR) Naoto OHBAYASHI (~June, OMFR) Shin NAKAMURA (~June, OMFR) Atsushi KAIDA (~June, ORO) Ami KURIBAYASHI (~June, OMFR) Junichiro SAKAMOTO (~June, OMFR)
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	Kohki TOHYAMA (\sim June, ORO)
	Wamasing NATNICHA (\sim June, OMFR)
	Yomtako SUPASITH (\sim June, OMFR)
	Arisa OKI (\sim June, OMFR)
	Carulina MESQUITA (\sim June, ORO)

(1) Outline

Main objective of this department is to provide opportunities to learn and study image diagnosis for oral and maxillofacial lesions and radiation oncology for oral cancer. It also makes clinical contribution to diagnosis and radiotherapy for above described lesions.

(2) Research

· Differential diagnosis for oral and maxillofacial lesions using MRI including diffusion-

weighted MRI and dynamic MRI and development of novel MRI diagnosis

 \cdot Clinical study on the prediction of prognosis after oral cancer treatment using CT diagnosis

 \cdot Clinical study on radio therapy for oral cancer and development of novel the rapeutic modalities

 \cdot Molecular and cellular study on signal transduction, DNA repair, and cell cycle checkpoint following irradiation

(3) Education

Our department is a branch of radiology and radiation oncology specifically dealing with image diagnosis for oral and maxillofacial legions and radiotherapy for oral cancer. The educational policy for post-graduates is to cultivate the ability to extract problems and to resolve them by themselves. Our department also aims to make them obtain certificate of specialists for oral radiology and oral radiation oncology.

(4) Lectures & Courses

Basic lectures for radiation physics, radiation biology, radiology, and radiation oncology are provided for under-graduates. Film conference on oral and maxillofacial lesions, cancer board on oral cancer, journal club, and research in progress are regularly held especially for post-graduates.

(5) Clinical Services & Other Works

Our clinic provides image diagnosis for oral and maxillofacial lesions mainly using CT and MRI, and radiotherapeutic treatment for oral cancer using external beam radiation (IMRT) and brachytherapy.

(6) Clinical Performances

Our clinic provides high quality image diagnosis for oral and maxillofacial lesions and a high level of treatment outcomes for oral cancer by high precision radiotherapy and brachytherapy.

(7) **Publications**

[Original Articles]

- Hitomi Nojima, Atsushi Kaida, Hiroyuki Harada, Masako Akiyama, Masahiko Miuraa. Effect of Ablative Dose Irradiation on Redistribution and Radioresponse in a Mouse Xenograft Model. Radiat Res. 2022.12; 198(6); 632-638
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Dental Anesthesiology and Orofacial Pain Management

Professor Shigeru MAEDA

Associate Professor Ryo WAKITA,

Junior Associate Professor Tomoka MATSUMURA

Assistant Professors Yukiko BABA, Yoko YAMAZAKI, Takuya FUNAYAMA, Takaya ITO

Specially Appointed Assistant Professor Chihiro SUZUKI, Hiroko IMURA, Yu SATO, Midori ISHIDA, Naomi SHIMADA

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Research Students Hidemasa KUSUNOKI, Satoshi YAMADA

(1) Outline

Our department is responsible for both dental anesthesiology and orofacial pain control. In addition, orofacial pain control consists of orofaical pain clinic and TMD clinic (former TMJ clinic). In the field of dental anesthesiology, the aim is to provide safe and painless dental treatment. The education includes lectures and practical training on local anesthesia, general anesthesia, sedation, and monitoring. In addition, basic and clinical research is conducted to achieve the above objectives. The number of cases of general anesthesia and sedation is about 1,000 and 2,000, respectively, per year, which is the largest number of anesthesia management among public universities in Japan. In the field of oral and maxillofacial anesthesiology, the orofacial pain clinic and TMJ outpatient clinic are staffed by dedicated specialists.

(2) Research

- 1) Development of a non-invasive drug delivery system
- 2) Development of a new local anesthesia method for dentistry

- 3) Elucidation of the etiology of neuropathic pain in the maxillofacial region and its treatment
- 4) Clinical research on psychosedation and systemic management in dentistry

(3) Education

The purpose of our department is to provide knowledge and basic skills in local anesthesia for daily dental practice, sedation and general anesthesia for specialized anesthesia management, systemic management of patients with complications, and maxillofacial pain treatment. Lectures are given on dental anesthesia (general anesthesia, local anesthesia, sedation, cardiopulmonary resuscitation) and orofacial pain. In the section on general anesthesia, students learn the physiology of respiration and circulation, and the pharmacological effects and mechanisms of anesthetics. In the section on sedation, students learn about the differences between general anesthesia and sedation. As a first aid training, students learn not only basic life support but also advanced life support using a cardiopulmonary resuscitation training system. In ofofacial pain clinic, students are instructed on the basis of physiology and pharmacology as a field of neuroscience.

(4) Lectures & Courses

The specialty of dental anesthesia is to provide safe and painless dental care. For this purpose, information about the patient's health status is collected and evaluated, which is an important prerequisite for dental care, regardless of the administration of anesthetics. The importance of such patient assessment is emphasized to undergraduate students. In addition, the meaning of anesthesia management by dentists is discussed with the students. In graduate school, the main objective is to accumulate clinical experience and learn basic and clinical research methods and concepts while aiming for certification and specialist training. After graduation, students are expected to obtain research funding and become involved in clinical practice, research, and education as potential supervisors.

(5) Clinical Services & Other Works

In the operating room, about 1,000 cases of general anesthesia are performed annually for oral surgery. These include lengthy surgeries like as reconstruction with free flap, and 2 jaw osteotomies. In the outpatient dental anesthesia clinic, we perform more than 2,000 sedation procedures per year to treat patients, who is difficult to receive in general dentistry, as well as long procedures such as implant-related procedures. In addition, we respond promptly to emergencies that occur in our hospital on average several times a month, and if necessary, we collaborate with the ER of the medical school hospital. The Department of Orofacial Pain Clinic and the Department of Temporomandibular Joint Treatment are two of the few specialized outpatient clinics in Japan, and we accept referrals from inside and outside the hospital. In the Orofacial Pain Clinic, we mainly treat neuropathic pain and trigeminal neuralgia, and provide multidisciplinary treatment with medication, nerve blocks, oriental medicine and physical therapy.

(6) Clinical Performances

In the central operating room, appropriate management including general anesthesia is provided for all types of oral surgery. Postoperative management is provided in collaboration with the ICU for long surgeries. In the outpatient clinic, we provide intravenous sedation for extraction of wisdom teeth and implant surgery to ensure safe and stress-free dental treatment. For patients who are fearful of dental treatment or

with intellectual disabilities, general anesthesia and intravenous sedation are used. In the oro-facial pain clinic, we provide holistic care for all kinds of pain, abnormal sensation, nerve palsy, etc. in the oral and maxillofacial region, incorporating medication, physical therapy, Oriental medicine, and psychosomatic medicine.

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[Original Articles]

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Pediatric Dentistry / Special Needs Dentistry

Professor Tsutomu Iwamoto

Junior Associate Professor Satoko Kakino

Assistant Professor Yasuka Kusumoto, Kanae Wada, Atsushi Oishi, Asuna Sugimoto, Kaori Kohi(Apr-)

Project assistant professor Taiji Hoshiai(-Mar)

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[Original Articles]

- Aya Yamada, Keigo Yoshizaki, Kan Saito, Masaki Ishikawa, Yuta Chiba, Seira Hoshikawa, Mitsuki Chiba, Ryoko Hino, Yuriko Maruya, Hiroshi Sato, Keiji Masuda, Haruyoshi Yamaza, Takashi Nakamura, Tsutomu Iwamoto, Satoshi Fukumoto. GSK3beta inhibitor-induced dental mesenchymal stem cells regulate ameloblast differentiation. J Oral Biosci. 2022.12; 64(4); 400-409
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Orthodontic Science

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Junior Associate Profe	essor Yoshiro MATSUMOTO, Jun HOSOMICHI(-Nov)		
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	Risa USUMI(Apr-)		
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	Aiko ISHIZAKI(May-), Hideyuki ISHIDORI(Oct-)		
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	Misaki AOYAGI, Sun-min KIM(-Sep)		
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	Sasin SRITARA(-Mar)		
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	Aiko TAKADA, Yoshiyuki HAMADA		
	Akiyo FUJITA, Ahmad F J M SH ALSULAILI		
	Saranya SERIRUKCHUTARUNGSEE, Yixin LOU		
	Keita ISHIZUKA, Mirei KEITOKU, Rikima TAKANO		
	Eri MISAWA, Ruixin LI, Chun Shuo HUANG, Wenqian SUN		
	Masato AKAKURA, Shuntaro IWAKI, Takumi SUZUKI		
	Yuka TANAKA, Moe TANIGAWA, Naomi TOYAMA, Jiratchaya SRISUTHA		
	Doyoon KIM, Jia QI		
	Arisa KUBO, Rika KUWABARA, Midori WADA, Manaka MORO		
	Rune ISHIZAKA(Apr-), Marin KAWASAKI(Apr-), Mika KIKUCHI(Apr-)		
	Yuri KINOSHITA(Apr-), Yu TAKENOUCHI(Apr-)		
	Minami WATANABE(Apr-), Yaosen CHEN(Apr-)		
Graduate School Rese	arch Students Moe SATO(-Mar), Kasumi HATANO(-Mar), Masako KAWADA(-Mar)		
	Shuko ARAI(-Apr), Aiko ISHIZAKI(-Apr), Misa TAKAHASHI(-Mar)		
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(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]

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- Wirongrong Wongkitikamjorn, Jun Hosomichi, Eiji Wada, Hideyuki Maeda, Sirichom Satrawaha, Haixin Hong, Yukiko K Hayashi, Ken-Ichi Yoshida, Takashi Ono. Gestational Intermittent Hypoxia Induces Mitochondrial Impairment in the Geniohyoid Muscle of Offspring Rats. Cureus. 2022.05; 14(5); e25088

- 12. Sunmin Kim, Ikuo Yonemitsu, Hiroshi Takemura, Kunio Shimoda, Kazuhiro Suga, Kohei Soga, Takashi Ono, Motohiro Uo. Influence of different ligation methods on force and moment generation in a simulated condition of the maxillary crowded anterior dentition with linguo-version and rotation. Biomed Mater Eng. 2022.05; 33(6); 453-463
- 13. Misaki Aoyagi, Marie Oshima, Masamichi Oishi, Soma Kita, Koichi Fujita, Haruki Imai, Shuji Oishi, Hiroko Ohmori, Takashi Ono. Computational fluid dynamic analysis of the nasal respiratory function before and after postero-superior repositioning of the maxilla. PLoS One. 2022.04; 17(4); e0267677
- Narubhorn Ongprakobkul, Yuji Ishida, Kasumi Hatano-Sato, Kai Li, Sirima Petdachai, Risa Usumi-Fujita, Jun Hosomichi, Korapin Mahatumarat, Takashi Ono. Effects of local vs systemic administration of CXCR4 inhibitor AMD3100 on orthodontic tooth movement in rats. Am J Orthod Dentofacial Orthop. 2022.03;
- 15. Asuka Manabe, Takayoshi Ishida, Eiichiro Kanda, Takashi Ono. Evaluation of maxillary and mandibular growth patterns with cephalometric analysis based on cervical vertebral maturation: A Japanese cross-sectional study. PLoS One. 2022; 17(4); e0265272
- Kamaratih Anindya, Ohmori Hiroko, Aoyagi Misaki, Kanno Zuisei, Ono Takashi. Gastric emptying rate of a solid meal in patients with anterior open bite malocclusion: A preliminary study APOS Trends in Orthodontics. 2022; 12(2); 77-85

[Conference Activities & Talks]

- 1. Qi Jia. Bone response to buccal tooth movement by light continuous force in mice. The 13th Asian Pacific Orthodontic Congress. 2022.10.28 Seoul, Korea
- 2. Li Ruixin, Kato Chiho, Abe Yasunori, Fujita Akiyo, Ogawa Takuya, Ishidori Hideyuki, Misawa Eri, Okihara Hidemasa, Kokai Satoshi, Ono Takashi. Altered neuromuscular behavior during cortically-elicited rhythmic jaw movement in obese Zucker rat. The 81st Annual Meeting of the Japanese Orthodontic Society. 2022.10.01 Osaka, Japan
- 3. Sun Wenqian, Ogawa Takuya, Okihara Hidemasa, Ishidori Hideyuki, Misawa Eri, Kato Chiho, Ono Takashi. Impact of change in food properties on learning/memory function in the growing mice. The 81st Annual Meeting of the Japanese Orthodontic Society. 2022.10.01 Osaka, Japan
- 4. Lou Yixin, Matsumoto Yoshiro, Iseki Sachiko, Qi Jia, Ono Takashi. Observation of root resorption/repair and related cytokines by application/removal of light orthodontic force in rats. The 81st Annual Meeting of the Japanese Orthodontic Society. 2022.10.01 Osaka, Japan
- 5. Guan Hao, Yonemitsu Ikuo, Ikeda Yuhei, Ono Takashi. Reversible effects of functional mandibular lateral shift on masticatory muscles in the growing rats. The 81st Annual Meeting of the Japanese Orthodontic Society. 2022.10.01 Osaka, Japan

[Social Contribution]

1. EECD, 2020.04.01 - Now
Cariology and Operative Dentistry

Professor: Yasushi Shimada Associate Professor: Masavuki Otsuki Junior Associate Professor: Noriko Hiraish Assistant Professor: Takako Yoshikawa, Go Inoue, Rena Takahashi, Takaaki Sato, Specially Appointed Assistant Professor: NHM Khairul Matin, Takashi Hatayama, Tomoko Tabata, Nami Tsuchiyama (April \sim), Hisaichi Nakagawa (November \sim) Hospital Staff: Ayako Nakamoto, Motoi Takahashi, Nami Tsuchiyama (\sim March), Hisaichi Nakagawa (\sim March) , Yousuke Minato (April $\sim)$ Staff Assistant: Rieko Sugiyama Graduate Student: Kyoko Ishikawa (\sim March) , Meiken Hayashi (\sim March), Yosuke Minato (\sim March), Leila Nasiry Khanlar (\sim May), Ayaka Sato, Satoshi Akiya, Yuko Ogawa, Kiyoka Furusawa, Yutaro Motoyama, Ako Yamashita, QI Feng, Kittisak SANON, TAGHREED ABDULRAHMAN ALREFAIE, MULTUZA AYED ALI, Soe Kay Thwe Than Naing, Koudai Akabane, Hiroki Ishihara, Kouta Kibe, Mika Shimojima, CHEN XUEFEI,WEI Diantong, YANG Yi, Panchanit UBOLSA-ARD, Mahiro Iizuka, Hirotoshi Iwabuchi, Kei Ushijima, Tadamu Gondo, Shunsuke Takano, Yukiko Tsuji, ZENG Chen, ZHAO Mengtian, Abu Hasan Mohammad KHALED, Kyaw Htet, DU Zijuan, Khin Myanmar Kouta Kobayashi (April \sim), Azusa Takeuchi (April \sim), Ryohei Fujimori (April \sim), Shamima JAHAN (April \sim), ZENG SIQI (April \sim), Research Student: Mineo Kijima, Keitaro Dohi (April \sim), Riko Nakamura (April \sim), ZHU Tianmo (May \sim), FENG Shuo (May \sim), ELSEOUDY Nadar Ahmed Abdelaziz (April \sim), FAN Lin (October \sim),HE Yuzhengqiu (October \sim), Mustafa Ata Cakaloglu (December \sim), WANG Xinyu (December \sim)

(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 dentistry. 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]

- Kozo Yamaji, Akihiko Yokoyama, Kumiko Matsuzaki, Tsutomi sugaya, Yasushi Shimada, Naoko Ohara, Masahiro Yoshiyama . Effects of BMP-2 on bone response using gelatin hydrogel in estrogen-deficient rats Journal of Oral Tissue Engineering. 2022.12; 20(2); 41-46
- Noriko Hiraishi, Tadamu Gondo, Yasushi Shimada, Robert Hill, Fumiaki Hayashi. Crystallographic and Physicochemical Analysis of Bovine and Human Teeth Using X-ray Diffraction and Solid-State Nuclear Magnetic Resonance. J Funct Biomater. 2022.11; 13(4); 254
- Syed Ali Murtuza, Khairul Matin, Noriko Hiraishi, Yasushi Shimada. Optimal Surface Pre-Reacted Glass Filler Ratio in a Dental Varnish Effective for Inhibition of Biofilm-Induced Root Dentin Demineralization. Polymers (Basel). 2022.11; 14(22); 5015
- 4. Yuko Ogawa, Mahmoud Sayed, Noriko Hiraishi, Nadin Al-Haj Husain, Junji Tagami, Mutlu Özcan, Yasushi Shimada. Effect of Surface Pre-Reacted Glass Ionomer Containing Dental Sealant on the Inhibition of Enamel Demineralization. J Funct Biomater. 2022.10; 13(4); 189
- Hayata Imamura, Wenliang Zhu, Tetsuya Adachi, Noriko Hiraishi, Elia Marin, Nao Miyamoto, Toshiro Yamamoto, Narisato Kanamura, Giuseppe Pezzotti. Raman Analyses of Laser Irradiation-Induced Microstructural Variations in Synthetic Hydroxyapatite and Human Teeth. J Funct Biomater. 2022.10; 13(4); 200
- Han SH, Shimada Y, Sadr A, Tagami J, Tabata T, Nakagawa H, Yang SE. Effects of Material Thickness and Pretreatment on the Interfacial Gap of Translucent Zirconia Restorations with Self-adhesive Resin Cement. Operative dentistry. 2022.09; 47(5); 535-548
- Midori Kawamura, Yu Toida, Shuhei Hoshika, Md Refat Readul Islam, Yitong Li, Ye Yao, Yunqing Liu, Rafiqul Islam, Takaaki Sato, Yasushi Shimada, Hidehiko Sano. Influence of Novel Experimental Light-Cured Resin Cement on Microtensile Bond Strength. Polymers (Basel). 2022.09; 14(19); 4075
- 8. Yasushi Shimada, Takaaki Sato, Go Inoue, Hisaichi Nakagawa, Tomoko Tabata, Yuan Zhou, Noriko Hiraishi, Tadamu Gondo, Syunsuke Takano, Kei Ushijima, Hirotoshi Iwabuchi, Yukiko Tsuji, Sadr Alireza, Yasunori Sumi, Junji Tagami . Evaluation of Incipient Enamel Caries at Smooth Tooth Surfaces Using SS-OCT Materials. 2022.08; 15(17); 5947
- 9. Shimada Y, Sato T, Inoue G, Nakagawa H, Tabata T, Zhou Y, Hiraishi N, Gondo T, Takano S, Ushijima K, Iwabuchi H, Tsuji Y, Alireza S, Sumi Y, Tagami J. Evaluation of Incipient Enamel Caries at Smooth Tooth Surfaces Using SS-OCT. Materials (Basel, Switzerland). 2022.08; 15(17);
- Daniel Hovander, Grant Chyz, Yasushi Shimada, Junji Tagami, Alireza Sadr. Optical coherence tomography evaluation of deep dentin crack removal techniques JADA Foundational Science. 2022.08; 1(C); 100012
- 11. Yutaro Oda, Rena Takahashi, Toru Nikaido, Junji Tagami. Influence of the resin-coating technique on the bonding performance of self-adhesive resin cements in single-visit computer-aided design/computer-aided manufacturing resin restorations. Journal of Esthetic and Restorative Dentistry. 2022.06; 34(4); 721-728
- 12. Sanon K, Tichy A, Hatayama T, Thanatvarakorn O, Prasansuttiporn T, Wada T, Shimada Y, Hosaka K, Nakajima M. Addition of metal chlorides to a HOCl conditioner can enhance bond strength to smear layer deproteinized dentin. Dental materials : official publication of the Academy of Dental Materials. 2022.06; 38(8); 1235-1247
- Noriko Hiraishi, Mahmoud Sayed, Robert Hill, Ysushi Shimada. Solid-state NMR spectroscopy measurement of fluoride reaction by bovine enamel and dentin treated with silver diammine fluoride. Dent Mater. 2022.05; 38(5); 769-777

- 14. Ayako Okada, Susumu Imai, Tomohiro Kikuchi, Khairul Matin, Ryoko Otsuka, Tomohiko Terai, Takekazu Okumura, Takatsugu Yamamoto, Nobuhiro Hanada. Evaluation of the cariogenic potential of a probiotic candidate strain Lactobacillus gasseri YIT 12321. Arch Oral Biol. 2022.04; 136; 105364
- 15. SoeKayThwe ThanNaing, Ahmed Abdou, Mahmoud Sayed, Yasunori Sumi, Junji Tagami, Noriko Hiraishi. Dentin anti-demineralization potential of surface reaction-type pre-reacted glass-ionomer filler containing self-adhesive resin cement. Clin Oral Investig. 2022.02; 26(2); 1333-1342
- 16. Yu Toida, Shimpei Kawano, Rafiqul Islam, Fu Jiale, Afm A Chowdhury, Shuhei Hoshika, Yasushi Shimada, Junji Tagami, Masahiro Yoshiyama, Satoshi Inoue, Ricardo M Carvalho, Yasuhiro Yoshida, Hidehiko Sano. Pulpal response to mineral trioxide aggregate containing phosphorylated pullulan-based capping material. Dent Mater J. 2022.02; 41(1); 126-133
- 17. Sanon K, Hatayama T, Tichy A, Thanatvarakorn O, Prasansuttiporn T, Wada T, Ikeda M, Hosaka K, Nakajima M. Smear layer deproteinization with NaOCl and HOCl: Do application/wash-out times affect dentin bonding of one-step self-etch adhesives? Dental materials journal. 2022.01; 41(3); 353-362
- 18. Citra Kusumasari, Meiken Hayashi, Yasushi Shimada. Uncut Enamel for Optimizing Bonded Composite Restoration on Multiple Diastema Closure Cases Journal of Dentistry Indonesia. 2022; 29(2); 140-146
- 19. Yoshikawa T, Arakawa M. Effects of C-factor on Dentin Bonding using Various Adhesive Systems. Niger J Clin Pract. 2022.03; 25(3); 255-260
- 1. Nakane A, Wei D, Nakamoto A, Moriya K, Hiraishi N, Otsuki M, Kato J, Shimada Y. Clinical application of Er:YAG laser for removal of melanin pigmentation Journal of Japanese Society for Laser Dentistry. 2022.01; 31(3); 74-77

[Books etc]

1. A Brand New Take: Dentistry's Challenge in the Lead-up to 2040. 2022.05

[Misc]

- 1. Noriko Hiraishi, Mahmoud Sayed, Motoi Takahashi, Toru Nikaido, Junji Tagami. Clinical and primary evidence of silver diamine fluoride on root caries management. Jpn Dent Sci Rev. 2022.11; 58; 1-8
- 1. Hisaichi NAKAGAWA, Yasushi SHIMADA. Introduction of swept-source optical coherence tomography (SS-OCT) for caries diagnosis Journal of Japanese Society for Laser Dentistry. 2022.12; 32(2); 23-31
- 2. Rena Takahashi. Practice of resin coating technique for vital teeth Adhesive Dentistry. 2022.04; 40(1); 14-17
- 3. Yasushi Shimada, Junji Tagami, Yasunori Sumi. Diagnostic capability of optical coherence tomography for dental caries 2022.04; 70(4); 3-11
- 4. Yasushi Shimada. Diagnosis of dental caries using optical coherence tomography The Journal of The Stomatological Society, Japan. 2022.03; 89(1); 7-12

[Conference Activities & Talks]

- 1. ZHAO MENGTIAN, Sato Takaaki, Khaled Abu Hasan Mohammad, Shimada Yasushi. The influence of phosphoric acid and primer treatment on morphological evaluation of the adhesive resin cement/enamel interface. The 157th Meeting of the Japanese Society of Conservative Dentistry 2022.11.11 Okayama
- 2. Sanon Kittisak, Hiraishi Noriko, Hatayama Takashi, Nakajima Masatoshi, Shimada Yasushi. Papain gel enhances bond strength to eroded dentin. The157th Meeting of the Japanese Society of Conservative Dentistry 2022.11.10 Okayama
- 3. Noriko Hiraishi. Bioactive Effect of S-PRG released ions on mineral precipitation and reaction with enamel and dentin. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 2022.11.04
- 4. Yu TOIDA, Midori KAWAMURA, Shuhei HOSHIKA, Yunqing LIU, Takaaki SATO, Yasushi SHIMADA, Hidehiko SANO. Evaluation of mechanical property of a newly developed light-cured resin cement. International Dental Materials Congress 2022 2022.11.04

- 5. Hatayama Takashi. Direct resin-bonded fixed dental prothesis with digital workflow: A New Technique. 5th Brawijaya Scientific Meeting in Dentistry 2022.07.17 Web
- 6. Yasushi Shimada, Hirotoshi Iwabuchi, Kei Ushijima, Tadamu Gondo, Syunsuke Takano, Yukiko Tsuji, Takaaki Sato, Hisaichi Nakagawa, Tomoko Tabata, Takashi Hatayama, Yasunori Sumi . 3D evaluation of smooth surface enamel caries using OCT. 100th General Session & Exhibition of the IADR 2022.06.25
- 7. Takaaki Sato, Tomoko Tabata, Kodai Akabane, Mengtian Zhao, Abu Hasan, Mohammad Khaled, Yasunori Sumi, Junji Tagami, Yasushi Shimada. Influence of Phosphoric Acid Etching on the Dentin-Enamel Junction. 100th General Session & Exhibition of the IADR 2022.06.24
- 8. Tonprasong W, Inokoshi M, Tamura M, Yoshihara K, Takahashi R, Wada T, Nozaki K, Minakuchi S. Porphyromonas gingivalis adhesion on highly polished tooth-colored materials. 2022 IADR/APR General Session & Exhibition 2022.06.24 web
- 9. Xuefei Chen, Go Inoue, Hidenori Hamba, Masaomi Ikeda, Yasushi Shimada . Remineralization Enhancement of Dentin Lesion Using the Combination of SDF+GIC.. The International Association for Dental Research 100th General Session & Exhibition 2022.06.23 ChengDu, China (Web)
- 10. Yi Yang, Go Inoue, Keiichi Hosaka, Masaomi Ikeda, Yasushi Shimada. The effect of deproteinizing pretreatment on bonding performance and acid resistance to eroded dentin. IAD 2022@Sapporo The International Congress on Adhesive Dentistry 2022.06.03 Hokkaido University Conference Hall
- 11. Go Inoue, Yasunori Sumi, Yasushi Shimada. Observation of the gap formation of a newly developed self-adhesive resin composite by OCT. The International Congress on Adhesive Dentistry 2022.06.03 Sapporo, Hokkaido Japan
- 12. Tashiro H, Miki H, Tagami J, Takagaki T, Hosaka K, Sato T, Hatayama T, Shimada Y. Clinical performance of mono-block direct composite crown restorations. IAD2022@Sapporo 2022.06.03
- 13. Sato T, Tashiro H, Miki H, Otani K, Nishimura M, Takahashi M, Hosaka K, Tagami J, Shimada Y. Clinical Effectiveness of direct composite vs. zirconia resin-bonded fixed dental prostheses. IAD2022@Sapporo 2022.06.03
- 14. Miki H, Tashiro H, Tagami J, Takagaki T, Hosaka K, Sato T, Hatayama T, Shimada Y. Survival of the anterior mono-block direct composite crown. IAD2022@Sapporo 2022.06.03
- 15. Yasushi Shimada. Dental OCT system for diagnosis of caries and tooth crack. The International Congress on Adhesive Dentistry 2022.06.03 Sapporo
- 16. Yasushi Shimada, Hisaichi Nakagawa, Tomoko Tabata, Takaaki Sato, Sadr Alireza, Yasunori Sumi, Junji Tagami. Diagnosis of occlusal and proximal caries using SS-OCT. The International Congress on Adhesive Dentistry 2022.06.03 Sapporo
- 17. Rena Takahashi, Saki Uchiyama, Yuna Kanamori, Shin Rozan, Yutaro Oda, Takaaki Sato, Junichi Shinagawa, Masanao Inokoshi, Toru Nikaido, Junji Tagami, Yasushi Shimada. Comparison of the bond strength of CAD/CAM inlay restorations with a specific cement. The International Congress on Adhesive Dentistry 2022.06 Sapporo, Japan
- Panchanit Ubolsa-ard, Mahmoud Sayed, Noriko Hiraishi, Yasushi Shimada. Collagen Morphology and Remineralization Using S-PRG On Demineralized Dentin . The 100th, the IADR/APR General Session & Exhibition, June 20-25, 2022 2022.06 virtual meeting
- 19. 1. Noriko Hiraishi, Aifang Han, Fumiaki Hayashi, Junji Tagamia, Yasusi Shimada. Zirconia Adhesion of Phosphoric Acid Ester Monomers Studied by NMR. The 100th, the IADR/APR General Session & Exhibition 2022.06 a virtual meeting
- Takako Yoshikawa, Alireza Sadr, Yasushi Shimada. Polymerization Behavior of Composites at Top/Bottom of Cavity using Different Light Cure. The International Congress on Adhesive Dentistry 2022.06.03 Web
- 1. Rena Takahashi, Taka
aki Sato, Motoi Takahashi, Yuna Kanamori , Yasushi Shimada. Effect of resin
 coating technique and cleaning method of dentin after removal of temporary sealing material on bond
 strength of CAD/CAM inlay restorations . 2022.12.03 Tokyo

- 2. Tadamu Gondo, Noriko Hiraishi, Yasushi Shimada. Crystallographic Comparison of Bovine and Human Extraction Teeth by Rietveld Analysis in X-ray Diffraction. The Stomatological Society, Japan 87th 2022.12
- 3. Xuefei Chen, Go Inoue, Yasushi Shimada. Time-dependent structural change in artificial demineralized dentin after silver diammine fluoride and glass ionomer treatment. The 157th Meeting of the Japanese Society of Conservative Dentistry 2022.11.11 Okayama, Japan
- 4. Hirotoshi Iwabuchi,Go Inoue,Masaomi Ikeda,Yasushi Shimada. The evaluation of acid-resistance and bond strength of an experimental calcium-containing adhesive system on enamel. The 157th Meeting of the Japanese Society of Conservative Dentistry 2022.11.10 Okayama,Japan
- 5. Matin Khairul, Ryoko Otsuka, Ayako Okada, Toshimitsu Fujii, Kenichi Nebuka, Yasushi Shimada, Kazuhito Satomura. Search for human oral pathogens in commercial food samples using next-generation sequencing. 2022.11.10
- 6. Motoi Takahashi , Rena Takahashi , Yasushi Shimada. Direct composite restoration for the esthetic and functional disorder with a digital workflow : A case report. The 157th The Japanese Society of Conservative Dentistry 2022 Fall Conference 2022.11 Okayama
- Tadamu Gondo, Noriko Hiraishi, Rika Kurogoushi, Tsutomu Iwamoto, Yasushi Shimada. Extraction of microbiome DNA from root and crown caries and comparison of bacterial composition. The 157 The Japanese Society of Conservative Dentistry 2022.11
- 8. Kei Ushijima, Noriko Hiraishi, Masaomi Ikeda, Yasushi Shimada. Tensile bond strength of resin cement to water glass penetrated to zirconia. The 157 The Japanese Society of Conservative Dentistry 2022.11
- 9. Go Inoue, Yasushi Shimada. The effect on tooth adherent of Calcium containing primer system. The 3rd Dentin Pulp Treatment Association 2022.09.10 Sapporo
- Mika Shimojima, Noriko Hiraishi, Kodai Akabane, Feng QI, Masayuki Otsuki, Yasushi Shimada. Effect of In-office Bleaching Agent with S-PRG Filler on Enamel. 156th Congress of The Japanese Society of Conservative Dentistry 2022.06 a virtual meeting.
- 11. Kodai Akabane, Noriko Hiraishi, Mika Shimojima, Feng QI, Masayuki Otsuki, Yasushi Shimada. Bleaching Effect of In-office Bleaching Agent with S-PRG Filler. 156th Congress of The Japanese Society of Conservative Dentistry 2022.06 a virtual meeting.
- 12. Yasushi Shimada. Diagnosis of dental caries using optical coherence tomography Potentialities and limitations. The 76th Annual Meeting of the Japanese Stomatological Society 2022.04.22 Fukuoka International Congress Center

[Social Contribution]

- 1. Editorial board (Takako Yoshikawa), Asian Pacific Journal of Dentistry, 2016.01.01 Now
- 2. Sensors Guest Editor (Yasushi Shimada), 2020.09 Now
- 3. Materials Guest Editor (Yasushi Shimada), 2021.01 Now
- 4. Functional Materials for Dental Restorations, Hokkaido University, Hokkaido Summer Institute 2022, Hokkaido University, 2022.08

Masticatory Function and Health Science

Professor: Kenji FUEKI Associate professor: Wataru KOMADA Junior associate professor: Hiroshi CHUREI Assistant professor : Shiho OHTAKE, Reina NEMOTO, Yuka INAMOCHI, Kairi HAYASHI, Hiroyuki ISHIYAMA Project assistant professor: Miho Sato, Mina TAKITA, Mayuko MASTUMURA Clinical staff: Sinya OISHI, Yasuyuki KOWAKA, Tomoyuki MIHARA, Wataru YANAKA, Hiroko KIMURA, Teisuke AKIMOTO

(1) **Outline**

This department researches the association between oral function with prosthetic treatments and health, and provides dental care and education on prosthodontics, sports dentistry, and TMD.

(2) Research

Research on the association between oral function and health, AI and data science, dental education, dental materials, dental allergy, sports dentistry, and TMD

(3) Education

Basic and clinical education on prosthodontics (fixed prosthodontics and removable partial denture), sports dentistry, and TMD

(4) Lectures & Courses

Evidence-based clinical education

(5) Clinical Services & Other Works

Dental care at prosthetic clinic, advanced dental clinic, dental allergy clinic, sports dentistry clinic, and TMD clinic

(6) Clinical Performances

Prosthetic treatments using digital technology, examination of allergies to dental materials, specialized treatment to sports injury using mouse guard and face guard, diagnosis and treatment of TMD

(7) **Publications**

[Original Articles]

- Shoko Tobe, Hiroyuki Ishiyama, Akira Nishiyama, Keisuke Miyazono, Hiroko Kimura, Kenji Fueki. Effects of Jaw-Opening Exercises with/without Pain for Temporomandibular Disorders: A Pilot Randomized Controlled Trial International Journal of Environmental Research and Public Health. 2022.12; 19(24); 16840
- Inamochi Y, Kohno EY, Wada J, Murakami N, Takaichi A, Arai Y, Ueno T, Fueki K, Wakabayashi N.. Knowledge acquisition efficacy of a remote flipped classroom on learning about removable partial dentures J Prosthodont Res. 2022.11;
- 3. Saleh O, Nozaki K, Matsumura M, Yanaka W, Abdou A, Miura H, Fueki K. Emergence angle: Comprehensive analysis and machine learning prediction for clinical application. Journal of prosthodontic research. 2022.11;
- 4. Shintaro Shimizu, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tatsuhiko Anzai, Kunihiko Takahashi, Toshiaki Ueno, Kenji Fueki. Quantitative text analysis of the mechanisms of tooth injury: Analysis of accidents in five sports that occurred in 15 years under school control. Dent Traumatol. 2022.11;
- Kairi Hayashi, Yasuo Takeuchi, Shintaro Shimizu, Gen Tanabe, Hiroshi Churei, Hiroaki Kobayashi, Toshiaki Ueno. Continuous Oral Administration of Sonicated P. gingivalis Delays Rat Skeletal Muscle Healing Post-Treadmill Training. International Journal of Environmental Research and Public Health. 2022.10; 19(20);
- Shiho Otake, Shinya Oishi, Taisuke Ozaki, Masaomi Ikeda, Wataru Komada. Effect of Method of Removing Caries-Affected Dentin on the Bond Strength of Composite Resin to Root Canal Dentin. Healthcare (Basel). 2022.10; 10(11);
- 7. Ruri Tsukahara, Wataru Komada, Shinya Oishi, Shu Yoshimatsu, Hiroyuki Miura, Kenji Fueki. Fracture strength of flared root canals reinforced using different post and core materials. J Prosthodont. 2022.10;
- 8. Jia Deng, Yuta Fukushima, Kosuke Nozaki, Hideyuki Nakanishi, Erica Yada, Yuki Terai, Kenji Fueki, Keiji Itaka. Anti-Inflammatory Therapy for Temporomandibular Joint Osteoarthritis Using mRNA Medicine Encoding Interleukin-1 Receptor Antagonist. Pharmaceutics. 2022.08; 14(9);
- 9. Kay Thwe Ye Min Soe, Hiroyuki Ishiyama, Akira Nishiyama, Masahiko Shimada, Shigeru Maeda . Effect of Different Maxillary Oral Appliance Designs on Respiratory Variables during Sleep International Journal of Environmental Research and Public Health. 2022.05; 19(11); 6714
- 10. Tanabe G, Hattori M, Obata S, Takahashi Y, Churei H, Nishiyama A, Ueno T, Sumita YI. Case report: Psychoacoustic analysis of a clarinet performance with a custom-made soft lip shield worn to prevent mucosal erosion of lower lip. Front Psychol. 2022.04; 13; 852866
- 11. Mizutani Koji, Mikami Risako, Tsukui Akira, Nagai Shigeyuki, Pavlic Verica, Komada Wataru, Iwata Takanori, Aoki Akira. Novel flapless esthetic procedure for the elimination of extended gingival metal tattoos adjacent to prosthetic teeth: Er:YAG laser micro-keyhole surgery(和訳中) Journal of Prosthodontic Research. 2022.04; 66(2); 346-352
- 12. Oishi S, Komada W, Tsukahara R, Yoshimatsu S, Kondo D, Omori S, Nozaki K, Miura H, Fueki K. A composite resin core with a new zirconia tube reduces the surface strain at the cervical area of a mandibular molar: A model tooth study. Journal of prosthodontic research. 2022.03;
- Kenji Fueki, Yuka Inamochi, Eiko Yoshida-Kohno, Noriyuki Wakabayashi. Short-term effect of thermoplastic resin removable partial dentures on periodontal health: A randomized cross-over trial. J Prosthodont Res. 2022.01; 66(1); 167-175
- 14. Ruman Uddin Chowdhury, Hiroshi Churei, Gen Tanabe, Yuriko Yoshida, Kairi Hayashi, Hidekazu Takahashi, Takahiro Wada, Motohiro Uo, Takahiro Mizobuchi, Nafees Uddin Chowdhury, Toshiaki Ueno. Useful design of custom-made mouthguard for athletes undergoing orthodontic treatment with brackets and wires. J Dent Sci. 2022.01; 17(1); 308-315
- 1. Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study Journal of oral and sleep medicine. 2022.05; 8(3); 64-72

[Misc]

- Toshikazu Yasui, Yoshinobu Maeda, Anthony Clough, Melvin Choy, Kazunori Nakajima, Rieko Koushi, Kazunori Ikebe, Paul Picciniinni, Hiroshi Suzuki, Hidehisa Matsumura, Yuto Tanaka, Masashi Yoshida, Tsung-Chieh Yang, David Kumamoto, Kung Rock Kwon, Tomotaka Takeda, Kairi Hayashi, Sylvaine Goupy, Ashraf Samy Ghanem, Naoki Tsukimura, Hiroshi Churei, Gen Tanabe, Siegfried Marquardt, Richard Lee Sungbok, Tomoyo Gonda, Kazunari Kimoto, Nanaho Katsutani. Statements from the 2019 Second International Workshop on Sports Dentistry in Osaka Japan. International Journal of Sports Dentistry. 2022.11; 15(1); 7-16
- 2. M T John, M Omara, N Su, T List, S Sekulic, B Häggman-Henrikson, C M Visscher, K Bekes, D R Reissmann, K Baba, O Schierz, N Theis-Mahon, K Fueki, T Stamm, L Bondemark, I Oghli, A van Wijk, P Larsson. RECOMMENDATIONS FOR USE AND SCORING OF ORAL HEALTH IMPACT PROFILE VERSIONS. J Evid Based Dent Pract. 2022.03; 22(1); 101619
- Kenji Fueki, Yuka Inamochi, Junichiro Wada, Yuki Arai, Atsushi Takaichi, Natsuko Murakami, Takeshi Ueno, Noriyuki Wakabayashi. A systematic review of digital removable partial dentures. Part I: Clinical evidence, digital impression, and maxillomandibular relationship record. J Prosthodont Res. 2022.01; 66(1); 40-52
- 4. Atsushi Takaichi, Kenji Fueki, Natsuko Murakami, Takeshi Ueno, Yuka Inamochi, Junichiro Wada, Yuki Arai, Noriyuki Wakabayashi. A systematic review of digital removable partial dentures. Part II: CAD/CAM framework, artificial teeth, and denture base. J Prosthodont Res. 2022.01; 66(1); 53-67
- 1. FUEKI Kenji. Evaluation of Objective Masticatory Performance and Future Challenges The Journal of the Stomatological Society, Japan. 2022.03; 89(1); 1-6
- 2. A systematic review of digital removable partial dentures Ann Jpn Prosthodont Soc. 2022.01; 14(1); 17-24

[Conference Activities & Talks]

- Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Mechanical evaluation of face guards fabricated by stereolithographic three- dimensional printing. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 (IDMC2022) 2022.11.04 Taipei, Taiwan
- 2. Hiroshi Churei, Kairi Hayashi, Gen Tanabe, Yuumi Takahashi, Kairi Togawa, Shintaro Shimizu, Chenyuan Li, Chang Liu, Thida Aung, Qiushuang Zhu, Zequn Li, Yunchia Lian, Akihito Kumagai, Toshiaki Ueno.. Relationship between appropriate heating temperature and drooping distance of poly-olefin sheet materials for mouthguard. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 2022.11.04 HYBRID ACADEMIC CONFERENCE, Taiwan
- 3. Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Ayumu Murata, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Evaluation of core and cushion materials of face guards made by stereolithography additive manufacturing. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA) 2022.10.25 Osaka, Japan
- 4. Saleh O, Nozaki K, Matsumura M, Yanaka W, Miura H, Fueki K. Development of an emergence angle estimation program by machine learning. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16
- 5. Omnia Saleh, 野崎浩佑, 松村茉由子, 谷中 航, 三浦宏之, 笛木賢治. 機械学習によるエマージェンスアング ル推定プログラムの開発. 日本補綴学会第 131 会学術大会 2022.07.15 大阪
- 6. Hattori M, Tanabe G, Sumita YI, Obata S, Churei H, Ueno T. Does playing music influence the rehabilitation of a maxillofacial defect patient?. 40th Annual PAMA International Symposium 2022.06.25 Chicago (USA)+Web
- 7. Chenyuan Li, Hiroshi Churei, Chang Liu, Qiushuang Zhu, Zequn Li, Gen Tanabe, Toshiaki Ueno. . Questionnaire survey on safety awareness for boxers in China. 2022 IADR (100th)/IADR APR(5th) 2022.06.20 web/ China
- 8. Kenji Fueki, Yuka Inamochi. Patient-reported outcomes and periodontal health after prosthetic treatment with thermoplastic resin removable partial dentures. FDCU International Symposium 2022 2022.05.18 Web

- 9. Saleh Omnia, Nozaki Kosuke, Matsumura Mayuko, Yanaka Wataru, Abdou Ahmed, Miura Hiroyuki, Fueki Kenji. Emergence angle three dimensional analyses and classification(和訳中). 口腔病学会雑誌 2022.03.01
- 10. Saleh Omnia, Nozaki Kosuke, Matsumura Mayuko, Yanaka Wataru, Abdou Ahmed, Miura Hiroyuki, Fueki Kenji. 歯の萠出角の三次元的分析と分類 (Emergence angle three dimensional analyses and classification). 口腔病学会雑誌 2022.03.01
- 1. Matsumura M, Nozaki K, Yanaka W, Beniya R, Matsumuto A, Wakabayashi N, Fueki K. Effect of cement space on color tone of anterior CADCAM crowns. 2022.12.18
- 2. Hiroyuki Ishiyama. The effects of Oral appliance therapy for obstructive sleep apnea on temporomandibular joint and masticatory muscles side effects and prevention. The 21th Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2022.11.20
- 3. Shoko Tobe, Hiroyuki Ishiyama, Keisuke Miyazono, Hiroko Kimura, Akira Nishiyama. Optimal intensity of jaw-opening exercise for functional pain in temporomandibular disorders: a randomized controlled trial. The 27th Annual Meeting of the Japanese Society of Orafacial Pain 2022.10.09
- 4. Yuka Inamochi. A questionnaire survey on medical and dental collaboration: ECCO project. Japan Research Society for Dementia and Oral Function 3rd annual meeting 2022.08.06 online meeting
- 5. Shiho Otake. A case report of occlusal recovery using minor tooth movement. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16
- 6. Hiroyuki Ishiyama, Akira Nishiyama. A case of suspected sleep apnea for morning headache attributed to temporomandibular disorders. The 35th Annual Meeting of the Japanese Society for the Temporomandibular Joint 2022.07.02

[Social Contribution]

- 1. Associate editor of Annals of Dentistry University of Malaya, 2019.04 Now
- 2. Associate editor of Journal of Prosthodontic Research, the Japan Prosthodontic Society, 2019.07 Now

Pulp Biology and Endodontics

Professor: Takashi OKIJI

Associate Professor: Nobuyuki KAWASHIMA

Junior Associate Professor: Satoshi WATANABE

Assistant Professor: Arata EBIHARA, Kento TAZAWA (August \sim), Kentaro HASHIMOTO, Yoshiko IINO, Keisuke SUNADA-NARA (\sim July)

Specially Appointed Assistant Professor Sonoko NODA, Keiichiro MAKI (April \sim), Shunsuke KIMURA (April \sim)

Hospital Staff:

Sonoko NODA (~ March), Mayuko FUJII, Keiichiro MAKI (~ March), Shunsuke KIMURA (~ March), Akira KOUNO (~ March), Yasuhiro HOSHIHARA, Shinya YAMAUCHI (~ March), Nanami NIKAIDO (~ March), Hiroko SOEDA, Taro NAKATSUKASA (~ March), Yamato OKADA (April ~)

Graduate Student: Saleh Sherif Adel Abdelfattah (~ March), Yamato OKADA, Shion ORIKASA (~ March), Kunlanun DUMRONGVTE (~ March), Myint THU (~ September), Thoai Quoc KIEU (~ September), Hayate UNNO, Satoshi OMORI, Hiroki OKUDA, Jiayi LIU, Aseel ALCHAWOOSH, Peifeng HAN, Moe Sandar KYAW, Yuka KASUGA, Souta MOCHIZUKI, Nyein Chan Ko, Ryota ITO, Keiko HIRANO, Ziniu YU, Shihan WANG, Risako YAMAMOTO (April ~), Phu Yadanar Aung Myint (April ~), Faisal Turki A ALGHAMDI (October ~), Xiyuan BAI(April ~), Khaing Nyein Pwint, Chunmei REN, Kazuhisa SATAKE, Kentaro NATORI (April ~), Koki Toyoda (April ~), Risa OHSHIMA (April ~)

Research Student: Sousuke IZAWA (\sim March), Yadanar Su Phyo (\sim September), Takuya KAWAMURA, Risako YAMAMOTO (\sim March), Phu Yadanar Aung Myint (\sim March), Chen Yanyan, Harutaka KOMAKI (April \sim), Yoko HOSHINO (April \sim), Luo Yanshan (October \sim)

(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 dental pulp stem cells
- Importance of tissue-resident M2-like LYVE-1+ macrophages in the dental pulp tissue
- Effects of BCL9 signaling on osteo-/odontoblastic differentiation of dental pulp stem cells

2. Evaluation of efficacy- and safety-related properties of laser-activated root canal irrigation

3. Evaluation of newly developed endodontic sealers and pulp capping materials

• Cytotocompatibility of an experimental sealer containing surface reaction type pre-reacted glassionomer (S-PRG) to osteoblastic cells

• Evaluation of strontium aluminate and distrontium cerate as new hydraulic endodontic cements

4. Nickel-titanium rotary root canal instrumentation

• Effect of different downward loads on canal centering ability, vertical force, and torque generation during nickeltitanium rotary instrumentation.

• Effect of kinematics on the torque/force generation, surface characteristics, and shaping ability of a nickel titanium rotary glide path instrument.

• Effect of rotational modes on torque/force generation and canal centering ability during rotary root canal instrumentation with differently heat-treated nickel-titanium instruments.

• Evaluation of mechanical properties and shaping ability of different nickel-titanium rotary instruments.

• Impact of radial lands on the reduction of torque/force generation of a heat-treated nickel-titanium rotary instrument.

• Influence of different kinematics on stationary and dynamic torque/screw-in force generation during nickeltitanium rotary instrumentation.

• Influence of rotational speed on torque/force generation and shaping ability during root canal instrumentation with continuous rotation and optimum torque reverse motion.

(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,

- \cdot Nonsurgical root canal therapy,
- \cdot Root canal retreatment,
- · Endodontic microsurgery,
- · Internal tooth bleaching, and
- \cdot 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. Dumrongvute K, Adel S, Wada T, Kawashima N, Piyachon C, Kurabayashi T, Okiji T, Uo M. Distrontium cerate as a radiopaque component of hydraulic endodontic cement. Materials. 2021.12; 15(1): 284

2. Orikasa S, Kawashima N, Tazawa K, Hashimoto K, Sunada-Nara K, Noda S, Fujii M, Akiyama T, Okiji T. Hypoxiainducible factor 1 α induces osteo/odontoblast differentiation of human dental pulp stem cells via Wnt/ β -catenin transcriptional cofactor BCL9. Scientific Reports. 2022.01; 12(1): 682

3. Thein HSS, Hashimoto K, Kawashima N, Noda S, Okiji T. Evaluation of the anti-inflammatory effects of surfacereaction-type pre-reacted glass-ionomer filler containing root canal sealer in lipopolysaccharide-stimulated RAW264.7 macrophages. Dental Materials Journal. 2022.02; 41(1); 150-158

4. Zaw ZCT, Kawashima N, Kaneko T, Okiji T. Angiogenesis during coronal pulp regeneration using rat dental pulp cells: Neovascularization in rat molars in vivo and proangiogenic dental pulp cell-endothelial cell interactions in vitro. Journal of Dental Sciences. 2022.02; 17(3): 1160-1168

5. Nakatsukasa T, Ebihara A, Kimura S, Maki K, Nishijo M, Tokita D, Okiji T. Impact of radial lands on the reduction of torque/force generation of a heat-treated nickel-titanium rotary instrument. Applied Sciences. 2022.03; 12(5); 2620

6. Kieu TQ, Tazawa K, Kawashima N, Noda S, Fujii M, Nara K, Hashimoto K, Han P, Okiji T. Kinetics of LYVE-1positive M2-like macrophages in developing and repairing dental pulp in vivo and their pro-angiogenic activity in vitro. Scientific Reports. 2022.03; 12(1); 5176

7. Maki K, Ebihara A, Unno H, Omori S, Nakatsukasa T, Kimura S, Okiji T. Effect of different downward loads on canal centering ability, vertical force, and torque generation during nickel-titanium rotary instrumentation. Materials. 2022.04; 7(15); 2724

8. Kyaw MS, Ebihara A, Maki K, Kimura S, Nakatsukasa T, Htun PH, Thu M, Omori S, Okiji T. Effect of kinematics on the torque/force generation, surface characteristics, and shaping ability of a nickel-titanium rotary glide path instrument: An ex vivo study. International Endodontic Journal. 2022.05; 55(5); 531-543

9. Adel S, Hashimoto K, Kawashima N, Wada T, Uo M, Okiji T. Biocompatibility and pro-mineralization effect of tristrontium aluminate cement for endodontic use. Journal of Dental Sciences. 2022.07; 17(3); 1193-1200

10. Murano H, Kaneko T, Zaw SYM, Sone PP, Zaw ZCT, Okada Y, Sunakawa M, Katsube K-I, Okiji T. Pulp inflammation induces Kv1.1 K+ channel down-regulation in rat thalamus. Oral Diseases. 2022.09; 28(6); 1674-1681

11. Thu M, Ebihara A, Kyaw MS, Omori S, Maki K, Kimura S, Unno H, Okiji T. Influence of different kinematics on stationary and dynamic torsional behavior of JIZAI nickel-titanium rotary instruments: An in vitro study. Journal of Dental Sciences. 2022.10; in press

12. Omori S, Ebihara A, Hirano K, Kasuga Y, Unno H, Nakatsukasa T, Kimura S, Maki K, Hanawa T, Okiji T. Effect of rotational modes on torque/force generation and canal centering ability during rotary root canal instrumentation with differently heat-treated nickel-titanium instruments. Materials. 2022.10; 15(19); 6850

13. Okada Y, Kawashima N, Noda S, Murano H, Han P, Hashimoto K, Kaneko T, Okiji T. VEGFA promotes odonto/ osteoblastic differentiation in dental pulp stem cells via ERK/p38 signaling. Journal of Dental Sciences. 2022.10; in press

14. Liu J, Watanabe S, Mochizuki S, Kouno A, Okiji T. Comparison of vapor bubble kinetics and cleaning efficacy of different root canal irrigation techniques in the apical area beyond the fractured instrument. Journal of Dental Sciences. 2022.11; in press

15. Unno H, Ebihara A, Hirano K, Kasuga Y, Omori S, Nakatsukasa T, Kimura S, Maki K, Okiji T. Mechanical properties and root canal shaping ability of a nickel-titanium rotary system for minimally invasive endodontic treatment: a comparative in vitro study. Materials. 2022.11; 15(22); 7929

16. Alchawoosh A, Hashimoto K, Kawashima N, Noda S, Nozaki K, Okiji T. Hydraulic calcium silicate-based root canal sealers mitigate proinflammatory cytokine synthesis and promote osteogenesis in vitro. Journal of Dental Sciences. 2022.12; in press

17. Thu M, Ebihara A, Maki K, Nishijo M, Kimura S, Nakatsukasa T, Kyaw MS, Okiji T. Effect of different axial speed patterns on cyclic fatigue resistance of rotary nickel-titanium instruments. BMC Oral Health. 2022.12; 22(1): 617

18. Tazawa K, Azuma MM, Furusho H, Stashenko P, Sasaki H. Revisiting the role of IL-1 signaling in the development of apical periodontitis. Frontiers in Dental Medicine. 2022.12; in press

[Books etc]

- 1. Okiji T. MTA update 2021-2022. Hyoron Publishers, 2022.07
- 2. Okiji T, Noiri Y, Muramatsu T. Diseases of the periapical tissue. Endodontics, 6th Ed. Nagasue Shoten Inc., p. 51-65, 2022.03
- 3. Okiji T, Muramatsu T. Diseases of the dental pulp. Endodontics, 6th Ed. Nagasue Shoten Inc., p. 36-50, 2022.03
- 4. Okiji T, Kawashima N. Physiology of dental pain. Endodontics, 6th Ed. Nagasue Shoten Inc., p. 29-35, 2022.03

[Misc]

- 1. Okiji T. Future perspectives of MTA. The Nippon Dental Review. 2022.01; 82(1); 74
- 2. Okiji T. Current status of MTA. . The Nippon Dental Review. 2022.01; 82(1); 26-36.
- 3. Okiji T. Answer from the author. The Journal of the Japanese Society for Dental Materials and Devices. 2022.05; 41(2); 123
- 4. Yamamoto R, Watanabe S, Okiji T. Outcomes of primary root canal therapy: An updated systematic review of longitudinal clinical studies published between 2003 and 2020. The Quintessence. 2022.12; 41(12); 188-190
- 5. Okiji T, Shigetani Y, Yoshiba K, Ohshima H. GaAlAs diode laser-induced mineralized tissue formation in dentin/ pulp complex: A review. The Journal of Japan Society for Laser Surgery and Medicine. 2022.07; 43(2); 113-119
- 6. Watanabe S, Okiji T. Application of root canal irrigation using Er:YAG Laser. The Journal of Japan Society for Laser Surgery and Medicine. 2022.07; 43(2);98-112

- 7. Okuda H, Watanabe S, Okiji T. Accuracy of cold sensibility testing on teeth with full-coverage restorations: a clinical study. The Quintessence. 2022.02; 41(2); 223-225
- 8. Hirano K, Watanabe S, Okiji T. The impact of an enhanced infection control protocol on molar root canal treatment outcome a randomized clinical trial. The Quintessence. 2022.05; 41(5); 219-221
- 9. Natori K, Watanabe S, Okiji T. External cervical resorption-Treatment outcomes and determinants: A retrospective cohort study with up to 10years of follow-up. The Quintessence. 2022.10; 41(10); 182-184
- 10. Kasuga Y, Okiji T. Factors related to the outcomes of cracked teeth after endodontic treatment. The Nippon Dental Review. 2022.01; 82(1); 140-141
- 11. Hirano K, Okiji T. Factors associated with extraction following root canal filling in adults. The Nippon Dental Review. 2022.05; 82(5); 136-137
- 12. Ito R, Okiji T. Root-end surgery or nonsurgical retreatment: Are there differences in long-term outcome? The Nippon Dental Review. 2022.09; 82(9); 144-145

[Conference Activities & Talks]

1. Tazawa K, Chen D, King, P, Sasaki H. Challenge To identify lymphatic vessels in mouse dental pulp. School of Dentistry Research Day. 2022.02.17, Ann Arbor, USA

2. Kawashima N. MTA: Anti-inflammatory actions & insight of its mechanisms strontium ranelate: A candidate of new pulp capping material. 5th International Symposium of Iranian Association of Endodontists. 2022.03.02, Virtual Meeting

3. Okiji T. Mineral trioxide aggregate: Properties and clinical applications. Academy of Endodontics. 2022.03.06, Tokyo

4. Satake K , Shimogishi M , Watanabe T, Watanabe S, OKIJI T Microbiome analysis of samples obtained from treatment-resistant apical periodontitis with 16S rRNA gene sequencing. The 156th Meeting of the Japanese Society of Conservative Dentistry. 2022.06.16, Virtual Meeting

5. Liu J, Watanabe S, Mochizuki S, Kouno A, Okiji T. Evaluation of the ability of Er:YAG laser-activated irrigation to clean the apical area beyond the fractured instrument. The 156th Meeting of the Japanese Society of Conservative Dentistry. 2022.06.16, Virtual Meeting

6. Unno H, Ebihara A, Hirano K, kasuga Y, Omori S, Maki K, Kikuna S, Okaji T. Evaluation of stress generation and apical transportation during root canal preparation with TruNatomy NiTi rotary instruments. The 156th Meeting of the Japanese Society of Conservative Dentistry. 2022.06.16, Virtual Meeting

7. Omori S, Maki K, Kimura S, Nakatsukasa T, Unno H, Ebihara A, Okiji T. Effect of various rotational modes on the stress generation and shaping ability during nickel-titanium rotary root canal instrumentation. The 156th Meeting of the Japanese Society of Conservative Dentistry. 2022.06.16, Virtual Meeting

8. Kyaw MS, Maki K, Kimura S, Thu M, Ebihara A, Okiji T. Effect of root canal curvature location and preset torque settings on torque/force generation and shaping ability of a nickel titanium rotary glide path instrument. The 156th Meeting of the Japanese Society of Conservative Dentistry. 2022.06.16, Virtual Meeting

9. Kieu QT, Tazawa K, Kawashima N, Noda S, Fujii M, Sunada-Nara K, Hashimoto K, Han P, Okiji T. LYVE-1+ M2macrophages: identification in dental-pulp and their pro-angiogenic activity in-vitro. The 100th General Session & Exhibition of the IADR. 2022.06.23, Virtual Meeting

10. Wang S, Sunada-Nara K, Kawashima N, Han P, Okiji T. MicroRNA-27a downregulates proinflammatory cytokines expression in LPS-stimulated human pulp cells. The 100th General Session & Exhibition of the IADR. 2022.06.23, Virtual Meeting

11. Yu Z, Sunada-Nara K, Kawashima N, Kieu QT, Han P, Okiji T. MicroRNA-27a upregulates osteoblastic markersexpression in human dental pulp cells. The 100th General Session & Exhibition of the IADR. 2022.06.23, Virtual Meeting 13. Han P, Sunada-Nara K, Kawashima N, Wang S, Kieu QT, Yu Z, Okiji T. MicroRNA-146b suppresses proinflammatory mediators synthesis in lipopolysaccharide-stimulated dental pulp cells. The 100th General Session & Exhibition of the IADR. 2022.06.23, Virtual Meeting

14. Watanabe S. Basic endodontics based on evidence + α . The 59th Oral Studio Web Seminar. 2022.06.28, Virtual Meeting

15. Thu M, Ebihara A, Kyaw MS, Omori S, Maki K, Kimura S, Unno H, Okiji T. Influence of different kinematics on stationary and dynamic torque/screw-in force generation during nickel-titanium rotary instrumentation. The 43rd Meeting of Japan Endodontic Association. 2022.07.9-25, Virtual Meeting

16. Alchawoosh A, Hashimoto K, Kawashima N, Okiji T. Anti inflammatory effects of hydraulic calcium silicate based endodontic sealers on lipopolysaccharide stimulated macrophages. The 43th Meeting of Japan Endodontic Association. 2022.07.9-25, Virtual Meeting

17. Mochizuki S, Watanabe S, Liu J, Okiji T. Evaluation of the cleaning ability of different irrigation techniques in conservatively instrumented root canals. The 43rd Meeting of Japan Endodontic Association. 2022.07.9-25, Virtual Meeting

18. Takuya Kawamura, Satoshi Watanabe, Akira Kouno, Takashi Okiji. Comparative evaluation and effect of establishing apical patency before root canal irrigation on the removability of intracanal calcium hydroxide pastes. The 43rd Meeting of Japan Endodontic Association. 2022.07.9-25, Virtual Meeting

19. Okiji T. Endodontics considerations in the management of traumatized teeth. Clinical Workshop, Japan Association of Dental Traumatology. 2022.07, Virtual Meeting

20. Watanabe S. Advanced endodontics to solve difficulty. The 62nd OralStudio Web Seminar. 2022.07.26, Virtual Meeting

21. Okiji T. Clinical endodontics in TMDU: microendodontics, NiTi rotary instrumentation and MTA. 58th C. D. E., Part II, Dental Alumni Association Tokyo Medical & Dental University. 2022.07.31, Tokyo

22. Watanabe S. First step for endodontic surgery. The 64th OralStudio Web Seminar. 2022.08.23, Virtual Meeting

23. Okiji T, Watanabe S. Evidence-based endodontics. Post-graduate education course, Tokyo Dental Association. 2022.08.28, Tokyo

24. Okiji T. Diagnosis and management of traumatized teeth: Endodontic considerations. Clinical Workshop, Japan Association of Dental Traumatology. 2022.09.11, Tokyo

25. Watanabe S. Omnibus of adjunct endodontics. The 66th OralStudio Web Seminar. 2022.09.27, Virtual Meeting

26. Okiji T. Essence of root canal retreatment. 1D Dental Seminar. 2022.10.03, Virtual Meeting

27. Watanabe S. Problem solving in Endodontics. The 29th Seminar for Specialist in Japan Endodontic Association. 2022.11.01, Virtual Meeting

28. Hirano K, Kimura S, Maki K, Unno H, Omori S, Kasuga Y, Ebihara A, Okiji T. Effect of different pecking depth on stress generation and shaping ability of XP-endo Shaper nickel-titanium rotary instruments. The 157th Meeting of the Japanese Society of Conservative Dentistry. 2022.11.10, Okayama

29. Alchawoosh A, Hashimoto K, Thein HSS, Kawashima N, Okiji T. Investigating the anti-inflammatory effect of hydraulic silicate-based endodontic materials in comparison with MTA. The 157th Meeting of the Japanese Society of Conservative Dentistry. 2022.11.10, Okayama

30. Kyaw MS, Maki K, Kimura S, Thu M, Omori S, Ebihara A, Okiji T. Effect of root canal curvature location and preset torque settings on torque/force generation and shaping ability of a nickel titanium rotary instrument. The 157th Meeting of the Japanese Society of Conservative Dentistry. 2022.11.11, Okayama

31. Watanabe S. Discussion of cleaning efficacy using Er:YAG laser. The 25th Anniversary Forum for Er:YAG laser. 2022.11.13, Tokyo

32. Okiji T. Endodontic management of traumatized teeth. Clinical Workshop, Japan Association of Dental Traumatology. 2022.11.13, Tokyo

33. Kasuga Y, Kimura S, Maki K, Unno H, Oomori S, Ebihara A, Okiji T. Evaluation of mechanical properties of heattreated nickel-titanium rotary endodontic instruments. The 87th Annual Meeting of the Stomatological Society. 2022.12.02, Tokyo

34. Tonami K, Umemori S, Noritake K, Hideshima M, Ebihara A, Ridan C, Sunaga M, Kinoshita A, Nitta H. Development of an insurance claim training application using Microsoft Excel macro. The 87th Annual Meeting of the Stomatological Society. 2022.12.03, Tokyo

[Awards & Honors]

Han Peifeng. Pulp Biology & Regeneration Group Travel Award, IADR, 2022. 06

Advanced Prosthodontics

Professor - Noriyuki Wakabayashi

Associate Professor - Takeshi Ueno, Yuka Sumita (Carrere up) (~ March 2022, Maxillofacial Prosthetics)

Junior Associate Professor - Kosuke Nozaki (August \sim)

Assistant Professors - Atsushi Takaichi, Kensuke Takakusaki, Mariko Hattori (\sim March 2022, Maxillofacial Prosthetics), Natsuko Murakami, Toshiki Yamazaki, Junnichiro Wada (Sabbatical)

Restart Postdoctoral (RPD) Research Fellowships: Yuka Kajima

Project Assistant Professor - Mihoko Haraguchi (~ March 2022, Maxillofacial Prosthetics), Mai Murase (~ March 2022, Maxillofacial Prosthetics)

Hospital Staff - Hisami Okawara, Kim Eung Yeol, Kazuaki Sakamoto, Hirokazu Sato, Shintaro Suzuki, Tomiharu Nagayama, Yoko Hayashi, Tanabe Gen (\sim March 2022 Quit, Maxillofacial Prosthetics), Fujita Haruka (\sim March 2022, Maxillofacial Prosthetics), Tani Hiroko (May \sim)

Speech-Language-Hearing Therapist - Masaki Keita (Clinic for Speech Therapy)

Graduate Students

- Amr Gamal, Yurika Ishioka, Yuji Uchida, Miona Utsumi, Qu Wenrui, Wu huaze, Yoshio Kobayashi, Kohei Komine, San Win Thant, Jiang Mengtian, Zou Shiqi, Huichuan Xu, Satsuki Tanaka, Zhang Yihui, Zhao Qian, Zhang Maorui, Zheng Jingpu, Ding Zhiyuan, Thida Phyo, Asuka Hirata, Hein Linn Htat, Hitomi Matsuno, Yang Shiyi, Lyu Huaxin, Bin Li, Ali Ahmed Sameir Mohamed (April \sim), Alkrayem Bilal Lukman (October \sim)

(\sim March 2022, Maxillofacial Prosthetics)

Tani Hiroko (\sim March), Gao Yuan, Wang Yujia, Towithelertkul Cheewin, Yu Hongli, Chugh Anshul, Han Xuewei, Ali Islam Elsayed, Bai Ziyi, Wang Jiangyu, Zhang Fan, Pradhan Nehasha

Part-time Special Student - Koki Abe, Tetsu Sato, Dong Jialin, Ali Ahmed Sameir Mohamed (\sim March 2022, Maxillofacial Prosthetics), Pang Xinyu (April \sim), Miao Menghan (October \sim)

Clinical Professor - Masaru Yatabe

Part-time Lecturer (Faculty of Dentistry) - Yuki Arai, Yasuha Ikawa, Keigo Isoshima, Hideaki Inagawa, Shusuke Inukai, Yuki Iwaki, Keiichiro Uchikura, Hirofumi Uchida, Takeshi Ootubo, Chie Okamoto, Masahiro Ona, Taihei Kasai, Ryunosuke Kazama, Hayato Kumagai, Masato Kotake, Hirohumi Sato, Natsuki Suzuki, Takashi Sekinishi, Yusuke Toyoshima, Yasuo Nakajima, Kohji Nagata, Kazutoshi Nakamura, Gen Nabeshima, Youko Hayashi, Hironari Hyama, Kazuyuki Handa, Shiro Hibi, Masahiro Hirasawa, Kengo Fujiki, Ichiro Minami, Chie Watanabe (~ March 2022, Maxillofacial Prosthetics) Arai Takayuki, Elbashti Mahmoud Ellarousi, Hatano Noriko, Teruyama Yuko, Yesiboli Yeerken (April ~)

Part-time Lecturer (Graduated School) - Hideharu Hibi, Kazuhiro Hori (~ March 2022, Maxillofacial Prosthetics) Ozawa Shogo, Tanigawa Chihiro, Inohara Ken, Mukohyama Hitoshi (April ~)

Visiting Researcher - Abouelezz Marwa Ahmed Mohamed Abdelrahman

(1) **Outline**

Department of Advanced Prosthodontics made a fresh start in April 2022, accepting the staff from the Department of Maxillofacial Prosthetics because of the discontinuation. Historically, our Department has inherited the clinical and research backgrounds that the First Department of Prosthodontics and the Department of Masticatory Function Rehabilitation were proud of, and we specialized in removable partial prosthodontics. Now we are responsible for bridging the gap between basic sciences and clinical research on development of the prosthetic materials and technologies, as well as teaching and training dental professionals as our future human resources.

(2) Research

- 1. Treatment Planning, Treatment and Evaluation in Prosthodontics
- 2. Design Optimization of Prosthodontic Biomaterials
- 3. Biological Evaluation of Oral Tissues in Prosthodontic Patients
- 4. Educational Development in Prosthodontics

Grants-in-Aid for Scientific Research

Grants-in-Aid for Scientific Research(C): Noriyuki Wakabayashi, Takeshi Ueno, Shunsuke Inukai, Kosuke Nozaki, Kimihiro Yamashita, Masahiro Ona, Atsushi Takaichi, Yuka Kashima Cront in Aid for Young Scientista, Kauji Nakata, Yuguka Tayashima, Ujagrij Okamana, Kanguka Takakugaki

Grant-in-Aid for Young Scientists: Kouji Nakata, Yusuke Toyoshima, Hisami Okawara, Kensuke Takakusaki, Gen Nabeshima, Hideaki Inagawa, Yasuha Ikawa

Private Grant

Nissin Dental Products INC. (Noriyuki Wakabayashi)

Nissin Dental Products INC. (Noriyuki Wakabayashi)

MITSUI & CO., LTD. (Noriyuki Wakabayashi)

Tokuyama Dental Corporation (Noriyuki Wakabayashi)

Tokuyama Dental Corporation (Kosuke Nozaki)

Yamaha Corporation: Raising of music dentistry (Yuka Sumita)

Yamaha Corporation, Yamaha Music Foundation: Effect of music exercise on oral function (Yuka Sumita) The MIKIYA Science And Technology Foundation: Structured infrastructure construction of expert skill for the application of AI technology to medical diagnosis (Yuka Sumita)

Innovation Idea Contest 2022: Development of a speech examination equipment Speech-EX (Mariko Hattori)

WISE Program

Huichuan Xu, Bin Li, Miona Utsumi, Zhao Qian, Kohei Komine, Zhang Maorui, Yu Hongli, Jiang Mengtian

(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

Extension Course TMDU International Faculty Development Course (IFDC). 31 January, 8 April, 15 April, 22 April, 1 July 2022.

(4) Lectures & Courses

This Department 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 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 complaints of the patients. The ultimate goal is to improve the oral health-related quality of life of patients.

The Department also manages the clinic for Maxillofacial Prosthetics and the clinic for Speech Therapy that do the prosthodontic and/or prosthetic treatment for patients with defects in oral and/or maxillofacial regions.

(7) Publications

[Original Articles]

- Nakai H, Inokoshi M, Nozaki K, Yoshihara K, Matsukawa A, Nagaoka N, Tonprasong W, Minakuchi S. Osteoblast Response of Additively Manufactured Zirconia and Alumina-Toughened Zirconia. Materials (Basel). 2022.12; 15(23); 8685
- 2. Gao Y, Hattori M, Zhang M, Elbashti ME, Sumita YI. Evaluating the feasibility and accuracy of digitizing a maxillary defect model simulating various trismus conditions. Int J Prosthodont. 2022.12; online.;
- 3. Hattori M, Patzelt SBM, Stadler S, Kohal RJ, Vach K, Elbashti ME, Sumita YI. Computerized optical scanning of ears: An in vitro evaluation with an intraoral scanner. J Prosthet Dent. 2022.12; online.;

- 4. Saleh Omnia, Nozaki Kosuke, Matsumura Mayuko, Yanaka Wataru, Miura Hiroyuki, Fueki Kenji. Texture-Based Neural Network Model for Biometric Dental Applications JOURNAL OF PERSONALIZED MEDICINE. 2022.12; 12(12);
- 5. Eung-Yeol Kim, Junichiro Wada, Kazuki Sakamoto, Yurika Ishioka, Yuki Arai, Natsuko Murakami, Toshiki Yamazaki, Hironari Hayama, Miona Utsumi, Shusuke Inukai, Noriyuki Wakabayashi. Effect of Scanning Origin Location on Data Accuracy of Abutment Teeth Region in Digital Impression Acquired Using Intraoral Scanner for Removable Partial Denture: A Preliminary In Vitro Study Journal of Clinical Medicine. 2022.12; 11(24); 7392
- 6. Ali IE, Murase M, Yonehara Y, Sumita YI. Time and cost of maxillofacial prosthetic treatment: The need for assessment. Jpn Dent Sci Rev. 2022.11; 58; 67-68
- Inamochi Y, Kohno EY, Wada J, Murakami N, Takaichi A, Arai Y, Ueno T, Fueki K, Wakabayashi N.. Knowledge acquisition efficacy of a remote flipped classroom on learning about removable partial dentures J Prosthodont Res. 2022.11;
- 8. Wang Y, Hattori M, Liu R, Sumita YI. Digital acoustic analysis of the first three formant frequencies in patients with a prosthesis after maxillectomy. J Prosthet Dent. 2022.11; online.;
- 9. Trang BNH, Kanazawa M, Murakami N, Wakabayashi N, Hada T, Sahaprom N, Komagamine Y, Minakuchi S. Stress distribution of one-piece and two-piece mini-Implant overdentures with various attachment systems and diameters: A finite element analysis. Journal of prosthodontic research. 2022.11;
- Saleh O, Nozaki K, Matsumura M, Yanaka W, Abdou A, Miura H, Fueki K. Emergence angle: Comprehensive analysis and machine learning prediction for clinical application. Journal of prosthodontic research. 2022.11;
- 11. Chie Watanabe, Junichiro Wada, Koji Mizutani, Tomiharu Nagayama, Hirofumi Uchida, Yo Shibata, Noriyuki Wakabayashi. Radiographic predictive factors for 10-year survival of removable partial denture abutment teeth: Alveolar bone level and density Journal of Prosthodontic Research. 2022.11;
- 12. Zhao Qian, Ueno Takeshi, Chen Peng, Nozaki Kosuke, Tan Tianbo, Hanawa Takao, Wakabayashi Noriyuki. Fabrication of micro-/submicro-/nanostructured surfaces on Ti-Zr alloy by varying H2SO4/H2O2 treatment conditions and investigations of fundamental properties of a typical surface SURFACES AND INTERFACES. 2022.11; 34;
- Towithelertkul C, Sumita YI, Murakami T, Notake R, Akiyama M, Yoshimura R, Wakabayashi N. Radiation attenuation properties of materials used to fabricate radiotherapy prostheses in vitro study. J Oral Sci. 2022.10; 64(4); 274-278
- 14. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of Nitrogen Gas Post-Curing and Printer Type on the Mechanical Properties of 3D-Printed Hard Occlusal Splint Material Polymers. 2022.10; 14(19); 3971
- 15. Kajima Yuka, Takaichi Atsushi, Htata Hein Linn, Hanawa Takao, Wakabayashi Noriyuki. Recrystallization behavior of selective laser melted Co-Cr-Mo alloys with several heat treatment times MATERIALS SCIENCE AND ENGINEERING A-STRUCTURAL MATERIALS PROPERTIES MICROSTRUCTURE AND PROCESSING. 2022.10; 856;
- 16. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of 3D Printer Type and Use of Protection Gas during Post-Curing on Some Physical Properties of Soft Occlusal Splint Material Polymers. 2022.10; 14(21); 4618
- 17. Hattori M, Haraguchi M, Semper-Hogg W, Kohal RJ, Sumita YI. Prosthodontic rehabilitation on a patient with limited mouth opening related to rheumatoid arthritis: A clinical report. Int J Maxillofac Prosthetics. 2022.09; 5(1); 18-21
- 18. Ali ASM, Hattori M, Sumita YI. Consonant evaluation during fabrication of a removable prosthesis for a cleft lip and palate patient: A clinical report. Int J Maxillofac Prosthetics. 2022.09; 5(1); 22-24
- 19. Haraguchi M, Towithelertkul C, Ali IE, Han X, Sumita YI. An indirect-direct technique with hot water for fabricating a cast metal crown under an existing removable partial denture. J Prosthet Dent. 2022.09; online.;

- 20. Towithelertkul C, Haraguchi M, Tanabe G, Fujita H, Ali IE, Han X, Sumita YI. Two-piece detachable interlocking mold for low-dose-rate brachytherapy: A dental technique for radiotherapy prosthesis fabrication. J Prosthet Dent. 2022.08; online.;
- 21. Ali IE, Hattori M, Sumita YI, Wakabayashi N. Effect of cut-out rescan procedures on the accuracy of an intraoral scanner used for digitizing an ear model: An in vitro study. J Prosthodont. 2022.08; online.;
- Jia Deng, Yuta Fukushima, Kosuke Nozaki, Hideyuki Nakanishi, Erica Yada, Yuki Terai, Kenji Fueki, Keiji Itaka. Anti-Inflammatory Therapy for Temporomandibular Joint Osteoarthritis Using mRNA Medicine Encoding Interleukin-1 Receptor Antagonist. Pharmaceutics. 2022.08; 14(9);
- Murase M, Tani H, Sumita YI, Ino S, Taniguchi H. Nutritional assessment in a maxillectomy patient from the preoperative period to definitive obturator insertion: A case report. J Prosthodont Res. 2022.07; 66(3); 514-518
- 24. Elbashti ME, Aswehlee AM, Rahman MA, Sumita YI, Bornstein MM, Schimmel M, Abou-Ayash S, Molinero-Mourelle P. Triangular mesh reduction of digitized maxillectomy defects for prosthetic rehabilitation: A 3D deviation study. J Dent. 2022.07; 122; 104090
- 25. Nozaki K, Nagai A, Endo T, Hashimoto K, Yamashita K.. Electrical polarization and ionic conduction properties of β -tricalcium phosphate bioceramics with controlled vacancies by sodium ion substitution Ceramics International. 2022.06; 48(11); 15791-15799
- 26. Han X, Haraguchi M, Sumita YI. Effect of a lingual augmentation prosthesis for preventing salivation after subtotal glossectomy: A clinical report. Int J Maxillofac Prosthetics. 2022.05; 5(1); 13-17
- 27. Zhang F, Hattori M, Sumita YI. Facial prosthesis fabricated from dental material for an exposed reconstruction plate: A clinical report. Int J Maxillofac Prosthetics. 2022.05; 5(1); 10-12
- 28. Tan T, Zhao Q, Kuwae H, Ueno T, Chen P, Tsutsumi Y, Mizuno J, Hanawa T, Wakabayashi N. Surface properties and biocompatibility of sandblasted and acid-etched titanium-zirconium binary alloys with various compositions. Dental materials journal. 2022.04; 41(2); 266-272
- 29. Takakusaki K, Murakami N, Wada J, Kasai T, Matsuno H, Yamazaki T, Iwasaki N, Yatabe M, Takahashi H, Wakabayashi N. Effect of retention hole designs in artificial teeth on failure resistance of the connection with thermoplastic resin. Dental materials journal. 2022.04; 41(4); 573-579
- 30. Tanabe G, Hattori M, Obata S, Takahashi Y, Churei H, Nishiyama A, Ueno T, Sumita YI. Case report: Psychoacoustic analysis of a clarinet performance with a custom-made soft lip shield worn to prevent mucosal erosion of lower lip. Front Psychol. 2022.04; 13; 852866
- 31. Chiaki Tsutsumi-Arai, Yuki Arai, Chika Terada-Ito, Takahiro Imamura, Seiko Tatehara, Shinji Ide, Noriyuki Wakabayashi, Kazuhito Satomura. Microbicidal effect of 405-nm blue LED light on Candida albicans and Streptococcus mutans dual-species biofilms on denture base resin. Lasers Med Sci. 2022.03; 37(2); 857-866
- 32. Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Influence of high-speed sintering protocols on translucency, mechanical properties, microstructure, crystallography, and low-temperature degradation of highly translucent zirconia. Dent Mater. 2022.02; 38(2); 451-468
- Hattori M, Murase M, Sumita YI. Hoarseness evaluation and prosthetic rehabilitation after maxillofacial surgery: A clinical report. Int J Maxillofac Prosthetics. 2022.02; 4; 43-46
- 34. Saito N, Mikami R, Mizutani K, Takeda K, Kominato H, Kido D, Ikeda Y, Buranasin P, Nakagawa K, Takemura S, Ueno T, Hosaka K, Hanawa T, Shinomura T, Iwata T. Impaired dental implant osseointegration in rat with streptozotocin-induced diabetes. Journal of periodontal research. 2022.01; 57(2); 412-424
- 35. Fueki Kenji, Inamochi Yuka, Wada Junichiro, Arai Yuki, Takaichi Atsushi, Murakami Natsuko, Ueno Takeshi, Wakabayashi Noriyuki. A systematic review of digital removable partial dentures. Part I: Clinical evidence, digital impression, and maxillomandibular relationship record(和訳中) Journal of Prosthodontic Research. 2022.01; 66(1); 40-52

- 36. Takaichi Atsushi, Fueki Kenji, Murakami Natsuko, Ueno Takeshi, Inamochi Yuka, Wada Junichiro, Arai Yuki, Wakabayashi Noriyuki. A systematic review of digital removable partial dentures. Part II: CAD/CAM framework, artificial teeth, and denture base(和訳中) Journal of Prosthodontic Research. 2022.01; 66(1); 53-67
- 37. Yamaguchi J, Chiba R, Komuro H, Ihara K, Nozaki K, Nagai A, Furukawa T, Sasano T. Local Injection of Hydroxyapatite Electret Ameliorated Infarct Size After Myocardial Infarction. Circulation reports. 2022.01; 4(1); 38-47
- 38. Chowdhury RU, Churei H, Tanabe G, Yoshida Y, Hayashi K, Takahashi H, Wada T, Uo M, Mizobuchi T, Chowdhury NU, Ueno T. Useful design of custom-made mouthguard for athletes undergoing orthodontic treatment with brackets and wires. J Dent Sci. 2022.01; 17(1); 308-315
- Uchida H, Wada J, Watanabe C, Nagayama T, Mizutani K, Mikami R, Inukai S, Wakabayashi N.. Effect of night denture on tooth mobility in denture wearers with sleep bruxism: a pilot randomized controlled trial. Journal of Prosthodontic Research. 2022; 66(4); 564-571
- 40. Uchikura K, Murakami N, Yamazaki T, Lyu H, Nagata K, Ona M, Iwasaki N, Takahashi H, Wakabayashi N. Fracture resistance of CAD/CAM restorative materials in mismatched removable partial denture rests: An in vitro experimental and finite element analysis Dental materials journal. 2022.05; 41(3); 466-472
- Huaxin Lyu, Natsuko Murakami, Toshiki Yamazaki, Junichiro Wada, Miona Utsumi, Noriyuki Wakabayashi. Evaluation of PEEK and zirconia occlusal rest designs for removable partial dentures based on finite element analysis J Prosthodont Res. 2022.05;
- 1. Junichiro Wada. Prosthetic strategies for efficient use and protection of weakened abutment teeth Annals of Japan Prosthodontic Society. 2022.01; 14(1); 38-45

[Books etc]

1. Nozaki K, Saleh O, Arakawa S, Miura H. Water-Formed Deposits Fundamentals and Mitigation Strategies. Elsevier, 2022.03

[Misc]

- 1. Ali IE, Sumita YI. Medication-related osteonecrosis of the jaw: Prosthodontic considerations. Jpn Dent Sci Rev. 2022.11; 58; 9-12
- Ali IE, Chugh A, Towithelertkul C, Hattori M, Sumita YI. The rising challenge of mucormycosis for maxillofacial prosthodontists in the Covid-19 pandemic: A literature review. J Prosthodont Res. 2022.07; 66(3); 395-401
- 3. Elbashti ME, Molinero-Mourelle P, Aggarwal H, Aswehlee AM, Schimmel M, Abou-Ayash S, Yamamori T, Baba K, Sumita YI. Feasibility and accuracy of using intraoral scanners to digitize maxillectomy defects for prosthetic rehabilitation: A systematic review. Int J Maxillofac Prosthetics. 2022.05; 5(1); 3-9
- 4. Kenji Fueki, Yuka Inamochi, Junichiro Wada, Yuki Arai, Atsushi Takaichi, Natsuko Murakami, Takeshi Ueno, Noriyuki Wakabayashi. A systematic review of digital removable partial dentures. Part I: Clinical evidence, digital impression, and maxillomandibular relationship record. J Prosthodont Res. 2022.01; 66(1); 40-52
- 5. Atsushi Takaichi, Kenji Fueki, Natsuko Murakami, Takeshi Ueno, Yuka Inamochi, Junichiro Wada, Yuki Arai, Noriyuki Wakabayashi. A systematic review of digital removable partial dentures. Part II: CAD/CAM framework, artificial teeth, and denture base. J Prosthodont Res. 2022.01; 66(1); 53-67
- Junichiro Wada, Koji Mizutani, Noriyuki Wakabayashi. The Successful Concept of Removable Partial Denture in Patient with Periodontitis: How to Preserve and Involve the Fragile Abutment Tooth in RPD? Part 3. Prosthodontic Approach for Fragile Abutment Tooth Protection The Quintessence. 2022.12; 41(12); 82-101
- 2. Junichiro Wada, Koji Mizutani, Noriyuki Wakabayashi. The Successful Concept of Removable Partial Denture in Patient with Periodontitis: How to Preserve and Involve the Fragile Abutment Tooth in RPD? Part 2. Removable Partial Denture Designing to Protect and Utilize Abutment Tooth The Quintessence. 2022.10; 41(10); 74-92

- 3. Junichiro Wada, Koji Mizutani, Noriyuki Wakabayashi. The Successful Concept of Removable Partial Denture in Patient with Periodontitis: How to Preserve and Involve the Fragile Abutment Tooth in RPD? Part1. Prosthodontic Treatment Following Periodontal Management The Quintessence. 2022.08; 41(8); 36-55
- 4. A systematic review of digital removable partial dentures Ann Jpn Prosthodont Soc. 2022.01; 14(1); 17-24
- 5. Wada J, Takaichi A, Wakabayashi N. Clinical procedure of magnetic attachment-Let's reconfirm its usefulness with the opportunity of insurance listing- The Nipponn Dental Review. 2022.01; 82(1); 88-95

[Conference Activities & Talks]

- 1. Hattori M. Digital evaluation in musicians' dentistry: An effective tool for performance. Digitodontics Webinar Series 2022.11.22 (Webinar)
- 2. Kanae Wada, Junichiro Wada, Hanae Kanazawa, Janna Waltimo-Siren, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Nano-mechanical Properties of Primary Molar Enamel with Enamel Hypoplasia, Early Enamel Demineralized, and Sound Enamel. International Association of Pediatric Dentistry (IAPD) 2nd Global Summit 2022.11.12 Roma, Italy
- 3. Kanae Wada, Junichiro Wada, Hanae Kanazawa, Janna Waltimo-Siren, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Kiillevaurioalentaa merkittävästi maitohampaan pintakovuutta. Finnish Dental Journal 2022.11.10 Helsinki, Finland
- 4. Nakai H, Inokoshi M, Nozaki K, Minakuchi S. Cell viability and osteogenic ability of additively manufactured zirconia. International Dental Materials Congress 2022 2022.11.04 hybrid (web, Taipei)
- 5. Kanae Wada, Junichiro Wada, Hanae Kanazawa, Janna Waltimo-Siren, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila.. Mechanical and Histological Properties of Primary Molar Enamel with Enamel Hypoplasia. Biomaterials and Medical Devices Research Program of BioCity Turku, Turku Biomaterials Days 2022.10.27 Turku, Finland
- 6. Yuka KAJIMA, Atsushi TAKAICHI, Takao HANAWA, Noriyuki WAKABAYASHI. Effect of several heat treatment times on the microstructure and mechanical behavior of selective laser melted Co–Cr–Mo alloys . The 6th International Symposium on Visualization in Joining & Welding Science through Advanced Measurements and Simulation&The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA) 2022.10.25 Osaka
- 7. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of Nitrogen Post-Curing on Surface Conditions of 3D-Printed Splint. The Academy of Dental Materials 2022 Meeting 2022.10.01 Athens, Greece
- 8. Tanabe G, Hattori M, Mizuguchi D, Masaki K, Wang Y, Hasegawa S, Tohara H, Sumita YI. Effect of voice training on maxillofacial function; a preliminary survey. Musicians' and Performing Artists' Health and Performance Conference 2022 (MHPC22) 2022.09.23 Oslo (Norway)+Web
- 9. Hattori M, Tanabe G, Patzelt SBM, Schulze D, Sumita YI. Visualization of oral function during playing a wind instrument by a lateral dental impression: a proof-of-concept investigation. Musicians' and Performing Artists' Health and Performance Conference 2022 (MHPC22) 2022.09.22 Oslo (Norway)+Web
- 10. Junichiro Wada, Kanae Wada, Mona Gibreel, Sufyan Garoushi, Pekka K. Vallittu, Lippo Lassila. Effect of Post-curing at Nitrogen Gas on Mechanical Properties of Water-stored 3D-printed Hard Occlusal Splint. The 2022 annual Conference of the European Prosthodontic Association 2022.09.22 Siena, Italy
- 11. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of printer types on mechanical properties of 3D-printed splint. The PAN EUROPEAN REGION of the International Association for Dental Research (PER-IADR Oral Health Research Congress) 2022.09.16 Marseille, France
- 12. Kanae Wada, Junichiro Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of nitrogen gas on mechanical properties of 3D-printed splint. The PAN EUROPEAN REGION of the International Association for Dental Research (PER-IADR Oral Health Research Congress 2022.09.16 Marseille, France

- Merve Uctasli, Junichiro Wada, Kanae Wada, Lippo Lassila. Different types of CAD/CAM materials surface morphology examination and clinical indications.. The 26th Turkish Dental Association International Dental Meeting 2022 2022.09.08 Istanbul, Turkey
- 14. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of Post-curing at Nitrogen Gas on Mechanical Properties of Water-stored 3D-printed Soft Occlusal Splint. Scandinavian Society for Prosthodontic Dentistry 2022.08.19 Aarhus, Denmark
- 15. Saleh O, Nozaki K, Matsumura M, Yanaka W, Miura H, Fueki K. Development of an emergence angle estimation program by machine learning. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16
- 16. Sumita YI. Digitized acoustic evaluation: An objective approach to improve speech in head and neck cancer patients. Digitodontics Webinar Series 2022.07.07 (Webinar)
- 17. Hattori M, Tanabe G, Sumita YI, Obata S, Churei H, Ueno T. Does playing music influence the rehabilitation of a maxillofacial defect patient?. 40th Annual PAMA International Symposium 2022.06.25 Chicago (USA)+Web
- 18. Tonprasong W, Inokoshi M, Tamura M, Yoshihara K, Takahashi R, Wada T, Nozaki K, Minakuchi S. Porphyromonas gingivalis adhesion on highly polished tooth-colored materials. 2022 IADR/APR General Session & Exhibition 2022.06.24 web
- 19. Hattori M. Maxillofacial prosthodontics Speech analysis. Seminar with Faculty of Dentistry University of Malaya, TMDU-UM Maxillofacial Prosthodontics lecture series 2022.05.11 (Web Seminar)
- 20. Hattori M. TMDU maxillofacial prosthodontics cases Sharing session. Seminar with Faculty of Dentistry University of Malaya, TMDU-UM Maxillofacial Prosthodontics lecture series 2022.04.27 (Web Seminar)
- Matsuno H, Li B, Okawara H, Toyoshima Y, Murakami N, Wakabayashi N. Effect of Tension and Compression on Dynamic Alveolar Histomorphom. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2022 2022.12.18 Tokyo
- Komine K, Murakami N, Yamazaki T, Utsumi M, Li B, Ona M, Wakabayashi N. Effect of restorative material thickness on thermal stress. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2022 2022.12.18 Tokyo
- 3. Utsumi M, Murakami N, Yamazaki T, Sakamoto K, Lyu H, Komine K, Kim EY, Wada J, Wakabayashi N. Accuracy of light-cured reline material in direct reline of removable partial dentures. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2022 2022.12.18 Tokyo
- 4. Lyu H, Murakami N, Yamazaki T, Zou S, Ding Z, Wada J, Wakabayashi N. Stress Analysis of PEEK and Zirconia Occlusal rest designs for Removable Partial Dentures. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2022 2022.12.18 Tokyo
- 5. Hirata A, Takakusaki K, Tanimoto M, Nakamura R, Komine K, Murakami N, Nozaki K, Wakabayashi N. Adhesion of *C. albicans* to the light-cured denture base relining material. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2022 2022.12.18 Tokyo
- 6. Kim E, Wada J, Sakamoto K, Ishioka Y, Arai Y, Murakami N, Yamazaki T, Hayama H, Utsumi M, Inukai S, Wakabayashi N. Effect of scanning origin location on data accuracy of digital impression acquired using an intraoral scanner for partially edentulous dental arch. Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2022 2022.12.18 Tokyo
- 7. Matsumura M, Nozaki K, Yanaka W, Beniya R, Matsumuto A, Wakabayashi N, Fueki K. Effect of cement space on color tone of anterior CADCAM crowns. 2022.12.18
- 8. Ali IE, Hattori M, Sumita YI, Wakabayashi N. Effect of cut-out rescan procedures on the accuracy of an intraoral scanner used for digitizing an ear model: An in vitro study. The 87th Annual Meeting of the Stomatological Society, Japan 2022.12.03 Tokyo (Japan)
- 9. Towithelertkul C, Sumita YI, Wakabayashi N. Radiation attenuation properties of materials used to fabricate radiotherapy prostheses in vitro study. The 87th Annual Meeting of the Stomatological Society, Japan 2022.12.02 Tokyo (Japan)

- 10. Hattori M, Sumita YI. Fabrication of music splint as dental treatment for wind instrumental player. The 1st Annual Meeting of Japanese Performing Arts Medicine Association 2022.07.18 Tokyo (Japan)
- 11. Sumita YI, Ito E, Bai Z, Hattori M. How to increase the ability of eating? Consideration of musical exercises. The 1st Annual Meeting of Japanese Performing Arts Medicine Association 2022.07.18 Tokyo (Japan)
- 12. Nishiyama A, Tanabe G, Hattori M, Churei H, Sumita YI, Ueno T. Dental problems that the person teaching the instrumentalist believes affect the performance. The 1st Annual Meeting of Japanese Performing Arts Medicine Association 2022.07.18 Tokyo (Japan)
- 13. Tanabe G, Obata S, Hattori M, Churei H, Nishiyama A, Ueno T, Mori T, Sumita YI. Exploring the relation between Musical Instrument Performance and Oral Sciences -Current state and policy for a massive questionnaire survey of instrumentalists through academia-industry collaboration. The 1st Annual Meeting of Japanese Performing Arts Medicine Association 2022.07.18 Tokyo (Japan)
- 14. Murase M, Tani H, Sumita YI. Fabrication of maxillofacial prosthesis using digital technology for a maxillectomy patient with sever trismus. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.17 Osaka (Japan)+Web
- 15. Effect of retention hole designs in artificial teeth on failure resistance of the connection with thermoplastic resin. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16 Osaka
- 16. Hattori M. Evening Session 3: Potential of prosthodontics for oral hypofunction -Swallowing, articulation, and sleep breathing-. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16 Osaka (Japan)+Web
- 17. Hattori M, Yamatani Y, Sumita YI. Fabrication of metal based maxillofacial prosthesis for the mandibular defect patient after tumor resection using digital technology. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16 Osaka (Japan)+Web
- 18. Haraguchi M, Towithelertkul C, Tanabe G, Fujita H, Han X, Sumita YI. Two-piece detachable interlocking mold for low-dose-rate brachytherapy: A dental technique for radiotherapy prosthesis fabrication. The 39th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2022.06.24 Miyazaki (Japan)+Web
- 19. Hattori M, Gao Y, Wang Y, Sumita YI. Fabrication of mandibular suction prosthesis using piezography technique for maxillofacial defect patients. The 39th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2022.06.24 Miyazaki (Japan)+Web
- Sumita YI. Educational Seminar. The 13rd Educational Seminar of Japan Society for Head and Neck Cancer 2022.06.20 (Web)
- 21. Haraguchi M, Tsushima F, Yoshimura R, Sumita YI, Michi Y, Harada H. Prosthetic rehabilitations for 4 patients with maxillary defect caused by recent cancer treatments. The 46th Annual Meeting of Japan Society for Head and Neck Cancer 2022.06.17 Nara (Japan)+Web
- 22. Sumita YI. Symposium 1. The 46th Annual Meeting of Japan Society for Head and Neck Cancer 2022.06.17 Nara (Japan)+Web
- 23. Atsushi Takaichi. Present of manufacturing dental prosthesis by Selective laser melting method. 2022.06.11
- 24. Murase M, Tani H, Sumita YI. A case of effective nutritional intake of oral function with maxillofacial treatment for head and neck cancer patient. The 37th Annual Meeting of Japanese Society for Clinical Nutrition and Metabolism 2022.05.31 Yokohama (Japan)+Web
- 25. Tanabe G, Hattori M, Tani H, Sumita YI. Two case reports of speech aid repair support for patients with cleft lip and palate. The 46th Annual Meeting of Japanese Cleft Palate Association 2022.05.27 Kagoshima (Japan)+Web
- 26. Harazono Y, Tonouchi E, Ishibashi R, Masaki K, Anzai E, Takahara N, Morita K, Yoda T. A clinical study on treatment strategy for patients with submucous cleft palate. The 46th Annual Meeting of Japanese Cleft Palate Association 2022.05.26 Kagoshima (Japan)+Web

- 27. Zhang F, Hattori M, Sumita YI. Research of skin color acrylic resin based on CIELAB color system. The 79th Annual Meeting of Japanese Society for Dental Materials and Devices 2022.05.21 Morioka (Japan)
- 28. Takaichi A, Thant SW, Mohamed A, Kajima Y, Ashida M, Hanawa T, Wakabayashi N. Ultraviolet treatment of Co-Cr alloy to enhance adhesion of PMMA . 2022.05.21 Morioka
- 29. Kajima Y, Takaichi A, Hein Linn Htat, Hanawa T, Wakabayashi N. Effects of heat treatment times on recrystallization process of Co-Cr-Mo alloys fabricated by selective laser melting. 2022.05.21 Morioka

[Awards & Honors]

1. The 2021 Japanese Academy of Maxillofacial Prosthetics Best Paper Award (Zhang M), Japanese Academy of Maxillofacial Prosthetics, 2022.06

Department of Regenerative and Reconstructive Dental Medicine

Professor Eriko MARUKAWA Assistant Professor Hidemi NAKATA, Masahiro SHIMOGISHI, Maiko YAMAMOTO, Masaki SHIBASAKI Clinical Fellow Taketo TOMODA, Shintaro NAKAMURA, Kaori YOKOTA, Akihiro TAKAHASHI, Mika TSUNO, Tomoya KUBOUCHI, Konosuke TOYAMA, Rei WAKUTA, Mei ISHIKAWA

(1) **Outline**

Prosthodontic 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 chlodronate 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]

 Kensuke Inoue / Hidemi Nakata / Hiromi Taninokuchi / Yuta Takahashi / Shohei Kasugai / Shinji Kuroda. Microbiological Comparison of Different Sealing Materials for the Access Holes of Implant Restorations Oral Health and Preventive Dentistry. 2022.03; Oral Health Prev Dent 2022; 20: 119–126; 119-126

[Conference Activities & Talks]

- 1. Atsushi Oka, Hidemi Nakata, Shinji Kuroda, Akira Aoki, Eriko Marukawa. Effect of VEGF/HGF signaling inhibition in peri-implantitis tissue. 87th the stomatological socity congress 2022.12.02
- 2. KUBOUCHI T,SHIMOGISHI M,SHIBASAKI M,SATO M,HYODO K,TERAUCHI M,YODA T,MARUKAWA E. Investigation of Refit Dental in maxillary sinus floor augmentation: 5-years follow-up study. The 26th Annual Meeting and Academic conference of Japanese Society of Japanese Academy of Maxillofaicial Implants 2022.11.27
- 3. SHIMOGISHI M,SHIBASAKI M,WATANABE T,MARUKAWA E. Investigation of risk factors that regulate the peri-implant microbiota. The 26th Annual Meeting and Academic conference of Japanese Society of Japanese Academy of Maxillofaicial Implants 2022.11.27
- 4. SATO M,SHIBASAKI M,TERAUCHI M,SHIMOGISHI M,KUBOUCHI T,YODA T,MARUKAWA E. Long-term 5 years Follow-up Study of Hydroxyapatite/Collagen Composite Applied in Ridge Augmentation. The 26th Annual Meeting and Academic conference of Japanese Society of Japanese Academy of Maxillofaicial Implants 2022.11.26
- 5. WAKUTA R,,SHIMOGISHI M,MARUKAWA E. Evaluation of the efficacy and safety of implants with buttress thread design: A one-year observational study. The 52nd Annual Meeting of the Japanese Society of Oral Implantology 2022.09.24
- 6. OGURA M,NAKAMURA S,SHIMOGISHI M,MARUKAWA E. Comparison of covering material over the lateral window on maxillary sinus augmentation. The 52nd Annual Meeting of the Japanese Society of Oral Implantology 2022.09.24
- 7. Atsushi Oka, Hidemi Nakata, Shinji Kuroda, Akira Aoki, Shohei Kasugai, Eriko Marukawa. Effect of VEGF signaling inhibition on collagen degradation in peri-implantitis-associated fibroblasts. 52th Japanese socity of Implantology congress 2022.09.23

Plastic and Reconstructive Surgery

Professor:Mori Hiroki Assistant Professor:Uemura Noriko Graduate Student:Homma Tsutomu, Hamanaga Mayuko, Yamamoto Mao, Ishii Yoshitaka, Kato Sayuri, Akazawa Satoshi

(1) Outline

Plastic surgery is a surgical science that treats congenital or acquired changes in shape and color of the body surface and adapts individuals to society. It is a "creating surgery" of appearance and function, utilizing tissue transplantation, regenerative medicine, and nonsurgical treatments.

(2) Research

Plastic and Reconstructive Surgery : MORI Hiroki

- 1. Pre and post operative breast or facial contour evaluation usning 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. Adipogenesis in a external negative pressure lymphedema model A new possibility of scaffold transplantation
- 5. Blood circulation study of the surgical flap using indocyanine green angioraphy and multi slice CT
- 6. Study to elucidate the mechanism of gynecomastia from the viewpoint of adipogenesis
- 7. Investigation of the effect of multi-platelet plasma on early functional recovery of neural anastomosis

(3) 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 remolding of nearly all external body structures.

(4) Clinical Performances

We cover the whole field of plastic surgery. In particular, we deal with the following field; congenital anormaly (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.

(5) Publications

[Original Articles]

- 1. Hidaka T, Mori H, Shimizu H, Takahashi S, Tanaka K, Okazaki M. Comparison of Lumbar Artery and Superior Gluteal Artery Perforator Flaps for Breast Reconstruction: Multislice CT-Based Anatomical Study. Ann Plast Surg. 2022.12; 89(6); e39-e44
- 2. Tanaka K, Suesada N, Homma T, Hidaka T, Mori H, Okazaki M, Sugawara T, Tsutsumi T, Asakage T. Early postoperative complications and their measures after skull base reconstruction: A study from the standpoint of plastic and reconstructive surgeons. Auris, nasus, larynx. 2022.10; 49(5); 845-855
- 3. Ishida N, Usami S, Tanaka K, Mori H. Use of a Fascial Reverse Dorso-Ulnar Metacarpal Bone Flap for Non-union of the Distal Phalanx of the Thumb: A Case Report. The journal of hand surgery Asian-Pacific volume. 2022.10; 27(5); 902-906
- 4. Oda G, Nakagawa T, Mori H, Onishi I, Fujioka T, Mori M, Kubota K, Hanazawa R, Hirakawa A, Ishikawa T, Okamoto K, Uetakesszsz H. Factors predicting upstaging from clinical N0 to pN2a/N3a in breast cancer patients. World journal of clinical oncology. 2022.09; 13(9); 748-757
- 5. Wen Shuheng, Unuma Kana, Makino Yohsuke, Mori Hiroki, Uemura Koichi. Fatal consequence after MiraDry treatment: Necrotizing fasciitis complicated with streptococcal toxic shock syndrome(タイトル 和訳中) Legal Medicine. 2022.09; 58; 1-4
- 6. Usami S, Kawahara S, Inami K, Hirase Y, Mori H. Identifying Predictors of Radiographic Distal Phalangeal Nonunion After Fingertip Replantation. The Journal of hand surgery. 2022.08;
- 7. Tanaka K, Suesada N, Homma T, Mori H, Tsutsumi T, Asakage T, Okazaki M. Muscle-penetration method: Cable nerve grafting with well vascularized surrounding tissue and shortest graft length. Journal of plastic, reconstructive & aesthetic surgery : JPRAS. 2022.07; 75(7); 2387-2440
- 8. Tanaka Kentaro, Suesada Nobuko, Homma Tsutomu, Mori Hiroki, Sugawara Takashi, Tsutsumi Takeshi, Asakage Takahiro, Okazaki Mutsumi. The different concepts of surgical managements between anterior and lateral skull base reconstructions based on surgical purposes(和訳中) Auris: Nasus: Larynx. 2022.04; 49(2); 271-278
- 9. Usami S, Inami K, Kawahara S, Hirase Y, Shimizu H, Mori H. Investigation of Predictors of Successful Replantation of Distal Digits at the Nail Bed Level: The Contribution of Digital Nerve Repair to Survival Rate. Plastic and reconstructive surgery. 2022.02; 149(4); 889-896
- Nakagawa T, Oda G, Mori H, Uemura N, Onishi I, Sagawa N, Fujioka T, Mori M, Kubota K, Ishikawa T, Okamoto K, Uetake H. Prognosis of Subcutaneous Mastectomy for Special Types of Breast Cancer. Medicina (Kaunas, Lithuania). 2022.01; 58(1);
- 11. Uemura N, Aoyagi K, Tanaka K, Okazaki M, Mori H. Laser Removal of Buccal Skin Coloration Caused by India Ink Injection for Cancer Marking. Eplasty. 2022; 22; QA2
- 1. Haruka KOGA, Hiroki MORI, Tsutomu HOMMA, Sayuri KATO, Naoya ISHIDA, Kentaro TANAKA, Masayuki YAGI, Koji MORISHITA. Extensive Cutaneous Necrosis of Hand and Forearm Due to Extravasation of Norepinephrine Requiring Fascia Transplantation and Anterolateral Thigh Flap -A Case Report 2022.09; 35(3); 116-121

[Conference Activities & Talks]

- Mori H, Saiga M, Watanabe S, Kato S, Sasada S, Yamamoto M, Ogiya A, Narui K, Seki H, Nagura N, Ishitobi M. Nipple malposition in nipple-sparing mastectomy and breast reconstruction -Multicenter collaborative study in Japan-. PRS KOREA 2022 2022.11.11 Seoul
- 2. Mori H. Current status of breast reconstruction in Japan, and treatment options at Tokyo Medical and Dental University. 2022 Precision diagnosis and treatment of breast cancer symposium 2022.11.06 WEB(中 国河南省唐山市)

- 3. Namiki Takeshi, Nojima Kohei, Hayashi Masahiro, Kawaguchi Masakazu, Suzuki Tamio, Ishikawa Masashi, Tanemura Atsushi, Katayama Ichiro, Mori Taisuke, Yamazaki Naoya, Mori Hiroki, Sasaki Yoshiyuki, Yokozeki Hiroo, Okiyama Naoko. Overexpression of NUAK2 and phospho-Akt(S473) has a significant impact on development and progression in acral melanomas(タイトル和訳中). 日本研究皮膚 科学会年次学術大会・総会プログラム 2022.10.01
- 4. Usami S, Inami K, Hirase Y. Free-style local digital artery perforator flap for digital resurfacing. IFSSH, IFSHT & FESSH COMBINED CONGRESS 2022.06.06 London

Head and Neck Surgery

Professor: Takahiro Asakage Junior Associate Professor: Yosuke Ariizumi, Kazuchika Ohno Assistant Professor: Akihisa Tasaki Specially Appointed Assistant Proffesor:Ryuhei Okada, Yumiko Tateishi, Hiroaki Kawabe Senior Resident: Ryosuke Takahashi Graduate Student: Toshifumi Tomioka, Sadahiro Kishishita, Ryosuke Takahashi, Masaru Yokomura, Yuta Hoshi, Ai Watanabe

(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]

- Miyauchi M, Akashi T, Furukawa A, Uchida K, Tamura T, Ando N, Kirimura S, Shintaku H, Yamamoto K, Ito T, Miura K, Kayamori K, Ariizumi Y, Asakage T, Kudo A, Tanabe M, Fujii Y, Ishibashi H, Okubo K, Murakami M, Yamada T, Takemoto A, Bae Y, Eishi Y, Ohashi K. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocr Pathol. 2022.12; 33(4); 506-518
- 2. Wakiyama H, Furusawa A, Okada R, Inagaki F, Kato T, Furumoto H, Fukushima H, Okuyama S, Choyke PL, Kobayashi H.. Opening up new VISTAs: V-domain immunoglobulin suppressor of T cell activation (VISTA) targeted near-infrared photoimmunotherapy (NIR-PIT) for enhancing host immunity against cancers Cancer Immunology Immunotherapy. 2022.12; 71(12); 2869-2879
- 3. Moriya T, Hashimoto M, Matsushita H, Masuyama S, Yoshida R, Okada R, Furusawa A, Fujimura D, Wakiyama H, Kato T, Choyke PL, Kusumoto Y, Chtanova T, Kobayashi H, Tomura M.. Near-infrared photoimmunotherapy induced tumor cell death enhances tumor dendritic cell migration Cancer Immunology Immunotherapy. 2022.12; 71(12); 3099-3106
- 4. Kota Yokoyama, Junichi Tsuchiya, Hiroaki Kawabe, Takahiro Asakage, Ukihide Tateishi. A rare case of primary intraosseous carcinoma of the mandible with perineural extension mimicking neurolymphomatosis on [18F] -FDG PET/CT Eur J Nucl Med Mol Imaging. 2022.12;
- 5. Naoyuki Sakihama, Ryuhei Okada, Naoto Takahashi, Naoki Fushimi, Tomoki Ooka, Hiroaki Kawabe, Yosuke Ariizumi, Kazuchika Ohno, Yutaka Ueki, Niro Tayama, Takeshi Tsutsumi, Takahiro Asakage. Post-intubation laryngeal injury after COVID-19 treatment causing dyspnea: A report of six cases. Auris Nasus Larynx. 2022.12;
- 6. Hiroaki Wakiyama, Takuya Kato, Aki Furusawa, Ryuhei Okada, Fuyuki Inagaki, Hideyuki Furumoto, Hiroshi Fukushima, Shuhei Okuyama, Peter L Choyke, Hisataka Kobayashi. Treg-Dominant Tumor Microenvironment Is Responsible for Hyperprogressive Disease after PD-1 Blockade Therapy. Cancer Immunol Res. 2022.11; 10(11); 1386-1397
- 7. Takuya Kato, Hiroshi Fukushima, Aki Furusawa, Ryuhei Okada, Hiroaki Wakiyama, Hideyuki Furumoto, Shuhei Okuyama, Seiichiro Takao, Peter L Choyke, Hisataka Kobayashi. Selective depletion of polymorphonuclear myeloid derived suppressor cells in tumor beds with near infrared photoimmunotherapy enhances host immune response. Oncoimmunology. 2022.11; 11(1); 2152248
- 8. Kazuchika Ohno, Motomi Nasu, Hidetoshi Matsui, Yoshifumi Baba, Takushi Yasuda, Jun Sakuma, Kenichiro Ikeda, Takashi Maruo, Takumi Okuda, Norihiko Narita, Hisayuki Kato, Taiji Kawasaki, Hiroshi Sato, Kunihiko Tokashiki, Naoki Akisada, Hajime Ishinaga, Ken Akashi, Kenji Okami, Kosuke Murayama, Soichiro Yamamoto, Yuji Kumakura, Kenro Kawada, Akihiro Shiotani, Takahiro Asakage. Real-world treatment patterns and outcomes in Japanese patients with cervical esophageal cancer. Esophagus. 2022.10; 19(4); 576-585
- 9. Kato T, Okada R, Furusawa A, Wakiyama H, Furumoto H, Fukushima H, Okuyama S, Choyke PL, Kobayashi H.. Comparison of the Effectiveness of IgG Antibody versus F(ab') 2 Antibody Fragment in CTLA4-Targeted Near-Infrared Photoimmunotherapy Molecular Pharmaceutics. 2022.10; 19(10); 3600-3611
- 10. Asuka Fujino, Yoji Tanaka, Daisu Abe, Yosuke Ariizumi, Motoki Inaji, Taketoshi Maehara. A New Technique for the Endoscopic Reconstruction of Skull Base Defects Using Multiple-balloon Catheters. Neurol Med Chir (Tokyo). 2022.10; 62(10); 483-487
- 11. Fukushima H, Kato T, Furusawa A, Okada R, Wakiyama H, Furumoto H, Okuyama S, Kondo E, Choyke PL, Kobayashi H.. Intercellular adhesion molecule-1-targeted near-infrared photoimmunotherapy of triple-negative breast cancer Cancer Science. 2022.09; 113(9); 3180-3192
- Fuyuki F Inagaki, Takuya Kato, Aki Furusawa, Ryuhei Okada, Hiroaki Wakiyama, Hideyuki Furumoto, Shuhei Okuyama, Peter L Choyke, Hisataka Kobayashi. Disialoganglioside GD2-Targeted Near-Infrared Photoimmunotherapy (NIR-PIT) in Tumors of Neuroectodermal Origin. Pharmaceutics. 2022.09; 14(10); 2037

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- 16. Yuki Saito, Akihiro Homma, Naomi Kiyota, Makoto Tahara, Nobuhiro Hanai, Takahiro Asakage, Kazuto Matsuura, Ichiro Ota, Tomoya Yokota, Daisuke Sano, Takeshi Kodaira, Atsushi Motegi, Koichi Yasuda, Shunji Takahashi, Kaoru Tanaka, Takuma Onoe, Susumu Okano, Yoshinori Imamura, Yosuke Ariizumi, Ryuichi Hayashi. Human papillomavirus-related oropharyngeal carcinoma. Jpn J Clin Oncol. 2022.07; 52(7); 700-706
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- 19. Takahiro Asakage. [Common Sense in Head and Neck Surgery for Malignant Skull Base Disease:Lack of Common Sense in Neurosurgery] . No Shinkei Geka. 2022.05; 50(3); 578-585
- 20. Yoshinori Imamura, Naomi Kiyota, Makoto Tahara, Nobuhiro Hanai, Takahiro Asakage, Kazuto Matsuura, Ichiro Ota, Yuki Saito, Daisuke Sano, Takeshi Kodaira, Atsushi Motegi, Koichi Yasuda, Shunji Takahashi, Tomoya Yokota, Susumu Okano, Kaoru Tanaka, Takuma Onoe, Yosuke Ariizumi, Akihiro Homma. Systemic therapy for salivary gland malignancy: current status and future perspectives. Jpn J Clin Oncol. 2022.04; 52(4); 293-302
- 21. Takahiro Asakage. Epidemiology and treatment of head and neck malignancies in the AYA generation. Int J Clin Oncol. 2022.03; 27(3); 465-472
- 22. Yasuko Aoyagi, Yoshihito Kano, Kohki Tohyama, Shotaro Matsudera, Yuichi Kumaki, Kenta Takahashi, Takahiro Mitsumura, Yohei Harada, Akemi Sato, Hideaki Nakamura, Eisaburo Sueoka, Naoko Aragane, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Keiichi Akahoshi, Hiroaki Ono, Toshiaki Ishikawa, Masanori Tokunaga, Tsuyoshi Nakagawa, Noriko Oshima, Reiko Nakamura, Masatoshi Takagi, Takahiro Asakage, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Yusuke Kinugasa, Sadakatsu Ikeda. Clinical utility of comprehensive genomic profiling in Japan: Result of PROFILE-F study. PLoS One. 2022.03; 17(3); e0266112
- 23. Imamura Y, Kiyota N, Tahara M, Hanai N, Asakage T, Matsuura K, Ota I, Saito Y, Sano D, Kodaira T, Motegi A, Yasuda K, Takahashi S, Yokota T, Okano S, Tanaka K, Onoe T, Ariizumi Y, Homma A. Systemic therapy for salivary gland malignancy: current status and future perspectives. Japanese journal of clinical oncology. 2022.02; 52(4); 293-302
- 24. Ryuji Yasumatsu, Yasushi Shimizu, Nobuhiro Hanai, Shin Kariya, Tomoya Yokota, Takashi Fujii, Kiyoaki Tsukahara, Mizuo Ando, Kenji Hanyu, Tsutomu Ueda, Hitoshi Hirakawa, Shunji Takahashi, Takeharu Ono, Daisuke Sano, Moriyasu Yamauchi, Akihito Watanabe, Koichi Omori, Tomoko Yamazaki, Nobuya Monden, Naomi Kudo, Makoto Arai, Syuji Yonekura, Takahiro Asakage, Takahiro Nekado, Takayuki Yamada, Akihiro Homma. Outcomes of long-term nivolumab and subsequent chemotherapy in Japanese
patients with head and neck cancer: 2-year follow-up from a multicenter real-world study. Int J Clin Oncol. 2022.01; 27(1); 95-104

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[Misc]

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- Ryuhei Okada, Takuya Kato, Aki Furusawa, Fuyuki Inagaki, Hiroaki Wakiyama, Daiki Fujimura, Shuhei Okuyama, Hideyuki Furumoto, Hiroshi Fukushima, Peter L. Choyke, Hisataka Kobayashi. Selection of Antibody and Light Exposure Regimens Alters Therapeutic Effects of EGFR-targeted Near-infrared Photoimmunotherapy. 第 60 回日本癌治療学会学術集会 2022.10.21 兵庫
- 2. Takahiro Asakage. Chairperson Symposium 8: Oral Cavity Cancer. 1st Joint Meeting of Tri-Head and Neck Society 2022 2022.09.23 WEB
- 3. Ryuhei Okada. Near-infrared photoimmunotherapy: A newly developed cancer therapy. 1st Joint Meeting of Tri-Head and Neck Society 2022 2022.09.22 Seoul, Korea
- 4. Akihiro Homma, Kazuto Matsuura, Rikiya Onimaru, Daisuke Yoshida, Hirotaka Shinomiya, Akira Ohkoshi, Ryuichi Hayashi,, Yuki Saito, Hiroyuki Tachibana, Kiyoto Shiga, Tsutomu Ueda, Yukinori Asada, Hirokazu Uemura, Akira Seto, Takeshi Beppu, Kazuki Ishikawa, Masashi Mikami, Kenichi Nakamura, Haruhiko Fukuda, Naomi Kiyota, Head and Neck Cancer Study Group of Japan Clinical Oncology Group (JCOG-HNCSG).. Dose-finding and efficacy confirmation trial of the super selective intra-arterial infusion of Cisplatin and concomitant radiotherapy for locally advanced maxillary sinus cancer (JCOG1212): Results of the efficacy confirmation phase in the T4a cohort.. the American Society of Clinical Oncology Annual Meeting 2022.06.03 Chicago

Radiation Therapeutics and Oncology

Professor Ryoichi Yoshimura
Lecturers Kazuma Toda
Research Associates Hirofumi Kuwabara, Takuya Nagano
Hospital Staff members Daigoro Matsubara, Aya Usami
Graduate Students
Yoshinao Takada, Masahiro Yoshida, Kazuma Sasamura, Yuji Uehara

(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.

(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 619 patients, including 178 head and neck cancer patients, 75 prostate cancer patients, 54 breast cancer patients, 44 lung cancer patients, and 21 esophageal cancer patients, were treated at our hospital in 2020.

Maxillofacial and Neck Reconstruction

(6) Clinical Performances

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

(7) Publications

[Original Articles]

- 1. Towithelertkul C, Sumita YI, Murakami T, Notake R, Akiyama M, Yoshimura R, Wakabayashi N. Radiation attenuation properties of materials used to fabricate radiotherapy prostheses in vitro study. J Oral Sci. 2022.10; 64(4); 274-278
- 2. Murakami N, Watanabe M, Uno T, Sekii S, Tsujino K, Kasamatsu T, Machitori Y, Aoshika T, Kato S, Hirowatari H, Kaneyasu Y, Nakagawa T, Ikushima H, Ando K, Murata M, Yoshida K, Yoshioka H, Murata K, Ohno T, Okonogi N, Saito AY, Ichikawa M, Okuda T, Tsuchida K, Sakurai H, Yoshimura R, Yoshioka Y, Yorozu A, Okamoto H, Inaba K, Kato T, Igaki H, Itami J. Large volume was associated with increased risk of acute non-hematologic adverse events in the hybrid of intracavitary and interstitial brachytherapy for locally advanced uterine cervical cancer: preliminary results of prospective phase I/II clinical trial JAPANESE JOURNAL OF CLINICAL ONCOLOGY. 2022.04; 52(8); 851-860
- 3. Kudo A, Tateishi U, Yoshimura R, Tsuchiya J, Yokoyama K, Takano S, Kobayashi N, Utsunomiya D, Hata M, Ichikawa Y, Tanabe M, Hosono M, Kinuya S. Safety and response after peptide receptor radionuclide therapy with 177Lu-DOTATATE for neuroendocrine tumors in phase 1/2 prospective Japanese trial Journal of Hepato-Biliary-Pancreatic Sciences. 2022.04; 29(4); 487-499
- Aya Usami, Kota Yokoyama, Junichi Tsuchiya, Yoshihiro Umezawa, Kazuma Toda, Ukihide Tateishi, Ryoichi Yoshimura. F] FDG Avidity and Low EOB Uptake Proportional to the Irradiation Dose. Diagnostics (Basel). 2022.02; 12(2);
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- 6. Noji R, Tohyama K, Kugimoto T, Kuroshima T, Hirai H, Tomioka H, Michi Y, Tasaki A, Ohno K, Ariizumi Y, Onishi I, Suenaga M, Mori T, Okamoto R, Yoshimura R, Miura M, Asakage T, Miyake S, Ikeda S, Harada H, Kano Y. Comprehensive Genomic Profiling Reveals Clinical Associations in Response to Immune Therapy in Head and Neck Cancer. Cancers. 2022.07; 14(14);

- 1. Murakami T, Daisaki H, Takino K, Sasamori K, Otani S, Yoshimura R. Proposal of a new quantitative index of co-registration accuracy for PET/CT. nuclear medicine 2022.08.01
- 2. Kimura K, Yoshida S, Tsuchiya J, Tanaka H, Yokoyama M, Matsuoka Y, Fujii Y, Yoshimura R, Tateishi U. Clinical Significance of the Vesical Imaging Reporting and Data System in Predicting the Therapeutic Effect of Bladder-Sparing Treatment in Muscle-Invasive Bladder Cancer. Annual meeting of the Japan Radiological Society abstracts 2022.03.01

Cognitive Neurobiology

Professor: Naofumi Uesaka Lecturer: Daisuke Tanaka Assistant Professor Atsuya Takeuchi

Graduate Students Moe Tanigawa Nozomi Utsumi Midori Wada Ryo Masumura Yang Sun Ibin Han

(1) **Outline**

Our goal is to understand how each brain cell or group of brain cells generates complex brain functions and how dysfunction of each cell causes brain diseases. To answer these questions, we use a variety of techniques, including neurophysiology, molecular biology, and genetics. We promote researches and aim to find novel concepts in brain development, brain function, and brain diseases.

(2) Research

1. Functional development of the brain

We are studying the mechanism of selective strengthening and elimination of synapses (synapse elimination) during postnatal development.

2. Glial function

We aim to discover novel functions of glial cells.

3. Crosstalk between oral function and brain function in the health and disease. We aim to elucidate the information processing of oral sensation in the brain and brain disease caused by oral dysfunction.

4) Brain diseases

We aim to elucidate the mechanisms by which brain diseases develop and become malignant.

(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

We plan to actively accept a diverse range of students and staff from various backgrounds, including biology, engineering, dentistry, and medicine, regardless of academic field. We will educate them to be able to either develop innovative methods, hit innovative hypotheses, or make innovative discoveries. For this reason, we place importance on creating an environment and atmosphere where staff and students can actively share their opinions in daily discussions and study sessions. By reading our papers and papers on the latest research findings and conducting research with staff and senior students, students can learn how to acquire and analyze data, conduct research, and write papers. Let's work together to make innovative discoveries by cooperating with each other and doing research every day toward the major goal of elucidating brain development, brain function, and brain diseases.

(5) Publications

[Original Articles]

- 1. Yuki Nagasawa, Sayaka Katagiri, Kazuharu Nakagawa, Tomomitsu Hirota, Kanako Yoshimi, Aritoshi Uchida, Masahiro Hatasa, Keiji Komatsu, Takahiko Shiba, Yujin Ohsugi, Naofumi Uesaka, Takanori Iwata, Haruka Tohara. Xanthan gum-based fluid thickener decreases postprandial blood glucose associated with increase of Glp1 and Glp1r expression in ileum and alteration of gut microbiome 2022.11;
- 2. Itami C, Uesaka N, Huang JY, Lu HC, Sakimura K, Kano M, Kimura F. Endocannabinoid-dependent formation of columnar axonal projection in the mouse cerebral cortex. Proceedings of the National Academy of Sciences of the United States of America. 2022.09; 119(37); e2122700119

- 1. 増村嶺、上阪直史. Cerebellar oligodendrocytes during development shape cerebellar circuit and behaviors. 第45回日本分子生物学会 2022.11.30
- 2. Tanaka DH, Mukae S, Han I, Nonaka S, Tanabe T, Uesaka N. Water deprivation-active neurons in the hypothalamus induce hedonic "liking" reactions for water. 2022 年度 日本味と匂学会 第 56 回大会 2022.08.23 仙台
- 3. 上阪 直史. From Astrocyte to Neuron signaling in developmental synapse remodeling. 第3回先端脳科 学国際シンポジウム 2022.03.30 山梨県甲府市
- 4. 上版 直史、狩野 方伸. Astrocyte-Neuron signaling in developmental synapse remodeling. 第 99 回日本 生理学会大会 2022.03.17 東北大学、宮城

Molecular Craniofacial Embryology and Oral Histology

Staffs and Students Professor Sachiko ISEKI Associate Professor Makoto TABATA Junior Associate Professor Vuki YOSHIMOTO Assistant Professor Noritaka ADACHI Part-time lecturers Masa-Aki IKEDA, Masaki TAKECHI, Youichirou NINOMIYA, Daisuke KOYABU, Keigo ARAKI, Masato Graduate Students ChengXue JIN, YuYan WANG, HanYang WANG Graduate Students (Others) Shintaro YAMAZAKI (Maxillofacial Surgery) Lou Yixin (Orthodontic Science) Research students Yukiko HOSHINO (Office of New Drug V, Pharmaceuticals and Medical Devices Agency) NAMANGKALAKUL Worachat (Chulalongkorn University) Rika TAKEUCHI (Jichi Medical University)

(1) Outline

(1) Outline

The research in this field is focused on elucidating the developmental mechanisms of cell proliferation, differentiation, and morphogenesis of the oral and maxillofacial region, and on applying the results of this research to regenerative medicine.

Within this area, graduate students will find their own research topics and formulate their own problems as much as possible independently with the advice of their academic advisors. In addition, to solve this problem, students will acquire knowledge and methods of molecular biology and molecular embryology, and mammalian embryo manipulation techniques including cell-tissue-organ culture methods, whole embryo culture methods, etc., as necessary, while developing sensitivity, cultivating logical construction skills, and developing the ability to write papers in English.

(2) Research

(2) 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

(3) Publications

[Original Articles]

1. Lu Zhao, Yoshiro Matsumoto, Sachiko Iseki, Takashi Ono. Effects of short-term orthodontic force application on the root at different developmental stages in rat maxillary molars. Am J Orthod Dentofacial Orthop. 2022.12;

- 2. Gabriella Lania, Monica Franzese, Adachi Noritaka, Marchesa Bilio, Gemma Flore, Annalaura Russo, Erika D'Agostino, Claudia Angelini, Robert G Kelly, Antonio Baldini. A phenotypic rescue approach identifies lineage regionalization defects in a mouse model of DiGeorge syndrome. Disease Models & Mechanisms. 2022.08;
- 3. Wataru Takagi, Fumiaki Sugahara, Shinnosuke Higuchi, Rie Kusakabe, Juan Pascual-Anaya, Iori Sato, Yasuhiro Oisi, Nobuhiro Ogawa, Hiroshi Miyanishi, Noritaka Adachi, Susumu Hyodo, Shigeru Kuratani. Thyroid and endostyle development in cyclostomes provides new insights into the evolutionary history of vertebrates. BMC Biol. 2022.04; 20(1); 76
- 4. Kano Sakurako, Higashihori Norihisa, Thiha Phyo, Takechi Masaki, Iseki Sachiko, Moriyama Keiji. The role of the histone methyltransferase SET domain bifurcated 1 during palatal development BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2022.04; 598; 74-80
- 5. Inagaki Y, Ogawa T, Tabata MJ, Nagata Y, Watanabe R, Kawamoto T, Moriyama K, Tanaka T. Correction to: Identification of OPN3 as associated with non-syndromic oligodontia in a Japanese population. Journal of human genetics. 2022.04; 67(4); 245
- 6. Nuri Takashi, Ota Masato, Ueda Koichi, Iseki Sachiko. Quantitative Morphologic Analysis of Cranial Vault in Twist1(+/-) Mice: Implications in Craniosynostosis PLASTIC AND RECONSTRUCTIVE SURGERY. 2022.01; 149(1); 28E-37E

[Misc]

- 1. 吉本 由紀、大石 由美子. 筋疾患と慢性炎症 医学のあゆみ. 2022.07; 282(1); 43-48
- 2. Fabienne Lescroart, Camille E Dumas, Noritaka Adachi, Robert G Kelly. Emergence of heart and branchiomeric muscles in cardiopharyngeal mesoderm. Exp Cell Res. 2022.01; 410(1); 112931

- 1. 吉本 由紀, 上住 聡芳, 上住 円, 田中 かおり, 余 昕怡, 黒澤 珠希, 山家 新勢, 前原 一満, 大川 恭行, 外丸 祐介, 宿南 知. 腱・靭帯分化誘導システムにおけるシングルセル解析. 第 45 回日本分子生物学会年会 2022.11.30
- Sachiko Iseki. FGF18 Modulates M2-like Macrophage Polarization by Inducing CCL2-CCR2 Axis in Calvarial Bone Healing. Craniofacial Morphogenesis and Tissue Regeneration, Gordon Research Conference. 2022.10.18 Ventura, CA, United States
- 3. Lou Yixin, Matsumoto Yoshiro, Iseki Sachiko, Qi Jia, Ono Takashi. ラットにおける light orthodontic force の応用/除去による歯根吸収/修復と関連サイトカインの観察 (Observation of root resorption/repair and related cytokines by application/removal of light orthodontic force in rats). 日本矯正歯科学会大会プログラム・抄録集 2022.10.01
- 4. 金成学, 足立礼孝, 井関祥子, 太田正人. FGF18 は歯根形成を制御する. 第 62 回日本先天異常学会学術集会 2022.07.29 金沢市文化ホール
- 5. 山家 新勢、余 昕怡、吉本 由紀、樋口 真之輔、秋山 治彦、安達 泰治、宿南 知佐. 線維軟骨性エンテーシ スの形成・維持に寄与する細胞群の特性解析. 第 40 回日本骨代謝学会学術集会 2022.07.22
- 6. 井関祥子. craniosynostosis の発症メカニズム. 第 65 回日本形成外科学会総会 · 学術集会 2022.04.22
- 7. 武智正樹、星野裕紀子、Mehran Moazen、小薮大輔、Erwin Pauws、井関祥子. 頭蓋縫合早期癒合症モデル マウスにおける頭蓋骨成長の幾何学的形態測定解析. 第 127 回日本解剖学会総会・全国学術集会 2022.03.27 オンライン
- 8. 井関 祥子. 形づくり (頭蓋顎顔面形態形成). 口腔病学会雑誌 2022.03.01
- 1. Noritaka Adachi, Marchesa Bilio, Antonio Baldini, Robert G. Kelly. Cardiopharyngeal mesoderm origins of musculoskeletal and connective tissues in the mammalian pharynx. The 62th Japanese Teratology Society, Annual meeting 2022.07.29 Kanazawa Bunka Hall
- 2. Noritaka Adachi, Marchesa Bilio, Antonio Baldini, Robert G. Kelly. Cardiopharyngeal mesoderm contribution to the mammalian pharynx. The 127th Japanese Association of Anatomists, Annual meeting 2022.03.27 Osaka University (online meeting)

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Hideto Kameda, Masahiro Shinohara

Research Student : Shiho Hidaka : Kei Gouchi :Rika Kodama (2022.1-) :Risa Kawatsura Collaborator :Yuki Kasahara

(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]

- Fujioka A, Nagano M, Ikegami K, Masumoto KH, Yoshikawa T, Koinuma S, Nakahama KI, Shigeyoshi Y. Circadian expression and specific localization of synaptotagmin17 in the suprachiasmatic nucleus, the master circadian oscillator in mammals. Brain research. 2022.11; 148129
- Hidaka S, Mouri Y, Akiyama M, Miyasaka N, Nakahama KI. GPR110, a receptor for synaptamide, expressed in osteoclasts negatively regulates osteoclastogenesis. Prostaglandins, leukotrienes, and essential fatty acids. 2022.06; 182; 102457
- 3. Kawatsura Risa, Hara Yusuke, Akiyama Masako, Tachikawa Noriko, Nakahama Ken-Ichi. Gap junctional intercellular communication attenuates osteoclastogenesis induced by activated osteoblasts BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2022.03; 597; 71-76

Maxillofacial Surgery

Professor: Tetsuya YODA

Associate Professor: Yoshiyuki SASAKI, Kei-ichi MORITA Junior Associate Professor: Hiroyuki YOSHITAKE, Namiaki TAKAHARA Assistant Professor: Nobuyoshi TOMOMATSU, Yousuke HARAZONO, (Apr.) Yasuhiro KURASAWA, Masahiko TERAUCHI Special Assistant Professor: Hirokazu KACHI, Erina TONOUCHI, Takasuke INADA, (Apr.) Tomomi SAKUMA, Tomoki KANEMARU, Yusoon KIM, (Mar.) Yasuhiro KURASAWA, Masahiko TERAUCHI Hospital Staff: Erina NAKAMURA, Narumi OSHIBE, (Apr.) Eri ANZAI, (Mar.) Yu AKAIKE, Taishi NAKAMURA Graduate Student: Hongfei ZHU, Noboru MARUTA, Shintarou YAMAZAKI, Rina TAJIMA, Karen KUROYAMA, Koutaro YAMAZAKI, (Apr.) Yuka KWAK, Migyuan HSIAO, Vu Viet Duc, (Mar.) Yu AKAIKE, Taishi NAKAMURA Social Graduate Student: Mari SHIBATA, Takuya IWASAKI, (Apr.) Yu AKAIKE, Taishi NAKAMURA Student: Souichi ROKUSHIMA, Yuuko KATSUKI, (Apr.) Motoko SEKI, (May.) YaXuan YU, (Mar.) Chizuko KOMURO, Vu Viet Duc, (Spt.) Junya KUMAGAI Clinical Professor: (Apr.) Fumiaki SATO, Takashi MISHIMAGI, (Mar.) Hirovuki WAKE Part-time Lecturer: Masashi YAMASHIRO, Jin SATO, Hideo MIYACHI, Akiko KOBAYASHI, Kazuhiro YAGIHARA, Yutaka SATO, Kazuto KUROHARA, Katsuya AIKOU, Yoshio OHYAMA, Ryousuke NAGAOKA, Toshiyuki YAMADA, Katsuya HYODO,

Daisuke YAMAMOTO, (Apr.) Youhei TSUTAKI, Tomohisa KITAMURA,

(May.) Hiroki MASUDA, (Oct.)Junya KUMAGAI

(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, facical 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 injures 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. Masahiro Hakariya, Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Takanori Iwata, Nobuhiko Yui. Suppressed Migration and Enhanced Cisplatin Chemosensitivity in Human Cancer Cell Lines by Tuning the Molecular Mobility of Supramolecular Biomaterials. Macromolecular Bioscience. 2022.12; e2200438
- 2. N Yamakawa, M Umeda, Y Yoshii, K Mitsudo, M Noguchi, J Kusukawa, A Katakura, H Nakayama, M Sasaki, T Noguchi, M Ueda, H Bukawa, K Yagihara, A Horie, A Miyazaki, D Chikazu, K Tomihara, K Mishima, M Otsuru, S Asoda, S Fujiwara, Y Ohyama, H Kurita, H Kawamata, M Fukuda, Y Shintani, T Kobayashi, T Kanno, I Oh-Iwa, K Kawano, Y Yamashita, W Kobayashi, Y Ohiro, K Uzawa, Y Ota, T Kirita. Multicenter retrospective study of nivolumab for recurrent/metastatic oral squamous cell carcinoma. Oral Dis. 2022.12;
- 3. Y Kurasawa, A Iida, K Narimatsu, H Sekiya, Y Maruoka, Y Michiwaki. Effects of Perioperative Oral Management in Patients with Cancer JOURNAL OF CLINICAL MEDICINE. 2022.11; 11(21);
- 4. M Shibata, A Ishikawa, J Ishii, E Anzai, H Yagishita, T Izumo, J Sumino, M Katsurano, Y Kim, H Kanda, M Ushijima, K Yagihara, T Yoda. Stiffness as measured with strain elastography is a prognostic factor for pT1/T2 tongue squamous cell carcinoma with muscle-layer invasion. Oral Surg Oral Med Oral Pathol Oral Radiol. 2022.11; 22;
- 5. M Shibata, K Yagihara, J Ishii, H Kanda, A Ishikawa. Two cases of secretory carcinoma in the minor salivary glands Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2022.11; 34; 850-857
- 6. N Takahara, S Nakagawa, K Sumikura, T Yoda. Comparison of magnetic resonance imaging findings in patients with intermittent closed lock and acute closed lock of the temporomandibular joint: a cross-sectional retrospective study. Oral Radiol. 2022.10;
- 7. Yuka Tanaka-Takemura, Yoshinori Arisaka, Masahiro Hakariya, Hiroki Masuda, Ryo Mikami, Ruriko Sekiya-Aoyama, Takanori Iwata, Tetsuya Yoda, Takashi Ono, Nobuhiko Yui. Independent roles of molecular mobility and zeta potential on supramolecular surfaces in the sequence of RAW264.7 macrophage responses Macromolecular bioscience. 2022.09; in press(11); e2200282
- 8. C Michikawa, V Gopalakrishnan, AM Harrandah, TV Karpinets, RR Garg, RA Chu, YP Park, SS Chukkapallia, N Yadlapalli, KC Erikson-Carter, FO Gleber-Netto, E Sayour, A Progulske-Fox, EKI Chan, X Wu, J Zhang, C Jobin, JA Wargo, CR Pickering, JN Myers, N Silver. Fusobacterium is enriched in oral cancer and promotes induction of programmed death-ligand 1 (PD-L1). Neoplasia. 2022.09; 31; 100813

- Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Phototethering of collagen onto polyetheretherketone surfaces to enhance osteoblastic and endothelial performance Macromolecular Bioscience. 2022.08; 22(8); 2200115
- J Iwanaga, S Ibaragi, T Okui, V Divi, Y Ohyama, K Watanabe, J Kusukawa. Cutaneous branch of the nerve to the mylohyoid muscle: Potential cause of postoperative sensory alteration in the submental area. Ann Anat. 2022.08; 243; 151934
- 11. N Tomomatsu, N Takahara, K Nakakuki, Y Kurasawa, T Iwasaki, T Yoda. Study of Morphological Changes in the Inferior Turbinate After Le Fort I Osteotomy. The Journal of craniofacial surgery. 2022.06;
- 12. Shigehiro Abe, Atsushi Kaida, Kazunori Kanemaru, Keiichiro Nakazato, Naoko Yokomizo, Yutaka Kobayashi, Masahiko Miura, Toshio Miki, Chiaki Hidai, Hisataka Kitano, Tetsuya Yoda. Differences in the stemness characteristics and molecular markers of distinct human oral tissue neural crest-derived multilineage cells. Cell Prolif. 2022.06; e13286
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- 15. M Shibata, A Ishikawa, J Ishii, E Anzai, H Yagishita, T Izumo, J Sumino, M Katsurano, Y Kim, H Kanda, M Ushijima, K Yagihara, T Yoda. Stiffness of tongue squamous cell carcinoma measured using strain elastography correlates with the amount of collagen fibers in the tumor. Oral Radiol. 2022.04; 38(2); 278-287
- M Shibata, N Takahara, N Tomomatsu, Y Kurasawa, Y Sasaki, T Yoda. Risk factors of neurosensory disturbances at 1 year postoperatively after bilateral sagittal split osteotomy Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology. 2022.04;
- M Yumoto, Y Mizuno, Y Isozaki, KO Ito, T Yoda, T Sato. Analysis of Masticatory Muscle Tendon-aponeurosis Hyperplasia by Using Next-generation Sequencing. In vivo (Athens, Greece). 2022.03; 36(2); 563-569
- M Terauchi, E Marukawa, K Hyodo, T Iwasaki, A Wada, H Harada, T Yoda. Conservative surgical treatment of odontogenic myxoma with preservation of the inferior alveolar nerve Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2022.03; 34(2); 156-163
- D Husein, A Alamoudi, Y Ohyama, H Mochida, B Ritter, Y Mochida. Identification of the C-terminal region in Amelogenesis Imperfecta causative protein WDR72 required for Golgi localization. Sci Rep. 2022.03; 12(1); 4640
- Y Harazono, K Morita, E Tonouchi, E Anzai, N Takahara, T Kohmoto, I Imoto, T Yoda. TP63 mutation mapping information in TP63 mutation-associated syndromes Advances in Oral and Maxillofacial Surgery. 2022.01; 5;
- 21. Yasuyuki Michi, Hiroyuki Harada, Yu Oikawa, Kohei Okuyama, Takuma Kugimoto, Takeshi Kuroshima, Hideaki Hirai, Yumi Mochizuki, Hiroaki Shimamoto, Hirofumi Tomioka, Hirokazu Kachi, Jun-Ichiro Sakamoto, Kou Kayamori, Tetsuya Yoda. Clinical manifestations of diffuse large B-cell lymphoma that exhibits initial symptoms in the maxilla and mandible: a single-center retrospective study. BMC Oral Health. 2022.01; 22(1); 20
- 22. T Aragaki, S Nakamura, K Sakamoto, M Suzuki, T Yoda, T Kurabayashi. MRI findings of a dermoid cyst in the floor of the mouth with "sac of marbles" sign: An immunohistopathological study(和訳中) Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2022.01; 34(1); 80-84
- 23. Yosuke Harazono, Kou Kayamori, Junichiro Sakamoto, Yu Akaike, Yasuhiro Kurasawa, Fumihiko Tsushima, Yoshiyuki Sasaki, Hiroyuki Harada, Tetsuya Yoda. Retrospective analysis of schwannoma in the oral and maxillofacial region: clinicopathological characteristics and specific pathology of ancient change. Br J Oral Maxillofac Surg. 2022.01; 60(3); 326-331

- 24. C Michikawa, PA Torres-Saavedra, NL Silver, PM Harari, MS Kies, DI Rosenthal, QT Le, RC Jordan, DY Duose, S Mallampati, S Trivedi, R Luthra, II Wistuba, AA Osman, O Lichtarge, RL Foote, U Parvathaneni, DN Hayes, CR Pickering, JN Myers. Analysis in Pathologically High-Risk Human Papillomavirus-Negative Head and Neck Cancer From a Phase 2 Clinical Trial: NRG Oncology Radiation Therapy Oncology Group 0234. Adv Radiat Oncol. 2022; 7(6); 100989
- 25. Y Ohyama, M Ogawa, S Yokoo. Novel Management for Severe Odontogenic Maxillary Sinusitis Based on Pathophysiology. Case Rep Dent. 2022; 2022; 1614739

[Books etc]

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- 2. 高原楠旻. 下顎枝矢状分割術における Superfixsorb® Mx SSRO プレートの使用経験. 帝人メディカルテク ノロジー株式会社 2022.11 帝人メディカルテクノロジー株式会社
- 3. M Terauchi, K Narita, S Yamanaka, T Yoda, E Marukawa. Amorphous Mg–Ca Coatings for Hydrophilicity Protection of Dental Implant Surfaces. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DeJI2MA) 2022.10.25 東京
- 4. 高原楠旻. 2 級症例に対する私の取り組み. ジョンソン・エンド・ジョンソン株式会社 2022.06
- 5. T Tsujikawa, K Ohno, S Saburi, J Mitsuda, K Yoshimura, A Kimura, H Morimoto, G Ohmura, A Arai, H Ogi, S Shibata, Y Ariizumi, A Tasaki, R Takahashi, Y Tateishi, H Kawabe, S Ikeda, K Morita, T Tsunoda, T Akashi, M Kurata, I Imoto, Y Shimizu, A Watanabe, Y Asada, R Hayashi, Y Saito, H Ozawa, K Tsukahara, N Oridate, A Horii, T Maruo, N Hanai, H Inohara, H Iwai, T Fujii, K Nibu, S Iwae, T Ueda, R Yasumatsu, H Umeno, M Masuda, K Itoh, S Hirano, T Asakage. Tumor immune characterization identifies age-stratified biomarkers for nivolumab in patients with head and neck squamous cell carcinoma: A nationwide collaborative study in Japan.. American Association for Cancer Research (AACR) Annual Meeting 2022; 2022 Apr 8-13. 2022.04.08 Philadelphia (PA)
- 1. Kano S, Hikita R, Kobayashi Y, Tomomatsu N, Yoda T, Moriyama K. A case of mandibular retrognathia with maxillary transverse deficiency treated by SARPE and SSRO. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 2. Miyazaki T, Kadota C, Tsunashima A, Tomomatsu N, Yoda T, Higashihori N, Moriyama K. An asymmetric mandibular prognathism case with reverse occlusal cant treated by SSRO and mandibular recontouring. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 3. Hiroyuki YOSHITAKE. Cadaver Surgical Training for Total Joint Replacement of Temporomandibular Joint. 2022.08.27

Maxillofacial Orthognathics

Professor and Chair Keiji MORIYAMA Associate Professor Takuya OGAWA Junior Associate Professor Norihisa HIGASHIHORI Assistant Professor Michiko TSUJI, Yukiho KOBAYASHI, Masayoshi UEZONO, Chiho KADOTA, Takeshi OGASAWARA Specially Appointed Assistant Professor Hideyuki YOSHIZAWA Dental Resident Sonhwa KANG, Takayuki MIYAZAKI, Nanase IGARASHI, Yuki NIKI, Atsuhiro INOUE, Sakurako KANO, Yuki SAGAWA Doctoral Program : Medical and Dental Sciences Track Hidekazu MATSUMOTO, Yoshiya KAISAKA, Faisal Alkherainej, Aina OKAWARA, Misato SHIMIZU, Ryoto MACHIDA, Aye Chan Myo, Hanae ARAI, Ayako SUZUKI, Yuri TAKAGIWA, Satoka TAKEUCHI, Shen Huiyu, Nao UKITA, Suzu CHIDA, Mikiko TERASHIMA, Daigo YAMAHARA, Yunaho YONEMITSU, Liu Yinan, Lu Yeming, Aung Thet Khine, Aoi BEPPU, Kazuhisa MIZUMA, Ye Thiha, Pyae Phyo Htun Doctoral Program : Joint Degree Program (Chulalongkorn University) Nicha Kositkittiwanit, Wasupol Sodsook, Ploysongsang Kwanrat Graduate International Research Student Program Kanako HORI, Mayu Oiwa, Yuichiro OMORI, Ami TSUNASHIMA, Shintaro ARIKATA, Shiori OKUBO, Konosuke YOSHITANI, Wang Junyan, Yuzuki ISHIZEKI, Yoshiki HAYASHI, Lu Liu, Kenjiro MATSUMURA Part-time Lecturer Shoichi SUZUKI, Tatsuo KAWAMOTO, Naoto SUDA, Yoshiyuki KATO, Yasuo ISHIWATA, Yoshiyuki BABA, Toshimoto TENGAN, Masahiko YOKOZEKI, Shigetoshi HIYAMA, Shigeki TAKAHASHI, Takumi TAKAHASHI, Yuji OGIHARA, Maristela Sayuri ARAI, Jun MIYAMOTO, Junichi TAKADA, Rina HIKITA, Tsutomu MATSUMOTO, Yuko YASUDA,

(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

Hiroyuki KAMIMOTO, Yumi INAGAKI

(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. Cheng ES, Tsuji M, Suzuki S, Moriyama K. An overview of the intraoral features and craniofacial morphology of growing and adult Japanese cleidocranial dysplasia subjects. European Journal of Orthodontics. 2022.12; 44(6); 711-722
- Kirino S, Suzuki M, Ogawa T, Takasawa K, Adachi E, Gau M, Takahashi K, Ikeno M, Yamada M, Suzuki H, Kosaki K, Moriyama K, Yoshida M, Morio T, Kashimada K. Clinical report: Chronic liver dysfunction in an individual with an AMOTL1 variant. European Journal of Medical Genetics. 2022.11; 65(11); 104623
- 3. Takahashi Y, Date H, Oi H, Takeya Adachi, Imanishi N, Kimura E, Takizawa H, Kosugi S, Matsumoto N, Kosak Ki, Matsubara Y, Ando Y, Anzai T, Ariga T, Fukushima Y, Furusawa Y, Ganaha A, Goto Y, Hata K, Honda M, Iijima K, Ikka T, Imoto I, Kaname T, Kobayashi M, Kojima S, Kurahashi H, Kure S, Kurosawa K, Maegaki Y, Makita Y, Morio T, Narita I, Nomura F, Ogata T, Ozono K, Oka A, Okamoto N, Saitoh S, Sakurai A, Takada F, Takahashi T, Tamaoka A, Umezawa A, Yachie A, Yoshiura K, Chinen Y, Eguchi M, Fujio K, Hosoda K, Ichikawa T, Kawarai T, Kosho T, Masuno M, Nakamura A, Nakane T, Ogi T, Okada S, Sakata Y, Seto T, Takahashi Y, Takano T, Ueda M, Yagasaki H, Yamamoto T, Watanabe A, Hotta Y, Kubo A, Maruyama H, Moriyama K, Nanba E, Sakai N, Sekijima Y, Shimosegawa T, Takeuchi t, Usami S, Yamamoto K, Mizusawa H. Six years' accomplishment of the Initiative on Rare and Undiagnosed Diseases: nationwide project in Japan to discover causes, mechanisms, and cures. Journal of Human Genetics. 2022.09; 67(9); 505-513
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- Soe KM, Ogawa T, Moriyama K. Molecular mechanism of hyperactive tooth root formation in oculo-facio-cardio-dental syndrome. Frontiers in Physiology. 2022.07; 13; 946282
- 8. Oo LT, Miyamoto J, Takada J, Moriyama K. Correlation between the position of the glenoid fossa and condylar translational movement in skeletal Class III mandibular asymmetry patients. European Journal of Orthodontics. 2022.05; 44(3); 294-302
- 9. Kano S, Higashihori N, Thiha P, Takechi M, Iseki S, Moriyama K. The role of the histone methyltransferase SET domain bifurcated 1 during palatal development Biochemical and Biophysical Research Communications. 2022.04; 598; 74-80
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- 11. Suga T, Nagamine T, Tu TTH , Moriyama K, Toyofuku A. Orthognathic Surgery for Patients with Neurodevelopmental Disorders Requires Careful Decision-making by a Multidisciplinary Team. Innovations in Clinical Neuroscience. 2022; 19(4-6); 9-10
- Igarashi N, Miyata K, Loo TM, Chiba M, Hanyu A, Nishio M, Kawasaki H, Zheng H, Toyokuni S, Kon S, Moriyama K, Fujita Y, Takahashi A. Hepatocyte growth factor derived from senescent cells attenuates cell competition-induced apical elimination of oncogenic cells. Nature communications. 2022.07; 13(1); 4157
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- 2. Sagawa Y, Ogawa T, Matsuyama Y, Nakagawa Kang J, Yoshizawa Araki M, Unnai Yasuda Y, Tumurkhuu T, Ganburged G, Bazar A, Tanaka T, Fujiwara T, Moriyama K. Association between maternal smoking during pregnancy and short root anomaly in offspring. the 55th Annual Congress of the KAO and the 13th Asian Pacific Orthodontic Congress(APOC) 2022.10.28 Korea / ondemand
- 3. Inoue A, Higashihori N, Takeuchi S, Moriyama K. A case report of Parry-Romberg syndrome with mandibular prognathism treated by surgical orthodontic treatment. the 55th Annual Congress of the KAO and the 13th Asian Pacific Orthodontic Congress(APOC) 2022.10.28 Korea / ondemand
- 4. Wijarn S, Uezono M, Ogasawara T, Techalertpaisarn P, Moriyama K. Evaluation of the effect of Flute Design on Orthodontic Miniscrews Stability Using Human Bone Analogue. 2022.10.05 Osaka / Ondemand
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- 6. Uezono M, Ogawa T, Kang J, Moriyama K. Correlation between inferior turbinate and alveolar bone bridge following secondary bone grafting for unilateral cleft lip and palate patients. 14th International Cleft and Craniofacial Congress 2022.07.11 Scotland / ondemand
- 7. Yamahara D, Uezono M, Ogasawara T, Takakuda K, Moriyama K. HAp/Col Enhances Bone Forma4on around Orthodon4c Anchorage Devices in Microminipigs. 2022 IADR/APR General Session & Exhibition 2022.06.20 ondemand
- 8. Okawara A, Matsuyama Y, Yoshizawa Araki M, Unnai Yasuda Y, Ogawa T, Tumurkhuu T, Ganburged G, Bazar A, Fujiwara T, Moriyama K. Association between child abuse and oral habits in Mongolian adolescents. 2022 IADR/APR General Session & Exhibition 2022.06.20 ondemand

- 9. Faisal A, Matsumoto T, Yoshizawa H, Miyamoto J, Moriyama K. Three-dimensional Evaluation of Orofacial Movements in Patients with Facial Asymmetry. 2022 IADR/APR General Session & Exhibition 2022.06.20 ondemand
- 10. Moriyama K. 3D Evaluation of the Tongue and Oral Cavity before and after Orthognathic Surgery for Mandibular Prognathism. 28th Australian Orthodontic Virtual Congress 2022.03.11 ondemand
- 1. Ogawa T, Soe KM, Moriyama K. Molecular mechanism of radiculomegaly in oclulo-facio-cardio-dental syndrome. The 67th Annual Meeting of the Japan Society of Human Genetics 2022.12.14
- 2. Kobayashi Y, Moriyama K. Analysis of expression and function of superoxide dismutase 3 (SOD3) in the periodontal tissue during orthodontic tooth movement of rat molars. The 87th Annual Meeting of the Stomatological Society 2022.12.02
- 3. Yoshizawa H, Alkherainej F, Matsumoto T, Miyamoto J, Moriyama K. Evaluation of orofacial movements during articulaton in patients with asymmetric mandibular prognathism. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 4. Sagawa Y, Ogawa T, Matsuyama Y, Kang J, Yoshizawa(Araki) M, Unnai(Yasuda) Y, Fujiwara T, Moriyama K. Association between maternal smoking during pregnancy and short root anomaly in offspring. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 5. Ogasawara T, Uezono M, Pooktuantong O, Chantarawaratit P, Moriyama K. Optimization of loading condition for maxillary molar intrusion with midpalatal miniscrew-attached extension arm. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 6. Igarashi N, Takahashi A, Moriyama K. Analysis of SASP factors derived by senescent oseteblasts. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 7. Shimizu M, Uezono M, Ogasawara T, Nakajima Y, Moriyama K. A trial to develop a new three-dimensional reconstruction method of the mandible using cephalograms. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 8. Tsuji M, Cheng E, Suzuki S, Moriyama K. Intraoral features and craniofacial morphology of growing and adult cleidocranial dysplasia patients. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 9. Arikata S, Higashihori N, Yoshizawa H, Okubo S, Yosjitani K, Ukita N, Yonemitsu Y, Kamimoto H, Kang J, Kadota-Watanabe C, Tsuji M, Moriyama K. Characteristics of tooth abnormalities and palatal morphology of patients with Down syndrome. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 10. Okubo S, Higashihori N, Kang J, Arikata S, Yoshitani K, Terashima M, Kamimoto H, Sagawa K, Furusawa M, Yoshizawa H, Kadota-Watanabe C, Tsuji M, Moriyama K. Assessment of myofunctional therapy for strengthening the orbicularis oris muscle in Down syndrome patients. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 11. Machida R, Ogawa T, Soe KM, Moriyama K. Molecular mechanism of hyperactive root formation in oculo-facio-cardio-dental syndrome. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 12. Kano S, Hikita R, Kobayashi Y, Tomomatsu N, Yoda T, Moriyama K. A case of mandibular retrognathia with maxillary transverse deficiency treated by SARPE and SSRO. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05

- 13. Miyazaki T, Kadota C, Tsunashima A, Tomomatsu N, Yoda T, Higashihori N, Moriyama K. An asymmetric mandibular prognathism case with reverse occlusal cant treated by SSRO and mandibular recontouring. The 81st Annual Meeting of the Japanese Orthodontic Society & The 9th Joint Symposium of the Japanese Orthodontic Society and Korean Association of orthodontists 2022.10.05
- 14. Niki Y, Higashihori N, Inoue A, Hori K, Kadota C, Moriyama K. Effects of tongue-jaw bone relationship on respiratory function during sleep in skeletal Class II patients. The 32nd Annual Meeting of the Japanese Society for Jaw Deformities 2022.06.09 Niigata / ondemand
- 15. Inoue A, Higashihori N, Takeuchi S, Nakakuki K, Yoda T, Moriyama K. A case report of Parry-Romberg syndrome with mandibular prognathism treated by surgical orthodontic . The 32nd Annual Meeting of the Japanese Society for Jaw Deformities 2022.06.09 Niigata / ondemand
- 16. Kang J, Ogawa T, Yokouchi R, Inagaki Y, Funahasi K, Uezono M, Moriyama K. A Study of Timing of Alveolar Bone Graft in Patients with UCLP, a retrospective study. The 46th Annual Meeting of Japanese Cleft Palate Association 2022.05.26 kagoshima
- 17. Kano S, Higashihori N, Moriyama K. Influence of the histone methyltransferase SETDB1 during palatal development. The 46th Annual Meeting of Japanese Cleft Palate Association 2022.05.26 kagoshima
- 18. Ogawa T. Cosidering the timing of alveolar bone grafting from cases of completion of orthodontic treatment in our department. The 46th Annual Meeting of Japanese Cleft Palate Association 2022.05.26 Kagoshima

[Patents]

- 1. MEDICAL DEVICE, DEVICE STRUCTURES FOR DENTISTRY, FOR HEAD AND NECK SURGERY AND FOR ORTHOPEDIC SURGERY, AND METHOD FOR BONDING MEDICAL DEVICE TO BONE, Patent Number : US11234747
- 2. MEDICAL DEVICE, DEVICE STRUCTURES FOR DENTISTRY, FOR HEAD AND NECK SURGERY AND FOR ORTHOPEDIC SURGERY, AND METHOD FOR BONDING MEDICAL DEVICE TO BONE, Patent Number : US11234747

Department of Reconstructive Plastic Surgery

Professor: Kentaro Tanaka Assistant Professor (Hospital): Naoya Ishida Graduate students: Naoya Ishida, Kyoichi Murakami

(1) **Outline**

This department is reconstructive plastic surgery as a hospital clinical department. Mainly in charge of various reconstructive surgeries using microsurgery, especially head and neck reconstruction. It is natural to perform standard reconstructive surgery for typical resection cases, but we also provide safe and high-quality reconstructive surgery for difficult cases in which the number of cases is small and standard treatment has not been established. In addition to primary reconstruction performed at the same time as tumor resection, we are actively working on secondary reconstruction surgery for residual deformities and paralysis after surgery. In collaboration with other departments related to the head and neck region, we will promote research centered on the development of new surgical techniques that balance aesthetic and function and emphasize postoperative QOL of patients.

(2) Research

1. Development of head and neck reconstruction technique with emphasis on function and aesthetic

2. Research on nerve regeneration mechanism after nerve transplantation

3. Measurement of volume changes after tissue transplantation using a new animal model

4. Does improvement of peripheral capillary patency contribute to maintenance of transplanted adipose tissue volume?

5. First step to approach the "quality" of autograft tissue - Focusing on functional recovery of sweat glands after surgery

6. Development of new reconstructive techniques and functional evaluation methods for facial paralysis

7. Development of a limb-preserving surgical method emphasizing walking function for patients with diabetic foot gangrene

(3) Education

Pre- and post-graduate education in plastic surgery is provided in cooperation with the Department of Plastic and Reconstructive Surgery.

As a clinical department, plastic surgery is mainly in charge of reconstructing the shape and function of the body surface, and its area includes the whole body. Therapeutics (mostly surgery) have a higher weight than diagnostics, and because they often deal with conspicuous parts such as the face, neck, and hands and feet, it is characterized by the need for treatment results that take into account appearance. For medical students, plastic surgery is the most basic clinical department in the surgical department. , believes that mastering primary care for injuries and burns is essential for physicians. In addition, we would like them to understand the positioning of plastic surgery within the hospital and the importance of team medical care in cooperation with each department. First of all, we aim to provide an education that will make students interested in plastic surgery and that lectures and practical training will be a place of excitement.

(4) Lectures & Courses

Pre- and post-graduate education in plastic surgery is provided in cooperation with the Department of Plastic and Reconstructive Surgery.

[learning goal]

1: Know the meaning of plastic surgery and understand its position in surgery. In particular, recognize the relevance, competition, and congruence with other surgical departments.

2: Know the historical background of plastic surgery and understand the social necessity.

3: Understand the instruments and procedures in basic plastic surgery procedures (cutting and suturing, skin grafting, skin flaps, and other tissue transplantation), and as a result, know how much functional and cosmetic restoration can be achieved.

4: Recognize and understand plastic surgery diseases (skin plastic surgery, cranial plastic surgery, face, trunk, limb plastic surgery, cosmetic surgery).

5: Understand possible plastic surgical organ and tissue transplantation in the future.

6: Recognize artificial substances that can be substituted for living tissue, and cultivate insight into the future development of tissue substitutes.

[Knowledge and skills to be acquired]

1: Explain what plastic surgery is and why it is necessary.

2: Can advise patients or doctors of each department about what diseases are included in plastic surgery and take appropriate measures.

3: Can judge what kind of treatment method should be taken for each patient.

4: Be able to handle instruments used in basic plastic surgery procedures, select sutures, and be able to discuss scientifically what kind of procedures should be used.

In post-graduate education, after initial clinical training and training in plastic surgery for four years, a training program will be organized so that students can acquire qualifications as certified physicians of the Japan Society of Plastic and Reconstructive Surgeons. My goal is to be a clinician who is working on activities and pioneering the front line of plastic surgery, and at the same time, to be a researcher.

(5) Clinical Services & Other Works

Practice a high level of reconstructive surgery using microsurgical techniques. In particular, the number of cases of head and neck reconstruction is large, and in the 15 years since 2007, we have a clinical record of over 1000 cases. Above all, it is one of the leading facilities in Japan for skull base reconstruction surgery. Based on these experiences, we are able to provide safe and high-quality reconstructive surgery for difficult-to-treat cases that cannot be treated at other hospitals.

We have actively presented our medical research results at academic conferences in Japan and overseas, and have published many papers in English and Japanese. We have extensive exchanges with other universities and center hospitals, and actively participate in multi-institutional joint research.

(6) Clinical Performances

Our university is located in the center of Tokyo and consists of a medical school and a dental school, and society expects us to be specialists in the treatment of the head and neck region. Our department routinely performs reconstructive surgery using microsurgery. In particular, reconstructive surgery centered on head and neck reconstruction and skull base reconstruction is performed.

We not only perform various standard reconstructive surgeries for typical resection cases. We continue to provide safe and high-quality reconstructive surgery for difficult cases for which no standard treatment has been established and for surgical cases that are only performed at our hospital nationwide. In addition to primary reconstruction performed at the same time as tumor resection, we are actively working on secondary reconstruction surgery for residual deformities and paralysis after surgery.

Taking advantage of our advanced reconstructive surgery techniques, we are willing to perform reconstructive surgery for difficult-to-treat cases not only in the head and neck region but also in other parts of the body. The clinical departments that have treated us jointly are as follows. Head and Neck Surgery, Otolaryngology, Neurosurgery, Respiratory Surgery, Esophagogastric Surgery, Colorectal Surgery, Hepatobiliary and Pancreatic Surgery, Cardiovascular Surgery, Peripheral Vascular Surgery, Orthopedic Surgery, Urology, Ophthalmology, Dermatology, Perinatal and Gynecology , Oral and Maxillofacial Surgery, Maxillofacial Prosthodontics, Implantology, etc. very diverse.

(7) Publications

[Original Articles]

- 1. Hidaka Takeaki, Mori Hiroki, Shimizu Hiroaki, Takahashi Susumu, Tanaka Kentaro, Okazaki Mutsumi. Comparison of Lumbar Artery and Superior Gluteal Artery Perforator Flaps for Breast Reconstruction Multislice CT-Based Anatomical Study ANNALS OF PLASTIC SURGERY. 2022.12; 89(6); e39-e44
- Ishida N, Usami S, Tanaka K, Mori H. Use of a Fascial Reverse Dorso-Ulnar Metacarpal Bone Flap for Non-union of the Distal Phalanx of the Thumb: A Case Report The Journal of Hand Surgery Asian-Pacific. 2022.10; 27(5); 902-906
- 3. Kentaro Tanaka, Nobuko Suesada, Tsutomu Homma, Takeaki Hidaka, Hiroki Mori, Mutsumi Okazaki, Takashi Sugawara, Takeshi Tsutsumi, Takahiro Asakage. Early postoperative complications and their measures after skull base reconstruction: A study from the standpoint of plastic and reconstructive surgeons. Auris Nasus Larynx. 2022.10; 49(5); 845-855
- 4. Tomioka Y, Sekino M, Gu J, Kurita M, Yamashita S, Miyamoto S, Iida T, Kanayama K, Yoshimura K, Nakagawa M, Akazawa S, Kagaya Y, Tanaka K, Sunaga Y, Ueda K, Kawahara T, Tahara Y, Okazaki M. Wearable, wireless, multi-sensor device for monitoring tissue circulation after free-tissue transplantation: a multicentre clinical trial. Sci Rep. 2022.10; 12(1); 16532
- 5. Kentaro Tanaka, Nobuko Suesada, Tsutomu Homma, Hiroki Mori, Takeshi Tsutsumi, Takahiro Asakage, Mutsumi Okazaki. Muscle-penetration method: Cable nerve grafting with well vascularized surrounding tissue and shortest graft length. J Plast Reconstr Aesthet Surg. 2022.07; 75(7); 2387-2440
- 6. Uemura N, Aoyagi K, Tanaka K, Okazaki M, Mori H. Laser Removal of Buccal Skin Coloration Caused by India Ink Injection for Cancer Marking. Eplasty. 2022; 22; QA2

Cell Biology

Professor : Takao Nakata Junior Associate Professor : Tomohiro Ishii Assistant Professor : Toshifumi Asano Assistant Professor : Shogo Yoshihara 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. Our goal in undergraduate course is to provide students with fundamental knowledge and skill to analyze microscopic samples of normal human body. 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**

- 1. Tomohiro Ishii. Development and application of optogenetic tools. IMEG Symposium 2022.09.15 Kumamoto
- 2. Hironori Inaba, Tomohiro Ishii, Toshifumi Asano, Satoko Nakamura, Hidemasa Goto, Takao Nakata. Trial of image classification AI creation group work using histology virtual slides. the 127th Annual Meeting of The Japanese Association of Anatomists 2022.03.26 Online
- 3. Tomohiro Ishii, Hironori Inaba, Toshifumi Asano, Satoko Nakamura, Takao Nakata. Histology education using virtual slides. The 127th Annual Meeting of The Japanese Association of Anatomists 2022.03.26 Online

4. Qianqian Miao, Hironori Inaba, Takao Nakata. Spatiotemporal analyses on the crosstalk between RhoA and Rac1 using optogenetics. the 127th Annual Meeting of The Japanese Association of Anatomists 2022.03.25 Online

Medical Biochemistry

Professor Hiroshi Asahara

Assistant Professor Kyoko Arimoto-Matsuzaki

(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 organaized the course of Biochemmistry for the undergraduate students.

2 : Master course

We organized the course of Biochemmistry for the master students.

(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. Joshua Agbemefa Kuleape, Shakhawoat Hossain, Caleb Kwame Sinclear, Takanobu Shimizu, Hiroaki Iwasa, Junichi Maruyama, Kyoko Arimoto-Matsuzaki, Hiroshi Nishina, Yutaka Hata. DNA Damage Triggers the Nuclear Accumulation of RASSF6 Tumor Suppressor Protein via CDK9 and BAF53 To Regulate p53 Target Gene Transcription. Mol Cell Biol. 2022.02; 42(2); e0031021
- 2. Caleb Kwame Sinclear, Junichi Maruyama, Shunta Nagashima, Kyoko Arimoto-Matsuzaki, Joshua Agbemefa Kuleape, Hiroaki Iwasa, Hiroshi Nishina, Yutaka Hata. Protein kinase C α activation switches YAP1 from TEAD-mediated signaling to p73-mediated signaling. Cancer Sci. 2022.04; 113(4); 1305-1320

[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 Appication of split-GFP reassembly assay to the study of the in vitro myogenesis and myofusion. Springer,

Joint Surgery and Sports Medicine

Hideyuki Koga Tomomasa Nakamura, Kazumasa Miyatake, Mai Katakura

Department of Cartilage Regeneration Yusuke Nakagawa, Ryohei Takada

Masaaki Isono, Aritoshi Yoshihara Tang Guo, Kei Sato, Yusuke Amano, Shoichi Hasegawa Tetsuya Tachibana, Zhu Ling, Qu Zhen, Yang Yang Riko Yamashita, Ryu Yoshida, Tatsunobu Ikeda Chisa Ishihata, Ryota Seki, Wataru Shirahata, Toyohiro Katsumata

Miyoko Ojima, Miho Okada

(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

(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. Takanori Wakayama, Yoshitomo Saita, Masashi Nagao, Sayuri Uchino, Sei-Ichi Yoshihara, Kunikazu Tsuji, Hideyuki Koga, Yohei Kobayashi, Hirofumi Nishio, Yasumasa Momoi, Hiroshi Ikeda, Kazuo Kaneko, Muneaki Ishijima. Intra-Articular Injections of the Adipose-Derived Mesenchymal Stem Cells Suppress Progression of a Mouse Traumatic Knee Osteoarthritis Model. Cartilage. 2022.12; 13(4); 148-156
- 2. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Changes in subjective knee function and psychological status from preoperation to 6 months post anterior cruciate ligament reconstruction. J Exp Orthop. 2022.12; 9(1); 114

- 3. Naoto Watanabe, Kazumasa Miyatake, Ryohei Takada, Takahisa Ogawa, Yusuke Amano, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa. The prevalence and treatment of osteoporosis in patients undergoing total hip arthroplasty and the levels of biochemical markers of bone turnover. Bone Joint Res. 2022.12; 11(12); 873-880
- 4. Yusuke Nakagawa, Hideyuki Koga, Tomomasa Nakamura, Masafumi Horie, Hiroki Katagiri, Nobutake Ozeki, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta, Toshifumi Watanabe. Mid-term clinical outcomes of a posterior stabilized total knee prosthesis for Japanese patients: A minimum follow-up of 5 years. J Orthop Sci. 2022.12;
- 5. Shunichi Fujii, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Comparison of adhesion of thawed and cultured synovial mesenchymal stem cells to the porcine meniscus and the relevance of cell surface microspike. BMC Molecular and Cell Biology. 2022.12; 23(1); 53
- 6. Ryuichi Nakamura, Masaki Amemiya, Fumiyoshi Kawashima, Akira Okano. Ankle-Angle-Adjusting Fibular Osteotomy in Closed Wedge High Tibial Osteotomy. Arthroscopy Techniques. 2022.12; 11(12); e2169-e2175
- 7. Koji Murofushi, Daisuke Yamaguchi, Hiroki Katagiri, Kenji Hirohata, Hidetaka Furuya, Sho Mitomo, Tomoki Oshikawa, Koji Kaneoka, Hideyuki Koga, Kazuyoshi Yagishita. Validity of the KOJI AWARENESS self-screening test for body movement and comparison with functional movement screening. PLoS One. 2022.12; 17(12); e0277167
- 8. Hiroki Katagiri, Bruce B Forster, Lars Engebretsen, Jae-Sung An, Takuya Adachi, Yukihisa Saida, Kentaro Onishi, Hideyuki Koga. Epidemiology of MRI-detected muscle injury in athletes participating in the Tokyo 2020 Olympic Games. Br J Sports Med. 2022.12; 57(4); 218-224
- 9. Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Nobutake Ozeki, Takashi Hoshino, Masaki Amemiya, Ichiro Sekiya. Simultaneous Correction of Varus Deformity and Posterior Tibial Slope by Modified Hybrid Closed-Wedge High Tibial Osteotomy. Arthrosc Tech. 2022.11; 11(11); e2081-e2089
- 10. Masaki Amemiya, Ryuichi Nakamura, Mitsuo Yoshimura, Tomoharu Takagi. Proximal tibiofibular joint (PTFJ) dislocation due to Ehlers-Danlos syndrome: posterolateral open-wedge high tibial osteotomy combined with medial closed-wedge distal femoral osteotomy can correct the severe valgus deformity with a markedly increased tibial posterior slope. BMJ Case Reports. 2022.11; 15(11);
- 11. Naoto Watanabe, Ryohei Takada, Takahisa Ogawa, Kazumasa Miyatake, Masanobu Hirao, Chisato Hoshino, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa. Short stature and short distance between the anterior acetabular rim to the femoral nerve are risk factors for femoral nerve palsy following primary total hip arthroplasty using the modified Watson-Jones approach. Orthop Traumatol Surg Res. 2022.10; 108(6); 103351
- 12. Takahiro Tanimoto, Kentaro Endo, Yuriko Sakamaki, Nobutake Ozeki, Hisako Katano, Mitsuru Mizuno, Hideyuki Koga, Ichiro Sekiya. Human synovial mesenchymal stem cells show time-dependent morphological changes and increased adhesion to degenerated porcine cartilage. Scientific Reports. 2022.10; 12(1); 16619
- 13. Masaaki Isono, Jun Takeuchi, Ami Maehara, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga, Yoshinori Asou, Kunikazu Tsuji. Effect of CD44 signal axis in the gain of mesenchymal stem cell surface antigens from synovial fibroblasts in vitro Heliyon. 2022.10; 8(10); e10739
- 14. Seiji Noda, Tadashi Hosoya, Yoji Komiya, Yasuhiro Tagawa, Kentaro Endo, Keiichiro Komori, Hideyuki Koga, Yasuhiro Takahara, Kazutaka Sugimoto, Ichiro Sekiya, Tetsuya Saito, Fumitaka Mizoguchi, Shinsuke Yasuda. synovial fibroblast subset in arthritic joints has high osteoblastic and chondrogenic potentials in vitro. Arthritis Res Ther. 2022.09; 24(1); 224
- 15. Hiroki Katagiri, Mikio Shioda, Yusuke Nakagawa, Toshiyuki Ohara, Nobutake Ozeki, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga. Risk Factors Affecting Return to Sports and Patient-Reported Outcomes After Opening-Wedge High Tibial Osteotomy in Active Patients. Orthop J Sports Med. 2022.09; 10(9); 23259671221118836

- 16. Ichiro Sekiya, Sho Sasaki, Yugo Miura, Hayato Aoki, Hisako Katano, Noriya Okanouchi, Makoto Tomita, Jun Masumoto, Hideyuki Koga, Nobutake Ozeki. Medial tibial osteophyte width strongly reflects medial meniscus extrusion distance and medial joint space width moderately reflects cartilage thickness in knee radiographs. JMRI.(Journal of Magnetic Resonance Imaging). 2022.09; 56(3); 824-834
- 17. Kenji Hirohata, Junya Aizawa, Takehiro Ohmi, Shunsuke Ohji, Sho Mitomo, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita, Tetsuya Jinno, Atsushi Okawa. Reactive strength index during single-limb vertical continuous jumps after anterior cruciate ligament reconstruction: cross-sectional study. BMC Sports Sci Med Rehabil. 2022.08; 14(1); 150
- 18. Sho Mitomo, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita. Association Between Knee Extension Strength at 3 and 6 Months After Anterior Cruciate Ligament Reconstruction. J Sport Rehabil. 2022.08; 1-9
- 19. Takuya Adachi, Hiroki Katagiri, Jae-Sung An, Lars Engebretsen, Ukihide Tateishi, Yukihisa Saida, Hideyuki Koga, Kazuyoshi Yagishita, Kentaro Onishi, Bruce B Forster. Imaging-detected bone stress injuries at the Tokyo 2020 summer Olympics: epidemiology, injury onset, and competition withdrawal rate. BMC Musculoskelet Disord. 2022.08; 23(1); 763
- 20. Xueying Zhang, Ying Zhang, Meng Zhang, Yusuke Nakagawa, Camila B Caballo, Hazel H Szeto, Xiang-Hua Deng, Scott A Rodeo. Evaluation of SS-31 as a Potential Strategy for Tendinopathy Treatment: An In Vitro Model. Am J Sports Med. 2022.08; 50(10); 2805-2816
- 21. Ichiro Sekiya, Hideyuki Koga, Hisako Katano, Mitsuru Mizuno, Yuji Kohno, Koji Otabe, Nobutake Ozeki. Second-look arthroscopy after meniscus repair and synovial mesenchymal stem cell transplantation to treat degenerative flaps and radial tears of the medial meniscus: A case report. J Orthop Sci. 2022.07; 27(4); 821-834
- 22. Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Cross-sectional study on relationships between physical function and psychological readiness to return to sport after anterior cruciate ligament reconstruction. BMC Sports Sci Med Rehabil. 2022.06; 14(1); 97
- 23. Mituru Mizuno, Takahisa Matsuzaki, Nobutake Ozeki, Hisako Katano, Hideyuki Koga, Takanori Takebe, Hiroshi Yoshikawa, Ichiro Sekiya. Cell membrane fluidity and ROS resistance define DMSO tolerance of cryopreserved synovial MSCs and HUVECs. Stem Cell Research & Therapy. 2022.05; 13(1); 177
- 24. Guo Tang, Yoshinori Asou, Etsuko Matsumura, Yusuke Nakagawa, Kazumasa Miyatake, Hiroki Katagiri, Tomomasa Nakamura, Hideyuki Koga, Keiichiro Komori, Ichiro Sekiya, Yoich Ezura, Kunikazu Tsuji. Short cytoplasmic isoform of IL1R1/CD121a mediates IL1 β induced proliferation of synovium-derived mesenchymal stem/stromal cells through ERK1/2 pathway. Heliyon. 2022.05; 8(5); e09476
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- 2. Ryohei Takada, Kazumasa Miyatake, Naoto Watanabe, Tetsuya Jinno, Toshitaka Yoshii, Hideyuki Koga, Atsushi Okawa. Development of non-invasive augmented reality-based navigation system for total hip arthroplasty. The 66th Annual Congress of the Korean Orthopaedic Association 2022.10.13 Seoul, Korea
- 3. Hideyuki Koga. MRI signs for lateral meniscus posterior root tears in ACL injuries. 5th International conference on meniscus sience and surgery 2022.07.07 Luxembourg (web)
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- 5. Hideyuki Koga. Root tears of the medial meniscus: the Asian perspective. 5th International conference on meniscus sience and surgery 2022.07.07 Luxembourg (web)
- 6. Hideyuki Koga. Meniscus centralization. 16th International Workshop on Osteoarthritis Imaging 2022.07.06 Tokyo, Japan
- 7. Hideyuki Koga. Meniscus centralization. Advanced Knee Program 2022.07.02 Singapore (web)

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- 10. Hideyuki Koga. Let's save the lateral meniscus -How to deal with complex tears: root and extrusion-. 20th ESSKA 2022.04.27 Paris, France
- 11. Mai Katakura. Foot and ankle epidemiology in professional ballet; an analysis of 588 medical attention injuries and 255 time-loss injuries. 20th ESSKA 2022.04.27 Paris, France
- 12. Hideyuki Koga. Meniscus centralization. Advanced Knee Program -Exploring the Knee- 2022.04.02 Singapore (web)
- 13. Hideyuki Koga. Arthroscopic centralization of the meniscus. 3rd International Knee Day (web) 2022.03.10
- 14. Aritoshi Yoshihara, Yusuke Nakagawa, Hideyuki Koga. Morphological Risk Factors for the Occurrence of Lateral Meniscus Posterior Root Tear in Anterior Cruciate Ligament-Injured Patients. 3rd International Knee Day (Web) 2022.03.10
- 15. Hideyuki Koga. All about the meniscus: Degenerative tears. 13th SLARD (Latin American Society of Arthroscopy, Knee and Sport) International Congress(web) 2022.03.02 Cartagena de Indias, Colombia (web)
- 16. Aritoshi Yoshihara, Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Tomomasa Nakamura, Kunikazu Tsuji, Ichiro Sekiya, Hideyuki Koga. Proliferated Synovial Cells Migrate To The Surface Of Articular Cartilage In A Rat Knee Arthritis Model. ORS 2022 2022.02.04
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- 18. Yang Yang, Kazumasa Miyatake, Yusuke Nakagawa, Tomomasa Nakamura, Hiroki Katagiri, Mai Katakura, Kunikazu Tsuji, Ichiro Sekiya, Hideyuki Koga. The Relationship Between Synovial Mesenchymal Stem Cells and Bone Morphology in Patients with Different Types of Hip Osteoarthritis. ORS 2022 2022.02.04

Pharmacology

Staffs and Students

Assistant Professor Yukihiko TAMURA

Researchers

Noriko HIRAISHI (Cariology and Operative Dentistry) Yasuka KUSUMOTO (Pediatric Dentistry) Shinji Kuroda(Regenerative Dental Medicine) Hidemi Nakata(Regenerative Dental Medicine) Nami TSUCHIYAMA(Cariology and Operative Dentistry) Graduate Students Kenya YONEDA (Regenerative Dental Medicine) Michiko OZAWA C.Supachatwong (Regenerative Dental Medicine) Jason Hou (Regenerative Dental Medicine) Meng Sikun (Regenerative Dental Medicine) Rizwangul Ali(Regenerative Dental Medicine) Hsin-Ying Lu(Regenerative Dental Medicine) Gonndou Tadamu(Cariology and Operative Dentistry) Lecturers Yoshihiro WAKI Kenichi NAGANO Hiroyuki SETO Toshimi SATO Genki KATO Kiichi NONAKA Fumie SATO

(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 for dental clinicians to know huge knowledge of drugs and how to use them for patients. For these purposes, 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 in medical and dental fields and the last with drugs of particular importance in dentistry. Dental students learn the principle of pharmacology through laboratory practice. Following this learning, they must acquire an adequate background for drug use in general practice.

(3) Publications

[Original Articles]

- 1. Sikun Meng, Taishi Yokoi, Jingyang Kang, Yukihiko Tamura, Masakazu Kawashita, Eriko Marukawa, Shohei Kasugai, Shinji Kuroda and Hidemi Nakata. Modification of hydroxyapatite by doping lithium through acid-base reaction. Journal of the Ceramic Society of Japan. 2022.09; 130(9); 1-5
- Jason Hou, Yukihiko Tamura, Hsin-Ying Lu, Yuta Takahashi, Shohei Kasugai, Hidemi Nakata and Shinji Kuroda. An In Vitro Evaluation of Selenium Nanoparticles on Osteoblastic Differentiation and Antimicrobial Properties against Porphyromonas gingivalis Nanomaterials. 2022.05; 12(11); 1850-1866
- 3. Lu Hsin-Ying, Hou Jason, Takahashi Yuta, Tamura Yukihiko, Kasugai Shohei, Kuroda Shinji, Nakata Hidemi. Periodontal Pathogen Adhesion, Cytotoxicity, and Surface Free Energy of Different Materials for an Implant Prosthesis Screw Access Hole MEDICINA. 2022.02; 58(329); 1-14

- 1. Sikun Meng, Taishi Yokoi, Yukihiko Tamura, Jingyang Kang, Masakazu Kawashita, Eriko Marukawa, Shohei Kasugai and Hidemi Nakata. Properties of Lithium-doped Hydroxyapatite/Chitosan Composite as a Potential Bioactive Bone Substitute. The 7th International Symposium on Biomedical Engineering 2022.11.25 オンライン・オンデマンド
- 2. Reziwanguli AILI, Shinji KURODA, Yukihiko TAMURA, Eriko MARUKAWA, Shohei KASUGAI, Hidemi NAKATA. Evaluation of Cross-linked Membranes of Fish Gelatin and Hydroxyapatite. 2022 IADR/APR General Session & Exhibition 2022.06.22 ON LINE VIRTUAL EXPERIENCE
- 3. Yukihiko TAMURA, Pornpoj FUANGTHARNTHIP, Yasuka KUSUMOTO, Tsutomu IWAMOTO, Yoshihiro WAKI. Pharmacological role of metallothionein in drug-induced gingival overgrowth. The 8th International Symposium on Metallomics 2022.06.11 Kanazawa
- 4. Yukihiiko Tamura, Yasuka Kusumoto, Tsutomu Iwamoto, Yoshihiro Waki. Induction of metallothionein expression by Ciclosporin. The 95th Annual Meeting of the Japanese Pharmacological Society 2022.03.09 福岡

Biochemistry

Professor Testuro Watabe Associate Professor Miki Yokoyama Assistant Professor Katarzyna Anna Podyma-Inoue, Miho Kobayashi Technical staff Megumi Naito Part-time Lecturer Yasuhiro Yoshimatsu, Jun Ishihara, Yuta Ikami Collaborative Researcher Kazuki Takahashi, Kazue Terasawa Graduate student Maki Saito, Kashio Fujiwara, Hisae Katsumata, Noriko Shibao, Honoka Hirose, Qianqian Miao

(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 lympangiognesis

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 antiogenesis and lymphaniogenesis in tumor microenvironment. In addition, we elucidated the molecular mechanism for anti-angiogenesis by vasohibin-1 (VASH1). We are conducting basic research aimed at suppressing tumor progression through the functional analysis of VASH1.

(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) Unraveling of the physiological role of VASH1 as a detyrosination enzyme

VASH1, which is induced expression by VEGF stimulation in endothelial cells, was re-identified as a enzyme of detyrosination. Detyrosination is one of the post-translational modification of microtubules, It is known that detyrosinated microtubules play key role for several physiological phenomena, such as chromosome partition in mitosis or functional beating of heart. We are conducting basic research aimed at molecularly elucidating of role as a detyrosination enzyme in physiological function of VASH1.

(5) Structural basis for chaperone-mediated autophagy

A mechanism for appropriately removing unnecessary proteins is indispensable for maintaining intracellular homeostasis. Intracellular proteolytic reactions can be broadly divided into lysosome-mediated pathways and proteasome-mediated pathways. In the lysosome-mediated pathway, lysosomes often fuse with vesicles containing target proteins (endosomes, phagosomes, autophagosomes, etc.). In contrast, chaperone-mediated autophagy (hereinafter abbreviated as CMA) has a unique mode in which the target protein is recruited by the chaperone onto the lysosomal membrane and directly incorporated into the lysosome. CMA was discovered as a phenomenon that is activated by serum removal, but in recent years it has been reported that CMA plays an important role in maintaining pluripotency of embryonic stem cells and maintaining the function of hematopoietic stem cells. On the other hand, it has been pointed out that CMA dysfunction causes neurodegenerative diseases or myopathy, and conversely, excessive CMA causes malignant transformation in cancer. However, while research on the functional importance of CMA is progressing, many unclear points remain in the molecular mechanism of CMA.

Lysosomal-associated membrane protein 2A (LAMP2A) provides a scaffold for the substrate protein chaperone to bind to the lysosomal membrane in CMA. LAMP2A is a single-transmembrane glycoprotein that is abundant in the lysosomal membrane. Most of the LAMP2A protein resides on the luminal side of the lysosome, and the short peptide portion of only 11 amino acid residues protruding to the cytoplasm side serves as a scaffold. The lumen side of LAMP2A is composed of two homologous subdomains, and we have reported by crystallographic analysis that the subdomains have a unique triangular prism structure (β -prism) (BBRC, 2016). However, it was unclear what structure the entire molecule of LAMP2A would take to provide a scaffold.

We analyzed the homophilic interaction of LAMP2A molecules, using expanded genetic code technologies that generate photo-crosslinking and/or steric hindrance at specified interfaces. As a result, it was clarified that LAMP2A has a structure in which specific faces of the triangular prisms of the subdomain close to the membrane face each other, and that CMA activity decreases when this structure cannot be obtained. This result suggests that the interaction between LAMP2A within the lysosomal lumen defines the proper arrangement of the short peptide moiety on the lysosomal membrane, which is a great clue to elucidate the molecular mechanism of CMA centered on LAMP2A (Autophagy, 2021).

We also succeeded in demonstrating cross-linking between LAMP2A and the chaperone Hsc70, whose direct interaction had not been demonstrated in CMA (ECR, 2022).

(6) HSPGs, Exosomes and EMT

Metastasis is the cause of the death in a majority of human cancers. Tumor-derived, small extracellular vesicles (exosomes) are suggested to play important roles in different steps of metastatic cascade. Tumor-derived exosomes has been shown to participate in tumor progression by mediating epithelial-to-mesenchymal transition (EMT), stimulating the invasion, migration, angiogenesis. Heparan sulfate proteoglycans (HSPGs) are strategically localized on the cell surface and serves as receptors for a number of extracellular ligands. HSPG-dependent signals regulate tumor proliferation, angiogenesis and metastasis. HSPGs have been also implicated in the formation/uptake of tumor-derived exosomes, but the detailed mechanisms still remain to be characterized. We are working on the characterization of exosomal cargo and identification of the molecules responsible for exosome-recipient cell interactions as well as pathways involved in the internalization of exosomes focusing on the role of HSPGs in those events.

(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. Miho Kobayashi, Kashio Fujiwara, Kazuki Takahashi, Yusuke Yoshioka, Takahiro Ochiya, Katarzyna A. Podyma-Inoue, Tetsuro Watabe. Transforming growth factor- β -induced secretion of extracellular vesicles from oral cancer cells evokes endothelial barrier instability via endothelial-mesenchymal transition Inflammation and Regeneration. 2022.09; 42(1); 38
- 2. Kazuki Takahashi, Katarzyna A. Podyma-Inoue, Maki Saito, Shintaro Sakakitan, Akinari Sugauchi, Keita Iida, Sadahiro Iwabuchi, Daizo Koinuma, Kyoko Kurioka, Toru Konishi, Susumu Tanaka, Atsushi Kaida, Masahiko Miura, Shinichi Hashimoto, Mariko Okada, Toshihiro Uchihashi, Kohei Miyazono, Tetsuro Watabe. TGF- β generates a population of cancer cells residing in G1 phase with high motility and metastatic potential via KRTAP2-3 Cell Reports. 2022.09; 40; 111411
- 3. Kei Takahashi, Ko Abe, Shimpei I Kubota, Noriaki Fukatsu, Yasuyuki Morishita, Yasuhiro Yoshimatsu, Satoshi Hirakawa, Yoshiaki Kubota, Tetsuro Watabe, Shogo Ehata, Hiroki R Ueda, Teppei Shimamura, Kohei Miyazono. An analysis modality for vascular structures combining tissue-clearing technology and topological data analysis. Nat Commun. 2022.09; 13(1); 5239
- 4. Nakayama K, Nishijo T, Miyazawa M, Watabe T, Azuma M, Sakaguchi H. Hapten sensitization to vaginal mucosa induces less recruitment of dendritic cells accompanying TGF- β -expressing CD206⁺ cells compared with skin. Immunity, inflammation and disease. 2022.04; 10(4); e605
- 5. Yuta Ikami, Kazue Terasawa, Kensaku Sakamoto, Kazumasa Ohtake, Hiroyuki Harada, Tetsuro Watabe, Shigeyuki Yokoyama, Miki Hara-Yokoyama. The two-domain architecture of LAMP2A regulates its interaction with Hsc70 Experimental Cell Research. 2022.02; 411(1);
- 6. Toshihiro Inubushi, Ayaka Fujiwara, Takumi Hirose, Gozo Aoyama, Toshihiro Uchihashi, Naoki Yoshida, Yuki Shiraishi, Yu Usami, Hiroshi Kurosaka, Satoru Toyosawa, Susumu Tanaka, Tetsuro Watabe, Mikihiko Kogo, Takashi Yamashiro. Ras signaling and RREB1 are required for the dissociation of medial edge epithelial cells in murine palatogenesis. Disease Models & Mechanisms. 2022.02; 15(2);

[Misc]

- 1. Yuta Ikami, Kazue Terasawa, Tetsuro Watabe, Shigeyuki Yokoyama, Miki Hara-Yokoyama. The two-domain architecture of LAMP2A within the lysosomal lumen regulates its interaction with HSPA8/Hsc70 Autophagy Reports. 2022.05; 1(1); 205-209
- 2. Yasuhiro Yoshimatsu, Tetsuro Watabe. Emerging roles of inflammation-mediated endothelial-mesenchymal transition in health and disease. Inflammation and Regeneration. 2022.02; 42(1); 9
- 1. Tetsuro Watabe. Development of novel therapeutic strategies targeting tumor microenvironment networks. Japanese Journal of Lymphology. 2022.06; 45(1); 15-18
- 2. Endothelial destabilization by tumor-derived exosome 2022; in press;
[Conference Activities & Talks]

- 1. 小林 美穂, 廣瀬 穂香, 中山 雅敬, 渡部 徹郎. 加齢に伴う血管内皮細胞の減少とストレス応答性の関係. 第 30 回日本血管生物医学会学術集会(CVMW2022) 2022.12.16
- 2. 小林 美穂、藤原 花汐、高橋 和樹、吉岡 祐亮、落谷 孝広、渡部 徹郎. 口腔扁平上皮がん細胞由来細胞外小 胞による血管不安定化機構. 第 87 回 口腔病学会学術大会 2022.12.03 東京
- 3. 小林 美穂, 廣瀬 穂香, 小林 ゆめ, 渡部 徹郎. Vasohibin-1 が細胞内輸送に及ぼす影響とその役割. 第45回日 本分子生物学会年会 2022.12.01 幕張
- 4. Tetsuro Watabe. Targeting tumor microenvironment networks for developing novel the rapeutic strategies.. KVBM2022 2022.11.25 Korea
- 5. Miho Kobayashi, Honoka Hirose, Masanori Nakayama, Tetsuro Watabe. Relationship between age-dependent vascular endothelial cell decline and stress responsiveness. The 22nd International Vascular Biology Meeting (IVBM2022) 2022.10.14 Oakland, USA
- 6. Katarzyna A. Inoue. TGF- β generates cancer cells residing in G1 phase with high motility by inducing Slug/HMGA2-independent EMT. Virtual TGF- β Meeting 2022.08.17 on-line
- 7. 小林 美穂, 藤原 花汐, 鈴木 康弘, 若林 育海, 中山 雅敬, 佐藤 靖史, 渡部 徹郎. 微小管の翻訳後修飾による細胞内輸送調節を介したシグナル伝達制御機構とその役割. 第 74 回日本細胞生物学会大会 2022.06.30 東京
- 8. Katarzyna A. Inoue, Kazuki Takahashi, Maki Saito, Shintaro Sakakitani, Toru Konishi, Daizo Koinuma, Akinari Sugauchi, Atsushi Kaida, Yasuhiro Yoshimatsu, Toshihiro Uchihashi, Masahiko Miura, Kohei Miyazono, Tetsuro Watabe. TGF-β-induced cell cycle arrest is correlated with increased migration and metastasis of oral squamous cell carcinoma. 第46回日本リンパ学会総会 2022.06.04 東京都
- 9. 高橋 和樹, 勝又 寿枝, 小林 美穂, 池田 行徳, 篠原 満利恵, 前田 健太郎, 吉松 康裕, 松永 行子, 渡部 徹郎. 内 皮間葉移行 (EndoMT) レポーター内皮細胞を用いた EndoMT の可視化とがん細胞の脈管内侵入機序の解明. 第 46 回日本リンパ学会総会 2022.06.04 東京
- 10. 小林 美穂. 口腔がん細胞が放出するエクソソームによる血管不安定化機構. 第7回 日本血管生物医学会若 手研究会 2022.03.05 淡路島(オンライン ハイブリッド)
- 1. Hisae Katsumata, Kazuki Takahashi, Miho Kobayashi, Kentaro Maeda, Yasuhiro Yoshimatsu, Yukiko Matsunaga, Tetsuro Watabe. Detection of partial endothelial-mesenchymal transition (EndoMT) states using EndoMT reporter endothelial cells. 2022.12.03
- 2. Miho Kobayashi. Relationship between vascular homeostasis and aging. MBSJ2022 2022.12.02
- 3. Katarzyna A. Podyma-Inoue, Kazuki Takahashi, Akinari Sugauchi, Keita Iida, Sadahiro Iwabuchi, Daizo Koinuma, Kyoko Kurioka, Toru Konishi, Susumu Tanaka, Atsushi Kaida, Masahiko Miura, Shinichi Hashimoto, Mariko Okada, Toshihiro Uchihashi, Kohei Miyazono, Tetsuro Watabe. TGF- β enhances metastasis of oral cancer via generation of a population of cancer cells in G1 phase with high motility. The 81st Annual Meeting of the Japanese Cancer Association 2022.09.30 Tokyo
- 4. Shiori Tokizaki, Katarzyna A. Inoue, Kazuki Takahashi, Takehisa Matsumoto, Mikako Shirouzu, Hiroyuki Harada, Tetsuro Watabe. Development of novel Fc chimeric receptor targeting all transforming growth factor- β isoforms. The 81st Annual Meeting of the Japanese Cancer Association 2022.09.29 Tokyo
- 5. Shiori Tokizaki, Katarzyna A. Inoue, Kazuki Takahashi, Hiroyuki Harada, Tetsuro Watabe. Development of novel Fc chimeric receptor targeting all TGF- β isoforms. The 46th Meeting of the Japanese Society of Lymphology 2022.06.04 Tokyo
- 6. Kazue Terasawa, Yuta Ikami, Tatsuro Seike, Kensaku Sakamoto, Tetsuro Watabe, Shigeyuki Yokoyama, Miki Yokoyama. Homophilic interaction of the beta-prism domains of LAMP2A in the lysosomal lumen is important for chaperone-mediated Autophagy . The 95th Annual Meeting of the Japanese Biochemical Society 2022.11.11 NAGOYA CONGRESS CENTER

[Others]

 2022.09 Twitter TMDU - Tokyo Medical and Dental University @TMDUniversity

The finding will lead to the development of novel therapeutic agents that target the blood vessels during the formation of pre-metastatic niches (PMNs) mediated by cancer cell-derived extracellular vesicles (EVs).

Cell Signaling

Professor(Principal Investigator)Tomoki NAKASHIMA Assistant Professor Mikihito 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

- Bingzi Dong, Masahiro Hiasa, Yoshiki Higa, Yukiyo Ohnishi, Itsuro Endo, Takeshi Kondo, Yuichi Takashi, Maria Tsoumpra, Risa Kainuma, Shun Sawatsubashi, Hiroshi Kiyonari, Go Shioi, Hiroshi Sakaue, Tomoki Nakashima, Shigeaki Kato, Masahiro Abe, Seiji Fukumoto, Toshio Matsumoto. Osteoblast/osteocyte-derived interleukin-11 regulates osteogenesis and systemic adipogenesis. Nat Commun. 2022.11; 13(1); 7194
- 2. Yu Yamashita, Mikihito Hayashi, Mitsuru Saito, Tomoki Nakashima. Osteoblast lineage cells-derived Sema3A regulates bone homeostasis independently of androgens Endocrinology. 2022.08;
- 3. Masayuki Tsukasaki, Noriko Komatsu, Takako Negishi-Koga, Nam Cong-Nhat Huynh, Ryunosuke Muro, Yutaro Ando, Yuka Seki, Asuka Terashima, Warunee Pluemsakunthai, Takeshi Nitta, Takashi Nakamura, Tomoki Nakashima, Shinsuke Ohba, Haruhiko Akiyama, Kazuo Okamoto, Roland Baron, Hiroshi

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4. Takehito Ono, Ryosuke Denda, Yuta Tsukahara, Takashi Nakamura, Kazuo Okamoto, Hiroshi Takayanagi, Tomoki Nakashima. Simultaneous augmentation of muscle and bone by locomomimetism through calcium-PGC-1 α signaling Bone Research. 2022.08; 10(1); 1-14

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1. Ono T, Nakashima T. Oral bone biology Journal of oral biosciences. 2022.02; 64(1); 8-17

[Conference Activities & Talks]

1. Takehito Ono, Ryosuke Denda, Yuta Tsukahara, Takashi Nakamura, Kazuo Okamoto, Hiroshi Takayanagi, Tomoki Nakashima. Simultaneous augmentation of muscle and bone by the locomomimetic drug LAMZ. The 8th Annual Meeting of Japan Muscle Society 2022.08.06 The University of Tokyo

Periodontology

From January. 2022 [Professor] Takanori Iwata [Photoperiodontics Professor] Akira Aoki [Associate Professor] Sayaka Katagiri [Junior Associate Professor] Yasuo Takeuchi [Assistant Professor] Koji Mizutani, Yuichi Ikeda(~Jun), Takahiko Shiba(~Mar), Shogo Maekawa(Sep \sim), Yujin Ohsugi(Apr \sim) [Specially appointed Assistant Professor] Hideyuki Takamatsu(~Mar), Shunsuke Fukuba(Apr~Mar), Yosuke Tsuchiya(Apr \sim), Munehiro Okada(Apr \sim) [Clinical Fellow] Kohei Takeda(~Mar), Natsumi Saito, Hiromi Niimi, Munehiro Okada, Tomoaki Kariya (~Mar), Ayako Kawada (\sim Mar), Kazuki Miyata (Apr \sim), Yuri Ito (Apr \sim), Aiko Fujino (Apr \sim), Yumine Kiuchi (Sep \sim), Yuya Hamada(Sep~), Takahiro Naito (Apr~) [Graduate Students] Ryo Sato(~Mar), Daiki Tanaka (~Mar), Takashi Nemoto (~Mar), Hiromi Kominato (\sim Mar), Ryo Mikami, Tsuyoshi Shimohira, Shunsuke Takeuchi, Masahiro Hatasa, Anhao Liu, Shu Takemura, Keita Nakagawa, Takahiko Nagai, Masahiro Hakariya, Kazuki Morita, Lisa Yagasaki, Mako Yokose, Sumiko Yoshida, Sakura Hayashi, Jiacheng Wang, Peiya Lin, Shiwei Sun, Ryota Kobayashi, Eri Sakaniwa, Tatsuro Seike, Kanji Tabata, Keita Toyoshima, Daichi Yamaki, Chihiro Imai(Apr~), Junya Watanabe(Apr~), Naoki Toyoda(Apr~), Chen Lu(Apr \sim), AKINAGA Moreira Bruna(Oct \sim), Mingran Zhang (Apr \sim), Jingyi Gao(Oct \sim) [Adult graduate student] Fumihoko Kimura, Ito Hirasawa [Graduate Research Student] Mai Kitamura(~Mar), Miki Dobashi(~Mar), Akane Ochiai, Sakurako Kawamoto,

Hiroe Nakashima, Yugo Itoh(Apr~), Saki Goto(Apr~), Ye Yint Kaung Myint(Oct~) [Clinical Professor] Hiroaki Kobayashi, Shigenari Kikuchi, Hiroaki Tsutioka [Adjunct Lecturer] 53 [Registered dentist] 74

[Assistant Administrative Staff] Hiroka Watanabe (\sim Mar), Keiko Odaka(Apr \sim)

(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 application of lasers/LEDs in periodontal therapy

(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

- Ohsugi Y, Hatasa M, Katagiri S, Hirota T, Shimohira T, Shiba T, Komatsu K, Tsuchiya Y, Fukuba S, Lin P, Toyoshima K, Maekawa S, Niimi H, Iwata T, Aoki A. High-frequency pulsed diode laser irradiation inhibits bone resorption in mice with ligature-induced periodontitis Journal of Clinical Periodontology. 2022.12; 49(12); 1275-1288
- 2. Mikami R, Sudo T, Fukuba S, Takeda K, Matsuura T, Kariya T, Takeuchi S, Ochiai A, Kawamoto S, Toyoshima K, Mizutani K, Arakawa S, Aoki A, Iwata T. Prognostic factors affecting periodontal regenerative therapy using recombinant human fibroblast growth factor-2: A 3-year cohort study. Regenerative therapy. 2022.12; 21; 271-276
- 3. Quan BD, Sadeghi R, Ikeda Y, Ganss B, Hamilton DW, Christopher MA, Sone ED. Screening of functionalized collagen membranes with a porcine periodontal regeneration model. Oral Diseases. 2022.12; epub;
- 4. Hakariya M, Arisaka Y, Masuda H, Yoda T, Iwata T, Yui N. Suppressed migration and enhanced cisplatin chemosensitivity in human cancer cell lines by tuning the molecular mobility of supramolecular biomaterials. Macromolecular Bioscience. 2022.12; 23(2); 2200438
- 5. Morita K, Nakamura A, Machida M, Kawasaki T, Nakanishi R, Ichida J, Iwata T, Umezawa A, Akutsu H. Efficient reprogramming of human fibroblasts using RNA reprogramming with DAPT and iDOT1L under normoxia conditions Regeneration Therapy. 2022.12; 21; 389-397
- 6. Ikeda E, Tanaka D, Glogauer M, Tenenbaum H C , Ikeda Y. Healing effects of monomer and dimer resveratrol in a mouse periodontitis model. BMC Oral Health. 2022.11; 22(1); 460
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- 9. Tamura A, Kang TW, Tonegawa A, Arisaka Y, Masuda H, Mikami R, Iwata T, Yoda T, Yui N. Supramolecular Surface Coatings with Acetylated Polyrotaxane-Based Triblock Copolymers for Thermal Regulation of Cell Adhesion and Fabrication of Cell Sheets. Biomacromolecules. 2022.11; 23(11); 4860-4871
- Yao Y, Raymond JE, Kauffmann F, Maekawa S, Sugai JV, Lahann J, Giannobile WV. Multicompartmental Scaffolds for Coordinated Periodontal Tissue Engineering. Journal of dental research. 2022.11; 101(12); 1457-1466
- 11. Hayashi K, Takeuchi Y, Shimizu S, Tanabe G, Churei H, Kobayashi H, Ueno T. Continuous oral administration of sonicated *P. gingivalis* delays rat skeletal muscle healing post-treadmill training International Journal of Environmental Research and Public Health. 2022.10; 19(20);
- 12. Tanaka-Takemura Y, Arisaka Y, Hakariya M, Masuda H, Mikami R, Sekiya-Aoyama R, Iwata T, Yoda T, Ono T, Yui N. Independent roles of molecular mobility and zeta potential on supramolecular surfaces in the sequence of RAW264.7 macrophage responses. Macromolecular bioscience. 2022.09; 22(11); 2200282
- Maekawa S, Cho YD, Kauffmann F, Yao Y, Sugai JV, Zhong X, Schmiedeler C, Kinra N, Moy A, Larsson L, Lahann J, Giannobile WV. BMP Gene-Immobilization to Dental Implants Enhances Bone Regeneration. Advanced materials interfaces. 2022.08; 9(22);
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- 16. Lin T, Taniguchi Y, Aoki A, Chen CC. Management of furcation-involved molar using Er:YAG laser-assisted bone regenerative therapy: A case report Journal of Dental Science. 2022.06; 17(4); 1836-1838
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- 22. Sato R, Matsuura T, Akizuki T, Fukuba S, Okada M, Nohara K, Takeuchi S, Hoshi S, Ono W, Maruyama K, Izumi Y, Iwata T. Influence of the bone graft materials used for guided bone regeneration on subsequent peri-implant inflammation: an experimental ligature-induced peri-implantitis model in Beagle dogs International Journal of Implant Dentistry. 2022.01; 21(8); 3
- 23. Shiba T, Katagiri S, Komatsu K, Nemoto T, Takeuchi Y, Chen B, Zhou YS, Iwata T. Treatment of peri-implantitis caused by malpositioning and an extra implant: a case report International Journal of Periodontics & Restorative Dentistry. 2022.01; 42(1); e15-e20

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- 25. Uchida H, Wada J, Watanabe C, Nagayama T, Mizutani K, Mikami R, Inukai S, Wakabayashi N.. Effect of night denture on tooth mobility in denture wearers with sleep bruxism: a pilot randomized controlled trial. Journal of Prosthodontic Research. 2022; 66(4); 564-571

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- 1. MIzutani K, Aoki A. Periodontal therapy by dental lasers. Current therapy of Peri-implantitis . Quintessence, 2022.12

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- 4. Fujii Y, Liu L, Yagasaki L, Inotsume M, Chiba T, Asahara H. Cartilage Homeostasis and Osteoarthritis International Journal of Molecular Sciences. 2022.06; 23(11); 6316
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- 4. Junichiro Wada, Koji Mizutani, Noriyuki Wakabayashi. The Successful Concept of Removable Partial Denture in Patient with Periodontitis: How to Preserve and Involve the Fragile Abutment Tooth in RPD? Part1. Prosthodontic Treatment Following Periodontal Management The Quintessence. 2022.08; 41(8); 36-55
- 5. Aoki A. For special features on "Lasers in field of teeth and dental pulp- Unique reseraches on application of LED" Journal of Japan Society for Laser Surgery and Medicine . 2022.07; 43(2); 74
- 6. Kitanaka Y, Takeuchi Y, Hiratsuka K, Nitta H, Iwata T, Aoki A. Application of antimicrobial photodynamic therapy in periodontal treatment 2022.06; 32(1); 9-14

- Aoki A, Yoshinari N. In memories of Hajime Yamamoto Journal of Japanese Society of Laser Dentistry. 2022.06; 32(1);
- 8. Aoki A, Shinoki T. Dental Talk, "25th Anniverasry Symposium of Er:YAG laser releasement", Variable applications and advancement of Er:YAG laser Dental MAgazine. 2022.06; (181); 10-14

[Conference Activities & Talks]

- 1. Maekawa S. Periodontal Regeneration Updates 2022 and Challenges-. International Conference of Taiwan Academy of Laser and Holistic Dentistry 2022.11.13 Online
- 2. Katagiri S. Porphyromonas gingivalis impairs glucose uptake in skeletal muscle associated with altering gut microbiota. UCh TMDU Joint Symposium 2022.11.08 Online
- 3. Aoki A. Current status of Er: YAG laser therapy in management of peri-implant disease. 10th Annual Meeting of Italian Society of Laser Dentistry (SILO) 2022.10.07 online
- 4. Iwata T. Bacterial Analysis between Periodontitis and Peri- implantitis. The 14th Asian Pacific Society of Periodontology Meeting 2022 2022.08.30 Bangkok
- 5. Iwata T. Periodontal Regeneration with Cell Sheet Engineering. The 14th Asian Pacific Society of Periodontology Meeting 2022 2022.08.29 Bangkok
- 6. Fukuba S, Okada M, Sato R, Takeuchi S, Ikeda Y, Yamaki D, Iwata T. Clinical outcomes of periodontal regeneration with carbonate apatite in treatments of intrabony defects, Class II and Class II furcation involvement: a 9-month prospective case series. EuroPerio 10 2022.06.15 Copenhagen
- 7. Yoshida S, Hatasa M, Ohsugi Y, Tsuchiya Y, Liu A, Niimi H, Morita K, Shimohira T, Sasaki N, Maekawa S, Shiba T, Hirota T, Noritake K, Nitta H, Katagiri S, Iwata T. Porphyromonas gingivalis administration induces obesity, modifies gene expression in the liver and brown adipose tissue in pregnant mice, and causes underweight in fetuses. Europerio 10 2022.06.15 Copenhagen
- 8. Maekawa S. To Preserve/ To Build Alveolar Bone for Optimal Implant Dentistry. National Conference of Taiwan National Association of Dental Implantology 2022.04.23 Online
- 9. Maekawa S. Modern Periodontal Tissue Regeneration. CE Seminar Harvard School of Dental Medicine 2022.03.15 Online
- 1. Aoki A. Lasers and Bone Regeneration in clinical practice. CDE Lecture in TMDU Alumni meeting, "Knowing and Making Bone" 2022.12.11 Tokyo
- 2. Aoki A. Periodontal Er:YAG Laser Operation- Less pain, Clean healing, Early healing. CDE practical course of TMDU alumni association 2022.12.11 Tokyo
- 3. Liu A, Hayashi M, Tsuchiya Y, Iwata T, Nakashima T. Spatio-temporal analysis of the pathogenesis of periodontitis via novel mouse periodontitis model. The 87th Annual Meeting of the Stomatological Society of Japan 2022.12.02
- 4. Oka A, Nakata H, Kuroda S, Aoki A, Marukawa E. Effect of VEGF/HGF signaling inhibition in peri-implantitis tissue. 2022.12.02 Tokyo
- 5. Tabata R, Nakagawa T, Martin K, Ohtsuki M, Aoki A, Shimada K. Quantification of biofilm in vitro using OCT. 34th Annual meeting of Japanese Society of Laser Dentistry 2022.11.27 Tokyo
- 6. Kawamura R, Mizutani K, Hamada K, Tsukuda M, Iwata T, Aoki A. Evaluation of Er:YAG laser's contact chip in frenurectomy. 34th Annual meeting of Japanese Society of Laser Dentistry 2022.11.26 Tokyo
- 7. Eguro T, Nishiwaki T, Mizoguchi T, Aoki A. Application of Er:YAG laser in second stage surgery using surgical guide plate. 34th Annual meeting of Japanese society of Laser Dentistry 2022.11.26 Tokyo
- 8. Aoki A. Comprehensive periodontal pocket treatment using scaler and Er:YAG laser. The 157th Japanese Society of Conservative Dentistry 2022.11.10
- 9. Yamaguchi Y, Saitou A, Horie M, Aoki A, Patrick M, Kai K. Role of hepatocyte growth factor in epithelial-mesenchymal interactions of in vitro human periodontitis model. The 95th Annual Meeting of the Japanese Biochemical Society 2022.11.09 Nagoya

- 10. Aoki A. Saving teeth at age of 80- Controlling and preventing periodontitis and caries. 29th Annual festa of teeth and gingival health of citizen 2022.11.05 Tokyo
- 11. Oka A, Nakata N, Kuroda S, Aoki A, Kasugai S, Marukawa E. Effect of VEGF signaling inhibition on collagen degradation in peri-implantitis-associated fibroblasts. 52nd Annual meeting of Japanese society of oral implantology 2022.09.23 Nagoya
- 12. Shimohira T, Ohsugi Y, Shiba T, Komatsu K, Lin P, Liu A, Toyoshima K, Katagiri S, Aoki A. Application of near-infrared photo therapy on medicine-related osteonecrosis of the jaw in model mice. The 64th annual meeting of Japanese association for oral biology 2022.09.17
- 13. Aoki A. Effect of various lasers and current clinical application. 278th FD workshop in graduate school of Meikai University 2022.09.15 Sakado
- 14. Maekawa S. Step to Giant Leap! One Step for Studying Abroad -. 2022.09.12 Online
- 15. Matsuda S, Sugaya T, Kato S, Nemoto E, Takeuchi Y, Daichi Kita D, Numabe Y, Nishida T, Ogata Y, Shin K, Nagano T, Morozumi T, Komatsu Y, Dewake N, Kamiya Y,Kitamura M, Taguchi Y, Takashiba S, Yumoto H, Yamashita A, Yoshinaga Y, Yoshimura, A, Kawaguchi H. Identification of new periodontal examination to evaluate the association between periodontitis and systemic diseases -multi centered clinical study-. 2022.09.02 Sendai
- 16. Wang J, M o rita K, Hatasa M, Niimi H, I wata T. The establishment of matrix-assisted differentiation into neural crest cells from human induced pluripotent stem cells. 2022.09.02 Sendai
- 17. Takahiko Shiba. Optimal treatment for peri-implantitis based on the latest literatures and bacterial analyses. 2022.08.28
- 18. Aoki A. Application of Er:YAG laser in Minimally invasive flapless periodontal pocket surgery. The 20th memorial meeting of the Japan Association for Oral dental L and lights 2022.07.10 Fukuoka
- 19. Liu A, Hayashi M, Tsuchiya Y, Iwata T, Nakashima T. Spatio-temporal analysis of the pathogenesis of periodontitis via novel mouse periodontitis model. The 7th Annual Meeting of Japanese Society for Osteoimmunology 2022.06.30 Okinawa, Japan
- 20. Takeuchi Y, Takamatsu H, Ito A, Kiuchi Y, Hamada Y, Naito R, Ishihara K, Hosokawa M, Izumi Y, Aoki A, Iwata T. The ability of trypsin-like enzyme activity test for the assessment of periodontopathic bacterial level and clinical periodontal condition. 2022.06.16
- 21. Aoki A. Past, present, and future of Er:YAG laser in periodontal treatment. Reiwa 4th meeting of Japanese society of Nippon dental universityy 2022.06.04 Online
- 22. Ohsugi Y, Hatsa M, Katagiri S, Hirota T, Shimohira T, Shiba T, Komatsu K, Tsuchiya Y, Fukuba S, Maekawa S, Niimi H, Iwata T, Aoki A. Effect of diode laser irradiation on inhibition of periodontitis in ligature-induced periodontitis model in mice. The 65th Spring Meeting of Japanese Society of Periodontology 2022.06.03 Tokyo
- 23. Aoki A. Application of Er:YAG laser in periodontal therapy. 2022.01.20 virtual

[Awards & Honors]

1. Best Presentation Award of The 87th Annual Meeting of the Stomatological Society of Japan (Liu A), 2022.12

Inorganic Biomaterials

Professor Masakazu Kawashita Associate Prof. Taishi Yokoi Assistant Prof. Masaya Shimabukuro

(1) Outline

In this department, we are conducting research on biomaterials (especially ceramic biomaterials) that contribute to the treatment of cancer and bone diseases. Specifically, various material synthesis methods such as the sol-gel method are used to synthesize cancer therapeutic materials (particularly fine particles) and bone filling materials, and evaluate their chemical, physical, and biological properties. By doing so, we aim to obtain knowledge that will lead to clinical application.

(2) Research

1. Development of Biomaterials for Intra-arterial Treatment of Cancer

Radioactive microspheres 20-30 $\mu\,$ m in diameter are useful for the radiotherapy of cancers, especially for tumors located deep inside the body. Also, ferromagnetic microspheres 20-30 $\mu\,$ m in diameter are useful as thermoseeds for inducing hyperthermia in deep-seated cancers under alternating magnetic field. In this department, we try to develop novel biomaterials for minimally invasive treatment of cancer by using various synthetic techniques.

2. Development of Bioactive Materials for Bone Repair

It has been found from 1970 that some ceramics can bond to living bone without fibrous tissues. They are called "bioactive" ceramics and clinically used as improtant bone substitutes. however, in a clinical field, novel bioactive materials showing excellent bone-bonding ability are required. In this laboratory, we try to develop novel bioactive materials by using various synthetic techniques.

3. Study on Osteoconductive Mechanism of Hydroxyapatite

Hydroxyapatite (HAp) is widely used as an artificial bone or a coating material for metallic biomaterials because it bonds to living bone (shows osteoconductivity). However, the details of the expression mechanism of its osteoconductivity have not been clarified yet. In this department, we are focusing on the initial adsorption of serum proteins such as albumin, fibronectin (Fn) and laminin (Ln) on HAp and hypothesize that some serum protein which specifically adsorbs on HAp causes the osteoconductivity of HAp.

4. Study on Organically Modified Octacalcium Phosphates

Octacalcium phosphate (OCP) is a precursor phase of hydroxyapatite (HAp) in bones and teeth, and has a high affinity for the hard tissues. OCP has been studied as bioabsorbable artificial bones. OCP has a layered structure, and various organic molecules can be incorporated into the OCP interlayers. We develop functional bone-repairing materials and ceramic materials that achieve both diagnosis and therapy utilizing the unique property of OCP.

(3) Lectures & Courses

Students aim to be able to comprehensively and comprehensively understand the structure, physical properties, chemical properties, reactions with biomolecules and cells, etc. of ceramic biomaterials. Their final goal is to

learn cutting-edge science and technology related to ceramic biomaterials and to acquire the ability to propose and design ceramic biomaterials that are useful for medical treatment.

(4) **Publications**

- 1. T. Yokoi, M. Watanabe, T. Goto, S. Meng, T. Sekino, M. Shimabukuro, M. Kawashita. Synthesis of octacalcium phosphate containing glutarate ions with a high incorporation fraction Materials. 2022.12; 16(1); 64
- Yokoi T, Watanabe M, Goto T, Meng S, Sekino T, Shimabukuro M, Kawashita M. Synthesis of Octacalcium Phosphate Containing Glutarate Ions with a High Incorporation Fraction. Materials (Basel, Switzerland). 2022.12; 16(1);
- M. Hashimoto, S. Takahashi, K. Kawahara, D. Yokoe, T. Kato, T. Ogawa, M. Kawashita, H. Kanetaka. Effect of citric acid content on magnetic property of magnetite particles for detecting virus Journal of the Ceramic Society of Japan. 2022.11; 130(11); 882-888
- 4. Tan Janice Lay Tin, Shimabukuro Masaya, Kishida Ryo, Ishikawa Kunio. Fabrication and histological evaluation of ant-nest type porous carbonate apatite artificial bone using polyurethane foam as a porogen Journal of Biomedical Materials Research Part B: Applied Biomaterials . 2022.10;
- 5. Sikun Meng, Taishi Yokoi, Jingyang Kang, Yukihiko Tamura, Masakazu Kawashita, Eriko Marukawa, Shohei Kasugai, Shinji Kuroda, Hidemi Nakata. Modification of hydroxyapatite by doping lithium through acid-base reaction Journal of the Ceramic Society of Japan. 2022.09; 130(9); 802-806
- 6. Sikun Meng, Taishi Yokoi, Jingyang Kang, Yukihiko Tamura, Masakazu Kawashita, Eriko Marukawa, Shohei Kasugai, Shinji Kuroda, Hidemi Nakata. Modification of hydroxyapatite by doping lithium through acid-base reaction Journal of the Ceramic Society of Japan. 2022.09; 130; 802-808
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[Books etc]

1. Masaya Shimabukuro. Innovative Bioceramics in Translational Medicine I. 2022.01

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[Conference Activities & Talks]

- 1. Masaya Shimabukuro, Koichiro Hayashi, Taishi Yokoi, Masakazu Kawashita, Kunio Ishikawa. Surface Functionalization of Honeycomb Scaffolds Consisting of Carbonate Apatite for Bone Regeneration and Infection Prevention. Visual-JW 2022 & DEJI2MA-2 2022.10.25
- 2. T. Yokoi, T. Goto, T. Sekino, M. Kawashita. Effects of incorporation of dicarboxylate ions into octacalcium phosphate on a topotactic transformation into hydroxyapatite: Reactivity and morphology. The 32nd Symposium & Annual Meeting of the International Society for Ceramics in Medicine (Bioceramics 32) 2022.09.21

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- 5. M. Shimabukuro, T. Hanawa, M. Kawashita. Antibacterial and pro-osteogenic porous titanium dioxide layer formed by micro-arc oxidation in the electrolyte with silver ion. The 17th International Workshop on Biomaterials in Interface Science 2022.08.24
- 6. L. Chang, H. Kanetaka, T. Mokudai, M. Kawashita, I. Mizoguchi. Evaluation of biocompatible and antibacterial properties of visible-light-responsive TiO2-xNx photocatalyst prepared by chemical treatment and elevated temperatures. The 17th International Workshop on Biomaterials in Interface Science 2022.08.24
- 7. S. Meng, H. Nakata, S. Kuroda, Y. Tamura, T. Yokoi, M. Kawashita, J. Kang, E. Marukawa and S. Kasugai. Preparation and characterization of a lithium-doped hydroxyapatite/chitosan composite scaffold. Academy of Osseointegration 2022 Annual Meeting 2022.02
- 8. Taishi Yokoi. Development of octacalcium phosphate-based functional biomaterial. The 25th SANKEN International Symposium 2022.01.06 Online

Global Health Promotion

Professor: Takeo Fujiwara, MD, MPH, PhD Associate Professor: Nobutoshi Nawa, MD, MPH, PhD Associate Professor: Ayako Morita, PhD Junior Associate Professor: Yukako Tani, PhD Assistant Professor: Yusuke Matsuyama, PhD Research Fellow of Japan Society for the Promotion of Science: Aya Isumi, PhD Research Fellow of Japan Society for the Promotion of Science: Satomi Doi, PhD Project Assistant Professor: Yui Yamaoka, PhD Specially Appointed: Tomoki Kawahara, MD

(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 indiviual factors (e.g., genetic factor) and environmental factors, especially social detreminants, their inter actions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statics; acquire attitudes toward social contribution through writeing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or preogran to prevent diseases in a real life setting.

(2) Research

The main focus of the department is as follows:

Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
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)
- 8. Infectious Disease Epidemiology (descriptive epidemiology about COVID-19, research on behavioral change)

(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 detreminants, their inter actions; make causal inference applying a life-course perspective on diseease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writeing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or preogram 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 adnvaced 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**

- 1. Marie Kobayashi, Yusuke Matsuyama, Nobutoshi Nawa, Aya Isumi, Satomi Doi, Takeo Fujiwara. Association between Community Social Capital and Access to Dental Check-Ups among Elementary School Children in Japan. Int J Environ Res Public Health. 2022.12; 20(1);
- 2. Hirama C, Zeng Z, Nawa N, Fujiwara T^{*}. Association between Cooperative Attitude and High-Risk Behaviors on the Spread of COVID-19 Infection among Medical Students in Japan. Int J Environ Res Public Health. 2022.12; 19(24);
- 3. Yamaoka Y, Doi S, Isumi A, Fujiwara T^{*}. Health and social relationships of mothers of children in special education schools. Res Dev Disabil. 2022.12; 131; 104374
- 4. Yu Par Khin, Yusuke Matsuyama, Takeo Fujiwara. Association between social capital and COVID-19 preventive behaviors: Country-level ecological study. Int J Disaster Risk Reduct. 2022.11; 82; 103335
- 5. Yusuke Matsuyama, Takahiro Tabuchi. Stepwise tobacco price increase and smoking behavioral changes in Japan: the JASTIS 2017-2021 longitudinal study. Nicotine Tob Res. 2022.11;
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- 11. Yuko Segawa, Tetsuya Jinno, Masaaki Matsubara, Yusuke Matsuyama, Takeo Fujiwara, Atsushi Okawa. A cross-sectional study evaluating patients' preferences for Salter innominate osteotomy. J Orthop Sci. 2022.10;
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- 15. Saimon Y, Doi S, Fujiwara T^{*}. No moderating effect of coping skills on the association between bullying experience and self-esteem: Results from K-CHILD study. Front Psychol. 2022.10; 13; 1004482
- 16. Keitaro Miyamura, Nobutoshi Nawa, Hisaaki Nishimura, Kiyohide Fushimi, Takeo Fujiwara. Association between heat exposure and hospitalization for diabetic ketoacidosis, hyperosmolar hyperglycemic state, and hypoglycemia in Japan. Environ Int. 2022.09; 167; 107410
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- 73. Mishima Y, Nawa N, Asada M, Nagashima M, Aiso Y, Nukui Y, Fujiwara T, Shigemitsu H. The Impact of Antibiotic Time Outs in Multidisciplinary ICU Rounds for Antimicrobial Stewardship Program on Patient Survival: A Controlled Before-and-After Study. Critical Care Explorations. 2022; (in press);
- 74. Hirama C, Zeng Z, Nawa N, Fujiwara T. Association between cooperative attitude and high-risk behaviors on spread of COVID-19 infection among medical students in Japan. International Journal of Environmental Research and Public Health. 2022; (in press);
- 75. Kobayashi M, Matsuyama Y, Nawa N, Isumi A, Doi S, Fujiwara T. Association between community social capital and access to preventive dental care among elementary school children in Japan. International Journal of Environmental Research and Public Health. 2022; (in press);
- 76. Hanafusa M, Ito Y, Ishibashi H, Nakaya T, Nawa N, Sobue T, Okubo K, Fujiwara T. Association between Socioeconomic Status and Net Survival after Primary Lung Cancer Surgery: A Tertiary University Hospital Retrospective Observational Study in Japan. Japanese Journal of Clinical Oncology. 2022; (in press);
- 77. Yusuke Matsuyama, Aya Isumi, Satomi Doi, Takeo Fujiwara. Impacts of the COVID-19 Pandemic Exposure on Child Dental Caries: Difference-in-Differences Analysis. Caries Res. 2022; 56(5-6); 546-554
- 78. Shuji Hibiya, Kazuo Ohtsuka, Kento Takenaka, Ami Kawamoto, Yusuke Matsuyama, Yumi Udagawa, Maiko Motobayashi, Hiromichi Shimizu, Toshimitsu Fujii, Eiko Saito, Masakazu Nagahori, Ryuichi Okamoto, Mamoru Watanabe. Mucosal healing of small intestinal stricture is associated with improved prognosis post-dilation in Crohn's disease. BMC Gastroenterol. 2022.05; 22(1); 218

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- 1. Hirota T*, McElory E, Fujiwara T, Boden JM. Editorial: Longitudinal data analysis in child and adolescent mental health. Front Psychiatry. 2022.10; 13; 1038190
- 2. Fujiwara T. Impact of adverse childhood experience on physical and mental health: A life-course epidemiology perspective. Psychiatry Clin Neurosci. 2022.08;

[Conference Activities & Talks]

- 1. Mitsuyuki Numasawa, Nobutoshi Nawa, Kumiko Yamaguchi, Kanako Noritake, Jun Tsuruta, Mina Nakagawa. Comparison of readiness for interprofessional learning among medical, dental, and nursing students before the start of clinical practice. AMEE 2022 2022.08.29 The Virtual Conference
- 1. The importance of formative assessment in a human anatomy course summative assessment. 2022.08.06
- 2. Remote interprofessional learning for younger undergraduate students' early exposure. 2022.08.05
- 3. Results of a survey to develop a data analysis system to support institutional research. The 54th Annual Meeting of the Japan Society for Medical Education 2022.08.05 Gunma
- 1. Sagawa Y, Ogawa T, Matsuyama Y, Nakagawa KJ, Araki YM, Yasuda UY, Tumurkhuu T, Ganburged G, Bazar A, Tanaka T, Fujiwara T, Moriyama K. Association between maternal smoking during pregnancy and short root anomaly in offspring. Annual Congress of the KAO and the 13th Asian Pacific Orthodontic Conference 2022.10.01

[Awards & Honors]

- 1. 2021 Highest Altmetric Scores Award, American Geriatrics Society, 2022.05
- 2. Best Presentation Award at the 81st Annual Meeting of the Japanese Society of Public Health, 日本公衆 衛生学会, 2022.10

Department of Parasitology & Tropical Medicine

Professor ISHINO Tomoko Assistant Professor KUMAGAI Takashi Lecturer SHINZAWA Naoaki Project Lecturer NAGAOKA Hikaru Visiting Lecturer KOBAYASHI Daisuke Visiting Lecturer Suganuma Masumi Graduate Student ARIMOTO Shou Graduate Student ADDO Gyan Daniel Kweku Graduate Student KUBOTA Rie Graduate Student AZERIGYIK Faustus Akankperiwen Graduate Student LADZEKPO Danielle Graduate Student MAHAZU Samiratu Graduate Student OWUSU Kofi Baffour-awuah Graduate Student Oundavong Sunti Graduate Student Mark Tetteh-Tsifoanya Graduate Student Quratul-ain Issahaque Graduate Student Peter Bolah Graduate Student Frederick Ofosu Appiah Graduate Student SHINOZAKI Momoka Graduate Student OKADA Rena Technical Assistant MURAYAMA Hisako Technical Assistant SEKINE Takashi

(1) **Outline**

Parasitic diseases continue to have a significant impact on people's lives in many countries of the world, and their control is an important public health challenge. Malaria, one of the world's major infectious diseases, is a parasitic disease that infects more than 200 million people worldwide and kills 600,000 people annually, mainly in Africa. The mortality rate is particularly high among infants under the age of five, with one child dying every two minutes. Although more than 200 million people are infected with schistosomiasis worldwide, the disease is regarded as a "neglected tropical disease" for which no effective countermeasures have been taken. We will continue our research on these parasitic diseases with the goal of elucidating the mechanisms of infection and their interactions with the host. These basic research will also lead to the development of vaccines and drugs in collaboration with researchers around the world, including those in endemic areas.

This department was established primarily to conduct research in the field of zoology, and has a long history of active research on helminths, among other parasitic diseases. In 2021, Dr. Ishino joined this department as a professor and focus on malaria research, together with other important parasitic diseases, such as schistosomiasis. Our aim of malaria research is the elucidation of the molecular mechanisms of parasite infection via specific interaction between parasite and host molecules. To achieve this, research will be conducted on Plasmodium berghei, a rodent malaria parasite, and Plasmodium falciparum, which cause lethal symptoms in humans, by reverse genetics, live imaging techniques, and transcriptome analyses. In addition, the mechanisms of drug resistance acquisition and the development of new vaccines will also be conducted. In the case of schistosomiasis, we are studying the mechanism of small RNAs transfer between parasites by extracellular vesicles. In addition, field studies are being conducted in endemic areas such as Ghana and Laos, with the aim of developing new diagnostic tools and vaccines for parasitic diseases.

(2) Research

(1) Elucidation of the host cell infection mechanism of Plasmodium:

Plasmodium efficiently invades and infects variously different cells in its life cycle. In particular, we will focus on elucidating the mechanism of sporozoites, which are responsible for malaria transmission from mosquitoes to humans, reach and infect hepatocytes. We have previously identified several secreted proteins involved in sporozoite infection of the liver by reverse-genetic technology of Plasmodium berghei, and have elucidated part of the mechanisms how sporozoites reach the hepatocytes. In the future, we aim to comprehensively understand the infection mechanism from the viewpoint of host-parasite interaction. The same approach will lead to the elucidation of the mechanisms of infection of erythrocytes and sexual reproduction in the mosquito body. Based on the knowledge obtained from research, we aim to develop methods to prevent infection/transmission in collaboration with researchers in endemic areas.

(2) Research on drug resistance mechanisms of Plasmodium falciparum:

Artemisinin combination therapy, which combines artemisinin as the main drug and a partner drug with a different mechanism of action and half-life, is the first choice for malaria drug therapy. However, parasite resistant to artemisinin and/or partner drugs is widespread in endemic areas, and is a major obstacle to malaria eradication. We have been searching for drug-resistant genes by whole genome sequencing of clinical isolates from endemic areas. Furthermore, we are utilizing genome editing technology to analyze the function of these drug resistance genes in order to elucidate the mechanism of drug resistance acquisition. The findings obtained are expected to be useful for the development of drug treatment strategies in malaria-endemic areas.

(3) Elucidation of the egg-laying induction mechanism through extracellular vesicles of the schistosome:

Schistosoma japonicum is a vasoactive species that lays eggs through the conjugation of males and females within the blood vessels. We are studying extracellular vesicles as a ways of communication for reproduction between males and females. Parasites treated with calpeptin, an inhibitor of extracellular vesicle secretion, showed a decrease in the number of egg laying as well as extracellular vesicle secretion. Based on this finding, we are currently analyzing the function of calpeptin in the secretion of extracellular vesicles and induction of egg laying by RNAi knockdown of the calpain gene family.

(4) Research Support for the Noguchi Memorial Institute for Medical Research in Ghana:

We will conduct parasite research focusing on malaria as a member of collaboration teams between TMDU and NMIMR. In Ghana, about 5 million people, corresponding to 1/6 of the total population, are infected with malaria annually. In order to tackle problems that have large social impacts, we will focus particularly on the transmission stage via mosquitoes, and aim to develop novel vaccines based on the basic research. In addition, the knowledge, experience and resources from endemic areas will be returned to basic research and to the education of medical students. We also accept young researchers from the NMIMR as PhD students and conducting research with them for the continuous future collaboration.

(3) Education

The number of cases of parasite infection in Japan has decreased significantly since the end of World War II due to various efforts, including the implementation of testing and drug administration by local communities, schools, and workplaces. On the other hand, recent dramatic changes in the social environment, changing dietary habits, and advances in refrigeration technology have led to major changes in the types of parasitic diseases detected in Japan. In addition, with the increase in logistics and human immigration and travel, the increase in imported cases from endemic regions of parasitic diseases has had a significant impact on the safety and security of our country. It is critical to keep our knowledge and clinical treatments up-to-date to prepare for emerging and re-emerging infectious diseases. Furthermore, the fact that the majority of neglected tropical diseases are parasitic diseases clearly indicates that parasitic diseases are an issue that needs to be addressed internationally.

In order to promote the students' ability to understand, think and discuss health and welfare in the world, this department gives lectures on Parasitology, Medical Zoology, and Tropical Medicine. In addition, during the project semester at the School of Medicine, we teach the "basis" of basic research on malaria topics. Through these educational efforts, we aim to develop future clinicians and researchers who can take leadership positions internationally in the field of health and medical care.

- 1. The actual situation of parasitic diseases in Japan and their diagnosis, treatment, etc.
- 2. The situation of parasitic diseases in the world and preventive tools
- 3. Biological understanding of the mechanism of parasite infection, together with its life cycle
- 4. Basic knowledge of tropical diseases and international health initiatives
- 5. Neglected tropical diseases and strategies taken by the international community

(4) Lectures & Courses

Lectures on parasitology and medical zoology will be given in a systematic manner. The history of the discovery and conquest of each parasitic disease will be introduced in order to foster the ability to deal with emerging and reemerging infectious diseases in the future. By observing actual parasite specimens on their own, students will spontaneously promote understanding of parasites from a biological perspective.

Through practical training, the course aims to cultivate the ability to find questions and solve them on one's own. Students are encouraged to participate in practical training and field research to cultivate the ability to find real problems and solve them.

(5) Clinical Services & Other Works

We provide advice on the diagnosis of parasitic diseases in collaboration with medical institutions both on and off campus.

Research aimed at developing diagnostic methods, therapeutics and vaccines for parasitic infections is being conducted. In addition, as part of international collaboration research, we conduct surveys as well as basic research in endemic areas to contribute to disease control, development of new vaccines, and elucidation of the mechanisms to acquire the resistance against drugs.

(6) **Publications**

- 1. Sex-inducing effects toward planarians widely present among parasitic flatworms 2022.12; 26(1); 105776
- Mahazu S, Prah I, Ota Y, Hayashi T, Nukui Y, Suzuki M, Hoshino Y, Akeda Y, Suzuki T, Ishino T, Ablordey A, Saito R. Klebsiella Species and Enterobacter cloacae Isolates Harboring bla(OXA-181) and bla(OXA-48): Resistome, Fitness Cost, and Plasmid Stability. Microbiology spectrum. 2022.12; 10(6); e0332022
- 3. Huang Wei-Chiao, Mabrouk Moustafa T., Zhou Luwen, Baba Minami, Tachibana Mayumi, Torii Motomi, Takashima Eizo, Locke Emily, Plieskatt Jordan, King C. Richter, Coelho Camila H., Duffy Patrick E., Long Carole, Tsuboi Takafumi, Miura Kazutoyo, Wu Yimin, Ishino Tomoko, Lovell Jonathan F.. Vaccine co-display of CSP and Pfs230 on liposomes targeting two Plasmodium falciparum differentiation stages COMMUNICATIONS BIOLOGY. 2022.08; 5(1); 773
- 4. Naoaki Shinzawa, Chisako Kashima, Hiroka Aonuma, Kei Takahashi, Masayuki Shimojima, Shinya Fukumoto, Erisha Saiki, Daisuke S. Yamamoto, Shigeto Yoshida, Hiroyiki Matsuoka, Yoshihiro Kawaoka, Hirotaka Kanuka. Generation of Transgenic Mosquitoes Harboring a Replication-Restricted Virus Frontiers in Tropical Diseases. 2022.05; 3; 850111
- Kumagai T, Shimogawara R, Ichimura K, Iwanaga S. Calpain inhibitor suppresses both extracellular vesicle-mediated secretion of miRNAs and egg production from paired adults of Schistosoma japonicum. Parasitology international. 2022.04; 87; 102540
- 6. Miura K, Takashima E, Pham TP, Deng B, Zhou L, Huang WC, Diouf A, Gebremicale YT, Tachibana M, Ishino T, Richter King C, Lovell JF, Long CA, Tsuboi T. Elucidating functional epitopes within the N-terminal region of malaria transmission blocking vaccine antigen Pfs230. NPJ vaccines. 2022.01; 7(1); 4

- 7. Cha SJ, Yu X, Gregory BD, Lee YS, Ishino T, Opoka RO, John CC, Jacobs-Lorena M. Identification of Key Determinants of Cerebral Malaria Development and Inhibition Pathways. mBio. 2022.01; 13(1); e0370821
- Daniel Addo-Gyan, Haruka Matsushita, Enya Sora, Tsubasa Nishi, Masao Yuda, Naoaki Shinzawa, Shiroh Iwanaga. Chromosome splitting of Plasmodium berghei using the CRISPR/Cas9 system. PLoS One. 2022; 17(2); e0260176
- 9. Kubota R, Ishino T, Iwanaga S, Shinzawa N. Evaluation of the Effect of Gene Duplication by Genome Editing on Drug Resistance in Plasmodium falciparum. Frontiers in cellular and infection microbiology. 2022; 12; 915656
- 10. Eriko Hamasaki, Natsuki Wakita, Hiroki Yasuoka, Hikaru Nagaoka, Masayuki Morita, Eizo Takashima, Takayuki Uchihashi, Tetsuya Takeda, Tadashi Abe, Ji-Won Lee, Tadahiro Iimura, Moin A Saleem, Naohisa Ogo, Akira Asai, Akihiro Narita, Kohji Takei, Hiroshi Yamada. The Lipid-Binding Defective Dynamin 2 Mutant in Charcot-Marie-Tooth Disease Impairs Proper Actin Bundling and Actin Organization in Glomerular Podocytes. Front Cell Dev Biol. 2022; 10; 884509
- 11. Eizo Takashima, Bernard N Kanoi, Hikaru Nagaoka, Masayuki Morita, Ifra Hassan, Nirianne M Q Palacpac, Thomas G Egwang, Toshihiro Horii, Jesse Gitaka, Takafumi Tsuboi. Meta-Analysis of Human Antibodies Against Plasmodium falciparum Variable Surface and Merozoite Stage Antigens. Front Immunol. 2022; 13; 887219
- Ricardo Correia, Bárbara Fernandes, Rute Castro, Hikaru Nagaoka, Eizo Takashima, Takafumi Tsuboi, Akihisa Fukushima, Nicola K Viebig, Hilde Depraetere, Paula M Alves, António Roldão. Asexual Blood-Stage Malaria Vaccine Candidate PfRipr5: Enhanced Production in Insect Cells. Front Bioeng Biotechnol. 2022; 10; 908509
- Hiroshi Yamada, Tadashi Abe, Hikaru Nagaoka, Eizo Takashima, Ryo Nitta, Masahiro Yamamoto, Kohji Takei. Recruitment of Irgb6 to the membrane is a direct trigger for membrane deformation. Front Cell Infect Microbiol. 2022; 12; 992198
- 14. Eizo Takashima, Hikaru Nagaoka, Ricardo Correia, Paula M Alves, António Roldão, Dennis Christensen, Jeffrey A Guderian, Akihisa Fukushima, Nicola K Viebig, Hilde Depraetere, Takafumi Tsuboi. A novel asexual blood-stage malaria vaccine candidate: PfRipr5 formulated with human-use adjuvants induces potent growth inhibitory antibodies. Front Immunol. 2022; 13; 1002430
- Takashi Kumagai, Emilie Louise Akiko Matsumoto-Takahashi, Hirofumi Ishikawa, Sengdeuane Keomalaphet, Phonepadith Khattignavong, Pheovaly Soundala, Bouasy Hongvanthong, Kei Oyoshi, Yoshinobu Sasaki, Yousei Mizukami, Shigeyuki Kano, Paul T. Brey, Moritoshi Iwagami. Detection of Schistosoma mekongi DNA in Human Stool and Intermediate Host Snail Neotricula aperta via Loop-Mediated Isothermal Amplification Assay in Lao PDR Pathogens. 2022.11; 11(12); 1413

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1. Tachibana Mayumi, Takashima Eizo, Morita Masayuki, Sattabongkot Jetsumon, Ishino Tomoko, Culleton Richard, Torii Motomi, Tsuboi Takafumi. Plasmodium vivax transmission-blocking vaccines: Progress, challenges and innovation(和訳中) Parasitology International. 2022.04; 87; 1-9

[Conference Activities & Talks]

- 1. Mahazu Samiratu, Prah Isaac, Ota Yusuke, Hayashi Takaya, Nukui Yoko, Suzuki Masato, Hoshino Yoshihiko, Akeda Yukihiro, Suzuki Toshihiko, Ishino Tomoko, Ablordey Anthony, Saito Ryoichi. Genetic analysis of carbapenemase-producing Enterobacter cloacae and Klebsiella species(タイトル和訳中). 日本 臨床微生物学会雑誌 2022.12.01
- 2. Tomoko Ishino. Molecular mechanisms of malaria transmission to mammals via mosquito vectors. 第 20 回あわじ感染と免疫国際フォーラム 2022.09.08 大阪
- 3. Kumagai T. Calpain inhibitor suppresses both extracellular vesicle-mediated secretion of miRNAs and egg production from paired adults of Schistosoma japonicum. 15th International Congress of Parasitology 2022.08.22 Copenhagen

 Tomoko Ishino. Molecular mechanisms of malaria parasite transmission from mosquitoes to mammals.. 第 91 回日本寄生虫学会 2022.05.29 帯広、北海道

Forensic Medicine

Professor Koichi UEMURA

Associate Professor Toshihiko AKI Kana UNUMA

Assistant Professor Takeshi FUNAKOSHI

Specially Appointed Assistant Professor Ryo WATANABE

Graduate Student Tomomi SANO Shuheng WEN Sho AOKI Moeka NOMURA Miyu KOMATSU Shotaro NAGANO Hikari TACHIBANA Kurumi MATSUMOTO

Research Student Masatoshi KIMURA

(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**

- Toya M, Minegishi S, Utsuno H, Ohta J, Namiki S, Unuma K, Uemura K, Sakurada K. Forensic Characteristics of Physical Elder Abuse and Current Status and Issues of Collaboration between Forensic Medicine Departments and Related Institutions in Japan. International journal of environmental research and public health. 2022.11; 19(22);
- Shuheng Wen, Kana Unuma, Takeshi Funakoshi, Toshihiko Aki, Koichi Uemura. Contraction Band Necrosis with Dephosphorylated Connexin 43 in Rat Myocardium after Daily Cocaine Administration. Int J Mol Sci. 2022.10; 23(19);
- 3. Makino Yohsuke, Unuma Kana, Nolte Kurt B., Adolphi Natalie L.. Accuracy of forensic pathologists in incorporating post-mortem CT (PMCT) in forensic death investigation JOURNAL OF FORENSIC SCIENCES. 2022.09; 67(6); 2351-2359
- 4. Wen Shuheng, Unuma Kana, Makino Yohsuke, Mori Hiroki, Uemura Koichi. Fatal consequence after MiraDry treatment: Necrotizing fasciitis complicated with streptococcal toxic shock syndrome(和訳中) Legal Medicine. 2022.09; 58; 1-4
- 5. Wen Shuheng, Unuma Kana, Uemura Koichi. Two fatal cases due to inadvertent discharge of carbon dioxide fire suppressant: Intoxication or asphyxiation? JOURNAL OF FORENSIC AND LEGAL MEDICINE. 2022.08; 90; 102390
- 6. Shuheng Wen, Kana Unuma, Yohsuke Makino, Hiroki Mori, Koichi Uemura. Fatal consequence after MiraDry® treatment: Necrotizing fasciitis complicated with streptococcal toxic shock syndrome. Leg Med (Tokyo). 2022.05; 58; 102095
- Saki Minegishi, Hajime Utsuno, Jun Ohta, Shuuji Namiki, Maiko Toya, Nozomi Sumi, Kana Unuma, Hisako Saitoh, Hirotaro Iwase, Koichi Uemura, Koichi Sakurada. Sixty-eight cases of postmortem pink teeth observed in dental autopsies of unidentified cadavers Journal of Forensic Sciences. 2022.02;
- 8. Toshihiko Aki, Takeshi Funakoshi, Kana Unuma, Koichi Uemura. Inverse regulation of GSDMD and GSDME gene expression during LPS-induced pyroptosis in RAW264.7 macrophage cells. Apoptosis. 2022.01;
- Unuma K, Kaga H, Funakoshi T, Nomura M, Aki T, Uemura K. Thymic involution caused by repeated cocaine administration includes apoptotic cell loss followed by ectopic adipogenesis. PloS one. 2022; 17(11); e0277032
- 10. Sho Aoki, Takeshi Funakoshi, Toshihiko Aki, Koichi Uemura. Aggregation-prone A53T mutant of α -synuclein exaggerates methamphetamine neurotoxicity in SH-SY5Y cells: Protective role of cellular cholesterol. Toxicol Rep. 2022; 9; 2020-2029

[Misc]

- 1. Shuheng Wen, Toshihiko Aki, Takeshi Funakoshi, Kana Unuma, Koichi Uemura. Role of Mitochondrial Dynamics in Cocaine's Neurotoxicity. Int J Mol Sci. 2022.05; 23(10);
- 2. Toshihiko Aki, Kana Unuma, Koichi Uemura. The Role of Peroxiredoxins in the Regulation of Sepsis. Antioxidants (Basel). 2022.01; 11(1);

Health Policy and Informatics

Professor:Kiyohide FUSHIMI Associate Professor:Daisuke SHINJO Graduate Student : Akira HOMMA, Kyoko HIRANO, Mihoko OTA, Takuaki TANI, Shoko YOSHIDA, Keisuke KONDO, Kimie MORI, Toshiaki SHIBATA, Masato KOIZUMI, Yukiko TSUKAO, Hiromichi Otaka, Ai Shinjo, Tomonori TAKEUCHI, Kenichi MIYAMOTO, Kei YAMAMOTO, Yasuyuki FUSEDA Graduate Research Student:Asako TSUKAZAKI

(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

- 1. Yasuhiro Inooka, Hayato Yamana, Yusuke Shinoda, Haruhi Inokuchi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Nobuhiko Haga. Predictive Factors for Oral Intake Recovery After Acute Stroke: Analysis of a Japanese Nationwide Inpatient Database. Dysphagia. 2022.12; 37(6); 1623-1632
- Yuki Hirano, Hidehiro Kaneko, Takaaki Konishi, Hidetaka Itoh, Satoru Matsuda, Hirofumi Kawakubo, Kazuaki Uda, Hiroki Matsui, Kiyohide Fushimi, Hiroyuki Daiko, Osamu Itano, Hideo Yasunaga, Yuko Kitagawa. ASO Visual Abstract: Short-Term Outcomes of Epidural Analgesia in Minimally Invasive Esophagectomy for Esophageal Cancer: Nationwide Inpatient Data Study in Japan. Ann Surg Oncol. 2022.12; 29(13); 8237-8238
- 3. Yuki Hirano, Hidehiro Kaneko, Takaaki Konishi, Hidetaka Itoh, Satoru Matsuda, Hirofumi Kawakubo, Kazuaki Uda, Hiroki Matsui, Kiyohide Fushimi, Hiroyuki Daiko, Osamu Itano, Hideo Yasunaga, Yuko Kitagawa. Short-Term Outcomes of Epidural Analgesia in Minimally Invasive Esophagectomy for Esophageal Cancer: Nationwide Inpatient Data Study in Japan. Ann Surg Oncol. 2022.12; 29(13); 8225-8234

- 4. Takaki Hirano, Mikio Nakajima, Hiroyuki Ohbe, Richard H Kaszynski, Yudai Iwasaki, Yuki Arakawa, Yusuke Sasabuchi, Kiyohide Fushimi, Hiroki Matsui, Hideo Yasunaga. Corticosteroid use with extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: A nationwide observational study. Resusc Plus. 2022.12; 12; 100308
- 5. Takaaki Konishi, Michimasa Fujiogi, Daisuke Shigemi, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Risk Factors for Postoperative Bleeding Following Breast Cancer Surgery: A Nationwide Database Study of 477,108 Cases in Japan. World J Surg. 2022.12; 46(12); 3062-3071
- 6. Tetsuya Ishimaru, Michimasa Fujiogi, Nobuaki Michihata, Takaaki Konishi, Kaori Morita, Hiroki Matsui, Kazuaki Uda, Kiyohide Fushimi, Hiroshi Kawashima, Jun Fujishiro, Hideo Yasunaga. Perioperative outcomes of laparoscopically assisted anorectoplasty versus conventional procedures for anorectal malformation: a retrospective nationwide database study. Pediatr Surg Int. 2022.12; 38(12); 1785-1791
- 7. Hiraku Kumamaru, Yoshihiro Kakeji, Kiyohide Fushimi, Koichi Benjamin Ishikawa, Hiroyuki Yamamoto, Hideki Hashimoto, Minoru Ono, Tadashi Iwanaka, Shigeru Marubashi, Mitsukazu Gotoh, Yasuyuki Seto, Yuko Kitagawa, Hiroaki Miyata. Cost of postoperative complications of lower anterior resection for rectal cancer: a nationwide registry study of 15,187 patients. Surg Today. 2022.12; 52(12); 1766-1774
- 8. Miki Mizuta, Kunio Tarasawa, Kiyohide Fushimi, Kenji Fujimori. Effect of Postoperative Pain Management after Robot-Assisted Radical Prostatectomy: A Study on Reducing Hospital Length of Stay and Medical Costs Using Japanese Nationwide Database. Tohoku J Exp Med. 2022.12; 259(1); 27-35
- 9. Reiko Yamaura, Tetsuji Kaneko, Koichi Benjamin Ishikawa, Shunya Ikeda, Kiyohide Fushimi, Tsutomu Yamazaki. Factors Associated With Time to Achieve Physical Functional Recovery in Patients With Severe Stoke After Inpatient Rehabilitation: A Retrospective Nationwide Cohort Study in Japan. Arch Rehabil Res Clin Transl. 2022.12; 4(4); 100229
- 10. Takuaki Tani, Shinobu Imai, Kiyohide Fushimi. Rehabilitation of Patients With Acute Ischemic Stroke Who Required Assistance Before Hospitalization Contributes to Improvement in Activities of Daily Living: A Nationwide Database Cohort Study. Arch Rehabil Res Clin Transl. 2022.12; 4(4); 100224
- Satoshi Kuhara, Ryutaro Matsugaki, Hanaka Imamura, Hideaki Itoh, Yasushi Oginosawa, Masaru Araki, Kiyohide Fushimi, Shinya Matsuda, Satoru Saeki. A survey of the implementation rate of cardiac rehabilitation for patients with heart disease undergoing device implantation in Japan. J Arrhythm. 2022.12; 38(6); 1049-1055
- Kensuke Matsuda, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Koichi Sugimoto. Institutional factors associated with early mortality of newly diagnosed acute promyelocytic leukemia. Blood Cancer J. 2022.12; 12(12); 167
- 13. Hideaki Oyama, Rintaro Moroi, Kunio Tarasawa, Yusuke Shimoyama, Takeo Naito, Atsushi Sakuma, Hisashi Shiga, Yoichi Kakuta, Kiyohide Fushimi, Kenji Fujimori, Yoshitaka Kinouchi, Atsushi Masamune. Depression is associated with increased disease activity in patients with ulcerative colitis: A propensity score-matched analysis using a nationwide database in Japan. JGH Open. 2022.12; 6(12); 876-885
- 14. Satoshi Shoji, Shun Kohsaka, Hiraku Kumamaru, Kyohei Yamaji, Shiori Nishimura, Hideki Ishii, Tetsuya Amano, Kiyohide Fushimi, Hiroaki Miyata, Yuji Ikari. Cost reduction associated with transradial access in percutaneous coronary intervention: A report from a Japanese nationwide registry. Lancet Reg Health West Pac. 2022.11; 28; 100555
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- 97. Kota Yano, Rintaro Moroi, Hisashi Shiga, Kunio Tarasawa, Yusuke Shimoyama, Masatake Kuroha, Shin Hamada, Yoichi Kakuta, Kiyohide Fushimi, Kenji Fujimori, Yoshitaka Kinouchi, Atsushi Masamune. Analysis of the disease activity of ulcerative colitis with and without concomitant primary sclerosing cholangitis: An investigation using a nationwide database in Japan. JGH Open. 2022.01; 6(1); 50-56
- 98. Jun Suzuki, Yusuke Sasabuchi, Shuji Hatakeyama, Hiroki Matsui, Teppei Sasahara, Yuji Morisawa, Toshiyuki Yamada, Kiyohide Fushimi, Hideo Yasunaga. Additional effect of azithromycin over β -lactam alone for severe community-acquired pneumonia-associated acute respiratory distress syndrome: a retrospective cohort study. Pneumonia (Nathan). 2022.01; 14(1); 1

- 99. Takaaki Konishi, Michimasa Fujiogi, Nobuaki Michihata, Takayoshi Niwa, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Impact of body mass index on short-term outcomes after differentiated thyroid cancer surgery: a nationwide inpatient database study in Japan. Eur Thyroid J. 2022.01; 11(1); e210081
- 100. Yamada Toru, Suzuki Risa, Ichimura Naoya, Mabuchi Suguru, Nagamine Yuiko, Sassa Chihiro, Tohda Shuji. Clinical Evaluation of Reverse Transcription-Polymerase Chain Reaction and Rapid Antigen Tests of Tongue Swabs for Detecting COVID-19(和訳中) Journal of Hospital General Medicine. 2022.01; 4(1); 12-20
- 101. Nakano Y, Mandai S*, Genma T, Akagi Y, Fujiki T, Ando F, Susa K, Mori T, Iimori S, Naito S, Sohara E, Uchida S, Fushimi K, Rai T*.. Nationwide mortality associated with perioperative acute dialysis requirement in major surgeries. Int J Surg. 2022.08; 104; 106816

Life Sciences and Bioethics

Masayuki Yoshida Yusuke Ebana Hiroko Kohbata Mizuko Osaka

(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

- Niwano T, Hosoya T, Kadowaki S, Toyofuku E, Naruto T, Shimizu M, Ohnishi H, Koike R, Morio T, Imai K, Yoshida M, Yasuda S. An adult case of suspected A20 haploinsufficiency mimicking polyarteritis nodosa. Rheumatology (Oxford, England). 2022.11; 61(11); e337-e340
- 2. Kirino S, Suzuki M, Ogawa T, Takasawa K, Adachi E, Gau M, Takahashi K, Ikeno M, Yamada M, Suzuki H, Kosaki K, Moriyama K, Yoshida M, Morio T, Kashimada K. Clinical report: Chronic liver dysfunction in an individual with an AMOTL1 variant. European journal of medical genetics. 2022.11; 65(11); 104623
- Hiroko Terui-Kohbata, Noriko Tanabe, Masayuki Yoshida. Attitudes towards reproductive genetic testing for HBOC among public healthy people, cancer patient and clinical genetic professionals OSP Journal of Health Care and Medicine. 2022.09; 3(2); 1-7
- 4. Ito S, Hashimoto H, Yamakawa H, Kusumoto D, Akiba Y, Nakamura T, Momoi M, Komuro J, Katsuki T, Kimura M, Kishino Y, Kashimura S, Kunitomi A, Lachmann M, Shimojima M, Yozu G, Motoda C, Seki T, Yamamoto T, Shinya Y, Hiraide T, Kataoka M, Kawakami T, Suzuki K, Ito K, Yada H, Abe M, Osaka M, Tsuru H, Yoshida M, Sakimura K, Fukumoto Y, Yuzaki M, Fukuda K, Yuasa S. The complement C3-complement factor D-C3a receptor signalling axis regulates cardiac remodelling in right ventricular failure. Nature communications. 2022.09; 13(1); 5409
- 5. Ito S, Hashimoto H, Yamakawa H, Kusumoto D, Akiba Y, Nakamura T, Momoi M, Komuro J, Katsuki T, Kimura M, Kishino Y, Kashimura S, Kunitomi A, Lachmann M, Shimojima M, Yozu G, Motoda C, Seki T, Yamamoto T, Shinya Y, Hiraide T, Kataoka M, Kawakami T, Suzuki K, Ito K, Yada H, Abe M, Osaka

M, Tsuru H, Yoshida M, Sakimura K, Fukumoto Y, Yuzaki M, Fukuda K, Yuasa S. The complement C3-complement factor D-C3a receptor signalling axis regulates cardiac remodelling in right ventricular failure. Nature communications. 2022.09; 13(1); 5409

- Inoue R, Nishi H, Osaka M, Yoshida M, Nangaku M. Neutrophil Protein Kinase R Mediates Endothelial Adhesion and Migration by the Promotion of Neutrophil Actin Polymerization. Journal of immunology (Baltimore, Md. : 1950). 2022.05; 208(9); 2173-2183
- 7. Takashi Ikenouchi MD, Yuki Shimizu MD, Miki Amemiya MD, Tatsuaki Kamata MD, Tasuku Yamamoto MD, Takuro Nishimura MD, PhD, Yukihiro Inamura MD, PhD, Akira Sato MD, Osamu Inaba MD, PhD, Susumu Tao MD, PhD, Masateru Takigawa MD, PhD, Yusuke Ebana MD, PhD, Shinsuke Miyazaki MD, PhD, FHRS, Masahiko Goya MD, PhD, Junichi Nitta MD, PhD, Tetsuo Sasano MD, PhD, Tetsushi Furukawa MD, PhD. THE IMPACT OF DEVELOPMENTAL ORIGIN OF NON-PULMONARY VEIN TRIGGERS LOCATION ON CLINICAL AND GENETICAL FEATURES OF ATRIAL FIBRILLATION PATIENTS Heart Rhythm. 2022.05; 19(5); S357-S358
- 8. Inoue R, Nishi H, Osaka M, Yoshida M, Nangaku M. Neutrophil Protein Kinase R Mediates Endothelial Adhesion and Migration by the Promotion of Neutrophil Actin Polymerization. Journal of immunology (Baltimore, Md. : 1950). 2022.04;
- 9. Yoshida M. More Than Clean, Sustainable, and Renewable Energy Source: New Therapeutic Role for Hydrogen? JACC. Basic to translational science. 2022.02; 7(2); 162-163

[Conference Activities & Talks]

- 1. Kanae Iwata, Masayuki Yoshida. Researchers' perception of electronic informed consent under the new Ethical Guidelines for Medical. PRIM&R Annual Conference 2022.12 web
- 青山 二郎, 大坂 瑞子, 吉田 雅幸. CXCL1 による好中球の接着促進は PAD4 による細胞質シトルリン化を 介して B2 インテグリンの活性化に関与する (CXCL1-induced Neutrophil Adhesion Enhancement Involves B2 Integrin Activation via Cytosolic Citrullination by PAD4). 日本循環器学会学術集会抄録集 2022.03.01
- 3. 大坂 瑞子, 吉田 雅幸. ペマフィブラートは高脂肪食を摂取した LDL 受容体欠損 (LDLR-/-) マウスにお いてヒストン H3 のシトルリン化阻害を介して好中球接着を抑制する (Pemafibrate Attenuates High-Fat Diet-Induced Neutrophil Adhesion via Inhibition of HistoneH3 Citrullination in LDLR-/- Mice). 日本循 環器学会学術集会抄録集 2022.03.01
- 4. 江花有亮. JAXA 人を対象とする生命科学 · 医学系研究における被験者保護と研究不正の防止. 宇宙航空研 究開発機構 JAXA 2022.10.29
- 5. 江花有亮. 医療 AI 技術と被験者保護に関するレビュー. 第4回日本メディカル AI 学会学術集会 2022.06.11 仙台市

Forensic Dentistry

Professor Koichi SAKURADA Lecturer Hajime UTSUNO Assistant Professor Saki MINEGISHI Graduate Student Shuuji NAMIKI Graduate Student Maiko TOYA Graduate Student Nozomi SUMI Graduate Student Muhammad Garry Syahriza HANAFI

(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]

- Satomi Mizuno, Sachiko Ono, Yohsuke Makino, Shigeki Tsuneya, Susumu Kobayashi, Namiko Ishii, Ayaka Sakuma, Koichi Sakurada, Saki Minegishi, Hajime Utsuno, Fumiko Chiba, Rutsuko Yamaguchi, Suguru Torimitsu, Hirotaro Iwase. Validity of dental findings for identification by postmortem computed tomography. Forensic Sci Int. 2022.11; 341; 111507
- Maiko Toya, Saki Minegishi, Hajime Utsuno, Jun Ohta, Shuuji Namiki, Kana Unuma, Koichi Uemura, Koichi Sakurada. Forensic Characteristics of Physical Elder Abuse and Current Status and Issues of Collaboration between Forensic Medicine Departments and Related Institutions in Japan. Int J Environ Res Public Health. 2022.11; 19(22);
- 3. Tomoko Akutsu, Isao Yokota, Ken Watanabe, Kochi Toyomane, Takayuki Yamagishi, Koichi Sakurada. Precise and comprehensive determination of multiple body fluids by applying statistical cutoff values to a multiplex reverse transcription-PCR and capillary electrophoresis procedure for forensic purposes. Leg Med (Tokyo). 2022.05; 58; 102087
- 4. Minegishi S, Utsuno H, Ohta J, Namiki S, Toya M, Sumi N, Unuma K, Saitoh H, Iwase H, Uemura K, Sakurada K. Sixty-eight cases of postmortem pink teeth observed in dental autopsies of unidentified cadavers. Journal of forensic sciences. 2022.05; 67(3); 1280-1287
- 5. Saki Minegishi, Hisako Saitoh, Hajime Utsuno, Jun Ohta, Shuuji Namiki, Maiko Toya, Nozomi Sumi, Koichi Sakurada. Association of Cadaveric Factors with the Degree and Region of Discoloration on Pink Teeth: An Approach to Serial Cases. Appled Sciences. 2022.04; 12; 4242
- 6. Mariko Kazuta, Utsuno Hajime, Yohsuke Makino, Saki Minegishi, Hirotaro Iwase, Koichi Sakurada. A post-mortem computed tomography imaging method for predicting the anteroposterior and superoinferior positions of the Japanese adult eyeball in the orbit. Forensic Imaging. 2022.04; 29; 200504

[Books etc]

1. Masanori Takahashi, Tamiyuki Tsuzuki, Yoshihiro Yamada, Koichi Sakurada. Forensic Dental Science 2nd edition. Nagasueshoten, 2022.02 (ISBN : 978-4-8160-1402-4)

[Conference Activities & Talks]

- 1. Hajime Utsuno, Shuuji Namiki, Yohsuke Makino, Saki Minegishi, Maikmo Toya, Nozomi Sumi, Hirotaro Iwase, Koichi Sakurada. Landmark comparisons of the alar region in the prediction of the ala of the nose using post-mortem computed tomography images. The Nineteenth Biennial Scientific Meeting of the International Association for Craniofacial Identification 2022.07.29 Liverpool, UK
- 1. Koichi Sakurada. Present situation of training related to forensic odontology for police dentists in Tokyo. Tenth Death Investigation Personal Identification System Society 2022.12.18 Zoom
- 2. Saki Minegishi, Kana Unuma, Koichi Uemura, Koichi Sakurada. Study on a relationship between dental findings of unidentified cadavers and their situations discovered. The 59th Annual Meeting of the Japanese Association of Criminology 2022.11.26 Bunkyo-ku, Tokyo

- 3. Saki Minegishi, Hisako Saitoh, Hajime Utsuno, Jun Ohta, Syuji Namiki, Maiko Toya, Nozomi Sumi, Koichi Sakurada. Association of cadaveric factors with the degree and region of discoloration on pink teeth. The 91st Kanto District Meeting of the Japanese Society of Legal Medicine 2022.10.08 Chiba city
- 4. Tomoko Akutsu, Isao Yokota, Ken Watanabe, Kochi Toyomane, Takayuki Yamagishi, Koichi Sakurada. Effects of types and combinations of target body fluids on test results in body fluid identification by multiplex RT-PCR. The 91st Kanto District Meeting of the Japanese Society of Legal Medicine 2022.10.08 Chiba city
- 5. Maiko Toya, Saki Minegishi, Hajime Utsuno, Jun Ohta, Shuuji Namiki, Kana Unuma, Koichi Uemura, Koichi Sakurada. Forensic characteristics of physical elder abuse and current status and issues of collaboration between forensic medicine departments and related institutions. The 18th Japan Academy for the prevention of the Elder Abuse 2022.09.10 Adachi-ku
- 6. Koichi Sakurada, Saki Minegishi, Keiji Inoue, Tkakashi Nakajima, Hitoshi Terada. Relationship between pink teeth phenomenon observed in dental autopsies of unidentified cadavers and cadaveric conditions. 19th National Convention of Police Dental Association 2022.08.06 Osaka city
- 7. Hiroko Oka, Akiko Takeuchi, Tosihiko Suzuki, Rieka Katsuragi, Hisako Saitoh, Koichi Sakurada, Yumi Yamashita. Current status of forensic dentistry at the education and research center related to investigation of the cause of death -Summary report of 2021 and changes from 2019-. 19th National Convention of Police Dental Association 2022.08.06
- 8. Jun Ohta, Saki Minegishi, Nao Noda, Hajime Utsuno, Koichi Sakurada. Changes in the properties of saliva identification markers due to changes in the state of saliva samples. The 106th Congress of the Japanese Society of Legal Medicine 2022.06.09 Nagoya city
- 9. Hajime Utsuno, Mariko Kazuta, Yosuke Makino, Hisako Saitoh, Syuji Namiki, Saki Minegishi, Maiko Toya, Jun Ohta, Hirotaro Iwase, Koichi Sakurada . Study on the positional relationship between the orbit and the eyeball of the Japanese adult skull using postmortem CT images. The 106th Congress of the Japanese Society of Legal Medicine 2022.06.09 Nagoya city
- Nozomi Sumi, Saki Minegishi, Shuuji Namiki, Maiko Toya, Jun Ohta, Koichi Sakurada. Study on discoloration mechanism in pink teeth phenomenon - Basic study using bovine teeth -. 16th Annual Scientific Meeting of Japanese Society of Forensic Dental Science 2022.05.15 Yokohama city
- 11. Hisako Saitoh, Saki Minegishi, Suguru Torimitsu, Fumiko Chiba, MIka Nagasawa, Namiko Ishii, Hirotaro Iwase, Koichi Sakurada. Estimation of the human birth year by radiocarbon concentrations of the whole crown powder of mandibular first premolar. 16th Annual Scientific Meeting of Japanese Society of Forensic Dental Science 2022.05.15 Yokohama city

[Social Contribution]

- 1. Personal identification using dental findings and others $(43\ \mathrm{cases})$, 2022.01.01 2022.12.31
- 2. 2022 Personal identification training program (First) (Koichi Sakurada) , Tokyo Dental Association , Japan Dental Association Building, 2022.07.24
- 3. 2022 Personal identification training program in Kanagawa (Koichi Sakurada) , Kanagawa Dental Association, Tsurumi University, 2022.10.23
- 4. Arakawa Dental Association Lecture (Koichi Sakurada) , Arakawa Dental Association , Workshop for the Police Cooperating Medical Association, Arakawa Dental Association Building, 2022.12.07
- 5. For
ensic Odontology seminar of Iwate Dental Association (Koichi Sakurada) , Iwate Dental Association ,
 Seminar, Iwate Dental Association Building, 2022.12.10

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 pharmaceutics 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

Dental Education Development

Professor: Ikuko MORIO Junior Associate Professor: Naoko SEKI Graduate Student: Mio NAITO Graduate Student: Ai OHSATO Graduate Student: Shin-ru LIAO Graduate Student: Kittichai SIREERAT

(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 healthcare sciences learn the basics of medical/dental curriculum: educational objectives, strategies and assessment/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. International Faculty Development Course (IFDC) (at TMDU)

2. International Course for Clinical Dentistry (ICCD)

3. Virtual Workshop for Collaborative Course Provision between Melbourne Dental School and Tokyo Medical and Dental University (TMDU)

(4) **Publications**

- 1. Cheng ES, Tsuji M, Suzuki S, Moriyama K. An overview of the intraoral features and craniofacial morphology of growing and adult Japanese cleidocranial dysplasia subjects. European Journal of Orthodontics. 2022.12; 44(6); 711-722
- 2. Liao SR, Seki N, Akiyama M, Shinada K, Morio I. Perceived stress and career planning awareness of Japanese and Taiwanese undergraduate dental hygiene students Journal of Dental Sciences. 2022.11;
- 3. Seki N, Sreerat K, Foxton R, Liao SR, Morio I. Critical thinking education for dental schools in Asia: Perceptions of educators Journal of Dental Sciences. 2022.09;

- 4. Kanamori Y, Seki N, Foxton R, Moross J, Komagamine Y, Mizutani K, Hosaka K, Kanazawa M, Hatayama T, Komada W, Yonemitsu I, Akiyama M, Kaewmanee PC, Kaewsutha N, Nitta H, Wakabayashi N, Morio I. Fostering globally competent dental students through virtual team-working, problem-solving and person-centred multi-disciplinary care planning. Journal of Dental Sciences. 2022.07;
- 5. Pravitharangu N, Miyamoto JJ, Yoshizawa H, Matsumoto T, Suzuki S, Chantarawaratit P, Moriyama K . Vowel sound production and its association with cephalometric characteristics in skeletal Class III subjects. European Journal of Orthodontics. 2022.06;
- Naito M, Shinada K, Seki N, Akiyama M, Yamamoto R, Onishi T, Taniyama K, Morio I. Effects of two-year oral health information provision on changes in gingival crevicular fluid in male day-night shift workers Journal of Dental Sciences. 2022.05; 17(4); 1463-1470
- 7. Sireerat K, Seki N, Akiyama M, Kinoshita A, Morio I. Critical thinking disposition among Thai dental students Journal of Dental Education. 2022.03; 1-8
- Ohsato A, Seki N, Nguyen TTT, Moross J, Sunaga M, Kabasawa Y, Kinoshita A, Morio I. Evaluating e-learning on an international scale: An audit of computer simulation learning materials in the field of dentistry Journal of Dental Sciences. 2022.01; 17(1); 535-544

[Misc]

- Seki N. Evaluation from overseas on the Model Core Curriculum for Dental Education in Japan/AY 2016 revision (Revision on the Model Core Curriculum) The Journal of Japanese Dental Education Association. 2022.12; 38(3); 17
- 2. Morio I, Seki N, Fujitani M, Fujii M, Stegaroiu R, Kawaguchi Y. International activities and challenges of the Japanese Dental Science Federation member societies Journal of Japanese Dental Science Federation. 2022.12; 1(1); 22-26
- 3. N. Seki, K. Sireerat. Assessment for Critical Thinking in Dental Education The Journal of the Stomatological Society, Japan. 2022.03; 89(1); 19

[Conference Activities & Talks]

- 1. Sireerat K, Seki N, Akiyama M, Kinoshita A, Morio I.. Differences in the critical thinking disposition of Thai dental students during pre-clinical and clinical training. ADEE Palma Annual Meeting 2022 2022.08.25 Meliá Palma Bay and Convention Centre, Palma, Spain
- 1. Shin-Ru LIAO, Naoko SEKI, Kittichai SIREERAT, Ikuko Morio. Critical thinking development in Asian dental education. The 87th Annual Meeting of the Stomatological Society 2022.12.03 Tokyo
- 2. KANAMORI Yuna, SEKI Naoko, NORITAKE Kanako, MOROSS Janelle, SUNAGA Masayo, TONAMI Ken-ichi, MORIO Ikuko, KINOSHITA Atsuhiro, NITTA Hiroshi. Dental English course for trainee residents at Tokyo Medical and Dental University (TMDU) Hospital. The 41st General and Scientific Meeting of the Japanese Dental Education Association 2022.07.23 Web

[Patents]

1. MEDICAL DEVICE, DEVICE STRUCTURES FOR DENTISTRY, FOR HEAD AND NECK SURGERY AND FOR ORTHOPEDIC SURGERY, AND METHOD FOR BONDING MEDICAL DEVICE TO BONE, Patent Number : US11234747

Oral Health Promotion

Professor Associate Professor Assistant Professor Assistant Professor Assistant Professor Office administrator Registered Resident Graduate Student

Jun Aida Yusuke Matsuyama Takashi Zaitsu Shiho Kino Akiko Oshiro Miho Ishimaru Kotomi Ito Hiromi Nishiyama Takashi Tanemura Jin Aoki Tomoya Saito Srinarupat Jarassri Yuko Inoue Duc Ho Satomi Shimada Masuko Sayo

(1) **Outline**

In "clinical practice," patients are diagnosed and treated, but "epidemiology" is used to diagnose people in society, and "public health" is used to maintain and promote the health of population in society through this process. The Department of Health Promotion Dentistry aims to promote people's health through epidemiology, public health, and the clinical and field activities of Fresh Breath Clinic.

Epidemiology" is also useful for future clinicians. Epidemiology is indispensable to determine the characteristics of one's own clinic and the condition of patients objectively from data, and to provide evidence-based prevention and treatment.

Public health" is an essential study for those who work in public administration at the national, prefectural, and municipal levels. Public health dentists work to maintain and promote the health of society. It is important to acquire a public health knowledge in order to contribute to the population health.

We also conduct dental examinations at health centers and companies, as well as at the "Fresh Breath Clinic," which specializes in the treatment of halitosis. Halitosis is the third most common dental and oral health concern, and is a factor that hinders people's communication in the workplace and in the community. As a department of a university hospital specializing in halitosis treatment, which is rare in the world, we provide state-of-the-art halitosis treatment equipped with measuring instruments, which are few in Japan, to contribute to well-being. Here, as dentists and dental hygienists, we are able to acquire a few special skills.

By acquiring such special expertise, we are training people who can contribute to the promotion of people's health as "epidemiological researchers," "administrative professionals," and "clinicians who can use epidemiology to understand their own patients' conditions and determine the best treatment based on data and evidence, and who can also provide halitosis treatment," as one-of-a-kind human resources.

(2) Research

Major research themes in the field

- · Research on causal inference between oral and general health
- · Research on health inequalities and social determinants of health
- · Research on the construction of a diagnosis and treatment system for halitosis

(3) Education

1) Graduate education

Doctoral Course Health Promotion Dentistry Advanced Theory (1st year), Seminar (1-2 years), Research Practice (2-3 years)

Graduate School of Medical and Dental Sciences Course Advanced Theory Health Science Course

Master's Course Environmental and Social Medicine and Dentistry

2) Undergraduate education

For first-year students of the School of Dentistry Module 01 "Introduction to Dentistry": Unit 03 "Current Dentistry", Unit 04 "Early Clinical Experience Practicum

For second-year students of the School of Dentistry Module 04 "Society and Environment": Unit 02 "Lifestyle and Health

For third-year students of the School of Dentistry Module 10 "Prevention and Health Care": Unit 01 "Prevention of Oral Diseases (Lecture and Practice)", Unit 02 "Prevention of Oral Diseases (Practical Training)

For fourth-year students of the School of Dentistry Module 19 "Research Experience Practicum

For 5th and 6th year students of the School of Dentistry Module 29 "Comprehensive Clinical Practice

For fourth-year students of the Department of Oral Health Sciences Module 29: Clinical Practice

(4) Lectures & Courses

1) Graduate education

The program will train dental professionals who can conduct research and regional diagnosis from epidemiology, statistics, and public health. To this end, cutting-edge research will be conducted in an international network with an understanding of international research context.

In the advanced course, basic, clinical, and epidemiological studies on oral disease prevention and oral health promotion will be reviewed. Lectures and discussions will be held on prevention of oral diseases, dental public health, epidemiology of oral diseases, social aspects of oral diseases, primary health care and health promotion, and the relationship between health care systems and educational systems and oral health promotion.

2) Undergraduate Education

Lifestyle and Health": To help students understand the relationship between health and social systems and the environment, and to acquire the knowledge, skills, and attitudes necessary to become dentists who can help people promote their health.

Prevention of Oral Diseases I & II": To acquire the knowledge, skills, and attitudes necessary for students to

become dentists who practice prevention and health management of oral diseases.

(5) 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.

(6) Publications

- 1. Marie Kobayashi, Yusuke Matsuyama, Nobutoshi Nawa, Aya Isumi, Satomi Doi, Takeo Fujiwara. Association between Community Social Capital and Access to Dental Check-Ups among Elementary School Children in Japan. Int J Environ Res Public Health. 2022.12; 20(1);
- Andrew Stickley, Naoki Kondo, Yosuke Inoue, Mariko Kanamori, Shiho Kino, Yuki Arakawa, Martin McKee. Worry about crime and loneliness in nine countries of the former Soviet Union 2022.12; 101316
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- 5. Yu Par Khin, Yusuke Matsuyama, Takeo Fujiwara. Association between social capital and COVID-19 preventive behaviors: Country-level ecological study. Int J Disaster Risk Reduct. 2022.11; 82; 103335
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- 15. Takaaki Ikeda, Yusuke Matsuyama, Masayasu Murakami, Ken Osaka. Duration of Education and Back Pain: Lessons from English Schooling Reforms. Am J Epidemiol. 2022.09;
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- 20. Inoue Y, Zaitsu T, Oshiro A, Ishimaru M, Taira K, Takahashi H, Aida J, Tamiya N. Association of marital status and access to dental care among the Japanese population: a cross-sectional study. BMC oral health. 2022.07; 22(1); 278
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- 24. Hollis Haotian Chai, Sakura Kiuchi, Ken Osaka, Jun Aida, Chun-Hung Chu, Shiqian Sherry Gao. Knowledge, Practices and Attitudes towards Silver Diamine Fluoride Therapy among Dentists in Japan: A Mixed Methods Study. Int J Environ Res Public Health. 2022.07; 19(14);
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- 39. Srinarupat J, Zaitsu T, Oshiro A, Prasertsom P, Niyomsilp K, Kawaguchi Y, Aida J. Associations of the number of remaining natural teeth and oral health behaviors with subjective chewing problems based on the Thailand National Oral Health Survey 2017. Journal of oral science. 2022.04; 64(3); 190-193
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- T Kuno, Y Miyamoto, M Iwagami, M Ishimaru, M So, M Takahashi, N N Egorova. The association of hemoglobin drop with in-hospital outcomes in COVID-19 patients. QJM. 2022.01; 114(11); 789-794
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- 64. Yu Sun, Masao Iwagami, Nobuo Sakata, Tomoko Ito, Ryota Inokuchi, Kazuaki Uda, Shota Hamada, Miho Ishimaru, Jun Komiyama, Naoaki Kuroda, Satoru Yoshie, Tatsuro Ishizaki, Katsuya Iijima, Nanako Tamiya. Development and validation of a risk score to predict the frequent emergency house calls among older people who receive regular home visits. BMC Prim Care. 2022; 23(1); 132
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[Books etc]

- 1. Miho Ishimaru, Sachiko Ono, Hideo Yasunaga. How to understand papers of dental clinical epidemiological study.. Shinko Igaku Syupansya, 2022.05 (ISBN : 978-4-8800-2919-1)
- 2. Miho Ishimaru, Tuguo Fukui, Makoto Takagi, Kazunari Komuro. Konnichinotiryoshishin2022. Igakusyoin, 2022.01 (ISBN : 978-4-2600-4777-7)

[Misc]

- 1. Richard G Watt, Jun Aida. Time to take oral health seriously. Lancet Healthy Longev. 2022.11; 3(11); e727-e728
- 2. Jun Aida, Kenji Takeuchi, Michiko Furuta, Kanade Ito, Yuji Kabasawa, Georgios Tsakos. Burden of Oral Diseases and Access to Oral Care in an Ageing Society. Int Dent J. 2022.08; 72(4S); S5-S11
- 3. 財津崇. 専門家に聞きたい ちょっと気になる症状 「口のにおい」 栄養と料理 2022 年 6 月号. 2022.05;

[Conference Activities & Talks]

- 1. 木野志保、上野恵子、西岡大輔、近藤尚己、相田潤. 生活保護受給と満たされない歯科医療ニーズの関連. 第 81 回公衆衛生学会総会 2022.10
- 2. Aida Jun. Data generation and utilization towards prevention of oral diseases. The 53rd Asia-Pacific Academic Consortium for Public Health Conference 2022.09.23 Manila, Philippines
- 3. Masuko Sayo, Zaitsu Takashi, Oshiro Akiko, Shimada Satomi, Ishimaru Miho, Kino Shiho, Aida Jun. Association of dental check-up with work absenteeism among Japanese workers(タイトル和訳中). 日本公 衆衛生学会総会抄録集 2022.09.01
- 4. Shimada Satomi, Zaitsu Takashi, Oshiro Akiko, Ishimaru Miho, Kino Shiho, Aida Jun. Association of oral health problems with work(タイトル和訳中). 日本公衆衛生学会総会抄録集 2022.09.01
- 5. 相田潤. Relation between Oral and General Health: Beyond the Critiques. Lunch Talk in Oral Health Academic Clinical Programme (ORH ACP) 2022.04.22 オンライン
- 1. Factors affecting continuous employment of newly graduated and reinstated dental hygienists attended a training course. 2022.07
- 2. Sachiko Ono, Miho Ishimaru, Akira Okada, Yosuke Ono, Hideo Yasunaga.. The post-extraction bleeding between direct oral anticoagulant user and warfarin user.. Japan Epidemiology Association 2022.01
- 1. Sagawa Y, Ogawa T, Matsuyama Y, Nakagawa KJ, Araki YM, Yasuda UY, Tumurkhuu T, Ganburged G, Bazar A, Tanaka T, Fujiwara T, Moriyama K. Association between maternal smoking during pregnancy and short root anomaly in offspring. Annual Congress of the KAO and the 13th Asian Pacific Orthodontic Conference 2022.10.01

[Awards & Honors]

- 1. 2021 Highest Altmetric Scores Award, American Geriatrics Society, 2022.05
- 2. Best Presentation Award at the 81st Annual Meeting of the Japanese Society of Public Health, 日本公衆 衛生学会, 2022.10

Educational Media Development

Professor KINOSHITA Atsuhiro Assistant Professor SUNAGA Masayo Graduate Student AKIYAMA Kyoko

(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. Live broadcast lectures have been implemented using zoom between clinics and students' homes since 2021. 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.

• We examine the effects of utilization and evaluation method with SIMROID, a patient robot for attitude education and communication education with patients in dentistry.

(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-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. Kittichai Sireerat, Naoko Seki, Masako Akiyama, Atsuhiro Kinoshita, Ikuko Morio. Critical thinking disposition among Thai dental students J Dent Educ. 2022.03; 1-8
- Sachi Umemori, Kanako Noritake, Ken-ichi Tonami, Son Hoang Le, Masayo Sunaga, Yasuyuki Kimura, Yuna Kanamori, Ayako Sekiguchi, Hiroshi Nitta. The Effects of Providing Advance Notice and Stress-Coping Traits on Physiological Stress of Patients during Dental Treatment International Journal of Environmental Research and Public Health. 2022.02; 19(5);
- 3. Ai Ohsato, Naoko Seki, Tam Thi Thanh Nguyen, Janelle Moross, Masayo Sunaga, Yuji Kabasawa, Atsuhiro Kinoshita, Ikuko Morio. Evaluating e-learning on an international scale: An audit of computer simulation learning materials in the field of dentistry. J Dent Sci. 2022.01; 17(1); 535-544

[Conference Activities & Talks]

1. Kittichai Sireerat, Naoko Seki, Masako Akiyama, Kouji Araki, Atsuhiro Kinoshita, Ikuko Morio. Differences in the critical thinking disposition of Thai dental students during pre-clinical and clinical training. the ADEE Palma annual meeting 2022, 24-26 August 2022.08.24 Palma de Mallorca

Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD Junior Associate Professor: Kaoruko Seino, PhD Research Fellow: Yuri Tashiro, MPharm, MPH, PhD; AL-SOBAIHI Saber, RN, MPH, PhD;

Graduate Student: Alemi Sharifullah, MD; Romnalin Thonglor, MPH; Kouki Akahoshi, MD;Ayano Miyashita, MSc; Yasushi Sakuramoto MD, MPH, MPA; Hideko Sato, RN, MPH; Anderson Bendera, MD; Kamila Dost, MD; Eugene Meshi, MSc; Zia-ul-haq Safi, MD; Minh Tri Tran Xuan, MD; Thao Vi, MD; Iftikhar Halimza, MD; Angelica Latorre, MPH; Ana Kriselda Rivera, MPH; Uyanga Munkhdavaa; Nalusha Quadros, DMD; Pichaya Jaroongjittanusonti, MD; Prangkhwan Jiaranaisilawong, MD; Jeanne Hamidou

(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 covrage 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

- Bendera A, Nakamura K, Seino K, Al-Sobaihi S. Factors associated with low uptake of medical male circumcision among adolescent boys in Tanzania: A multinomial logistic regression modeling. HIV/AIDS - Research and Palliative Care. 2022.12; 14; 565-575
- Meshi EB, Nakamura K, Seino K, Alemi S. Equity in water, sanitation, hygiene, and waste management services in healthcare facilities in Tanzania. Public health in practice (Oxford, England). 2022.12; 4; 100323

- 3. Thonglor R, Nakamura K, Seino S. Sociodemographic characteristics and functional health among Thai older adults in skipped generation households. Health and Social Care in the Community. 2022.11; 30(6); e5213-e5222
- 4. Nakamura K, Siongco KLL, Moncatar TRT, Tejero LMS, De La Vega SAF, Seino K, et al. Sobaihi Kaoruko Seino Thang Van Vo Fely Marilyn E. Lorenzo Carmelita C. Canila. In-service training programme for health and social care workers in the Philippines to strengthen interprofessional collaboration in caring for older adults: a mixed methods study. BMC Health Research Policy and Systems. 2022.11; 20(suppl 1); 111
- 5. Nakamura K, Siongco KLL, Moncatar TJRT, Tejero LMS, De La Vega SAF, Bonito SR, Javier R, Tsutsui T, Tri Han TD, Vo MTH, Tashiro Y, Al-Sobaihi S, Seino K, Van Vo T, Lorenzo FME, Canila CC. In-service training programme for health and social care workers in the Philippines to strengthen interprofessional collaboration in caring for older adults: a mixed-methods study. Health research policy and systems. 2022.11; 20(Suppl 1); 111
- 6. Thonglor R, Nakamura K, Seino K.. The association between living arrangements and subjective health and well-being among older adults in Thailand: a special focus on skip-generation households. Journal of Rural Medicine. 2022.10; 17(4); 196-204
- 7. Meshi EB, Nakamura K, Seino K, Alemi S. Equity in water, sanitation, hygiene, and waste management services in healthcare facilities in Tanzania. Public Health in Practice. 2022.10; 4; 100323
- 8. Thonglor Romnalin, Nakamura Keiko, Seino Kaoruko. The association between living arrangements and subjective health and well-being among older adults in Thailand: a special focus on skip-generation households(タイトル和訳中) Journal of Rural Medicine. 2022.10; 17(4); 205-213
- 9. Thonglor R, Nakamura K, Seino K. The association between living arrangements and subjective health and well-being among older adults in Thailand: a special focus on skip-generation households. Journal of rural medicine : JRM. 2022.10; 17(4); 205-213
- 10. Thonglor R, Nakamura K, Seino K. Sociodemographic characteristics and functional health among Thai older adults in skipped generation households. Health & social care in the community. 2022.07;
- 11. Miyashita A, Nakamura K, Ohnishi M, Bintabara D, Shayo F, Maro I, Sato H, Seino K, Kibusi S. . Reaching patients with noncommunicable diseases in rural Tanzania using mobile devices and community trust. JMIR mHealth uHealth. 2022.03; 10(3); e29407
- 12. Ramani-Chander A, Joshi R, van Olmen J, Thrift AG, Nakamura K, et al.. Applying systems thinking to identify enablers and challenges to scale-up interventions for hypertension and diabetes in low-income and middle-income countries: protocol for a longitudinal mixed-methods study. BMJ Open. 2022.03; 12; e053122
- Miyashita A, Nakamura K, Ohnishi M, Bintabara D, Shayo FK, Maro II, Sato H, Seino K, Kibusi S. Reaching Patients With Noncommunicable Diseases in Rural Tanzania Using Mobile Devices and Community Trust: Qualitative Study. JMIR mHealth and uHealth. 2022.03; 10(3); e29407
- 14. Alemi S, Nakamura K, Seino K, Hemat S.. Status of water, sanitation, and hygiene and standard precautions in healthcare facilities and its relevance to COVID-19 in Afghanistan Environmental Health and Preventive Medicine. 2022.02; 27; 6
- 15. Alemi Sharifullah, Nakamura Keiko, Seino Kaoruko, Hemat Shaflqullah. Status of water, sanitation, and hygiene and standard precautions in healthcare facilities and its relevance to COVID-19 in Afghanistan(和 訳中) Environmental Health and Preventive Medicine. 2022; 27; 1 of 9-9 of 9
- Bendera A, Nakamura K, Seino K, Al-Sobaihi S. Factors Associated with Low Uptake of Medical Male Circumcision Among Adolescent Boys in Tanzania: A Multinomial Logistic Regression Modeling. HIV/AIDS (Auckland, N.Z.). 2022; 14; 565-575

[Misc]

1. Vo MTH, Thonglor R, Moncatar TR, Han TDT, Tejativaddhana P, Nakamura K. Fear of falling and associated factors among older adults in Southeast Asia: a systematic review. Public Health. 2022.08;

[Conference Activities & Talks]

- 1. Nakamura K.. Western Pacific Region (WPR): Network of the Alliance for Healthy Cities. WHO 2022 European Healthy Cities Annual Business Meeting and Technical Conference. 2022.11.23 Copenhagen
- 2. Nakamura K, Seino K, Alemi S.. Planetary Health Education at a Graduate School, Tokyo Medical and Dental University.. Planetary Health Alliance Annual Meeting, 2022. 2022.11.01 Boston MA
- 3. Nakamura K. Experience in accrreditation process: lessons WPRO Alliance for Healthy Cities. WHO Regional Meeting with Multisectoral Partners on Urban Governance for Health and Well-being in South-East Asia Region. 2022.09.28 Bangkok
- 4. Sato Hideko, Nakamura Keiko, Miyashita Ayano, Kibusi Stephen, Seino Kaoruko, Tashiro Yuri, Ohnishi Mayumi. タンザニア農村部での NCD 患者に対する地域医療従事者の備え (Preparedness of Community Health Workers in Rural Tanzania towards NCD Patients). 日本公衆衛生学会総会抄録集 2022.09.01
- 5. Tran Thao Vi, Nakamura Keiko, Seino Kaoruko, Tashiro Yuri. ベトナムにおける医学生の喫煙状況とたば こ規制に対する意識調査 (Medical students' smoking status and attitudes to tobacco control in Vietnam). 日本公衆衛生学会総会抄録集 2022.09.01
- 6. Tran Xuan Minh Tri, Nakamura Keiko, Seino Kaoruko, Tashiro Yuri. ベトナムにおける幼児期の発達に関 連する家庭環境因子 (Home environment factors associated with early childhood development in Vitenam). 日本公衆衛生学会総会抄録集 2022.09.01
- 7. Nakamura K.. Getting funding: Global experience and challenges in implementation research and knowledge translation.. Regional Short Course Training on Implementation Research 2022.07.21 Manila, Philippines
- 8. Nakamura K.. Indicators for monitoring and evaluation of Healthy Cities. The First Online Seminar of the Alliance for Healthy Cities 2022.07.21
- 9. Nakamura K.. Climate Change and City Action taken in Healthy Cities.. "Climate Change and City" NDC Forum 2022.05.30 Erdenet, Mongolia

Rehabilitation Medicine

Professor Associate Professor Adjunct Lecturer Assistant Professor Atsushi OKAWA Tomoko SAKAI Tetsuya JINNO Chisato HOSHINO

Graduate Student

Yuji TAKAHASHI Kenji HIROHATA Tomoko KAWASAKI Keigo NANJO Koji IKEMATSU Megumi NAKANO

(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

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

- 1. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Changes in subjective knee function and psychological status from preoperation to 6 months post anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2022.12; 9(1); 114
- Ryo Onuma, Tadashi Masuda, Fumihiko Hoshi, Tadamitsu Matsuda, Tomoko Sakai, Atsushi Okawa, Tetsuya Jinno. Separated center-of-pressure measurements reveal new characteristics of reduced anticipatory postural adjustments during gait initiation in patients with Parkinson's disease. Physiother Theory Pract. 2022.11; 38(13); 2544-2553
- 3. Ryo Onuma, Fumihiko Hoshi, Hiroshi R
 Yamasaki, Tomoko Sakai, Tetsuya Jinno. New quantitative evaluation of anticipatory postural adjustments using a smartphone in patients with Parkinson's disease. Physiother Theory Pract. 2022.11; 1-6

- 4. Naoto Watanabe, Ryohei Takada, Takahisa Ogawa, Kazumasa Miyatake, Masanobu Hirao, Chisato Hoshino, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa. Short stature and short distance between the anterior acetabular rim to the femoral nerve are risk factors for femoral nerve palsy following primary total hip arthroplasty using the modified Watson-Jones approach. Orthop Traumatol Surg Res. 2022.10; 108(6); 103351
- 5. Mitomo S, Aizawa J, Hirohata K, Ohji S, Ohmi T, Ohara T, Koga H, Yagishita K. Association Between Knee Extension Strength at 3 and 6 Months After Anterior Cruciate Ligament Reconstruction. Journal of sport rehabilitation. 2022.08; 1-9
- Murofushi K, Oshikawa T, Kaneoka K, Akuzawa H, Yamaguchi D, Mitomo S, Furuya H, Hirohata K, Yagishita K. Differences in trunk and lower extremity muscle activity during squatting exercise with and without hammer swing. Scientific reports. 2022.08; 12(1); 13387
- 7. Hirohata K, Aizawa J, Ohmi T, Ohji S, Mitomo S, Ohara T, Koga H, Yagishita K, Jinno T, Okawa A. Reactive strength index during single-limb vertical continuous jumps after anterior cruciate ligament reconstruction: cross-sectional study. BMC sports science, medicine & rehabilitation. 2022.08; 14(1); 150
- Murofushi Koji, Yamaguchi Daisuke, Katagiri Hiroki, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Oshikawa Tomoki, Kaneoka Koji, Koga Hideyuki. The relationship between movement self-screening scores and pain intensity during daily training The Journal of Medical Investigation. 2022.08; 69(3-4); 204-216
- Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Association between landing biomechanics, knee pain, and kinesiophobia in athletes following anterior cruciate ligament reconstruction: A cross-sectional study PM&R. 2022.07;
- Aizawa J, Hirohata K, Ohji S, Ohmi T, Mitomo S, Koga H, Yagishita K. Cross-sectional study on relationships between physical function and psychological readiness to return to sport after anterior cruciate ligament reconstruction. BMC sports science, medicine & rehabilitation. 2022.06; 14(1); 97
- 11. Tomoko Kawasaki, Shunsuke Ohji, Junya Aizawa, Tomoko Sakai, Kenji Hirohata, Hironobu Kuruma, Hirohisa Koseki, Atsushi Okawa, Tetsuya Jinno. Correlation between the Photographic Cranial Angles and Radiographic Cervical Spine Alignment. Int J Environ Res Public Health. 2022.05; 19(10);
- 12. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa. Difference in tapered wedge stem alignment between supine and lateral position in cementless total hip arthroplasty via modified Watson-Jones anterolateral approach. Eur J Orthop Surg Traumatol. 2022.04; 32(3); 497-503
- Masanobu Hirao, Kazumasa Miyatake, Ryohei Takada, Tetsuya Tachibana, Atsushi Okawa, Tetsuya Jinno. Periprosthetic fragility fracture of the femur after primary cementless total hip arthroplasty. Mod Rheumatol. 2022.04; 32(3); 626-633
- 14. Tomoko Sakai, Chisato Hoshino, Megumi Nakano, Yu Fujiwara, Atsushi Okawa. Rehabilitation Characteristics of Acute-stage COVID-19 Survivors Managed with Extracorporeal Membrane Oxygenation in the Intensive Care Unit. Prog Rehabil Med. 2022.03; 7; 20220015
- 15. Murofushi Koji, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho. Variations in upper limb and trunk muscles activation during isometric exercises with or without exertion of control ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(3); 251-258
- Ikeda T, Sato R, Ninomiya K, Suzuki K, Hirakawa K, Jinno T. Nutritional Factors Related to Muscle Weakness 1 Year after Total Hip Arthroplasty: A Case-Control Study. Annals of nutrition & metabolism. 2022; 78(2); 73-79
- 17. Murofushi Koji, Oshikawa Tomoki, Kaneoka Koji, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Akuzawa Hiroshi, Yagishita Kazuyoshi. The effect of external-focus using a paper balloon on the activity of upper limb and trunk muscles during static and dynamic tasks ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(4); 345-355
- Murofushi K, Yamaguchi D, Katagiri H, Hirohata K, Furuya H, Mitomo S, Oshikawa T, Kaneoka K, Koga H. The relationship between movement self-screening scores and pain intensity during daily training. The journal of medical investigation : JMI. 2022; 69(3.4); 204-216

- Murofushi K, Yamaguchi D, Katagiri H, Hirohata K, Furuya H, Mitomo S, Oshikawa T, Kaneoka K, Koga H, Yagishita K. Validity of the KOJI AWARENESS self-screening test for body movement and comparison with functional movement screening. PloS one. 2022; 17(12); e0277167
- 20. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Strength normalized to muscle volume rather than body weight is more accurate for assessing knee strength following anterior cruciate ligament reconstruction ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(1); 7-13

Gerodontology and Oral Rehabilitation

Professor MINAKUCHI Shunsuke

Associate Professor INOKOSHI Masanao

Junior Associate Professor KOMAGAMINE Yuriko

Assistant Professor MOTOMURA Kazuo, HAMA Yohei, SUZUKI Hiroyuki, SOEDA Hitomi, SOEDA Yumika

Dental Resident UEDA Kaori, UEHARA Yoko, YAMAMOTO Mao, SHIMIZU Kento, YANAGIHARA Yuiko, YAMAGUCHI Kohei, WATANABE Masataka,

Graduate Student YOSHINAKA Shin, TONPRASONG Watcharapong, KATADA Haruko, LIU Hengyi, BUI Ngoc Huyen Trang, AKIYAMA Yo, OKADA Mitsuzumi, KASHIWAZAKI Kenta, NAMANO Sahaprom, KHIN Pyae Sone, QI Keyu, XU Kaiqi, FUTATSUYA Ryota, KIKUTA Miho, SUNAMI Akiho, SEKIMOTO Yu, CHANG Chun Wei, WU Shanglin, REN Xiangyu,

Research Student KUNISAWA Kiko, HAYAKAWA Wakako, FUKASE Madoka, ZHOU Wenming, WANG Bohua, WU Di, An Nguyen, LWIN Phyo Aung, Ba Htoo Chit, OKKAR Kyaw, TANG Bohan

Staff TERADA Mito

Adjunct lecturer

ANDO Kazuo, OWATARI Tsuneto, SAKAGUCHI Hideo, SATO Koetsu, HIRANO Shigezo, KOMATSU Yoshihiko, TOBITA Ayako, ARAKIDA Toshio, ITO Junji, INOUE Minoru, UCHIDA Tatsuro, OSADA Eiji, KOBAYASHI Shoji, TAKAHASHI Noboru, TAKEUCHI Satoshi, TAKEUCHI Shuhei, TANOUE Mariko, TERANAKA Satoshi, TOMIOKA Eiji, BABA Yuya, HIRATSUKA Tomohiro, HIRANO Yasuyoshi, HIRAYAMA Daisuke, YAMAGA Eijiro, YOSHIZAKI Taro, YONEYAMA Takeyoshi, WATANABE Ikki, SATO Yusuke, INOUE Mari, NEGORO Masatoshi, HADA Tamaki, ONUMA Hiraku, HATANO Keita, OTAKE Ryosuke, OGAWA Takahiko, IKEBE Kazunori, CHO Fuizu, NAKANODA Shinichi, FUJISHIMA Ichiro, SHIMIZUBATA Makoto

(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) Stress analyses of implant overdenture
- 9) Factorial analysis of complete denture prosthesis
- 10) Resilient denture lining material
- 11) CAD/CAM system for fabricating complete dentures
- 12) Evaluations of masticatory performance using color-changeable chewing gum
- 13) Development of novel restorative materials for root caries
- 14) Development of novel aesthetic, strong and ageing resistant highly translucent zirconia
- 15) 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.

(3) Clinical Performances

We manage the prosthodontic and special care departments.

(4) **Publications**

- 1. Soeda Y, Komagamine Y, Kanazawa M, Hada T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures from custom disks with a milled recess. The Journal of prosthetic dentistry. 2022.12;
- Nakai H, Inokoshi M, Nozaki K, Yoshihara K, Matsukawa A, Nagaoka N, Tonprasong W, Minakuchi S. Osteoblast Response of Additively Manufactured Zirconia and Alumina-Toughened Zirconia. Materials (Basel). 2022.12; 15(23); 8685
- 3. Masataka Watanabe, Manabu Kanazawa, Daisuke Sato, Yoko Uehara, Anna Miyayasu, Maiko Iwaki, Yuriko Komagamine, Sai Tun Naing, Awutsadaporn Katheng, Yuriko Kusumoto, Kazuyoshi Baba, Shunsuke Minakuchi. Oral function of implant-assisted removable partial dentures with magnetic attachments using short implants: A prospective study Tokyo Medical and Dental University. 2022.12;
- 4. Tonprasong W, Inokoshi M, Shimizubata M, Yamamoto M, Hatano K, Minakuchi S. Impact of direct restorative dental materials on surface root caries treatment. Evidence based and current materials development: A systematic review. Jpn Dent Sci Rev. 2022.11; 58; 13-30
- 5. Hama Y, Hosoda A, Kubota C, Guo R, Soeda H, Yamaguchi K, Okada M, Minakuchi S. Factors related to masticatory performance in junior and senior high school students and young adults: A cross-sectional study. Journal of prosthodontic research. 2022.11;
- 6. Trang BNH, Kanazawa M, Murakami N, Wakabayashi N, Hada T, Sahaprom N, Komagamine Y, Minakuchi S. Stress distribution of one-piece and two-piece mini-Implant overdentures with various attachment systems and diameters: A finite element analysis. Journal of prosthodontic research. 2022.11;
- Inokoshi M, Soeda Y, Akiyama Y, Ueda K, Kubota K, Minakuchi S. Fully Digital Workflow for the Fabrication of Three-Dimensionally Printed Surgical Splints for Preventing Postoperative Bleeding: A Case Report. Int J Environ Res Public Health. 2022.10; 19(19); 12773

- 8. Sai Tun Naing, Manabu Kanazawa, Tamaki Hada, Maiko Iwaki, Yuriko Komagamine, Anna Miyayasu, Yoko Uehara, Shunsuke Minakuchi. In vitro study of the effect of implant position and attachment type on stress distribution of implant-assisted removable partial dentures. J Dent Sci. 2022.10; 17(4); 1697-1703
- 9. Zhang F, Spies BC, Willems E, Inokoshi M, Wesemann C, Cokic SM, Hache B, Kohal RJ, Altmann B, Vleugels J, Van Meerbeek B, Rabel K. 3D printed zirconia dental implants with integrated directional surface pores combine mechanical strength with favorable osteoblast response. Acta Biomater. 2022.09; 150; 427-441
- Kimoto Katsuhiko, Kimoto Suguru, Hoshi Noriyuki, Sato Yusuke, Yoneyama Yoshikazu, Takebe Jun, Ichikawa Tetsuo, Murata Hiroshi, Nishimura Masahiro, Minakuchi Shunsuke, Kawai Yasuhiko. Clinical efficacy of mandibular complete dentures with a resilient liner: study protocol for a multicenter randomized controlled trial TRIALS. 2022.09; 23(1);
- 11. Suzuki H, Furuya J, Nakagawa K, Hidaka R, Nakane A, Yoshimi K, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Changes in Nutrition-Intake Method and Oral Health through a Multidisciplinary Team Approach in Malnourished Older Patients Admitted to an Acute Care Hospital. Int J Environ Res Public Health. 2022.08; 19(16);
- 12. Furuya J, Suzuki H, Hidaka R, Matsubara C, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Miyake S, Minakuchi S. Association between oral health and advisability of oral feeding in advanced cancer patients receiving palliative care: a cross-sectional study. Support Care Cancer. 2022.07; 30(7); 5779-5788
- 13. Suzuki H, Furuya J, Matsubara C, Aoyagi M, Shirobe M, Sato Y, Tohara H, Minakuchi S. Comparison of the Amount of Used and the Ease of Oral Care between Liquid and Gel-Type Oral Moisturizers Used with an Oral Care Simulators. Int J Environ Res Public Health. 2022.07; 19(13); 8158
- Čokić SM, Cóndor M, Vleugels J, Van Meerbeek B, Van Oosterwyck H, Inokoshi M, Zhang F. Mechanical properties-translucency-microstructure relationships in commercial monolayer and multilayer monolithic zirconia ceramics. Dent Mater. 2022.05; 38(5); 797-810
- 15. Inokoshi M, Yoshihara K, Kakehata M, Yashiro H, Nagaoka N, Tonprasong W, Xu K, Minakuchi S. Preliminary Study on the Optimization of Femtosecond Laser Treatment on the Surface Morphology of Lithium Disilicate Glass-Ceramics and Highly Translucent Zirconia Ceramics. Materials (Basel). 2022.05; 15(10); 3614
- 16. Ryosuke Otake, Manabu Kanazawa, Maiko Iwaki, Yumika Soeda, Tamaki Hada, Awutsadaporn Katheng, Yuriko Komagamine, Shunsuke Minakuchi. Patient-reported outcome and cost-effectiveness analysis of milled and conventionally fabricated complete dentures in a university clinic: A retrospective study. J Prosthet Dent. 2022.04;
- Maiko Iwaki, Manabu Kanazawa, Naoki Kodama, Kenichi Matsuda, Shunsuke Minakuchi, Shogo Minagi, Kazunori Ikebe, Hiroshi Nitta. Current Educational Settings for the Undergraduate Curriculum of Complete Denture Prosthodontics in 29 Japanese Dental Schools. J Prosthodont Res. 2022.04; 67(1); 1-3
- 18. Khanlar LN, Takagaki T, Abdou A, Inokoshi M, Ikeda M, Takahashi A, Yoshihara K, Nagaoka N, Nikaido T, Blatz MB, Tagami J. Effect of Air-Particle Abrasion Protocol and Primer on The Topography and Bond Strength of a High-Translucent Zirconia Ceramic. J Prosthodont. 2022.03; 31(3); 228-238
- Furuya J, Suzuki H, Hidaka R, Koshitani N, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Minakuchi S, Miyake S. Factors affecting the oral health of inpatients with advanced cancer in palliative care. Support Care Cancer. 2022.02; 30(2); 1463-1471
- Tangpothitham S, Pongprueksa P, Inokoshi M, Mitrirattanakul S. Effect of post-polymerization with autoclaving treatment on monomer elution and mechanical properties of 3D-printing acrylic resin for splint fabrication. J Mech Behav Biomed Mater. 2022.02; 126; 105015
- Liu H, Inokoshi M, Nozaki K, Shimizubata M, Nakai H, Cho Too TD, Minakuchi S. Influence of high-speed sintering protocols on translucency, mechanical properties, microstructure, crystallography, and low-temperature degradation of highly translucent zirconia. Dent Mater. 2022.02; 38(2); 451-468

- 22. Hada T, Kanazawa M, Miyamoto N, Liu H, Iwaki M, Komagamine Y, Minakuchi S. Effect of different filler contents and printing directions on the mechanical properties for photopolymer resins. International Journal of Molecular Sciences. 2022.02; 23(4);
- 23. Katheng A, Kanazawa M, Komagamine Y, Iwaki M, Namano S, Minakuchi S. Effect of post-rinsing time and method on accuracy of denture base manufactured with stereolithography. J Adv Prosthodont. 2022.02; 14(1); 45-55
- 24. Uehara Yoko, Kanazawa Manabu, Miyayasu Anna, Watanabe Masataka, Katheng Awutsadaporn, Sato Daisuke, Minakuchi Shunsuke. Comparison of general satisfaction, oral health-related quality of life, and patient's self-assessment between mandibular single-implant overdentures and experimental removable complete dentures: A randomized crossover clinical trial JOURNAL OF DENTISTRY. 2022.02; 117;
- 25. Yanagida Ryosuke, Hara Koji, Iida Takatoshi, Tohara Takashi, Tamada Yasushi, Minakuchi Shunsuke, Namiki Chizuru, Okumura Takuma, Tohara Haruka. Jaw-Opening Force as a Useful Index for Dysphagia: A Cross-Sectional and Multi-Institutional Study Gerontology. 2022.01; 68(11); 1258-1265
- 26. Meguro A, Ohara Y, Iwasaki M, Edahiro A, Shirobe M, Igarashi K, Motokawa K, Ito M, Watanabe Y, Kawai Y, Hirano H. Denture wearing is associated with nutritional status among older adults requiring long-term care: A cross-sectional study. Journal of dental sciences. 2022.01; 17(1); 500-506
- 27. Iwasaki M, Ohara Y, Motokawa K, Hayakawa M, Shirobe M, Edahiro A, Watanabe Y, Awata S, Okamura T, Inagaki H, Sakuma N, Obuchi S, Kawai H, Ejiri M, Ito K, Fujiwara Y, Kitamura A, Nofuji Y, Abe T, Iijima K, Tanaka T, Son BK, Shinkai S, Hirano H. Population-based reference values for tongue pressure in Japanese older adults: A pooled analysis of over 5,000 participants. Journal of prosthodontic research. 2022.01;
- 28. Mikami Y, Motokawa K, Shirobe M, Edahiro A, Ohara Y, Iwasaki M, Hayakawa M, Watanabe Y, Inagaki H, Kim H, Shinkai S, Awata S, Hirano H. Relationship between Eating Alone and Poor Appetite Using the Simplified Nutritional Appetite Questionnaire. Nutrients. 2022.01; 14(2);
- 29. Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 560-567
- 30. Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes with immediate- loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 70-77
- 31. Sai Tun Naing, Kanazawa M, Hada T, Iwaki M, Komagamine Y, Miyayasu A, Uehara Y, Minakuchi S. In vitro study of the effect of implant position and attachment type on stress distribution of implant-assisted removable partial dentures. Journal of Dental Sciences. 2022;
- 32. Kenichiro Ozaki, Satoshi Teranaka, Haruka Tohara, Shunsuke Minakuchi, Satoru Komatsumoto. Oral Management by a Full-Time Resident Dentist in the Hospital Ward Reduces the Incidence of Pneumonia in Patients with Acute Stroke. Int J Dent. 2022; 2022; 6193818
- 33. Minakuchi Shunsuke. Philosophy of Oral Hypofunction GERODONTOLOGY. 2022.03; 39(1); 1-2
- 1. Inokoshi M. Oral rehabilitation by applying appropriate anterior guidance and increasing the vertical dimension: A case report. Ann Jpn Prosthodont Soc. 2022.07; 14(3); 269-272
- 2. Latest evidence of dental zirconia ceramics from material science. Ann Jpn Prosthodont Soc. 2022.04; 14(2); 124-130
- 3. 副田弓夏, 金澤学, 秋山洋, 大竹涼介, 羽田多麻木, QI Keyu, NAMANO Sahaprom, 駒ヶ嶺友梨子, 岩城麻 衣子, 水口俊介, 新保秀仁, 武山丈徹, 溝越眺, 大久保力廣. Comparison of oral health-related quality of life and patient satisfaction between 3D-printed complete dentures and conventional complete dentures: a crossover randomized clinical trial (interim report) 日本デジタル歯科学会誌 (Web). 2022; 12(1);

[Conference Activities & Talks]

- 1. Inokoshi M. Contemporary dental zirconia ceramics as restorative materials. International Dental Materials Congress 2022 2022.11.05 hybrid (web, Taipei)
- 2. Inokoshi M, Nakai H, Minakuchi S. Comparison of four-point and biaxial flexural strength for strength-gradient yttria-stabilized zirconia. International Dental Materials Congress 2022 2022.11.04 hybrid (web, Taipei)
- 3. Xu K, Inokoshi M, Liu H, Minakuchi S. Influence of femtosecond laser irradiation on crystallography of highly translucent dental zirconia. International Dental Materials Congress 2022 2022.11.04 hybrid (web, Taipei)
- 4. Nakai H, Inokoshi M, Nozaki K, Minakuchi S. Cell viability and osteogenic ability of additively manufactured zirconia. International Dental Materials Congress 2022 2022.11.04 hybrid (web, Taipei)
- Tamaki HADA, Manabu KANAZAWA, Maiko IWAKI, Anna MIYAYASU, Motohiro UO, Shunsuke MINAKUCHI. Evaluation of mechanical properties of custom blocks for digital dentures fabricated using a new polymerization method. International Dental Materials Congress 2022 (IDMC2022) 2022.11.04 Taipei
- 6. Sahaprom Namano, Manabu Kanazawa, Awutsadaporn Katheng, Bui Ngoc Huyen Trang, Tamaki Hada, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. Trueness and eco-efficiency analysis of the support structure reduction for SLA printed maxillary denture.. PER-IADR Oral Health Research Congress 2022.09.17 Marseille, France
- 7. Tonprasong W, Inokoshi M, Tamura M, Yoshihara K, Takahashi R, Wada T, Nozaki K, Minakuchi S. Porphyromonas gingivalis adhesion on highly polished tooth-colored materials. 2022 IADR/APR General Session & Exhibition 2022.06.24 web
- 8. BUI Ngoc Huyen Trang, Manabu Kanazawa, Daisuke Sato, Masataka Watanabe, Yoko Uehara, Maiko Iwaki, Yuriko Komagamine, Sai Tun Naing, Yuriko Kusumoto, Yuka Abe, Kazuyoshi Baba, Shunsuke Minakuchi. Masticatory Function With Implant-assisted Removable Partial Dentures Using Short Implants. 2022 IADR/APR General Session 2022.06.22 Web
- 9. Inokoshi M, Yoshihara K, Kakehata M, Yashiro H, Nagaoka N, Tonprasong W, Xu K, Minakuchi S. Morphological analysis of femtosecond laser irradiated lithium disilicate glass-ceramics and highly translucent zirconia A preliminary study. The International Congress on Adhesive Dentistry 2022.06.03 hybrid (web, Sapporo)
- 10. Rena Takahashi, Saki Uchiyama, Yuna Kanamori, Shin Rozan, Yutaro Oda, Takaaki Sato, Junichi Shinagawa, Masanao Inokoshi, Toru Nikaido, Junji Tagami, Yasushi Shimada. Comparison of the bond strength of CAD/CAM inlay restorations with a specific cement. The International Congress on Adhesive Dentistry 2022.06 Sapporo, Japan
- 11. Sahaprom Namano, Manabu Kanazawa, Awutsadaporn Katheng, Bui Ngoc Huyen Trang, Tamaki Hada, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. The effect of support structures on the precision of SLA 3D printing dentures: an in vitro study. FDCU International Symposium 2022: Artificial Intelligence and Personalized Dental Medicine- the Future Dentistry. 2022.05.18
- 12. Yanagida Ryosuke, Hara Koji, Nakagawa Kazuharu, Namiki Chizuru, Iida Takatoshi, Tohara Takashi, Tamada Yasushi, Minakuchi Shunsuke, Yamaguchi Kohei, Yoshimi Kanako, Nakane Ayako, Tohara Haruka. Association between Jaw-opening forceand dysphagia in older adults. 30th Annual Meeting of Dysphagia Research Society 2022.03.17
- 1. The influence of wearing complete dentures on walking stability in edentulous older adults -Investigation by 3-axis accelerometers-. 2022.12.18
- 2. Development of new sports mouth guards using 4D printing technology. The 33rd Annual Meeting of Japanese Academy of Sports Dentistry 2022.12.04
- 3. Yamamoto M, Inokoshi M, Kikuta M, Minakuchi S. Flexural strength of 4-META/MMA-TBB resin containing bioactive agents. Annual Scientific Meeting of Japan Prosthodontic Society Kyushu Branch 2022 2022.11.20 hybrid (web, Sasebo)

- 4. Usefulness of Oral Environment Assessment by Multiple Professionals on Intraoral Video Taken with a Tablet Device. 2022.11.20
- 5. Inokoshi M. Basic properties of novel strength-gradient zirconia and its clinical application. The 2nd Resin-bonded zirconia fixed dental prosthesis research meeting 2022.07.23 hybrid (web, Tokyo)
- Liu H, Inokoshi M, Xu K, Nakai H, Minakuchi S. Meta-analysis for the influence of speed sintering protocols on the translucency of dental zirconia. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.17 hybrid (web, Osaka)
- 7. Hitomi Soeda, Hiroyuki Suzuki, Anna Miyayasu, Keita Hatano, Yumika Soeda, Ikki Watanabe, Shoji Kobayashi, Eiji Osada, Shigezo Hirano, Kazuo Ando, Shunsuke Minakuchi. A consideration of effective model practice on complete denture in the time of COVID-19. 2022.07.17
- 8. Xu K, Inokoshi M, Yoshihara K, Liu H, Minakuchi S. Surface roughness of highly translucent dental zirconia after femtosecond laser irradiation. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16 hybrid (web, Osaka)
- 9. Inokoshi M. Learning from cases: Mandatory knowledge regarding systemic diseases on home-visit dental treatment. The 131st Annual Meeting of the Japan Prosthodontic Society 2022.07.16 hybrid (web, Osaka)
- 10. The influence of wearing a complete denture on control of head position during walking exercise in edentulous older adults. 2022.07.16
- 11. Effect of different filler contents on the mechanical properties for photopolymer resins for 3D printing. 2022.07.16
- 12. Inokoshi M. Expectations for S-PRG filler-containing dental materials in the super-aging society. The 33rd Annual Meeting of Japanese Society of Gerodontology 2022.06.11 hybrid (web, Niigata)
- 13. Inokoshi M, Soeda Y, Akiyama Y, Ueda K, Kubota K, Minakuchi S. Fully digital workflow for the fabrication of surgical splints for preventing postoperative bleeding. The 33rd Annual Meeting of Japanese Society of Gerodontology 2022.06.11 hybrid (web, Niigata)
- 14. Ueda K, Kubota K, Inokoshi M, Morizawa M, Minakuchi S. Influence of radiographic cervical length of extracted tooth on post-operative bleeding in patients on anticoagulation therapy. The 33rd Annual Meeting of Japanese Society of Gerodontology 2022.06.11 hybrid (web, Niigata)

[Social Contribution]

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

Dysphagia Rehabilitation

(1) Publications

- 1. Mina Kawashima, Kanako Yoshimi, Kazuharu Nakagawa, Kohei Yamaguchi, Miki Ishii, Shohei Hasegawa, Rieko Moritoyo, Ayako Nakane, Haruka Tohara. Usefulness and Validity of a Jaw-Closing Force Meter in Older Adults Geriatrics. 2022.12;
- 2. Yoshizawa A, Nakagawa K, Yoshimi K, Hashimoto M, Aritaki K, Ishii M, Yamaguchi K, Nakane A, Kawabata A, Hirai T, Yoshii T, Ikeda M, Okawa A, Tohara H. Analysis of swallowing function after anterior/posterior surgery for cervical degenerative disorders and factors related to the occurrence of postoperative dysphagia. The spine journal : official journal of the North American Spine Society. 2022.12;
- 3. Saiki A, Yoshimi K, Nakagawa K, Nagasawa Y, Yoshizawa A, Yanagida R, Yamaguchi K, Nakane A, Maeda K, Tohara H. Effects of thickened carbonated cola in older patients with dysphagia. Scientific reports. 2022.12; 12(1); 22151
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- Akino Saiki, Kanako Yoshimi, Kazuharu Nakagawa, Yuki Nagasawa, Akira Yoshizawa, Ryosuke Yanagida, Kohei Yamaguchi, Ayako Nakane, Keisuke Maeda, Haruka Tohara. Effects of thickened carbonated cola in older patients with dysphagia Scientific reports. 2022.12;
- 7. Yuki Nagasawa, Sayaka Katagiri, Kazuharu Nakagawa, Tomomitsu Hirota, Kanako Yoshimi, Aritoshi Uchida, Masahiro Hatasa, Keiji Komatsu, Takahiko Shiba, Yujin Ohsugi, Naofumi Uesaka, Takanori Iwata, Haruka Tohara. Xanthan gum-based fluid thickener decreases postprandial blood glucose associated with increase of Glp1 and Glp1r expression in ileum and alteration of gut microbiome 2022.11;
- 8. 中根綾子、戸原玄. 口腔ケアで改善する嚥下機能(1) マウスピュアブランドサイト掲載コラム. 2022.11;
- 9. Tamai T, Hara K, Nakagawa K, Namiki C, Yamaguchi K, Yoshimi K, Yanagida R, Hasegawa S, Nakane A, Okumura T, Ishii M, Tohara H. Strength and morphology of a suprahyoid muscle and their relationship to forward head posture in healthy older adults. Geriatrics & gerontology international. 2022.09; 22(9); 779-784
- 10. Tamai Tomoe, Hara Koji, Nakagawa Kazuharu, Namiki Chizuru, Yamaguchi Kohei, Yoshimi Kanako, Yanagida Ryosuke, Hasegawa Shohei, Nakane Ayako, Okumura Takuma, Ishii Miki, Tohara Haruka. Strength and morphology of a suprahyoid muscle and their relationship to forward head posture in healthy older adults(タイトル和訳中) Geriatrics & Gerontology International. 2022.09; 22(9); 779-784

- 11. Suzuki H, Furuya J, Nakagawa K, Hidaka R, Nakane A, Yoshimi K, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Changes in Nutrition-Intake Method and Oral Health through a Multidisciplinary Team Approach in Malnourished Older Patients Admitted to an Acute Care Hospital. Int J Environ Res Public Health. 2022.08; 19(16);
- 12. Ayako Nakane, Kazuharu Nakagawa, Kohei Yamaguchi, Kanako Yoshimi, Yoshiko Hara, Haruka Tohara. Cough Test Results during Screening for Silent Aspiration Are Affected by Risk Factors for Silent Cerebral Infarct in Older Adults with Chronic Disease International Journal of Environmental Research and Public Health. 2022.08; 19;
- 13. Namiki Chizuru, Hara Koji, Yanagida Ryosuke, Nakagawa Kazuharu, Yamaguchi Kohei, Okumura Takuma, Tamai Tomoe, Kurosawa Yukiko, Komatsu Tomoko, Tohara Haruka. Association between Tongue Pressure and Jaw-Opening Force in Older Adults INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH. 2022.08; 19(16);
- 14. Furuya J, Suzuki H, Hidaka R, Matsubara C, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Miyake S, Minakuchi S. Association between oral health and advisability of oral feeding in advanced cancer patients receiving palliative care: a cross-sectional study. Support Care Cancer. 2022.07; 30(7); 5779-5788
- 15. Suzuki H, Furuya J, Matsubara C, Aoyagi M, Shirobe M, Sato Y, Tohara H, Minakuchi S. Comparison of the Amount of Used and the Ease of Oral Care between Liquid and Gel-Type Oral Moisturizers Used with an Oral Care Simulators. Int J Environ Res Public Health. 2022.07; 19(13); 8158
- 16. Kohei Yamaguchi, Kazuharu Nakagawa, Kanako Yoshimi, Chantaramanee Ariya, Ayako Nakane, Takuma Okumura, Haruka Tohara . Higher extracellular water/total body water ratio is associated with lower tongue and grip strength Journal of Prosthodontic Research. 2022.06;
- 17. Yamaguchi K, Nakagawa K, Yoshimi K, Ariya C, Nakane A, Okumura T, Tohara H. Higher extracellular water/total body water ratio is associated with lower tongue and grip strength: a cross-sectional study. Journal of prosthodontic research. 2022.06;
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- Miki Ishii, Kazuharu Nakagawa, Kanako Yoshimi, Takuma Okumura, Shohei Hasegawa, Kohei Yamaguchi, Ayako Nakane, Tomoe Tamai, Yuki Nagasawa, Akira Yoshizawa, Haruka Tohara. Time Spent Away from Bed to Maintain Swallowing Function in Older Adults Gerontology. 2022.04;
- 20. Tamura A, Yamaguchi K, Yanagida R, Miyata R, Tohara H. At-Home Orthodontic Treatment for Severe Teeth Arch Malalignment and Severe Obstructive Sleep Apnea Syndrome in a Child with Cerebral Palsy. International journal of environmental research and public health. 2022.04; 19(9);
- 21. Shimizu A, Fujishima I, Maeda K, Murotani K, Ohno T, Nomoto A, Nagami S, Nagano A, Sato K, Ueshima J, Inoue T, Shimizu M, Ishida Y, Kayashita J, Suenaga M, Mori N. Association between food texture levels consumed and the prevalence of malnutrition and sarcopenia in older patients after stroke. European journal of clinical nutrition. 2022.04;
- 22. Wakasugi Y, Susa C, Murata S, Aida J, Sasaki J, Furuya J, Tohara H. Factors Affecting Hospitalization and Death of Older Patients Who Need Long-Term Care-The Necessity of the Support for Dysphagia in Home Dental Care. Geriatrics (Basel, Switzerland). 2022.03; 7(2); 37
- 23. Yanagida Ryosuke, Hara Koji, Iida Takatoshi, Tohara Takashi, Tamada Yasushi, Minakuchi Shunsuke, Namiki Chizuru, Okumura Takuma, Tohara Haruka. Jaw-Opening Force as a Useful Index for Dysphagia: A Cross-Sectional and Multi-Institutional Study Gerontology. 2022.01; 68(11); 1258-1265
- 24. Chantaramanee A, Nakagawa K, Yoshimi K, Nakane A, Yamaguchi K, Tohara H. . Comparison of Tongue Characteristics Classified According to Ultrasonographic Features Using a K-Means Clustering Algorithm. Diagnostics (Basel). 2022.01; 12(2); 264
- 25. Kunieda K, Sugiyama J, Nomoto A, Ohno T, Shigematsu T, Fujishima I. Compensatory swallowing methods in a patient with dysphagia due to lateral medullary syndrome-vacuum and prolonged swallowing: A case report. Medicine. 2022.01; 101(1); e28524
- 26. Yamaguchi K, Nakagawa K, Yoshimi K, Chantaramanee A, Nakane A, Okumura T, Tohara H. The Cross-Sectional Area of the Middle and Base of the Tongue is Associated with Swallowing-Related Muscle Strength Dysphagia. 2022;
- 27. Ozaki K, Teranaka S, Tohara H, Minakuchi S, Komatsumoto S. Oral Management by a Full-Time Resident Dentist in the Hospital Ward Reduces the Incidence of Pneumonia in Patients with Acute Stroke. International journal of dentistry. 2022; 2022; 6193818
- 28. 戸原玄. 喉頭挙上に必要な筋肉は鍛えられますか? 歯科衛生士. 2022;
- 29. Saori Yoshida, Kohei Yamaguchi, Yusuke Taniguchi, Kota Isshi, Hirofumi Kido, Haruka Tohara. Design of palatal and lingual augmentation prostheses by using an intraoral scanner for a patient after a glossectomy: A clinical report The Journal of Prosthetic Dentistry. 2022.02;
- 1. Tomoe Tamai, Koji Hara, Kazuharu Nakagawa, Chizuru Namiki, Kohei Yamaguchi, Kanako Yoshimi, Ryosuke Yanagida, Shohei Hasegawa, Ayako Nakane, Takuma Okumura, Miki Ishii, Haruka Tohara. Strength and morphology of a suprahyoid muscle and their relationship to forward head posture in healthy older adults Geriatrics & amp; Gerontology International. 2022.09; 22(9); 779-784
- 2. Chizuru Namiki, Koji Hara, Ryosuke Yanagida, Kazuharu Nakagawa, Kohei Yamaguchi, Takuma Okumura, Tomoe Tamai, Yukiko Kurosawa, Tomoko Komatsu, Haruka Tohara. Association between Tongue Pressure and Jaw-Opening Force in Older Adults. International journal of environmental research and public health. 2022.08; 19(16);
- 3. Hiroyuki Suzuki, Junichi Furuya, Kazuharu Nakagawa, Rena Hidaka, Ayako Nakane, Kanako Yoshimi, Yukue Shimizu, Keiko Saito, Yasuhiro Itsui, Haruka Tohara, Yuji Sato, Shunsuke Minakuchi. Changes in Nutrition-Intake Method and Oral Health through a Multidisciplinary Team Approach in Malnourished Older Patients Admitted to an Acute Care Hospital. International journal of environmental research and public health. 2022.08; 19(16);
- 4. Shohei Hasegawa, Kazuharu Nakagawa, Kanako Yoshimi, Kohei Yamaguchi, Ayako Nakane, Miki Ishii, Takuma Okumura, Koji Hara, Shunsuke Minakuchi, Haruka Tohara. Jaw-retraction exercise increases anterior hyoid excursion during swallowing in older adults with mild dysphagia. Gerodontology. 2022.03; 39(1); 98-105
- Akiko Nomoto, Akio Shimizu, Tomohisa Ohno, Haruka Tohara, Momoyo Hashidume, Machiko Hatano, Ichiro Fujishima. Poor oral health and anorexia in older rehabilitation patients Gerodontology. 2022.03; 39(1); 59-66

[Books etc]

1. TOHARA Haruka, NAKAGAWA Kazuharu, YANAGIDA Ryosuke. The journal of Dental hygiene. Ishiyaku Publishers,Inc., 2022.03

[Misc]

1. 戸原玄. たとえ逆立ちしていても食道は水や食べ物を胃に送る ニュートン別冊 人体完全ガイド 改訂第3 版. 2022.02;

[Conference Activities & Talks]

- 1. MORITOYO.R, NAKAGAWA.K, HASEGAWA.S, ISHII.M, TOHARA.H. Jaw-Closing Force for the Older Adults without Occlusion. HATTON AWARDS 2023 国内二次選考会 2022.11.19 東京医科歯科大学
- 2. Ryosuke Yanagida. An overview on Oral Hypofunction, Oral Frailty and Dysphagia Rehabilitation. Chiang Mai University, Dent CMU Research Club 2022.11.11 Chiang Mai, Thailand
- 3. 小森彩加, 須佐千明, 道脇幸博 他. 4 次元 CT の領域分割で抽出された嚥下中の食塊の通過経路と臨床応用の可能性. 2022.09.23 幕張メッセ 国際会議場
- 4. Kanako Yoshimi, Kazuharu Nakagawa, Akino Saiki, Yosuke Kawai, Takuji Koike, Haruka Tohara. Development of screening device of swallowing function using near-infrared fluorescence . 12th annual congress 2022.09.16 Leuven, Beigium

- 5. Kazuharu Nakagawa, Aritoshi Uchida, Kanako Yoshimi, Yuki Nagasawa, Miki Ishii, Kohei Yamaguchi, Haruka Tohara. Factors affecting changes in activity and muscle mass in an animal model of social isolation. 12th annual congress 2022.09.15 Leuven, Beigium
- 6. Rieko Moritoyo, Kazuharu Nakagawa, Kohei Yamaguchi, Shohei Hasegawa, Miki Ishii, Kanako Yoshimi, Ayako Nakane, Haruka Tohara. Diet level is associated with jaw closing force in older adults without functional occlusal support. European Society for Swallowing Disorders 2022 2022.09.15 Leuven, Belgium
- Nagasawa Y, Nakagawa K, Yoshimi K, Uchida A, Tohara H. . Effect of xanthan gum-based fluid thickener for dysphagia patients with diabetes mellitus.. 2022 ESSD annual meeting 2022.09.14 Sep.16, 2022, Leuven, Belgium.
- 8. Miki Ishii, Kazuharu Nakagawa, Kanako Yoshimi, Takuma Okumura, Shohei Hasegawa, Kohei Yamaguchi, Ayako Nakane, Haruka Tohara. Application of Bioimpedance Analysis at Homes and in Nursing Homes: Relationship between Nutrition and Swallowing Function. the 30th Annual Meeting of the Dysphagia Research Society 2022.03.18 Online
- 9. Yanagida Ryosuke, Hara Koji, Nakagawa Kazuharu, Namiki Chizuru, Iida Takatoshi, Tohara Takashi, Tamada Yasushi, Minakuchi Shunsuke, Yamaguchi Kohei, Yoshimi Kanako, Nakane Ayako, Tohara Haruka. Association between Jaw-opening forceand dysphagia in older adults. 30th Annual Meeting of Dysphagia Research Society 2022.03.17
- 10. Yamaguchi K, Nakagawa K, Yoshimi K, Chantaramanee A, Nakane A, Okumura T, Tohara H. Relationship Between Characeteristics And Swallowing Related Muscle Strength Of The Middle Part And Base Of The Tongue. Dysphagia research society 2022.03
- 1. Usefulness of Oral Environment Assessment by Multiple Professionals on Intraoral Video Taken with a Tablet Device. 2022.11.20
- 2. Effects of thickener on the gastrointestinal tract : A Basic Study Using rats. 2022.09.24
- 3. Thickened fizzwater included indigestible dextrin improved dyslipidemia in a patient with dysphagia. 2022.09.24
- 4. Akino Saiki, Kanako Yoshimi, Kazuharu Nakagawa, Haruka Tohara. Effect and utilization of carbonated thickened beverages for patients with dysphagia. The 28th Annual Meeting of the Japanese Society of Dysphagia Rehabilitation 2022.09.24
- 5. Flexible 2-step angulation endoscope is useful for observation of the posterior tracheal wall. 2022.09.23
- 6. Changing clothes helps adult patients with dysphagia to prevent aspiration. 2022.09.23
- 7. Rieko Moritoyo,Kazuharu Nakagawa,Kohei Yamaguchi, Shohei Hasegawa, Miki Ishii, Kanako Yoshimi, Ayako Nakane, Haruka Tohara. Relationship between jaw closing force and diet level in older adults without occlusal support.. The 28th Annual Meeting of The Japanese Society of Dysphagia Rehabilitation 2022.09.23
- 8. Mina Kawashima, Kazuharu Nakagawa, Miki Ishii, Rieko Moritoyo, Kohei Yamaguchi, Kanako Yoshimi, Ayako Nakane, Haruka Tohara. Is mouth closing force useful as a way to provide an indication of oral function of older adults?. The 28th Annual Meeting of the Japanese Society of Dysphagia Rehabilitation 2022.09.23 Chiba, Japan
- 9. Gradual reduction in liquid consistency during training was effective in acquiring a safe swallow using a straw in a post-surgery tongue cancer patient: A case report. The 28th Annual Meeting of the Japanese Society of Dysphagia Rehabilitation 2022.09.22
- 10. A Vision-based Oral and Swallowing Capability Quantification Approach with Smartphones. Information Processing Society of Japan Multimedia, Distributed, Cooperative, and Mobile Symposium 2022.07.14
- 11. Changes in swallowing function in older adults with cervical spine disease before and after surgery -Kinematic analysis during chewing and swallowing-. 2022.06.12

- 12. Akino Saiki, Kanako Yoshimi, Kazuharu Nakagawa, Yuki Nagasawa, Akira Yoshizawa, Taishi Yamada, Ayako Nakane, Kohei Yamaguchi, Haruka Tohara. Research on new swallowing function evaluation using near-infrared fluorescence system. The 33rd Annual Meeting of the Japanese Society of Geriatric Dentistry 2022.06.11
- 13. A study on older patients with loss of molar occlusal support and oral intake without dentures. 2022.06.11
- 14. Rieko Moritoyo, Ayako Nakane. Dysphagia after radiotherapy for tonsillar carcinoma. 2022.06.10

[Others]

1. Low jaw strength reflects hard to swallow in old age, 2022.04 AAAS EurekAlert! The Global Source for Science News

Laboratory Medicine

Professor Shuji TOHDA Junior Associate Professor Tadashi KANOUCHI Junior Associate Professor Mai ITOH Assistant Professor Ayako NOGAMI Graduate Students Toshihisa SATTA, Chisuzu ITO, Kotomi NOGUCHI, Haruka KUMADA

(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 thepapy

- 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 techeque 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**

- 1. Takahiro Mitsumura, Tsukasa Okamoto, Mizuho Tosaka, Takashi Yamana, Sho Shimada, Yuki Iijima, Rie Sakakibara, Sho Shibata, Takayuki Honda, Tsuyoshi Shirai, Masahiro Ishizuka, Junichi Aiboshi, Haruhiko Furusawa, Tomoya Tateishi, Meiyo Tamaoka, Hidenobu Shigemitsu, Hirokuni Arai, Yasuhiro Otomo, Shuji Tohda, Tatsuhiko Anzai, Kunihiko Takahashi, Shinsuke Yasuda, Yasunari Miyazaki. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Jpn J Infect Dis. 2022.09; 75(5); 504-510
- 2. Yusuke Ota, Chihiro Tani Sassa, Masayo Kashiwagi, Chikako Okawara, Shuji Tohda, Ryoichi Saito. Complete Genome Sequence of an Enterobacter roggenkampii Strain with Reduced Carbapenem Susceptibility Isolated from a Home-Visit Nursing Agency. Microbiol Resour Announc. 2022.08; e0035322
- Yuasa S, Nakajima J, Takatsuki Y, Takahashi Y, Tani-Sassa C, Iwasaki Y, Nagano K, Sonobe K, Yoshimoto T, Nukui Y, Takeuchi H, Tanimoto K, Tanaka Y, Kimura A, Ichimura N, Tohda S.. Viral load of SARS-CoV-2 Omicron is not high despite its high infectivity Journal of Medical Virology. 2022.07; 94(11); 5543-5546
- 4. Hamada Satomi, Sasaki Kanae, Kito Hotaka, Tooyama Yui, Ihara Kensuke, Aoyagi Eiko, Ichimura Naoya, Tohda Shuji, Sasano Tetsuo. Effect of the recording condition on the quality of a single-lead electrocardiogram HEART AND VESSELS. 2022.06; 37(6); 1010-1026
- 5. Hamada Satomi, Sasaki Kanae, Kito Hotaka, Tooyama Yui, Ihara Kensuke, Aoyagi Eiko, Ichimura Naoya, Tohda Shuji, Sasano Tetsuo. single-lead ECG の品質に記録条件が及ぼす影響 (Effect of the recording condition on the quality of a single-lead electrocardiogram) Heart and Vessels. 2022.06; 37(6); 1010-1026
- 6. Chihiro Tani-Sassa, Yumi Iwasaki, Naoya Ichimura, Katsutoshi Nagano, Yuna Takatsuki, Sonoka Yuasa, Yuta Takahashi, Jun Nakajima, Kazunari Sonobe, Yoko Nukui, Hiroaki Takeuchi, Kousuke Tanimoto, Yukie Tanaka, Akinori Kimura, Shuji Tohda. Viral loads and profile of the patients infected with SARS-CoV-2 Delta, Alpha, or R.1 variants in Tokyo. J Med Virol. 2022.04; 94(4); 1707-1710
- 7. Satoru Aoyama, Shunichiro Yasuda, Huixin Li, Daisuke Watanabe, Yoshihiro Umezawa, Keigo Okada, Ayako Nogami, Osamu Miura, Norihiko Kawamata. A novel chimeric antigen receptor (CAR) system using an exogenous protease, in which activation of T cells is controlled by expression patterns of cell **■** surface proteins on target cells. International Journal of Molecular Medicine. 2022.04; 49(4);
- 8. Ryoichi Saito, Jun Nakajima, Isaac Prah, Masatomo Morita, Samiratu Mahazu, Yusuke Ota, Ayuka Kobayashi, Shuji Tohda, Hajime Kamiya, Hideyuki Takahashi, Makoto Ohnishi. Penicillin- and Ciprofloxacin-Resistant Invasive Neisseria meningitidis Isolates from Japan. Microbiol Spectr. 2022.04; e0062722
- 9. Saito T, Itoh M, Tohda S. TYRO3 knockdown suppresses the growth of myeloid leukaemia cells. Anticancer Research. 2022.04; 42(4); 1757-1761
- Kawahara Tomoki, Ueki Yutaka, Nawa Nobutoshi, Miyamae Shigeru, Hanafusa Mariko, Goto Yuki, Tohda Shuji, Fujiwara Takeo. Characteristics of SARS-CoV-2 super-spreaders in Japan JOURNAL OF INFECTION. 2022.02; 84(2); e6-e9
- Kameda Takahiro, Horiuchi Yuna, Shimano Shitsuko, Yano Kouji, Lai Shao-Jui, Ichimura Naoya, Tohda Shuji, Kurihara Yuriko, Tozuka Minoru, Ohkawa Ryunosuke. Effect of myeloperoxidase oxidation and N-homocysteinylation of high-density lipoprotein on endothelial repair function BIOLOGICAL CHEMISTRY. 2022.02; 403(3); 265-277

- 12. Yamada Toru, Suzuki Risa, Ichimura Naoya, Mabuchi Suguru, Nagamine Yuiko, Sassa Chihiro, Tohda Shuji. Clinical Evaluation of Reverse Transcription-Polymerase Chain Reaction and Rapid Antigen Tests of Tongue Swabs for Detecting COVID-19(和訳中) Journal of Hospital General Medicine. 2022.01; 4(1); 12-20
- 1. Kimura M, Nishiyama Y, Ueda H, Kitajo A, Arimatsu T, Kuboki M, Takahata A, Saito M, Sakashita C, Okada K, Umezawa Y, Nagao T, Yamamoto M, Tohda S, Tanabe M, Mori T, Nogami A. Perioperative management of laparoscopic cholecystectomy in a patient with paroxysmal nocturnal haemoglobinuria undergoing ravulizumab treatment 2022; 63(4); 260-264

[Misc]

 Nogami A., Sasaki K.. Therapeutic Advances in Immunotherapies for Hematological Malignancies Therapeutic Advances in Immunotherapies for Hematological Malignancies. International Journal of Molecular Sciences . 2022.09; 23; 11526

[Conference Activities & Talks]

- 1. Kota Yoshifuji, Yotaro Motomura, Makiko Saito, Ayako Nogami, Genji Kawade, Shiori Watabe, Kouhei Yamamoto, Takahiko Mori, Toshikage Nagao.. TPL2, a New Prognostic Factor and a Potential Therapeutic Target in ABC-DLBCL.. 64th ASH Annual Meeting and Exposition. 2022.12.11 New Orleans
- 2. Satoru Aoyama, Ayako Nogami, Sadakatsu Ikeda, Takehiko Mori. Novel protease-mediated double antigen recognizing Chimeric Antigen Receptor (CAR) enhances directionality of CAR-T cell activity and improves target cell specificity.. 64th American Society of Hematology (ASH) annual Meeting and Exposition 2022.12.10
- Yamazaki A., Fujii Y., Kameda T., Ichimura N., Tohda S., and Ohkawa R.. Investigation of Assays for Cholesterol Content of Erythrocytes Membrane. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 1. Makiko Saito, Satoshi Koi, Kana Bando, Hiroki Fujiwara, Yuki Osada, Kota Yoshifuji, Keisuke Tanaka, Keigo Okada, Ayako Nogami, Yoshihiro Umezawa, Toshikage Nagao, Chizuko Sakashita, Masahide Yamamoto, Shuji Tohda, Takehiko Mori. Clostridioides difficile infection among patients with hematological disorders. The 84th Annual Meeting of the Japanese Society of Hematology 2022.10.15 Fukuoka International Congress Center

Intensive Care Medicine

Professor and Chairman Kenji Wakabayashi (2021.10.1 -)

Specially Appointed Professor Hideo Takahashi (2017.4.1 -)

Associate Professor Toyomu Ugawa (2018.11.1 -)

Junior Associate Professor Michio Nagashima (2017.4.1 - 2022.3.31) Hideo Yamanouchi (2019.4.1 -) Nobuyuki Nosaka (2022.4.1 -)

Assistant Professor Takahiro Masuda (Intensive Care Unit) (2014.4.1 -) Fumi Maruyama (Intensive Care Unit) (2017.2.1 -) Nobuyuki Nosaka (2020.4.1 -2022.3.31)

Specially Appointed Assistant Professor Nobuhiro Shiota (2017.4.1 -) Ryo Uchimido (Intensive Care Unit) (2020.4.1 -) Yuka Mishima (Intensive Care Unit) (2017.4.1 -) Toshihiro Kubo (Intensive Care Unit) (2019.10.1 -)

Fellow: Taiga Nagase (Anesthesiology) (2020.4.1 -) Kouki Kiyama
(2022.4.1 -)

Postgraduate students: Shotaro Matsumoto (2016.4.1 - 2022.9.30) Nobuhiro Shiota (2017.4.1 -) Yoichi Iki (2018.4.1 -) Michiko Abe (2019.4.1 -) Yuka Mishima (2019.4.1 -) Ryo Uchimido (2020.4.1 -) Toshihiro Kubo(2021.4.1-) Ichiro Osawa(2021.4.1-)

Adjunct lecturer Yoshito Ujike (2017.4.1 -) Eriko Takezawa (2017.4.1 -2022.3.31) Satoru Hashimoto(2022.10.1 -) Shotaro Matsumoto(2022.10.1 -)

(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

We proceed big data analysis and translational research to gain a better understanding of the pathophysiology of diseases in intensive care. The department is also involved in a number of problem-solving studies in daily clinical practice and in medical education research.

(3) Education

We provide lectures for 4th year student of school of medicine (Mechanical ventilation and ARDS, Nutrition in ICU, End-stage care in ICU, PICS). We also provide programs in ICU for clinical clerkship for 5th ad 6th-year student of school of medicine. Residents have great opportunity to study patient management with multiple procedures in ICU.

(4) Lectures & Courses

We provide the unique educational conference called "academic day" every Tuesday for not only students but residents and Fellows.

(5) Clinical Services & Other Works

Intensivists are responsible for respiratory, circulatory and metabolic management and treatment of critically ill patients. We conduct multidisciplinary rounds every weekday morning to formulate and implement the most appropriate management and treatment strategy for each patient involving pharmacists, dietitians, rehabilitation staff, and clinical engineers. Risk Assessment System (RAS), a unique initiative started in March 2017 to prevent adverse events in the general ward of our hospital by making rounds of all wards during the daytime on weekdays, with a total of 400 consultations per year.

(6) Clinical Performances

Early mobilization and early nutrition are implemented to improve the outcome of critically ill patients. We support the intensive care management of each department day and night. Furthermore, this year, we took on the challenge of crowdfunding to create an cartoon to raise awareness of post-intensive care syndrome (PICS).

(7) **Publications**

[Original Articles]

1. Maruyama F, Masuda T, Nosaka N, Wakabayashi K. Case of laryngeal venous malformations requiring repeated advanced airway management in the perioperative course. Clinical case reports. 2022.12; 10(12); e6687

- 2. Maruyama F, Masuda T, Nosaka N, Wakabayashi K. Case of laryngeal venous malformations requiring repeated advanced airway management in the perioperative course. Clinical case reports. 2022.12; 10(12); e6687
- 3. Hanafusa M, Nawa N, Goto Y, Kawahara T, Miyamae S, Ueki Y, Nosaka N, Wakabayashi K, Tohda S, Tateishi U, Fujiwara T. Effectiveness of remdesivir with corticosteroids for COVID-19 patients in intensive care unit: a hospital-based observational study. Journal of medical virology. 2022.09; 95(1); e28168
- 4. Kensuke Hirasawa, Gurpreet K Singh, Jurrien H Kuneman, Tea Gegenava, Frank van der Kley, David Hautemann, Johan H C Reiber, Nina Ajmone Marsan, Jeroen J Bax, Victoria Delgado. Feature-tracking computed tomography left atrial strain and long-term survival after transcatheter aortic valve implantation. Eur Heart J Cardiovasc Imaging. 2022.08;
- 5. Jan Stassen, Stephan M Pio, See Hooi Ewe, Gurpreet K Singh, Kensuke Hirasawa, Steele C Butcher, David J Cohen, Philippe Généreux, Martin B Leon, Nina Ajmone Marsan, Victoria Delgado, Jeroen J Bax. Left Ventricular Global Longitudinal Strain in Patients with Moderate Aortic Stenosis. J Am Soc Echocardiogr. 2022.08; 35(8); 791-800.e4
- 6. Jan Stassen, See Hooi Ewe, Steele C Butcher, Mohammed R Amanullah, Bart J Mertens, Kensuke Hirasawa, Gurpreet K Singh, Kenny Y Sin, Zee Pin Ding, Stephan M Pio, Ching-Hui Sia, Nicholas Chew, William Kong, Kian Keong Poh, David Cohen, Philippe Généreux, Martin B Leon, Nina Ajmone Marsan, Victoria Delgado, Jeroen J Bax. Prognostic implications of left ventricular diastolic dysfunction in moderate aortic stenosis. Heart. 2022.08; 108(17); 1401-1407
- 7. Jurrien H Kuneman, Steele C Butcher, Gurpreet K Singh, Xu Wang, Kensuke Hirasawa, Frank van der Kley, Martin B Leon, Juhani Knuuti, Philippe Pibarot, Nina Ajmone Marsan, Victoria Delgado, Jeroen J Bax. Prognostic Implications of Change in Left Ventricular Ejection Fraction After Transcatheter Aortic Valve Implantation. Am J Cardiol. 2022.08; 177; 90-99
- 8. Jan Stassen, See Hooi Ewe, Gurpreet K Singh, Steele C Butcher, Kensuke Hirasawa, Mohammed R Amanullah, Stephan M Pio, Kenny Y K Sin, Zee P Ding, Ching-Hui Sia, Nicholas W S Chew, William K F Kong, Kian Keong Poh, Martin B Leon, Philippe Pibarot, Victoria Delgado, Nina Ajmone Marsan, Jeroen J Bax. Prevalence and Prognostic Implications of Discordant Grading and Flow-Gradient Patterns in Moderate Aortic Stenosis. J Am Coll Cardiol. 2022.08; 80(7); 666-676
- 9. Saito S, Tatsumoto N, Cao DY, Nosaka N, Nishi H, Leal DN, Bernstein EA, Shimada K, Arditi M, Bernstein KE, Yamashita M. Overexpressed Angiotensin Converting Enzyme in Neutrophils Suppresses Glomerular Damage in Crescentic Glomerulonephritis. American journal of physiology. Renal physiology. 2022.08; 323(4); F411-F424
- Kensuke Hirasawa, Federico Fortuni, Philippe J van Rosendael, Nina Ajmone Marsan, Jeroen J Bax, Victoria Delgado. Association between computed tomography-derived tricuspid annular dimensions and prognosis: insights from whole-beat computed tomography assessment. Eur Heart J Cardiovasc Imaging. 2022.07; 23(8); 1090-1097
- Jan Stassen, Xavier Galloo, Kensuke Hirasawa, Pieter van der Bijl, Martin B Leon, Nina Ajmone Marsan, Jeroen J Bax. Interaction between secondary mitral regurgitation and left atrial function and their prognostic implications after cardiac resynchronization therapy. Eur Heart J Cardiovasc Imaging. 2022.07;
- 12. Jurrien H Kuneman, Gurpreet K Singh, Stephan Milhorini Pio, Kensuke Hirasawa, David Hautemann, Frank van der Kley, Nina Ajmone Marsan, Juhani Knuuti, Victoria Delgado, Jeroen J Bax. Sex differences in left ventricular remodelling in patients with severe aortic valve stenosis. Eur Heart J Cardiovasc Imaging. 2022.06; 23(6); 781-789
- 13. Jan Stassen, See Hooi Ewe, Steele C Butcher, Mohammed R Amanullah, Kensuke Hirasawa, Gurpreet K Singh, Kenny Y K Sin, Zee P Ding, Stephan M Pio, Ching-Hui Sia, Nicholas W S Chew, William K F Kong, Kian Keong Poh, David J Cohen, Philippe Généreux, Martin B Leon, Nina Ajmone Marsan, Victoria Delgado, Jeroen J Bax. Moderate aortic stenosis: importance of symptoms and left ventricular ejection fraction. Eur Heart J Cardiovasc Imaging. 2022.06; 23(6); 790-799

- 14. Xavier Galloo, Jan Stassen, Kensuke Hirasawa, Surenjav Chimed, Bernard Cosyns, Nina Ajmone Marsan, Victoria Delgado, Pieter van der Bijl, Jeroen J Bax. Impact of baseline left ventricular volume on left ventricular reverse remodeling after cardiac resynchronization therapy. Heart Rhythm. 2022.06; 19(6); 927-936
- 15. Jan Stassen, Xavier Galloo, Surenjav Chimed, Kensuke Hirasawa, Nina Ajmone Marsan, Victoria Delgado, Pieter van der Bijl, Jeroen J Bax. Clinical implications of left atrial reverse remodelling after cardiac resynchronization therapy. Eur Heart J Cardiovasc Imaging. 2022.06; 23(6); 730-740
- 16. Jan Stassen, Xavier Galloo, Kensuke Hirasawa, Surenjav Chimed, Nina Ajmone Marsan, Victoria Delgado, Pieter van der Bijl, Jeroen J Bax. Right ventricular-pulmonary artery coupling in cardiac resynchronization therapy: evolution and prognosis. ESC Heart Fail. 2022.06; 9(3); 1597-1607
- 17. Jan Stassen, Pieter van der Bijl, Xavier Galloo, Kensuke Hirasawa, Edgard A Prihadi, Nina Ajmone Marsan, Jeroen J Bax. Prognostic Implications of Right Ventricular Free Wall Strain in Recipients of Cardiac Resynchronization Therapy. Am J Cardiol. 2022.05; 171; 151-158
- 18. Jan Stassen, Mand Khidir, Xavier Galloo, Kensuke Hirasawa, Juhani Knuuti, Nina Ajmone Marsan, Victoria Delgado, Pieter van der Bijl, Jeroen J Bax. Prognostic implications of staging cardiac remodeling in patients undergoing cardiac resynchronization therapy. Int J Cardiol. 2022.05; 355; 65-71
- 19. Surenjav Chimed, Pieter van der Bijl, Rodolfo de Paula Lustosa, Kensuke Hirasawa, Idit Yedidya, Federico Fortuni, Enno van der Velde, Jose M Montero-Cabezas, Nina Ajmone Marsan, Bernard J Gersh, Victoria Delgado, Jeroen J Bax. Prognostic Relevance of Right Ventricular Remodeling after ST-Segment Elevation Myocardial Infarction in Patients Treated With Primary Percutaneous Coronary Intervention. Am J Cardiol. 2022.05; 170; 1-9
- 20. Catherina Tjahjadi, Steele C Butcher, Thomas Zegkos, Ching Hui Sia, Kensuke Hirasawa, Vasileios Kamperidis, Jinghao Nicholas Ngiam, Raymond C C Wong, Georgios Efthimiadis, Jeroen J Bax, Victoria Delgado, Nina Ajmone Marsan. Differences in Characteristics and Outcomes Between Patients With Hypertrophic Cardiomyopathy From Asian and European Centers. J Am Heart Assoc. 2022.05; 11(10); e023313
- 21. Junji Matsuda, Taishi Yonetsu, Shunichi Kato, Giichi Nitta, Yasuaki Hada, Ken Negi, Yoshinori Kanno, Toshihiko Nakao, Takayuki Niida, Yuji Matsuda, Eisuke Usui, Kensuke Hirasawa, Tomoyuki Umemoto, Hideki Morita, Osamu Inaba, Yutaka Matsumura, Tetsuo Sasano. The impact of lesion complexity on predicting mortality of coronary artery disease patients after out-of-hospital cardiac arrest. Intern Emerg Med. 2022.04;
- 22. Noda Kotaro, Nosaka Nobuyuki, Hara Nobuhiro, Yokota Takanori, Shigemitsu Hidenobu, Takahashi Hideo. We Should Pay Attention to "Referred Pain": A Case of Acute Myocardial Infarction That Masked and Delayed the Diagnosis of Esophageal Perforation(和訳中) Internal Medicine. 2022.04; 61(8); 1295-1298
- Jan Stassen, Xavier Galloo, Kensuke Hirasawa, Nina Ajmone Marsan, Pieter van der Bijl, Victoria Delgado, Jeroen J Bax. Tricuspid regurgitation after cardiac resynchronization therapy: evolution and prognostic significance. Europace. 2022.03;
- 24. Mishima Y, Nosaka N, Oi K, Gu Y, Arai H. Tracheobronchial aspergillosis presenting with black mucus plugs and tracheal ulcers. Clinical case reports. 2022.02; 10(2); e05456
- 25. Jan Stassen, See Hooi Ewe, Kensuke Hirasawa, Steele C Butcher, Gurpreet K Singh, Mohammed R Amanullah, Kenny Y K Sin, Zee P Ding, Stephan M Pio, Nicholas W S Chew, Ching-Hui Sia, William K F Kong, Kian Keong Poh, David J Cohen, Philippe Généreux, Martin B Leon, Nina Ajmone Marsan, Victoria Delgado, Jeroen J Bax. Left ventricular remodelling patterns in patients with moderate aortic stenosis. Eur Heart J Cardiovasc Imaging. 2022.02;
- 26. Gurpreet K Singh, Farnaz Namazi, Kensuke Hirasawa, Pieter van der Bijl, Aniek L van Wijngaarden, N Mai Vo, Gregg W Stone, Nina Ajmone Marsan, Victoria Delgado, Jeroen J Bax. Extramitral Valvular Cardiac Involvement in Patients With Significant Secondary Mitral Regurgitation. Am J Cardiol. 2022.01; 162; 143-149

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1. Kensuke Hirasawa, Masaki Izumo. Role of 3D Transesophageal Echocardiography for Transcatheter Mitral Valve Repair-A Mini Review. Front Cardiovasc Med. 2022.02; 9; 815304

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata

Postgraduate student Xue Bingyang, Tsubura Noda, Shotaro Mizuno, Tatsuki Akahoshi, Yuna Kusakabe, Takuya Suzuoka

(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

- 1. Xue B, Ishiwata Y, Kawano Y, Takahashi H, Negishi K, Aoyama T, Nagata M. Paliperidone-Induced Acute Hyperglycemia Is Caused by Adrenaline Secretion via the Activation of Hypothalamic AMP-Activated Protein Kinase. Biological & pharmaceutical bulletin. 2022.11; 45(11); 1669-1677
- 2. Kawano Y, Obana M, Nagata M, Mano Y, Katsuyama M, Yamamoto Y, Maeda-Minami A, Negishi K, Takagi M, Shimada S, Aoyama T. The antiplatelet effect of mirtazapine is mediated by co-blocking 5-HT_{2A} and α ₂-adrenergic receptors on platelets: An in vitro human plasma-based study. European journal of pharmacology. 2022.02; 917; 174640
- 3. Takagi M, Ogawa C, Iehara T, Aoki-Nogami Y, Ishibashi E, Imai M, Kimura T, Nagata M, Yasuhara M, Masutani M, Yoshimura K, Tomizawa D, Ogawa A, Yonemori K, Morishita A, Miyamoto S, Takita J, Kihara T, Nobori K, Hasebe K, Miya F, Ikeda S, Shioda Y, Matsumoto K, Fujimura J, Mizutani S, Morio T, Hosoi H, Koike R. First phase 1 clinical study of olaparib in pediatric patients with refractory solid tumors. Cancer. 2022.05;

Medical Education Research and Development

Professor Masanaga YAMAWAKI Junior Associate Professor Eriko OKADA Junior Associate Professor Yasuhiro ITSUI Assistant Professor Nobutoshi NAWA Attending Staff Ayako KASHIMADA

(1) **Outline**

Our aim is to carry out the mission of the university, "cultivating professionals with knowledge and humanity, thereby contributing to people's well-being," from the perspective of educational management. The basis of our department is to contribute to the education, research, clinical practice, and management & operation of the university in cooperation with other departments and sections. Medical education will continue from undergraduate education to lifelong learning. Our department is in charge of "coordination and support" of education for 6 years of undergraduate and 2 years of junior residency period, and of cultivating future Clinician Scientists and Scientific Clinicians.

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

We are developing the following research from the perspective of medical education.

 $\cdot~$ Study on evaluation for clinical ability acquisition

We are studying educational and evaluation system on how to learn and continue to practice in under- and post-graduate clinical training.

 $\cdot\,$ Research on career education

Research on career education for doctors is being conducted with development of entrepreneurship education program for doctors.

 $\cdot\,$ Research on research ethics education of medical students and residents

Development and verification of a model evaluation program for research ethics education by an interdisciplinary approach.

· Research on patient medication and drug swallowing using design thinking

Research on patient medication and drug swallowing using design thinking is being conducted in search for new treatment strategy for dysphagia.

 $\cdot\,$ Research on team medical care and multidisciplinary education

We are conducting research on team medical care and multidisciplinary collaborative education.

 $\cdot\,$ Research on health prevention and patient education

We are conducting research on the development of patient education programs related to

health promotion for the super-elderly. In addition, we are also conducting preventive research on lifestyle-related diseases in Kyo-tango Longevity Cohort Study.

 \cdot Other research on medical education

We are also conducting research on cognitive mechanism and cerebral processing in clinical reasoning, on competence evaluation in pre- and post-graduate clinical medical education, on multifaceted evaluation in medical communication and research on community-based medicine.

(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, our education program revealed one of the most competitive among all national teaching hospitals.

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

- 1. Ishii E, Nawa N, Hashimoto S, Shigemitsu H, Fujiwara T*. Development, validation, and feature extraction of a deep learning model predicting in-hospital mortality using Japan's largest national ICU database: a validation framework for transparent clinical Artificial Intelligence (cAI) development. Anaesth Crit Care Pain Med. 2022.10; 42(2); 101167
- 2. Miyamura K, Nawa N, Isumi A, Doi S, Ochi M, Fujiwara T. Impact of exposure to secondhand smoke on the risk of obesity in early adolescence. Pediatric research. 2022.08;

- 3. Furumoto Yohei, Araki Akihiro, Matsumoto Taichi, Nozaka Takahito, Yauchi Masato, Kobayashi Katsumasa, Nitta Sayuri, Okada Eriko. Experience of disruption of capsule endoscopy after prolonged retention(和訳中) DEN Open. 2022.04; 2(1); 1 of 5-5 of 5
- 4. Goto Yuki, Yamada Toru, Nagamine Yuiko, Mabuchi Suguru, Akaishi Yu, Yoshida Shoko, Suzuki Risa, Masanaga Yamawaki. Epidemiology and clinical characteristics of outpatients with suspected COVID-19: A prospective observational study from the COVID-19 outpatient center at a university hospital(和訳中) Journal of Hospital General Medicine. 2022.03; 4(2); 57-65
- Nishimura H, Nawa N, Ogawa T, Fushimi K, Fujiwara T. Association of ambient temperature and sun exposure with hip fractures in Japan: A time-series analysis using nationwide inpatient database. Sci Total Environ. 2022.02; 807(Pt 1); 150774
- Koyama T, Nawa N, Itsui Y, Okada E, Fujiwara T. Facilitators and barriers to implementing shared decision making: A cross-sectional study of physicians in Japan. Patient education and counseling. 2022.01; S0738-3991(22); 00042-00048
- 7. Satomura Y, Bessho K, Nawa N, Kondo H, Ito S, Togawa T, Yano M, Yamano Y, Inoue T, Fukui M, Onuma S, Fukuoka T, Yasuda K, Kimura T, Tachibana M, Kitaoka T, Nabatame S, Ozono K. Novel gene mutations in three Japanese patients with ARC syndrome associated mild phenotypes: a case series. Journal of Medical Case Reports. 2022; (in press);
- 8. Yoshimoto T, Nawa N, Uemura M, Sakano T, Fujiwara T. The impact of interprofessional communication through ICT on health outcomes of older adults receiving home care in Japan a retrospective cohort study. Journal of General and Family Medicine. 2022; (in press);
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- 11. Koyama Y, Fujiwara T, Doi S, Isumi A, Morita A, Matsuyama Y, Tani Y, Nawa N, Mashiko H, Yagi J.. The Great East Japan Earthquake Follow-up study for Children (GEJE-FC) team. Heart rate variability in 2014 predicted delayed onset of internalizing problems in 2015 among children affected by the 2011 Great East Japan Earthquake. J Psychiatric Research. 2022; (in press);
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- 14. Koyama Y, Nawa N, Ochi M, Surkan PJ, Fujiwara T. Joint roles of oxytocin- and dopamine-related genes and childhood parenting experience in maternal supportive social network. Child Psychiatry & Human Development. 2022; (in press);
- Hanafusa M, Nawa N, Goto Y, Kawahara T, Miyamae S, Ueki Y, Nosaka N, Wakabayashi K, Tohda S, Tateishi U, Fujiwara T. Effectiveness of remdesivir with corticosteroids for COVID-19 patients in intensive care unit: a hospital- based observational study. Journal of Medical Virology. 2022; (in press);
- Furukawa S, Nawa N, Yamaoka Y, Fujiwara T. Concerns and needs of people with intellectual disabilities and their caregivers during the COVID-19 pandemic in Japan. Journal of Intellectual Disabilities. 2022; (in press);
- Ishii E, Nawa N, Hashimoto S, Shigemitsu H, Fujiwara T. Development, Validation, and Feature Extraction of a Deep Learning Model Predicting In-Hospital Mortality Using Japan's Largest National ICU Database: A Validation Framework for Transparent Clinical AI Development. Anaesthesia Critical Care & Pain Medicine. 2022; (in press);

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- Kobayashi M, Matsuyama Y, Nawa N, Isumi A, Doi S, Fujiwara T. Association between community social capital and access to preventive dental care among elementary school children in Japan. International Journal of Environmental Research and Public Health. 2022; (in press);
- 22. Hanafusa M, Ito Y, Ishibashi H, Nakaya T, Nawa N, Sobue T, Okubo K, Fujiwara T. Association between Socioeconomic Status and Net Survival after Primary Lung Cancer Surgery: A Tertiary University Hospital Retrospective Observational Study in Japan. Japanese Journal of Clinical Oncology. 2022; (in press);

[Conference Activities & Talks]

- 1. Mitsuyuki Numasawa, Nobutoshi Nawa, Kumiko Yamaguchi, Kanako Noritake, Jun Tsuruta, Mina Nakagawa. Comparison of readiness for interprofessional learning among medical, dental, and nursing students before the start of clinical practice. AMEE 2022 2022.08.29 The Virtual Conference
- 1. The importance of formative assessment in a human anatomy course summative assessment. 2022.08.06
- 2. Remote interprofessional learning for younger undergraduate students' early exposure. 2022.08.05
- 3. Results of a survey to develop a data analysis system to support institutional research. The 54th Annual Meeting of the Japan Society for Medical Education 2022.08.05 Gunma

Acute Critical Care and Disaster Medicine

Professor Yasuhiro Otomo Associate Professor Koji Morishita Lecturer Shusuke Mori Assistant professor Wataru Takayama Assistant professor Yutaka Ueki Assistant professor Kyuhei Miyakawa Assistant professor Atsushi Senda Assistant professor Keita Nakatsutsumi Assistant professor Satoshi Fujie Assistant professor Akira Suekane Specially Appointed Assistant professor Tomohiro Adachi Specially Appointed Assistant professor Yohei Iwasaki Specially Appointed Assistant professor Kei Ito Specially Appointed Assistant professor Hiroki Matsui Specially Appointed Assistant professor Akihiro Fujita Staff Shimpei Asada Staff Hazuki Koguchi Staff Naoki Kawahara Emergency Life-saving Technician Nagisa kato Emergency Life-saving Technician Rei Kitahara Mizuki Harashima Emergency Life-saving Technician

(1) Outline

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

(2) Research

- \cdot Analysis of inflammatory mediators in septic patients
- \cdot Analysis of lipid mediators with mass spectrometry
- \cdot Interventional research of concentrated fibrinogen and blood transfusion in patients with massive blood loss
- · Investigation of neutrofil function in severely septic patients
- \cdot Statistical analysis using Japan Trauma Databank

(3) Education

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.

(4) Clinical Services & Other Works

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.

(5) Publications

- 1. Koji Morishita, Kozo Katase, Masahiro Ishikane, Yasuhiro Otomo. Motivating factors for frontline healthcare workers during the COVID-19 pandemic: A survey in Japan. Curr Psychol. 2022.12; 1-9
- 2. Morishita K, Katase K, Ishikane M, Otomo Y. Motivating factors for frontline healthcare workers during the COVID-19 pandemic: A survey in Japan. Current psychology (New Brunswick, N.J.). 2022.12; 1-9
- 3. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Japanese journal of infectious diseases. 2022.09; 75(5); 504-510
- 4. Mitsumura Takahiro, Okamoto Tsukasa, Tosaka Mizuho, Yamana Takashi, Shimada Sho, Iijima Yuki, Sakakibara Rie, Shibata Sho, Honda Takayuki, Shirai Tsuyoshi, Ishizuka Masahiro, Aiboshi Junichi, Furusawa Haruhiko, Tateishi Tomoya, Tamaoka Meiyo, Shigemitsu Hidenobu, Arai Hirokuni, Otomo Yasuhiro, Tohda Shuji, Anzai Tatsuhiko, Takahashi Kunihiko, Yasuda Shinsuke, Miyazaki Yasunari. SARS-CoV-2 RNA コピー数と COVID-19 死亡率との関連、ならびにそれが重症患者における死亡率の 予測能に及ぼす影響 (Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases) Japanese Journal of Infectious Diseases. 2022.09; 75(5); 504-510
- 5. Morishita K, Kudo A, Uchida T, Kurashima N, Toba M, Ito K, Otomo Y. Unexpected Mechanical Ventilation Dysfunction in a Coronavirus Disease Patient With Severe Pneumonia Due to the Oxygen Flowsensor Failure. J Patient Saf. 2022.08; 18(5); e867-e868
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- 7. Sasaki Y, Nakakuki K, Ikeda M, Sumi Y, Miura H, Imazu Y, Otomo Y. Undergraduate medical and dental science students' interest and support needs in medical volunteer activities during times of disasters Japanese Journal of Disaster Medicine. 2022.04; 27; 102-109
- Masayuki Yagi, Junichi Aiboshi, Mitsuaki Kojima, Shunsuke Yoshikawa, Koji Morishita, Masahito Kaji, Yasuhiro Otomo. Life-saving case of cardiopulmonary arrest by secondary aortoenteric fistula formed in the anastomotic site between the inferior mesenteric artery and aortic graft. Acute Med Surg. 2022.03; 9(1); e2744
- 9. Yagi Masayuki, Aiboshi Junichi, Kojima Mitsuaki, Yoshikawa Shunsuke, Morishita Koji, Kaji Masahito, Otomo Yasuhiro. 下腸間膜動脈と大動脈グラフト間の吻合部位に形成した二次性 aortoenteric fistula による心肺停止から救命が可能であった 1 例 (Life-saving case of cardiopulmonary arrest by secondary aortoenteric fistula formed in the anastomotic site between the inferior mesenteric artery and aortic graft) Acute Medicine & Surgery. 2022.03; 9(1); 1 of 4-4 of 4

- 10. Ishii Euma, Nawa Nobutoshi, Matsui Hiroki, Otomo Yasuhiro, Fujiwara Takeo. Letter to the Editor への 回答 日本の三次救急医療センターにおける日本人患者と外国人患者の疾患パターンと転帰の比較 (Response to the Letter to the Editor on "Comparison of Disease Patterns and Outcomes Between Non-Japanese and Japanese Patients at a Single Tertiary Emergency Care Center in Japan") Journal of Epidemiology. 2022.02; 32(1-2); 114
- 11. Ito Kei, Endo Akira, Kobayashi Masanori, Otomo Yasuhiro. Multi-stage endoscopic therapy により管理 しえた主膵管の完全途絶を呈する重度膵損傷 1 症例報告 (Severe pancreatic injury with total disruption of main pancreatic duct successfully managed by multi-stage endoscopic therapy: a case report) Acute Medicine & Surgery. 2022.02; 9(1); 1 of 4-4 of 4
- 12. Ishii Euma, Nawa Nobutoshi, Matsui Hiroki, Otomo Yasuhiro, Fujiwara Takeo. 日本の三次救急医療セン ターにおける日本人患者と外国人患者の疾患パターンと転帰の比較 (Comparison of Disease Patterns and Outcomes Between Non-Japanese and Japanese Patients at a Single Tertiary Emergency Care Center in Japan) Journal of Epidemiology. 2022.02; 32(1-2); 80-88
- Hirotaka Aoki, Koji Morishita, Marie Takahashi, Rea Machida, Kousuke Hirata, Atsushi Kudoh, Tsuyoshi Shirai. Elicitation of Diagnosis Strategy During Scanning Chest X-Rays from Eye Tracking Stimulated Retrospections 13th International Conference on Applied Human Factors and Ergonomics. 2022.01;
- 14. Fujita A, Nakatsutsumi K, Takahashi T, Suzuki T, Nakashima C, Ito K, Endo A, Otomo Y. Effective hemostasis by preperitoneal pelvic packing for common iliac vein injury without pelvic fracture in severe blunt trauma: a case report. Acute medicine & surgery. 2022.01; 9(1); e771
- 15. Yagi M, Aiboshi J, Kojima M, Yoshikawa S, Morishita K, Kaji M, Otomo Y. Life-saving case of cardiopulmonary arrest by secondary aortoenteric fistula formed in the anastomotic site between the inferior mesenteric artery and aortic graft. Acute medicine & surgery. 2022.01; 9(1); e2744
- 16. Ito K, Endo A, Kobayashi M, Otomo Y. Severe pancreatic injury with total disruption of main pancreatic duct successfully managed by multi-stage endoscopic therapy: a case report. Acute medicine & surgery. 2022.01; 9(1); e735
- 17. Kojima Mitsuaki, Endo Akira, Shiraishi Atsushi, Shoko Tomohisa, Otomo Yasuhiro, Coimbra Raul. 大量 輸血を行う高齢・非高齢外傷患者における血漿/赤血球比と生存の関連 後方視的コホート研究 (Association between the plasma-to-red blood cell ratio and survival in geriatric and non-geriatric trauma patients undergoing massive transfusion: a retrospective cohort study) Journal of Intensive Care. 2022.01; 10; 1 of 12-12 of 12
- 18. Wada T, Shiraishi A, Gando S, Kabata D, Yamakawa K, Fujishima S, Saitoh D, Kushimoto S, Ogura H, Abe T, Mayumi T, Otomo Y. Association of antithrombin with development of trauma-induced disseminated intravascular coagulation and outcomes. Frontiers in immunology. 2022; 13; 1026163
- Koji Morishita, Ryuzo Abe, Kazuhide Matsushima, Takane Suzuki, Takaaki Nakada, Norio Sato, Tomohiro Muronoi, Hiroaki Watanabe, Yasuhiro Otomo. The Advanced Surgical Skills for Exposure in Trauma Course in Japan; the current status and issues Japanese Journal of Acute Care Surgery. 2022.12; 12(1); 54-59
- 2. Akiko Kuge, Koji Morishita, Shimpei Asada, Keita Nakatsutsumi, Wataru Takayama, Emi Kiuchi, Yasuhiro Otomo. A patient with post COVID–19 vaccination presented with convulsions and cardiogenic shock due to adrenal crisis and Takotsubo cardiomyopathy diagnosed with autoimmune polyendocrine syndromes type II and Addison's disease JJAAM. 2022.12; 33; 1016-1021
- 3. Haruka KOGA, Hiroki MORI, Tsutomu HOMMA, Sayuri KATO, Naoya ISHIDA, Kentaro TANAKA, Masayuki YAGI, Koji MORISHITA. Extensive Cutaneous Necrosis of Hand and Forearm Due to Extravasation of Norepinephrine Requiring Fascia Transplantation and Anterolateral Thigh Flap -A Case Report 2022.09; 35(3); 116-121
- 4. 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. Koji Morishita. Japanese Trauma System Current Issue, Introduction of TMDU activity . Khon Kaen Hospital Trauma Meeting 2022.11.24 Khon Kaen, Thailand
- 2. Koji Morishita. Trauma Systems: Japanese Perspective. TRAUMA 2022 Hybrid & Asian Trauma Congress 2022 2022.11.18 New Delhi, India
- 3. Koji Morishita. Trauma System in Japan. Khon Kaen University Trauma meeting 2022.11.15 Khon Kaen, Thailand
- 4. Adachi T, Morishita K,Nakatsutsumi K, Kojima M, Senda A, Suzuki K, Aiboshi J, Otomo Y. LIPID METABOLIC PROFILE IN MESENTERIC LYMPH AFTER INTESTINAL ISCHEMIA/REPERFUSION. The American Association for the Surgery of Trauma for the 81st Annual Meeting of AAST & Clinical Congress of Acute Care Surgery 2022.09.21

General Dentistry

Professor Hiroshi NITTA
Associate Professor Akira NISHIYAMA
Junior Associate Professor Masayuki HIDESHIMA
Junior Associate Professor Ken-ichi TONAMI
Junior Associate Professor Kanako NORITAKE
Assistant Professor Sachi UMEMORI
Project Assistant Professor Yuna KANAMORI
Project Assistant Professor Daisuke KIDO
Project Assistant Professor Yasuyuki KIMURA
Project Assistant Professor Hitan SOU
Project Assistant Professor Naoko HARADA
Hospital Staff Hiraku OONUMA
Hospital Staff Shoko KAIDA
Hospital Staff Yutaro KITANAKA
Hospital Staff Yukako KUSUNOKI
Hospital Staff Hideyuki TAKAMATSU
Hospital Staff Akitaka HATTORI
Hospital Staff Akiyo FUJITA
Hospital Staff Hirohito MIKI
Hospital Staff Yuko MITSUMA
Hospital Staff Mai MIYACHI
Graduate student Ayako SEKIGUCHI

(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

- Shoko Tobe, Hiroyuki Ishiyama, Akira Nishiyama, Keisuke Miyazono, Hiroko Kimura, Kenji Fueki. Effects of Jaw-Opening Exercises with/without Pain for Temporomandibular Disorders: A Pilot Randomized Controlled Trial International Journal of Environmental Research and Public Health. 2022.12; 19(24); 16840
- 2. Zaitsu T, Inoue Y, Oshiro A, Nishiyama A, Kawaguchi Y, Aida J. Association of visual display terminal time with prevalence of temporomandibular disorder among Japanese workers. Journal of occupational health. 2022.11; 64(1); e12370
- 3. Noritake K, Oshima K, Fukuda H, Tano R, Oshiro A, Nitta H, Miura H. Factors Affecting the Career Continuation of Newly Graduated and Reinstated Dental Hygienists Who Participated in a Technical Training Program in Japan. International journal of environmental research and public health. 2022.10; 19(20); 13360
- 4. Akiyo Fujita, Chiho Kato, Yasunori Abe, Hideyuki Ishidori, Ruixin Li, Phyo Thura Aung, Takuya Ogawa, Hidemasa Okihara, Satoshi Kokai, Takashi Ono. Unilateral nasal obstruction affects development of cortical orofacial motor representation in the cortical masticatory area of growing rats Neuroscience Letters. 2022.07; 783; 136700

- 5. Risako Mikami, Koji Mizutani, Yusuke Matsuyama, Tomohito Gohda, Hiromichi Gotoh, Norio Aoyama, Takanori Matsuura, Daisuke Kido, Kohei Takeda, Natsumi Saito, Takeo Fujiwara, Yuichi Izumi, Takanori Iwata. Association of type 2 diabetes with periodontitis and tooth loss in patients undergoing hemodialysis. PLoS One. 2022.05; 17(5); e0267494
- 6. Kay Thwe Ye Min Soe, Hiroyuki Ishiyama, Akira Nishiyama, Masahiko Shimada, Shigeru Maeda . Effect of Different Maxillary Oral Appliance Designs on Respiratory Variables during Sleep International Journal of Environmental Research and Public Health. 2022.05; 19(11); 6714
- 7. Kimura-Ono A, Maekawa K, Kuboki T, Nawachi K, Fujisawa M, Sato H, Aita H, Koyama S, Hideshima M, Sato Y, Wake H, Nagao K, Kodaira-Ueda Y, Tamaki K, Sadamori S, Tsuga K, Nishi Y, Sawase T, Koshino H, Masumi SI, Sakurai K, Ishibashi K, Ohyama T, Akagawa Y, Hirai T, Sasaki K, Koyano K, Yatani H, Matsumura H, Ichikawa T, Ohkawa S, Baba K. Prosthodontic treatment can improve the ingestible food profile in Japanese adult outpatients. Journal of prosthodontic research __D_22_00017. 2022.05;
- Maiko Iwaki, Manabu Kanazawa, Naoki Kodama, Kenichi Matsuda, Shunsuke Minakuchi, Shogo Minagi, Kazunori Ikebe, Hiroshi Nitta. Current Educational Settings for the Undergraduate Curriculum of Complete Denture Prosthodontics in 29 Japanese Dental Schools. J Prosthodont Res. 2022.04; 67(1); 1-3
- 9. Sachi Umemori, Kanako Noritake, Ken-ichi Tonami, Son Hoang Le, Masayo Sunaga,Yasuyuki Kimura,Yuna Kanamori, Ayako Sekiguchi, Hiroshi Nitta. The Effects of Providing Advance Notice and Stress-Coping Traits on Physiological Stress of Patients during Dental Treatment International Journal of Environmental Research and Public Health. 2022.02; 19(5); 2540
- Akitaka Hattori, Ken-ichi Tonami, Jun Tsuruta, Masayuki Hideshima, Yasuyuki Kimura, Hiroshi Nitta, Kouji Araki. Effect of the haptic 3D virtual reality dental training simulator on assessment of tooth preparation. Journal of Dental Sciences. 2022.01; 17(1); 514-520
- 11. Suzuki H, Sugimoto K, Kubota-Miyazawa A, Noritake K, Umemori S, Araki K, Adachi N, Otsuka H, Yoshida N. A survey of oral health status, subjective oral symptoms and oral health behaviors among first-year dental students at a Japanese university. Journal of oral science. 2022.01; 64(1); 85-90
- 12. Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 560-567
- Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes with immediate- loaded two-implant-supported mandibular overdentures: Results of a 5-year prospective study. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 70-77
- 14. Suzuki Hitomi, Sugimoto Kumiko, Kubota-Miyazawa Ayako, Noritake Kanako, Umemori Sachi, Araki Kouji, Adachi Naoko, Otsuka Hiromi, Yoshida Naomi. A survey of oral health status, subjective oral symptoms and oral health behaviors among first-year dental students at a Japanese university. Journal of Oral Science. 2022.01; 64(1); 85-90
- 15. Tanabe G, Hattori M, Obata S, Takahashi Y, Churei H, Nishiyama A, Ueno T, Sumita YI. Case Report: Psychoacoustic Analysis of a Clarinet Performance With a Custom-Made Soft Lip Shield Worn to Prevent Mucosal Erosion of Lower Lip. Frontiers in psychology. 2022; 13; 852866
- 1. Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study Journal of oral and sleep medicine. 2022.05; 8(3); 64-72

[Books etc]

1. Miyachi Mai. Sleep Apnea Treatment for Dentist. Quintessence Publishing, 2022.08 (ISBN : 978-4-7812-0889-3)

[Misc]

- 1. TONAMI Ken-ichi. Issue and countermeasure of medical mistrust in Japan Scientific Journal of Japan Institute for Advanced Dentistry. 2022.11; 28(3); 182-185
- 2. Kitanaka Y, Takeuchi Y, Hiratsuka K, Nitta H, Iwata T, Aoki A. Application of antimicrobial photodynamic therapy in periodontal treatment 2022.06; 32(1); 9-14
- 3. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part15 The Introduction of Sleep Dentistry into General Dentists and the Prospect of the OSA Treatment. the Quintessence. 2022.03; 41(3); 172-179
- 4. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part14 Case Study:Treatment of Obstructive Sleep Apnea the Quintessence. 2022.02; 41(2); 166-178
- 5. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part13 The Screening and Clinical Diagnosis of Pediatric Obstructive Sleep Apnea and Its Treatment Options. the Quintessence. 2022.01; 4(1); 202-207

[Conference Activities & Talks]

- 1. Mitsuyuki Numasawa, Nobutoshi Nawa, Kumiko Yamaguchi, Kanako Noritake, Jun Tsuruta, Mina Nakagawa. Comparison of readiness for interprofessional learning among medical, dental, and nursing students before the start of clinical practice. AMEE 2022 2022.08.29 The Virtual Conference
- 2. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Janelle Moross, Jun Tsuruta. Remote interprofessional learning during the COVID-19 pandemic for younger undergraduate students' early exposure to medicine . AMEE 2022 2022.08.27
- 3. Rena Takahashi, Saki Uchiyama, Yuna Kanamori, Shin Rozan, Yutaro Oda, Takaaki Sato, Junichi Shinagawa, Masanao Inokoshi, Toru Nikaido, Junji Tagami, Yasushi Shimada. Comparison of the bond strength of CAD/CAM inlay restorations with a specific cement. The International Congress on Adhesive Dentistry 2022.06 Sapporo, Japan
- 1. Ken-ichi Tonami, Sachi Umemori, Kanako Noritake, Masayuki Hideshima, Arata Ebihara, Cao Ridan, Masayo Sunaga, Atsuhiro Kinoshita, Hiroshi Nitta. Development of an insurance claim training application using Microsoft Excel macro. The 87th Annual Meeting of The Stomatological Society 2022.12.03 Tokyo
- 2. Sachi Umemori, Miho Ishimaru, Yuji Uchimura, Ken-ichi Tonami, Kanako Noritake, Masayo Sunaga, Atsuhiro Kinoshita, Yasushi Shimada, Hiroshi Nitta, Jun Aida2. Analysis of factors affecting the prognosis of composite resin restorations using the Data Ware House system(DWH). The 87th Annual Meeting of The Stomatological Society 2022.12.03 Tokyo
- 3. Rena Takahashi, Taka
aki Sato, Motoi Takahashi, Yuna Kanamori , Yasushi Shimada. Effect of resin
 coating technique and cleaning method of dentin after removal of temporary sealing material on bond
 strength of CAD/CAM inlay restorations . 2022.12.03 Tokyo
- 4. MAI MIYACHI. Airway Analysis and A Fully Digital Workflow of Oral Appliance for the Treatment of Obstructive Sleep Apnea. The 21st Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2022.11.21 Okinawa Bankoku Shinryokan
- 5. Shoko Tobe, Hiroyuki Ishiyama, Keisuke Miyazono, Hiroko Kimura, Akira Nishiyama. Optimal intensity of jaw-opening exercise for functional pain in temporomandibular disorders: a randomized controlled trial. The 27th Annual Meeting of the Japanese Society of Orafacial Pain 2022.10.09
- 6. Remote interprofessional learning for younger undergraduate students' early exposure. 2022.08.05
- 7. TONAMI Ken-ichi, UMEMORI Sachi, NORITAKE Kanako, KANAMORI Yuna, NITTA Hiroshi. Development of perception of human relationship is different between online class and experiential learning. The 54th Annual Meeting of the japan Society for Medical Education 2022.08.05 Takasaki
- 8. Kanako Noritake, Sachi Umemori, Yuna Kanamori, Ken-ichi Tonami, and Hiroshi Nitta. How should early clinical exposure be implemented under the Covid-19 infection spread?. The 54th Annual Meeting of the japan Society for Medical Education 2022.08 Gunma

- 9. NITTA Hiroshi. The evaluation method in the dentist clinical training system. The 41st General and Scientific Meeting of the Japanese Dental Education Association 2022.07.24 Web
- 10. KANAMORI Yuna, SEKI Naoko, NORITAKE Kanako, MOROSS Janelle, SUNAGA Masayo, TONAMI Ken-ichi, MORIO Ikuko, KINOSHITA Atsuhiro, NITTA Hiroshi. Dental English course for trainee residents at Tokyo Medical and Dental University (TMDU) Hospital. The 41st General and Scientific Meeting of the Japanese Dental Education Association 2022.07.23 Web
- 11. Tonami Ken-chi, Umemori Sachi, Noritake Kanako, Kanamori Yuna, Nitta Hiroshi. Task concerning informed consent expected to solve using prospect theory. The 41st General and Scientific Meetnig of the Japanese Dental Educaion Association 2022.07.23
- 12. Masayuki HIDESHIMA. Adoption to the social insurance system and clinical practice guidelines for magnetic attachment. The 131st Annual Meeting of the japan Prosthodontic Society, Clinical Lecture Series 4,Knowledge and skills of magnetic attachment for prosthodontists 2022.07.17 Osaka
- 13. Hiroyuki Ishiyama, Akira Nishiyama. A case of suspected sleep apnea for morning headache attributed to temporomandibular disorders. The 35th Annual Meeting of the Japanese Society for the Temporomandibular Joint 2022.07.02
- 14. A case of suspected sleep apnea for morning headache attributed to temporomandibular disorders. 2022.07
- 15. Factors affecting continuous employment of newly graduated and reinstated dental hygienists attended a training course. 2022.07
- 16. Miyachi Mai. Medical-dental collaboration in sleep-disordered breathing treatment Let's ask each other - What we want to ask the medical department about CPAP treatment. The 47th annual meeting of Japanese society of sleep research 2022.06.30

[Others]

 Prognosis of treatment effect for sleep apnea with oral appliance therapy - videoendoscopic evaluation for the predicting model -, 2022.04 Masayuki HIDESHIMA Grant-in-Aid for Scientific Research(C) 2022 Research No. 22K10051 Research Period 2012-2024 Principal Investigator Masayuki HIDESHIMA Research Fund \3,200,000

Psychosomatic Dentistry

Professor Akira Toyofuku Junior Associate Professor Motoko Watanabe Assistant Professor Yasuyuki Kimura Hospital Staff Chihiro Takao Hospital Staff Chizuko Maeda Hospital Staff Risa Tominaga Graduate Student Mitsuhiro Asami Graduate Student Atsushi Ito Graduate Student Hong Chaoli Graduate Student Hong Chaoli Graduate Student Chihiro Takao Graduate Student Kiyokazu Iwawaki Graduate Student Liu Zhenyan Graduate Student Gayatri Nayanar Graduate Student Chizuko Maeda

Lecturer (part-time) Haruhiko Motomura Lecturer (part-time) Jiro Kurata Lecturer (part-time) Takahiko Naganine

(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 trough 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-Dopamin 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

- 1. Chaoli Hong, Yoshinori Hayashi, Suzuro Hitomi, Ryoko Kurisu, Kentaro Urata, Ikuko Shibuta, Akira Toyofuku, Koichi Iwata, Masamichi Shinoda. Astrocytic and microglial interleukin-1 β mediates complement C1q-triggered orofacial mechanical allodynia. Neurosci Res. 2022.11;
- 2. Ayano Katagiri, Kazuo Tsubota, Lou Mikuzuki, Shigeru Nakamura, Akira Toyofuku, Takafumi Kato, David A Bereiter, Koichi Iwata. Diquafosol sodium reduces neuronal activity in trigeminal subnucleus caudalis in a rat model of chronic dry eye disease. Neurosci Lett. 2022.10; 792; 136939

- 3. Satoko Sumi, Takahiko Nagamine, Koji Sumi, Reona Aijima, Kyoko Oka, Akira Toyofuku. Case report: Open bite as an extrapyramidal side effect with aripiprazole, a dopamine partial agonist. Front Psychiatry. 2022.09; 13; 976387
- 4. Satoshi Kasahara, Chihiro Takao, Ko Matsudaira, Naoko Sato, Trang Thi Huyen Tu, Shin-Ichi Niwa, Kanji Uchida, Akira Toyofuku. Case report: Treatment of persistent atypical odontalgia with attention deficit hyperactivity disorder and autism spectrum disorder with risperidone and atomoxetine. Front Pain Res (Lausanne). 2022.08; 3; 926946
- 5. Masafumi Utsunomiya, Hirofumi Matsuoka, Miho Takenoshita, Akira Toyofuku, Hiroko Miura, Yoshihiro Abiko. The influence of intolerance of uncertainty on the correlation between the severity of symptoms and satisfaction with oral state in patients with burning mouth syndrome. Clin Oral Investig. 2022.07;
- 6. Motoko Watanabe, Tetsuo Nakabayashi, Gayatri Nayanar, Chihiro Takao, Chizuko Maeda, Trang Thi Huyen Tu, Haruhiko Motomura, Akira Toyofuku. Case Report: Auditory Hallucination Induced by Amitriptyline for the Treatment of Atypical Odontalgia. Front Psychiatry. 2022.05; 13; 863485
- 7. Motoko Watanabe, Chihiro Takao, Zhenyan Liu, Gayatri Nayanar, Takayuki Suga, Chaoli Hong, Trang Thi Huyen Tu, Tatsuya Yoshikawa, Miho Takenoshita, Haruhiko Motomura, Takahiko Nagamine, Akira Toyofuku. The Effectiveness and Adverse Events of Amitriptyline and Aripiprazole in Very Elderly Patients With BMS. Front Pain Res (Lausanne). 2022.03; 3; 809207
- 8. Takayuki Suga, Takahiko Nagamine, Trang T H Tu, Keiji Moriyama, Akira Toyofuku. Orthognathic Surgery for Patients with Neurodevelopmental Disorders Requires Careful Decision-making by a Multidisciplinary Team. Innov Clin Neurosci. 2022; 19(4-6); 9-10

[Misc]

- Durga Paudel, Osamu Uehara, Sarita Giri, Koki Yoshida, Tetsuro Morikawa, Takao Kitagawa, Hirofumi Matsuoka, Hiroko Miura, Akira Toyofuku, Yasuhiro Kuramitsu, Tohru Ohta, Masanobu Kobayashi, Yoshihiro Abiko. Effect of psychological stress on the oral-gut microbiota and the potential oral-gut-brain axis. Jpn Dent Sci Rev. 2022.11; 58; 365-375
- 2. T T H Tu, M Watanabe, A Toyofuku, U Yojiro. Phantom bite syndrome. Br Dent J. 2022.06; 232(12); 839-840
- 3. Psychostomatology: The psychosomatic status and approaches for the management of patients with inflammatory oral mucosal diseases Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2022.02; 34; 200-208

[Conference Activities & Talks]

- 1. 木村康之, 則武加奈子, 礪波健一, 新田浩, 豊福明. 臨床研修歯科医向け歯科医療安全教育プログラムの開発. 第 87 回口腔病学会学術大会 2022.12.03 東京
- 2. 高橋周平、Paudel Durga、吉田光希、森川哲郎、宇都宮雅史、Giri Sarita、佐藤淳、松岡紘史、豊福明、 安彦善裕. 口腔扁平苔癬患者の心身医学的背景とアプローチーシステマチックレビュー. 第 37 回日本歯科心 身医学会総会 · 学術大会 2022.07.09 web 開催
- 1. Chizuko Maeda, Motoko Watanabe, Risa Tominaga, Akira Toyohuku. Current trends of the out-patients with oral psychosomatic disorders during pandemic of COVID-19 at our department in 2021. 2022.11.04

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 provides 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

- $\cdot\,$ Needs assessment in health care and in professional development in health science fields
- $\cdot~$ Curriculum development for professionals of the future needs in health sciences

(3) Education

Undergraduate schools

Courses

- \cdot School of medicine (1st year): Medical Introductory Courses
- · Schools of medicine/dentistry (2nd/3rd years): Global Communication for Health Professionals
- \cdot School of medicine (4th year): Preparation for Clinical Clerkship
- \cdot 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
- \cdot Health Sciences Leadership Program: Problem-solving in the Health Sciences

Graduate school

Course

- · [Master level] Public Health Biology
- · [Master level] Health Systems Management

(4) Clinical Services & Other Works

Medical Hospital Kazuki TAKADA (Rheumatology) Comprehensive Patient Care

(5) Publications

[Misc]

1. Kazuki Takada. 22. Clinical Clerkship White Paper on Medical Education 2022. 2022.07; 79-83

Department of General Medicine

Masayoshi Hashimoto Toru Yamada Masashi Beppu Suguru Mabuchi Yu Akaishi Shoko Yoshida Risa Suzuki Yuki Goto Takahiro Shinohara Mari Fukuhara

Masako Sugihara Yuya Ando Akane Futami Hiroshi Koike Kota Hada Kaname Dateoka Mari Miya

Shuji Ouchi Hiroki Nin Hiroki Sekiguchi Maki Goto Risa Narita Kouki Kiyama Azusa Aoshima Seiya Sato Ryota Takaishi Tsukasa Tabuchi Rio Tsuruwaka Hironori Yamada

(1) Outline

"Ambition" and "Passion" Keys for Family Medicine/General Medicine Share your "Ambition" with us. You may think it impossible to become true. Believe me, we are here for you. We can take it with all our strength and our heart Exert your passionate ebullience We are ready to support you.

Backgrounds and Aims

TMDU General Medicine/Family Medicine Network (TMUDGM/FM-N) is a network of hospitals and clinics which engage in practice, education, and research related to general medicine/family medicine or primary health care. More than ten healthcare institutions join the TMUDGM/FM-N in Tokyo Ward and a few prefectures surrounding Tokyo, Japan. The TMUDGM/FM-N is also known as a network for physicians and other professionals who engage in these activities. Members of the TMUDGM/FM-N build a weak tie with each other or facility, and collaborate closely in each activity.

The TMUDGM/FM-N engages in following activities for people in community all over the world to stay in healthy and happy lives:

1. To conduct research more efficiently and provide effective practices in general medicine/family medicine and primary health care.

2. To foster general medicine, family physicians, general practitioners, and healthcare professionals, who can practice in the field of general medicine/family medicine and primary health care

3. To nurture more advanced personnel who can educate general medicine/family physicians, healthcare professionals, educators, or researchers in the field of general medicine/family medicine and primary health care.

Our Activity

Education

The TMUDGM/FM-N provide educations about general medicine/family medicine, and primary healthcare, for each generation of healthcare professionals, such as medical students, junior residents, and senior residents. As well, we provide inter-professional educations for the various medical professionals. Although some of our educations are provided in TMDU, lots of parts are undertaken in clinics and hospitals in community.

The TMUDGM/FM-N weighs importance on career-long education for general medicine/family physicians and other collaborating healthcare professionals. As well, we have activities of continuous medical education on themes related to general medicine/family medicine.

Graduate School

The TMUDGM/FM-N provides education and research for TMDU Graduate School of Medical and Dental Sciences. The TMUDGM/FM-N accepts international students from all over the world.

In our graduate school, we want students to learn how to resolve problems in the real community via research. Our research should not be mere finding or exploring the facts, but contribute towards people in communities. Research is only one of the tools for resolving problems in communities, improving clinical practices, and contributing to patients and people in community. Therefore, we should keep in our mind to implement the research findings into the real world.

To enable students to fulfill our aims above mentioned, we provide didactic lectures about general medicine/family medicine, biostatistics, clinical epidemiology, qualitative research, how to build questionnaire and so on. However, attending these lectures for students is not enough to resolve problems in communities and they should: approach the target community or field; get familiar with the people living there; feel known or unknown needs from the people living there; and suggest some resolution for their needs or problems. These processes require students not only technical and academic skills, but also communication or social skills. As well, these processes train students to learn by their own mistakes. Therefore, we provide students safe environments to think their own interests for themselves.

Research

The TMUDGM/FM-N conducts research several themes in general medicine/family medicine, communication, community medicine, and medical education. We especially focus on the behavioral aspects of patients and medical professionals, as well as collaborations between specialties or healthcare professionals. We use both quantitative and qualitative approaches.

The examples of ongoing research are as follows:

1. Research on the relationship between the characteristic of physicians and patients' medical seeking behavior or their health status

- 2. Research on non-verbal communication using artificial intelligence (AI)
- 3. reliability and validity of apparatus used in primary care setting (ultrasound, etc.)
- 4. Cost-effectiveness of the home care
- 5. Collaboration between primary care physicians and occupational physicians
- 6. To establish the method to build better team in medical setting
- 7. Relationship between the basis of the family medicine and health outcomes
- 8. Inter-professional education for students in medical school

9. Home visiting care for elderly in community

10. Other researches of family medicine/general medicine

Practice

The TMUDGM/FM-N provides care for the people living in their own community, in their own clinics or hospitals besides at outpatient department and wards in TMDU university hospital. Our practice is based on the principles and methods for the general medicine/family medicine, or primary healthcare. Additionally, we weigh importance on the collaboration between specialties, between healthcare professionals, between medical facilities, and between healthcare system and community. Moreover, we try to learn about the newest evidences for all the disease we can be involved.

(2) Publications

- Yuya Ando, Toshifumi Yodoshi, Takashi Yoshioka. Comment on "Food processing and risk of Crohn's disease and ulcerative colitis: A European Prospective Cohort Study". Clin Gastroenterol Hepatol. 2022.11;
- 2. Ando Y, Ono Y, Sano A, Fujita N, Ono S. Subacute Thyroiditis after COVID-19: A Literature Review. The American journal of tropical medicine and hygiene. 2022.09; 107(5); 1074-1082
- 3. Y Ando, Y Ono, A Sano, N Fujita, S Ono, Y Tanaka. Clinical characteristics and outcomes of pheochromocytoma crisis: a literature review of 200 cases. J Endocrinol Invest. 2022.07;
- 4. Uchihara Masaki, Ehara Jun, Iwanami Keiichi, Kitamura Koichi, Suzuki Toshihiko, Ishizuka Noriyoshi, Yamada Toru, Hiraoka Eiji. Chylous Ascites Due to Hyperthyroidism and Heart Failure(和訳中) Internal Medicine. 2022.07; 61(13); 1995-1998
- Yuya Ando, Yosuke Ono, Yoshinori Miura. Salmon-pink skin rashes in adult-onset Still's disease. Am J Med Sci. 2022.06; 365(2); e17-e18
- 6. Yuya Ando, Satoko Senda, Yosuke Ono. Skin rash following amoxicillin treatment. Eur J Intern Med. 2022.05; 102; 114-115
- 7. Yuya Ando, Azusa Sano, Yosuke Ono. Primary central nervous system lymphoma mimicking brain hemorrhage. Am J Med Sci. 2022.05; 364(4); e19-e20
- 8. Yuya Ando, Yosuke Ono, Sachiko Ono. Pheochromocytoma-related posterior reversible encephalopathy syndrome. Am J Med Sci. 2022.04; 364(3); e29-e30
- 9. Goto Yuki, Yamada Toru, Nagamine Yuiko, Mabuchi Suguru, Akaishi Yu, Yoshida Shoko, Suzuki Risa, Masanaga Yamawaki. COVID-19 が疑われた外来患者の疫学および臨床的特徴 大学病院の COVID-19 外来センターで実施した前向き観察研究 (Epidemiology and clinical characteristics of outpatients with suspected COVID-19: A prospective observational study from the COVID-19 outpatient center at a university hospital) Journal of Hospital General Medicine. 2022.03; 4(2); 57-65
- Ando Y, Ono S, Ono Y, Miura Y. Hypertrichosis and topical corticosteroid use. Cleveland Clinic journal of medicine. 2022.02; 89(2); 71-72
- 11. Taiju Miyagami, Toru Yamada, Yohei Kanzawa, Shunsuke Kosugi, Kazuya Nagasaki, Hiroyuki Nagano, Taro Shimizu, Kazutoshi Fujibayashi, Gautam A Deshpande, Toshio Naito. Large-Scale Observational Study on the Current Status and Challenges of General Medicine in Japan: Job Description and Required Skills International Journal of General Medicine. 2022.01; 15; 975-984
- Yamada Toru, Suzuki Risa, Ichimura Naoya, Mabuchi Suguru, Nagamine Yuiko, Sassa Chihiro, Tohda Shuji. Clinical Evaluation of Reverse Transcription-Polymerase Chain Reaction and Rapid Antigen Tests of Tongue Swabs for Detecting COVID-19(和訳中) Journal of Hospital General Medicine. 2022.01; 4(1); 12-20

13. Yamada Toru, Suzuki Risa, Ichimura Naoya, Mabuchi Suguru, Nagamine Yuiko, Sassa Chihiro, Tohda Shuji. COVID-19 検出を目的とした舌スワブ検体での逆転写 PCR 法と迅速抗原検査による臨床評価 (Clinical Evaluation of Reverse Transcription-Polymerase Chain Reaction and Rapid Antigen Tests of Tongue Swabs for Detecting COVID-19) Journal of Hospital General Medicine. 2022.01; 4(1); 12-20

Infectious Diseases

Professor GU Yoshiaki Associate professor / lecturer TAGASHIRA Yasuaki Assistant professor KURITA Takashi Assistant professor (Division of Infection Control and Prevention) IDE Satoshi Project researcher AGATA Chikako Project researcher SAKAGUCHI Mikiyo Secretary FUNADA Eriko

(1) Outline

The Department of Infectious Diseases is in charge of research and education with a focus on clinical infectious diseases. We are in charge of clinical practice of infectious diseases and infection prevention and control at Tokyo Medical and Dental University Hospital. We conduct epidemiological research on infectious diseases and other researches, as well as educational activities on infectious diseases in general.

In addition, as the core of TMDU's "Platform Project for Multilayered Efforts to Conquer Infectious Disease Pandemics," the department plays a role in promoting infectious disease research and education at the university.

(2) Research

We conduct clinical and epidemiological research on infectious diseases from various perspectives, with a focus on research on the proper use of antimicrobials and the control of hospital-acquired infections.

Among these, we are focusing on hospital epidemiology research related to antimicrobial resistance (AMR), which has become a major problem in Japan and worldwide, and research aimed at changing the behavior of healthcare workers and the general public by investigating their awareness of AMR.

In collaboration with the Tokyo Metropolitan Government, we are also conducting research on the response of medical institutions and public health to the COVID-19 pandemic.

(3) Education

We are committed to training the infectious disease specialists who will lead the future. Since infectious diseases are related to all aspects of healthcare, it is also important to increase the number of physicians who are trained in basic infectious disease treatment and infection prevention and control. Education for multiple professions is also important. We are committed to human resource development by providing education at various stages.

Pre-graduate education

We are in charge of lectures and practical training related to clinical infectious disease treatment and infection prevention and control, focusing on lectures for third-year medical students and clinical clerkship for five/six-year medical students. We devise ways for students to learn with interest the basics of clinical infectious diseases that all physicians and health care workers should learn.

Post-graduate education

We offer programs that match your previous experience and career plans, including initial residency , major residency, and fellowship to become a specialist.

Graduate Education

We aim to train professionals to tackle infectious diseases from multiple perspectives, with a focus on clinical infectious diseases and infectious disease epidemiology.

Topics include AMR control, hospital epidemiology, and control of hospital acquired infections.

Continuing Education

In all areas of clinical practice, you will be involved in the treatment of infectious diseases to a greater or lesser extent. We contribute to lifelong education by providing information on the diagnosis and treatment of infectious diseases.

We are also involved in education for pharmacists, nurses, clinical laboratory technicians, and other professionals.

(4) Lectures & Courses

The program aims to train professionals to tackle infectious diseases from multiple perspectives, with a focus on clinical infectious diseases and infectious disease epidemiology.

(5) Clinical Services & Other Works

We are in charge of the Department of Infectious Diseases and the Division of Infection Control and Prevention at Tokyo Medical and Dental University Hospital.

The Department of Infectious Diseases is a new department established in October 2021. Focusing on consultations from various departments, our department diagnoses and treats a variety of infectious diseases that occur mainly in inpatients. The department identifies the microorganisms that are causing symptoms of infections such as fever and other suspected infectious diseases, and selects the most appropriate treatment according to the microorganisms and the patient's condition.

The Division of Infection Control and Prevention is responsible for preventing infectious diseases that occur in the hospital, preventing their spread, and providing a safe environment for patients to receive medical care. We work as a multidisciplinary team in cooperation with all related departments.

We are working to promote the proper use of antimicrobial agents to prevent antimicrobial resistance (AMR), which has become a major problem in recent years. The Department of Infectious Diseases and the Department of Infection Control are working together to monitor the use of antimicrobials and to improve AMR control and treatment outcomes by optimizing the treatment of infectious diseases.

Outside of the university, we have a project with the Tokyo Metropolitan Government for the "Project for Strengthening the Capacity of Small and Medium-Sized Hospitals to Respond to Infectious Disease Health Crises in the Post-Coronary Era" as a three-year plan starting in FY2022. We are also involved in a variety of other activities, including academic conferences and public activities.

(6) Clinical Performances

The Department of Infectious Diseases provides clinical consultation services in response to consultations from various departments. It provides support to each department by dealing with various infectious diseases regardless of the organ, and contributes to the diagnosis and treatment of infectious diseases throughout the University Hospital. The Division of Infection Control and Prevention focuses on the prevention of infectious diseases. Through these activities, the department plays a role in supporting advanced medical care at the university hospital.

(7) Publications

- 1. Kusama Yoshiki, Miyahara Mitsuoki, Ishikane Masahiro, Suzuki Kumiko, Gu Yoshiaki, Sasaki Jun, Ohmagari Norio. Physician practices in the diagnosis and treatment of infectious diseases in home care settings: A questionnaire study(タイトル和訳中) Global Health & Medicine. 2022.10; 4(5); 268-272
- 2. Hongo M, Harada Y, Shimizu T, Gu Y. Acute cytomegalovirus infection in a 61-year-old woman. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2022.08; 194(32); E1109-E1111-E1111
- 3. Nomoto H, Ishikane M, Gu Y, Yamamuro R, Osawa R, Hosokawa N, Sahara T, Nakamura-Uchiyama F, Fukushima K, Sekiya N, Imamura A, Fujikura Y, Kawana A, Nagata K, Tamura K, Kutsuna S, Ohmagari N. Nationwide descriptive epidemiological study of patients with COVID-19 evacuated from Wuhan, China, to Japan from January to February 2020. Japanese journal of infectious diseases. 2022.08; 76(1); 20-26
- 4. Saito N, Kitazawa J, Horiuchi H, Yamamoto T, Kimura M, Inoue F, Matsui M, Minakawa S, Itoga M, Tsuchiya J, Suzuki S, Hisatsune J, Gu Y, Sugai M, Kayaba H. Interhospital transmission of vancomycin-resistant Enterococcus faecium in Aomori, Japan. Antimicrobial resistance and infection control. 2022.07; 11(1); 99
- 5. Inoue Kenji, Kobayashi Seiichi, Sato Keigo, Kanno Hitoshi, Kantou Rina, Naganuma Yuka, Kawamura Naomi, Oike Yasunori, Kobayashi Michio, Yanai Masaru, Suzuki Akira, Kurai Hanako, Miyairi Isao, Kutsuna Satoshi, Gu Yoshiaki. Regional Antimicrobial Stewardship Program in a Provincial Medical Zone in Japan: a Multifaceted Approach(和訳中) Japanese Journal of Infectious Diseases. 2022.07; 75(4); 347-354
- 6. Yusuke Ota, Isaac Prah, Yoko Nukui, Ryuji Koike, Ryoichi Saito. blaKPC-2-Encoding IncP-6 Plasmids in Citrobacter freundii and Klebsiella variicola Strains from Hospital Sewage in Japan. Appl Environ Microbiol. 2022.04; e0001922
- 7. 具 芳明. 新型コロナウイルス (COVID-19) ワクチンの現状と今後 長野県薬誌りんどう. 2022.04; (561); 13-15
- 8. Mishima Y, Nosaka N, Oi K, Gu Y, Arai H. Tracheobronchial aspergillosis presenting with black mucus plugs and tracheal ulcers. Clinical case reports. 2022.02; 10(2); e05456
- 9. Ishibashi N, Pauwels I, Tomori Y, Gu Y, Yamaguchi T, Handa T, Yamaoka M, Ito D, Sakimoto T, Kimura T, Takizawa K, Sato R, Sakashita T, Ooyama A, Versporten A, Goossens H, Tarumoto N, Maesaki S, Tanahashi N. Point Prevalence Surveys of Antimicrobial Prescribing in a Non-Acute Care Hospital in Saitama Prefecture, Japan. The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale. 2022; 2022; 2497869
- Kusama Y, Miyahara M, Ishikane M, Suzuki K, Gu Y, Sasaki J, Ohmagari N. Physician practices in the diagnosis and treatment of infectious diseases in home care settings: A questionnaire study. Global health & medicine. 2022; 4(5); 268-272
- 1. Hidetoshi Nomoto, Hiroki Saito, Masahiro Ishikane, Yoshiaki Gu, Norio Ohmagari, Didier Pittet, Hiroyuki Kunishima, Benedetta Allegranzi, Masaki Yoshida. First nationwide survey of infection prevention and control among healthcare facilities in Japan: impact of the national regulatory system. Antimicrobial resistance and infection control. 2022.11; 11(1); 135

[Conference Activities & Talks]

1. 田頭 保彰, 高松 茜, 切替 照雄. SARS-CoV-2 における COVID-19 の重症度とスパイクおよびヌクレオカプシド タンパク質に対する免疫グロブリンの存在との相関 (Correlation of COVID-19 severity and immunoglobulin presence against spike and nucleocapsid proteins in SARS-CoV-2). 感染症学雑誌 2022.03.01

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio Lecturer : SAITO Kenta Assistant Professor: KAWAGISHI Masahiko Assistant Professor: SATO Keisuke Graduate Student : HANAOKA Miho Graduate Student, MD-PhD Course : NAKAI-KADOWAKI Nori Affiliated Researcher: SUGIZAKI Ayana Lab Manager, Administrative Assistant: TAGUCHI Mie

(1) Outline

Our research group uses both cell biological and biophysical methods to address problems in basic cellular morphology. Specifically, we are interested in the basic molecular mechanism of cytoskeletal dynamics and intercellular communication and have been gaining important insights through our work with methodologies ranging from transgenic animals to cutting-edge spectroscopies. Our active faculty members are engaged in the training of both graduate and medical students through various training programs, research seminars, and journal clubs, and lots of exciting collaborative research efforts with colleagues around the world are now in progress.

(2) Research

We are cell biologists and biophysicists who study how the dynamics of cytoskeletal proteins are regulated. We are also interested in the intracellular communications that support cellular functions, especially those of the nervous system. Visualization or live cell imaging is a key to approach our common research interests, and our work spans multiple disciplines or methodologies such as microscopies, spectroscopies, and probe developments. Our lab has focused in three major directions we are taking with several collaborators.

(1) By utilizing newly developed probe technique POLArIS for fluorescence polarization microscopy, we are now focusing on discovering previously unknown phenomena around cytoskeletal structures, and deciphering their functional significance.

We have been collaborating with Dr. Tomomi Tani, microscopist at the Marine Biological Laboratory at Woods Hole (now at the National Institute of Advanced Industrial Science and Technology) on this matter.

(2) We also try to establish effective probes to detect functional intracellular communication to find the logics of neuronal signal transductions.

(3) In addition to live cell imaging, we are interested in development of spectroscopic techniques such as fluorescent correlation spectroscopy and Raman spectroscopy.

Regarding Raman spectroscopy, we have a long-standing collaboration with Prof. Kazuhiko Misawa at Tokyo University of Agriculture and Technology.

By combining cutting edge microscopic and spectroscopic technologies with molecular genetics and modelling, we try to solve questions such as: How cytoskeletal dynamics are regulated? How the cell shape is controlled? How the function of the nervous system is maintained?

(3) 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.

(4) **Publications**

[Misc]

1. Takase H, Arai A, Iwasaki Y, Imai A, Nagao T, Kawagishi M, Ishida T, Mochizuki M. Challenges in the diagnosis and management of vitreoretinal lymphoma - Clinical and basic approaches. Progress in retinal and eye research. 2022.02; 101053

[Conference Activities & Talks]

- 1. Keisuke Sato, Nori Nakai-Kadowaki, Ayana Sugizaki, Kazuyoshi Chiba, Kenta Saito, Masahiko Kawagishi, Yuri Tomabechi, Shalin B. Mehta, Hirokazu Ishii, Naoki Sakai, Hiromasa Ka, Mikako Shirouzu, Tomomi Tani, Sumio Terada. Development of POLArIS, a versatile probe for multi-color/multi-target orientation imaging in living cells. Cell Bio 2022 2022.12.04 Washington, DC
- 2. Nori Nakai, Keisuke Sato, Tomomi Tani, Masahiko Kawagishi, Hiromasa Ka, Kenta Saito, Sumio Terada. EXPANDED REPERTOIRE OF POLARIS, A VERSATILE FLUORESCENT PROBE FOR MOLECULAR ORIENTATION. Biophysical Society 66th Annual Meeting 2022.02.23 USA
- 3. Nori Nakai, Keisuke Sato, Tomomi Tani, Masahiko Kawagishi, Hiromasa Ka, Kenta Saito, Sumio Terada. EXPANDED REPERTOIRE OF POLARIS, A VERSATILE FLUORESCENT PROBE FOR MOLECULAR ORIENTATION.. Biophysical Society 66th Annual Meeting 2022.02.23
- 4. Nakai Nori, Sato Keisuke, Tani Tomomi, Kawagishi Masahiko, Ka Hiromasa, Saito Kenta, Terada Sumio. Expanded repertoire of polaris, a versatile fluorescent probe for molecular orientation. 66th Biophysical Society Annual Meeting 2022.02.20 San Francisco, California, USA
- 1. Nori Nakai-Kadowaki , Keisuke Sato, Tomomi Tani, Masahiko Kawagishi, Hiromasa Ka, Kenta Saito, Sumio Terada. Nanobody-based POLArIS: a versatile molecular orientation probe with options of colors and fluorescence polarization orientations. 2022.09.29
- 2. Nori Nakai-Kadowaki, Keisuke Sato, Tomomi Tani, Masahiko Kawagishi, Hiromasa Ka, Kenta Saito, Sumio Terada. Development of nanobody-based POLArIS orientation probes enabled multi-color/multi-target molecular orientation imaging. The 74th Annual Meeting of the Japanese Society for Cell Biology 2022.06.30 Tokyo, Japan
- 3. Keisuke Sato, Ayana Sugizaki, Kazuyoshi Chiba, Kenta Saito, Masahiko Kawagishi, Shalin B. Mehta, Mikako Shirouzu, Tomomi Tani, Sumio Terada. Development of POLArIS, a versatile probe for molecular orientation, and its application to the analysis of actin dynamics in living cells. The 74th Annual Meeting of the Japanese Society for Cell Biology 2022.06.29 Tokyo, Japan
- 4. Keisuke Sato, Ayana Sugizaki, Kazuyoshi Chiba, Kenta Saito, Masahiko Kawagishi, Shalin B. Mehta, Mikako Shirouzu, Tomomi Tani, Sumio Terada. Development of POLArIS, a versatile probe for molecular orientation, and its application to the analysis of cytoskeleton dynamics. 2022.01.08 Nagoya

Systems Neurophysiology

Professor Izumi Sugihara Associate Professor Yuriko Sugiuchi Lecturer Yoshiko Izawa Lecturer Mayu Takahashi JSPS Postdoctoral fellow Yuanjun Luo Support Member Satomi Amano Students (dorcor) 7

(1) Outline

Department of Systems Neurophysiology, formarly 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 four "elective research course" students.

(5) Publications

[Original Articles]

- 1. Takahashi M, Sugiuchi Y, Shinoda Y.. Neural substrates for generation of oblique saccades Equilibrium Research. 2022.04; 81(2); 67-78
- 2. Takahashi Mayu, Sugiuchi Yuriko, Na Jie, Shinoda Yoshikazu. Brainstem Circuits Triggering Saccades and Fixation Journal of Neuroscience. 2022.02; 42(5); 789-803
- 3. Spaeth Ludovic, Bahuguna Jyotika, Gagneux Theo, Dorgans Kevin, Sugihara Izumi, Poulain Bernard, Battaglia Demian, Isope Philippe. Cerebellar connectivity maps embody individual adaptive behavior in mice Nature Communications. 2022.01; 13(1); 580
- 4. Nguyen-Minh Viet, Wang Tianzhuo, Khoa Tran-Anh, Sugihara Izumi. Heterogeneity of intrinsic plasticity in cerebellar Purkinje cells linked with cortical molecular zones iScience. 2022.01; 25(1); 103705

[Conference Activities & Talks]

- 1. Takahashi Mayu, Sugiuchi Yuriko, Shinoda Yoshikazu. Brainstem neural circuits for triggering saccades. The Journal of Physiological Sciences 2022.12.01
- 2. Mayu Takahashi. Brainstem neural circuits for saccades. Johns Hopkins Cerebellum Seminars 2022.08.30
- 3. Mayu Takahashi, Yuriko Sugiuchi, Yoshikazu Shinoda. Neural substrates for generation of oblique saccades -Branching patterns of single tectofugal neurons. Neural Control of Movement, Annual Meeting 2022.07.26 Dublin, Ireland
- 4. Mayu Takahashi. Neural circuits suppressing brainstem omnipause neuron activity and triggering saccadic eye movements. Neural Control of Movement, Satellite Meeting in honor of Mike King 2022.07.25 Dublin, Ireland
- 5. Mayu Takahashi. Neural Circuits Triggering Saccades and Fixation. 第 99 回日本生理学会大会 2022.03.16 仙台

Molecular Neuroscience

Professor Kohichi Tanaka Assistant Professor Yuichi Hiraoka Assistant Professor Tetsuo Ohnishi

Graduate Student (doctor course) Bi Haining Zhao Di

Graduate Student (master course) Mahito Mitumasa

(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. Attention-deficit/hyperactivity disorder (ADHD) is a common neuropsychiatric disorder in children. We report the generation of mice expressing only 20% of normal levels of the GLT1. These mice exhibit ADHD-like phenotypes, including hyperactivity, impulsivity and impaired memory. These findings indicate that GLT1 dysfunction may underlie ADHD-like symptoms.

2. Role of glial engulfment in motor learning

Synaptic pruning is a fundamental process of neuronal circuit refinement in learning and memory. Accumulating evidence suggests that glia participates in sculpting the neuronal circuits through synapse engulfment. However, whether glial involvement in synaptic pruning has a role in memory formation remains elusive. In this study, we developed a genetic strategy for visualizing phagocytic events to reveal the involvement of glial phagocytosis in the pruning process. We found that Bergmann glia (BG) have a high phagocytic capacity in naive healthy mouse cerebellar cortex (Fig. 2). Furthermore, we found that synaptic engulfment by cerebellar BG frequently occurred upon cerebellum-dependent motor learning in mice. We observed increases in pre- and postsynaptic nibbling by BG along with a reduction in spine volume after learning. Pharmacological blockade of phosphatidylserine (PS)-dependent phagocytosis with Annexin V inhibited both the spine volume reduction and improvement of

the learned behavior. These results indicate that BG contribute to the refinement of the mature cerebellar cortical circuit through synaptic engulfment during motor learning.

3. Generation of vasoactive intestinal peptide (VIP)tTA knock-in mice

The suprachiasmatic nucleus (SCN), the central circadian clock in mammals, is a neural network consisting of various types of GABAergic neurons, which can be differentiated by the co-expression of specific peptides such as vasoactive intestinal peptide (VIP), arginine vasopressin (AVP), and gastrin-releasing peptide (GRP). VIP is expressed in about 10% of SCN neurons and has been considered as a critical factor for the circadian rhythmicity and synchronization of individual SCN neurons. However, the precise mechanisms of how VIP neurons regulate SCN circuits remain incompletely understood. Here, we generated ViptTA knock-in mice that express tetracycline transactivator (tTA) specifically in VIP neurons by inserting tTA sequence at the start codon of Vip gene. The specific and efficient expression of tTA in VIP neurons was verified using EGFP reporter mice. In addition, combined with Avp-Cre mice, ViptTA mice enabled us to simultaneously apply different genetic manipulations to VIP and AVP neurons in the SCN. Furthermore, because the transcription of the endogenous Vip coding sequence was blocked in the ViptTA allele, VIP was completely absent in homozygous mice of the line. Consistently, homozygous ViptTA mice showed impaired circadian behavioral rhythms similar to those of Vip knockout mice, such as attenuated rhythmicity and shortened circadian period. In contrast, heterozygous mice demonstrated normal circadian behavioral rhythms comparable to wild-type mice. These data suggest that ViptTA mice are a valuable genetic tool to express exogenous genes specifically in VIP neurons in both normal and VIP-deficient mice, facilitating the study of VIP neuronal roles in the SCN neural network.

(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. Yosuke M Morizawa, Mami Matsumoto, Yuka Nakashima, Narumi Endo, Tomomi Aida, Hiroshi Ishikane, Kaoru Beppu, Satoru Moritoh, Hitoshi Inada, Noriko Osumi, Eiji Shigetomi, Schuichi Koizumi, Guang Yang, Hirokazu Hirai, Kohichi Tanaka, Kenji F Tanaka, Nobuhiko Ohno, Yugo Fukazawa, Ko Matsui. Synaptic pruning through glial synapse engulfment upon motor learning. Nat Neurosci. 2022.11; 25(11); 1458-1469

2. Peng Yubo, Tsuno Yusuke, Matsui Ayako, Hiraoka Yuichi, Tanaka Kohichi, Horike Shin-ichi, Daikoku Takiko, Mieda Michihiro. Cell Type-Specific Genetic Manipulation and Impaired Circadian Rhythms in Vip(tTA) Knock-In Mice FRONTIERS IN PHYSIOLOGY. 2022.05; 13; 895633

Neuropathology

Professor: Hitoshi Okazawa Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone, Kyota Fujita Project Associate Professor: Hidenori Homma Lecturer: Hikari Tanaka Assistant Administrative Staff: Xuemei Zhang Secretary: Marie Tanaka Graduate Student : Kanoh Kondo(~ 2022.3), Yuki Yoshioka, Jin Meihua, Jin Xiaocen, Huang Yong, Sumire Takayama

(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

[Outline]

Following studies have been intensively carried out in our laboratory with various techniques including molecular biology, cell biology, biochemistry, Drosophila models, and mice models.

1)Investigation of molecular pathologies of neurodegenerative disease.

2)Development of new therapies for neurodegeneration.

3)Development of new seed drug for mental retardation.

4)Investigation of molecular function of Oct3/4.

[This year's progress]

Mind your Qs: polyQ-binding protein 5 scaffolds the nucleolus.

We find that PQBP5/NOL10, an intrinsically disordered protein, scaffolds the nucleolus under normal and stressed conditions and is bound by polyglutamine disease proteins.

Everyone has that one friend who's the life of the party, bringing people together and keeping everyone connected. Now, we find that an unusually structured protein plays a similar role in bringing a diverse group of proteins together and keeping them connected and functional.

In a study published recently in Nature Communications, we have revealed that an intrinsically disordered protein (IDP) is crucial for the stability of an organelle called the nucleolus.

Cognitive and Behavioral Medicine

The nucleolus is critical for transcribing ribosomal DNA, which encodes crucial components of the ribosome, an essential organelle for cellular maintenance, differentiation, and stress responses. Many proteins that are part of the nucleolus are IDPs that are susceptible to deformation and dysfunction in response to stressors such as temperature changes, low oxygen conditions, or dehydration.

We previously identified the IDP polyglutamine binding protein 5 (PQBP5), also known as nucleolar protein 10 (NOL10), in a screen for proteins that bind to polyglutamine (polyQ) tract sequences in proteins that cause polyQ diseases. PQBP5/NOL10 was later found to be a component of the nucleolus. the integrity of which has been implicated in the pathophysiology of neurodegenerative diseases.

To determine whether PQBP5/NOL10 is involved in maintaining the structural integrity of the nucleolus, we investigated its molecular characteristics, nucleolar sublocalization, relationship with other nucleolar proteins, and stress responses.

Unexpectedly, we found that PQBP5/NOL10 is a core structural element of the nucleolus, forming a meshwork that supports other nucleolar substructures. Even more intriguingly, unlike other nucleolar proteins that disperse to the nucleoplasm under osmotic stress conditions, PQBP5/NOL10 remains in the nucleolus and anchors reassembly of the nucleolar structure.

In addition, we found that PQBP5/NOL10 can essentially be sponged up by polyQ disease proteins, both in cells and in mice. This leads to deformation or even disappearance of the nucleoli.

Taken together, these findings indicate that PQBP5/NOL10 is an essential protein needed to maintain the structure of the nucleolus.

Given that polyQ proteins form aggregates with a dense core that often excludes polyQ-binding proteins, PQBP5/NOL10 may initially interact with soluble forms of these proteins before being pulled into larger inclusions. Aggregation inhibitors that prevent inclusion formation could therefore affect PQBP5/NOL10 distribution, and thus nucleolar stability, providing a novel approach to treating polyQ diseases.

(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 nerurodegenerative diseases.

(5) Publications

[Original Articles]

1. Shiwaku H, Katayama S, Kondo K, Nakano Y, Tanaka H, Yoshioka Y, Fujita K, Tamaki H, Takebayashi H, Terasaki O, Nagase Y, Nagase T, Kubota T, Ishikawa K, Okazawa H, Takahashi H. Autoantibodies against NCAM1 from patients with schizophrenia cause schizophrenia-related behavior and changes in synapses in mice. Cell Rep Med. 2022.04; 3(4); 100597

[Misc]

1. Tanaka H, Okazawa H. PQBP1: The Key to Intellectual Disability, Neurodegenerative Diseases, and Innate Immunity. Int J Mol Sci. 2022.06; 23(11); 6227

[Conference Activities & Talks]

- 1. Hitoshi Okazawa. Tau activates microglia via the PQBP1-cGAS-STING pathway to promote brain inflammation. The 51st Annual Meeting of the Japanese Society for Immunology(JSI2022) 2022.12.08 Kumamoto-Jo Hall(Kumamoto)
- 2. Hikari Tanaka, Kanoh Kondo, Kyota Fujita, Hidenori Homma, Kazuhiko Tagawa, Xiaocen Jin, Meihua Jin, Yuki Yoshioka, Sumire Takayama, Hitoshi Okazawa. HMGB1 signaling phosphorylates Ku70 and impairs DNA damage repair in Alzheimer's disease pathology. NEURO2022 2022.07.03 Okinawa Convention Center(Okinawa)
- 3. Meihua Jin, Hiroki Shiwaku, Hikari Tanaka, Yuki Yoshioka, Xiaocen Jin, Kanoh Kondo, Kyota Fujita, Hidenori Homma, Hitoshi Okazawa. Tau activates microglia via the PQBP1-cGAS-STING pathway to promote brain inflammation. NEURO2022 2022.07.01 Okinawa Convention Center(Okinawa)
- 4. Kyota Fujita, Hidenori Homma, Hikari Tanaka, Meihua Jin, Xiaocen Jin, Yong Huang, Yuki Yoshioka, Kanoh Kondo, Hiroki Shiwaku, Kazuhiko Tagawa, Hitoshi Okazawa. DNA damage in embryonic neural stem cell determines FTLDs' fate via early-stage neuronal necrosis. 63rd Annual Meeting of the Japanese Society of Neurology 2022.05.20 Tokyo International Forum(Tokyo)
- 5. Hikari Tanaka, Hidenori Homma, Kyota Fujita, Kanoh Kondo, Xiaocen Jin, Meihua Jin, Yuki Yoshioka, Sumire Takayama, Kazuhiko Tagawa, Hitoshi Okazawa. Effect of YAP-dependent necrosis in the ultra early stage on Alzheimer's disease pathology. 63rd Annual Meeting of the Japanese Society of Neurology 2022.05.20 Tokyo International Forum(Tokyo)
- 6. Meihua Jin, Hiroki Shiwaku, Hikari Tanaka, Takayuki Obita, Sakurako Ohuchi, Yuki Yoshioka, Xiaocen Jin, Kanoh Kondo, Kyota Fujita, Hidenori Homma, Kazuyuki Nakajima, Mineyuki Mizuguchi, Hitoshi Okazawa. Tau activates microglia via the PQBP1-cGAS-STING pathway to promote brain Inflammation. The 14th CBIR Symposium Inspiring the Next Generation(online) 2022.02.17

[Patents]

1. Methods for treating spinocerebellar ataxia type I using RPA1, Patent Number : EP 3056210

Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui Associate Professor;Takeshi Yoshida Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Shintaro Horie Assistant Professor; Tae Igarashi, Kengo Uramoto, Yuka Ohnishi, Noriko Nakao, Taiju Ito Graduate student; keijia Cao, Yuxin Fang, Ran Du, Xie Shi Qi, Xuejiao Li

(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 immunoregulartion 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 in 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. Mako Ota-Itadani, Hiroyuki Takahashi, Zaixing Mao, Tae Igarashi-Yokoi, Takeshi Yoshida, Kyoko Ohno-Matsui. Deep learning-based 3D OCT imaging for detection of lamina cribrosa defects in eyes with high myopia. Sci Rep. 2022.12; 12(1); 22195
- 2. Jianping Xiong, Ran Du, Shiqi Xie, Hongshuang Lu, Changyu Chen, Tae Lgarashi-Yokoi, Kengo Uramoto, Yuka Onishi, Takeshi Yoshida, Koju Kamoi, Kyoko Ohno-Matsui. Papillary and Peripapillary Hemorrhages in Eyes With Pathologic Myopia. Invest Ophthalmol Vis Sci. 2022.11; 63(12); 28
- Rosie Clark, Alfred Pozarickij, Pirro G Hysi, Kyoko Ohno-Matsui, Cathy Williams, Jeremy A Guggenheim,
 Education interacts with genetic variants near GJD2, RBFOX1, LAMA2, KCNQ5 and LRRC4C to confer susceptibility to myopia. PLoS Genet. 2022.11; 18(11); e1010478
- 4. Ran Du, Shiqi Xie, Hongshuang Lu, Changyu Chen, Jianping Xiong, Kengo Uramoto, Hiroyuki Takahashi, Yuka Onishi, Koju Kamoi, Noriko Nakao, Yuxin Fang, Kyoko Ohno-Matsui. Hospital-based study of risk factors associated with development of myopic macular neovascularization in highly myopic eyes. Ophthalmic Res. 2022.10;
- 5. Hongshuang Lu 1 , Ran Du, Shiqi Xie, Jianping Xiong, Changyu Chen, Muka Moriyama, Tae Igarashi-Yokoi, Hiroyuki Takahashi, Koju Kamoi, Kengo Uramoto, Noriko Nakao, Kyoko Ohno-Matsui. ANOMALIES OF CHOROIDAL VENOUS STRUCTURE IN HIGHLY MYOPIC EYES Retina . 2022.09; 42(9); 1655-1664
- Izumi Hashimoto, Hiroshi Takase, Satoru Kase, Yuko Iwasaki, Daisuke Kobayashi, Kyoko Ohno-Matsui. Clinicopathological analysis of secondary retinal vasoproliferative tumor/reactive retinal astrocytic tumor successfully treated by endoresection. Retin Cases Brief Rep. 2022.09;
- 7. Hongshuang Lu, Ran Du, Shiqi Xie, Jianping Xiong, Changyu Chen, Muka Moriyama, Tae Igarashi-Yokoi, Hiroyuki Takahashi, Koju Kamoi, Kengo Uramoto, Noriko Nakao, Kyoko Ohno-Matsui. ANOMALIES OF CHOROIDAL VENOUS STRUCTURE IN HIGHLY MYOPIC EYES. Retina. 2022.09; 42(9); 1655-1664

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- 12. Hiroyuki Takahashi, Kengo Uramoto, Kyoko Ohno-Matsui. Nd:YAG laser ablation of internal limiting membrane to treat myopic macular retinoschisis: Case series. Retin Cases Brief Rep. 2022.08;
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- 22. Shintaro Horie, Hiroshi Takase, Takeshi Yoshida, Kyoko Ohno-Matsui. Sympathetic ophthalmia in eye with pathologic myopia. Am J Ophthalmol Case Rep. 2022.02; 25; 101295

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- 24. Koju Kamoi, Kaoru Uchimaru, Arinobu Tojo, Toshiki Watanabe, Kyoko Ohno-Matsui. HTLV-1 uveitis and Graves' disease presenting with sudden onset of blurred vision. Lancet. 2022.01; 399(10319); 60
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- 28. Shiqi Xie, Koju Kamoi, Tae Igarashi-Yokoi, Kengo Uramoto, Hiroyuki Takahashi, Noriko Nakao, Kyoko Ohno-Matsui. Structural Abnormalities in the Papillary and Peripapillary Areas and Corresponding Visual Field Defects in Eyes With Pathologic Myopia. Invest Ophthalmol Vis Sci. 2022.04; 63(4); 13
- 29. Koju Kamoi, Toshiki Watanabe, Kaoru Uchimaru, Akihiko Okayama, Seiko Kato, Toyotaka Kawamata, Hisako Kurozumi-Karube, Noe Horiguchi, Yuan Zong, Yoshihisa Yamano, Isao Hamaguchi, Yasuhito Nannya, Arinobu Tojo, Kyoko Ohno-Matsui. Updates on HTLV-1 Uveitis. Viruses. 2022.04; 14(4);
- 1. A case of acute retinal pigment epithelitis following COVID-19 vaccination 2022.09; 15(9); 602-607
- 2. A case of acute retinal pigment epithelitis following COVID-19 vaccinationEffectiveness of the Low-Addition Contact Lenses for Asthenopia Patients 2022.08; 39(8); 1134-1138

[Misc]

- 1. Shintaro Horie, Kyoko Ohno-Matsui. Progress of Imaging in Diabetic Retinopathy-From the Past to the Present. Diagnostics (Basel). 2022.07; 12(7); 1684
- 2. Salomon Yves Cohen, Catherine Vignal-Clermont, Liem Trinh, Kyoko Ohno-Matsui. Tilted disc syndrome (TDS): New hypotheses for posterior segment complications and their implications in other retinal diseases. Prog Retin Eye Res. 2022.05; 101020
- 3. Ran Du, Kyoko Ohno-Matsui. Novel Uses and Challenges of Artificial Intelligence in Diagnosing and Managing Eyes with High Myopia and Pathologic Myopia. Diagnostics (Basel). 2022.05; 12(5); 1210
- 4. Kai Xiong Cheong, Lingqian Xu, Kyoko Ohno-Matsui, Charumathi Sabanayagam, Seang Mei Saw, Quan V Hoang. An evidence-based review of the epidemiology of myopic traction maculopathy. Surv Ophthalmol. 2022.03;
- 5. Takase H, Arai A, Iwasaki Y, Imai A, Nagao T, Kawagishi M, Ishida T, Mochizuki M. Challenges in the diagnosis and management of vitreoretinal lymphoma Clinical and basic approaches. Progress in retinal and eye research. 2022.02; 101053
- 6. Kyoko Ohno-Matsui, Hendrik P N Scholl. Having One of the Fastest Growing Unmet Needs in Ophthalmology Reflected in Editorial Activities: Myopia. Ophthalmic Res. 2022.01; 65(1); 1-3

[Conference Activities & Talks]

- 1. Ohno-Matsui K. Current Classification of Myopic Maculopathy. Wilmer Retina Festival-Johns Hopkins CME 2022.12.03
- 2. Ohno-Matsui K. Imaging advances in pathologic myopia. The 15th Asia-Pacific Vitreo-retina Society(APVRS) 2022.11.20 Nangang, Taipei

- 3. Zong Y, Kamoi K, Ando N, Kurozumi-Karube H, Yang M, Zhang J, Ohno-Matsui K. In vitro investigation of the possibility of HTLV-1 infection to human resident cells in the eye. The Japanese Society of HTLV-1 and Associated Diseases 2022.11.05 Tokyo, Chiyoda (Hitotsubashi University Auditorium)
- 4. Yang M, Kamoi K, Zong Y, Zhang J, Ando N, Kurozumi-Karube H, Ohno-Matsui K. In vitro simulation of the intraocular environment of ATL patient by primary retinal epithelial cell. The Japanese Society of HTLV-1 and Associated Diseases 2022.11.04 Tokyo, Chiyoda (Hitotsubashi University Auditorium)
- 5. Ohno-Matsui K. Posterior staphyloma in pathologic myopia. 36th Mexican Society of Ophthalmology 2022.10.05 web
- 6. Ohno-Matsui K. Vitreous imaging with ultra with wide-field OCT and AI-based 3D observation. 36th Mexican Society of Ophthalmology 2022.10.05
- 7. Yasuda S, Ito T, Shimizu G, Yoshida T, Ohno-Matsui K. Novel features of the choroid observed with retromode imaging in cases with vkh disease and posterior scleritis. AAO 2022 2022.10.02
- Stanga PE, Moussa MS, Sadda SR, Ohno-Matsui K, Staurenghi G, Fawzi A, Papayannis A. Vitreous-macular-choroidal and peripheral OCT: Cross-sectional, en face, angio 3-D, widefield and intraoperative imaging. AAO 2022 2022.10.02 California, USA
- 9. Ohno-Matsui K. Structural abnormalities in the papillary and peripapillary areas and corresponding vf defects in eyes with pathologic myopia. AAO 2022 2022.10.01 California, USA (web)
- Xie S, Kamoi K, Igarashi-Yokoi T, Uramoto K, Takahashi H, Nakao N, Ohno-Matsui K. Structural abnormalities in the papillary and peripapillary areas and corresponding vf defects in eyes with pathologic myopia.. AAO 2022 2022.10.01 web
- 11. Ohno-Matsui K. Intervortex vein anastomoses in high myopia and its implication to other chorioretinal diseases . AAO 2022 2022.09.30 California, USA (web)
- 12. Du R, Xie S, Lu H, Chen C, Xiong J, Uramoto K, Takahashi H, Onishi Y, Kamoi K, Nakao N, Fang Y, Ohno-Matsui K.. Hospital-based study of risk factors associated with development of myopic macular neovascularization in highly myopic eyes.. AAO 2022 2022.09.30 web
- 13. Ohno-Matsui K. Pathologic Myopia. Invited Lecture at Columbia University Stanley Chang Lecture 2022.09.28 New York, USA
- 14. Ohno-Matsui K. Classification of myopic maculopathy. 37th Asia Pacific Myopia Society APMS2022 2022.09.24 webinar
- 15. Ohno-Matsui K. Abnormalities of choroidal vasculature in pathologic myopia. World Ophthalmology Congress 2022 2022.09.11 web
- 16. Ohno-Matsui K. Intervortex anastomoses in high myopes and its implication for other retinal diseases. EURETINA2021 2022.09.02 web
- 17. Ohno-Matsui K. Imaging of Vitreous. EURETINA2021 2022.09.01 web
- Ohno-Matsui K. Anomalies of choroidal venous structure in highly myopia. 45TH ANNUAL MACULA SOCIETY MEETING 2022 2022.08.10 Berlin, Germany
- 19. Ohno-Matsui K. Longitudinal Scleral Curvature Patterns in Highly Myopic Children/Adolescents. Kanagawa Retina Forum 2022.07.29 web
- 20. Wakabayashi T, Yonekawa Y, Ohno-Matsui K, Cohen SY, Rowland C, Pulido JS. 6-Year-Old Girl with Myopia and Peripapillary Serious Retinal Detachment. The American Society of Retina Specialists 2022 40th Annual Meeting 2022.07.13 New York, USA
- Ohno-Matsui K. Longitudinal Scleral Curvature Patterns in Highly Myopic Children/Adolescents. 9th International symposium of Asia Pacific Retinal Imaging Society 2022.07.02 web

- 22. Igarashi-Yokoi T, Takahashi H, Kamoi K, Uramoto K, Nakao N, Ohno-Matsui K . Anomalies of choroidal venous structure in highly myopic eyes. The 4th Annual Meeting of Japan Myopia Society 2022.05.14 Knowledge Capital (web)
- 23. Chen C, Du R, Xie S, Lu H, Xiong J, Wang Y, Nakao N, Takahashi H, Igarashi-Yokoi T, Kamoi K, Ohno-Matsui K. The morphological features of sclera shape in younger high myopia patients. The 4th Annual Meeting of Japan Myopia Society 2022.05.14 Knowledge Capital (web)
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- 25. Xie S, Kamoi K, Igarashi-Yokoi T, Uramoto K, Takahashi H, Nakao N, Ohno-Matsui K. Lamina cribrosa defects in eyes with pathologic myopia. The 4th Annual Meeting of Japan Myopia Society 2022.05.14 Knowledge Capital (web)
- 26. Ohno-Matsui K. Ultra widefield OCT imaging of scleral curvature changes in highly myopic children and adolescents. International Retinal Imaging Society (IntRIS) 2022.05.07 web
- 27. Yuan Zong, Koju Kamoi, Hisako Kurozumi-Karube, Kyoko Ohno-Matsui. Safety of aflibercept for the eye under HTLV-1 infection status in vitro. ARVO Annual Meeting 2022 2022.05.04 Denver, CO, USA
- 28. Ohno-Matsui K. Intervortex anastomoses in pathologic myopia. The 17th Retina en Platique 2022.03.25 web
- 29. Hiroshi Takase. Retinochoroidal sarcoidosis. EURETINA Webinar 2022.02.17 Web

[Awards & Honors]

- 1. The J. Donald M. Gass Medal , The Macula Society, 2022.02
- 2. The Power List 2022, The Ophthalmologist, 2022.04

[Others]

- 1. Pathologic myopia The major cause of visual impairment, 2022.02 Ohno-Matsui Kyoko. TMDU Research Activities 2021-2022 p.24
- 2. High Myopia, 2022.11 Chairman .The 15th Asia-Pacific Vitreo-retina Society (APVRS), 2022.11.18, Nangang, Taipei

Otorhinolaryngology

Professor: Takeshi Tsutsumi Associate Professor: Yoshiyuki Kawashima Junior Associate Professor: Taku Ito Assistant Professor: Tarou Fujikawa, Keiji Honda, Ayako Nishio Hospital Staff: Tomoki Ooka, Keisuke Kondo Graduate Student: Ayako Maruyama, Bai Jing, Ayame Yamazaki, Hiroki Watanabe, Natsuki Aoki, Tomoki Ooka, Kaori

(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) Biomarker 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 clerkshipIII, 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. Sakihama N, Okada R, Takahashi N, Fushimi N, Ooka T, Kawabe H, Ariizumi Y, Ohno K, Ueki Y, Tayama N, Tsutsumi T, Asakage T. Post-intubation laryngeal injury after COVID-19 treatment causing dyspnea: A report of six cases. Auris, nasus, larynx. 2022.12;
- 2. Tanaka Kentaro, Suesada Nobuko, Homma Tsutomu, Hidaka Takeaki, Mori Hiroki, Okazaki Mutsumi, Sugawara Takashi, Tsutsumi Takeshi, Asakage Takahiro. Early postoperative complications and their measures after skull base reconstruction: A study from the standpoint of plastic and reconstructive surgeons AURIS NASUS LARYNX. 2022.10; 49(5); 845-855
- 3. Tanaka K, Suesada N, Homma T, Mori H, Tsutsumi T, Asakage T, Okazaki M. Muscle-penetration method: Cable nerve grafting with well vascularized surrounding tissue and shortest graft length. Journal of plastic, reconstructive & aesthetic surgery : JPRAS. 2022.04; 75(7); 2387-2440
- 4. Tanaka Kentaro, Suesada Nobuko, Homma Tsutomu, Mori Hiroki, Sugawara Takashi, Tsutsumi Takeshi, Asakage Takahiro, Okazaki Mutsumi. 手術目的に基づく前頭蓋底再建と側方頭蓋底再建における術式の コンセプトの差 (The different concepts of surgical managements between anterior and lateral skull base reconstructions based on surgical purposes) Auris Nasus Larynx. 2022.04; 49(2); 271-278
- 5. 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

[Conference Activities & Talks]

- 1. Takeshi Tsutsumi. "Endoscopic Surgery for Petrous Apex Lesions" Panel Discussion/Round Table 19 "Usefulness of the Endoscope in Lateral Skull Base Surgery". 4th World Congress of Endoscopic Ear Surgery 2022.12.05
- 2. Takeshi Tsutsumi. "Exoscope Application" Panel Discussion/Round Table 19 "Ergonomics in Ear Surgery". 4th World Congress of Endoscopic Ear Surgery 2022.12.05
- 3. 白 静, 伊藤 卓, 川島 慶之, 藤川 太郎, 本田 圭司, 渡邊 浩基, 倉田 奈都子, 堤 剛. C57BL/6J マウスを用い た、出生後の耳石発生に関する Ex Vivo でのマイクロ CT 分析 (Ex Vivo Micro-CT Analysis of Postnatal Otoconia Development in C57BL/6J Mice). 日本耳科学会総会 · 学術講演会抄録集 2022.10.01
- 4. Takeshi Tsutsumi, Ayame Yamazaki, Tomoki Ooka, Hiroki Watanabe, Takamori Takeda, Keiji Honda, Taku Ito. Post-rotatory unsteadiness is induced by the output to otolith-ocular reflex pathway.. 31th Barany Society Meeting 2022.05.09
- 5. Tsutsumi T, Asakage T, Kawashima Y, Ariizumi Y.. Short-term outcome of 69 external auditory canal cancer treated at a single institution. Joint Meeting of Otorhinolaryngology Head and Neck Surgery 2022.04.06
- 6. Tsutsumi T, Asakage T, Kawashima Y, Kiyokawa Y.. Surgical outcome of 69 external auditory canal cancer treated at a single institution. 7th East Asian Symposium on Otology 2022.03.24

Neurology and Neurological Science

Professor YOKOTA Takanori Associate Professor NISHIDA Yoichiro Junior Associate Professor KUWAHARA Hiroya, HATTORI Takaaki Assistant Professor ISHIGURO Taro, YAGI Yohsuke, ONO Daisuke, Suzuki Motohiro Project Professor SANJO Nobuo, UCHIHARA Toshiki, NAGATA Tetsuya Project Associate Professor NAKAYAMA Tojo Project Junior Associate Professor HARA Rintaro Project Assistant Professor YOSHIOKA Kotaro, HIRATA Kosei, ASAMI Yutaro Project Assistant Professor HIGASHI Miwa, SAKAUE Fumika, OHARA Masahiro Project Researcher AMANO Akiko, SU SU Lei Mon, TOMORI Takahito Graduate Student HASEGAWA Jyuri, MIYASHITA Akiko, SANO Tatsuhiko, ICHINOSE Keiko, MARUOKA Hiroyuki, YAMADA Akane, KINA Satoko, SATO Takefumi, MIURA Motoki, MATSUDA Sakino, YANAGIDAIRA Mitsugu, OHTANI Tai, SHINYA Akiko, TOIDE Nozomi, TAMAKI Kana, IWASE Ryo, MATSUBAYASHI Taiki, SHIMANO Kaoru, AMANO Eiichiro, FUKUSIMA Meiko, YASUURA Asuka, NODA Kotaro, KURODA Takayuki, KUROIWA Nobuaki, NATSUI Hirokazu, KATSUYAMA Maho, AOYAMA Hisashi, YANO Yui, SONOHARA Terutaka, JIA Chunyan, CHEN Qingmeng, THUNYARUT Bannawongsil, YASUURA Asuka, YASUDA Kazuma, YAMAMOTO Shota, KOYAMA Kanako Resident KIZUKA Narumi, MIYAKE Ryo, KAWAI Honami, Watanabe Yui, YOSHIHAMA Rei, Matsumoto Masayoshi, Izumi Takao, Takashima Ryoko, Sanjo Yuta

(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 32 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]

- Matsuda H, Okita K, Motoi Y, Mizuno T, Ikeda M, Sanjo N, Murakami K, Kambe T, Takayama T, Yamada K, Suehiro T, Matsunaga K, Yokota T, Tateishi U, Shigemoto Y, Kimura Y, Chiba E, Kawashima T, Tomo Y, Tachimori H, Kimura Y, Sato N. Clinical impact of amyloid PET using (18)F-florbetapir in patients with cognitive impairment and suspected Alzheimer's disease: a multicenter study. Annals of nuclear medicine. 2022.12; 36(12); 1039-1049
- 2. Ohara M, Sanjo N, Kanouchi T, Yokota T. Entrapment partly participates in the longitudinal progression of neuropathy with anti-MAG antibodies. Revue neurologique. 2022.11;
- 3. Chen Q, Hattori T, Tomisato H, Ohara M, Hirata K, Yokota T, Alzheimer's Disease Neuroimaging Initiative. Turning and multitask gait unmask gait disturbance in mild-to-moderate multiple sclerosis: Underlying specific cortical thinning and connecting fibers damage. Human brain mapping. 2022.11;
- 4. Masaaki Niino, Shoko Fukumoto, Tatsusada Okuno, Nobuo Sanjo, Hikoaki Fukaura, Masahiro Mori, Takashi Ohashi, Hideyuki Takeuchi, Yuko Shimizu, Juichi Fujimori, Izumi Kawachi, Jun-ichi Kira, Eri Takahashi, Yusei Miyazaki, Nobuhiro Mifune. Health related quality of life in Japanese patients with multiple sclerosis Journal of Neurology. 2022.11; 270; 1011-1018
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[Conference Activities & Talks]

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- 2. Yokota T. Blood-Brain-Barrier penetrating DNA/RNA Heteroduplex Oligonuclotide (HDO)can regulate genes of microglia and lymphocytes by systemic administration. The 34th annual meeting of the Japanese Society for Neuroimmunology 2022.10.21 長崎
- 3. Tojo Nakayama, Timothy Yu. アンチセンスオリゴを用いた神経疾患に対する個別化医療の取り組み. Neuro2022(第45回日本神経科学大会・第65回日本神経化学会大会・第32回日本神経回路学会大会) 2022.07.03 沖縄
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- 18. 大谷 泰, 赤座実穂, 叶内 匡, 夏井洋和, 川端茂徳, 渡部泰士, 石田洸樹, 宮野由貴, 足立善昭, 関原謙, 横田隆徳, . 生体磁場計測装置を用いた単一の運動単位の電気活動評価. 第 14 回 CBIR/ONSA/大学院セミナー共済 若 手インスパイアシンポジウム 2022.02.17
- 19. Ohara M,Nagata T,Iwata Hara R,Takagi K,Sato K,Maeda Y,Wada T,Yokota T. Cationic oligopeptides enhance the therapeutic potential of ligand-conjug DNA/RNA heteroduplex . 第 14 回 CBIR/ONSA/大 学院セミナー共済 若手インスパイアシンポジウム 2022.02.17
- 1. Tojo Nakayama, Timothy Yu. Precision gene therapeutics for epileptic encephalopathy with antisense oligonucleotides. 2022.09.21
- 2. Individualized clinical trials using oligonucleotides for Neurological rare disorders. 2022.08.02
- 3. Developing antisense oligonucleotide therapy for Dentatorubral-pallidoluysian atrophy (DRPLA). 2022.08.02
- 4. Individualized medicine with antisense oligonucleotides for rare neurological disorders. 2022.07.15
- 5. Neurological adverse events following COVID-19 vaccination. 2022.05.21

[Patents]

- 1. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : CA 2859581
- 2. CARRIER FOR USE IN DELIVERING DRUG, CONJUGATE, COMPOSITION COMPRISING SAME, AND METHOD FOR ADMINISTRATING SAME, Patent Number : EP 3072506
- 3. CARRIER FOR USE IN DELIVERING DRUG, CONJUGATE, COMPOSITION COMPRISING SAME, AND METHOD FOR ADMINISTRATING SAME, Patent Number : EP 3072506
- 4. α -SYNUCLEIN EXPRESSION INHIBITOR, Patent Number : US11234995
- 5. α -SYNUCLEIN EXPRESSION INHIBITOR, Patent Number : US11234995
- 6. DOUBLE-STRANDED NUCLEIC ACID COMPLEX HAVING OVERHANG, Patent Number : US 11260134
- 7. DOUBLE-STRANDED NUCLEIC ACID COMPLEX HAVING OVERHANG, Patent Number \div US 11260134

[Awards & Honors]

- 1. 35th Research Encouragement Award, Tokyo Medical and Dental University Medical Alumni Association, 2022.03
- 2. Research Encouragement Program for Fostering Researchers (Drug Discovery-Related Fields) 2022, Japan Agency for Medical Research and Development, 2022.11

[Others]

- 1. How a two-faced molecule can silence problematic genes, 2022.02 AAAS EurekAlert! The Global Source for Science News
- 2. How a two-faced molecule can silence problematic genes, 2022.02 AAAS EurekAlert! The Global Source for Science News

Psychiatry and Behavioral Sciences

Professor, Chair Hidehiko TAKAHASHI Professor Takayuki OKADA Associate Professor Genichi SUGIHARA Associate Professor Takashi TAKEUCHI Associate Professor (tenure track) Hiroki SHIWAKU Junior Associate Professor Daisuke JITOKU, Junya FUJINO Junior Associate Professor (carrier up) Miho MIYAJIMA Junior Associate Professor (faculty) Shunsuke TAKAGI Assistant Professor Takehiro TAMURA, Yukiko MATSUMOTO, Nanase KOBAYASHI Junior Assistant Professor Shun NIIYA Senior Resident Ryuta GOSHIMA, Yusei YAMAGUCHI, Yukiaki KOIZUMI, Yuuki Yamamoto **Clinical Psychologist** Kazunori MURAKAMI, Hisahi YAMADA, Ryoko NAKAJIMA, Hikaru TANIGUCHI, Ayako KUSANO **Psychiatric Social Worker** Yoshifumi KANEKO, Akinori MONTA, Mai KUDO, Masae NAKANISHI **Occupational Therapist** Tomoko SHIRATO Graduate Students (Doctoral Course) Masaki OHYA, Hironobu NAKAMURA, Marino KAWAMOTO, Kazushige HIRAKAKAWA, Takao KANAI, Yuki SHIDEI, Mariko SUNAHARA, Kouichi TABATA, Kyoji MARUO, Kentaro NAGAO, Shiori NOGUCHI, Yoritsugu IIDA, Chenyu QIAN, Masaaki SHIMIZU, Masanori ICHIHASHI, Yukiko MOTOKAWA, Saori TOYODA, Yukiaki KOIZUMI, Ryuta GOSHIMA, Yusei YAMAMOTO, Mao OTAKE, Ikuko ARAKAWA, Takehiro IBARAKI, Marika OKAMURA, Yoshinori SASAKI, Wataru NAKAGAWA, Mayo FUHIWARA, Sayaka OZAKA, Shiho MATSUOKA, Kazuhiro KOSUGI, Hiroyuki TANAKA, Takahiro KAWATA, Yuka BANDO Graduate Students (Master Course) Sayuri ISHII

(1) **Outline**

The theme of our research is to investigate the pathogenesis of psychiatric disorders such as schizophrenia, mood disorders, and addiction based on brain science, to develop objective diagnostic methods and novel treatments and establish psychosocial therapeutic approaches based on objective and scientific techniques and evidence. Our investigation focuses on the pathophysiology of psychiatric disorders using functional magnetic resonance

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imaging, nuclear medicine, and other modalities. We are also performing research to investigate the role of neurofeedback as a therapeutic strategy for mental disorders. Brain imaging studies are the most interesting and well-skilled lesion. Our study involves processing a large volume of brain data using machine learning and computational psychiatry to explore prospects for new discoveries and to predict pathological conditions through modeling. We are exploring neurofeedback as a novel therapeutic approach for psychiatric diseases and the role of artificial intelligence (AI) and computational psychiatry. Moreover, we are actively designing studies that can establish evidence-based approaches to address issues observed in routine clinical practice.

(2) Research

1) Studies in biological psychiatry

(i) Molecular and cellular studies to clarify the etiology and conditions of neuropsychiatric diseases We have performed translational and reverse translational research together with molecular, cellular, and behavioral analyses using animal models and clinical samples of DNA, serum, cerebrospinal fluid, and postmortem brain tissue obtained from patients with psychiatric disorders.

(ii) Study of sleep stages and behavior in neuropsychiatric diseases

Using an automatic analysis device (polysomnography), a study is being performed to investigate sleep stages and behavior in patients with various psychiatric disorders.

(iii) Neuroimaging in psychiatric disorders

We are actively incorporating AI technology in our research on brain structure and function and molecular imaging using magnetic resonance imaging and positron emission tomography to elucidate the pathogenesis of mental disorders, identify subtypes, and predict treatment response.

(iv) We are performing an observational study to retrospectively analyze information regarding electroconvulsive therapy (ECT). These data are submitted as performance reports from multi-institutional "ECT Training Facilities" accredited by the Japanese Society of General Hospital Psychiatry. Despite its long history in psychiatric clinical practice, the actual implementation of ECT in daily clinical practice remains unclear. This study will clarify the status of ECT in real-world Japanese medical facilities.

2) Psychopathological studies

Based on a psychotherapeutic approach, we are performing psychological studies of neuropsychiatric diseases with regard to phenomenology, anthropology, and linguistics. Other research activities include a review of fundamental psychiatric concepts and a basic study to establish a diagnostic classification of psychiatric disorders, which are important issues currently being widely recognized in clinical practice. In addition to studies on endogenous psychosis observed in schizophrenia and bipolar disorder, we are involved in psychoanalytical studies to better understand and develop psychotherapeutic modalities for neurosis and borderline personality disorder, which have gained increasing attention in recent times.

3) Research on liaison psychiatry and psycho-oncology

(i) Liaison psychiatry

In collaboration with dental hospitals, we are involved in research on the prevention of postoperative delirium. We are also performing research on delirium prevention in patients admitted to the physical department. We intend to perform research on perinatal mental health in the future.

(ii) Psycho-oncology

The concept of cancer disease is an important factor in the process by which a child accepts and adapts to cancer in his/her family. Therefore, we are analyzing textbooks used in elementary and junior high schools that could affect the development of the concept of cancer. Based on these data, from the perspective of psycho-oncology, we are attempting to prepare user-friendly home-based educational materials for parents to complement educational material available at school. We will verify the effects of these tools once they are operational.

4) Forensic psychiatry research

Our research includes projects for the development of forensic psychiatric evaluation methodology, risk assessment and management in forensic settings, and an investigation of the associations and mechanisms of criminal behavior. Our research encompasses a wide range of topics including the development of a method to assess the capacity to act for appraisal in the adult guardianship system.

(3) Education

Following the 2-year period of mandatory clinical training, during the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists and will undergo practical training at affiliated medical facilities to qualify as psychiatrists. Undergraduate education, which emphasizes clinical clerkship training after a systematic series of lecture courses and seminar-based classes, is designed to develop students' problem-solving skills and improve their motivation to learn neuropsychiatry, with support from external facilities.

(4) Lectures & Courses

During the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment, laws and regulations related to clinical practice and will acquire other general knowledge, all of which are essential for a comprehensive understanding of the biopsychosocial approaches to neuropsychiatric diseases.

(5) Clinical Services & Other Works

Clinical practice

Among all new outpatients who visit our department, based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10), approximately 30% are diagnosed with "mood disorders" (F3), 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 from other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance, dependence, and neurosis, necessitating intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. This facility is the psychiatric department of a general hospital and is involved with university education and training; therefore, most inpatients are diagnosed as F2, followed by F4 and F3 categories per ICD-10 codes. We also provide care and treatment for patients with sleep rhythm and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided modified ECT for inpatients and individual and group psychotherapy for patients admitted to our psychiatric ward, clinic, and day care center in close collaboration with rehabilitation facilities in the community. The day care (partial hospitalization) is a transitional element between inpatient and outpatient care and is indicated in a wide range of psychiatric disorders, such as schizophrenia, depression, bipolar disorder, adjustment disorder, and personality disorders.

Each member has its own aim, and the team provides care utilizing different types of frameworks. Our day care team places emphasis on the potentiality of the group and in our opinion, the collective efforts of the group could contribute to the therapeutic effect. This experience promotes good communication skills in patients and readaptation to social situations and social reintegration become easier.

(6) Clinical Performances

Per our policy, patients with schizophrenia are treated with clozapine, which is approved for the treatment of refractory schizophrenia. Following effective coordination with the Dental Hospital, we currently treat patients with oral pain or dysesthesia; this collaboration is a characteristic of our university. Our faculty includes board-certified specialists to treat patients who present with sleep disorders and epilepsy. In 2014, we introduced a psychoeducational program for patients with bipolar disorder, which focuses on relapse prevention. Additionally, we ensure close cooperation with the staff for an increasing number of liaison activities implemented for delirium prevention (particularly in surgical wards), interventions for patients with suicide attempts in the emergency room, and mental support for peripartum patients.

(7) Publications

[Original Articles]

- 1. Yawata T, Takagi S, Tamura T, Sugihara G, Takahashi H. Psychosis treatment in a patient with Parkinsonian type multiple system atrophy using modified electroconvulsive therapy: a case report. Psychogeriatrics : the official journal of the Japanese Psychogeriatric Society. 2022.12; 23(2); 364-367
- Tani Y, Fujiwara T, Sugihara G, Hanazato M, Suzuki N, Machida M, Amagasa S, Murayama H, Inoue S, Shobugawa Y. Neighborhood Beauty and the Brain in Older Japanese Adults. International journal of environmental research and public health. 2022.12; 20(1);
- 3. Matsumoto Y, Nishida S, Hayashi R, Son S, Murakami A, Yoshikawa N, Ito H, Oishi N, Masuda N, Murai T, Friston K, Nishimoto S, Takahashi H. Disorganization of Semantic Brain Networks in Schizophrenia Revealed by fMRI. Schizophrenia bulletin. 2022.12;
- 4. Takahiro Kawata, Genichi Sugihara, Yoichi Kakibuchi, Midori Tomitaka, Miho Miyajima, Eisuke Matsushima, Takashi Takeuchi, Hidehiko Takahashi. Attention-deficit hyperactivity symptoms and risk of alcohol use relapse. Neuropsychopharmacology Reports.. 2022.12; 43(1); 103-111
- Takahashi Y, Yamamoto T, Oyama J, Sugihara G, Shirai Y, Tao S, Takigawa M, Sato H, Sasaki M, Hirakawa A, Takahashi H, Goya M, Sasano T. Increase in Cerebral Blood Flow After Catheter Ablation of Atrial Fibrillation. JACC. Clinical electrophysiology. 2022.11; 8(11); 1369-1377
- 6. Rikumo Ode,Koichi Fujiwara, Miho Miyajima, Toshikata Yamakawa, Manabu Kano,Kazutaka Jin,Nobukazu Nakasato, Yasuko Sawai,Toru Hoshida,Masaki Murata, Satsuki Iwasaki,Yoshiko Watanabe, Yutaka Watanabe, Yoko Suzuki, Motoki Inaji, Naoto Kunii, Satoru Oshino, Hui Ming Khoo, Haruhiko Kishima, Taketoshi Maehara. Development of an epileptic seizure prediction algorithm using R-R intervals with self-attentive autoencoder Artificial Life and Robotics. 2022.11;
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- 9. Tamura Takehiro, Sugihara Genichi, Okita Kyoji, Mukai Yohei, Matsuda Hiroshi, Shiwaku Hiroki, Takagi Shunsuke, Daisaki Hiromitsu, Tateishi Ukihide, Takahashi Hidehiko. Dopamine dysfunction in depression: application of texture analysis to dopamine transporter single-photon emission computed tomography imaging Translational psychiatry. 2022.08; 12(1); 309
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- Shisei Tei, Junya Fujino. The educational value of sense of coherence for grief care. Front Psychol. 2022; 13; 1037637

[Conference Activities & Talks]

- 1. Junya Fujino, Qian Chenyu, Shisei Tei, Hidehiko Takahashi. Decision-making in situations involving group membership in autism spectrum disorder. 22nd World Congress of Psychiatry 2022.08 Bangkok and Virtual
- 2. Shisei Tei, Junya Fujino. Social anxiety, connections, and needs during the coronavirus disease 2019 pandemic. 22nd World Congress of Psychiatry 2022.08 Bangkok and Virtual
- 3. Rikumo Ode, Koichi Fujiwara, Miho Miyajima, Toshitaka Yamakawa, Manabu Kano, Taketoshi Maehara. R-R Intervals based Epileptic Seizure Prediction Algorithm Utilizing Self-attentive Autoencoder. 44th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2022.07.14 Glasgow, Scotland, UK
- 4. Junya Fujiino, Shisei Tei, Kohya Abe, Hidehiko Takahashi. Neurobiological mechanisms of burnout in medical professionals. 33rd CINP Hybrid World Congress of Neuropsychopharmacology 2022.06 Taiwan and Virtual
- 5. Junya Fujiino, Shisei Tei, Kohya Abe, Hidehiko Takahashi. Gray matter volume and burnout severity among medical professionals. 30th European Congress of Psychiatry 2022.06 Virtual
- 6. Shisei Tei, Junya Fujino. The dark side of social ties: coronavirus 2019-induced fear and intergroup conflicts. 30th European Congress of Psychiatry 2022.06 Virtual
- 7. Rikumo Ode, Koichi Fujiwara, Miho Miyajima, Toshitaka Yamakawa, Manabu Kano, Taketoshi Maehara. Development of an Epileptic Seizure Prediction Algorithm Using R-R Intervals with Self-attentive Autoencoder . The International Society of Artificial Life and Robotics (ISAROB) 2022.01.27 online
- 1. Miho Miyajima. Psycho-oncology in Clinical Brain Tumors: Focus on Epilepsy and Depression. The 40th Annual Meeting of the Japanese Brain Tumor Society 2022.12.06 Kamogawa Grand Hotel

Endovascular Surgery

Professor Kazutaka Sumita Assistant Professor Sakyo Hirai, Kyohei Fujita, Jiro Aoyama Clinical Fellow Shoko Fujii, Mariko Ishikawa, Hirotaka Sagawa Secretary 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]

- Fujita K, Fujii S, Hirai S, Yamaoka H, Ishikawa M, Karakama J, Miki K, Yoshimura M, Nemoto S, Sumita K. P2Y12 reaction units and ischemic and bleeding events after neuro-endovascular treatment. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2022.09; 31(9); 106631
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- 4. Yamaoka Hiroto, Fujita Kyohei, Fujii Shoko, Ayabe Fuga, Karakama Jun, Hirai Sakyo, Yoshimura Masataka, Yamamoto Shinji, Nemoto Shigeru, Sumita Kazutaka. 出血発症した解離性椎骨動脈瘤に合 併した外転神経麻痺の検討 (Clinical Course of Abducens Nerve Palsy in Patients with Ruptured Vertebral Artery Dissecting Aneurysms) JNET: Journal of Neuroendovascular Therapy. 2022.07; 16(7); 339-345
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- Kobayashi T, Nitta M, Shimizu K, Saito T, Tsuzuki S, Fukui A, Koriyama S, Kuwano A, Komori T, Masui K, Maehara T, Kawamata T, Muragaki Y. Therapeutic Options for Recurrent Glioblastoma-Efficacy of Talaporfin Sodium Mediated Photodynamic Therapy. Pharmaceutics. 2022.02; 14(2);
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NCNP Brain Physiology and Pathology

1. Staffs

Collaborative Professor Collaborative Professor Collaborative Professor Collaborative Professor Collaborative Associate Professor Collaborative Associate Professor

Mikio HOSHINO Tadafumi HASHIMOTO Noritaka ICHINOHE Yoshitsugu AOKI Yuichi YAMASHITA Shinji Oki

(1) Research

1) Investigation of the molecular machinery underlying brain development.

(Mikio Hoshino; Department of Biochemistry and Cellular Biology, National Institute of Neuroscience, NCNP)

We are investigating molecular machinery underlying nervous system development, especially focusing on neuron-subtype specification, nervous system regionalization and neuronal migration. We are also interested in human diseases/disorders caused by disorganized development of the nervous system. We published five papers in 2022.

2) Investigation of the pathomechanism of neurodegenerative disorders.

(Tadafumi Hashimoto, Department of Degenerative Neurological Diseases, National Institute of Neuroscience, NCNP)

In Alzheimer's disease (AD) and frontotemporal lobar degeneration (FTLD), aggregation and deposition of the pathogenic proteins in the brain are thought to cause progressive neurodegeneration. However, the detailed molecular mechanism is still unclear, and this remains a major obstacle to the development of disease-modifying therapies for dementia. We study the pathogenic proteins of AD and FTLD, such as A β , tau, TDP-43 or FUS, and elucidate the molecular mechanisms by which these proteins aggregate, accumulate, and exhibit neurodegeneration using patient brains, mouse or *Drosophila* models. This year, we found that phosphorylation of FUS by casein kinase 1 (CK1) δ/ϵ reduces its insolubility and toxicity using *Drosophila* and cell models (J Biol Chem, 2022), which may provide a clue to suppress FUS-induced neurotoxicity in FTLD or ALS.

3) Autism research using a primate model marmoset

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of

Neuroscience, NCNP)

Autism is a neurodevelopmental disorder characterized by impaired social skills and perseverance. Although autism has been studied in rodent models, no treatment for autism has yet been developed. New World monkey, marmosets are expected to be suitable for autism research because they are evolutionarily close to humans, and have advanced social skills and a well-developed prefrontal cortex. We have developed an autism model of marmosets to elucidate the pathogenesis of autism and to develop treatments. In particular, we are analyzing the marmoset autism model from multiple perspectives using molecular and cell biological methods, systems neuroscience approaches (electrophysiology, structural MRI, etc.), and behavioral techniques. This year, we have shown that the autism marmoset models, like human autism, have social deficits such as weak social gazing and a tendency to fixate on previously learned behaviors and poor adaptation to other learning paradigms (Nakagami et al., 2022, Frontiers in Psychiatry). In addition, the salivary cortisol level in the marmoset models was high, as in human autism, which is useful for studying the vulnerability to stress that individuals with autism have (Nakamura et al., 2022, Frontiers in Behavioral Neuroscience).

4) Development of state-of-the-art genetic therapies using human 3D tissue models for neuromuscular diseases

(Yoshitsugu Aoki, Department of Molecular Therapy, National, National Institute of Neuroscience, NCNP)

Our research group integrates molecular, pharmacologic, proteomic, and genomic methodologies to clarify the molecular mechanisms of disease pathogenesis and develop novel genetic or stem cell-based therapies for the diseases. Primarily, our research focuses on novel genetic therapies targeting messenger RNA and DNA. We also investigate RNA interference-based and genome editing therapies for several neuromuscular disorders. We have successfully shown the proof of concept of exon skipping in our unique animal models, such as canine X-linked muscular dystrophy in Japan and mdx52 mice with an exon 52 deletion of the Dmd gene. Recently, we have successfully developed an exon 53-skipping drug (viltolarsen: NS-065/NCNP-01) in collaboration with a Japanese pharmaceutical company (conditional approval in Japan and the US FDA).

Additionally, our group has drawn on research worldwide to create a picture of the current state-of-the-art 3D tissue platform using human urine-derived stem cells and induced pluripotent stem cell (iPSC) for pre-clinical investigations in gene therapy. Our

research entails several promising discoveries and offers hope to patients afflicted with the potentially life-limiting condition of neuromuscular diseases, including DMD.

5) Computational approach for psychiatric disorders

(Yuchi Yamashita, Department of Information Medicine, National, National Institute of Neuroscience, NCNP)

Computational psychiatry (CPSY) is a new research field that uses mathematical modeling of information processing in the brain to understand mental disorders as aberrant computation. In our laboratory, we conducted a series of CPSY experiments in which behavioral control mechanisms with hierarchical predictive processes were implemented through the physical (or simulated) actions of a humanoid robot driven by a hierarchical recurrent neural network. In 2022, we demonstrated that through developmental learning based on predictive processing/free energy principle, a phenomenon called "sensory attenuation" emerges through the integration of external and proprioceptive sensory modalities. It was further shown that differences in this integration style may explain characteristics of mental disorders such as autism spectrum disorders (ASD) or schizophrenia (Idei et al. Sci Rep, 2022). Additionally, we successfully developed an AI technology using a data-driven approach with deep learning that accurately predicts the progression from mild cognitive impairment to dementia (Wang et al. npj Digital Medicine, 2022).

6) Translational research on immune dysregulation-mediated CNS diseases

(Shinji Oki, Department of Immunology, National Institute of Neuroscience, NCNP) We have been investigating pathogenic involvement of immune dysregulation on intractable CNS diseases and analyzing two novel subset of functional helper T cells. First, we demonstrated that Eomes+ Th cells, a neurotoxic subset of novel functional helper T cell, cause neurodegeneration upon encounter with ORF1 antigen derived from retrotransposon LINE-1 (Takahashi et al. iScience 2022. Microglial incorporation and antigen presentation of ORF1 on MHC II are crucial for activation of Eomes+ Th cells and induction of neurotoxicity (Zhang et al. Cells 2023). Second, we revealed that Nrp-1 acts as an essential biomarker for self-reactive Th cells and we have successfully ameliorate symptoms of systemic autoimmunity in SLE-prone mice by targeting Nrp-1+ Th cells (Raveney et al. EMBO Mol Med 2022). As our data clearly indicate that a previously-unappreciated immune dysregulation by itself may orchestrate intractable pathogenesis of CNS diseases, we are now aiming to establish a novel class of strategy for therapeutic intervention of those CNS diseases.
(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]

- Sano T, Kawazoe T, Shioya A, Mori-Yoshimura M, Oya Y, Maruo K, Nishino I, <u>Hoshino M</u>, Murayama S, Saito Y. Unique Lewy pathology in myonic dystrophy type 1. *Neuropathology*. 2022 ;42(2):104-116.
- Hashimoto Y, Kuniishi H, Sakai K, Fukushima Y, Du X, Yamashiro K, Hori K, Imamura M, <u>Hoshino M</u>, Yamada M, Araki T, Sakagami H, Takeda S, Itaka K, Ichinohe N, Muntoni F, Sekiguchi M, Aoki Y. Brain Dp140 alters glutamatergic transmission and social behaviour in the mdx52 mouse model of Duchenne muscular dystrophy. *Prog Neurobiol.* 2022 ;216:102288.
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- Inoue YU, Miwa H, Hori K, Kaneko R, Morimoto Y, Koike E, Asami J, Kamijo S, Yamada M, <u>Hoshino M</u>, Inoue T. Targeting Neurons with Functional Oxytocin Receptors: A Novel Set of Simple Knock-In Mouse Lines for Oxytocin Receptor Visualization and Manipulation. eNeuro.;9(1):ENEURO.0423-21.2022.
- 5. Izumi R, Hino M, Nagaoka A, Shishido R, Kakita A, <u>Hoshino M</u>, Kunii Y, Yabe H. Dysregulation of DPYSL2 expression by mTOR signaling in schizophrenia: Multi-level study of postmortem brain. Neurosci Res. 175, 73-81, 2022
- Kishino Y, Matsukawa K, Matsumoto T, Miyazaki R, Wakabayashi T, Nonaka T, Kametani F, Hasegawa M, <u>Hashimoto T</u>, Iwatsubo T. Casein kinase 1δ/ε phosphorylates fused in sarcoma (FUS) and ameliorates FUS-mediated neurodegeneration. *J Biol Chem.* 2022; 298(8):102191.
- 7. Nakamura, M., Nakagami, A., Nakagaki, K., Yasue, M., Kawai, N., & <u>Ichinohe, N</u>. (2022). Prenatal valproic acid-induced autism marmoset model exhibits higher salivary cortisol levels. *Frontiers in behavioral neuroscience*, 2022; 16, 943759.
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- 9. Matsuno, H., Tsuchimine, S., O'Hashi, K., Sakai, K., Hattori, K., Hidese, S., Nakajima, S., Chiba, S., Yoshimura, A., Fukuzato, N., Kando, M., Tatsumi, M., Ogawa, S., <u>Ichinohe, N.</u>,

Kunugi, H., & Sohya, K. Association between vascular endothelial growth factor-mediated blood-brain barrier dysfunction and stress-induced depression. *Molecular psychiatry*, 2022: 27(9), 3822–3832.

- Kaneko, T., Komatsu, M., Yamamori, T., <u>Ichinohe, N.</u>, & Okano, H. Cortical neural dynamics unveil the rhythm of natural visual behavior in marmosets. *Communications biology*, 2022: 5(1), 108.
- Chesshyre M, Ridout D, Hashimoto Y, Ookubo Y, Torelli S, Maresh K, Ricotti V, Abbott L, Gupta VA, Main M, Ferrari G, Kowala A, Lin YY, Tedesco FS, Scoto M, Baranello G, Manzur A, Aoki Y, Muntoni F. Investigating the role of dystrophin isoform deficiency in motor function in Duchenne muscular dystrophy. J Cachexia Sarcopenia Muscle. 2022 Apr;13(2):1360-1372. doi: 10.1002/jcsm.12914. Epub 2022 Jan 26. PMID: 35083887; PMCID: PMC8977977.
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[Review Articles • Books]

- 1. Miyashita S, <u>Hoshino M.</u> Transit Amplifying Progenitors in the Cerebellum: Similarities to and Differences from Transit Amplifying Cells in Other Brain Regions and between Species. Cells, 11(4), 726, 2022
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- 4. Mochizuki H, Aoki M, Ikenaka K, Inoue H, Iwatsubo T, Ugawa Y, Okazawa H, Ono K, Onodera O, Kitagawa K, Saito Y, Shimohata T, Takahashi R, Toda T, Nakahara J, Matsumoto R, Mizusawa H, Mitsui J, Murayama S, Katsuno M; Future Vision Committee of Japanese Society of Neurology; Aoki Y, Ishiura H, Izumi Y, Koike H, Shimada H, Takahashi Y, Tokuda T, Nakajima H, Hatano T, Misawa S, Watanabe H. [Recommendations (Proposal) for promoting research for overcoming neurological diseases 2020]. Rinsho Shinkeigaku. 2022 Jun 24;62(6):429-442. Japanese. doi: 10.5692/clinicalneurol.cn-001695. Epub 2022 May 28. PMID: 35644579.
- 5. Mochizuki H, Aoki M, Ikenaka K, Inoue H, Iwatsubo T, Ugawa Y, Okazawa H, Ono K, Onodera O, Kitagawa K, Saito Y, Shimohata T, Takahashi R, Toda T, Nakahara J, Matsumoto R, Mizusawa H, Mitsui J, Murayama S, Katsuno M; Future Vision Committee of Japanese Society of Neurology; Aoki Y, Ishiura H, Izumi Y, Koike H, Shimada H, Takahashi Y, Tokuda T, Nakajima H, Hatano T, Misawa S, Watanabe H. [Recommendations (Proposal) for promoting research for overcoming neurological diseases 2020]. Rinsho Shinkeigaku. 2022 Jun 24;62(6):443-457. Japanese. doi: 10.5692/clinicalneurol.cn-001696. Epub 2022 May 28. PMID: 35644580.
- 6. Fumio Takahashi, Chenyang Zhang , Hirohiko Hohjoh , Ben Raveney , Takashi Yamamura , Nobuhiro Hayashi , Shinji Oki. Immune-mediated neurodegenerative trait provoked by multimodal derepression of long-interspersed nuclear element-1. *iScience*. 2022 ; 25(5):104278. doi: 10.1016/j.isci.2022.104278.
- 7. Ben Je Raveney, Yosif El-Darawish , Wakiro Sato , Yoshiyuki Arinuma , Kunihiro Yamaoka , Shohei Hori , Takashi Yamamura , Shinji Oki. Neuropilin-1 (NRP1) expression distinguishes self-reactive helper T cells in systemic autoimmune disease. *EMBO Mol Med.* 2022 ; 14(10):e15864. doi: 10.15252/emmm.202215864.

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Molecular Virology

Professor : Shoji YAMAOKA Associate Professor : Hiroaki TAKEUCHI Project Junior Associate Professor: Takaya HAYASHI Assistant Professor: Sayaka SUKEGAWA

Medical Technologist : Yoshio INAGAKI Secretary : Kumiko THORPE-MATSUI

-Students-Ph.D. course: Haruki KITAMURA,Kei TAGA

(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 our in out 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.

- Virological approaches for robust increase in lentiviral titer.

(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]

- Kitamura H., Sukegawa S., Matsuda K., Tanimoto K., Kobayakawa T., Takahashi K., Tamamura H., Tsuchiya K., Gatanaga H., Maeda K., and Takeuchi H.. 4-phenylquinoline-8-amine induces HIV-1 reactivation and apoptosis in latently HIV-1 infected cells. Biochemical and Biophysical Research Communications. 2022.12; 641; 139-147
- Tatsuya Iida, Jun Ando, Hajime Shinoda, Asami Makino, Mami Yoshimura, Kazue Murai, Makiko Mori, Hiroaki Takeuchi, Takeshi Noda, Hiroshi Nishimasu, Rikiya Watanabe. Compact wide-field femtoliter-chamber imaging system for high-speed and accurate digital bioanalysis. Lab on a Chip. 2022.10;
- 3. Kao S, Miyagi E, Mallorson R, Saito H, Sukegawa S, Mukherji A, Mateja A, Ferhadian D, Fabryova H, Clouse K, Strebel K.. The Myeloid-Specific Transcription Factor PU.1 Upregulates Mannose Receptor Expression but Represses Basal Activity of the HIV-LTR Promoter. Journal of Virology. 2022.07; 96(14);
- 4. Shigemi U, Yamamura Y, Matsuda M, Okazaki R, Kubota M, Ibe S, Nemoto M, Maejima-Kitagawa M, Sukegawa S, Imahashi M, Kikuchi T, Sugiura W, Iwatani Y, Hachiya A, Yokomaku Y; Evaluation of the Geenius HIV 1/2 confirmatory assay for HIV-2 samples isolated in Japan. Journal of clinical virology. 2022.07;
- 5. Yuasa S, Nakajima J, Takatsuki Y, Takahashi Y, Tani-Sassa C, Iwasaki Y, Nagano K, Sonobe K, Yoshimoto T, Nukui Y, Takeuchi H, Tanimoto K, Tanaka Y, Kimura A, Ichimura N, Tohda S.. Viral load of SARS-CoV-2 Omicron is not high despite its high infectivity Journal of Medical Virology. 2022.07; 94(11); 5543-5546
- 6. Nishiyama Takara, Takada Toru, Takeuchi Hiroaki, Iwami Shingo. Maternal embryonic leucine zipper kinase (MELK) optimally regulates the HIV-1 uncoating process JOURNAL OF THEORETICAL BIOLOGY. 2022.07; 545; 111152
- 7. Isaac Prah, Yoko Nukui, Shoji Yamaoka, Ryoichi Saito. Emergence of a high-risk Klebsiella michiganensis clone disseminating carbapenemase genes. Front Microbiol. 2022.05; 13; 880248
- Horiguchi Y, Naono N, Sakamoto O, Takeuchi H, Yamaoka S, Miyahara Y. Methodology to Detect Biological Particles Using a Biosensing Surface Integrated in Resistive Pulse Sensing. ACS applied materials & interfaces. 2022.05; 14(17); 20168-20178
- 9. Shinoda Hajime, Iida Tatsuya, Makino Asami, Yoshimura Mami, Ishikawa Junichiro, Ando Jun, Murai Kazue, Sugiyama Katsumi, Muramoto Yukiko, Nakano Masahiro, Kiga Kotaro, Cui Longzhu, Nureki Osamu, Takeuchi Hiroaki, Noda Takeshi, Nishimasu Hiroshi, Watanabe Rikiya. Automated amplification-free digital RNA detection platform for rapid and sensitive SARS-CoV-2 diagnosis COMMUNICATIONS BIOLOGY. 2022.05; 5(1); 473
- 10. Chihiro Tani-Sassa, Yumi Iwasaki, Naoya Ichimura, Katsutoshi Nagano, Yuna Takatsuki, Sonoka Yuasa, Yuta Takahashi, Jun Nakajima, Kazunari Sonobe, Yoko Nukui, Hiroaki Takeuchi, Kousuke Tanimoto, Yukie Tanaka, Akinori Kimura, Shuji Tohda. Viral loads and profile of the patients infected with SARS-CoV-2 Delta, Alpha, or R.1 variants in Tokyo. J Med Virol. 2022.04; 94(4); 1707-1710

- 11. Yao W, Strebel K, Yamaoka S, Yoshida T. Simian Immunodeficiency Virus SIVgsn-99CM71 Vpu Employs Different Amino Acids To Antagonize Human and Greater Spot-Nosed Monkey BST-2. Journal of virology. 2022.02; 96(4); e0152721
- 12. Arakawa M, Tabata K, Ishida K, Kobayashi M, Arai A, Ishikawa T, Suzuki R, Takeuchi H, Tripathi LP, Mizuguchi K, Morita E. Flavivirus recruits the valosin-containing protein (VCP)/NPL4 complex to induce stress granule disassembly for efficient viral genome replication. The Journal of biological chemistry. 2022.01; 298(3); 101597

[Misc]

1. Sayaka Sukegawa and Hiroaki Takeuchi. Toward the unveiling of HIV-1 dynamics: Involvement of monocytes/macrophages in HIV-1 infection Frontiers in Virology. 2022.07;

[Conference Activities & Talks]

- 1. Hiroaki Takeuchi. Identification of host factors regulating HIV-1 latency and their potential therapeutic targets in HIV-1 latency reversal. The 2nd France-Japan symposium on HIV/AIDS and infectious disease basic research 2022.11.05 Tokyo, Japan
- 2. Human mannose receptor 1 attenuates HIV-1 infectivity in a virus isolate-specific manner. 2022.05.23
- 3. DNA-repair factor complex contributes to maintenance of HIV-1 latency. 2022.05.23
- 4. HIV-1 replication and latency is modulated by host Solute Carrier Protein (SCP) expression levels in human cells. Cold Spring Harbor Laboratory Retrovirus meeting 2022.05.23 USA, NY
- 5. Farkašová H, Sukegawa S, Miyagi E, Taylor L, Kao S, Ferhadian D, Schaal H, Hillebrand F, Strebel K.. HIV-1 Vpr induces degradation of Gelsolin, a myeloid cell-specific host factor that reduces viral infectivity by inhibiting expression and packaging of the HIV-1 Env glycoprotein.. Cold Spring Harbor Laboratory Retrovirus meeting 2022.05.23 USA, NY
- 6. Miyagi E, Kao S, Mallorson R, Saito H, Sukegawa S, Mukherji A, Ferhadian D, Fabryova H, Clouse K, Strebel K.. The myeloid-specific transcription factor PU.1 upregulates mannose receptor expression but represses basal activity of the HIV-LTR promoter.. Cold Spring Harbor Laboratory Retrovirus meeting 2022.05.23 USA, NY
- 1. Human mannose receptor 1 protein has the potential to attenuate HIV-1 infectivity in a virus isolate-specific mannerer. 2022.11.15
- 2. Essential contribution of a novel host cell factor SCP in regulating latent HIV-1 provirus expression. 2022.11.15
- 3. DNA maintenance factor complex contributes to regulate of HIV-1 latency. 2022.11.14
- 4. The multiple function of Human mannose receptor 1 (hMRC1) in HIV-1 replication. 2022.07.24

[Others]

1. Resourceful viral protein combats monkey and human defenses differently, 2022.03 AAAS EurekAlert! The Global Source for Science News

Biodefense Research

Professor Toshiaki Ohteki Associate Professor Taku Sato Adjunct Lecturer Yasuhiro Murakawa Adjunct Lecturer Nobuyuki Onai Assistant Professor Masashi Kanayama Graduate Student Megumi Akiyama Graduate Student Hajime Sato Graduate Student Hajime Sato Graduate Student Shun Ishikawa Graduate Student Yuta Izumi Graduate Student Yuta Izumi Graduate Student Eriko Ohashi Research Technician Kisho Shiseki Research Technician Tomiki Hayashi Staff 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 myeloid cells

1) Identification of novel sources of dendritic cells and macrophages

Dendritic cells (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) in response to viral and self-nucleic acids. We have discovered the DC progenitors in the mouse bone marrow, and named common DC progenitors (CDPs) (Immunity 2013; Nat Immunol 2007). Interestingly, we found that 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.

During stress response, monocytes actively influx into various tissues and differentiate into macrophages, which are involved in inflammation, tissue repair, and cancer growth. In addition to CDPs, we recently found human common monocyte progenitors (cMoPs) in human bone marrow and umbilical cord blood (Immunity 2017; Int Immunol 2018). Human cMoP gives rise to only monocytes but not other hematopoietic cells including DCs. Given that monocytes are involved in chronic myelomonocytic leukemia (CMML) and monocyte-derived tumor-associated macrophages (TAMs) promote tumor development, we, in collaboration with a pharmaceutical company, have generated an antibody-drug conjugate (ADC) that selectively targets human cMoP. When this ADC was administered to the CMML PDX model, leukemia cells almost completely disappeared from the bone marrow and peripheral blood. In addition, upon ADC administration into tumor-bearing humanized mice, both peripheral blood monocytes and intratumoral TAMs disappeared, leading to the shrinkage of tumor mass (Front Immunol 2021). Since monocytes are also involved in various inflammatory diseases, the application of human monocyte lineage-specific ADCs to these diseases is also expected.

2) Impairment of brain function by microglial enhancer in aging and Alzheimer's disease (AD)

The decline in tissue regeneration and homeostasis associated with life-stage progression is closely related to the functional alteration of macrophages. Microglia, a macrophage in the brain, is actively contributing to the brain development and maintenance during young age (regenerative microglia). However, with age, microglial inflammatory trait becomes prominent with impaired phagocytosis and brain-derived neurotrophic factor (BDNF) production etc (inflammatory microglia). As a result, functional neurons and synapses are decreased and destroyed. However, the overall picture and entire process of the microglial functional alteration and causative epigenomic transformation have not been clarified.

Using a novel RIKEN technology that can detect the active enhancer region at single base level, we are trying to identify the enhancers responsible for the microglial transformation during life-stage progression and AD development. To date, we have succeeded to identify 36,320 new microglial enhancers including 937 regions that become different with age, and the analysis of coding regions regulated by the enhancers using Hi-C technology is in progress. As enhancers are activated in a cell-type specific manner, one can expect the development of novel technology that specifically controls the age-related functional alteration of microglia.

- 2. Research on tissue stem cells
- 1) Tissue homeostasis and its breakdown on the basis of immune cell-tissue stem cell interplay

Even under the steady-state, type I interferons (IFNs) are consistently produced, albeit in trace amounts, so called "physiologic type I IFNs". We previously reported that the physiologic 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 achievement, we examined the significance of physiologic type I IFNs in intestinal stem cells (ISCs) and found that it reduces the number and function of ISCs, resulting in the promoted differentiation into secretory progenitors (Nat Cell Biol 2020). Similarly, physiologic type I IFNs impaired the stemness of colonic stem cells (CSCs), leading to the defective colonic regeneration with lethality in a DSS colitis model (Sci Rep 2020).

Although several types of cells are synchronously involved in the damage-induced epithelial regeneration, it remains unclear to what degree each population contributes to the overall epithelial regeneration. Using a combination of genetic lineage tracing, single-cell gene expression profiling, and organoid-formation assays, we characterized the heterogeneity of epithelial stem cells in the radiation-damaged intestine. As a result, we found that the main cell of origin after intestinal injury originated from Lgr5+ cells (Sci Rep 2020).

2) Establishment of human tongue cancer organoid biobank

Squamous cell carcinoma occurs in the oral cavity, esophagus, lungs, and cervix. Tongue cancer accounts for about 60% of oral cancer, and the 5-year survival rate is extremely low for advanced tongue cancer, and the recurrence rate after radical treatment is also high. Similarly, squamous cell carcinoma of the esophagus, which is characteristic of Asian countries including Japan, has a very high recurrence rate after curative treatment. As a multicenter collaborative study, our research group has succeeded in constructing an organoid library specialized for human tongue cancer and human esophageal squamous cell carcinoma, which has never been reported (34 cases of tongue cancer and 18 cases of esophageal cancer, ongoing). In addition, we have established cancer organoids that are resistant to anticancer drugs used in clinical treatment (4 cases of tongue cancer and 4 cases of esophageal cancer, ongoing). Using these unique resources, the elucidation of the mechanism for acquiring anticancer drug resistance and the search for drug discovery are in progress.

(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. Loems Ziegler-Heitbrock, Toshiaki Ohteki, Florent Ginhoux, Ken Shortman, Hergen Spits. Reclassifying plasmacytoid dendritic cells as innate lymphocytes. Nat Rev Immunol. 2022.10; 23(1); 1-2
- 2. Guangwei Cui, Akihiro Shimba, Jianshi Jin, Taisaku Ogawa, Yukiko Muramoto, Hitoshi Miyachi, Shinya Abe, Takuma Asahi, Shizue Tani-Ichi, Johannes M Dijkstra, Yayoi Iwamoto, Kirill Kryukov, Yuanbo Zhu, Daichi Takami, Takahiro Hara, Satsuki Kitano, Yan Xu, Hajime Morita, Moyu Zhang, Lynn Zreka, Keishi Miyata, Takashi Kanaya, Shinya Okumura, Takashi Ito, Etsuro Hatano, Yoshimasa Takahashi, Hiroshi Watarai, Yuichi Oike, Tadashi Imanishi, Hiroshi Ohno, Toshiaki Ohteki, Nagahiro Minato, Masato Kubo, Georg A Holländer, Hideki Ueno, Takeshi Noda, Katsuyuki Shiroguchi, Koichi Ikuta. A circulating subset of iNKT cells mediates antitumor and antiviral immunity. Sci Immunol. 2022.10; 7(76); eabj8760

[Conference Activities & Talks]

- Yasuhiro Kamii, Koji Hayashizaki, Toshio Kanno, Yoshimasa Takahashi, Toshiaki Ohteki, Yusuke Endo. Interleukin-27 supports metabolic adaptation of Natural killer T cells and effector responses. 第 51 回日 本免疫学会学術集会 2022.12.09 熊本
- 2. Taku Sato, Toshiaki Ohteki, Takeshi Namiki . Characterization of tissue macrophages involved in the pathogenesis of type I interferonopathy . 第 51 回日本免疫学会学術集会 2022.12.09 熊本
- 3. Masashi Kanayama. B cell: an amplifier of myeloid cell production triggered by infection. 第 51 回日本免疫学会学術集会 2022.12.09 熊本
- 1. Taku Sato, Toshiaki Ohteki. Intestinal stem cells and their niche. The 40th Annual Meeting of the Japanese Society for Bone and Mineral Research 2022.07.22

Pathological Cell Biology

Professor : Shigeomi SHIMIZU Associate Professor : Norio SHIMIZU Project Associate Professor : Satoshi TORII, Kimiko SHIMIZU, Masatsune TSUJIOKA, Shinya HONDA Assistant Professor : Hirofumi YAMAGUCHI, Youichi NIBE Project Assistant Professor : MHajime SAKURAI, Minkyong SHIN, Graduate Student : Tomoyo YOSHIDA, Kazuma OHSHIMA, Chinami OGAWA Research Assistant : Hikaru KUROSAWA, Naomi KOJIMA Secretary : Hitomi Fukabori, Setsu TAMAI

(1) Outline

- 1) Molecular mechanisms of Golgi membrane associated degradation (GOMED)
- 2) Physiological and pathological roles of GOMED in mammals 3) Development of GOMED-inducing drugs
- 4) Analysis of non-apoptotic cell death
- 5) Physiological and pathological roles of cell death in mammals
- 6) Analysis of organellar communication with cytosol
- 7) Development of novel anti- Epstein-Barr virus (EBV)drug (S-FMSU).
- 8) 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 proteolysis and cell death, the cell death-related diseases, the physiological and pathological roles of GOMED, and development of anti-EBV drugs and 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 GOMED and cell death, the cell death-related diseases, the physiological and pathological roles of GOMED, and development of an exhaustive pathogenic microbial screening system.

(4) Publications

[Original Articles]

1. Sakurai HT, Arakawa S, Noguchi S, Shimizu S. FLIP-based autophagy-detecting technique reveals closed autophagic compartments. Scientific reports. 2022.12; 12(1); 22452

- 2. Hajime Tajima Sakurai, Satoko Arakawa, Saori Noguchi, Shigeomi Shimizu. FLIP-based autophagy-detecting technique reveals closed autophagic compartments. Sci Rep. 2022.12; 12(1); 22452
- 3. Yanagi T, Kikuchi H, Susa K, Takahashi N, Bamba H, Suzuki T, Nakano Y, Fujiki T, Mori Y, Ando F, Mandai S, Mori T, Takeuchi K, Honda S, Torii S, Shimizu S, Rai T, Uchida S, Sohara E. Absence of ULK1 decreases AMPK activity in the kidney, leading to chronic kidney disease progression. Genes to cells. 2022.11; 28(1); 5-14
- 4. Matsuda H, Nibe-Shirakihara Y, Tamura A, Aonuma E, Arakawa S, Otsubo K, Nemoto Y, Nagaishi T, Tsuchiya K, Shimizu S, Ma A, Watanabe M, Uo M, Okamoto R, Oshima S. Nickel particles are present in Crohn's disease tissue and exacerbate intestinal inflammation in IBD susceptible mice. Biochemical and biophysical research communications. 2022.02; 592; 74-80
- 5. Hiroki Matsuda, Yoichi Nibe-Shirakihara, Akiko Tamura, Emi Aonuma, Satoko Arakawa, Kana Otsubo, Yasuhiro Nemoto, Takashi Nagaishi, Kiichiro Tsuchiya, Shigeomi Shimizu, Averil Ma, Mamoru Watanabe, Motohiro Uo, Ryuichi Okamoto, Shigeru Oshima. Nickel particles are present in Crohn's disease tissue and exacerbate intestinal inflammation in IBD susceptible mice. Biochem Biophys Res Commun. 2022.02; 592; 74-80
- 6. 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
- 7. 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
- 8. 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. Arakawa S, Honda S, Torii S, Tsujioka M, Shimizu S.. Monitoring of Atg5-independent Mitophagy. Methods in Molecular Biology,"Mitophagy".

[Conference Activities & Talks]

1. 山口啓史. Wipi3 分子による新規オートファジー機構 (GOMED) の制御とインスリン分泌への影響. 2021 年 度難治疾患研究所発表会 2022.03.08 東京

Pediatrics and Developmental Biology

Professor: Tomohiro MORIO Associate Professor: Masatoshi TAKAGI, Kenchi KASHIMADA Senior Assistant Professor: Kenichi KASHIMADA, Takeshi ISODA Assistant Professor: Tomoko MIZUNO, Kei TAKASAWA, Taku ISHII, Tomohiro UDAGAWA, Manabu SUGIE, Akihiro HOSHINO, Yohei YAMAGUCHI, Kazuyuki ITO, Akira NISHIMURA, Hitoshi IRABU, Taisuke YAMAUCHI Project Assistant Professor:Fumiko Ozaki Graduate Students:Akira NISHIMURA, Kazuaki MATSUMOTO, Kengo MORIYAMA, Kento INOUE, Haruka HIROKI, Maki GAU, Aoi MORISHITA, Yuko AKUTSU, Takahiro TOMODA, Makito SAKURAI, Mika OKUTSU, Toru KANAMORI, Eriko ADACHI, Yusuke NOGUCHI, Shuya KANEKO, Shizuka KIRINO, Dan TOMOMASA, Etsushi TOYOFUKU, Shizuka KATSUZAKI, Hisae NAKATANI, Asami SHIMBO, Shiori EGUCHI, Daiki NIIZATO, Analia Gisela Yogi, Ayaka HANADA, Graduate Research Student:Riski MUHAIMIN

Department of Child Health and Development Professor: Hirokazu KANEGANE Assistant Professor: Masaki SHIMIZU

Department of Pediatrics, Neonatal and Maternal Medicine Professor: Masatoshi TAKAGI Assistant Professor: Susumu HOSOKAWA Project Assistant Professor: Chikako MORIOKA, Hitoshi IRABU

Department of Lifecourse Clinical Immunology Professor: Masaaki MORI

(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 be dside. Our current main projects are

1. Identification of responsible genes for inborn errors of immunity (IEI).

2. Development of the rapeutic approach for IEI

- 3. Development of innovative techniques for ex vivo cell therapy after hematopoietic stem cell transplantation.
- 4. Multicenter Registry for pediatric Pulmonary arterial hypertension (PAH) (Congenital Heart Disease related

PAH (JACPHR) and Idiopathic/heritable PAH (JAPHR))

5. Multicenter Registry study on Kawasaki Disease with coronary artery aneurysm

6. Basic study on the profile changes of umbilical cord blood and umbilical cord-derived mesenchymal stem cells in various intrauterine environments

7. Investigation of profile changes in stem cells from human exfoliated deciduous teeth (SHED) in children with cerebral palsy due to periventricular leukomalacia

- 8. Elucidating the molecular mechanisms of gonadal development
- 9. Molecular pathology of congenital adrenal diseases and disorder of sex development
- 10. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
- 11. Study of autoimmunity in Opsoclonus Myoclonus Syndrome
- 12. Development of gene therapy for Ataxia Telangiectasia
- 13. Study of molecular biology in systemic vascular stenosis
- 14. Genetic background of leukemia development
- 15. Study using single cell sequencing analysis in pediatric leukemia
- 16. Development of novel CAR-NK cell therapy for child cancer
- 17. Identifying the molecular pathology of metabolic syndrome in 21 hydroxylase deficiency
- $18.\ 3D$ genome structure and molecular mechanism in leukemia
- 19. Mechanistic insight into activation of super-enhancer in T cell commitment
- 20. Genetic analysis and development of the rapeutic approach for epilepsy syndrome
- 21. Clarifying immunological profiles of the patients with autoimmune diseases
- 22. Developing a methodology for the diagnosis of cytokine storm syndrome by exploiting a novel biomarker
- 23. Development of newborn screening for treatable childhood diseases including spinal muscular atrophy
- 24. Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease
- 25. Research in pathophysiology and prognostic predictor of nephritis /nephrotic syndrome
- 26. Molecular mechanisms and pathology of kidney disease with IEI or hereditary kidney disease

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Sci-ence, Hiroshima University, 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, Kyoto University, Tokyo University and many other laboratories.

• Hematology/Oncology/Immunology Group (Basic Research) Immunology

We have explored inborn error of immunity (IEI) candidate genes using the whole-exome analysis (WES) method using next-generation sequencers and have identified several candidate mutations. Molecular characterization of these candidates has also been conducted parallelly. Transplant outcomes of 566 IEI (WAS, CID, HLH, CGD, PIRD) cases using the Transplant Registry Unified Management Program (TRUMP) database were reported (Miyamoto, Kajiwara, Morio). We reported that XIAP deficiency is caused by maternal gonadal mosaicism (Tomomasa, Kanakane). Also, we are working with domestic and overseas researchers to analyze the pathogenesis of IEI and to develop therapeutic methods. A phase II clinical trial is underway to evaluate the efficacy and safety of sirolimus in the treatment of lymphoid enlargement, enteritis, and cytopenia associated with patients with IEI (Endo). As adoptive immunotherapy to promote immunological reconstitution after transplantation, we have developed virus-specific T cell therapy for refractory viral infections and are pursuing the clinical trial (Kamiya and Morio).

Oncology

In the research for the diseases related to DNA damage response pathways, we have elucidated the usefulness of PARP inhibitors for neuroblastoma by targeting homologous recombination repair and reported the results of phase I physician-led clinical trials for refractory pediatric solid tumors (Takagi). A multi-omics analysis using RNA-seq, methylation analysis, and whole exon analysis was performed on 84 cases of infant leukemia, and found that the undifferentiated IRX group with RAS pathway abnormalities showed resistance to treatment (Nishimura, Takagi).

Cardiology Group

< Basic Research >

We are struggling to elucidate the mechanism of pulmonary arterial hypertension. Our current project is to examine a role of BMP9 in PAH. (Sakurai and Hosokawa)

< Clinical Research >

"Multicenter Registry for pediatric pulmonary arterial hypertension (PAH) (Congenital Heart Disease related PAH (JACPHR) and Idiopathic/heritable PAH (JAPHR))"

"Effectiveness evaluation of live attenuated vaccines for patients using immunosuppresants" (Ishii)

"Multicenter Registry study on Kawasaki Disease with coronary artery aneurysm"

• Neurology Group

< Basic research >

We are trying to establish the gene therapy using viral vectors for ataxia telangiectasia (AT), one of the major neurodegenerative diseases. Another project is to establish diagnostic tools for early detection and early treatment of spinal muscular atrophy (SMA). We are also investigating the pathological mechanism of Moyamoya syndrome.

To clarify the cytoprotective effects of astrocytes in oxygen-glucose deprivation condition, we are investigating the role of nuclear receptor 4A (NR4A) subfamily and another cytoprotective transcription factor related to hypoxia-induced factor-1 α (HIF-1 α) with murine astrocyte-enriched cultures (collaborative project with Hiroshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

< Clnical research >

"Genetic analysis and development of the rapeutic 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" "Development of newborn screening for treatable childhood diseases including spinal muscular atrophy" "Establishment of quantitative evaluation of pediatric cerebellum-dependent motor learning through prism adaptation and the application to central nervous system diseases"

Endocrinology – Metabolism Group Molecular mechanisms of gonadal development

To understand the pathophysiology of DSD, our current research is focusing on elucidating the molecular mechanisms of sex determination and gonadal development, especially in the aspect of the transcriptional network of sex determination and gonadal development. Another our target is to identify the precise functions of transcription factors, such as NR5A1 (SF1), FOXL2, and SOX9, in gonadal development.

Molecular analysis of pathological mechanisms in congenital adrenal hyperplasia (CAH), including developing a novel methodology for analysing the responsible gene, CYP21A2.

One of our major tasks is supervising the CAH neonatal mass-screening in Tokyo. Currently, large number of CAH patients we treat, and clarifying the clinical details and we are focusing on clarifying the long term prognosis of the disease. In addition to adrenal insufficiency and androgen excess, metabolic syndrome during adulthood is reported to be another major concern of CAH. The precise pathophysiology is not known. We are looking at elucidating the molecular mechanisms of the metabolic syndrome in CAH patients by using mice model.

Identifying novel molecules of congenital endocrinological and congenital metabolic diseases

We aim to identify novel molecules responsible for development of congenital endocrine disorders such as insulin resistance. Current ongoing projects will be integrated systematically, and will be applicable to develop innovative approach for the treatment of congenital endocrine and metabolic disorder, including regenerative medicine.

• Rheumatology 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, developing a methodology for the diagnosis of cytokine storm syndrome by exploiting a novel biomarker, and Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease are other our current projects. In addition, in joint research with the department of rheumatology, we are analyzing the

current status and effectiveness of treatment for childhood and adult onset of collagen disease.

• Neonatology group

We will compare and analyze the gene expression profiles of mesenchymal stem cells collected from umbilical cords and dental pulp to elucidate their relationship with disease establishment and to accumulate basic data for cell therapy.

We will collect umbilical cord-derived mesenchymal stem cells with various background factors, such as intrauterine infection and fetal growth restriction, and examine the relationship between profile changes and disease establishment.

As basic data for exploring the possibility of dental pulp stem cell therapy for periventricular leukomalacia, a complication of preterm infants, we are collecting stem cells from human exfoliated deciduous teeth of children with cerebral palsy due to periventricular leukomalacia and analyzing their profile.

• 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 immunological and epidemiological studies on therapeutic effects of oral immunotherapy against food allergy.

• Nephrology Group

Research in pathophysiology and prognostic predictor of nephritis /nephrotic syndrome

A multicentre study with associated hospitals is underway to identify disease pathogenesis and pathogenic factors by analysing patient epidemiological data, peripheral blood cell fraction analysis and serum, urinary protein and miRNA profiling.

Searching for biomarkers associated with the severity, response to treatment and long-term prognosis of idiopathic nephritis and idiopathic nephrotic syndrome, aiming to construct disease models and elucidate the molecular basis of the disease using organoids.

(3) Education

Block Lecture

The systematic lecture was performed for M4 students. Half of the lectures "were performed using an active-learning" style. Eighteen frames of the active-learning and two frames of team -based learning (TBL) were provided. Although one frame of active-learning alone cannot cover the whole area of pediatrics, we believe that the active learning is very useful because it can enhance students' application skills.

Project semester

This provides the opportunities of basic research for the 4th grade students for half a year. Every year, a few students are 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) for 5th-year medical students in pediatrics was shortened from 1 month (4 weeks) to 2 weeks due to the pandemic of COVID-19. Each student spent two weeks in one of the two groups (hematology, immunology, cardiology, neurology, Endocrinology-metabolism, nephrology, Rheumatology, neonatology).

Lectures were given to all students six times in two weeks selected from a lot of topics such as diagnostics, congenital heart disease, neonates, infusion, EEG, endocrinology, leukemia, immunodeficiency infections, and the role of the Child Life Specialist in pediatrics, and student conferences were held on Tuesday, Wednesday, and Thursday for further understanding of the clinical practice program.

We struggled to provide ward practice to the students even though the time to practice was limited due to the pandemic.

Two 6th-year medical students were accepted for clinical training in pediatrics, and they joined a practice for two weeks in a medical group of their choice as an advanced program.

In terms of post-graduate education, at least one month of basic clinical education was provided to the first and second year of clinical residents at on-campus. For the second semester clinical residents at the university, we

provided a wide range of more specialized clinical education to prepare them to become pediatric specialists.

(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 raked 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 inborn errors of immunity, 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 FY2020, we performed HCT for 10 cases (10 allo-HCT). In addition, Two HCTs were performed in collaboration with the hematology department.

For a relapsed ALL case, CAR-T cas performed.

Our experience of HCT exceeds 230 cases including more than 100 cases with primary immunodeficiency diseases, so far.

Clinical trial

Clinical trials led by the pediatric department of Tokyo Medical and Dental University are ongoing.

"Phase 2 study of the efficacy and safety of sirolumus in patients with primary immunodeficiency"

"Cell therapy for treatment-resistant viral infections after hematopoietic cell transplantation using antigen-specific T cells against multiple viruses generated from blood donors with at least half-matched HLA" Clinical trial (Phase I/II) as a GCTP-compliant regenerative medicine technology based on the Law for Ensuring the Safety of Regenerative Medicine.

"Clinical Phase II Study of hematopoietic stem cell transplantation for ataxia telangiectasia and related diseases" is carried out"

• Cardiology 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 2022, the number of inpatients was 83, which consisted of 47 congenital heart disease, 13 pulmonary hypertension, 6 Kawasaki Disease, 6 arrhythmia, and 5 others. Cardiac catheterizations were performed in 49 patients and cardiac surgery was performed in 21 patients (16 open-heart surgery), which consisted of 9 VSDs, 4 ASDs, 1 TOF, 1 DORV, 1 PDA, 1 CoA, 1 severeTR.. The number of outpatients was 1,826, echocardiogram was performed in 1227, Treadmill exercise-induced electrocardiogram was perform in 113, and Holter 24hr electrocardiogram was performed in 75 patients.

• Neurology Group

We provide medical care in a wide range of pediatric nerologic 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. We also provide nucleic acid drug and gene therapy for patients with spinal muscular atrophy. We focus on diagnosis, genetic analysis and treatment for rare neurologic diseases.

• Endocrinology- Metabolism Group

We provide comprehensive diagnostic and treatment services for children with disorders of endocrinology and metabolism, including and diabetes, such as disorders of growth, pubertal development, Ca/P metabolism (including skeletal dysplasia), gonadal development and adrenal cortex function. Especially, we are focusing on providing advanced medical service for congenital adrenal hyperplasia (CAH) and disorders of sex development (DSD). Our institute is one of the DSD central facilities approved by the Japanese Society for Pediatric Endocrinology (JSPE). For social contribution, we supervise the neonatal screening system for CAH in Tokyo metropolitan city and peer support group of type 1 diabetes, "Tokyo Wakamatsu-kai".

• Nephrology Group

Nephrology Group provides diagnosis and treatment for patients with various kidney diseases. We perform kidney biopsy (30/year) and imaging examination. Percutaneous needle renal biopsy under general anaesthesia is performed in patients with nephritis and nephrotic syndrome in infancy, in collaboration with anaesthetists. Last year, seven percutaneous needle renal biopsies under general anaesthesia were performed. No major complications occurred and the procedure was performed safely.

We performed peritoneal dialysis for infants and provided acute hemodialysis for children who developed acute kidney injury. Also patients with tubulointerstitial nephritis and renal disease complicated by uveitis are treated.

• Rheumatology group

We treat children with rheumatic diseases, undiagnosed cases such as fever of unknown origin, and autoinflammatory syndrome represented by periodic fever. The emphasis is on the issues and challenges of transitional care in adulthood for pediatric rheumatic diseases.

• Neonatology group

Collaborating with other medical departments or special care groups in pediatrics, we are treating preterm infants (≥ 27 weeks gestation, birth weight ≥ 800 g), neonates with complications and babys 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 inborn errors of immunity. We perform hematopoietic stem cell transplan- tation 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 Group

Cardiology group performs diagnosis, evaluation of treatment and decision of treatment strategy for pediatric pulmonary hypertension patients. We actively treat severe idiopathic/hereditary pulmonary arterial hypertension (IPAH/HPAH) patients by upfront 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 incractable epilepsy, cerebellar ataxia, immune-mediated neurological disease, spinal muscular atrophy, involuntary movement, perinatal brain damage, infection of nervous system, acute encephalopathy/encephalitis, neurodegenerative disease.

• Endocrinology- Metabolism Group

The leader of our endocrinology group is a supervisor of congenital adrenal hyperplasia (CAH) newborn screening in Tokyo. We treat substantial number of 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 organizing a Type 1 DM patients' association (Wakamatsu-kai) and have the summer camp for diabetic children every year.

• Nephrology Group

We treat various pediatric kidney diseases, such as congenital nephrotic syndrome, refractory nephrotic syndrome, IgA nephropathy, Henoch-Scho " nlein purpura nephritis and tubulointerstitial nephritis with or without uveitis, etc. Chronic kidney disease management and dialysis treatment for children with acute renal failure. Acute hemodialysis and plasma exchange therapy for acute renal failure associated with hematological disease and collagen diseases, as well as autoimmune encephalitis, are also provided. Needle kidney biopsy performed to more than 30 patients for infants and over children. We cooperate in school urinalysis to prevent exacerbations of renal disease, we

• Rheumatology group

Clinically, our target is not only pediatric rheumatic disease, but also inflammatory diseases such as periodic fever, fever of unknown origin, and repeated arthritis affecting multiple joints. We are also actively involved in the expansion and standardization of treatment indications through participation in clinical trials and formulation of guidelines.

• 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. We introduce new biological medicines to the long-term management for sever persistent asthma patients.

(7) Publications

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[Misc]

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- 2. Intan Hakimah Ismail, Hirokazu Kanegane, Xiaodong Zhao. Editorial: Creating Awareness for Primary Immunodeficiencies in the Southeast and East Asia Regions. Front Immunol. 2022.05; 13; 920819
- 3. Kenichi Kashimada. When to eat and sleep matters to children's health. Pediatr Int. 2022.01; 64(1); e15063

[Conference Activities & Talks]

- 1. Franziska Auer, Adela Escuerdo, Ulrike Anne Friedrich, Polina Stepensky, Arndt Borkhardt, Sarah Elitzur, Masatoshi Takagi, Julia Hauer. Familial Predisposition to B-Cell Precursor Acute Lymphoblastic Leukemia Mediated By PAX5 Germline Variants.. The 64th ASH Annual Meeting and Exposition 2022.12.12 New Orleans, US
- 2. Carolin Escherich, Wenan Chen, Satoshi Miyamoto, Yui Namikawa, Wenjian Yang, David T. Teachey, Zhenhua Li, Elizabeth A. Raetz, Eric C Larsen, Meenakshi Devidas, Paul L. Martin, W Paul Bowman, Gang Wu, Ching-Hon Pui, Stephen P. Hunger, Masatoshi Takagi, Jun J. Yang, Mignon L. Loh. Rare Deleterious TCF3 Germline Variants and Predisposition to Acute Lymphoblastic Leukemia in Children.. The 64th ASH Annual Meeting and Exposition 2022.12.11 New Orleans, US
- 3. Hirokazu Kanegane. Advanced therapies: The future of BMT in Asia. IPOPI 4th Regional Asian PID Meeting 2022.11.19 Kuala Lumpur
- 4. Hirokazu Kanegane. Finding NEMO. The 1st National IEI Congress of China 2022 2022.11.12 Web 開催
- 5. Eriko Adachi, Kenichi Kashimada, Ryuichi Nakagawa, Kei Takasawa, Akito Sutani, Atsumi Tsuji-Hosokawa, Osamu Ohara. Allele frequency of deletions or large conversions in Japanese 21 hydroxylase deficiency patients was 20%. The 12th Biennial Scientific Meeting of the Asia Pacific Paediatric Endocrine Society 2022 2022.10.06 Seoul, KOREA (Web)
- 6. Shizuka Kirino, Analia Gisela Yogi, Eriko Adachi, Maki Gau, Hisae Nakatani, Toru Kanamori, Tomohiro Udagawa, Kei Takasawa, Kenichi Kashimada, Tomohiro Morio. The first family case of 46,XX DSD due to pathogenic variant of WT1 Zinc Finger domain 4. The 12th Biennial Scientific Meeting of the Asia Pacific Paediatric Endocrine Society 2022 2022.10.06 Seoul, KOREA (Web)
- 7. Analia Gisela Yogi, Kenichi Kashimada, Ryosei Iemura, Hisae Nakatani, Kei Takasawa, Maki Gau, Takeru Yamauchi, Masayuki Yoshida, Tomohiro Morio. A case of BMP2 defficiency with short stature. The 12th Biennial Scientific Meeting of the Asia Pacific Paediatric Endocrine Society 2022 2022.10.06 Seoul, KOREA (Web)
- 8. Atsumi Tsuji-Hosokawa, Kazuhiro Watanabe, Atsuko Hashimoto, Nobuyuki Ishige, Harumi Yajima, Akito Sutani, Hisae Nakatani, Maki Gau, Kei Takasawa, Kenichi Kashimada. The LC-MS/MS pilot study assay for 21-hydroxylase deficiency newborn screening revealed the high relevancy of 21DOF, (4AD + 17 α OHP)/F, and 11DOF/17 α OHP. The 12th Biennial Scientific Meeting of the Asia Pacific Paediatric Endocrine Society 2022 2022.10.06 Seoul, KOREA (Web)
- 9. Hirokazu Kanegane. Hematopoietic stem cell transplantation for PID. 17th Congress of Asian Society for Pediatric Research (ASPR 2022) 2022.09.17 Web 開催
- Franziska Auer, Adela Escudero, Mikko Sipola, Anna Viitasalo, Mina Morcos, Ulrike Anne Friedrich, Aleksandra Pandyra, Arndt Borkhardt, Masatoshi Takagi, Julia Hauer. PAX5 Deficiency and Germline Susceptibility to Pediatric Leukemia. 27th European Hemathology Association Congress (EHA2022) 2022.06.09 Vienna, Austria
- 11. Yohei Yamaguchi, Susumu Hosokawa, Yusuke Kajikawa, Yasuhiro Maejima, Mitsuaki Isobe, Tetsushi Furukawa, Shozaburo Doi. Pathophysiological Role of Dexmedetomidine for Monocrotaline-induced Pulmonary Arterial Hypertension in Rats. 55th Annual Meeting of the Association for European Paediatric and Congenital Cardiology 2022.05.26 Geneva
- Hirokazu Kanegane. A B-Cell Deficient Japanese Girl with ZIP7 Deficiency Caused by Novel Compound Heterozygous Variants in SLC39A7. 13th International Congress of Immunodeficiency Diseases 2022.04.24 Web 開催
- 13. Hirokazu Kanegane. ALPS & ALPS-like and IPEX & IPEX-like. . 4th Asia-Pacific Society for Immunodeficiencies Congress 2022.04.02 Web 開催
- 14. Hirokazu Kanegane. An Approach to Antibody Deficencies.. 4th Asia-Pacific Society for Immunodeficiencies Congress 2022.04.01 Web 開催
- 1. EBV reactivation and nephrotic syndrome associated with chronic GVHD after allogeneic hematopoietic cell transplantation for GATA2 deficiency. 2022.11.26

- 2. Sinusoidal obstruction syndrome during induction remission therapy for FUS-ERG-positive BCP-ALL. 2022.11.26
- 3. A case of unrelated bone marrow transplantation with a lemtuzumab-based conditioning regimen for XIAP deficiency. 2022.11.26
- 4. BCP-ALL Inotuzumab ozogamicin successfully controlled the TCF3-HLF-positive acute lymphoblastic leukemia before hematopoietic cell transplantation. 2022.11.25
- 5. A PAX5 germline variant in a patient with common variable immunodeficiency complicated with B-cell acute lymphoblastic leukemia. 2022.11.25
- 6. Polatuzumab vedotin, bendamustine and rituximab (Pola-BR) for diffuse large B cell lymphoma in a patient with Bloom syndrome. 2022.11.25
- 7. Cytokine monitoring for disease status evaluation in a patient with chronic active Epstein-Barr virus infection. 2022.11.25
- 8. Umbilical cord blood transplantation for a patient with CHARGE syndrome and severe combined immunodeficiency. 2022.11.25
- 9. Non-coding RNA transcription and super-enhancer activation facilitate 3D genome structure. 2022.09.29
- 10. Role of Hematopoietic Cell Transplant Coordinator in transition from childhood to adulthood. 2022.05.14
- 11. Stem cell transplantation for XLP1 with EBV-associated hemophagocytic lymphohistiocytosis. 2022.05.14
- 12. International retrospective study of allogeneic HCT for X-linked agammaglobulinemia. 2022.05.13
- 13. A lemtuzumab-containing reduced intensity conditioning for two cases with PI3K-delta syndrome. 2022.05.13
- 14. Allogeneic hematopoietic cell transplantation for asymptomatic patients with SAP deficiency. 2022.05.13
- 15. Cellular therapy within the framework of regenerative medicine. 2022.05.12
- 16. A nation-wide study of congenital complement deficiency in Japan. 2022.02.12
- 17. Infection prevention for patients with inborn errors of immunity; second report from a nationwide survey in Japan. 2022.02.12
- 18. A case of bone marrow transplantation to activated P13KDelta syndrome type 1 (APDS1). 2022.02.12

[Others]

1. 2022.02

Macrophage activation syndrome -Pathogenesis and treatment strategy(SHIMIZU Masaki)

Rheumatology

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	Hisanori HASEGAWA
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	Naoki KIMURA(2)
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	Akio YAMAMOTO, Youji KOMIYA,
	Yasuhiro TAGAWA, Seiji NODA
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Affiliated Hospital	Hiroyuki HAGIYAMA, Kenji NAGASAKA,
	Akito TAKAMURA, Makoto SOEJIMA,
	Yusuke MATSUO, Toshihiro MATSUI,
	Fumiaki KONDO, Wakako KAWSAKI,
	Masami TOKURA, Riku YOSHITUKA,
	Tomoko NIWANO, Yuriko YAGYU,
	Takahiro NAKAHARA, Takuna TSUBATA,
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	Hiroyuki BABA, Daisuke KAWADA,
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	Motohiko SATO
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Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,
Instutute of global affairs

(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. Komiya Y, Sugihara T, Hirano F, Matsumoto T, Kamiya M, Sasaki H, Hosoya T, Kimura N, Ishizaki T, Mori M, Tohma S, Yasuda S, Matsui T. Factors associated with impaired physical function in elderly rheumatoid arthritis patients who had achieved low disease activity. Modern rheumatology. 2022.12;
- 2. Ho Lee, Shotaro Chubachi, Ho Namkoong, Takanori Asakura, Hiromu Tanaka, Shiro Otake, Kensuke Nakagawara, Atsuho Morita, Takahiro Fukushima, Mayuko Watase, Tatsuya Kusumoto, Katsunori Masaki, Hirofumi Kamata, Makoto Ishii, Naoki Hasegawa, Norihiro Harada, Tetsuya Ueda, Soichiro Ueda, Takashi Ishiguro, Ken Arimura, Fukuki Saito, Takashi Yoshiyama, Yasushi Nakano, Yoshikazu Mutoh, Yusuke Suzuki, Koji Murakami, Yukinori Okada, Ryuji Koike, Yuko Kitagawa, Akinori Kimura, Seiya Imoto, Satoru Miyano, Seishi Ogawa, Takanori Kanai, Koichi Fukunaga, . Characteristics of hospitalized patients with COVID-19 during the first to fifth waves of infection: a report from the Japan COVID-19 Task Force. BMC Infect Dis. 2022.12; 22(1); 935
- 3. Watase M, Masaki K, Chubachi S, Namkoong H, Tanaka H, Lee H, Fukushima T, Otake S, Nakagawara K, Kusumoto T, Asakura T, Kamata H, Ishii M, Hasegawa N, Oyamada Y, Harada N, Ueda T, Ueda S, Ishiguro T, Arimura K, Saito F, Yoshiyama T, Nakano Y, Mutoh Y, Suzuki Y, Edahiro R, Sano H, Sato Y, Okada Y, Koike R, Kitagawa Y, Tokunaga K, Kimura A, Imoto S, Miyano S, Ogawa S, Kanai T, Fukunaga K, Japan COVID-19 Task Force. Impact of accumulative smoking exposure and chronic obstructive pulmonary disease on COVID-19 outcomes: report based on findings from the Japan COVID-19 task force. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2022.12; 128; 121-127
- 4. Tomoko Niwano, Tadashi Hosoya, Saori Kadowaki, Etsushi Toyofuku, Takuya Naruto, Masaki Shimizu, Hidenori Ohnishi, Ryuji Koike, Tomohiro Morio, Kohsuke Imai, Masayuki Yoshida, Shinsuke Yasuda. An adult case of suspected A20 haploinsufficiency mimicking polyarteritis nodosa. Rheumatology (Oxford). 2022.11; 61(11); e337-e340
- 5. Nakagawara Kensuke, Chubachi Shotaro, Namkoong Ho, Tanaka Hiromu, Lee Ho, Azekawa Shuhei, Otake Shiro, Fukushima Takahiro, Morita Atsuho, Watase Mayuko, Sakurai Kaori, Kusumoto Tatsuya, Asakura Takanori, Masaki Katsunori, Kamata Hirofumi, Ishii Makoto, Hasegawa Naoki, Harada Norihiro, Ueda Tetsuya, Ueda Soichiro, Ishiguro Takashi, Arimura Ken, Saito Fukuki, Yoshiyama Takashi, Nakano Yasushi, Mutoh Yoshikazu, Suzuki Yusuke, Edahiro Ryuya, Murakami Koji, Sato Yasunori, Okada Yukinori, Koike Ryuji, Kitagawa Yuko, Tokunaga Katsushi, Kimura Akinori, Imoto Seiya, Miyano Satoru, Ogawa Seishi, Kanai Takanori, Fukunaga Koichi. Impact of upper and lower respiratory symptoms on COVID-19 outcomes: a multicenter retrospective cohort study RESPIRATORY RESEARCH. 2022.11; 23(1); 315
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- 20. Tetsuya Saito, Nikunj M Shukla, Fumi Sato-Kaneko, Yukiya Sako, Tadashi Hosoya, Shiyin Yao, Fitzgerald S Lao, Karen Messer, Minya Pu, Michael Chan, Paul J Chu, Howard B Cottam, Tomoko Hayashi, Dennis A Carson, Maripat Corr. Small Molecule Calcium Channel Activator Potentiates Adjuvant Activity. ACS Chem Biol. 2022.01; 17(1); 217-229
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- 22. Mari Kamiya, Fumitaka Mizoguchi, Shinsuke Yasuda. Amelioration of inflammatory myopathies by glucagon-like peptide-1 receptor agonist via suppressing muscle fibre necroptosis Journal of Cachexia, Sarcopenia and Muscle. 2022.06; 13(4); 2118-2131
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[Conference Activities & Talks]

- Hosoya Tadashi, Oba Seiya, Komiya Yoji, Kawata Daisuke, Kamiya Mari, Iwai Hideyuki, Miyamoto Sho, Kanno Takayuki, Ainai Akira, Suzuki Tadaki, Hasegawa Hideki, Yasuda Shinsuke. Infection and Immunity II(The underlying mechanism of the deterioration in obese patients with COVID-19). 日本免 疫学会総会,学術集会記録 2022.11.01
- 2. Mari Kamiya, Marina Tsuchida, Hirokazu Sasaki, Natuka Umezawa, Shinsuke Yasuda. Glucagon-like peptide-1 receptor agonist ameliorates inflammatory myopathies via suppressing muscle fiber necroptosis. The 51st Annual Meeting of the Japanese Society for Immunology 2022.12.09 Kumamoto, Japan
- 3. Shinsuke Yasuda, Mari Kamiya, Fumitaka Mizoguchi, Kimito Kawahata, Dengli Wang, Masahiro Nishibori, Jessica Day, Cynthia Louis, Ian P Wicks, Hitoshi Kohsaka . Targeting Necroptosis in Muscle Fibers in Polymyositis. ACR Convergence 2022 2022.11.13 Philadelphia, Pennsylvania, USA
- 4. Mari Kamiya, Fumitaka Mizoguchi, Hirokazu Sasaki, Natsuka Umezawa, Shinsuke Yasuda. Agonistic stimulation of Glucagon-like peptide-1 receptor ameliorated inflammatory myopathies through suppressing muscle fiber necroptosis. EULAR2022 2022.06.02 Bella Center Copenhagen, Copenhagen, Denmark

5. Mari Kamiya, Fumitaka Mizoguchi, Shinsuke Yasuda. Agonistic stimulation of Glucagon-like peptide-1 receptor ameliorates experimental polymyositis through inhibiting muscle fiber necroptosis. 66th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2022.04.26 Yokohama, Japan

[Awards & Honors]

- 1. MRCR Top Reviewer Award 2021, 2022.03
- 2. JCR2022 ICW Excellent Abstract Award, Japan College of Rheumatology, 2022.04
- 3. Excellence in Research Awards, Tokyo Medical and Dental University, 2022.10

[Others]

1. Targeting necroptosis for inflammatory myopathies, 2022.03 AAAS EurekAlert! The Global Source for Science News

Dermatology

Professor: Naoko OKIYAMA Associate Professor: Takeshi NAMIKI Head of medical office:Hana TAKESHITA Assistant Professor: Yuutaro IWAMOTO, Rina OOTAKE, Azusa KANAZAWA Senior Resident: Atsushi ODA, Shizuka OZASA, Mituki YAMAMOTO, Hideki SHIMA, Mika FUJIWARA Resident:Yua HARIMOTO, Ittki SUGITA, Kenta MORIMOTO Adjunct Doctor:Tadatsune IIDA, Yuuki ICHIMURA, Risa KONISHI, Tomoko FUJIMOTO, Makiko NISHIDA, Minako INAZAWA Doctoral Student: Taku NAMATAME, Chie UCHIDA Project Researcher : Hind ALBUSANI Technical Assistant: Chiyako MIYAGISHI Staff Assistant:Misa MIWA, 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) 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 theories (STAT6 decoy ODN) for severe atopic dermatitis in the clinic.

(3) Publications

[Original Articles]

- 1. Okiyama Naoko, Tanaka Ryota. 免疫チェックポイント阻害剤による様々な臓器における免疫関連有害事象 (Immune-related adverse events in various organs caused by immune checkpoint inhibitors) Allergology International. 2022.04; 71(2); 169-178
- 2. Kakurai Masakazu, Okiyama Naoko, Ogawa Tatsuya, Fukuzono Maki, Kubota Noriko, Fujisawa Yasuhiro, Kajita Tomohide, Ishii Akiko, Tamaoka Akira, Nomura Toshifumi. Intertwined vascular skin manifestations in a patient with Sjoegren syndrome: A case report(和訳中) Journal of Cutaneous Immunology and Allergy. 2022.02; 5(1); 22-23
- 3. Miyahara Hanako, Okiyama Naoko, Okune Mari, Konishi Risa, Miyamoto Masahide, Hara Monami, Iwabuchi Atsushi, Takada Hidetoshi, Nishino Ichizo, Nomura Toshifumi. Case of anti-nuclear matrix protein 2 antibody-positive juvenile dermatomyositis preceded by linear cutaneous lupus erythematosus on the face(和訳中) The Journal of Dermatology. 2022.01; 49(1); e18-e19
- 4. Imanaka Yoko, Nakagawa Yukinobu, Yamaoka Toshifumi, Kotobuki Yorihisa, Hayashi Misa, Katayama Ichiro, Ichimura Yuki, Okiyama Naoko, Fujimoto Manabu. Refractory dermatomyositis which developed in a patient with silicone breast implants(和訳中) Allergology International. 2022.01; 71(1); 158-160

[Misc]

- 1. Mouri M, Kanamori T, Tanaka E, Hiratoko K, Okubo M, Inoue M, Morio T, Shimizu M, Nishino I, Okiyama N, Mori M. Hepatic veno-occlusive disease accompanied by thrombotic microangiopathy developing during treatment of juvenile dermatomyositis and macrophage activation syndrome: A case report. Modern rheumatology case reports. 2022.11;
- 2. Wada S, Namiki T, Takano M, Miura K, Okiyama N. Kaposi sarcoma with HHV-8 immunoreactivity in a gastric lesion but not in skin lesions. Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG. 2022.11; 20(11); 1512-1514
- 3. Wada S, Namiki T, Takano M, Miura K, Okiyama N. Kaposi-Sarkom mit HHV-8-Immunreaktivität in einer Magenläsion, aber nicht in Hautläsionen. Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG. 2022.11; 20(11); 1511-1513
- 4. Ichimura Y, Ikei H, Konishi R, Zeniya M, Okai T, Nomura T, Negishi K, Okiyama N. Relevance of leukemia inhibitory factor to anti-melanoma differentiation-associated gene 5 antibody-positive interstitial lung disease. Rheumatology (Oxford, England). 2022.11;
- Ogawa T, Ishitsuka Y, Nakamura Y, Watanabe R, Okiyama N, Fujisawa Y, Fujimoto M, Roop DR, Nomura T. Loricrin Protects against Chemical Carcinogenesis. The Journal of investigative dermatology. 2022.07; 142(7); 2023-2026.e1
- Tanaka R, Ichimura Y, Kubota N, Konishi R, Nakamura Y, Mizuno S, Takahashi S, Fujimoto M, Nomura T, Okiyama N. The Role of PD-L1 on Langerhans Cells in the Regulation of Psoriasis. The Journal of investigative dermatology. 2022.07; 142(12); 3167-3174.e9
- 7. Nagamori T, Ishibazawa E, Yoshida Y, Izumi K, Sato M, Ichimura Y, Okiyama N, Nishino I, Azuma H. A Continuous Increase in CXC-Motif Chemokine Ligand 10 in a Case of Anti-Nuclear Matrix Protein-2-Positive Juvenile Dermatomyositis. Journal of medical cases. 2022.06; 13(6); 290-296
- 8. Kobayashi T, Nakano T, Ogata H, Sato N, Yamaide F, Yamashita Y, Chikaraishi K, Hino M, Nishino I, Ichimura Y, Okiyama N, Hamada H. A 10-year-old girl with low-grade B cell lymphoma complicated by anti-nuclear matrix protein 2 autoantibody-positive juvenile dermatomyositis. Rheumatology (Oxford, England). 2022.05; 61(6); e143-e145
- 9. Okune M, Okiyama N, Fukuzono M, Sasaki K, Nomura T. Development of systemic lupus erythematosus after dupilumab treatment in a case of atopic dermatitis. The Journal of dermatology. 2022.05; 49(5); 556-559
- 10. Fukuzono M, Okiyama N, Iwasaki R, Endo R, Sasaki K, Inoue S, Nomura T. Intravenous immunoglobulin-induced thrombocytopenia: a case report and review of the literature European journal of dermatology : EJD. 2022.05; 32(3); 373-376
- Okune Mari, Okiyama Naoko, Fukuzono Maki, Sasaki Katsuhito, Nomura Toshifumi. デュピルマブ治療後 に全身性エリテマトーデスを発症したアトピー性皮膚炎の1例 (Development of systemic lupus erythematosus after dupilumab treatment in a case of atopic dermatitis) The Journal of Dermatology. 2022.05; 49(5); 556-559
- 12. Okada Y, Izumi R, Hosaka T, Watanabe S, Shijo T, Hatchome N, Konishi R, Ichimura Y, Okiyama N, Suzuki N, Misu T, Aoki M. Anti-NXP2 antibody-positive dermatomyositis developed after COVID-19 manifesting as type I interferonopathy. Rheumatology (Oxford, England). 2022.04; 61(4); e90-e92

- Okiyama N, Tanaka R. Immune-related adverse events in various organs caused by immune checkpoint inhibitors. Allergology international : official journal of the Japanese Society of Allergology. 2022.04; 71(2); 169-178
- 14. Ichimura Yuki, Konishi Risa, Shobo Miwako, Inoue Sae, Okune Mari, Maeda Akemi, Tanaka Ryota, Kubota Noriko, Matsumoto Isao, Ishii Akiko, Tamaoka Akira, Shimbo Asami, Mori Masaaki, Morio Tomohiro, Kishi Takayuki, Miyamae Takako, Tanboon Jantima, Inoue Michio, Nishino Ichizo, Fujimoto Manabu, Nomura Toshifumi, Okiyama Naoko. Reliability of antinuclear matrix protein 2 antibody assays in idiopathic inflammatory myopathies is dependent on target protein properties(和訳中) The Journal of Dermatology. 2022.04; 49(4); 441-447
- 15. Ichimura Y, Konishi R, Shobo M, Inoue S, Okune M, Maeda A, Tanaka R, Kubota N, Matsumoto I, Ishii A, Tamaoka A, Shimbo A, Mori M, Morio T, Kishi T, Miyamae T, Tanboon J, Inoue M, Nishino I, Fujimoto M, Nomura T, Okiyama N. Reliability of antinuclear matrix protein 2 antibody assays in idiopathic inflammatory myopathies is dependent on target protein properties. The Journal of dermatology. 2022.04; 49(4); 441-447
- 16. Ichimura Y, Konishi R, Shobo M, Inoue S, Okune M, Maeda A, Tanaka R, Kubota N, Matsumoto I, Ishii A, Tamaoka A, Shimbo A, Mori M, Morio T, Kishi T, Miyamae T, Tanboon J, Inoue M, Nishino I, Fujimoto M, Nomura T, Okiyama N. Anti-nuclear matrix protein 2 antibody-positive inflammatory myopathies represent extensive myositis without dermatomyositis-specific rash. Rheumatology (Oxford, England). 2022.03; 61(3); 1222-1227
- 17. Hiraiwa T, Hanami Y, Okiyama N, Konishi R, Ichimura Y, Yamamoto T. Clinically amyopathic dermatomyositis with diffuse erosive erythema in a patient with anti-small ubiquitin-like modifier activating enzyme antibody. International journal of dermatology. 2022.02; 61(10); e389-e391
- Tanboon J, Inoue M, Saito Y, Tachimori H, Hayashi S, Noguchi S, Okiyama N, Fujimoto M, Nishino I. Dermatomyositis: Muscle Pathology According to Antibody Subtypes. Neurology. 2022.02; 98(7); e739-e749
- 19. Miyahara H, Okiyama N, Okune M, Konishi R, Miyamoto M, Hara M, Iwabuchi A, Takada H, Nishino I, Nomura T. Case of anti-nuclear matrix protein 2 antibody-positive juvenile dermatomyositis preceded by linear cutaneous lupus erythematosus on the face. The Journal of dermatology. 2022.01; 49(1); e18-e19
- 20. Tanaka R, Ichimura Y, Kubota N, Saito A, Nakamura Y, Ishitsuka Y, Watanabe R, Fujisawa Y, Mizuno S, Takahashi S, Fujimoto M, Okiyama N. Differential Involvement of Programmed Cell Death Ligands in Skin Immune Responses. The Journal of investigative dermatology. 2022.01; 142(1); 145-154.e8
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- 22. Konishi R, Tanaka R, Inoue S, Ichimura Y, Nomura T, Okiyama N. Evaluation of apremilast, an oral phosphodiesterase 4 inhibitor, for refractory cutaneous dermatomyositis: A phase 1b clinical trial. The Journal of dermatology. 2022.01; 49(1); 118-123
- 23. Ishitsuka Y, Ogawa T, Nakamura Y, Kubota N, Fujisawa Y, Watanabe R, Okiyama N, Fujimoto M, Roop DR, Ishida-Yamamoto A. Loricrin and NRF2 Coordinate Cornification. JID innovations : skin science from molecules to population health. 2022.01; 2(1); 100065
- 24. Imanaka Y, Nakagawa Y, Yamaoka T, Kotobuki Y, Hayashi M, Katayama I, Ichimura Y, Okiyama N, Fujimoto M. Refractory dermatomyositis which developed in a patient with silicone breast implants. Allergology international : official journal of the Japanese Society of Allergology. 2022.01; 71(1); 158-160

[Conference Activities & Talks]

- 1. Ichimura Yuki, Konishi Risa, Nomura Toshifumi, Fujimoto Manabu, Okiyama Naoko. Autoimmunity against melanoma differentiation-associated protein 5 induces interstitial lung disease in mice(タイトル和 訳中). 日本研究皮膚科学会年次学術大会・総会プログラム 2022.10.01
- 2. Okiyama Naoko. Comprehensive study of autoimmune diseases(タイトル和訳中). 日本研究皮膚科学会年 次学術大会 · 総会プログラム 2022.10.01

- 3. Iida Tadatsune, Namiki Takeshi, Kobayashi Daisuke, Yokozeki Hiroo, Okiyama Naoko. Macrophage activation promotes hypohidrosis(タイトル和訳中). 日本研究皮膚科学会年次学術大会・総会プログラム 2022.10.01
- 4. Namiki Takeshi, Nojima Kohei, Hayashi Masahiro, Kawaguchi Masakazu, Suzuki Tamio, Ishikawa Masashi, Tanemura Atsushi, Katayama Ichiro, Mori Taisuke, Yamazaki Naoya, Mori Hiroki, Sasaki Yoshiyuki, Yokozeki Hiroo, Okiyama Naoko. Overexpression of NUAK2 and phospho-Akt(S473) has a significant impact on development and progression in acral melanomas(タイトル和訳中). 日本研究皮膚 科学会年次学術大会・総会プログラム 2022.10.01
- 5. Ebata Satoshi, Yoshizaki Ayumi, Oba Koji, Kashiwabara Kosuke, Ueda Keiko, Uemura Yukari, Watadani Takeyuki, Fukasawa Takemichi, Miura Shunsuke, Yoshizaki-Ogawa Asako, Asano Yoshihide, Okiyama Naoko, Kodera Masanari, Hasegawa Minoru, Sato Shinichi. Safety and efficacy of rituximab in systemic sclerosis (DESIRES): a double-blind, investigator-initiated, randomised, placebo-controlled trial(タイトル 和訳中). 日本研究皮膚科学会年次学術大会・総会プログラム 2022.10.01
- 6. Nagashima Natsumi, Ugajin Tsukasa, Miyake Kensuke, Karasuyama Hajime, Namiki Takeshi, Okiyama Naoko. The clinical and histological characteristics of 'basophil-high' atopic dermatitis(タイトル和訳中). 日本研究皮膚科学会年次学術大会・総会プログラム 2022.10.01

NCCHD Child Health and Development

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Matsumoto, Kenji

(1) Research

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 multifanctorial 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 underlysing 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, allogenic 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.

(2) 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) Publications

[Original Articles]

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- Miyakawa K, Machida M, Kawasaki T, Nishi M, <u>Akutsu H</u>^{*}, Ryo A. Reduced Replication Efficacy of Severe Acute Respiratory Syndrome Coronavirus 2 Omicron Variant in "Mini-gut" Organoids. *Gastroenterology*. 2022 Aug;163(2):514-516.
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[Review Articles]

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Human Pathology

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(1) Outline

Pathology is the studies in which one theorizes and understands disease, as the language implies disease (pathos hardship) + theory (logus logic). Later, as research subjects that caused diseases were subdivided and research methods advanced, bacteriology (microbiology), parasitology (medical zoology), immunology, and molecular biology became independent from the category of pathology. In recent years, academic fields have been restructured beyond the framework of conventional academic fields, and there is a tendency for them to be further subdivided according to purposes, research subjects, and research methods. At present, pathology, based on morphology, is the study of understanding and organizing the causes of diseases (etiology), the formation of lesions (histogenesis), and disease status (pathogenesis). In the recent pathology, the fields of experimental pathology, in which hypotheses are experimentally proven using laboratory animals and cultured cells, and the fields of surgical pathology and diagnostic pathology, which are closely related to the clinical medicine, tend to be separated, and the number of pathologists engaged in the latter, which deals with human tissues, is increasing.

In the field of Human Pathology of TMDU, we aim to train pathologists who can accurately make pathological diagnosis of various human diseases, and at the same time, to develop pathologists who have a research mind capable of carrying out research that leads to improvement of pathological diagnosis, with the aim of elucidating the etiology, histogenesis and mechanism of human diseases.

(2) Research

About human cancer:

There are three main purposes.

(1) Carcinogenesis and histogenesis of cancers: For the understanging of G-I tract cancers, such as esophageal cancers, gastric cancers, colorectal cancers, and colitic cancers, and lung cancers, premalignant lesions will be clarified by histopathological analyses, clinicopathological analyses, and genetic analyses, and the process and molecular basis of carcinogenesis from premalignant lesions will be clarified.

(2) Objective diagnosis of pathological diagnosis related to cancer: Cancer originating from any organ is difficult to differentiate from benign tumors originating from that organ, and there are also borderline tumors of benign and malignant tumors. In addition, many of the pathological findings with clinical significance are based on subjective judgment, and the objectivity, reproducibility, and agreement rate among observers of the findings are problematic. In pathological diagnosis, it is important to apply computer, Ai, and image analysis technology, and establishment of new pathological diagnosis which integrates genome information and various marker expression information of which the advance is remarkable recently is required.

(3) Malignant tumor progression and mechanism of metastasis: In human esophageal cancer, gastric cancer, colorectal cancer, and lung cancer, early cancer is often found, and reduced operations and treatments such as endoscopic resection are often performed. However, there are some high-grade cases showing metastasis from the early stage, and it is necessary to diagnose them in the early stage and select an appropriate therapy. In the process of invasion of early cancers, it is important to clarify the pathological findings related to metastasis and recurrence and to clarify the molecular basis closely related to them. By establishing markers that can be applied to pathological diagnosis, more accurate pathological diagnosis will become possible. About chronic inflammatory diseases:

To clarify the etiology and origin of a chronic inflammatory disease of unknown origin by thoroughly analyzing the lesion site from a pathological standpoint. In addition, markers useful for diagnosis will be developed and applied to actual pathological diagnosis.

1) The possibility that intracellular latent infection in the deep organ of Propionibacterium acnes and rapid activation of autophagy and induction of Th1 immune response with the endogenous activation are causes of granuloma formation is studied on the sarcoidosis from the immunopathology viewpoint. Acne infection has been reported to be associated with diseases other than sarcoidosis, and its relationship to other diseases is also being studied.

2) Regarding the pathogenetic mechanism of chronic gastritis caused by infection of Helicobacter pylori on the surface of gastric mucosa, we found that Helicobacter pylori invades the lamina propria and translocates to regional lymph nodes of the stomach due to injury of the surface epithelium of the mucosa. Therefore, we investigated the possibility that Helicobacter pylori contributes to chronic inflammation of the gastric mucosa by directly stimulating immunocompetent cells in the mucosa and chronically stimulates the immune system in the paracortical region after influx to the lymph nodes. It is also known that the risk of developing gastric cancer varies depending on the structure of Helicobacter pylori. We are also developing test kits that can clarify the relationship between the structure of H. pylori and the risk of carcinogenesis and evaluate the risk of carcinogenesis by H. pylori.

3) Characteristic pathological findings observed in inflammatory colitis such as ulcerative colitis and Crohn's disease are analyzed, and their occurrence mechanism and significance are verified. In addition, evaluation of the activity of inflammation using biopsy materials and expression of molecular markers are studied.

4) Diagnosis of the type of systemic amyloidosis is very important for deciding the treatment plan of patients, but useful antibodies for diagnosis are not sufficiently available. Research is being conducted on the development and application of diagnostic antibodies that can improve the accuracy of pathological diagnosis.

(3) Education

In the graduate school doctoral program, the acquisition of the pathology medical specialist qualification is also made to be a goal with the doctor degree acquisition. First of all, training in autopsy, biopsy tissue diagnosis, rapid tissue diagnosis, tissue diagnosis of surgical specimens, etc., will be conducted, and training in the department of Diagnostic Pathology, TMDU hospital, as well as in the department of pathological diagnosis of the related hospitals will be conducted, with the aim of forming the basis for a "pathologist". During the training, participants will participate in various conferences or meetings in joint with clinical departments to announce pathological diagnoses, identify current problems in each clinical field, and discuss or collaborate with clinicians. While forming a basis as a pathologist, we will conduct research using clinicopathological, immunohistologic, and molecular pathological methods on issues directly related to the causes, diagnosis, and treatment of human diseases. The results will be published in academic meetings and academic journals in Japan and overseas.

(4) Lectures & Courses

What society calls for in medical care is proper diagnosis and treatment. Therefore, in the field of Human Pathology, the aim is to study the etiology, histogenesis, diagnosis, and treatment of human diseases with a strong awareness of problems and deep thought, while focusing on the study of clinical pathology, including histopathological diagnosis of autopsy, biopsy and surgically resected specimens. The results of the research should not only deepen the understanding of diseases, but also be useful for medical care and pathological diagnosis.

(5) Clinical Services & Other Works

As a general rule, all graduate students with a medical doctor's license are concurrently engaged in the Diagnostic Pathology department, TMDU hospital, where they are trained in pathological diagnosis and autopsy, with the aim of acquiring a qualification as a pathology specialist. In addition, staff and graduate students are working as part-time physicians at affiliated hospitals of TMDU in Tokyo, Kanagawa, Saitama, Chiba, and Ibaraki prefectures, which play a central role in supporting local medical care, to support pathological diagnosis and conduct joint research. In the field of Human Pathology, we hope to contribute to community medicine and society by improving the accuracy of pathological diagnosis. We are also actively cooperating in various academic activities, such as lecture presentations and conference participation in local hospitals. We also actively participate in and cooperate with the activities of various academic societies, including the Japanese Society of Pathology. In particular, we are involved in the management of the Japanese Society of Pathology and play a core role. Staff members also participate in and cooperate with various committees of ministries and agencies, including the Ministry of Health, Labour and Welfare.

(6) 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 the apeutic 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.

(7) Publications

[Original Articles]

- Miyauchi M, Akashi T, Furukawa A, Uchida K, Tamura T, Ando N, Kirimura S, Shintaku H, Yamamoto K, Ito T, Miura K, Kayamori K, Ariizumi Y, Asakage T, Kudo A, Tanabe M, Fujii Y, Ishibashi H, Okubo K, Murakami M, Yamada T, Takemoto A, Bae Y, Eishi Y, Ohashi K. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocr Pathol. 2022.12; 33(4); 506-518
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- 6. Shogo Wada, Takeshi Namiki, Moe Takano, Keiko Miura, Naoko Okiyama. Kaposi sarcoma with HHV-8 immunoreactivity in a gastric lesion but not in skin lesions. J Dtsch Dermatol Ges. 2022.11; 20(11); 1512-1514
- 7. Yoshimura Yusuke, Watanabe Shun, Yamanouchi Masayuki, Ikuma Daisuke, Mizuno Hiroki, Sekine Akinari, Hasegawa Eiko, Suwabe Tatsuya, Kono Kei, Kinowaki Keiichi, Ohashi Kenichi, Ubara Yoshifumi, Sawa Naoki. Tocilizumab Attenuates Anti-neutrophil Cytoplasmic Antibody-associated Nephritis Occurring During Abatacept and Adalimumab Therapy for Rheumatoid Arthritis: A Case Report. Intern Med. 2022.11;
- 8. Shinohara H, Kobayashi M, Hayashi K, Nogawa D, Asakawa A, Ohata Y, Kubota K, Takahashi H, Yamada M, Tokunaga M, Kinugasa Y, Oda G, Nakagawa T, Onishi I, Kinowaki Y, Kurata M, Ohashi K, Kitagawa M, Yamamoto K. Spatial and Quantitative Analysis of Tumor-Associated Macrophages: Intratumoral CD163-/PD-L1+ TAMs as a Marker of Favorable Clinical Outcomes in Triple-Negative Breast Cancer. International journal of molecular sciences. 2022.10; 23(21);
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- 19. Kataoka Toshiaki, Okudela Koji, Matsumura Mai, Baba Tomohisa, Kitamura Hideya, Arai Hiromasa, Suzuki Takeshisa, Koike Chihiro, Mutsui Hideaki, Sekiya Motoki, Sugiyama Misaki, Takemura Tamiko, Iwasawa Tae, Ogura Takashi, Ohashi Kenichi. Significant accumulation of KRAS mutations in bronchiolar metaplasia-associated honeycomb lesions of interstitial pneumonia. Oncol Lett. 2022.07; 24(1); 225
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- 35. Shogo Wada, Takeshi Namiki, Keiko Miura. Mononuclear variant of adult xanthogranuloma associated with B-cell acute lymphocytic leukemia. J Dermatol. 2022.01; 49(5); e161-e162
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[Conference Activities & Talks]

- 1. Kota Yoshifuji, Yotaro Motomura, Makiko Saito, Ayako Nogami, Genji Kawade, Shiori Watabe, Kouhei Yamamoto, Takahiko Mori, Toshikage Nagao.. TPL2, a New Prognostic Factor and a Potential Therapeutic Target in ABC-DLBCL.. 64th ASH Annual Meeting and Exposition. 2022.12.11 New Orleans
- 2. Junya Ito, Kensuke Miyake, Kazufusa Takahashi, Shigeyuki Shichino, Hajime Karasuyama. Transcriptomic and functional analyses uncover an immature subpopulation of basophils in the bone marrow and FoxO1 as a transcription factor involved in the regulation of basophil responsiveness. The 51st Annual Meeting of the Japanese Society 2022.12.08 Kumamoto

- 3. Kazufusa Takahashi, Kensuke Miyake, Ito Junya, Shimamura Hinano, Karasuyama Hajime. Difamilast, a selective phosphodiesterase 4 inhibitor, suppresses IL-4 production by basophils and ameliorates atopic dermatitis in a murine model. The 51st Annual Meeting of the Japanese Society 2022.12.08 Kumamoto
- 4. Kensuke Miyake, Kazufusa Takahashi, Junya Ito, Jun Nakabayashi, Shigeyuki Shichino, Soichiro Yoshikawa, Hajime Karasuyama. M2 macrophages present at resolution phase of inflammation display high efferocytic capacity and promote resolution of skin allergic inflammation. The 51st Annual Meeting of the Japanese Society 2022.12.07 Kumamoto

[Social Contribution]

- 1. The Japanese Society of Diagnostic Dermatopathology, Department of Pathology, Fukuoka University, 2005.04.17 Now
- 2. Ochanomizu Study Meeting of Dermatopathology, 2009.04 Now

Physiology and Cell Biology

Professor: Yoshikazu Isomura Associate professor: Riichiro Hira Assistant professor: Alain Rios Assistant professor: Masanori Kawabata Project Assistant professor: Kyohei Fujita

(1) Outline

One of the major goals of the Department of Physiology and Cell Biology is to elucidate the basic principles of the brain networks that are responsible for behavioral expression in rodents. Our neurophysiological research focuses mainly on the neural networks of the cerebral cortex, hippocampus, basal ganglia and thalamus that regulate particular behavioral tasks in rats; this research utilizes multichannel electrode-based multineuronal recording technology, Two-photon imaging of neural activity, optogenetics involving genetically modified animals and adeno-associated virus vectors, and theoretical analysis technologies.

(2) Research

Research Agenda – What do we want to know?

In the sensory, association and motor cortices in the cerebral cortex, the excitatory pyramidal cells and inhibitory interneurons form an intracortical circuit. These brain areas, which play important roles in appropriate behavioral expression, are connected with each other and form the interareal circuit that consists of complex intercortical and subcortical connections through the hippocampus, striatum, substantia nigra and thalamus.

In the 20th century, the spike (unit) activity of single neurons in the brain that are related to behavior was actively studied using the single-unit recording technique. From a technical point of view, however, it was extremely difficult to investigate neuron subtypes and axonal connections by this method. Therefore, we developed a new experimental technique and used it to initiate a study of the basic principles whereby neural networks, particularly those in the cerebral cortex, encode behavioral information.

Research Techniques – How do we find answers?

1. Operant Learning Task

With the conventional technique of operant conditioning, it took weeks to months to train rats to obtain rewards by pushing a lever with their forelimb. Therefore, we developed a "spout-lever" by integrating a lever and a spout, and this enabled us to train rats to perform the forelimb movement task in a short period of time. This method allows for more rapid generation of rats to perform particular behavioral tasks in physiological experiments.

2. Multineuronal Recording

Multineuronal recording is a physiological technique in which spike activities of a large number of neurons are simultaneously recorded using silicon probes (multichannel electrodes). Signals recorded with electrode are distinguished by spike sorting, an analysis technique, to separate the spike (unit) activity produced by each neuron. Multineuronal recording also makes it possible to simultaneously record local field potentials and spike activities to permit the analysis of functional synchronous oscillation activities such as gamma and ripple waves.

3. Optogenetics

To understand the mechanism of information processing in neuronal networks, it is useful to demonstrate causality by optogenetically manipulating signals flowing in the networks. We are conducting experiments using gene-expressing virus vectors as well as transgenic rats that express channelrhodopsin-2, which uses blue light to depolarize membrane potentials. In addition, we are conducting research to establish a multi-linc analysis technique that identifies axonal projections of recorded neurons by combining multineuronal recording technology with optogenetics.

4. Theoretical Analysis – Simulation Modeling

In collaboration with computational neuroscientists, we are conducting sophisticated and efficient theoretical analyses of multineuronal recording data. Our goal is to fuse experiment and theory by utilizing simulation and modeling techniques.

5. Two-photon imaging of neural activity

We are constructing a two-photon microscope with the world's largest field-of-view. Using this microscope, we will record more than 100,000 neuronal activities from the brain during task execution and clarify the mechanism by which neurons cooperatively express brain functions.

Research Methodologies - Pursuing Originality

Our research targets the brain networks in rats that are responsible for behavioral expression in order to understand essential brain mechanisms. Conventional neuroscience has often explored the functional localization in the brain by "averaging" brain activities. However, brain activities dynamically change every second, and there is no doubt that it is not just single areas that play a role in information processing, but rather the whole network, which consists of multiple areas. Therefore, we aim to perform truly original research by increasing the sophistication of our methods and extending our interests to multidisciplinary research without fear of failure, from the viewpoints of "from static to dynamic states" and "from points to lines."

see https://researchmap.jp/yoshikazuisomura/

(3) Education

The Department of Physiology and Cell Biology supports excellent next-generation researchers such as post-doctoral research fellows and graduate students through research activities that aim to elucidate the basic principles of brain networks. In principle, students define their research topics based on their future goals. One experimental setup is provided per one or two students/researchers. They receive curricula to learn a series of experimental techniques, join discussions that develop their logical thinking ability rather than simply increasing their knowledge, and receive opportunities to effectively conduct collaborative research in and out of the laboratory.

The Department is responsible for a lecture and laboratory practice on General Physiology for medical school students. It also provides research training for students during the project semester and MD-PhD courses that aim to foster basic researchers in the early stages of their education. The field of physiology is essential for comprehensively understanding body functions and providing the foundation for doctors to treat patients. We hope that you will voluntarily and actively participate in the activities of the department to immerse yourself in physiology.

(4) Lectures & Courses

We respect each one's independence and positive attitude, and foster a sense of social cooperation and responsibility.

(5) Publications

[Original Articles]

- 1. Keita Mitani, Masanori Kawabata, Yoshikazu Isomura, Yutaka Sakai. Automated and parallelized spike collision tests to identify spike signal projections iScience. 2022.09; 25(10); 105071
- 2. Koji Ikezoe, Naoki Hidaka, Satoshi Manita, Masayoshi Murakami, Shinichiro Tsutsumi, Yoshikazu Isomura, Masanobu Kano, Kazuo Kitamura. Cerebellar climbing fibers convey behavioral information of multiplex modalities and form functional modules bioRxiv. 2022.08; (preprint)
- 3. Soma S, Ohara S, Nonomura S, Yoshida J, Suematsu N, Pastalkova E, Sakai Y, Tsutsui K-I, Isomura Y. Hippocampal CA1 represents action and reward events instantly compared to the superficial and deep layers of the lateral entorhinal cortex bioRxiv. 2022.04; (preprint)

[Conference Activities & Talks]

- 1. Yoshikazu Isomura. Reward experience differently modifies action- and outcome-related activities along nigrostriatal system . JANUBET Symposium 2022 2022.09.21 Kyoto
- 2. Alain Rios, Satoshi Nonomura, Yutaka Sakai, Shigeki Kato, Kazuto Kobayashi, Masahiko Takada, Yoshikazu Isomura, Minoru Kimura. Dynamic and pathway-specific signaling in the dorsomedial striatum and dopamine neurons during behavioral adaptation. The 45th Annual Meeting of the Japan Neuroscience Society 2022.07.01 Okinawa convention center, Ginowan, Okinawa
- 3. Kawabata M, Rios AA, Sakairi T, Sakai Y, Isomura Y. Exploration of sensorimotor transformationrelated rodent cerebral cortices using a visual two-step response task. Neuroscience 2022, The 45th Annual Meeting of the Japan Neuroscience Society 2022.07.01 Okinawa convention center, Ginowan, Okinawa
- 4. Yoshikazu Isomura. Reward prediction and response in the hippocampus and basal ganglia . BSI KIST Seminar Series 2022 (online, KIST, Korea) 2022.06.08
- 5. Junichi Yoshida, Leila Khatami, Jorge Vera, Maritza Oñate, Julian Guarque Chabrera, Victoria Lovallo, Samantha Washburn, Yoshikazu Isomura, Farzan Nadim, Kamran Khodakhah. The Cerebellar Value Signaling to the Dopaminergic Centers . DOPAMINE 2022 (Centre Mont-Royal, Montreal, Canada) 2022.05.21
- 1. Visualization of neuronal activity by multiphoton excitation microscopy and its limitations. 2022.06.17

Stem Cell Regulation

Professor Tetsuya TAGA Junior Associate Professor Kouichi TABU Assistant Professor Yoshitaka MUROTA Administrative Assistant Maya MAKINO Technical Assistant Marika NODERA

(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) Development of bio-functional polymers and their applications for cancer stem cell regulation

(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. Aimaitijiang Alapati, Tabu Kouichi, Wang Wenqian, Nobuhisa Ikuo, Taga Tetsuya. Glioma cells remotely promote erythropoiesis as a self-expanding strategy of cancer stem cells GENES TO CELLS. 2022.01; 27(1); 25-42

[Misc]

- 1. Wenqian Wang, Kouichi Tabu, Alapati Aimaitijiang, Tetsuya Taga. Therapy-resistant nature of cancer stem cells in view of iron metabolism Inflammation and Regeneration. 2022.11; 42(1); 34
- 2. Yoshitaka Murota, Kouichi Tabu, Tetsuya Taga. Cancer Stem Cell-Associated Immune Microenvironment in Recurrent Glioblastomas Cells. 2022.06; 11(13); 2054
- 1. Tabu Kouichi, Taga Tetsuya. Cancer ego-system in glioma: an iron-replenishing niche network systemically self-organized by cancer stem cells 2022.11; 42(1); 54

[Conference Activities & Talks]

- 1. Yoshitaka Murota, Kouichi Tabu, Tetsuya Taga. Establishment of a high-content polymer array screening system to explore niche mimicries for cancerous cells. The 17th International Symposium of the Institute Network for Biomedical Science International Symposium on Tumor Biology in Kanazawa 2022 2022.10.14 Cancer Research Institute of Kanazawa University, Kanazawa, Japan
- 2. Kouichi Tabu, Shinji Kohsaka, Takuichiro Hide, Tetsuya Taga. Synthetic polymer microenvironment array chip based development of new cell phenomics for cancer stratification The 81st Annual Meeting of the Japanese Cancer Association. The 81st Annual Meeting of the Japanese Cancer Association 2022.10.01 Pacifico Yokohama, Yokohama, Japan
- 3. Yoshitaka Murota, Kouichi Tabu, Tetsuya Taga. Establishment of a high-content screening system for niche mimicries using polymer-immobilized microwell array plates. The 81st Annual Meeting of the Japanese Cancer Association 2022.09.30 Pacifico Yokohama, Yokohama, Japan
- 4. Tingting Zhang, Kouichi Tabuk, Yoshitaka Murota, Takuichiro Hide, Shunichiro Ogura, Tetsuya Taga. Exploration of glioma recurrence-related genes upregulated in highly invasive and 5-ALA-PDD escaping cells. The 81st Annual Meeting of the Japanese Cancer Association 2022.09.30 Pacifico Yokohama, Yokohama, Japan
- 5. Melig G, Nobuhisa I, Kiyoka S, Tsukahara R, Itabashi A, Kanai Y, Kanai M, Taga T. Rasip1-mediated maintenance of Sox17-transduced intra-aortic hematopoietic cluster cells. The 43rd Annual Meeting of the Japanese Society of Inflammation and Regeneration 2022.07.06 Awaji Yumebutai International Conference Center, Awaji, Japan
- 6. Tetsuya Taga, Kenji Kabashima. New regulatory mode of innate immunity, the organizers' opening remarks. The 15th World Congress on Inflammation 2022.06.08 Ergife Conference Center, Rome, Italy
- 7. Tetsuya Taga, Norihisa Bizen, Kouichi Tabu, Mei Wu, Christian Mangani, Rong Zhang, Mark Bradley. Identification of a niche-mimicking synthetic polymer scaffold that maintains neural stem cells in a growth factor- and serum-free system. The 19 th Stem Cell Research Symposium 2022.05.27 Awaji Yumebutai International Conference Center, Awaji, Japan
- 8. Norihisa Bizen, Tetsushi Kagawa, Toshinobu Nakamura, Hirohide Takebayashi, Toru Nakano, Tetsuya Taga. 5-methylcytosine hydroxylase Tet3 endows embryonic neural stem/precursor cells with astrogliogenic competence. The 19th Stem Cell Research Symposium 2022.05.27 Awaji Yumebutai International Conference Center, Awaji, Japan
- 9. Gerel Melig, Ikuo Nobuhisa, Kiyoka Saito, Ryota Tsukahara, Ayumi Itabashi, Yoshiakira Kanai, Masami Kanai, Tetsuya Taga. Investigating the function of Rasip1 in HSC-containing IAHCs of midgestation mouse embryos. The 19th Stem Cell Research Symposium 2022.05.27 Awaji Yumebutai International Conference Center, Awaji, Japan

Respiratory Medicine

Professor: Yasunari Miyazaki Junior Associate Professor: Furusawa Haruhiko, Assistant Professor: Tuyoshi Shirai, Takayuki Honda, Sho Shibata, Rie Sakakibara Masahiro Ishizuka (Research leave) Project Assistant Professor: Yuki Iijima, Sho Shimada, Takashi Yamana, yuka mishima Clinical Fellow:Wataru Inoue,Mizuki Mikoshiba,Natsushi Kubota,Yasuhisa takanashi,Kanako Furukawa Resident:Eiko Abe,Masafumi Soejima Ph.D. student; Seiko Takazawa, Hikaru Aoki, Shohei Yamashita, Takahiro Ando, Shun Endo, Jun Sugihara, Akifumi Mochizuki, Takashi Shimamura, Masaru Ito, Shinya Fujii, Nobuyuki Kondou, Goma Abe Professor, Department of Respiratory and Nervous System Science: Yuki Sumi Professor, Health Administration Center: Ryushi Tazawa Assistant Professor, Health Administration Center: Keiko Komatsuzaki Associate Professor, Department of Respiratory Physiology and Sleep Medicine: Tomoya Tateishi Associate Professor, Department of Pulmonary Immunotherapeutics: Tsukasa Okamoto Junior Assistant Professor, Department of Pulmonary Immunotherapeutics: Takahiro Mitsumura Specially-appointed Professor: Yasuhiro Setoguchi

(1) Outline

The lungs are in contact with the outside environment for breathing and are susceptible to external factors such as bacterial / viral infections, smoking, and dust exposure. Therefore, respiratory diseases include tumors, infectious diseases, allergic diseases, other inflammations, and congenital anomalies. In this field, we will foster researchers who are able to understand the pathophysiology of a wide range of respiratory diseases and to conduct research that approaches the mechanism of disease development having a scientific perspective.

(2) Research

- 1. Pathophysiology of hypersensitivity pneumonitis, identification of causative antigens in the environment
- 2. Pathophysiology in lung fibrosis
- 3. Pathophysiology of acute exacerbations in interstitial pneumonia
- 4. Pathophysiology of pulmonary fibrosis and emphysematous changes
- 5. Tumor immunity in mesothelioma
- 6. Examination of oral allergy syndrome and asthma desensitization
- 2. Airway remodeling mechanism in asthma model
- 6. Pathophysiology of sleep apnea
- 7. Development of treatment for antibacterial drug-resistant 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 lug diseases in Japan are referred to our clinic.

(7) Publications

[Original Articles]

- Okamoto T, Dobrinskikh E, Hennessy CE, Liu N, Schwarz MI, Evans CM, Fontenot AP, Yang IV, Schwartz DA. Muc5b plays a role in the development of inflammation and fibrosis in hypersensitivity pneumonitis induced by < i> Saccharopolyspora rectivirgula< /i> . American journal of physiology. Lung cellular and molecular physiology. 2022.09; 323(3); L329-L337
- 2. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Japanese journal of infectious diseases. 2022.09; 75(5); 504-510
- 3. Natsuka Umezawa, Hirokazu Sasaki, Haruhiko Furusawa, Daisuke Kawata, Chiina Hata, Shinsuke Yasuda. Development of vasculitis in a case with severe asthma treated with benralizumab and low-dose corticosteroid. Allergol Int. 2022.09;
- 4. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Japanese journal of infectious diseases. 2022.09; 75(5); 504-510
- 5. Mitsumura Takahiro, Okamoto Tsukasa, Tosaka Mizuho, Yamana Takashi, Shimada Sho, Iijima Yuki, Sakakibara Rie, Shibata Sho, Honda Takayuki, Shirai Tsuyoshi, Ishizuka Masahiro, Aiboshi Junichi, Furusawa Haruhiko, Tateishi Tomoya, Tamaoka Meiyo, Shigemitsu Hidenobu, Arai Hirokuni, Otomo Yasuhiro, Tohda Shuji, Anzai Tatsuhiko, Takahashi Kunihiko, Yasuda Shinsuke, Miyazaki Yasunari. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases(タイトル和訳中) Japanese Journal of Infectious Diseases. 2022.09; 75(5); 504-510

- 6. Mitsumura Takahiro, Okamoto Tsukasa, Tosaka Mizuho, Yamana Takashi, Shimada Sho, Iijima Yuki, Sakakibara Rie, Shibata Sho, Honda Takayuki, Shirai Tsuyoshi, Ishizuka Masahiro, Aiboshi Junichi, Furusawa Haruhiko, Tateishi Tomoya, Tamaoka Meiyo, Shigemitsu Hidenobu, Arai Hirokuni, Otomo Yasuhiro, Tohda Shuji, Anzai Tatsuhiko, Takahashi Kunihiko, Yasuda Shinsuke, Miyazaki Yasunari. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases(タイトル和訳中) Japanese Journal of Infectious Diseases. 2022.09; 75(5); 504-510
- 7. Komatsu M, Yamamoto H, Matsui S, Terasaki Y, Hebisawa A, Iwasawa T, Johkoh T, Baba T, Miyamoto A, Handa T, Tomii K, Waseda Y, Bando M, Ishii H, Miyazaki Y, Yoshizawa A, Takemura T, Kawabata Y, Hanaoka M, Ogura T, Tokyo Diffuse Lung Disease Study Group.. Respiratory lesions in IgG4-related disease: classification using 2019 American College of Rheumatology/European League Against Rheumatism criteria. ERJ open research. 2022.07; 8(3);
- Yuko Kawamoto, Yumiko Yatomi, Haruhiko Furusawa, Satoshi Hanzawa, Yasunari Miyazaki, Makoto Tanaka. Understanding the process of people with hypersensitivity pneumonitis Implementing continuous antigen avoidance and their affecting situations: A grounded theory study. Journal of Clinical Nursing. 2022.06; 1-12
- Kawamoto Y, Yatomi Y, Furusawa H, Hanzawa S, Miyazaki Y, Tanaka M. Understanding the process of people with hypersensitivity pneumonitis implementing continuous antigen avoidance and their affecting situations: A grounded theory study. Journal of clinical nursing. 2022.06;
- 10. Ikeda Tokuji, Ichiba Shingo, Sasaki Takashi, Sato Masaaki, Konoeda Chihiro, Okamoto Tsukasa, Miyazaki Yasunari, Nakajima Jun, Sakamoto Atsuhiro. A case of severe respiratory failure due to interstitial pneumonia successfully bridged to lung transplantation from a brain-dead donor using 109-day veno-arterial extracorporeal membrane oxygenation JOURNAL OF ARTIFICIAL ORGANS. 2022.06;
- 11. Ikeda T, Ichiba S, Sasaki T, Sato M, Konoeda C, Okamoto T, Miyazaki Y, Nakajima J, Sakamoto A. A case of severe respiratory failure due to interstitial pneumonia successfully bridged to lung transplantation from a brain-dead donor using 109-day veno-arterial extracorporeal membrane oxygenation. Journal of artificial organs : the official journal of the Japanese Society for Artificial Organs. 2022.06;
- Kawamoto Y, Yatomi Y, Furusawa H, Hanzawa S, Miyazaki Y, Tanaka M. Understanding the process of people with hypersensitivity pneumonitis implementing continuous antigen avoidance and their affecting situations: A grounded theory study. Journal of clinical nursing. 2022.06;
- 13. Ejima M, Okamoto T, Suzuki T, Miyazaki Y. Role of serum surfactant protein-D as a prognostic predictor in fibrotic hypersensitivity pneumonitis. Respiratory investigation. 2022.05; 60(3); 369-378
- 14. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. SARS-CoV-2 RNA copy number is a factor associated with the mortality of COVID-19 and improves the predictive performance of mortality in severe cases. Japanese journal of infectious diseases. 2022.05;
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- 16. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. SARS-CoV-2 RNA copy number is a factor associated with the mortality of COVID-19 and improves the predictive performance of mortality in severe cases. Japanese journal of infectious diseases. 2022.05; 75(5); 504-510
- 17. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. SARS-CoV-2 RNA copy number is a factor associated with the mortality of COVID-19 and improves the predictive performance of mortality in severe cases. Japanese journal of infectious diseases. 2022.05;

- 18. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. SARS-CoV-2 RNA copy number is a factor associated with the mortality of COVID-19 and improves the predictive performance of mortality in severe cases. Japanese journal of infectious diseases. 2022.05; 75(5); 504-510
- 19. Sakashita H, Uchibori K, Jin Y, Tsutsui T, Honda T, Sakakibara R, Mitsumura T, Nukui Y, Shirai T, Masuo M, Suhara K, Furusawa H, Yamashita T, Ohba T, Saito K, Takagiwa J, Miyashita Y, Inase N, Miyazaki Y. A phase II feasibility study of carboplatin and nab-paclitaxel for advanced non-small cell lung cancer patients with interstitial lung disease (YLOG0114). Thoracic cancer. 2022.03; 13(9); 1267-1275
- 20. Sakashita H, Uchibori K, Jin Y, Tsutsui T, Honda T, Sakakibara R, Mitsumura T, Nukui Y, Shirai T, Masuo M, Suhara K, Furusawa H, Yamashita T, Ohba T, Saito K, Takagiwa J, Miyashita Y, Inase N, Miyazaki Y. A phase II feasibility study of carboplatin and nab-paclitaxel for advanced non-small cell lung cancer patients with interstitial lung disease (YLOG0114). Thoracic cancer. 2022.03; 13(9); 1267-1275
- 21. Endo S, Honda T, Kawahara T, Sakakibara R, Mitsumura T, Okamoto T, Miyazaki Y. Profile of metastatic lung cancer patients susceptible to development of thromboembolism during immunotherapy. Cancer treatment and research communications. 2022.03; 31; 100547
- 22. Haruhiko Furusawa, Anna L Peljto, Avram D Walts, Jonathan Cardwell, Philip L Molyneaux, Joyce S Lee, Evans R Fernández Pérez, Paul J Wolters, Ivana V Yang, David A Schwartz. Common idiopathic pulmonary fibrosis risk variants are associated with hypersensitivity pneumonitis. Thorax. 2022.01;
- 23. Ejima M, Okamoto T, Suzuki T, Miyazaki Y. Role of serum surfactant protein-D as a prognostic predictor in fibrotic hypersensitivity pneumonitis. Respiratory investigation. 2022.01; 60(3); 369-378
- 24. Murakami T, Iijima Y, Ando T, Ejima M, Shirai T, Furusawa H, Okamoto T, Tateishi T, Tamaoka M, Miyazaki Y. Successful diagnosis of humidifier lung by individual provocation test to a responsible environment, a case report. Respiratory medicine case reports. 2022; 37; 101639
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- 27. Murakami T, Iijima Y, Ando T, Ejima M, Shirai T, Furusawa H, Okamoto T, Tateishi T, Tamaoka M, Miyazaki Y. Successful diagnosis of humidifier lung by individual provocation test to a responsible environment, a case report. Respiratory medicine case reports. 2022; 37; 101639
- 28. Murakami T, Iijima Y, Ando T, Ejima M, Shirai T, Furusawa H, Okamoto T, Tateishi T, Tamaoka M, Miyazaki Y. Successful diagnosis of humidifier lung by individual provocation test to a responsible environment, a case report. Respiratory medicine case reports. 2022; 37; 101639
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- 31. Endo S, Honda T, Kawahara T, Sakakibara R, Mitsumura T, Okamoto T, Miyazaki Y. Profile of metastatic lung cancer patients susceptible to development of thromboembolism during immunotherapy. Cancer treatment and research communications. 2022; 31; 100547

[Conference Activities & Talks]

- Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma(和訳中). 日本呼吸器学会誌 2022.04.01
- 2. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma(和訳中). 日本呼吸器学会誌 2022.04.01
- 3. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. 悪性胸膜中皮腫の腫瘍免疫微小環境の解明 (Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma). 日本呼吸器学会誌 2022.04.01
- 4. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. 悪性胸膜中皮腫の腫瘍免疫微小環境の解明 (Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma). 日本呼吸器学会誌 2022.04.01
- 5. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. 悪性胸膜中皮腫の腫瘍免疫微小環境の解明 (Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma). 日本呼吸器学会誌 2022.04.01
- 6. Amemiya Miki, Tao Susumu, Yonetsu Taishi, Yamamoto Tasuku, Niida Takayuki, Matsuda Yuji, Usui Eisuke, Matsuda Junji, Nakamura Rena, Nishimura Takuro, Takigawa Masateru, Umemoto Tomoyuki, Miyazaki Shinsuke, Maejima Yasuhiro, Goya Masahiko, Mitsumura Takahiro, Miyazaki Yasunari, Sasano Tetsuo. D-dimer Level at Admission Associated with Thrombosis in Hospitalized Patients with Coronavirus Disease 2019(COVID-19)(和訳中). 日本循環器学会学術集会抄録集 2022.03.01
- 7. Touyama Yoko, Tao Susumu, Yonetsu Taishi, Yamamoto Tasuku, Niida Takayuki, Matsuda Yuji, Usui Eisuke, Matsuda Junji, Nakamura Rena, Nishimura Takuro, Takigawa Masateru, Umemoto Tomoyuki, Miyazaki Shinsuke, Maejima Yasuhiro, Goya Masahiko, Mitsumura Takahiro, Miyazaki Yasunari, Sasano Tetsuo. The Difference of Cardiovascular Disease Associated with Mortality in Younger and Elderly Patients with Coronavirus Disease 2019(COVID-19)(和訳中). 日本循環器学会学術集会抄録集 2022.03.01
- 8. Touyama Yoko, Tao Susumu, Yonetsu Taishi, Yamamoto Tasuku, Niida Takayuki, Matsuda Yuji, Usui Eisuke, Matsuda Junji, Nakamura Rena, Nishimura Takuro, Takigawa Masateru, Umemoto Tomoyuki, Miyazaki Shinsuke, Maejima Yasuhiro, Goya Masahiko, Mitsumura Takahiro, Miyazaki Yasunari, Sasano Tetsuo. 新型コロナウイルス感染症 (COVID-19) に罹患した若年患者と高齢患者における死亡率と関連し た心血管疾患の差違 (The Difference of Cardiovascular Disease Associated with Mortality in Younger and Elderly Patients with Coronavirus Disease 2019(COVID-19)). 日本循環器学会学術集会抄録集 2022.03.01
- 9. Amemiya Miki, Tao Susumu, Yonetsu Taishi, Yamamoto Tasuku, Niida Takayuki, Matsuda Yuji, Usui Eisuke, Matsuda Junji, Nakamura Rena, Nishimura Takuro, Takigawa Masateru, Umemoto Tomoyuki, Miyazaki Shinsuke, Maejima Yasuhiro, Goya Masahiko, Mitsumura Takahiro, Miyazaki Yasunari, Sasano Tetsuo. 新型コロナウイルス感染症 (COVID-19) 入院患者における入院時 D ダイマー値と血栓症との関 連 (D-dimer Level at Admission Associated with Thrombosis in Hospitalized Patients with Coronavirus Disease 2019(COVID-19)). 日本循環器学会学術集会抄録集 2022.03.01

Cardiovascular Medicine

Professor Tetsuo Sasano Associate Professor Masahiko Goya, Yasuhiro Maejima Eiji Kaneko Shinsuke Miyazaki, Taishi Yonetsu Lecturer Yusuke Ebana Assistant Professor Tomoyuki Umemoto, Susumu Tao, Tomoyo Sugiyama, Takatoshi Shigeta, Takuro Nishimura, Kensuke Hirasawa, Makoto Araki, Medical Staff, Resident Yoshinori Kanno, Mari Omori, Miho Negishi, Hiroshi Yoshikawa, Eiko Sakai, Akira Nakashima, Masayuki Noda, Hiroyuki Masumoto

(1) Outline

Our focus is on overcoming cardiovascular diseases such as ischemic heart disease, arrhythmias, and heart failure through research, clinical practice, and education. We particularly emphasize translational research that bridges the gap between basic research and clinical applications, as well as collaborative research involving medical engineering using AI and biosensing devices. We are dedicated to activities such as coronary artery imaging, physiological assessment of coronary blood flow, clinical electrophysiological tests, catheter ablation, and comprehensive therapies for severe heart failure. Our clinical efforts are supported by grounded clinical research.

Based on these activities, our aim is to educate individuals who can excel not only in Japan but also on a global scale. We provide education to foster physician scientists in order to contribute to the advancement of cardiovascular medicine.

(2) Research

To elucidate the etiology and pathophysiology of cardiovascular diseases, analysis is conducted using techniques such as pathology, cell biology, molecular biology, and immunology, employing model animals and clinical specimens. Particularly, research is focused on fundamental electrophysiology and the underlying mechanisms of arrhythmias, the investigation of heart failure pathogenesis and novel therapeutic approaches, as well as the exploration of remote biosensing and precision medicine through the use of AI for proactive medical interventions.

(3) Education

We provide a wide range of medical care related to cardiovascular diseases, and our educational activities encompass all aspects of cardiovascular disorders. Particularly, we cover diverse conditions such as ischemic heart disease, arrhythmias, valvular heart disease, and cardiomyopathies, including heart failure as their ultimate manifestation. The scope extends to vascular lesions, spanning from atherosclerotic diseases to vasculitis.

Furthermore, we are engaged in pioneering diagnostic methods centered around imaging and electrophysiology,

as well as advanced catheter-based treatments and comprehensive approaches for severe heart failure. We have established an educational framework dedicated to these endeavors.

(4) Lectures & Courses

We aim to cultivate physician scientists who possess a research-oriented mindset focused not only on acquiring technical skills and knowledge, but also on unraveling pathophysiology and developing treatment methods.

(5) 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 research 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.

(6) Clinical Performances

Diagnostic and treatment approaches: Ischemic heart diseases (angina, myocardial infarction), heart failure, arrhythmias (tachyarrhythmias and bradyarrhythmias), acquired heart valve diseases, cardiomyopathies (including secondary cardiomyopathies like cardiac sarcoidosis), Takayasu arteritis (treating the largest number of patients domestically), congenital heart diseases, pulmonary hypertension, hypertension, and blood pressure regulation abnormalities (neurally mediated syncope).

Advanced and sophisticated medical interventions: Catheter-based treatments for complex coronary artery lesions, excimer laser coronary angioplasty, catheter ablation for refractory arrhythmias, removal of infected pacemakers, diagnosis and treatment for Takayasu arteritis, mechanical circulatory support for severe heart failure requiring cardiac transplantation, evaluation for heart transplantation candidacy.

(7) Publications

[Original Articles]

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[Misc]

1. Kensuke Hirasawa, Masaki Izumo. Role of 3D Transesophageal Echocardiography for Transcatheter Mitral Valve Repair-A Mini Review. Front Cardiovasc Med. 2022.02; 9; 815304

[Conference Activities & Talks]

- 1. 中釜 瞬, Candray Katherine, 山本 佑, 中釜 悠, 城戸 康年, 前嶋 康浩, 笹野 哲郎. 炎症性心筋症疑いに 合併した AV ブロック グローバル化時代における病因診断の再考 (AV block Associated with Suspected Inflammatory Cardiomyopathy: Rethinking the Etiological Diagnosis in the Globalized Era). 日本渡航医 学会誌 2022.09.01
- 阿部 史征, 宮崎 徹, 木村 文香, 田仲 明史, 矢部 顕人, 吉竹 貴克, 野本 英嗣, 鈴木 麻美, 栗原 顕, 小野 裕一, 大友 建一郎, 笹野 哲郎. COVID-19 流行による緊急 PCI での再灌流時間に与える影響. 日本心血管インター ベンション治療学会抄録集 2022.07.01
- 3. 宮崎 紘子, 木村 茂樹, 張 峻模, 三須 彬生, 立石 遼, 山口 正男, 山上 洋介, 島田 博史, 萬野 智子, 一色 亜美, 清水 雅人, 藤井 洋之, 鈴木 誠, 笹野 哲郎. Orbital atherectomy による石灰化プラーク減少の評価における 新規 OCT に搭載された人工知能の信頼性. 日本心血管インターベンション治療学会抄録集 2022.07.01
- 4. 菱刈 景一, 疋田 浩之, 津野 航, 吉川 宏, 矢野 弘崇, 伊藤 徳彦, 飯谷 宗弘, 村井 典史, 高橋 淳, 米津 太志, 笹 野 哲郎. PAD 患者における EVT 後の3剤併用療法と2剤併用療法の有用性. 日本心血管インターベンショ ン治療学会抄録集 2022.07.01
- 5. 菱刈 景一, 疋田 浩之, 村井 典史, 高橋 淳, 米津 太志, 笹野 哲郎. PAD 疾患に対するカテーテル以外の治 療法 EVT 後の抗血小板、抗凝固療法は?Short DAPT?. 日本心血管インターベンション治療学会抄録集 2022.07.01
- 6. 増田 怜, 土山 高明, 水沼 吉章, 佐々木 高史, 鯨岡 裕史, 山岡 広一郎, 新井 智之, 稲垣 大, 吉田 精孝, 木村 高志, 高橋 正雄, 北條 林太郎, 深水 誠二, 笹野 哲郎. ST 上昇型急性心筋梗塞に対するエキシマレーザーカテーテルアブレーションの長期予後への影響. 日本心血管インターベンション治療学会抄録集 2022.07.01
- 7. Nakagama Shun, Maejima Yasuhiro, Fan Qintao, Watanabe Yuka, Tamura Natsuko, Sasano Tetsuo. The critical role of ER selective autophagy in response to Doxorubicin-induced myocardial injury Shun Nakagama(和訳中). 日本小児循環器学会総会、学術集会抄録集 2022.07.01
- 8. 山上 洋介, 木村 茂樹, 宮崎 紘子, 張 峻模, 三須 彬生, 立石 遼, 山口 正男, 島田 博史, 萬野 智子, 一色 亜美, 清水 雅人, 藤井 洋之, 鈴木 誠, 笹野 哲郎. たこつぼ症候群の合併が疑われた特発性冠動脈解離の一例. 日本 心血管インターベンション治療学会抄録集 2022.07.01
- 9. 松田 和樹, 杉山 知代, 星野 昌弘, 羽田 昌浩, 三澤 透, 長嶺 竜宏, 上野 弘貴, 左山 耕大, 米津 太志, 笹野 哲 郎, 角田 恒和. 初発の非 ST 上昇型急性冠症候群における心臓 MRI で初めて同定された過去の無症候性心筋 梗塞の予測因子. 日本心血管インターベンション治療学会抄録集 2022.07.01
- 10. 左山 耕大, 杉山 知代, 星野 昌弘, 羽田 昌浩, 三澤 透, 長嶺 竜宏, 上野 弘貴, 松田 和樹, 米津 太志, 笹野 哲 郎, 角田 恒和. 初発の非 ST 上昇型急性心筋梗塞患者において、心臓 MRI で初めて同定された過去の無症候 性心筋梗塞が予後に与える影響. 日本心血管インターベンション治療学会抄録集 2022.07.01

- 11. 羽田 昌浩, 杉山 知代, 星野 昌弘, 三澤 透, 長嶺 竜宏, 上野 弘貴, 松田 和樹, 左山 耕大, 米津 太志, 笹野 哲 郎, 角田 恒和. 左前下行枝病変の微小血管障害の有無について左前下行枝のドップラーエコーでの血流速度 の診断能についての検討. 日本心血管インターベンション治療学会抄録集 2022.07.01
- 12. 三須 彬生, 木村 茂樹, 宮崎 紘子, 張 峻模, 立石 遼, 山口 正男, 山上 洋介, 島田 博史, 萬野 智子, 一色 亜美, 清水 雅人, 藤井 洋之, 鈴木 誠, 笹野 哲郎. 急性冠症候群における非責任病変の脂質プラークの経時的変化. 日本心血管インターベンション治療学会抄録集 2022.07.01
- 13. 杉山 知代, 星野 昌弘, 羽田 昌浩, 三澤 透, 長嶺 竜宏, 上野 弘貴, 松田 和樹, 左山 耕大, 米津 太志, 笹野 哲 郎, 角田 恒和. 急性冠症候群患者における OCT 上の冠動脈プラーク性状と CTA 上の冠動脈炎症・CMR 上 の全冠血流予備比との関連. 日本心血管インターベンション治療学会抄録集 2022.07.01
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[Awards & Honors]

1. The Best Doctors in Japan 2022–2023, Teladoc HEALTH, 2022.07

Cardiovascular Surgery

Professor : HirokuniARAI Associate Professor: Tomohiro MIZUNO Junior Associate Professor: Keiji OI, Eiki NAGAOKA Assistant Professor: Masafumi YASHIMA, Tatsuki FUJIWARA, Kiyotoshi OISHI, Masashi TAKESHITA Graduate Student: Dai TASAKI, Kenji SAKAI, Ryoji KINOSHITA, Kiyotoshi OISHI, Kenji YOKOYAMA Masashi TAKESHITA, Hironobu SAKURAI, Haruna SEKI, Tomoki TAHARA Hospital Staff: 3

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 regargitation. 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]

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- 4. Nagaoka E, Arai H. Mechanical simulation study of reapproximated sternum rigidity comparing sternal fixation devices. General thoracic and cardiovascular surgery. 2022.08; 71(2); 98-103
- 5. Takeshita M, Arai H, Nagaoka E, Oi K, Yashima M, Fujiwara T, Oishi K, Mizuno T. . Efficacy of singular and composite annular repositioning and subvalvular surgical techniques to treat functional tricuspid regurgitation due to leaflet tethering: Early results of a feasibility study European Journal of Cardio-Thoracic Surgery, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University. 2022.03; 62(3); ezac101
- 6. Kinoshita R, Arai H, Yashima M, Hachimaru T, Fujiwara T, Tamura K, Tanaka H, Oi K, Mizuno T, Nagaoka E. Mid-term results of mitral valve reconstruction with autologous pericardial patch for active infective endocarditis with extensive leaflet destruction. General thoracic and cardiovascular surgery. 2022.02; 70(8); 694-704
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- 2. Mizuno T. Emergent CABG with ECMO in AMI patients. MICAB: Minimally Circulatory Assisted On-Pump Beating CABG. 2022 International Coronary Congress 2022.12.01
- 3. Fujiwara T.. Two cases in which percutaneous left atrial appendage closure was not indicated. CSI FOCUS LAA & PFO 2022 2022.10.01 Tokyo,
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- 7. Tomohiro Mizuno. "One stage hybrid total aortic arch repair for extended aortic arch and descending
thoracic aortic disease". Asian Society of Cardiovascular and Thoracic Surgery $2022.03.26 \ \cancel{x} \ \cancel{y} \ \cancel{z} \ \cancel$

Nephrology

Professor: Shinichi UCHIDA Associate Professor: Eisei SOHARA Shotaro NAITO (Dept. of Blood Purification) Junior Associate Professor: Soichiro IIMORI (Endowed Chair) Assistant Professor: Koichiro SUSA Takayasu MORI (Dept. of Blood Purification) Fumiaki ANDO Shintaro MANDAI (Dept. of Blood Purification) Yutaro MORI (Tenure track) Tamami FUJIKI Project Assistant Professor Yuichiro AKAGI, Shingo SHIOJI Graduate Student: Yu HARA, Soichiro SUZUKI, Tomoki YANAGI, Takaaki KOIDE Hisazumi MATSUKI, Hideki YANAGAWA, Takefumi SUZUKI Hospital Staff: Nobuhisa MORIMOTO, Ayumi YAMAMURA, Asami HANIOKA Katsuo MORI, Hatsumi WATANABE, Keigo SAKAI Technician: Chieko IIJIMA, 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 focus of our research is to elucidate the mechanisms underlying blood pressure regulation and fluid homeostasis in the kidneys, understand the pathophysiology of their dysfunction and systemic effects, and develop therapeutic strategies to address these issues. The academic and research activities, which have been hampered by the COVID-19 pandemic since 2020, are expected to conclude by the end of 2022, allowing us to resume our activities, including on-site conferences.

In FY2022, our research efforts resulted in numerous award recipients at academic conferences. At the 65th Annual Meeting of the Japanese Society of Nephrology, Dr. Yutaro Mori received the Young Investigator Award (YIA), Dr. Naohiro Takahashi was honored with the Best Paper Award, and Dr. Taku Gemma and Dr. Yu Hara both received the Best Presentation Award. Dr. Yutaro Mori also received the 2021 Medical Association Award from the Tokyo Medical and Dental University Medical Association, as well as the 35th Research Encouragement Award from the alumni association. Additionally, Dr. Azuma Nanamatsu received the Excellence Award and the President's Award at the 12th Molecular Nephrology Forum and the 12th Renal Failure Research Meeting, respectively. Moreover, Dr. Ayumi Yamamura received the Best Presentation Award at the 54th Clinical Study Group on Body Fluids, and Dr. Shintaro Mandai was selected for the 4th Next Generation Researchers Unit in TMDU.

Our research findings were published in prestigious journals such as the International Journal of Surgery (Nakano Y, Mandai S, et al., IF: 13.4), Proceedings of the National Academy of Sciences (PNAS) (Hara Y, Ando F, et al., IF: 12.8), In Vitro Cellular and Developmental Biology (Nakano Y, Mandai S, et al.), and Genes to Cells (Yanagi T, Sohara E, et al.). We reported a total of 13 papers in English journals and issued two press releases. Additionally, our ongoing comprehensive genetic diagnosis utilizing next-generation sequencers and clinical research related to genome information are making significant contributions, facilitating the diagnosis of up to 123 patients annually.

(3) Education

Pre-Graduation Education:

The Nephrology Department is responsible for the education of medical students, which includes systematic lectures for third-year students, project semesters for fourth-year students, and clinical training for fifth- and sixth-year students.

Systematic Lectures:

The systematic lectures were conducted in collaboration with the Urology Department and Pathology Department. These intensive lectures focused on diseases within the field of renal and urological medicine and lasted for three weeks. Due to the COVID-19 pandemic, all lectures in FY2022 were conducted remotely via Zoom or video streaming. However, we enhanced the interactive nature of the lectures by utilizing Zoom's breakout room function and making activities such as Problem-Based Learning (PBL) more independent. PBL involved small group discussions for making differential diagnoses of scenario cases. We engaged nephrology staff and graduate students as tutors, with one tutor assigned to each two groups. Students appreciated the tutor's guidance, as it facilitated fruitful discussions.

Project Semester:

During this year's project semester, a fourth-year medical student chose nephrology and actively worked on a research project under the guidance of graduate student Dr. Takefumi Suzuki. The student achieved excellent experimental results and delivered an outstanding presentation during the final research presentation. We sincerely hope that the student will maintain an interest in nephrology after graduation and completion of initial training, and consider returning to the Nephrology Department.

Clinical Practice:

Clinical practice commenced in December of the fourth year, following the completion of the project semester. The Pre-Clinical Clerkship (PCC) ran from the end of November to February, during which small groups of students engaged in practical and comprehensive studies. The Clinical Clerkship (CC) in the fifth year involved practical training in hospital wards. CC students underwent two weeks of practical training per group, working with actual patients to study nephrological diseases. Despite the limitations imposed by the COVID-19 pandemic, we took measures to minimize the risk of infection for both patients and students, while ensuring an in-depth understanding of the pathophysiology of various nephrological diseases. The differential diagnosis exercise during clinical practice was renamed from mini-CEX (Clinical Evaluation Exercise) to WoSAC (Workplace-based Student Assessment with Clinical Reasoning focus) starting from FY2022, and it continued to be implemented. When it was not possible to directly interview hospitalized patients or perform physical examinations, the medical staff responsible for training assumed the role of patients and trained the students in

making differential diagnoses, describing examination findings, and formulating treatment plans while refining their medical skills. At the end of the training, a summary was provided by the faculty. We believe that these efforts are a testament to the dedication of the doctors and staff involved in student education. Additionally, lectures and examinations for Dentistry, Health Sciences, Dental Hygiene, and Master's degrees were also conducted by the nephrology faculty.

Post-Graduation Education:

Following two years of post-graduate initial training, students undergo further training as nephrologists at the university and affiliated hospitals. During this period, they are encouraged to address unresolved clinical issues and cultivate the mindset of academic doctors who strive to understand the essence of things. Research activities within the graduate school are thriving, and cutting-edge research is conducted to nurture physicians who excel in both basic and clinical medicine.

(4) Clinical Services & Other Works

Fiscal year 2022 began as the sixth wave of the novel coronavirus showed signs of subsiding. Similar to other hospitals, our staff became accustomed to dealing with COVID-19-positive patients and continued to provide daily care while maintaining the necessary precautions. The summer brought the eighth wave, followed by the ninth wave in winter. Although the future seemed uncertain and exhausting, the increase in vaccination rates, the availability of therapeutic drugs, and the weakening of the virus contributed to a steady decline in the mortality rate among infected patients. In March, at the end of the fiscal year, the university's COVID-19 treatment system was significantly relaxed in line with the government's policy to lift mask mandates.

The construction of the "Functional Enhancement Building" is currently underway on the Ochanomizu Station side of the university grounds. By the end of FY2022, the temporary construction enclosure will be removed, unveiling the completed building. The new facility will have hybrid functions, including an emergency room, operating rooms, and an intensive care unit. It is expected to serve as a center for providing emergency and highly advanced medical care at the university in the future.

In FY2022, outpatient enzyme replacement therapy for patients with Fabry disease was initiated. Additionally, from an infection control perspective, outpatient maintenance dialysis services, which were suspended in spring 2020, have now resumed, and the number of patients will gradually increase in the future.

The number of inpatients is gradually recovering after reaching its lowest point in FY2020, and there has been considerable improvement in the number of renal biopsies and surgeries. However, they are still only at approximately 80% of the previous level. Furthermore, the revision in April 2022 resulted in shorter DPC (Diagnosis Procedure Combination) days, presenting ongoing challenges for nephrology. Nevertheless, we remain committed to enhancing our medical care system by strengthening collaboration among medical diagnoses, promoting outpatient visits for dialysis-related complications, increasing the number of peritoneal dialysis cases, expanding one-day hospitalization for PTA (percutaneous transluminal angioplasty), and implementing diagnostic and treatment measures for rare and refractory renal diseases.

(5) Publications

[Original Articles]

- 1. Maho Hatano, Tomohiro Udagawa, Toru Kanamori, Akito Sutani, Takayasu Mori, Eisei Sohara, Shinichi Uchida, Tomohiro Morio, Masato Nishioka. A novel SLC5A2 heterozygous variant in a family with familial renal glucosuria Hum Genome Var. 2022.12; 9(1); 42
- 2. Yanagi T, Kikuchi H, Susa K, Takahashi N, Bamba H, Suzuki T, Nakano Y, Fujiki T, Mori Y, Ando F, Mandai S, Mori T, Takeuchi K, Honda S, Torii S, Shimizu S, Rai T, Uchida S, Sohara E. Absence of ULK1 decreases AMPK activity in the kidney, leading to chronic kidney disease progression. Genes to cells. 2022.11; 28(1); 5-14
- 3. Hara Y, Ando F, Oikawa D, Ichimura K, Yanagawa H, Sakamaki Y, Nanamatsu A, Fujiki T, Mori S, Suzuki S, Yui N, Mandai S, Susa K, Mori T, Sohara E, Rai T, Takahashi M, Sasaki S, Kagechika H, Tokunaga F, Uchida S. LRBA is essential for urinary concentration and body water homeostasis. Proceedings of the National Academy of Sciences of the United States of America. 2022.07; 119(30); e2202125119

- 4. Oki Y, Katsuma A, Okabe M, Watanabe M, Sagasaki M, Takahashi D, Kimura A, Kato J, Ueda H, Hataya H, Fujimaru T, Mori T, Sohara E, Uchida S, Miyazaki Y, Yokoo T. Different Clinical Courses of Nephronophthisis in Dizygotic Twins. Internal medicine (Tokyo, Japan). 2022.06;
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- Nakano Y, Susa K, Yanagi T, Hiraoka Y, Suzuki T, Mori T, Ando F, Mandai S, Fujiki T, Rai T, Uchida S, Sohara E.. Generation of NPHP1 knockout human pluripotent stem cells by a practical biallelic gene deletion strategy using CRISPR/Cas9 and ssODN. In Vitro Cell Dev Biol Anim. 2022.02; 58(2); 85-95
- 9. Yutaro Mori, Corby Fink, Takaharu Ichimura, Keisuke Sako, Makiko Mori, Nathan N Lee, Philipp Aschauer, Krishna M Padmanabha Das, SoonGweon Hong, Minsun Song, Robert F Padera, Astrid Weins, Luke P Lee, Mahmoud L Nasr, Gregory A Dekaban, Jimmy D Dikeakos, Joseph V Bonventre. KIM-1/TIM-1 is a Receptor for SARS-CoV-2 in Lung and Kidney. medRxiv. 2022.01;
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- 3. Kanamori T, Udagawa T, Murakoshi M, Adachi E, Okutsu M, Mori T, Sohara E, Uchida S. A Missense Mutation in Zinc Finger 4 of WT1 Might Lead to Focal Segmental Glomerular Sclerosis due to Its Mislocalization and Downstream Dysregulation. ASN Kidney Week 2022 2022.11 Orland
- 4. Suzuki S, Ando F, Hara Y, Fujiki T, Mandai S, Susa K, Mori T, Sohara E, Rai T, Uchida S. ZNF185 Prevents Stress Fiber Formation Through the Inhibition of RhoA in Endothelial Cells. ASN Kidney Week 2022 2022.11 Orland

- 5. Yanagi T, Kikuchi H, Takeuchi K, Susa K, Takahashi N, Nakano Y, Ando F, Mandai S, Mori T, Honda S, Torii S, Shimizu S, Rai T, Uchida S, Sohara E. ULK1-Regulated AMP Sensing Mechanism by AMPK Is Disrupted in CKD. ASN Kidney Week 2022 2022.11 Orland
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- 7. Ando F. Identification of the rapeutic targets for congenital nephrogenic diabetes insipidus. BENZON SYMPOSIUM No.66 2022.09
- 8. Fumiaki Ando. Identification of an A-Kinase Anchor Protein Essential for Urinary Concentration. The 42nd Annual Meeting of the Korean Society of Nephrology. Basic Science Symposium. 2022.05.27
- 9. Eisei SOHARA. Understanding Cystic Kidney Disease by Comprehensive Genetic Panel Test ~Emerging Role of Clinical Genetics in CKD~ . JSN/ASN Joint Symposium, The 65th Annual Meeting of the Japanese Society of Nephrology 2022.06.11 Kobe, Japan
- 1. Yutaro Mori. KIM-1 mediates fatty acid uptake by renal tubular cells to promote progressive diabetic kidney disease. The 65th Annual Meeting of the Japanese Society of Nephrology 2022.06.12 Kobe, On-line
- 2. Yutaro Mori. KIM-1 mediates fatty acid uptake by renal tubular cells to promote progressive diabetic kidney disease. The 65th Annual Meeting of the Japanese Society of Nephrology 2022.06.11 Kobe, On-line

[Awards & Honors]

- 1. Yutaro Mori. 2021 Medical Association Award, Tokyo Medical and Dental University Medical Association, 2022.02
- 2. Yutaro Mori. The 35th Research Excellence Award, Tokyo Medical and Dental University Medical Alumni Association, 2022.03
- 3. Yutaro Mori. Young Investigator Award, Japanese Society of Nephrology, 2022.06

[Others]

1. 【Press release】 Urgent dialysis during hospitalization for surgery predicts poor outcomes, 2022.09 AAAS EurekAlert! The Global Source for Science News

[Social Contribution]

- 1. Peer review for Journal of Zhejiang University-SCIENCE B, Zhejiang University Press and Springer Science+Business Media, 2021.10.21 2022.01.19
- Yutaro Mori. Zeroing in on the Role of KIM-1 in Diabetic Kidney Disease, National Institute of Diabetes and Digestive and Kidney Diseases, NIDDK Recent Advances & Emerging Opportunities, Kidney, Urologic, and Hematologic Diseases, 2022.01
- 3. Yutaro Mori. Peer review for Frontiers in Pharmacology, Frontiers, 2022.02.04

Comprehensive Reproductive Medicine

2023.1.1

Professor : Naoyuki MIYASAKA Associate Professor : Naoyuki YOSHIKI Project Professor : Masakazu TERAUCHI Junior Associate Professor : Kimio WAKANA Project Associate Professor : Tomonori ISHIKAWA Assistant Professor : Yuki IWAHARA, Noriko OSHIMA,Masaki SEKIGUCHI,Ayako FUDONO, Asuka HIROSE,Maki TAKAO,Michi SHIMADA Project Assistant Professor : Takashi NAKASUJI,Kazuki SAITO,Tamami ODAI HospitalStaff : Kotoi TSURANE,Yusuke KORI Graduate Student : Misako IWATA,Nobuyuki KIDERA,Kotoi TSURANE,Atsushi FUSEGI, Shiho HIDAKA,Hiroshi YOMOGITA,Yuan FANG,Junichiro MITSUI, Yuka ENOKUCHI,Shoko KATSUMATA,Masayasu SEGA,Yuri TERAMOTO,Akiyo TORIUMI

(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 clump)
- 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]

- Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. Body weight and body fat are negatively associated with severe dyspareunia in postmenopausal women. J Obstet Gynaecol Res. 2022.12; 48(12); 3279-3285
- 2. Kuniaki Ota, Toshifumi Takahashi, Junichiro Mitsui, Kishio Kuroda, Kenichiro Hiraoka, Kiyotaka Kawai. A case of discrepancy between three ERA tests in a woman with repeated implantation failure complicated by chronic endometritis BMC pregnancy and chlidbirth. 2022.12; 22(1); 891
- 3. Junichiro Mitsui, Kiyotaka Kawai, Makiko Tajima, Kenichiro Hiraoka, Viviane Casaroli, Yoshimi Sato, Yoshiaki Furusawa, Tomonori Ishikawa, Naoyuki Miyasaka . Effects of Hydrosalpinx on Endometrial Receptivity and Uterine Microbiome: An Interesting Case of Double Uterus with Unilateral Hydrosalpinx Endocrines. 2022.12; 3(4); 821-830
- Kidera N, Ishikawa T, Kawamura T, Miyasaka N. Impact of paternal age on IVF and pregnancy outcomes with only normal sperm parameters. Taiwanese journal of obstetrics & gynecology. 2022.11; 61(6); 1015-1020
- 5. Kotoi Tsurane, Kayoko Kaneko, Kazue Yoshida, Ryo Tanaka, Haruhiko Sago, Atsuko Murashima. Initiation of hydroxychloroquine therapy during pregnancy can cause adverse effects and alter pregnancy outcomes: A case of acute generalised exanthematous pustulosis induced by hydroxychloroquine in a patient with systemic lupus erythematosus Modern Rheumatology Case Reports. 2022.11;
- 6. Kotoi Tsurane, Nagayoshi Umehara, Tetsuo Nakayama, Kenji Okada, Momoko Inoue, Kohei Ogawa, Haruhiko Sago, Naoyuki Miyasaka, Koushi Yamaguchi. Pertussis, diphtheria, and tetanus antibodies seroprevalence in pregnant women and neonates, as a preliminary data for introduction of preconception or prenatal DTaP vaccination among Japanese society Vaccine. 2022.11; 40(49); 7122-7129
- 7. Fusegi A, Kanao H, Tsumura S, Murakami A, Abe A, Aoki Y, Nomura H. Minimally invasive radical hysterectomy and the importance of avoiding cancer cell spillage for early-stage cervical cancer: a narrative review J Gynecol Oncol. 2022.11; 34(1);
- 8. Terauchi M, Kimura T. Response: The introduction of 21st century abortion methods in Japan-Policy based on all WHO recommendations is needed. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2022.08;

- 9. Mitsutoshi Yamada, Tomonori Ishikawa, Takeshi Iwasa, Hajime Oishi, Satoko Osuka, Kenji Oka, Shuichi Ono, Masanori Ono, Makoto Orisaka, Haruhiko Kanasaki, Yasushi Kawano, Kazuhiro Kawamura, Hiroshi Kishi, Fuminori Kimura, Shinnosuke Kuroda, Akira Kuwahara, Hideyuki Kobayashi, Akira Komiya, Hidekazu Saito, Kenji Sato, Suguru Sato, Koji Shiraishi, Hiromitsu Shirasawa, Tatsuya Suzuki, Yasushi Takai, Seido Takae, Toshifumi Takahashi, Tsuyoshi Takiuchi, Masahito Tachibana, Isao Tamura, Hiroshi Tamura, Seung Chik Jwa, Tsuyoshi Baba, Miyuki Harada, Tetsuya Hirata, Atsushi Fukui, Yusuke Fukuda, Shinichiro Fukuhara, Tetsuo Maruyama, Yasushi Yumura, Osamu Yoshino, Yasushi Hirota, Akira Tsujimura, Naoaki Kuji, Yutaka Osuga. Guidelines for Reproductive Medicine in Japan. Reprod Med Biol. 2022.08; 21(1); e12483
- 10. Eri Maeda, Seung Chik Jwa, Yukiyo Kumazawa, Kazuki Saito, Arisa Iba, Ayako Yanagisawa-Sugita, Akira Kuwahara, Hidekazu Saito, Yukihiro Terada, Takashi Fukuda, Osamu Ishihara, Yasuki Kobayashi. Out-of-pocket payment and patients' treatment choice for assisted reproductive technology by household income: a conjoint analysis using an online social research panel in Japan. BMC Health Serv Res. 2022.08; 22(1); 1093
- Hidaka S, Mouri Y, Akiyama M, Miyasaka N, Nakahama KI. GPR110, a receptor for synaptamide, expressed in osteoclasts negatively regulates osteoclastogenesis. Prostaglandins, leukotrienes, and essential fatty acids. 2022.07; 182; 102457
- 12. Masakazu Terauchi, Tsuyoshi Higuchi. Women's Health Care Committee, Japan Society of Obstetrics and Gynecology: Annual report-2022. Journal of Obstetrics and Gynaecology Research. 2022.07;
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- 14. Ichikura, K, Shimizu S, Oshima N, Ariizumi Y, Fujie T, Yamauchi S, Ishikawa T, Nakajima Y, Fukase Y, Murayama N, Murase H, Tagaya H, Takeuchi T, Miyake S, Matsushima E. Cancer patients' preferences for psychological counseling: a cross-sectional study using full-profile conjoint analysis in Japan Journal of Psychosocial Oncology Research and Practice. 2022.07; 4(3);
- Tamami Odai, Masakazu Terauchi, Hidenori Umeki, Naoyuki Miyasaka, Yoshiaki Somekawa. Sleep apnea in postmenopausal women is associated with joint pain severity and fatigability: a cross-sectional study. Menopause. 2022.06; 29(6); 680-686
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- 17. Shiho Hidaka, Yuki Mouri, Masako Akiyama, Naoyuki Miyasaka, Ken-ichi Nakahama . GPR110, a receptor for synaptamide, expressed in osteoclasts negatively regulates osteoclastogenesis Prostaglandins, Leukotrienes and Essential Fatty Acids. 2022.06;
- 18. Yomogita H, Miyasaka N, Kanai-Azuma M. A Review of Delayed Delivery Models and the Analysis Method in Mice. Journal of developmental biology. 2022.05; 10(2);
- 19. Yomogita H, Miyasaka N, Kanai-Azuma M. A Review of Delayed Delivery Models and the Analysis Method in Mice. Journal of developmental biology. 2022.05; 10(2);
- 20. Terauchi M, Kimura T. Letter to the editor: Japan foresees early-stage medical abortion approval: Will this reduce barriers to access safe abortion? International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2022.04; 158(1); 227
- Egawa M, Kanda E, Ohtsu H, Nakamura T, Yoshida M. Number of Children and Risk of Cardiovascular Disease in Japanese Women: Findings from the Tohoku Medical Megabank. Journal of atherosclerosis and thrombosis. 2022.04;
- 22. Kotoi Tsurane, Katsusuke Ozawa, Minako Matsuda, Mayu Kuriyama, Izumi Honda, Naoki Shimojima, Kentaro Matsuoka & Naoyuki Miyasaka . Altering Appearance of Fetal Enteric Duplication Cysts: The Gut Signature Sign and Other Indications for Prenatal Diagnosis 2022.04; 9(1);

- Mayuko Kazama, Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. The Inverse Correlation of Isoflavone Dietary Intake and Headache in Peri- and Post-Menopausal Women Nutrients. 2022.03; 14; 1226
- 24. Yasuko Aoyagi, Yoshihito Kano, Kohki Tohyama, Shotaro Matsudera, Yuichi Kumaki, Kenta Takahashi, Takahiro Mitsumura, Yohei Harada, Akemi Sato, Hideaki Nakamura, Eisaburo Sueoka, Naoko Aragane, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Keiichi Akahoshi, Hiroaki Ono, Toshiaki Ishikawa, Masanori Tokunaga, Tsuyoshi Nakagawa, Noriko Oshima, Reiko Nakamura, Masatoshi Takagi, Takahiro Asakage, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Yusuke Kinugasa, Sadakatsu Ikeda. Clinical utility of comprehensive genomic profiling in Japan: Result of PROFILE-F study. PLoS One. 2022.03; 17(3); e0266112
- 25. Konishi A, Samura O, Muromoto J, Okamoto Y, Takahashi H, Kasai Y, Ichikawa M, Yamada N, Kato N, Sato H, Hamada H, Nakanami N, Machi M, Ichizuka K, Sunami R, Tanaka T, Yonetani N, Kamei Y, Nagamatsu T, Matsumoto M, Tairaku S, Fujiwara A, Nakamura H, Harada T, Watanabe T, Sasaki S, Kawaguchi S, Minami S, Ogawa M, Miura K, Suzumori N, Kojima J, Kotani T, Sasaki R, Baba T, Toyofuku A, Endo M, Takeshita N, Taketani T, Sase M, Matsubara K, Hayata K, Hamada Y, Egawa M, Kakinuma T, Matsushima S, Kitagawa M, Shiga T, Kurashina R, Hamada H, Takagi H, Kondo A, Miharu N, Yamashita M, Horiya M, Morimoto K, Takahashi K, Okamoto A, Sekizawa A, Sago H. Prevalence of common aneuploidy in twin pregnancies. Journal of human genetics. 2022.01; 67(5); 261-265
- 26. Kenichiro Hiraoka, Nozomi Uchida, Tomonori Ishikawa and Kiyotaka Kawai. Value of Meiotic Spindle Imaging on Fertilization and Embryo Development Following Human Oocyte Piezo-ICSI Fertility & Reproduction. 2022; 4(1); 26-31
- 1. Malignant transformation of lobular endocervical glandular hyperplasia to gastric-type crvical cancer: a case report 2022.01; 71(10); 155-160

[Books etc]

1. Masakazu Terauchi. Nutrition Challenges for Middle-Aged and Older Women. MDPI, 2022.10

- 1. Masakazu Terauchi, Yuki Ideno, Kunihiko Hayashi. The effect of shift work on daytime sleepiness in middle-aged female nurses: results from the Japan Nurses' Health Study. The 18th World Congress on Menopause 2022.10.28 Lisbon, Portugal
- 2. Masakazu Terauchi. APMF Panel Discussion: Overview, Challenges and Solutions for Midlife Women' s Health in Asia Pacific "S-Equol: a novel therapeutic option from Asian perspective". The 18th World Congress on Menopause 2022.10.27 Lisbon, Portugal
- 3. Masakazu Terauchi. The current practice of menopause management and the role of S-Equol in Japan. Equol Advisory Meeting 2022.10.27 Lisbon, Portugal
- 4. Atsushi Fusegi, Shiho Tsumura, Tsuyoshi Matsumoto, Atsushi Murakami, Akiko Abe, Makiko Omi, Terumi Tanigawa, Yoichi Aoki, Sachiho Netsu, Sanshiro Okamoto, Kohei Omatsu, Mayu Yunokawa, Hidetaka Nomura, Hiroyuki Kanao. Avoidance of tumor spillage during laparoscopic radical hysterectomy for early-stage cervical cancer: A propensity score-adjusted analysis. 第 64 回日本婦人科腫瘍学会学術講 演会 2022.07.14 福岡
- 5. Odai Tamami, Ohno Haruko, Nakamura Reiko, Tsukada Takafumi, Oshima Noriko, Wakana Kimio, Miyasaka Naoyuki. Primary pulmonary choriocarcinoma diagnosed by histopathologic and genetic examination(和訳中). 日本產科婦人科学会雑誌 2022.02.01

Urology

Professor and Chairman: Yasuhisa Fujii

Associate Professor: Soichiro Yoshida

Junior Associate Professor: Hajime Tanaka, Yuma Waseda (Department of Insured Medical Care Management) Assistant Professor: Shohei Fukuda, Yudai Ishikawa, Yuki Nakamura, Motohiro Fujiwara, Masaki Kobayashi Hospital Staff: Bo Fan, Takahiko Soma, Kasumi Yoshitomi, Shunya Matsumoto, Yusuke Aida, Yuya Maezawa Resident: Kensaku Ishihara

(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-weighed MRI to diagnosis, assessment of the rapeutic 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 the rapeutic 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 transure thral resection of bladder tumor, low-dose chemoradio therapy 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]

- Nishizawa M, Kudo T, Kijima T, Fujii Y. Failed endovascular abdominal aortic aneurysm repair due to Mycobacterium bovis infection following intravesical bacillus Calmette-Guérin therapy. J Vasc Surg Cases Innov Tech. 2022.12; 8(4); 807-812
- 2. Julia H Yuan, Hajime Tanaka, Dattatraya Patil, Kevin Hakimi, Shady Soliman, Margaret F Meagher, Ava Saidian, Arman Walia, Sohail Dhanji, Franklin Liu, Jonathan Afari, Mimi Nguyen, Luke Wang, Yosuke Yasuda, Kazutaka Saito, Yasuhisa Fujii, Viraj Master, Ithaar H Derweesh. Age-Related Differences in Oncological Outcomes in Renal Cell Carcinoma: Impact of Functional Conservation as Measured by Postoperative eGFR. Clin Genitourin Cancer. 2022.12;
- 3. Chen W, Yokoyama M, Kobayashi M, Fan B, Fukuda S, Waseda Y, Tanaka H, Yoshida S, Ai M, Fushimi K, Nonomura N, Fujii Y. Trends of radical cystectomy and comparisons of surgical outcomes among surgical approaches focusing on robot-assisted radical cystectomy: A Japanese nationwide database study Int J Urol. 2022.12;
- 4. Yuki Nakamura, Hiroshi Fukushima, Kasumi Yoshitomi, Takahiko Soma, Masaki Kobayashi, Bo Fan, Motohiro Fujiwara, Yudai Ishikawa, Shohei Fukuda, Yuma Waseda, Hajime Tanaka, Soichiro Yoshida, Minato Yokoyama, Yasuhisa Fujii. Significance of dorsal bladder neck involvement in predicting the progression of non-muscle-invasive bladder cancer. Int J Urol. 2022.12;
- 5. Yamaguchi Y, Yokoyama M, Takemoto A, Nakamura Y, Fukuda S, Uehara S, Tanaka H, Yoshida S, Matsuoka Y, Fujii Y. Succinate dehydrogenase-deficient malignant paraganglioma complicated by succinate dehydrogenase-deficient renal cell carcinoma. IJU case reports. 2022.11; 5(6); 480-483
- 6. Eri Fukagawa, Takeshi Yuasa, Kentaro Inamura, Kosuke Hamada, Motohiro Fujiwara, Yoshinobu Komai, Junji Yonese. large-cell neuroendocrine carcinoma of the prostate: A case report and literature review. IJU Case Rep. 2022.11; 5(6); 505-510
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- Yonese I, Ito M, Waseda Y, Kobayashi S, Toide M, Takazawa R, Koga F. Adverse Prognostic Impact of Diagnostic Ureterorenoscopy in a Subset of Patients with High-Risk Upper Tract Urothelial Carcinoma Treated with Radical Nephroureterectomy. Cancers. 2022.08; 14(16);

- Arita Y, Yoshida S, Shigeta K, Kwee TC, Edo H, Okawara N, Hashimoto M, Ishii R, Ueda R, Mikami S, Fujiwara M, Waseda Y, Kikuchi E, Fujii Y, Jinzaki M. Diagnostic Value of the Vesical Imaging-Reporting and Data System in Bladder Urothelial Carcinoma with Variant Histology. European urology oncology. 2022.08;
- 10. Arita Y, Yoshida S, Shigeta K, Kwee TC, Edo H, Okawara N, Hashimoto M, Ishii R, Ueda R, Mikami S, Fujiwara M, Waseda Y, Kikuchi E, Fujii YJinzaki M. Diagnostic Value of the Vesical Imaging-Reporting and Data System in Bladder Urothelial Carcinoma with Variant Histology Eur Urol Oncol . 2022.08;
- 11. Yamamoto S, Fukushima H, Fukuda S, Uehara S, Yasuda Y, Tanaka H, Yoshida S, Yokoyama M, Matsuoka Y, Fujii Y. Early cancer cachexia phenotype predicts survival of advanced urothelial cancer patients treated with pembrolizumab. Asia Pac J Clin Oncol . 2022.08; 18(4); 410-418
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- 7. Fukuda S, Tanaka H, Tanabe K, Tamiya T, Kobayashi M, Yajima S, Nakamura Y, Fujiwara M, Ishikawa Y, Yamamoto T, Araki S, Yoshida S, Yokoyama M, Matsuoka Y, Otsuka Y, Koga F, Fujii Y. Local recurrence following partial nephrectomy in patients with renal cell carcinoma: a multicenter study. The 117th annual meeting of the American Urological Association 2022.05.13 New Orleans, USA
- 8. Kobayashi M, Matsuoka Y, Uehara S, Tanaka Hiroshi, Nakamura Y, Uchida Y, Fukuda S, Tanaka Hajime, Yoshida S, Yokoyama M, Fujii Y. PIRADS score combined with positive core number on MRI-ultrasound fusion targeted prostate biopsy can predict the absence of pathological extraprostatic extension. AUA Annual Meeting 2022.05.13
- 9. Uchida Y, Yokoyama M, Nakamura Y, Fukuda S, Uehara S, Tanaka H, Yoshida S, Matsuoka Y, Fujii Y. ASSESSMENT OF ERECTILE AND EJACULATORY FUNCTIONS AFTER BLADDER-SPARING THERAPY AGAINST MUSCLE-INVASIVE BLADDER CANCER. the 22nd World Meeting of the International Society for Sexual Medicine 2022.05
- 10. Tanaka Hajime. Prognostic impact of pathological renal parenchymal infiltration in non-metastatic clear cell renal cell carcinoma. AUA Annual Meeting 2022
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- 13. Fan Bo. Incidence and significance of 20% decrease from new baseline estimated glomerular filtration rate after radical and partial nephrectomy. AUA Annual Meeting 2022

Gastrointestinal Surgery

Professor Yusuke KINUGASA Associate Professor Masanori TOKUNAGA, Takuya Okada Junior Associate Professor Shigeo, Haruki, Kenro KAWADA Assistant Professor Hisashi FUJIWARA, Kazuya YAMAGUCHI Yuya SATO, Toshiro TANIOKA, Shinichi YAMAUCHI Noriko IWATA, Marie HANAOKA, Ayumi TAKAOKA Graduate Student (Hospital Staff) Emi KANEMOTO, Yuya UMEBAYASHI, Toshifumi SAIO, Yudai YAMAMOTO, Takahiro IGAKI, Jun SAKUMA, Yoshiaki TOMI, Yamato YAMASHITA, Sodai ARAI, Sono ITO, Ryuta KAKUTA, Takashi SHIGENO, Miyako TAZAWA, Kei NAKAJIMA, Akitoshi NANKAKU, Masako MIZOGUCHI, Naoya ISHIBASHI, Masayoshi SAKANO, Hiroyuki SHIOBARA, Rumi SHIMANO, Fumio TSUKAMOTO, Syunsaku NAKAGAWA, Shiho MATSUNAGA, Hiroki YONEZAWA, Kyoko RYU, Mayuko OTOMO, Yoshihiro SAKAI, Yuta SUZUKI, Yukari FUJII, Yoshimi YAMASAKI, Souhei AKUTA, Hayato IKAWA, Yusuke YATABE, Toyoshi ODA, Misuzu Yamato, Mari Nakagawa

(1) Outline

The Department of Gastrointestinal Surgery is composed of three departments of esophageal surgery, gastric surgery, and colorectal surgery, and it conducts research on the entire gastrointestinal tract. We conduct clinical research based on clinical activities and basic research in specialized laboratories within and outside the department, which is applied to clinical practice. We provide up-to-date and high-level gastrointestinal surgery and pre- and post-graduate education.

(2) Research

- 1) Development of esophageal surgery.
- 2) Development of gastric surgery.
- 3) Development of colorectal surgery.

(3) 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.

(4) Lectures & Courses

Basic gastrointestinal and general surgery knowledge and skills are the program's cornerstones. The program aims to cultivate a high level of practical ability to quickly perform logical and objective medical treatment, backed up by the skill and kindness of a clinician.

(5) Clinical Services & Other Works

Not only to engage in specialized training and research activities within the university but also to contribute to community medicine while improving their abilities as gastrointestinal and general surgeons at the affiliated hospitals. They are also encouraged to study in Japan and overseas and to work at overseas bases.

(6) 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.

(7) Publications

[Original Articles]

- 2. Harunobu Sato, Kotaro Maeda, Yusuke Kinugasa, Hiroyasu Kagawa, Shunsuke Tsukamoto, Keiichi Takahashi, Hiroaki Nozawa, Yasumasa Takii, Tsuyoshi Konishi, Yoshito Akagi, Takeshi Suto, Shigeki Yamaguchi, Heita Ozawa, Koji Komori, Masayuki Ohue, Junichiro Hiro, Seiichi Shinji, Kazuhito Minami, Tomoharu Shimizu, Kazuhiro Sakamoto, Kay Uehara, Hiroshi Takahashi, Kenichi Sugihara. Management of inguinal lymph node metastases from rectal and anal canal adenocarcinoma Colorectal disease. 2022.10; 24(10); 1150-1163
- 3. Yuya Sato, Jun Sese, Takatoshi Matsuyama, Masaki Onuki, Shogo Mase, Keisuke Okuno, Katsumasa Saito, Naoto Fujiwara, Akihiro Hoshino, Kenro Kawada, Masanori Tokunaga, Yusuke Kinugasa. Preliminary study for developing a navigation system for gastric cancer surgery using artificial intelligence Surgery today. 2022.10; 52(12); 1753-1758
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- 9. Marie Hanaoka, Hitoshi Hino, Akio Shiomi, Hiroyasu Kagawa, Shoichi Manabe, Yusuke Yamaoka, Shunichiro Kato, Shinichi Yamauchi, Yusuke Kinugasa, Kenichi Sugihara. The Eastern Cooperative Oncology Group Performance Status as a prognostic factor of stage I-III colorectal cancer surgery for elderly patients: a multi-institutional retrospective analysis Surgery today. 2022.07; 52(7):p1081-1089(7); 1081-1089
- 10. Jun Watanabe, Shigeki Yamaguchi, Ichiro Takemasa, Masayoshi Yasui, Yasumitsu Hirano, Daisuke Nakano, Akio Shiomi, Shinya Munakata, Masanori Naito, Shunsuke Tsukamoto, Atsushi Ishibe, Yoshiaki Kuriu, Yasutake Uchima, Shinichiro Mori, Hideki Kanazawa, Go Wakabayashi, Takeshi Yamada, Muneaki Ezu, Masahiko Watanabe, Yusuke Kinugasa. Safety, efficacy, and operability of a newly developed absorbable adhesion barrier (GM142) in patients with primary rectal cancer scheduled for diverting ileostomy during laparoscopic surgery: Randomized controlled trial Annals of Gastroenterological Surgery. 2022.07; 6(4); 515-522
- 11. Keisuke Okuno, Masanori Tokunaga, Yusuke Kinugasa, Hideo Baba, Yasuhiro Kodera, Ajay Goel. A Transcriptomic Liquid Biopsy Assay for Predicting Resistance to Neoadjuvant Therapy in Esophageal Squamous Cell Carcinoma Annals of surgery. 2022.07; 276(1); 101-110
- 12. Kazutaka Yamada, Yasumitsu Saiki, Koji Komori, Akio Shiomi, Masashi Ueno, Masaaki Ito, Koya Hida, Seiichiro Yamamoto, Manabu Shiozawa, Soichiro Ishihara, Yukihide Kanemitsu, Hideki Ueno, Tatsuya Kinjo, Kotaro Maeda, Junichiro Kawamura, Fumihiko Fujita, Keiichi Takahashi, Tsunekazu Mizushima, Yasuhiro Shimada, Shin Sasaki, Eiji Sunami, Fumio Ishida, Keiji Hirata, Shinobu Ohnuma, Kimihiko Funahashi, Jun Watanabe, Yusuke Kinugasa, Shigeki Yamaguchi, Yojiro Hashiguchi, Masataka Ikeda, Takeshi Sudo, Yoshito Komatsu, Keiji Koda, Kazuhiro Sakamoto, Masazumi Okajima, Hideyuki Ishida, Yuichi Hisamatsu, Taiki Masuda, Shinichiro Mori, Kazuhito Minami, Seiji Hasegawa, Shungo Endo, Akinori Iwashita, Madoka Hamada, Yoichi Ajioka, Koichiro Usuku, Tokunori Ikeda, Kenichi Sugihara. Characteristics of anal canal cancer in Japan Cancer medicine. 2022.07; 11(14); 2735-2743
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- 17. Takashi Shigeno, Akihiro Hoshino, Shiho Matsunaga, Rumi Shimano, Naoya Ishibashi, Hajime Shinohara, Hiroyuki Shiobara, Chiharu Tomii, Katsumasa Saito, Naoto Fujiwara, Yuya Sato, Kenro Kawada, Masanori Tokunaga, Yusuke Kinugasa. The impact of lymphadenectomy on lymph node recurrence after performing various treatments for esophageal squamous cell carcinoma BMC surgery. 2022.05; 22(1); 171

- Takahiro Igaki, Daichi Kitaguchi, Shigehiro Kojima, Hiro Hasegawa, Nobuyoshi Takeshita, Kensaku Mori, Yusuke Kinugasa, Masaaki Ito. Artificial Intelligence-Based Total Mesorectal Excision Plane Navigation in Laparoscopic Colorectal Surgery Diseases of the colon and rectum. 2022.05; 65(5):e329-e333(5); e329-e333
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- 2. Yusuke Kinugasa. Current status of robotic colorectal cancer surgery in Japan. The 20th National Conference on Cancer Control 2022.09.30 WEB
- 3. Marie Hanaoka, Shunsaku Nakagawa, Naoya Ishibashi, Masako Mizoguchi, Miyako Tazawa, Noriko Iwata, Taiki Masuda, Shinichi Yamauchi, Masanori Tokunaga, Yusuke Kinugasa. Robotic rectal surgery with lateral lymph node dissection or combined resection of other organs. The 77th General Meeting of the Japanese Society of Gastroenterological Surgery 2022.07.21 Yokohama
- 4. 絹笠祐介. 当科におけるロボット支援下大腸切除術. 第12回城北大腸癌治療セミナー 2022.06.24 WEB
- 5. Yusuke Kinugasa. How to improve our routine procedure using robotic approach in colorectal cancer surgery?. The 50th Congress of KSELS & 12th International Symposium (KSELS 2022) 2022.04.29 WEB
- 6. Yusuke Kinugasa. Rectal cancer surgery based on anatomy. 2022 Colorectal Surgery Academic Exchange Conference 2022.01.23 WEB
- 7. 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 Associate professor Assistant professor Assistant professor Assistant professor Hospital assistant professor Graduate Student Kenichi Okubo Hironori Ishibashi Ryo Wakejima Katsutoshi Seto Syunichi Baba Ayaka Asakawa Yuya Ishikawa Mariko Hanafusa Yasuyuki Kurihara Yusuke Sugita Hirotomo Takahara Kuniyo Sueyoshi

(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

- \cdot Minimally invasive surgery for lung cancer
- \cdot Multimodal treatments for thoracic malignancies
- \cdot Surgery for metastatic lung tumors
- \cdot 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, 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**

- Ayaka Asakawa , Genji Kawade, Morito Kurata , Sho Fukuda , Iichiroh Onishi, Yuko Kinowaki , Sachiko Ishibashi, Masumi Ikeda, Shiori Watabe, Masashi Kobayashi, Hironori Ishibashi, Kenichi Okubo, Masanobu Kitagawa , Kouhei Yamamoto. Stratification of lung squamous cell carcinoma based on ferroptosis regulators: Potential for new therapeutic strategies involving ferroptosis induction. Lung Cancer. 2022.01; 165(24); 82-90
- 2. Hironori Ishibashi, Ryo Wakejima, Ayaka Asakawa, Yusuke Sugita, Yuya Ishikawa, Mariko Hanafusa, Shunichi Baba, Yasuhiro Nakashima, Katsutoshi Seto, Kenichi Okubo. Postoperative Delirium in Lung Cancer Anatomical Resection-Analysis of Risk Factors and Prognosis. World J Surg. 2022.05; 46(5); 1196-1206
- 3. Katsutoshi Seto, Junichi Shimizu, Katsuhiro Masago, Mitsugu Araki, Ryohei Katayama, Yukari Sagae, Shiro Fujita, Yoshitsugu Horio, Eiichi Sasaki, Hiroaki Kuroda, Kenichi Okubo, Yasushi Okuno, Toyoaki Hida+A89:G89. Sensitivity to dabrafenib and trametinib treatments in patients with non-small-cell cancer harboring BRAF compound mutations: A pooled analysis of BRAF p.V600E-positive advanced non-small-cell lung cancer. Cancer Genetics. 2022.08; 266-267; 1-6
- 4. Hiroshi Ueno, Hiroto Yamaoka, Sakyo Hirai, Kyohei Fujita, Mariko Ishikawa, Shoko Fujii, Yuki Aizawa, Yosuke Ishii, Masataka Yoshimura, Kenji Yamada, Yoshikazu Yoshino, Morito Kurata, Katsutoshi Seto, Hironori Ishibashi, Kenichi Okubo, Shigeru Nemoto, Kazutaka Sumita. Endovascular Treatment for Acute Ischemic Stroke After Video-Assisted Thoracoscopic Pulmonary Lobectomy in Patients With Lung Cancer: A Report of Four Cases and Literature Review. Journal of Stroke and Cerebrovascular Diseases [doi: 10.1016/j.jstrokecerebrovasdis.2022.106593]. 2022.08;
- 5. Kumiko Hayashi, Daichi Nogawa, Maki Kobayashi, Ayaka Asakawa, Yae Ohata, Shota Kitagawa, Kazuishi Kubota, Hisashi Takahashi, Miyuki Yamada, Goshi Oda, Tsuyoshi Nakagawa, Hiroyuki Uetake, Iichiroh Onishi, Yuko Kinowaki, Morito Kurata, Masanobu Kitagawa, Kouhei Yamamoto. Quantitative high-throughput analysis of tumor infiltrating lymphocytes in breast cancer. Frontiers in Oncology [doi:10.3389/fonc.2022.901591. eCollection]. 2022.09;
- 6. Mariko Hanafusa, Nobutoshi Nawa, Yuki Goto, Tomoki Kawahara, Shigeru Miyamae, Yutaka Ueki, Nobuyuki Nosaka, Kenji Wakabayashi, Shuji Tohda, Ukihide Tateishi, Takeo Fujiwara. Effectiveness of remdesivir with corticosteroids for COVID-19 patients in intensive care unit: A hospital-based observational study. Journal of Medical Virology [Accepted 21 September 2022]. 2022.09;
- 7. Hajime Shinohara, Maki Kobayashi, Kumiko Hayashi, Daichi Nogawa, Ayaka Asakawa, Yae Ohata, Kazuishi Kubota, Hisashi Takahashi, Miyuki Yamada, Masanori Tokunaga, Yusuke Kinugasa, Goshi Oda, Tsuyoshi Nakagawa, Iichiroh Onishi, Yuko Kinowaki, Morito Kurata, Kenichi Ohashi, Masanobu Kitagawa, Kouhei Yamamoto. Spatial and Quantitative Analysis of Tumor-Associated Macrophages: Intratumoral CD163-/PD-L1+ TAMs as a Marker of Favorable Clinical Outcomes in Triple-Negative Breast Cancer. International Journal of Molecular Sciences [doi:10.3390/ijms232113235]. 2022.10;
- 8. Mariko Hanafusa, Yuri Ito, Hironori Ishibashi, Tomoki Nakaya, Nobutoshi Nawa, Tomotaka Sobue, Kenichi Okubo and Takeo Fujiwara. Association between socioeconomic status and net survival after primary lung cancer surgery: a tertiary university hospital retrospective observational study in Japan Japanese Journal of Clinical Oncology [Accepted 13 December 2022]. 2022.12;

9. Minami Miyauchi, Takumi Akashi, Asuka Furukawa, Keisuke Uchida, Tomoki Tamura, Noboru Ando, Susumu Kirimura, Hiroshi Shintaku, Kurara Yamamoto, Takashi Ito, Keiko Miura, Kou Kayamori, Yosuke Ariizumi, Takahiro Asakage, Atsushi Kudo, Minoru Tanabe, Yasuhisa Fujii, Hironori Ishibashi, Kenichi Okubo, Masanori Murakami, Tetsuya Yamada, Akira Takemoto, Yuan Bae, Yoshinobu Eishi, Kenichi Ohashi. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocrine Pathology. 2022.12; 33(4); 506-518

[Others]

- 1. Successful excision of a giant subcarinal bronchogenic cyst by video assisted thoracoscopic surgery, 2022.02 General Thoracic and Cardiovascular Surgery. 2022 Feb;70(2):197-200 Hironori Ishibashi, Airi Kato, Yusuke Sugita, Yasuhiro Nakashima, Katsutoshi Seto, Ryo Wakejima, Kenichi Okubo
- Primary pulmonary choriocarcinoma with a genomic sequence, 2022.02 Pathology International. 2022 Feb;72(2):141-143 Iichiroh Onishi , Susumu Kirimura, Ryo Wakejima, Kenichi Okubo, Tamami Odai, Ryota Kakuta, Yoshihito Kano, Sadakatsu Ikeda, Takumi Akashi, Masanobu Kitagawa
- 3. Pulmonary Mucormycosis Involving the Left Main Bronchus and the Pulmonary Artery, 2022.04 Annals of Thoracic and Cardiovascular Surgery. 2022 Apr 6. doi: 10.5761/atcs.cr.22-00035. Online ahead of print. Katsutoshi Seto, Rika Nohara, Yusuke Sugita, Hironori Ishibashi, Kenichi Okubo
- 4. Reconstruction of the Bifurcation of Right Upper Bronchus Using Miyamoto's Technique for Typical Carcinoid, 2022.08 Ann Thorac Cardiovasc Surg. 2022 Aug 25. doi: 10.5761/atcs.cr.22-00084. Online ahead of print Ayaka Asakawa, Hironori Ishibashi, Kuniyo Sueyoshi, Erika Mori, Yasuhiro Nakashima, Masashi Kobayashi, and Kenichi Okubo

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara Visiting Professor Makoto Arai Visiting Professor Masato Hasegawa Associate Visiting Professor Takashi Shichita Associate Visiting Professor Yuichiro Mitaoka Graduate Student Mai Asakura, Akari Nakamura, Kyoka Iino, Ittetsu Nakajima, Risa Saito, Minako Shingai, Shiho Sasaki, Terumi Ono, Fumiya Seki (April~), Hikaru Ando (April~), Riku Takahashi (April~), Anri Saito (April~), Minato Maeda (April~), Lanyu Huang (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 psychiatric 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.

- [Takashi Shichita] To develop the therapeutic method for stroke and dementia, we will clarify the cellular and molecular mechanisms underlying sterile inflammation and tissue repair after brain tissue injury. In addition to the classical method of molecular biology and biochemistry, the latest analysis methods of immunology, neuroscience, and epigenetics are applied to our research.
- [Yuichiro Miyaoka] Our goal is to develop new therapeutic approaches for genetic disorders by using genome editing in human iPS cells. We introduce causative mutations of heart and liver diseases into human iPS cells to study the pathogenic mechanism by analyzing these cells with cellular and molecular biology techniques such as PCR and immuno-staining. We also seek for ways to improve genome editing technologies including CRISPR/Cas9 to achieve precise genome editing.

(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, stroke, and genetic disorders. 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

- T. Suzuki, S. Takagi, and T. Hara. Multiple gene transfer and all-in-one conditional knockout systems in mouse embryonic stem cells for analysis of gene function. *Front. Cell Dev. Biol.*, 10: 870629, 2022.
- K. Tsujihana*, K. Tanegashima*, Y. Santo, H. Yamada, S. Akazawa, R. Nakao, K. Tominaga, R. Saito, Y. Nishito, R. Hata, T. Nakamura, I. Murai, Y. Kono, M. Sugawa, M. Tanioka, G. Egawa, M. Doi, T. Isa, K. Kabashima, T. Hara#, and H. Okamura#. Circadian protection against bacterial skin infection by epidermal CXCL14-mediated innate immunity. *Proc. Natl. Acad. Sci. U.S.A.*, 119: e2116027119, 2022. *Co-first authors. #Co-corresponding authors.
- 3. K. Kitajima, M. Shingai, H. Ando, M. Hamasaki, and T. Hara. An interferon-γ/FLT3 axis positively regulates hemopoietic progenitor cell expansion from human pluripotent stem cells. *Stem Cells*, 40: 906-918, 2022.

- 4. H. Ishida, M. Miyashita, K. Oshima, I. Kawakami, K. Sekiyama, M. Kounoe, E. Seki, N. Arai, S. Takizawa, E. Nagata, M. Itokawa, and M. Arai. Carbonyl stress-sensitive brain regions in the patient with treatment-resistant schizophrenia with a glyoxalase 1 frameshift mutation: Autopsy study. *Psychiatry Res. Case Rep.*, 1: 100064, 2022.
- 5. S. Koike, Y. Miyaji, K. Suzuki, M. Miyashita, M. Itokawa, M. Arai, and Y. Ogasawara. Plasma unconjugated bile acids as novel biomarker for schizophrenia. *Biochem. Biophys. Res. Commun.*, 634: 70-74, 2022.
- 6. K. Tabata, M. Miyashita, S. Yamasaki, K. Toriumi, S. Ando, K. Suzuki, K. Endo, Y. Morimoto, Y. Tomita, S. Yamaguchi, S. Usami, M. Itokawa, M. Hiraiwa-Hasegawa, H. Takahashi, K. Kasai, A. Nishida, and M. Arai. Hair zinc levels and psychosis risk among adolescents. *Schizophrenia (Heidelb)*, 8: 107, 2022.
- 7. T. Inoue, T. Shinba, M. Itokawa, G. Sun, M. Nishikawa, M. Miyashita, K. Suzuki, N. Kariya, M. Arai, and T. Matsui. The development and clinical application of a novel schizophrenia screening system using yoga-induced autonomic nervous system responses. *Front. Physiol.*, 13: 902979, 2022.
- 8. I. Kushima, B. Aleksic, H. Kimura, M. Nakatochi, T. Lo, M. Ikeda, M. Arai, R. Hashimoto, S. Numata, Y. Okamura, T. Obara, T. Inada, and N. Ozaki. X chromosome aneuploidies and schizophrenia: association analysis and phenotypic characterization. *Psychiatry Clin. Neurosci.*, 76: 667-673, 2022.
- 9. A. Yoshikawa, I. Kushima, M. Miyashita, K. Suzuki, K. Iino, K. Toriumi, Y. Horiuchi, H. Kawaji, N. Ozaki, M. Itokawa, and M. Arai. Exonic deletions in IMMP2L in schizophrenia with enhanced glycation stress subtype. *PLoS ONE*, 17: e0270506, 2022.
- I. Kushima, M. Nakatochi, B. Aleksic, T. Okada, H. Kimura, H. Kato, M. Morikawa, T. Inada, K. Ishizuka, Y. Torii, Y. Nakamura, S. Tanaka, M. Imaeda, N. Takahashi, M. Yamamoto, K. Iwamoto, Y. Nawa, N. Ogawa, S. Iritani, Y. Hayashi, T. Lo, G. Otgonbayar, S. Furuta, N. Iwata, M. Ikeda, T. Saito, K. Ninomiya, T. Okochi, R. Hashimoto, H. Yamamori, Y. Yasuda, M. Fujimoto, K. Miura, M. Itokawa, M. Arai, M. Miyashita, K. Toriumi, K. Ohi, T. Shioiri, K. Kitaichi, T. Someya, Y. Watanabe, J. Egawa, T. Takahashi, M. Suzuki, T. Sasaki, M. Tochigi, F. Nishimura, H. Yamasue, H. Kuwabara, T. Wakuda, TA Kato, S. Kanba, H. Horikawa, M. Usami, M. Kodaira, K. Watanabe, T. Yoshikawa, T. Toyota, S. Yokoyama, T. Munesue, R. Kimura, Y. Funabiki, H. Kosaka, M. Jung, K. Kasai, T. Ikegame, S. Jinde, S. Numata, M. Kinoshita, T. Kato, C. Kakiuchi, K. Yamakawa, T. Suzuki, N. Hashimoto, S. Ishikawa, B. Yamagata, S. Nio, T. Murai, S. Son, Y. Kunii, H. Yabe, M. Inagaki, YI. Goto, Y. Okumura, T. Ito, Y. Arioka, D. Mori, and N. Ozaki. Cross-Disorder Analysis of Genic and Regulatory Copy

Number Variations in Bipolar Disorder, Schizophrenia, and Autism Spectrum Disorder. *Biol. Psychiatry*, 92: 362-374, 2022.

- K. Suzuki, S. Yamasaki, M. Miyashita, S. Ando, K. Toriumi, A. Yoshikawa, M. Nakanishi, Y. Morimoto, S. Kanata, S. Fujikawa, K. Endo, S. Koike, S. Usami, M. Itokawa, S. Washizuka, M. Hiraiwa-Hasegawa, HY. Meltzer, K. Kasai, A. Nishida, and M. Arai. Role of advanced glycation end products in the longitudinal association between muscular strength and psychotic symptoms among adolescents. *Schizophrenia (Heidelb)*, 8: 44, 2022.
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- R. Mizutani, S. Noguchi, R. Saiga, Y. Yamashita, M. Miyashita, M. Arai, and M. Itokawa. Schizophrenia-Mimicking Layers Outperform Conventional Neural Network Layers. *Front. Neurorobot.*, 16: 851471, 2022.
- T. Shinba, N. Kariya, S. Matsuda, M. Arai, M. Itokawa, and Y. Hoshi. Near-Infrared Time-Resolved Spectroscopy Shows Anterior Prefrontal Blood Volume Reduction in Schizophrenia but Not in Major Depressive Disorder. *Sensors (Basel)*, 22: 1594, 2022.
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- K. Endo, S. Yamasaki, M. Nakanishi, J. DeVylder, S. Usami, Y. Morimoto, D. Stanyon, K. Suzuki, M. Miyashita, M. Arai, S. Fujikawa, S. Kanata, S. Ando, M. Hiraiwa-Hasegawa, K. Kasai, and A. Nishida. Psychotic experiences predict subsequent loneliness among adolescents: A population-based birth cohort study. *Schizophr. Res.*, 239: 123-127, 2022.
- D. Arseni, M. Hasegawa, A. Murzin, F. Kametani, M. Arai, M. Yoshida, and B. Falcon. Structures of TDP-43 filaments from amyotrophic 1 lateral sclerosis with frontotemporal lobar degeneration, *Nature*, 601: 139-143, 2022.
- M. Schweighauser, D. Arseni, M. Bacioglu, M. Huang, S. Lövestam, Y. Shi, Y. Yang, W. Zhang, A. Kotecha, H. Garringer, R. Vidal, G. Hallinan, K. Newell, A. Tarutani, S. Murayama, M. Miyazaki, Y. Saito, M. Yoshida, K. Hasegawa, T. Lashley, T. Revesz, G. Kovacs, J. van Swieten, M. Takao, M. Hasegawa, B. Ghetti, M. Spillantini, B. Ryskeldi-Falcon, A. Murzin, M. Goedert, and A. Scheres. Age-dependent formation of TMEM106B amyloid filaments in human brains. *Nature*, 605: 310-3148, 2022.

- Y. Yang, Y. Shi, M. Schweighauser, X. Zhang, A. Kotecha, A. Murzin, H. Garringer, P. Cullinane, Y. Saito, T. Foroud, T. Warner, K. Hasegawa, R. Vidal, S. Murayama, T. Revesz, B. Ghetti, H. M. Hasegawa, T. Lashley, S. Scheres, and M. Goedert. Structures of α-synuclein filaments from human brains with Lewy pathology. *Nature*, 610: 791-795, 2022.
- 20. G. Takahashi, D. Kondo, M. Maeda, Y. Morishita, and Y. Miyaoka. Genome editing is induced in a binary manner in single human cells. *iSicence*, 25: 105619, 2022.
- D. Song*, G. Takahashi*, YW. Zheng, M. Matsuo-Takasaki, J. Li, M. Takami, Y. An, Y. Hemmi, N. Miharada, T. Fujioka, M. Noguchi, T. Nakajima, MK. Saito, Y. Nakamura, T. Oda, Y. Miyaoka#, and Y. Hayashi#. Retinoids rescue ceruloplasmin secretion and alleviate oxidative stress in Wilson's disease-specific hepatocytes. *Hum. Mol. Genet.*, 31: 3652, 2022. *Co-first authors. #Co-corresponding authors.

[Review Articles]

- K. Toriumi, M. Miyashita, K. Suzuki, K. Tabata, Y. Horiuchi, H. Ishida, M. Itokawa, and M. Arai. Role of glyoxalase 1 in methylglyoxal detoxification-the broad player of psychiatric disorders. *Redox Biol.*, 49: 102222, 2022.
- R. Koyama, and T. Shichita. Glial roles in sterile inflammation after ischemic stroke. *Neurosci. Res.*, doi: 10.1016/j.neures.2022.10.002.
- S. Sakai, and T. Shichita. Role of alarmins in poststroke inflammation and neuronal repair. *Semin. Immunopathol.*, doi: 10.1007/s00281-022-00961-5.

[Books]

Clinical Anatomy

Professor : Keiichi AKITA Professor: Akimoto NIMURA (Department of Functional Joint Anatomy) Junior Associate Professor : Kumiko YAMAGUCHI (Institute of Education Curricular Management Division) Junior Associate Professor : Kouji FUJITA(Department of Functional Joint Anatomy) Junior Associate Professor (Career Track) : Masayo HARADA Assistant Professor : Satoru MURO, Shigeru OKUHARA(November \sim December) Assistant Professor : Takuya IBARA (Department of Functional Joint Anatomy) Research Technician : Rintaro YAMAMOTO Staff Assistant : Mayuri IKEDA Parttime Lecturer : Kenji IBUKURO, Itsuko OKUDA, Shirou SUZUKI, Kenro CHIKAZAWA, Sachiyuki TSUKADA, Masahiro TSUTSUMI, Masataka NAKAZAWA, Tomoyuki YANO Graduate Student : Syuusaku HOSONO, Shouko MOUE, Ming Yan $HE(\sim March)$, Areeya JIAMJUNYASIRI, Atsuhiro FUKAI, Suthasinee THARNMANULARP, Ryo KARAKAWA, Hidehiko YOSHIMATSU, Georgina Isabella DJAMEH, Yuzuki SUGIYAMA(April \sim), Tong LIU(April \sim) Research student :

(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

- 1. Mio Norose, Akimoto Nimura, Masahiro Tsutsumi, Koji Fujita, Atsushi Okawa, Keiichi Akita. Anatomical study for elucidating the stabilization mechanism in the trapeziometacarpal joint. Sci Rep. 2022.12; 12(1); 20790
- 2. Ryo Karakawa, Hidehiko Yoshimatsu, Keisuke Kamiya, Yuma Fuse, Tomoyuki Yano, Satoru Muro, Keiichi Akita. An Anatomical Study of Posterior Trunk Recipient Vessels, and Comparisons of Outcome following Pedicled- and Free-Flap Transfers for Treatment of Sarcoma in the Posterior Trunk. J Reconstr Microsurg. 2022.11; 38(9); 683-693
- 3. Suthasinee Tharnmanularp, Akimoto Nimura, Masahiro Tsutsumi, Mio Norose, Sachiyuki Tsukada, Keiichi Akita. Medial patellofemoral ligament is a part of the vastus medialis obliquus and vastus intermedius aponeuroses attaching to the medial epicondyle. Knee Surg Sports Traumatol Arthrosc. 2022.11; 30(11); 3742-3750
- 4. Ryo Karakawa, Takaaki Konishi, Hidehiko Yoshimatsu, Yuma Fuse, Yohei Hashimoto, Hiroki Matsui, Kiyohide Fushimi, Tomoyuki Yano, Hideo Yasunaga. Comparison of short-term outcomes between pedicled- and free-flap autologous breast reconstruction: a nationwide inpatient database study in Japan. Breast Cancer. 2022.11; 29(6); 1067-1075
- 5. Ken Imai, Kenro Chikazawa, Emi Yonemori, Tomoyuki Kuwata. Visualizing the dissectable layer for vaginal hysterectomy with indigo carmine. Eur J Obstet Gynecol Reprod Biol. 2022.11; 278; 195-196
- 6. Kengo Nakatsuka, Ryo Karakawa, Yuma Fuse, Hidehiko Yoshimatsu, Tomoyuki Yano. Donor-site Chyle Leakage after Breast Reconstruction Using a Deep Inferior Epigastric Artery Perforator Flap. Plast Reconstr Surg Glob Open. 2022.10; 10(10); e4612
- Haruki Toda, Yuki Hashimoto, Takuya Ibara, Mitsunori Tada. Effect of vibrotactile stimulation of the hallux nail on segmental coordination: A secondary analysis using uncontrolled manifold analysis. J Biomech. 2022.08; 141; 111234
- Atsuhiro Fukai, Akimoto Nimura, Masahiro Tsutsumi, Hitomi Fujishiro, Koji Fujita, Junya Imatani, Keiichi Akita. Lateral Ulnar Collateral Ligament of the Elbow Joint: Reconsideration of Anatomy in Terms of Connection with Surrounding Fibrous Structures. J Bone Joint Surg Am. 2022.08; 104(15); 1370-1379
- Kenro Chikazawa, Shigeki Matsubara, Tomoyuki Kuwata. Difficulties in the Management of Placenta Accreta Spectrum Disorders are not Confined to Low-/Middle-Income Countries: A Possible Usefulness of Simulation Training. Rev Bras Ginecol Obstet. 2022.08; 44(8); 804-805

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- 11. Takayoshi Komemushi, Itsuko Okuda, Atsushi Komemushi, Yasuo Nakajima, Hidefumi Mimura, Akiyoshi Kajikawa. Matching the perforating branch of the internal thoracic artery and the deep inferior epigastric artery for breast reconstruction using multi-detector row computed tomography. Jpn J Radiol. 2022.06; 40(6); 624-629
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- 21. Tomoyuki Yano. Flaps vs Implants!!. San Antonio Breast Cancer Symposium Shenzhen 2022.01.23 Web

Systems BioMedicine

Professor Hiroshi ASAHARA

Junior Associate Professor Ryouta KURIMOTO Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA, Yuta Fujii Postdoctoral fellow Yutaro UCHIDA Graduate Students Maiko INOTSUME, Lin LIU, Lisa YAGASAKI, Suzu CHIDA, Masayasu SEGA, Mayu KOIKE, Risa SANADA, Nao WATANABE, Hiroki ONO, Mikoto KATAGIRI, Hifumi TAGUCHI, Waka MIYAMOTO

(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.

Revealed the molecular mechanism by which osteocytes regulate bone homeostasis.

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" and "Biochemistry Experimental Practice", 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.

In research education for undergraduate students, as part of the research practice program, a new research training system was established as the "Meister Training Course," covering basic and applied research from molecular biology to experiments using individual mice, in order to enhance their basic research skills.

(3) Publications

[Original Articles]

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- 2. Tomohiko Murakami, Yoshifumi Takahata, Kenji Hata, Kosuke Ebina, Katsutoshi Hirose, Lerdluck Ruengsinpinya, Yuri Nakaminami, Yuki Etani, Sachi Kobayashi, Takashi Maruyama, Hiroyasu Nakano, Takehito Kaneko, Satoru Toyosawa, Hiroshi Asahara, Riko Nishimura. Semaphorin 4D induces articular cartilage destruction and inflammation in joints by transcriptionally reprogramming chondrocytes. Sci Signal. 2022.11; 15(758); eabl5304
- 3. Takayoshi Sasako, Toshihiro Umehara, Kotaro Soeda, Kazuma Kaneko, Miho Suzuki, Naoki Kobayashi, Yukiko Okazaki, Miwa Tamura-Nakano, Tomoki Chiba, Domenico Accili, C Ronald Kahn, Tetsuo Noda, Hiroshi Asahara, Toshimasa Yamauchi, Takashi Kadowaki, Kohjiro Ueki. Deletion of skeletal muscle Akt1/2 causes osteosarcopenia and reduces lifespan in mice. Nat Commun. 2022.10; 13(1); 5655
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- 1. Hiroshi Asahara. Athlete Giftedness and Tendon. Molecular Medicine Department Retreat 2022.10.10 ス クリプス研究所
- 2. 劉琳、千葉朋希、淺原弘嗣. Generation and analysis of conditional Mkx knockout mice. 第 40 回日本骨代 謝学会学術集会 2022.07.22
- 3. Yutaro Uchida, Ryota Kurimoto, Tomoki Chiba, Yasuto Takeuchi, Noriko Gotoh, Hiroshi Asahara. Post-transcriptional regulation of breast cancer stemness by the novel RNA binding protein. 第 23 回 日本 RNA 学会年会 2022.07.21
- 4. Ryota Kurimoto, Waka Miyamoto, Maiko Inotsume, Tomoki Chiba, TakahideMatsushima, YutaroUchida, Yuta Fujii, Hiroshi Asahara.. Regulation of lung cancer metastasis by the RNA-modifying enzyme. 第 23 回日本 RNA 学会年会 2022.07.21
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[Others]

- 1. Connecting science to medicine: tendon-like tissue created from human stem cells, 2022.02 AAAS EurekAlert! The Global Source for Science News
- 2. Revealing the function of Mkx in periodontal ligament homeostasis, 2022.02 AAAS EurekAlert! The Global Source for Science News
- 3. Connecting science to medicine: tendon-like tissue created from human stem cells, 2022.02 AAAS EurekAlert! The Global Source for Science News
- 4. Revealing the function of Mkx in periodontal ligament homeostasis, 2022.02 AAAS EurekAlert! The Global Source for Science News

Comprehensive Pathology

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(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

In vivo and in vitro using mice as experimental models, immunohistological, virological, biochemical and molecular biological analyzes of cells of the blood system are performed.

1. Analysis of the mechanism of retrovirus-induced leukemia and development of its therapeutic model The function of host T cells plays an important role in the onset of tumors by Friend Leukemia Virus. We are analyzing what signaling mechanisms are activated by virus infection and how T cell functions are controlled.

2. Apoptosis induction using retrovirus-derived proteins and its application to gene therapy. Gp70 from Friend Leukemia Virus activates the pro-apoptotic pathway for DNA damage signals, highlighting host-derived genes. Using this system, we are applying it to treatments including gene therapy.

3. Molecular and pathological study on the mechanism of Myelodysplastic syndromes (MDS) onset. MDS is a disease that occurs in relatively elderly people, and causes peripheral blood cytopenias due to the frequent apoptosis in the bone marrow. We are analyzing the expression and regulation of molecules that cause apoptosis in MDS bone marrow cells from both hematopoietic cells and stromal cells.

4. Study on drug resistance of various hematopoietic diseases Analysis of drug resistance genes of various hematopoietic diseases and the movement of related molecules.

5. Comprehensive study on the mechanism of immune system formation and its breakdown with age. The formation of the immune system progresses rapidly after birth, reaches a peak during puberty, and then declines with age. As a result, it is not uncommon for elderly people after the age of 70 to have markedly reduced immune function, and are susceptible to infectious diseases, similar to AIDS. In order to elucidate the

mechanism of such age-related changes in the immune system, the age-related changes in the thymus, T cells, and the neuroendocrine immune system are analyzed at the molecular level.

6. Molecular pathological study on cancer growth and progression.

We mainly use human pathological tissue of the digestive system to analyze various substances related to the growth and progression of cancer using molecular pathological techniques.

(3) Education

Undergraduate education: Education is provided throughout the four years from the first grade to the fourth grade of specialized courses through the general pathology, each theory practice, PBL, block type learning, comprehensive diagnostics practice, BSL, and the like. The program is implemented in cooperation with the human pathology department, hospital pathology department, molecular pathology department, difficult research neuropathology department, and dentistry oral pathology course. At the case study meeting, CPE, which is held at the end of each discussion practice, a small number of students are in charge of one case, give presentations, and promote understanding of pathology through case experience.

(4) Lectures & Courses

Post-graduate education: Training of pathological, anatomy and surgical pathology for the purpose of acquiring the qualification of a pathological society-certified physician, as well as training in related hospitals. Through CPC and case study meetings with clinical departments, the aim is to deepen their understanding of clinical medicine. Regarding research, in addition to the usual pathological methods, we will use them according to the theme of each person such as immunopathology, virology, biochemistry and molecular biology methods, so that we can conduct advanced research.

(5) Clinical Services & Other Works

I the university hospital, surgical materials, biopsy materials, and various organs obtained by pathological dissection are subjected to immunohistological technic in addition to the usual morphological methods.

(6) Clinical Performances

To improve diagnostic accuracy, the methods of molecular pathology are also applied.

(7) Publications

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- 3. Anri Koyanagi, Iichiroh Onishi, Karin Muraoka, Ikue Sato, Shingo Sato, Tsuyoshi Kimura, Akio Kishida, Kouhei Yamamoto, Masanobu Kitagawa, Morito Kurata. Identification of the factor that leads human mesenchymal stem cell lines into decellularized bone Bioengineering (Basel). 2022.09; 9(10); 490
- Koyanagi A, Onishi I, Muraoka K, Sato I, Sato S, Kimura T, Kishida A, Yamamoto K, Kitagawa M, Kurata M. Identification of the Factor That Leads Human Mesenchymal Stem Cell Lines into Decellularized Bone. Bioengineering (Basel, Switzerland). 2022.09; 9(10);

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- 10. Asakawa A, Kawade G, Kurata M, Fukuda S, Onishi I, Kinowaki Y, Ishibashi S, Ikeda M, Watabe S, Kobayashi M, Ishibashi H, Okubo K, Kitagawa M, Yamamoto K. Stratification of lung squamous cell carcinoma based on ferroptosis regulators: Potential for new therapeutic strategies involving ferroptosis induction. Lung cancer (Amsterdam, Netherlands). 2022.01; 165; 82-90
- 11. Hayashi K, Nogawa D, Kobayashi M, Asakawa A, Ohata Y, Kitagawa S, Kubota K, Takahashi H, Yamada M, Oda G, Nakagawa T, Uetake H, Onishi I, Kinowaki Y, Kurata M, Kitagawa M, Yamamoto K. Quantitative high-throughput analysis of tumor infiltrating lymphocytes in breast cancer. Frontiers in oncology. 2022; 12; 901591
- Miyamoto R, Hirai T, Yoshii T, Onuma H, Inose H, Yuasa M, Matsukura Y, Morishita S, Yamamoto K, Koyanagi H, Sato S, Yagishita K, Okawa A. Surgical Strategy for Osteoid Osteoma Localized in Anterior Lumbar Vertebral Body: A Case Report. Spine surgery and related research. 2022; 6(4); 408-411
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- 2. 杉田佳祐, 倉田盛人, 大西威一郎, 山本浩平, 北川昌伸. CRISPR screening を用いた細胞間相互作用により誘 導される薬剤耐性関連分子の同定. 第 81 回日本癌学会学術総会 2022.09.30 パシフィコ横浜
- 3. 杉田 佳祐, 倉田 盛人, 大西 威一郎, 山本 浩平, 北川 昌伸. CRISPR screening を用いた細胞間相互作用によ り誘導される薬剤耐性関連分子の同定 (CRISPR screening revealed a new molecule of cell-cell interaction drug resistance.). 日本癌学会総会記事 2022.09.01
- 4. 大橋 彩香, 倉田 盛人, 新井 文子. EBV 陽性 T,NK 細胞腫瘍、慢性活動性 EBV 感染症に対する BCL2 阻害剤 の効果 (The Effects of BCL2 Inhibitors on Chronic Active EBV Infections, an Intractable T- or NK-cell Lymphoid Neoplasm). 日本癌学会総会記事 2022.09.01

- 5. 大西 威一郎, 小柳 杏莉, 村岡 香琳, 木村 剛, 岸田 晶夫, 北川 昌伸, 倉田 盛人. 脱細胞化骨を用いた、ヒト骨髄微 小環境モデルの構築 (Establishment of human bone-marrow microenvironment model using Decellularized bone). 日本癌学会総会記事 2022.09.01
- 6. Kinowaki Yuko, Fukumura Yuki, Matsuda Yoko, Akashi Takumi, Akahoshi Keiichi, Kobayashi Masanori, Ono Hiroaki, Kudo Atsushi, Tanabe Minoru, Kitagawa Masanobu. Pancreatic mixed neuroendocrine-non-neuroendocrine neoplasm: a case series of 6 patients(タイトル和訳中). 膵臓 2022.09.01
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- 8. 山本 浩平, 川出 玄二, 石橋 佐知子, 倉田 盛人, 大西 威一郎, 北川 昌伸. Diffuse large B-cell lymphoma にお ける 4-HNE 蓄積の臨床病理学的・分子学的意義 (Clinico-pathologic and molecular significance of 4-HNE accumulation in diffuse large B-cell lymphoma). 日本病理学会会誌 2022.03.01
- 9. 川出 玄二, 山本 浩平, 浅川 文香, 大西 威一郎, 倉田 盛人, 北川 昌伸. 肺癌における GPX4,FSP1 発現 と 4-HNE 蓄積の臨床病理学的検討 (Clinicopathological study of GPX4 and FSP1 expression and 4HNE accumulation in lung cancer). 日本病理学会会誌 2022.03.01

[Social Contribution]

- 1. Journal of Cancer Research and Clinical Oncology, Springer Nature, Journal of Cancer Research and Clinical Oncology, 2017.04.01 Now
- 2. Guest editor, International Journal of Molecular Sciences, 2021.08 2022.08

Molecular Oncology

Professor: Shinji TANAKA Associate Professor: Yoshimitsu AKIYAMA Assistant Professor: Shu SHIMADA Assistant Professor: Megumi HATANO Graduate Student: Kouya YASUKAWA Graduate Student: Kentaro UMEMURA Graduate Student: Atsushi KAMACHI Graduate Student: Raizo SUGIMOTO

(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 scirrhous 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]

- Asano D, Kudo A, Akahoshi K, Maekawa A, Murase Y, Ogawa K, Ono H, Ban D, Tanaka S, Tanabe M. Curative Surgery and Ki-67 Value Rather than Tumor Differentiation Predict the Survival of Patients with High-grade Neuroendocrine Neoplasms. Annals of Surgery. 2022.08; 276(2); e108-e113
- 2. Kabashima A, Matsuo Y, Ito S, Akiyama Y, Ishii T, Shimada S, Masamune A, Tanabe M, Tanaka S. cGAS-STING signaling encourages immune cell overcoming of fibroblast barricades in pancreatic cancer. Scientific reports. 2022.06; 12(1); 10466
- 3. Kato T, Kudo A, Kinowaki Y, Ishikawa Y, Watanabe S, Akahoshi K, Ogawa K, Ono H, Ban D, Tanaka S, Tanabe M. A novel classification of portal venous tumor invasion to predict residual tumor status after surgery in patients with pancreatic neuroendocrine neoplasms. J Cancer Res Clin Oncol. 2022.04; 148(4); 931-941
- 4. Maekawa A, Kudo A, Kishino M, Murase Y, Watanabe S, Ishikawa Y, Ueda H, Akahoshi K, Ogawa K, Ono H, Tanaka S, Kinowaki Y, Tanabe M. Hormonal tumor mapping for liver metastases of gastroenteropancreatic neuroendocrine neoplasms: a novel therapeutic strategy. J Cancer Res Clin Oncol. 2022.03; 148(3); 697-706
- 5. Wang J, Hirose H, Yokoyama Y, Ikeshima R, Tsujimura N, Bonkobara S, Takeda K, Hata T, Inoue A, Hiraki M, Ohtsuka M, Nishida N, Takahashi H, Haraguchi N, Tanaka S, Wu X, Mori M, Yamamoto H.. Functional assessment of miR-1291 in colon cancer cells. International Journal of Oncology. 2022.02; 60(2); 13
- 6. Zhang M, Sugita I, Komura D, Katoh H, Shimada S, Inazawa J, Tanaka S, Ishikawa S. Genomic landscape of a mouse model of diffuse-type gastric adenocarcinoma Gastric Cancer. 2022.01; 25(1); 83-95
- 7. Ishii T, Akiyama Y, Shimada S, Kabashima A, Asano D, Watanabe S, Ishikawa Y, Ueda H, Akahoshi K, Ogawa K, Ono H, Kudo A, Tanabe M, Tanaka S. Identification of a novel target of SETD1A histone methyltransferase and the clinical significance in pancreatic cancer Cancer Science. 2022;
- Ichihara M, Takahashi H, Nishida N, Ivan C, Okuzaki D, Yokoyama Y, Ohtsuka M, Miyoshi N, Uemura M, Tanaka S, Calin G, Mori M, Doki Y, Eguchi, H, Yamamoto H. Long noncoding RNA 01534 maintains cancer stemness by down-regulating endoplasmic reticulum stress response in colorectal cancer. Annals of Gastroenterological Surgery. 2022;
- Yamamoto Y, Shimada S, Akiyama Y, Tsukihara S, Sugimoto R, Kabashima A, Tokunaga M, Kinugasa Y, Kawakami Y, Tanaka S. RTP4 silencing provokes tumor-intrinsic resistance to immune checkpoint blockade in colorectal cancer. Journal of Gastroenterology. 2022;

[Misc]

1. Shimada S, Tanaka S. Molecular targeted drugs, comprehensive classification and preclinical models for the implementation of precision immune oncology in hepatocellular carcinoma International Journal of Clinical Oncology. 2022.07; 27(7); 1101-1109

- 1. Shinji Tanaka. Surgical oncology to elucidate molecular and immunological mechanisms for clinical application in hepato-biliary-pancreatic cancer (lecture). UCh-TMDU Joint Symposium 2022.11.08 Chile (on-line)
- 2. Atsushi Nara, Keiichi Akahoshi, Hiroki Ueda, Koichiro Morimoto, Masaru Takeuchi, Masahiro Yamane, Akira Ito, Shotaro Gan, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Shuichi Watanabe, Yoshiya Isikawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Usefulness of the Novel Rupture Severity Score (NRSS) in Determining the Timing of Transarterial Embolization (TAE) for Ruptured Hepatocellular Carcinoma. IASGO-CME 2022.10.26 Fukuoka
- 3. Shinji Tanaka. Workshop 9 : Molecular mechanisms of liver cancer (including HCC, CCC, metastatic liver cancer) , Molecular and immunological mechanisms of liver cancer; preclinical studies for clinical application (invited lecture). APASL Oncology 2022 2022.09.01 Takamatsu (on-line)

- 4. Hiroaki Ono, Yoshiki Murase, Daisuke Asano, Syuuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Evaluation of the efficacy of Ispinesib, a novel Eg5 inhibitor, for the treatment of high grade Pan-NENs. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.08 Kyoto
- 5. Shotaro Gan, Hiroki Ueda, Atsushi Nara, Akira Ito, Koichiro Morimoto, Hironari Yamashita, Munetaka Kimura, Kohei Yagi, Takeshi Ishii, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Discussion on the treatment of liver cysts at our hospital. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 6. Daisuke Asano, Atushi Kudo, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Shinji Tanaka, Minoru Tanabe. Reappraisal of surgical treatment for liver metastases of neuroendocrine neoplasms. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 7. Aya Maekawa, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Hormonaltumor mapping for liver metastases of gastroenteropancreatic neuroendocrine neoplasms. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 8. Yoshiya Ishikawa, Daisuke Asano, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Safe approach to dissect hepatoduodenal ligament during laparoscopic pancreaticoduodenectomy. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 9. Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The novel techniques of distal pancreatectomy using articulation forceps -introducing the desterity of a robotic system to a palaroscopic surgery. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 10. Akira Ito, Daisuke Asano, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Takeshi Ishii, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Strategy of pancreatic ductal adenocarcinoma treatment. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 11. Akira Ito, Daisuke Asano, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Takeshi Ishii, Yoshiya Ishikawa, Shuichi watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe . Strategy of pancreatic ductal adenocarcinoma treatment. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 12. Keiichi Akahoshi, Akira Ito, Atsushi Nara, Shotaro Gan, Takeshi Ishii, Kohei Yagi, Koichiro Morimoto, Hironari Yamashita, Munetaka Kimura, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Transpapillary or transmural drainage for postoperative pancreatic fistula after distal pancreatectomy. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 13. Koichiro Morimoto, Hiroki Ueda, Daisuke Asano, Yoshiya Ishikawa, Syuichi Watanebe, Keiichi Akahoshi, Hiroaki Ono, Atushi Kudo, Shinji Tanaka, Minoru Tanabe. Risk factors of postoperative cholangitis after hepatectomy with hepato-jejunostomy for malignancy-Clumping test predicts late refractory cholangitis. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 14. Hiroaki Ono, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Validation of surgical resection for pancreatic neuroendocrine neoplasms with simulataneous liver metastases. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 15. Takeshi Ishii, Keiichi Akahoshi, Koichirou Morimoto, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. A single-center retrospective study of 17 cases of pancreatic metastasis from renal cell carcinoma. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime

- 16. Hiroki Ueda, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical features of malignant insulinoma from single center experience. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 17. Atsushi Nara, Hiroki Ueda, Yukue Shimizu, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Hiroaki Ono, Shinji Tanaka, Minoru Tanabe. Evaluation of sarcopenia using preoperative InBody and short-term results after pancreaticoduodenectomy. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 18. Hironari Yamashita, Keiichi Akahoshi, Akira Ito, Shoutaro Gan, Atsushi Nara, Munetaka Kimura, Koichiro Morimoto, Kohei Yagi, Takeshi Ishi, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical outcome of pT1 pancreatic ductal adenocarcinoma-what is the risk factor of poor prognosis?. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 19. Kohei Yagi, Hiroaki Ono, Atsushi Kudo, Akira Ito, Atsushi Nara, Syotaro Gan, Munetaka Kimura, Hironari Yamashita, Takeshi Ishii, Daisuke Aasano, Syuichi Watanabe, Hiroki Ueda, Yoshiya Ishikawa, Keiichi Akahoshi, Shinji Tanaka, Minoru Tanabe. Significance of MGMT expression for streptozocin treatment of pancreatic neuroendocrine neoplasms. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 20. Hiroki Ueda, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical features of malignant insulinoma from single center experience. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10
- 21. Shinji Tanaka. Workshop 2: Innovative research of biomarkers for HBP cancers, Biomarker research and clinical application for treatment of hepato-biliary-pancreatic cancer (invited lecture). The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Matsuyama (on-line)
- 1. Shu Shimada, Yoshimitsu Akiyama, Shinji Tanaka. Intrinsic activation of β -catenin signaling by CRISPR/Cas9- mediated exon skipping contributes to immune evasion in HCC. The 81st Annual Meeting of the Japanese Cancer Association. 2022.09.30 Yokohama

[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

Associate Professor: Takumi AKASHI Assistant Professor: Iichiro Onishi ,Susumu KIRIMURA, Junko KUNIEDA ,Hiroshi Shintaku Project Assistant Professor: Keiko MIURA Secretary: Ayako UENO

(1) Outline

Missons 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) Development of novel markers significant for histopathological diagnosis
- 3) Clinico-pathological analysis of malignant mesothelioma
- 4) Clinico-pathological analysis of inflammatory bowel disease
- 5) Clinico-pathological analysis of glomerular disease
- 6) Clinico-pathological analysis of pancreatic neuroendocrine tumor
- 7) Clinico-pathological analysis of neuronal degenerative disease

(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 (40 case in a year), cytopathology services (9,517 cases in a year) and surgical pathology (11,695 cases in a year) for the clinicians of the affiliated hospital. Diagnosis is mostly done by the organ-subspecilized staffs. Clinico-pathological conferences have been held about two hundred times in 2022.

(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

- Miyauchi M, Akashi T, Furukawa A, Uchida K, Tamura T, Ando N, Kirimura S, Shintaku H, Yamamoto K, Ito T, Miura K, Kayamori K, Ariizumi Y, Asakage T, Kudo A, Tanabe M, Fujii Y, Ishibashi H, Okubo K, Murakami M, Yamada T, Takemoto A, Bae Y, Eishi Y, Ohashi K. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocr Pathol. 2022.12; 33(4); 506-518
- Shogo Wada, Takeshi Namiki, Moe Takano, Keiko Miura, Naoko Okiyama. Kaposi sarcoma with HHV-8 immunoreactivity in a gastric lesion but not in skin lesions. J Dtsch Dermatol Ges. 2022.11; 20(11); 1512-1514
- Usui E, Kanno Y, Yonetsu T, Kinowaki Y, Akashi T, Sasano T. Multimodality Imaging of Possible Healed Plaque Erosion Pathologically Validated by Directional Coronary Atherectomy Specimens. JACC. Cardiovascular interventions. 2022.11; 15(21); 2225-2227
- 4. Tatsumi A, Hirakochi H, Inoue S, Tanaka Y, Furuno H, Ikeda M, Ishibashi S, Taguchi T, Yamamoto K, Onishi I, Sachs Z, Largaespada DA, Kitagawa M, Kurata M. Identification of NRAS Downstream Genes with CRISPR Activation Screening. Biology. 2022.10; 11(11);
- 5. Shinohara H, Kobayashi M, Hayashi K, Nogawa D, Asakawa A, Ohata Y, Kubota K, Takahashi H, Yamada M, Tokunaga M, Kinugasa Y, Oda G, Nakagawa T, Onishi I, Kinowaki Y, Kurata M, Ohashi K, Kitagawa M, Yamamoto K. Spatial and Quantitative Analysis of Tumor-Associated Macrophages: Intratumoral CD163-/PD-L1+ TAMs as a Marker of Favorable Clinical Outcomes in Triple-Negative Breast Cancer. International journal of molecular sciences. 2022.10; 23(21);
- 6. Oda G, Nakagawa T, Mori H, Onishi I, Fujioka T, Mori M, Kubota K, Hanazawa R, Hirakawa A, Ishikawa T, Okamoto K, Uetake H. Factors predicting upstaging from clinical N0 to pN2a/N3a in breast cancer patients. World Journal of Clinical Oncology. 2022.09; 13(9); 748-757
- 7. Keisuke Goto, Kohei Ogawa, Tatsuo Fukai, Keiko Miura, Shigeto Yanagihara, Keiichiro Honma, Toru Motoi. Categorization of cutaneous epithelioid angiomatous nodule as epithelioid hemangioma or angiolymphoid hyperplasia with eosinophilia: Clinicopathologic, immunohistochemical, and molecular analyses of seven lesions. J Cutan Pathol. 2022.09; 49(9); 765-771
- 8. Koyanagi A, Onishi I, Muraoka K, Sato I, Sato S, Kimura T, Kishida A, Yamamoto K, Kitagawa M, Kurata M. Identification of the Factor That Leads Human Mesenchymal Stem Cell Lines into Decellularized Bone. Bioengineering (Basel, Switzerland). 2022.09; 9(10);

- 9. Kimura S, Onishi I, Kobayashi M. A Rare Case of Esophageal Metastasis of Invasive Mucinous Adenocarcinoma of the Lung. ACG case reports journal. 2022.08; 9(8); e00857
- 10. Kudo Ryo, Kano Yoshihito, Noji Rika, Kakuta Ryota, Onishi Iichiro, Kimura Kouichiro, Tanimoto Kousuke, Miya Fuyuki, Mitsumura Takahiro, Oshima Noriko, Ariizumi Yousuke, Nakagawa Tsuyoshi, Ishikawa Toshiaki, Miyake Satoshi, Ikeda Sadakatsu. Clinical utility of comprehensive genomic profiling for patients with cancer of unknown primary site ANNALS OF ONCOLOGY. 2022.07; 33; S500
- 11. Kusafuka K, Sato Y, Nakatani E, Baba S, Maeda M, Yamanegi K, Ueda K, Inagaki H, Otsuki Y, Kuroda N, Suzuki K, Iwai H, Imamura Y, Itakura J, Yamanaka S, Takahashi H, Ito I, Akashi T, Daa T, Hamada M, Yasuda M, Kawata R, Yamamoto H, Tachibana Y, Fukuoka J, Muramatsu A, Arai K, Suzuki M. The implicated clinical factors for outcomes in 304 patients with salivary duct carcinoma: Multi-institutional retrospective analysis in Japan. Head & neck. 2022.06; 44(6); 1430-1441
- Keisuke Goto, Shusuke Yoshikawa, Yoshio Kiyohara, Yoji Kukita, Keiko Miura, Takuma Oishi. Co-existence of BRAF V600E-mutated malignant melanoma and BRAF V600E-mutated Langerhans cell histiocytosis: A case report. J Cutan Pathol. 2022.04; 49(4); 393-398
- Takashi Hashimoto, Takeshi Namiki, Madoka Iikawa, Tsukasa Ugajin, Keiko Miura, Hiroo Yokozeki. Prurigo Nodularis in a Patient with Anaplastic Large Cell Lymphoma: A Potential Role for M2-Macrophages in Its Pathogenesis. Ann Dermatol. 2022.04; 34(2); 149-151
- 14. Tsuyoshi Nakagawa, Kumiko Hayashi, Ayumi Ogawa, Goshi Oda, Iichiro Onishi, Masahide Yamamoto, Mio Mori, Tomoyuki Fujioka, Toshiaki Ishikawa, Kentaro Okamoto, Hiroyuki Uetake. Bone Marrow Carcinomatosis in a Stage IV Breast Cancer Patient Treated by Letrozole as First-Line Endocrine Therapy. Case Rep Oncol. 2022.04; 15(1); 436-441
- 15. Takashi Ito, Yoshinobu Eishi, Daisuke Kobayashi, Takumi Akashi, Morio Koike, Kenichi Ohashi. A risk stratification for nodal metastasis in T1 colorectal cancer after successful therapeutic endoscopy. Gastrointest Endosc. 2022.03; 96(1); 131-134
- 16. Yasuko Aoyagi, Yoshihito Kano, Kohki Tohyama, Shotaro Matsudera, Yuichi Kumaki, Kenta Takahashi, Takahiro Mitsumura, Yohei Harada, Akemi Sato, Hideaki Nakamura, Eisaburo Sueoka, Naoko Aragane, Koichiro Kimura, Iichiro Onishi, Akira Takemoto, Keiichi Akahoshi, Hiroaki Ono, Toshiaki Ishikawa, Masanori Tokunaga, Tsuyoshi Nakagawa, Noriko Oshima, Reiko Nakamura, Masatoshi Takagi, Takahiro Asakage, Hiroyuki Uetake, Minoru Tanabe, Satoshi Miyake, Yusuke Kinugasa, Sadakatsu Ikeda. Clinical utility of comprehensive genomic profiling in Japan: Result of PROFILE-F study. PLoS One. 2022.03; 17(3); e0266112
- 17. Propylthiouracil-induced vasculitis presenting as purpuric plaques on cheeks. Clin Exp Dermatol. 2022.03; 47(3); 581-582
- Hiroki Arakawa, Takeya Adachi, Akihiro Miyagawa, Keiko Miura, Kentaro Ogata, Toyoko Inazumi. A case of aggressive and protuberant nodular fasciitis on the finger with repeated contact. Australas J Dermatol. 2022.02; 63(1); e102-e103
- 19. Ogawa A, Nakagawa T, Kumaki Y, Hosoya T, Oda G, Mori M, Fujioka T, Kubota K, Onishi I, Uetake H. Spontaneous regression of breast lymphoproliferative disorders after withdrawal of methotrexate in rheumatoid arthritis patients with Epstein-Barr virus infection: a case report and review of the literature. Journal of medical case reports. 2022.02; 16(1); 49
- Onishi Iichiroh, Kirimura Susumu, Wakejima Ryo, Okubo Kenichi, Odai Tamami, Kakuta Ryota, Kano Yoshihito, Ikeda Sadakatsu, Akashi Takumi, Kitagawa Masanobu. Primary pulmonary choriocarcinoma with a genomic sequence Pathology International. 2022.02; 72(2); 141-143
- Nakagawa T, Oda G, Mori H, Uemura N, Onishi I, Sagawa N, Fujioka T, Mori M, Kubota K, Ishikawa T, Okamoto K, Uetake H. Prognosis of Subcutaneous Mastectomy for Special Types of Breast Cancer. Medicina (Kaunas, Lithuania). 2022.01; 58(1);
- 22. Yumi Mochizuki, Maiko Tsuchiya, Jun Oyama, Akane Wada, Takuma Kugimoto, Takeshi Kuroshima, Hideaki Hirai, Hirofumi Tomioka, Hiroyuki Harada, Tohru Ikeda, Takumi Akashi. Left supraclavicular (Virchow's) node metastasis detected before primary infradiaphragmatic tumor: a case series. J Med Case Rep. 2022.01; 16(1); 33

- 23. Asakawa A, Kawade G, Kurata M, Fukuda S, Onishi I, Kinowaki Y, Ishibashi S, Ikeda M, Watabe S, Kobayashi M, Ishibashi H, Okubo K, Kitagawa M, Yamamoto K. Stratification of lung squamous cell carcinoma based on ferroptosis regulators: Potential for new therapeutic strategies involving ferroptosis induction. Lung cancer (Amsterdam, Netherlands). 2022.01; 165; 82-90
- 24. Shogo Wada, Takeshi Namiki, Keiko Miura. Mononuclear variant of adult xanthogranuloma associated with B-cell acute lymphocytic leukemia. J Dermatol. 2022.01; 49(5); e161-e162
- 25. Hayashi K, Nogawa D, Kobayashi M, Asakawa A, Ohata Y, Kitagawa S, Kubota K, Takahashi H, Yamada M, Oda G, Nakagawa T, Uetake H, Onishi I, Kinowaki Y, Kurata M, Kitagawa M, Yamamoto K. Quantitative high-throughput analysis of tumor infiltrating lymphocytes in breast cancer. Frontiers in oncology. 2022; 12; 901591
- 26. Daisuke Kobayashi, Keisuke Uchida, Asuka Furukawa, Takashi Ito, Luis Masuo Maruta, Heinrich Bender Kohnert Seidler, Aloisio Felipe-Silva, Masaki Sekine, Noboru Ando, Yuka Toyama, Yusuke Chino, Keiko Miura, Kurara Yamamoto, Takumi Akashi, Yoshinobu Eishi, Kenichi Ohashi. Immunohistochemical Differentiation between Western and East Asian Types of CagA-Positive Helicobacter pylori in Gastric Biopsy Samples Can J Gastroenterol Hepatol. 2022; 2022; 1371089
- 27. Mori M, Fujioka T, Ichikawa R, Inomata R, Katsuta L, Yashima Y, Yamaga E, Tsuchiya J, Hayashi K, Kumaki Y, Oda G, Nakagawa T, Onishi I, Kubota K, Tateishi U. Comparison of < sup> 18/sup> F-fluorothymidine Positron Emission Tomography/Computed Tomography and < sup> 18/sup> F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Patients with Breast Cancer. Tomography (Ann Arbor, Mich.). 2022.10; 8(5); 2533-2546
- 28. Noji R, Tohyama K, Kugimoto T, Kuroshima T, Hirai H, Tomioka H, Michi Y, Tasaki A, Ohno K, Ariizumi Y, Onishi I, Suenaga M, Mori T, Okamoto R, Yoshimura R, Miura M, Asakage T, Miyake S, Ikeda S, Harada H, Kano Y. Comprehensive Genomic Profiling Reveals Clinical Associations in Response to Immune Therapy in Head and Neck Cancer. Cancers. 2022.07; 14(14);

[Conference Activities & Talks]

- 1. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. Potential Utility of Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma as Prognostic marker of Nivolumab(タイトル和訳中). 肺癌 2022.11.01
- 2. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. 悪性胸膜中皮腫の腫瘍免疫微小環境の解明 (Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma). 日本呼吸器学会誌 2022.04.01

[Social Contribution]

- 1. The Japanese Society of Diagnostic Dermatopathology, Department of Pathology, Fukuoka University, 2005.04.17 Now
- 2. Ochanomizu Study Meeting of Dermatopathology, 2009.04 Now

Signal Gene Regulation

Professor (Bio-Matrix, Medical Biochemistry) HATA Yutaka 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**

- 1. Noriko Funato^{*}, Hiromi Yanagisawa. TBX1 targets the miR-200-ZEB2 axis to induce epithelial differentiation and inhibit stem cell properties. Scientific Reports. 2022.11; 12(1); 20188
- 2. Yuki Taga, Yu Iwasaki, Chisa Tometsuka, Noriko Funato, Yasutaka Shigemura, Masashi Kusubata, Kazunori Mizuno. Identification of a highly stable bioactive 3-hydroxyproline-containing tripeptide in human blood after collagen hydrolysate ingestion. NPJ Sci Food. 2022.06; 6(1); 29

[Books etc]

1. Kevin V. Urbano (Editor), Noriko Funato et al.,. Advances in Genetics Research. Vol 21. Nova Science Publishers, Inc., 2022.02 (ISBN : 978-1-68507-562-0)

[Misc]

1. Noriko Funato*. Craniofacial Phenotypes and Genetics of DiGeorge Syndrome. Journal Developmental Biology. 2022.05; 10(2); 18

[Others]

- 1. Grants-in-Aid for Scientific Research (C), 2022.04 "Elucidation of new transcription target of DiGeorge syndrome disease gene product TBX1 and its molecular mechanism" Noriko Funato
- Craniofacial Phenotypes and Genetics of DiGeorge Syndrome, 2022.06 Scholarly Community Encyclopedia https://encyclopedia.pub/entry/23098
- 3. 2022.10 PR TIMES https://prtimes.jp/main/html/rd/p/000000010.000083625.html

[Social Contribution]

- 1. QS Global Academic Survey (QS World University Rankings), 2020 2022
- 2. Times Higher Education (THE)'s Global Academic Reputation Survey, 2021 2022

Hematology

Professor: Takehiko Mori

Junior Associate Professor: Masahide Yamamoto, Toshikage Nagao Assistant Professor: Yoshihiro Umezawa, Keigo Okada, Kota Yoshifuji

Project Assistant Professor: Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory): Ayako Nogami

Senior Resident : Takuma Harada, Fumihiko Ouchi, Hikari Kanai, Momoko Chiba, Hiroki Hatsuzawa, Marie Yagi, Keisuke Tanaka

Graduate Student: Yotaro Motomura, Makiko Saito, Junichi Mukae, Yuma Noguchi, Mai Soejima

(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

Our laboratory has been engaged in various research activities, focusing on elucidation of "crosstalk among intracellular signaling pathways, involved in cell proliferation or tumorigenesis of hematopoietic malignancies" as well as "comprehensive mechanisms by which chemotherapeutic agents induce apoptosis in hematopoietic tumors". Based on those accomplishments, we are energetically pursuing new insights, supported by recent drastic advances in molecular biological and genetic analysis methods.

1) New molecular targets in refractory B-cell malignancies and the potential for therapeutic application.

2) Elucidation of the molecular mechanisms involved in formation of drug resistance in acute leukemias with specific oncogenic mutations.

3) Development of novel Chimeric Antigen Receptor (CAR) T cell technologies.

4) Analyses on pathogenesis-related genetic aberrations and their implication to clinical presentation in primary vitreoretinal lymphoma.

5) Analyses on pathogenesis of myeloproliferative neoplasms, mechanisms of drug resistance, and development of effective therapeutic methodologies.

6) Establishment, characterization of novel cell lines derived from hematopoietic tumors and their application in basic research,

7) Development of novel diagnostic methods and management of infectious complications immunocompromised patients.

(3) Education

Department of hematology is responsible for teaching basic and clinical hematology to the 3rd-year medical students in Hematology/Oncology block course. We are also responsible for the 5th- and 6th-year students in clinical clerkship to obtain basic knowledge and problem-solving abilities in hematology as well as general internal medicine. In the clerkship, we focus on the participation in the team, which would be helpful to proceed to the post-graduate training.

Even under the restriction due to COVID-19 pandemic, lectures based on case study and group work are provided.

In the resident training course, we provide training to acquire the basic skills of total health care including communications, diagnosis and treatment of various hematological disorders. Our training is based on the essential issues and skills to obtain the certificate of Hematology Specialist.

We always guide the young doctors, including Ph.D. students, to search for the solutions of their own questions by planning and performing basic and/or clinical studies. Our goal is to raise researchers with an excellent research mind.

(4) Lectures & Courses

As described in 3, our goal is to raise experts with ability to solve problems and provide total health care through learning clinical and basic hematology.

(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, hematopoietic cell transplantation, and CAR-T cell therapy.

(6) Clinical Performances

We provide the highest quality of patient care for a wide spectrum of blood diseases and cancers.

(7) Publications

- Nagao T, Yoshifuji K, Sadato D, Motomura Y, Saito M, Yamamoto K, Yamamoto K, Nogami A. Establishment and characterization of a new activated B-cell-like DLBCL cell line, TMD12. Experimental hematology. 2022.12; 116; 37-49
- 2. Kimura Shunichi, Shimizu Hiroaki, Miyazaki Takuya, Sakurai Masatoshi, Tanoue Susumu, Kayamori Kensuke, Ohwada Chikako, Yoshimura Kazuki, Nakasone Hideki, Ohashi Takuma, Shono Katsuhiro, Tachibana Takayoshi, Hatano Kaoru, Okada Keigo, Kimura Yuta, Seo Sachiko, Doki Noriko, Tanaka Masatsugu, Hatta Yoshihiro, Takahashi Satoshi, Kanda Yoshinobu. Impact of standard-dose dipeptidyl peptidase-4 inhibitors on the incidence of graft-versus-host disease after allogeneic hematopoietic cell transplantation BONE MARROW TRANSPLANTATION. 2022.12;
- 3. Nakamura Y, Mori T, Kako S, Yamazaki H, Kanda Y, Uchida N, Tanaka M, Nawa Y, Fukuda T, Ichinohe T, Atsuta Y, Onishi Y. Outcome of peripheral blood stem cell transplantation from HLA-identical sibling donors for adult patients with aplastic anemia. International journal of hematology. 2022.11;

- 4. Nogawa M, Watanabe N, Koike T, Fukuda K, Ishiguro M, Fujino H, Hirayama J, Shiba M, Handa M, Mori T, Okamoto S, Miyata S, Satake M.. Hemostatic function of cold stored platelets in a thrombocytopenic rabbit bleeding model Transfusion. 2022.09; 62(11); 2304-2313
- 5. Yokoyama Y, Nozawa E, Morita M, Ishikawa E, Mori T, Sakurai M, Kikuchi T, Matsuki E, Yamazaki R, Kataoka K, Jibiki A, Kawazoe H, Suzuki S, Nakamura T. Simultaneous quantification of dasatinib, nilotinib, bosutinib, and ponatinib using high-performance liquid chromatography-Photodiode array detection. Journal of clinical laboratory analysis. 2022.08; 36(8); e24598
- 6. Edahiro Y, Ito T, Gotoh A, Nakamae M, Kimura F, Koike M, Kirito K, Wada H, Usuki K, Tanaka T, Mori T, Wakita S, Saito TI, Kada A, Saito AM, Shimoda K, Sugimoto Y, Kurokawa T, Tomita A, Hashimoto Y, Akashi K, Matsumura I, Takenaka K, Komatsu N. Clinical characteristics of Japanese patients with polycythemia vera: results of the JSH-MPN-R18 study. International journal of hematology. 2022.07; 116(5); 696-711
- 7. Noji R, Tohyama K, Kugimoto T, Kuroshima T, Hirai H, Tomioka H, Michi Y, Tasaki A, Ohno K, Ariizumi Y, Onishi I, Suenaga M, Mori T, Okamoto R, Yoshimura R, Miura M, Asakage T, Miyake S, Ikeda S, Harada H, Kano Y. Comprehensive Genomic Profiling Reveals Clinical Associations in Response to Immune Therapy in Head and Neck Cancer. Cancers. 2022.07; 14(14);
- Mizuno K, Sakurai M, Kato J, Yamaguchi K, Abe R, Koda Y, Kataoka K, Mori T. Risk factor analysis for cytomegalovirus reactivation under prophylaxis with letermovir after allogeneic hematopoietic stem cell transplantation. Transplant infectious disease : an official journal of the Transplantation Society. 2022.07; 24(6); e13904
- 9. Masahide Yamamoto, Maho Sato, Yasushi Onishi, Yoji Sasahara, Hideki Sano, Masayoshi Masuko, Hirohisa Nakamae, Ken-Ichi Matsuoka, Takahide Ara, Kana Washio, Makoto Onizuka, Kenichiro Watanabe, Yoshiyuki Takahashi, Tsuneaki Hirakawa, Miwako Nishio, Chizuko Sakashita, Tohru Kobayashi, Akihisa Sawada, Tatsuo Ichinohe, Takahiro Fukuda, Yoshiko Hashii, Yoshiko Atsuta, Ayako Arai. Registry data analysis of hematopoietic stem cell transplantation on systemic chronic active Epstein-Barr virus infection patients in Japan. Am J Hematol. 2022.06; 97(6); 780-790
- 10. Yokota T, Ueno T, Soga Y, Ishiki H, Uezono Y, Mori T, Zenda S, Uchitomi Y.. J-SUPPORT research policy for oral mucositis associated with cancer treatment Cancer Med. 2022.06; 11(24); 4816-4829
- 11. Satoru Aoyama, Shunichiro Yasuda, Huixin Li, Daisuke Watanabe, Yoshihiro Umezawa, Keigo Okada, Ayako Nogami, Osamu Miura, Norihiko Kawamata. A novel chimeric antigen receptor (CAR) system using an exogenous protease, in which activation of T cells is controlled by expression patterns of cell **■** surface proteins on target cells. International Journal of Molecular Medicine. 2022.04; 49(4);
- 12. Sekiya T, Kasahara H, Takemura R, Fujita S, Kato J, Doki N, Katayama Y, Ozawa Y, Takada S, Eto T, Fukuda T, Ichinohe T, Takanashi M, Onizuka M, Atsuta Y, Okamoto S, Yoshimura A, Takaki S, Mori T. Essential Roles of the Transcription Factor NR4A1 in Regulatory T Cell Differentiation under the Influence of Immunosuppressants. Journal of immunology (Baltimore, Md. : 1950). 2022.04; 208(9); 2122-2130
- 13. Tsuyoshi Nakagawa, Kumiko Hayashi, Ayumi Ogawa, Goshi Oda, Iichiro Onishi, Masahide Yamamoto, Mio Mori, Tomoyuki Fujioka, Toshiaki Ishikawa, Kentaro Okamoto, Hiroyuki Uetake. Bone Marrow Carcinomatosis in a Stage IV Breast Cancer Patient Treated by Letrozole as First-Line Endocrine Therapy. Case Rep Oncol. 2022.04; 15(1); 436-441
- 14. Tachibana Т, Kondo Т, Uchida Ν. Doki Ν, Takada S. Takahashi S. Yano Τ, Fukuda T, Atsuta S. Mori Τ. Kohno А, Kimura Y, Nagamura-Inoue Т. On-Behalf-Of-The-Adult-Cmlmpn-Working-Group-Of-The-Japanese-Society-For-Transplantation-And-Cellular-Therap The clinical significance of BCR-ABL1 mutations in patients with Philadelphia chromosome-positive chronic myeloid leukemia who underwent allogeneic hematopoietic cell transplantation. Transplantation and cellular therapy. 2022.03; 28(6); 321.e1-321.e8
- 15. Hashimoto Y, Ito T, Gotoh A, Nakamae M, Kimura F, Koike M, Kirito K, Wada H, Usuki K, Tanaka T, Mori T, Wakita S, Saito TI, Kada A, Saito AM, Shimoda K, Sugimoto Y, Kurokawa T, Tomita A, Edahiro Y, Akashi K, Matsumura I, Takenaka K, Komatsu N.. Clinical characteristics, prognostic factors, and outcomes of patients with essential thrombocythemia in Japan: the JSH-MPN-R18 study Int J Hematol. . 2022.02; 115; 208-221

- 16. Motomura Y, Umezawa Y, Arimatsu T, Okada K, Miura O, Kumagai T. Successful treatment with bortezomib for refractory fever associated with myelodysplastic syndrome with underlying lymphoplasmacytic lymphoma. Clinical case reports. 2022.02; 10(2); e05372
- Aya Usami, Kota Yokoyama, Junichi Tsuchiya, Yoshihiro Umezawa, Kazuma Toda, Ukihide Tateishi, Ryoichi Yoshimura. F] FDG Avidity and Low EOB Uptake Proportional to the Irradiation Dose. Diagnostics (Basel). 2022.02; 12(2);
- 18. Masatoshi Sakurai, Yasuhito Nannya, Rie Yamazaki, Kentaro Yamaguchi, Yuya Koda, Ryohei Abe, Kenji Yokoyama, Seishi Ogawa, Takehiko Mori. Germline RUNX1 translocation in familial platelet disorder with propensity to myeloid malignancies. Ann Hematol. 2022.01; 101(1); 237-239
- Takehiko Mori, Yuya Koda, Jun Kato, Masatoshi Sakurai, Yoshifumi Uwamino, Naoki Hasegawa. Usefulness of the FilmArray Meningitis/Encephalitis Panel in diagnosis of central nervous system infection after allogeneic hematopoietic stem cell transplantation. Support Care Cancer. 2022.01; 30(1); 5-8
- 20. Hirohisa Nakamae, Masahide Yamamoto, Emiko Sakaida, Yoshinobu Kanda, Ken Ohmine, Takaaki Ono, Itaru Matsumura, Maho Ishikawa, Makoto Aoki, Akio Maki, Hirohiko Shibayama. Nilotinib vs. imatinib in Japanese patients with newly diagnosed chronic myeloid leukemia in chronic phase: 10-year follow up of the Japanese subgroup of the randomized ENESTnd trial. Int J Hematol. 2022.01; 115(1); 33-42
- 21. Nobuhiro Hiramoto, Hirohito Yamazaki, Yukinori Nakamura, Naoyuki Uchida, Makoto Murata, Tadakazu Kondo, Satoshi Yoshioka, Tetsuya Eto, Akinori Nishikawa, Takafumi Kimura, Tatsuo Ichinohe, Yoshiko Atsuta, Yasushi Onishi, Ritsuro Suzuki, Takehiko Mori, . Total body irradiation-containing conditioning regimens without antithymocyte globulin in adults with aplastic anemia undergoing umbilical cord blood transplantation. Ann Hematol. 2022.01; 101(1); 165-175
- 22. Kawajiri A, Kawase T, Tanaka H, Fukuda T, Mukae J, Ozawa Y, Eto T, Uchida N, Mori T, Ashida T, Kondo T, Onizuka M, Ichinohe T, Atsuta Y, Morishima S, Kanda J, HLA Working Group of the Japan Society for Hematopoietic Cell Transplantation.. Human leukocyte antigen (HLA) haplotype matching in unrelated single HLA allele mismatch bone marrow transplantation. Bone marrow transplantation. 2022.01; 57(3); 407-415
- 1. Nagao T, Bando K, Iura A, Kakuta R, Kano Y, Ikeda S, Nogami A, Tanaka Y, Kirimura S, Mori T.. Malignant paraganglioma mimicking multiple myeloma] The Japanese journal of clinical hematology. 2022.10; 63(10); 1373-1378
- 2. Kimura M, Nishiyama Y, Ueda H, Kitajo A, Arimatsu T, Kuboki M, Takahata A, Saito M, Sakashita C, Okada K, Umezawa Y, Nagao T, Yamamoto M, Tohda S, Tanabe M, Mori T, Nogami A. Perioperative management of laparoscopic cholecystectomy in a patient with paroxysmal nocturnal haemoglobinuria undergoing ravulizumab treatment 2022; 63(4); 260-264

[Misc]

- Takase H, Arai A, Iwasaki Y, Imai A, Nagao T, Kawagishi M, Ishida T, Mochizuki M. Challenges in the diagnosis and management of vitreoretinal lymphoma - Clinical and basic approaches. Progress in retinal and eye research. 2022.02; 101053
- Nogami A., Sasaki K.. Therapeutic Advances in Immunotherapies for Hematological Malignancies Therapeutic Advances in Immunotherapies for Hematological Malignancies. International Journal of Molecular Sciences . 2022.09; 23; 11526

- 1. Kota Yoshifuji, Yotaro Motomura, Makiko Saito, Ayako Nogami, Genji Kawade, Shiori Watabe, Kouhei Yamamoto, Takahiko Mori, Toshikage Nagao.. TPL2, a New Prognostic Factor and a Potential Therapeutic Target in ABC-DLBCL.. 64th ASH Annual Meeting and Exposition. 2022.12.11 New Orleans
- 2. Satoru Aoyama, Ayako Nogami, Sadakatsu Ikeda, Takehiko Mori. Novel protease-mediated double antigen recognizing Chimeric Antigen Receptor (CAR) enhances directionality of CAR-T cell activity and improves target cell specificity.. 64th American Society of Hematology (ASH) annual Meeting and Exposition 2022.12.10

- 3. Yu Uemura, Masahide Yamamoto, Masataka Ishimura, Hirokazu Kanegane, Akihisa Sawada, Akihiro Hirakawa, Ken-Ichi Imadome, Mayumi Yoshimori, Masashi Nagata, Norio Shimizu, Ryuji Koike,Ayako Arai. Phase II Study of a JAK1/2 Inhibitor Ruxolitinib for Systemic Chronic Active Epstein-Barr Virus Disease: An Investigator-Initiated Trial . 64th ASH Annual Meeting and Exposition 2022.12
- 1. Yoshihiro Umezawa,Hiroki Fujiwara,Satoshi Koi,Kana Bando,Makiko Saito,Yuuki Osada, Kota,Yoshifuji,Keisuke Tanaka, Keigo Okada, Ayako Nogami, Chizuko Sakashita, Toshikage Nagao, Masahide Yamamoto, Takehiko Mori. Analysis of BKPyV viremia after allogeneic hematopoietic cell transplantation. The 84th annual meeting of the Japanese society of hematology 2022.10.15 Fukuoka
- 2. Allogeneic stem cell transplantation for dehydrated hereditary stomatocytosis with PIEZO1 mutation. the 84th Annual Meeting of the Japanese Society of Hematology 2022.10.15 Fukuoka International Congress Center
- 3. Makiko Saito, Satoshi Koi, Kana Bando, Hiroki Fujiwara, Yuki Osada, Kota Yoshifuji, Keisuke Tanaka, Keigo Okada, Ayako Nogami, Yoshihiro Umezawa, Toshikage Nagao, Chizuko Sakashita, Masahide Yamamoto, Shuji Tohda, Takehiko Mori. Clostridioides difficile infection among patients with hematological disorders. The 84th Annual Meeting of the Japanese Society of Hematology 2022.10.15 Fukuoka International Congress Center
- 4. Marie Yagi, Keisuke Tanaka, Kota Yoshifuji, Keigo Okada, Yoshihiro Umezawa, Toshikage Nagao, Takehiko Mori, Masahide Yamamoto. Cessation of imatinib in patients with FIP1L1-PDGFRA positive myeloid neoplasm with eosinophilia. The 84th annual meeting of the Japanese society of hematology 2022.10.14
- 5. Yukinori Nakamura, Takehiko Mori, Shinichi Kako, Hiroto Yamazaki, Yos hinobu Kanda, Naoyuki Uchida, Masashi Tanaka, Yuichiro Nawa, Takahiro Fukuda, Tatsuo Ichinohe, Yuko Atsuta, Yasushi Onishi. Peripheral blood stem cell transplantation from HLA-identical sibling donors for aplastic anemia. 44th annual meeting of Japanese society for transplantation and cellular therapy 2022.05.14 Yokohama
- 6. Junko Ishizuka, Akiko Uchiyama, Tomohiro Morio, Takehiko Mori, Masahide Yamamoto et. al.. Role of Hematopoietic Cell Transplant Coordinator in transition from childhood to adulthood. 44th annual meeting of Japanese society for transplantation and cellular therapy 2022.05.14 Yokohama
- 7. Yuuki Osada, Yoshihiro Umezawa, Kana Bando,Satoshi Koi,Hiroki Fujiwara,Makiko Saito, Keigo Okada, Ayako Nogami, Toshikage Nagao, Chizuko Sakashita, Naohiro Kamiya, Toshiyuki Ohara, Kazuyoshi Yagishita, Takehiko Mori, Masahide Yamamoto. Efficacy of hyperbaric oxygen therapy for viral hemorrhagic cystitis after allogeneic HSCT. 44th anual meeting of Japanese society for transplantation and cellular therapy 2022.05.14 Yokohama
- Junichi Sugita, Tetsuya Nishida, Yukiyasu Ozawa, Jun Kato, Takehiko Mori, Keisuke Kataoka, Shinichiro Okamoto, Takanori Teshima. Post-hoc analysis for clinical trial of ECP in chronic graft-versus-host disease patients in Japan. 44th Annual meeting of Japanese society for Transplantation and Cellular therapy 2022.05.13

Molecular Endocrinology and Metabolism

Professor: Tetsuya Yamada Associate Professor: Kenji Ikeda Associate professor/lecturer : Chikara Komiya Assistant Professor: Kazutaka Tsujimoto, Kumiko Shiba, Masanori Murakami Clinical Fellow: Satoru Uchida,Ryoko Ishii, Katsunori Matsubara, Maasa Murata Resident: Sayo Sihkishima, Airi Nakayama Project Assistant Professor: Mitsuyuki Numasawa Graduate Students (Doctor' s course): Yoshihiro Niitsu, Akira Takeuchi, Kazunari Hara, Masato Horino, Jun Aoki, Rei Okazaki

(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 diabetes, 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) Mechanisms and development of new therapeutic strategies of diabetes and metabolic syndrome
- 2) Thermogenesis and energy metabolism
- 3) Induced molecular mechanism of thermogenic fat
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors

3. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including: 1) diabetes mellitus, diabetic complications, metabolic syndrome, and obesity

- 2) diseases of the thyroid, pituitary and adrenal glands.
- 3) primary and secondary hypertension
- 4) disorders of calcium metabolism

(2) Publications

[Original Articles]

Miyauchi M, Akashi T, Furukawa A, Uchida K, Tamura T, Ando N, Kirimura S, Shintaku H, Yamamoto K, Ito T, Miura K, Kayamori K, Ariizumi Y, Asakage T, Kudo A, Tanabe M, Fujii Y, Ishibashi H, Okubo K, Murakami M, Yamada T, Takemoto A, Bae Y, Eishi Y, Ohashi K. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocr Pathol. 2022.12; 33(4); 506-518
- Masanori Murakami, Na Sun, Fengxia Li, Annette Feuchtinger, Celso Gomez-Sanchez, Martin Fassnacht, Martin Reincke, Irina Bancos, Axel Walch, Matthias Kroiss, Felix Beuschlein. In Situ Metabolomics of Cortisol-Producing Adenomas. Clin Chem. 2022.12;
- Otsubo N, Fukuda T, Genhin C, Ishibashi F, Yamada T, Monzen K. Utility of Indices Obtained During Medical Checkups for Predicting Fatty Liver Disease in Non-obese People. Internal medicine (Tokyo, Japan). 2022.12;
- 4. Yujiro Nakano, Masanori Murakami, Kazunari Hara, Tatsuya Fukuda, Masato Horino, Akira Takeuchi, Yoshihiro Niitsu, Kumiko Shiba, Kazutaka Tsujimoto, Chikara Komiya, Minato Yokoyama, Kenji Ikeda, Takanobu Yoshimoto, Yasuhisa Fujii, Tetsuya Yamada. Long-term effects of primary aldosteronism treatment on patients with primary aldosteronism and chronic kidney disease. Clin Endocrinol (Oxf). 2022.11;
- 5. Ariadni Spyroglou, Laura Handgriff, Lisa Müller, Paul Schwarzlmüller, Mirko Parasiliti-Caprino, Carmina Teresa Fuss, Hana Remde, Anna Hirsch, Samuel Matthew O'Toole, Moe Thuzar, Luigi Petramala, Claudio Letizia, Elisa Deflorenne, Laurence Amar, Rok Vrckovnik, Tomaz Kocjan, Catherine D Zhang, Dingfeng Li, Sumitabh Singh, Takuyuki Katabami, Takashi Yoneda, Masanori Murakami, Norio Wada, Nobuya Inagaki, Marcus Quinkler, Ezio Ghigo, Mauro Maccario, Michael Stowasser, William M Drake, Martin Fassnacht, Irina Bancos, Martin Reincke, Mitsuhide Naruse, Felix Beuschlein. The metabolic phenotype of patients with primary aldosteronism: impact of subtype and sex a multicenter-study of 3566 Caucasian and Asian subjects. Eur J Endocrinol. 2022.09; 187(3); 361-372
- 6. Ikeda K, Tajima K, Tanabe Y, Poon ASY, Kajimura S. Activation of UCP1-Independent Ca2+ Cycling Thermogenesis by Wireless Optogenetics. Methods in Molecular Biology . 2022.02; 2448; 131-139
- 7. Kazunari Hara, Masanori Murakami, Yoshihiro Niitsu, Akira Takeuchi, Masato Horino, Kumiko Shiba, Kazutaka Tsujimoto, Chikara Komiya, Kenji Ikeda, Mika Tsuiki, Akiyo Tanabe, Toshihiro Tanaka, Minato Yokoyama, Yasuhisa Fujii, Mitsuhide Naruse, Tetsuya Yamada. Heterogeneous circulating miRNA profiles of PBMAH. Front Endocrinol (Lausanne). 2022; 13; 1073328

[Conference Activities & Talks]

- 1. Mitsuyuki Numasawa, Nobutoshi Nawa, Kumiko Yamaguchi, Kanako Noritake, Jun Tsuruta, Mina Nakagawa. Comparison of readiness for interprofessional learning among medical, dental, and nursing students before the start of clinical practice. AMEE 2022 2022.08.29 The Virtual Conference
- 2. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Janelle Moross, Jun Tsuruta. Remote interprofessional learning during the COVID-19 pandemic for younger undergraduate students' early exposure to medicine . AMEE 2022 2022.08.27
- 1. The importance of formative assessment in a human anatomy course summative assessment. 2022.08.06
- 2. Remote interprofessional learning for younger undergraduate students' early exposure. 2022.08.05
- 3. Results of a survey to develop a data analysis system to support institutional research. The 54th Annual Meeting of the Japan Society for Medical Education 2022.08.05 Gunma
- 4. Report on a Case in Tokyo Medical and Dental University from the Perspective of KPI. The 54th Annual Meeting of the Japan Society for Medical Education 2022.08.05 Gunma

[Works]

1. Excel VBA macros for building adjacency matrix, Software, GitHub, 2021.08 - Now

Hepatobiliary and Pancreatic Surgery

Director & Professor Minoru Tanabe MD, PhD Associate Professor Atsushi Kudo MD, PhD Lecturer Keiichi Akahoshi MD, PhD Hiroaki Ono MD, PhD Assistant Professor Hiroki Ueda MD, PhD Yoshiya Ishikawa MD, PhD Shuichi Watanabe MD, PhD Daisuke Asano MD, PhD

Graduate School Students Takeshi Ishii MD Aya Maekawa MD Kohei Yagi MD Hironari Yamashita MD Hiroyuki Ishida MD Koichiro Morimoto MD Munetaka Kimura MD Akira Ito MD Shotaro Gan MD Atsushi Nara MD Masaru Takeuchi MD(from April) Masahiro Yamane MD(from April)

(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:

- \cdot Biomolecular mechanisms of carcinogenesis, cancer growth, invasion and metastasis
- \cdot Molecular target therapy for malignant diseases
- \cdot Cancer stem cell
- \cdot Extended indication for hepatectomy

- \cdot The system of liver microcirculation
- · Laparoscopic surgery for hepatobiliary and pancreatic cancers
- \cdot Liver transplantation and organ preservation
- \cdot Treatments for neuroendocrine tumor
- · Innovation of imaging modality for hepatobiliary and pancreatic cancers
- \cdot Establishment of PDX model in hepatobiliary and pancreatic cancer

(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) Lectures & Courses

Undergraduate education: Educate and acquire knowledge as a surgeon in general and basic knowledge, then more practical knowledge and stages, in accordance with the actual case as much as possible in a one-on-one system with a supervising doctor. At the same time, they will teach you how to be a doctor and learn morals according to specific cases such as how to treat patients and issues of illness notification. Basic surgical procedures will be entrusted to postgraduate education, but the aim is to gain many clinical experiences by assisting many patients with hepatobiliary and pancreatic surgery as high-assistance surgery.

Post-graduate education: The primary purpose is to develop surgeons with a high level of consulting skills in cooperation with related hospitals. Instruct students to have a viewpoint. We want to not only provide surgeons and gastroenterologists with training that can be obtained, but also motivate internationally competitive specialists and surgical researchers to make a leap forward.

(5) Clinical Services & Other Works

Diseases of hepatobiliary, pancreatic, and splenic areas are the targets of our department, and we mainly focus on multidisciplinary treatments for malignant tumors centering on surgical treatment. The mission of the university is to push the limits of surgical indications for highly advanced and refractory cancers, using preoperative simulation using a workstation and resection / reconstruction with vascular complications. In addition, arthroscopic surgery will be developed as a minimally invasive treatment. As an important treatment option for patients with end-stage liver disease, we also make indications for living donor liver transplantation. In laparoscopic surgery, we will develop new surgical instruments and procedures to promote safer, reduced port surgery that minimizes abdominal wall destruction, and expand the indication of minimally invasive operations.

(6) Clinical Performances

In 2022, the influence of surgery restrictions by COVID-19 was strong, and the total number of surgeries was 182 (255 in 2019), 38 hepatectomy and 54 pancreatic resection. It is one of the top-class high volume facilities in Japan and covers a wide variety of surgical procedures from characteristic minimally invasive surgery to extended surgery.

Laparoscopic surgery accounts for more than half of all cases, and laparoscopic surgery is about half for both hepatectomy and pancreatic resection, and the number of cases is increasing year by year. We expanded robotic

pancreatectomy, which started in 2020, to include a new indication for pancreaticoduodenectomy: 7 robotic pancreaticoduodenectomies and 6 distal pancreatectomy were successfully performed.

The treatment of neuroendocrine tumors, which is a feature of our department, spans surgery, drug therapy, and radiotherapy, and we aim to improve results by performing multidisciplinary treatment. Last year, the cumulative number of first-visit patients exceeded 850, the largest number in Japan.

(7) **Publications**

[Original Articles]

- Miyauchi M, Akashi T, Furukawa A, Uchida K, Tamura T, Ando N, Kirimura S, Shintaku H, Yamamoto K, Ito T, Miura K, Kayamori K, Ariizumi Y, Asakage T, Kudo A, Tanabe M, Fujii Y, Ishibashi H, Okubo K, Murakami M, Yamada T, Takemoto A, Bae Y, Eishi Y, Ohashi K. PHOX2B is a Sensitive and Specific Marker for the Histopathological Diagnosis of Pheochromocytoma and Paraganglioma. Endocr Pathol. 2022.12; 33(4); 506-518
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- Morishita K, Kudo A, Uchida T, Kurashima N, Toba M, Ito K, Otomo Y. Unexpected Mechanical Ventilation Dysfunction in a Coronavirus Disease Patient With Severe Pneumonia Due to the Oxygen Flowsensor Failure. J Patient Saf. 2022.08; 18(5); e867-e868
- 4. Fujiwara S, Kobayashi M, Ohtsuka K, Tanabe M, Okamoto R. The Double-Max method: a novel method for gallbladder epithelial biopsy. VideoGIE. 2022.08; 7(9); 334-336
- 5. Kabashima A, Matsuo Y, Ito S, Akiyama Y, Ishii T, Shimada S, Masamune A, Tanabe M, Tanaka S. cGAS-STING signaling encourages immune cell overcoming of fibroblast barricades in pancreatic cancer. Scientific Reports. 2022.06; 12(1); 10466
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- Ishida H, Ogura T, Takahashi A, Miyamoto R, Matsudaira S, Amikura K, Tanabe M, Kawashima Y. Optimal Region of Lymph Node Dissection in Distal Pancreatectomy for Left-Sided Pancreatic Cancer Based on Tumor Location. Ann Surg Oncol. 2022.04; 29(4); 2414-2424
- 9. Kudo A, Tateishi U, Yoshimura R, Tsuchiya J, Yokoyama K, Takano S, Kobayashi N, Utsunomiya D, Hata M, Ichikawa Y, Tanabe M, Hosono M, Kinuya S. Safety and response after peptide receptor radionuclide therapy with 177 Lu-DOTATATE for neuroendocrine tumors in phase 1/2 prospective Japanese trial. J Hepatobiliary Pancreat Sci. 2022.04; 29(4); 487-499
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- 26. Nakamura M, Wakabayashi G, Tsuchida A, Nagakawa Y, Study group of Precision Anatomy for Minimally Invastive Hepato-Biliary-Pancreatic surgery(PAM-HBP surgery). Precision anatomy for minimally invasive hepatobiliary pancreatic surgery: PAM-HBP Surgery Project. J Hepatobiliary Pancreat Sci. 2022.01; 29(1); 1-3
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- Masanori Kobayashi, Shomei Ryozawa, Kazuo Ohtsuka, Minoru Tanabe, Ryuichi Okamoto. A convenient and reliable method for endoscopic mapping biopsy of cholangiocarcinoma using a double-lumen cytology device. VideoGIE. 2022.05; 7(5); 182-184

[Books etc]

- 1. Ban D, Tanabe M. The IASGO Textbook of Multi-Disciplinary Management of Hepato-Pancreato-Biliary diseases. Springer, 2022.06
- 2. Akahoshi K, Ishii T, Kudo A. Multidisciplinary Computational Anatomy. Springer, 2022

[Conference Activities & Talks]

- 1. Keiichi Akahoshi, Yoshiya Ishikawa, Daisuke Asano, Hiroki Ueda, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Safety methods to perform laparoscopic liver resection for liber cirrhosis. ACRLS 2022 2022.12.09 Nagoya
- 2. Minoru Tanabe. The tips of pancreatic oduodenectomy based on better understanding of surgical anatomy. IRCAD Taiwan 2022.12.04 Web
- 3. Atsushi Nara, Keiichi Akahoshi, Hiroki Ueda, Koichiro Morimoto, Masaru Takeuchi, Masahiro Yamane, Akira Ito, Shotaro Gan, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Shuichi Watanabe, Yoshiya Isikawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Usefulness of the Novel Rupture Severity Score (NRSS) in Determining the Timing of Transarterial Embolization (TAE) for Ruptured Hepatocellular Carcinoma. IASGO-CME 2022.10.26 Fukuoka
- 4. Minoru Tanabe. Are the current difficulty scores for laparoscopic liver surgery telling the whole story?. 18th World Congress of Endoscopic Surgery 2022 2022.10.07 Korea
- 5. Minoru Tanabe. STATE OF THE ART: CURRENT ASIAN APPROACH TO SURGICAL MANAGEMENT OF HCC. International Surgical Week 2022 2022.08.16 Vienna, Austria
- 6. Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe. HOW DO WE MANAGE STAPLER LACERATION OF PANCREATIC CAPSULE DURING LAPAROSCOPIC DISTAL PANCREATECTOMY?. International Surgical Week 2022 2022.08.15 Vienna, Austria
- 7. Yasuhito Iwao, Kota Sato, Norimichi Chiyonobu, Shigeru Yamazaki, Minoru Tanabe. Stage I pancreatic body cancer relapsed with needle tract seeding and left sided liver metastasis. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.09 Kyoto
- 8. Takeshi Ishii, Keiichi Akahoshi, Akira Ito, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe. Efficacy and safety of FOLFONI therapy for unresectable pancreatic cancer. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.09 Kyoto
- 9. Yuki Fukumura, Yuko Kinowaki, Yoko Matsuda, Masaru Takase, Yifare Maimaitiaili Maimaitiaili, Lu Rong, Keiichi Akahoshi, Minoru Tanabe, Keiichi Okano, Katsuhiro San, Akio Saiura, Masanori Kobayashi, Ko Tomishima, Toshio Fujisawa, Hiroyuki Isayama, Takashi Yao. Size- and age-related alterations of mucinous cystic neoplasm : a proposal on MCN progression. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.09 Kyoto
- 10. Hiroaki Ono, Yoshiki Murase, Daisuke Asano, Syuuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Evaluation of the efficacy of Ispinesib, a novel Eg5 inhibitor, for the treatment of high grade Pan-NENs. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.08 Kyoto
- 11. Yuko Kinowaki, Yuki Fukumura, Yoko Matsuda, Takumi Akashi, Keiichi Akahoshi, Masanori Kobayashi, Hiroaki Ono, Atsushi Kudo, Minoru Tanabe, Masanobu Kitagawa. Pancreatic mixed neuroendocrine-non-neuroendocrine neoplasm: a case series of 6 patients. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.08 Kyoto
- 12. Atsushi Kudo. Surgical management for PanNEN with distant metastases. Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS 2022.07.08
- 13. Shotaro Gan, Hiroki Ueda, Atsushi Nara, Akira Ito, Koichiro Morimoto, Hironari Yamashita, Munetaka Kimura, Kohei Yagi, Takeshi Ishii, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Discussion on the treatment of liver cysts at our hospital. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 14. Daisuke Asano, Atushi Kudo, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Shinji Tanaka, Minoru Tanabe. Reappraisal of surgical treatment for liver metastases of neuroendocrine neoplasms. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime

- 15. Aya Maekawa, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Hormonaltumor mapping for liver metastases of gastroenteropancreatic neuroendocrine neoplasms. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 16. Yoshiya Ishikawa, Daisuke Asano, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Safe approach to dissect hepatoduodenal ligament during laparoscopic pancreaticoduodenectomy. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 17. Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The novel techniques of distal pancreatectomy using articulation forceps -introducing the desterity of a robotic system to a palaroscopic surgery. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 18. Yasuhito Iwao, Kota Sato, Norimichi Chiyonobu, Suguru Miyazawa, Yuka Kanno, Minoru Tanabe. The controversy of EUS-FNA required for neoadjuvant therapy for pancreatic body and tail cancer: A case series. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 19. Akira Ito, Daisuke Asano, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Takeshi Ishii, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Strategy of pancreatic ductal adenocarcinoma treatment. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 20. Yoshiya Ishikawa. Pursuing the ideal pancreaticoduodenectomy —Laparoscopic and Robotic surgery—. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.11 Ehime
- 21. Keiichi Akahoshi, Akira Ito, Atsushi Nara, Shotaro Gan, Takeshi Ishii, Kohei Yagi, Koichiro Morimoto, Hironari Yamashita, Munetaka Kimura, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Transpapillary or transmural drainage for postoperative pancreatic fistula after distal pancreatectomy. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 22. Keiichi Akahoshi. Efforts to train young HBP surgeons in the era of minimally invasive surgery. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 23. Koichiro Morimoto, Hiroki Ueda, Daisuke Asano, Yoshiya Ishikawa, Syuichi Watanebe, Keiichi Akahoshi, Hiroaki Ono, Atushi Kudo, Shinji Tanaka, Minoru Tanabe. Risk factors of postoperative cholangitis after hepatectomy with hepato-jejunostomy for malignancy-Clumping test predicts late refractory cholangitis. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 24. Hiroaki Ono, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Validation of surgical resection for pancreatic neuroendocrine neoplasms with simulataneous liver metastases. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 25. Takeshi Ishii, Keiichi Akahoshi, Koichirou Morimoto, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. A single-center retrospective study of 17 cases of pancreatic metastasis from renal cell carcinoma. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 26. Hiroki Ueda, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical features of malignant insulinoma from single center experience. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 27. Atsushi Nara, Hiroki Ueda, Yukue Shimizu, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Hiroaki Ono, Shinji Tanaka, Minoru Tanabe. Evaluation of sarcopenia using preoperative InBody and short-term results after pancreaticoduodenectomy. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 28. Hironari Yamashita, Keiichi Akahoshi, Akira Ito, Shoutaro Gan, Atsushi Nara, Munetaka Kimura, Koichiro Morimoto, Kohei Yagi, Takeshi Ishi, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical outcome of pT1 pancreatic ductal adenocarcinoma-what is the risk factor of poor prognosis?. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime

- 29. Kohei Yagi, Hiroaki Ono, Atsushi Kudo, Akira Ito, Atsushi Nara, Syotaro Gan, Munetaka Kimura, Hironari Yamashita, Takeshi Ishii, Daisuke Aasano, Syuichi Watanabe, Hiroki Ueda, Yoshiya Ishikawa, Keiichi Akahoshi, Shinji Tanaka, Minoru Tanabe. Significance of MGMT expression for streptozocin treatment of pancreatic neuroendocrine neoplasms. The 34th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2022.06.10 Ehime
- 30. Atsushi Kudo. Multidisciplinary Treatment Strategies Centered on Surgery for NEN. The 81st Annual Meeting of the Japan Radiological Society 2022.04.15 Yokohama

[Awards & Honors]

- 1. Hiroki Ueda, Yokohama Award of International Surgical Week 2022, International Surgical Week 2022, 2022.08
- 2. Atsushi Nara, Best Poster Award, IASGO-CME, 2022.10

[Others]

- Plenary Session, 2022.06 Tanabe M, Moderator, Plenary session, The 34th Meeting of Japanese society of Hepato-Biliary-Pancreatic Surgery, 20220611, Ehime
- 2. Current treatment strategy for pancreatic neuroendocrine neoplasms(PNENs), 2022.06 Atsushi Kudo, Moderator, The 34th Meeting of Japanese society of Hepato-Biliary-Pancreatic Surgery, 20220611, Ehime
- 3. Managements of the small non-functioning PanNEN, 2022.07 Kudo A, Managements of the small non-functioning PanNEN, Joint Congress of the 26th Meeting of IAP and the 53rd Annual Meeting of JPS, 20220709, Kyoto
- HPB MALIGNANT, 2022.08 Minoru Tanabe, Moderator, ISDS MAIN SESSION, International Surgical Week 2022, 20220816, Vienna, Austria
- Robotic HPB Surgery, 2022.10 Minoru Tanabe, Chair, Luncheon Seminar, Robotic HPB Surgery, IASGO-CME, 20221026, Fukuoka

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa Associate Professor: Toshitaka Yoshii Junior Associate Professor: Yuko Segawa, Takashi Hirai Assistant Professor: Hidetoshi Kaburagi, Yu Matsukura, Yuki Funauchi, Satoru Eagawa Specially Appointed Assistant Professor: Naoto Watanabe, Kurando Utagawa, Takumi Kaku, Jun Hashimoto

「Department of Orthopaedic and Trauma Research」 Associate Professor: Hiroyuki Inose Junior Associate Professor: Yoto Oh Assistant Professor: Kentaro Yamada

「Joint Research Department of Advanced Technology in Medicine」 Joint Research Professor: Shigenori Kawabata Junior Associate Professor: Yuko Hoshino Adjunct Lecturer∶Kensuke Sekihara

「Joint Research Department of Functional Joint Anatomy」 Joint Research Professor: Akimoto Nimura Junior Associate Professor: Koji Fujita Assistant Professor: Takuya Ibara

「Joint Research Department of Nano-Bioscience」 Joint Research Professor: Yoshinori Asou Joint Research Professor: Kunikazu Tsuji Associate Professor: Munetaka Iwata Assistant Professor: Hailati Aini

(1) Outline

This field is responsible for "orthopedics" in conjunction with the department of Joint Surgery and Sports Medicine, and is involved in clinical activities, education, and research. Orthopedics deals with research on the musculoskeletal system, such as bones, cartilage, joints, tendons, ligaments, muscles, the spinal cord, and peripheral nerves, and treats various injuries and illnesses such as trauma, degenerative diseases, tumors, and bone disorders.

Correspondingly, extensive basic and clinical research are being conducted, including the reconstruction of the motor function of the spine and joints, clinical applications of regenerative medicine techniques, development of artificial materials and joints, biomechanical approaches, and pain control. In order to elucidate the pathophysiology of rare diseases and to develop state-of-the-art diagnostic testing methods, research is actively conducted not only by each specialty section but also in collaboration with related departments and external research facilities.

(2) Research

- 1. Research on osteochondral metabolism
- 2. Research for clinical application of artificial materials (bone, nerve)
- 3. Elucidation of the mechanism of spinal ligament ossification (AMED Research Grant)
- 4. Development of spinal cord magnetic field measuring instrument (joint research course)
- 5. Research on metastatic tumors
- 6. Clinical Study of Ossification of Posterior Longitudinal Ligament (AMED)
- 7. Clinical research on spinal cord function monitoring
- 8. Development of finger function analysis methods
- 9. Pathophysiology of atypical femoral fractures
- 10. Hyperbaric oxygen therapy for muscle trauma (hyperbaric therapy)

(3) Education

Journal Club (JC) is held three times a week on Tuesday, Thursday, and Friday at 7:30 am. On Tuesday, we cover clinical research papers in the field of orthopedic surgery and hold joint sessions with the department of Joint Surgery and Sports Medicine. On Thursday, we discuss basic research papers, and on Friday, we conduct Research Progress sessions related to clinical research. During the RP sessions, we also provide opportunities for graduate students to present their research and receive feedback from others than their direct supervisors. The RP sessions are primarily conducted in English to ease writing research papers.

As part of clinical education in orthopedics, we hold a monthly initial training seminar for residents, providing hands-on surgical training and lectures on basic research activities. We also mandate case presentation in English at the biannual in-house symposium. For lifelong education, we hold biannual post-graduate seminars and provide opportunities for post-graduate education from within and outside the institution.

(4) Lectures & Courses

Research in the field of orthopedics in our country is characterized by orthopedic specialists engaging in basic research while also practicing clinical medicine. As the name "surgeon scientist" suggests, many achievements related to bones, cartilage, and nerves have been accomplished through studying clinical problems rooted in practice. Our department has also created unique artificial bones and spinal function diagnostic equipment and publishes more than 30 English papers annually. Graduate students are taught basic research methods and directed towards these research directions. Even after graduating from graduate school to engage in clinical medicine, they can acquire an attitude towards conducting clinical research that summarizes treatment outcomes and will be useful for future medical care.

(5) Clinical Services & Other Works

The orthopaedic department, consisting of the fields of orthopaedics and sports medicine, provides highly specialized outpatient and surgical treatment for spinal surgery, hand surgery, bone and soft tissue tumors, knee surgery, and hip surgery. There are more than 40 orthopaedic specialists on staff. Regarding cervical ossification of the posterior longitudinal ligament, our facility is one of the few in the country that has achieved good results through anterior decompression and fixation surgery. In this area, we have also served as the research representative in the Ministry of Health, Labour and Welfare's survey on intractable diseases and are collaborating with researchers in the spinal cord and spine field nationwide to advance clinical research.

(6) Clinical Performances

In the spinal surgery, our goal is to achieve safe and reliable decompression and fixation, early mobilization, and a definite surgical outcome by introducing of navigation surgery and spinal cord evoked potential measurement. In particular, we are actively addressing anterior surgery for cervical OPLL, corrective fixation surgery for adult spinal deformities and osteoporotic vertebral fractures, as well as resection of spinal cord tumors. In addition, we have an outpatient clinic for bone metastases, and we are focusing on systematizing the treatment of terminal cancer patients and surgical treatment of multi-trauma patients.

(7) Publications

[Original Articles]

- Takanori Wakayama, Yoshitomo Saita, Masashi Nagao, Sayuri Uchino, Sei-Ichi Yoshihara, Kunikazu Tsuji, Hideyuki Koga, Yohei Kobayashi, Hirofumi Nishio, Yasumasa Momoi, Hiroshi Ikeda, Kazuo Kaneko, Muneaki Ishijima. Intra-Articular Injections of the Adipose-Derived Mesenchymal Stem Cells Suppress Progression of a Mouse Traumatic Knee Osteoarthritis Model. Cartilage. 2022.12; 13(4); 148-156
- 2. Shunichi Fujii, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Comparison of adhesion of thawed and cultured synovial mesenchymal stem cells to the porcine meniscus and the relevance of cell surface microspike. BMC Molecular and Cell Biology. 2022.12; 23(1); 53
- 3. Akira Yoshizawa, Kazuharu Nakagawa, Kanako Yoshimi, Motonori Hashimoto, Kota Aritaki, Miki Ishii, Kohei Yamaguchi, Ayako Nakane, Atsuyuki Kawabata, Takashi Hirai, Toshitaka Yoshii, Masaomi Ikeda, Atsushi Okawa, Haruka Tohara. Analysis of swallowing function after anterior/posterior surgery for cervical degenerative disorders and factors related to the occurrence of postoperative dysphagia. Spine J. 2022.12;
- 4. Naoto Watanabe, Kazumasa Miyatake, Ryohei Takada, Takahisa Ogawa, Yusuke Amano, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa. The prevalence and treatment of osteoporosis in patients undergoing total hip arthroplasty and the levels of biochemical markers of bone turnover. Bone Joint Res. 2022.12; 11(12); 873-880
- 5. Mio Norose, Akimoto Nimura, Masahiro Tsutsumi, Koji Fujita, Atsushi Okawa, Keiichi Akita. Anatomical study for elucidating the stabilization mechanism in the trapeziometacarpal joint. Sci Rep. 2022.12; 12(1); 20790
- 6. Gen Inoue, Masayuki Miyagi, Wataru Saito, Eiki Shirasawa, Kentaro Uchida, Naobumi Hosogane, Kei Watanabe, Keiichi Katsumi, Takashi Kaito, Tomoya Yamashita, Hiroyasu Fujiwara, Yukitaka Nagamoto, Kenya Nojiri, Satoshi Suzuki, Eijiro Okada, Seiji Ueda, Tomohiro Hikata, Yuta Shiono, Kota Watanabe, Hidetomi Terai, Koji Tamai, Yuji Matsuoka, Hidekazu Suzuki, Hirosuke Nishimura, Atsushi Tagami, Shuta Yamada, Shinji Adachi, Seiji Ohtori, Takeo Furuya, Sumihisa Orita, Kazuhide Inage, Toshitaka Yoshii, Shuta Ushio, Haruki Funao, Norihiro Isogai, Katsumi Harimaya, Seiji Okada, Kenichi Kawaguchi, Nobuhiko Yokoyama, Hidekazu Oishi, Toshio Doi, Katsuhito Kiyasu, Shiro Imagama, Kei Ando, Kazuyoshi Kobayashi, Daisuke Sakai, Masahiro Tanaka, Atsushi Kimura, Hirokazu Inoue, Atsushi Nakano, Shota Ikegami, Masayuki Shimizu, Toshimasa Futatsugi, Kenichiro Kakutani, Takashi Yurube, Kazuyoshi Nakanishi, Masashi Oshima, Hiroshi Uei, Yasuchika Aoki, Masahiko Takahata, Akira Iwata, Hirooki Endo, Shoji Seki, Hideki Murakami, Satoshi Kato, Katsuhito Yoshioka, Michio Hongo, Tetsuya Abe, Toshinori Tsukanishi, Masashi Takaso, Ken Ishii. Effect of low body mass index on clinical recovery after fusion surgery for osteoporotic vertebral fracture: A retrospective, multicenter study of 237 cases. Medicine (Baltimore). 2022.12; 101(52); e32330
- 7. Kanichiro Wada, Shiro Imagama, Yukihiro Matsuyama, Go Yoshida, Kei Ando, Kazuyoshi Kobayashi, Masaaki Machino, Shigenori Kawabata, Hiroshi Iwasaki, Masahiro Funaba, Tsukasa Kanchiku, Kei Yamada, Yasushi Fujiwara, Hideki Shigematsu, Shinichirou Taniguchi, Muneharu Ando, Masahito Takahashi, Hiroki Ushirozako, Nobuaki Tadokoro, Shinji Morito, Naoya Yamamoto, Akimasa Yasuda, Jun Hashimoto, Tunenori Takatani, Toshikazu Tani, Gentaro Kumagai, Toru Asari, Yoshiro Nitobe, Yasuyuki Ishibashi. Comparison of intraoperative neuromonitoring accuracies and procedures associated with alarms in anterior versus posterior fusion for cervical spinal disorders: A prospective multi-institutional cohort study. Medicine (Baltimore). 2022.12; 101(49); e31846
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- 9. Kenichiro Sakai, Toshitaka Yoshii, Yoshiyasu Arai, Takashi Hirai, Ichiro Torigoe, Hiroyuki Inose, Masaki Tomori, Kyohei Sakaki, Masato Yuasa, Tsuyoshi Yamada, Yu Matsukura, Takuya Oyaizu, Shingo Morishita, Atsushi Okawa. A comparative study of surgical outcomes between anterior cervical discectomy with fusion and selective laminoplasty for cervical spondylotic myelopathy. J Orthop Sci. 2022.11; 27(6); 1228-1233
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- Koji Fujita, Kana Matsuo, Takafumi Koyama, Kurando Utagawa, Shingo Morishita, Yuta Sugiura. Development and testing of a new application for measuring motion at the cervical spine. BMC Med Imaging. 2022.11; 22(1); 193
- 14. Suthasinee Tharnmanularp, Akimoto Nimura, Masahiro Tsutsumi, Mio Norose, Sachiyuki Tsukada, Keiichi Akita. Medial patellofemoral ligament is a part of the vastus medialis obliquus and vastus intermedius aponeuroses attaching to the medial epicondyle. Knee Surg Sports Traumatol Arthrosc. 2022.11; 30(11); 3742-3750
- 15. Naoto Watanabe, Ryohei Takada, Takahisa Ogawa, Kazumasa Miyatake, Masanobu Hirao, Chisato Hoshino, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa. Short stature and short distance between the anterior acetabular rim to the femoral nerve are risk factors for femoral nerve palsy following primary total hip arthroplasty using the modified Watson-Jones approach. Orthop Traumatol Surg Res. 2022.10; 108(6); 103351
- 16. Masashi Uehara, Shota Ikegami, Takashi Takizawa, Hiroki Oba, Noriaki Yokogawa, Takeshi Sasagawa, Kei Ando, Hiroaki Nakashima, Naoki Segi, Toru Funayama, Fumihiko Eto, Akihiro Yamaji, Kota Watanabe, Satoshi Nori, Kazuki Takeda, Takeo Furuya, Atsushi Yunde, Hideaki Nakajima, Tomohiro Yamada, Tomohiko Hasegawa, Yoshinori Terashima, Ryosuke Hirota, Hidenori Suzuki, Yasuaki Imajo, Hitoshi Tonomura, Munehiro Sakata, Ko Hashimoto, Yoshito Onoda, Kenichi Kawaguchi, Yohei Haruta, Nobuyuki Suzuki, Kenji Kato, Hiroshi Uei, Hirokatsu Sawada, Kazuo Nakanishi, Kosuke Misaki, Hidetomi Terai, Koji Tamai, Eiki Shirasawa, Gen Inoue, Kenichiro Kakutani, Yuji Kakiuchi, Katsuhito Kiyasu, Hiroyuki Tominaga, Hiroto Tokumoto, Yoichi Iizuka, Eiji Takasawa, Koji Akeda, Norihiko Takegami, Haruki Funao, Yasushi Oshima, Takashi Kaito, Daisuke Sakai, Toshitaka Yoshii, Bungo Otsuki, Shoji Seki, Masashi Miyazaki, Masayuki Ishihara, Seiji Okada, Shiro Imagama, Satoshi Kato. Factors Affecting the Waiting Time from Injury to Surgery in Elderly Patients with a Cervical Spine Injury: A Japanese Multicenter Survey. World Neurosurg. 2022.10; 166; e815-e822
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Koji Tamai, Eiki Shirasawa, Gen Inoue, Katsuhito Kiyasu, Yoichi Iizuka, Eiji Takasawa, Haruki Funao, Takashi Kaito, Toshitaka Yoshii, Masayuki Ishihara, Seiji Okada, Shiro Imagama, Satoshi Kato. Does surgery improve neurological outcomes in older individuals with cervical spinal cord injury without bone injury? A multicenter study. Spinal Cord. 2022.10; 60(10); 895-902

- 18. Masaaki Isono, Jun Takeuchi, Ami Maehara, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga, Yoshinori Asou, Kunikazu Tsuji. Effect of CD44 signal axis in the gain of mesenchymal stem cell surface antigens from synovial fibroblasts in vitro Heliyon. 2022.10; 8(10); e10739
- Shusaku Hosono, Koji Fujita, Akimoto Nimura, Keiichi Akita. Release of Cervical Muscle Tension Improves Psychological Stress and Symptoms of Moderate-to-Severe Atopic Dermatitis: a Case Series with 20 Patients. Dermatol Ther (Heidelb). 2022.10; 12(10); 2383-2395
- Yuko Segawa, Tetsuya Jinno, Masaaki Matsubara, Yusuke Matsuyama, Takeo Fujiwara, Atsushi Okawa. A cross-sectional study evaluating patients' preferences for Salter innominate osteotomy. J Orthop Sci. 2022.10;
- 21. Akihiro Tsuchiya, Koji Wada, Natsumi Tanaka, Kazue Hayakawa, Yoji Mikami, Atsushi Okawa, Emiko Horii, Junji Ito. Associations between Depressive Symptoms, Work Environment, and Lifestyle in < 40-year-old Male Orthopedic Physicians in Japan. JMA J. 2022.10; 5(4); 471-479</p>
- 22. Takashi Hirai, Toshitaka Yoshii, Hiroyuki Inose, Yu Matsukura, Yuki Funauchi, Satoru Egawa, Kurando Utagawa, Jun Hashimoto, Mariko Nishizawa, Kohei Yamamoto, Atsushi Okawa. Intraosseous Aggressive Schwannoma In The Lumbar Spine: A Case Report Spine Surgery and Related Research. 2022.10; Article ID: 2022-0168
- 23. Sara Sugiura, Haruhiko Shimura, Koji Fujita, Takahisa Ogawa, Akimoto Nimura. Comparison of ceftriaxone and cefazolin as prophylactic antibiotics for surgical site infection in orthopedic upper extremity surgery: The nationwide shortage of cefazolin in March 2019. J Orthop Sci. 2022.09;
- 24. Noriaki Yokogawa, Satoshi Kato, Takeshi Sasagawa, Hiroyuki Hayashi, Hiroyuki Tsuchiya, Kei Ando, Hiroaki Nakashima, Naoki Segi, Toru Funayama, Fumihiko Eto, Akihiro Yamaji, Satoshi Nori, Junichi Yamane, Takeo Furuya, Atsushi Yunde, Hideaki Nakajima, Tomohiro Yamada, Tomohiko Hasegawa, Yoshinori Terashima, Ryosuke Hirota, Hidenori Suzuki, Yasuaki Imajo, Shota Ikegami, Masashi Uehara, Hitoshi Tonomura, Munehiro Sakata, Ko Hashimoto, Yoshito Onoda, Kenichi Kawaguchi, Yohei Haruta, Nobuyuki Suzuki, Kenji Kato, Hiroshi Uei, Hirokatsu Sawada, Kazuo Nakanishi, Kosuke Misaki, Hidetomi Terai, Koji Tamai, Eiki Shirasawa, Gen Inoue, Kenichiro Kakutani, Yuji Kakiuchi, Katsuhito Kiyasu, Hiroyuki Tominaga, Hiroto Tokumoto, Yoichi Iizuka, Eiji Takasawa, Koji Akeda, Norihiko Takegami, Haruki Funao, Yasushi Oshima, Takashi Kaito, Daisuke Sakai, Toshitaka Yoshii, Tetsuro Ohba, Bungo Otsuki, Shoji Seki, Masashi Miyazaki, Masayuki Ishihara, Seiji Okada, Shiro Imagama, Kota Watanabe. Differences in clinical characteristics of cervical spine injuries in older adults by external causes: a multicenter study of 1512 cases. Sci Rep. 2022.09; 12(1); 15867
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[Conference Activities & Talks]

- 1. Yohei Tomaru, Makoto Kamegaya, Takashi Saisu, Jun Kakizaki, Yasuhiro Oikawa, Mitsuaki Morita, Yuko Segawa, Yuta Tsukagoshi, Hiroshi Kamada, Masashi Yamazaki. Epidemiology of Growing Pains, MRI and Ultrasonographic findings in Selective Cases. The 33rd Annual Meeting of the Japanese Pediatric Orthopaedic Association 2022.12.09 Yokohama
- 2. Toshitaka Yoshii. Surgical treatment of cervical OPLL-Current evidence. The 66th Annual Congress of the Korean Orthopaedic Association 2022 2022.10.14 Seoul, Korea (Hybrid)
- 3. Ryohei Takada, Kazumasa Miyatake, Naoto Watanabe, Tetsuya Jinno, Toshitaka Yoshii, Hideyuki Koga, Atsushi Okawa. Development of non-invasive augmented reality-based navigation system for total hip arthroplasty. The 66th Annual Congress of the Korean Orthopaedic Association 2022 2022.10.13 Seoul, Korea

- 4. Akimoto Nimura. Anatomical knowledge in relation to acromioclavicular joint dislocation. 49th Annual meeting of Japan shoulder society 2022.10.07 Yokohama, Kanagawa
- 5. Masahiro Tsutsumi, Isao Yamaguchi, Akimoto Nimura, Hajime Utsunomiya, Keiichi Akita, Shintarou Kudo. Anatomical characteristics of the hip flexion abduction external rotation (FABER) position using magnetic resonance imaging. The 20th Congress of the International Federation of Associations of Anatomist (IFAA) 2022.08.06 Web
- 6. Yoto Oh. Bone healing and the effect of patient factors and injury mechanism on fracture management. AO Trauma Course - Basic Principles of Fracture Management 2022.08 Yokohama
- 7. Yoto Oh. The 2018 AO/OTA Fracture and Dislocation Classification Compendium. AO Trauma Course Basic Principles of Fracture Management 2022.08 Yokohama
- 8. Yoto Oh. Fixation principles in osteoporotic bone—the geriatric patient. AO Trauma Course Basic Principles of Fracture Management 2022.08 Yokohama
- 9. Yoto Oh. Fractures in the growing skeleton—how are they different?. AO Trauma Course Basic Principles of Fracture Management 2022.08 Yokohama
- 10. Suthasinee Tharnmanularp, Akimoto Nimura, Masahiro Tsutsumi, Mio Norose, Sachiyuki Tsukada, Keiichi Akita. Medial patellofemoral ligament is a part of the vastus medialis obliquus and vastus intermedius aponeuroses attaching to the medial epicondyle. Japanese Orthopaedic Society of Knee, Arthroscopy and Sports Medicine Japanese Orthopaedic Society for Sports Medicine 2022 2022.06.18 Sapporo, Hokkaido
- 11. Yoto Oh, Toshitaka Yoshii, Atsushi Okawa. Development of a CT-based finite element analysis model for verifying the effect of preventing hip fractures by the shock-absorbing floor. 5th AOTrauma Asia Pacific Scientific Conference 2022.05.28 WEB
- 12. Yu Matsukrua, et al. A Multicenter Prospective Study of Surgical Outcomes for Cervical Posterior Longitudinal Ligament Ossification Focusing on the Duration of Symptoms. The 51st Annual Meeting of the Japanese Society for Spine Surgery and Related Research 2022.04.21 Yokohama

[Patents]

- 1. MAGNETIC MEASURING DEVICE, Patent Number : CN ZL201780013786.2
- 2. BIOMAGNETIC MEASUREMENT APPARATUS, BIOLOGICAL INFORMATION MEASUREMENT APARATUS, AND BIOMAGNETIC MEASUREMENT METHOD, Patent Number : US 11375934

[Awards & Honors]

1. Best 10 paper of the 5th AO Trauma Asia Pacific Scientific Conference (Yoto Oh), AO Trauma Asia Pacific, 2022.05

Diagnostic Radiology and Nuclear Medicine

Professor Ukihide Tateishi

Associate Professors Mitsuhiro Kishino,

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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 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

 \cdot CT: A total of three CT scanners are involved in diagnostic radiology: five in the radiology department and one in the ER center.

 \cdot MRI: A total of four MRI scanners are involved in diagnostic radiology: one 1.5-tesla scanners and four 3-tesla scanners. This has allowed for an increase in examinations.

 \cdot Ultrasound: The main examinations carried out by diagnostic radiologists are breast and abdominal examinations.

 \cdot 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.

 \cdot 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.

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 Non-FDG tracers (C-11 acetate, F-18 FLT, F-18 FAZA, F-18 PSMA1007) for malignancies were introduced.

(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. Kota Yokoyama, Junichi Tsuchiya, Hiroaki Kawabe, Takahiro Asakage, Ukihide Tateishi. A rare case of primary intraosseous carcinoma of the mandible with perineural extension mimicking neurolymphomatosis on [18F] -FDG PET/CT Eur J Nucl Med Mol Imaging. 2022.12;
- Hiroki Katagiri, Bruce B Forster, Lars Engebretsen, Jae-Sung An, Takuya Adachi, Yukihisa Saida, Kentaro Onishi, Hideyuki Koga. Epidemiology of MRI-detected muscle injury in athletes participating in the Tokyo 2020 Olympic Games. Br J Sports Med. 2022.12; 57(4); 218-224
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in patients with cognitive impairment and suspected Alzheimer's disease: a multicenter study Annals of Nuclear Medicine. 2022.12; 36(12); 1039-1049

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- 5. Kusumoto Shigeru, Munakata Wataru, Machida Ryunosuke, Terauchi Takashi, Onaya Hiroaki, Oguchi Masahiko, Iida Shinsuke, Nosaka Kisato, Suzuki Yasuhiro, Harada Yasuhiko, Miyazaki Kana, Maruta Masaki, Fukuhara Noriko, Toubai Tomomi, Kubota Nobuko, Ohmachi Ken, Yamamoto Kazuhito, Kumode Takahiro, Mizuno Ishikazu, Tabayashi Takayuki, Tsujimura Hideki, Takayama Nobuyuki, Asagoe Kohsuke, Yoshida Isao, Takamatsu Yasushi, Fukuhara Suguru, Takeuchi Mai, Tateishi Ukihide, Maruyama Dai, Tsukasaki Kunihiro, Nagai Hirokazu. Interim PET-Guided ABVD or ABVD/Escalated BEACOPP for Newly Diagnosed Advanced-Stage Classic Hodgkin Lymphoma (JCOG1305, INNOVATE-HL study) BLOOD. 2022.11; 140; 3718-3720
- 6. Shimada Wataru, Kimura Koichiro, Tanaka Hajime, Fukuda Shohei, Yoshida Soichiro, Fujii Yasuhisa. Significance of tumor shape irregularity: Radiomics analysis based on dynamic computed tomography for predicting pT3a upstaging in cT1b-2N0M0 renal cell carcinoma INTERNATIONAL JOURNAL OF UROLOGY. 2022.11; 29(11); 1387-1389
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- 9. Kida Tatsuya, Takahashi Nobuaki, Mori Masayuki X., Sun Jiacheng H., Oota Hideto, Nishino Kosuke, Okauchi Takashi, Ochi Yuta, Kano Daisuke, Tateishi Ukihide, Watanabe Yasuyoshi, Cui Yilong, Mori Yasuo, Doi Hisashi. N-Methylamide-structured SB366791 derivatives with high TRPV1 antagonistic activity: toward PET radiotracers to visualize TRPV1 RSC MEDICINAL CHEMISTRY. 2022.10; 13(10); 1197-1204
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- 14. Kudo Ryo, Kano Yoshihito, Noji Rika, Kakuta Ryota, Onishi Iichiro, Kimura Kouichiro, Tanimoto Kousuke, Miya Fuyuki, Mitsumura Takahiro, Oshima Noriko, Ariizumi Yousuke, Nakagawa Tsuyoshi,

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- 17. Yoshio Kitazume, Kento Takenaka, Kazuo Ohtsuka, Yasuo Ozawa, Koichiro Kimura, Ryosuke Watanabe, Junichi Tsuchiya, Toshimitsu Fujii, Masakazu Nagahori, Mamoru Watanabe, Ukihide Tateishi. Motility Mapping Quantification Using the Classical Optical Flow Algorithm for Small Bowel Crohn's Disease: Comparison with Balloon-assisted Enteroscopy Findings. Magn Reson Med Sci. 2022.05; Online ahead of print
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[Conference Activities & Talks]

- 1. Kishino Mitsuhiro, Takahashi Marie, Kimura Koichiro, Yamada Ayumi, Adachi Takuya, Watanabe Ryosuke, Kitazume Yoshio, Tateishi Ukihide. Clinical features of spontaneous muscle hemorrhage associated with COVID-19 infection. The Official Journal of the Japanese Society of Interventional Radiology 2022.05.01
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- 3. Kishino Mitsuhiro, Takahashi Marie, Kimura Koichiro, Yamada Ayumi, Adachi Takuya, Watanabe Ryosuke, Kitazume Yoshio, Tateishi Ukihide. Clinical features of spontaneous muscle hemorrhage associated with COVID-19 infection. The Official Journal of the Japanese Society of Interventional Radiology 2022.05.01
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- 11. Clinical Significance of the Vesical Imaging-Reporting and Data System in Predicting Therapeutic Effect of Bladder-Sparing Treatment in Muscle-Invasive Bladder Cancer. 2022.04.16
- 12. Imokawa Tomoki, Fujioka Tomoyuki, Satoh Yoko, Mori Mio, Yamaga Emi, Takahashi Kanae, Takahashi Keiko, Kawase Takahiro, Kubota Kazunori, Tateishi Ukihide. Deep Learning for Breast Cancer Classification in Dedicated Breast Positron Emission Tomography. Annual meeting of the Japan Radiological Society abstracts 2022.03.01
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- 15. Yamaga Emi, Fujioka Tomoyuki, Mori Mio, Yashima Yuka, Kubota Kazunori, Hayashi Makiko, Yamamuro Katsura, Oda Goshi, Nakagawa Tsuyoshi, Tateishi Ukihide. Evaluation of Detection for Breast Tumors using MR Elastography with External Vibration to the Back. Annual meeting of the Japan Radiological Society abstracts 2022.03.01
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- 17. Katsuta Leona, Fujioka Tomoyuki, Kubota Kazunori, Mori Mio, Yamaga Emi, Yashima Yuka, Nomura Kyoko, Oda Goshi, Nakagawa Tsuyoshi, Tateishi Ukihide. Comparison of the State-of-the-art Biopsy Systems for Ultrasound-guided Breast Biopsy using a Chicken Breast Phantom. Annual meeting of the Japan Radiological Society abstracts 2022.03.01
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ゲノム機能多様性分野

Department of Genomic Function and Diversity

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(1) 分野概要

免疫アレルギー疾患・生活習慣病・癌などの多因子疾患は、個人間の遺伝子配列の違い、すなわち遺伝子多型が積 み重なることによって発症に至ります。ゲノムワイド関連解析(GWAS)によって、様々な疾患の感受性遺伝子 多型が明らかにされましたが、病態解明は道半ばです。本分野では、ヒトゲノム、エピゲノム、トランスクリプ トームなどの様々なビッグデータを用いた解析に、分子生物学的手法を用いた解析を統合することによって、遺 伝子多型によってもたらされるゲノム機能の多様性を理解し、多因子疾患の病態解明を行います。また、個人の ゲノム情報に基づいた病態や薬剤応答性の予測法を開発し、いわゆるプレシジョン医療の確立を目指します。

(2) 研究活動

1. 多因子疾患の病因メカニズムを明らかにするために、ゲノムワイド関連解析 (GWAS) と expression QTL/splicing QTL 解析の統合を行い、特に疾患に関与する選択的スプライシングの網羅的同定を行った。

2. 関節リウマチや全身性エリテマトーデスの疾患感受性領域を明らかにするために、国際研究グループにおける GWASのメタ解析を進めている。

- 3. ポリジェニック・リスク・スコアを用いて、関節リウマチの重症化を予測する統計学的モデルを樹立した。
- 4. ロングリード・シークエンサーを用いて、疾患に関わる構造多型や反復配列多型を明らかにした。

(3) 教育活動

GWAS や eQTL/sQTL データを用いた多因子疾患の病態メカニズムの理解方法について、学部生、大学院生向け に講義を行った。

(4) 教育方針

GWAS や次世代シークエンサーなどの研究手法.技術の登場により、疾患に関わる様々なビッグデータが公共利用可能な時代になっています。我々はこれらのビッグデータを独自のアイディアのもとに利活用して、様々な疾患の病態解明につなげることのできる人材を育成します。

(5) 研究業績

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- 2. 高地 雄太. 【全身性エリテマトーデス-診断 · 治療の最新動向-】総論と SLE の発症メカニズム SLE の遺 伝学 日本臨床. 2022.05; 80(5); 757-762
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[講演·口頭発表等]

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- 2. 高地 雄太. 免疫アレルギー疾患のオミックス 多因子免疫疾患のゲノム解析と精密医療へのアプローチ. アレルギー 2022.08.01

[その他業績]

- 1. 「ポリジェニックリスクスコアは関節リウマチの関節破壊進行を予測する」— 関節リウマチのゲノムオー ダーメイド医療へ向けて —, 2022 年 01 月 Arthritis & Rheumatology
- 2. Predicting the progression of rheumatoid arthritis, 2022 年 03 月 AAAS EurekAlert! The Global Source for Science News
- 3. 「タンパク質構造を変化させる遺伝子多型を同定する手法を開発」 選択的スプライシングの複雑性を 読み解くことで疾患の病態解明に挑む —, 2022 年 08 月 Nature Communications
- 4. A new data analysis approach identifies disease-associated splicing variants, 2022 年 09 月 AAAS EurekAlert! The Global Source for Science News
- 5. 国際ゲノム解析により関節リウマチの遺伝的背景を解明 —個人のゲノム情報を活用した発症予測の社会実装に貢献—, 2022 年 11 月

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka

(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]

- Yuki Nagata, Ryo Watanabe, Christian Eichhorn, Seiko Ohno, Takeshi Aiba, Taisuke Ishikawa, Yukiko Nakano, Yoshiyasu Aizawa, Kenshi Hayashi, Nobuyuki Murakoshi, Tadashi Nakajima, Nobue Yagihara, Hiroyuki Mishima, Takeaki Sudo, Chihiro Higuchi, Atsushi Takahashi, Akihiro Sekine, Takeru Makiyama, Yoshihiro Tanaka, Atsuyuki Watanabe, Motomi Tachibana, Hiroshi Morita, Koh-Ichiro Yoshiura, Tatsuhiko Tsunoda, Hiroshi Watanabe, Masahiko Kurabayashi, Akihiko Nogami, Yasuki Kihara, Minoru Horie, Wataru Shimizu, Naomasa Makita, Toshihiro Tanaka. Targeted deep sequencing analyses of long QT syndrome in a Japanese population. PLoS One. 2022.12; 17(12); e0277242
- Yumi Inagaki, Takuya Ogawa, Makoto J Tabata, Yuki Nagata, Ryo Watanabe, Tatsuo Kawamoto, Keiji Moriyama, Toshihiro Tanaka. Correction to: Identification of OPN3 as associated with non-syndromic oligodontia in a Japanese population. J Hum Genet. 2022.04; 67(4); 245
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[Conference Activities & Talks]

1. Yuki Nagata, Toshihiro Tanaka. Targeted deep sequencing analyses of long QT syndrome in a Japanese population.. The 67th Annual Meeting of the Japan Society of Human Genetics 2022.12.14 Yokohama, Japan

2. Yuki Nagata, Toshihiro Tanaka. Targeted deep sequencing analyses of long QT syndrome in a Japanese population. ASHG annual meeting 2022 2022.10.25 Los Angels, USA

Applied Regenerative Medicine

Professor: Ichiro SEKIYA Junior Assistant Professor: Nobutake OZEKI Assistant Professor: Hisako KATANO Project Assistant Professor: Mitsuru MIZUNO, Kentaro ENDO Specially Appointed Researcher: Keiichiro KOMORI, Kimiko TAKANASHI Graduate Student: Kiyotaka HORIUCHI, Rei KUBOTA, Shunichi FUJII Yugo MIURA, Hideto FURUOKA, Takahiro TANIMOTO Seiya MATSUTA, Yusuke AIMONO, Hayato KODAMA, Misaki YAGI Technical Assistants: Kanako NAGANO, Jyunko MIURA Assistant Clerk: Harumi ANDO, Mayumi TSUKAMOTO

(1) Outline

Stem cell medicine and regenerative medicine have been developing remarkably in recent years, and the competition for the advancement of regenerative medicine products to obtain a global market has been growing. We conduct basic research in the field of stem cell medicine and regenerative medicine from the viewpoint of practical application of regenerative medicine that shows high efficacy against existing therapies, and perform translational researches. In addition, we apply the results of our studies clinically and eventually aim at industrialization.

(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

We are working on basic, translational, and clinical researches with the aim of establishing a new treatment for knee osteoarthritis. Since 2000, we have discovered that mesenchymal stem cells derived from synovium (synovial MSCs) can highly differentiate into cartilage and meniscus, and that transplantation of these cells promotes the natural healing process. After these basic and translational studies using medium-sized animals, we started a physician-led clinical trial of autologous synovial stem cells for meniscus injury in August 2017. A patent license agreement was signed with a company in March 2019, and based on the results of a clinical trial completed in June 2019, we started a company-initiated clinical trial as a validation study in January 2023. In addition, we began a clinical study "Intra-articular injection of synovial MSCs for osteoarthritis of the knee" in December 2017 under the financial support of AMED Research for Practical Application of Regenerative Medicine (Principal Investigator: Ichiro Sekiya) to develop a treatment method using a new route of administration of synovial MSCs, and completed the observation period for all research subjects in March 2020. We plan to conduct a comparative study as a physician-initiated clinical trial from April 2023. In addition, we developed MRI 3D analysis software that can automatically display cartilage and meniscus in knee joints in collaboration with a
company. This software has been installed in a volume analyzer that is being commercialized in 2019 and is now widely used in orthopedic practice in Japan.

(4) **Publications**

[Original Articles]

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- 3. Shunichi Fujii, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Comparison of adhesion of thawed and cultured synovial mesenchymal stem cells to the porcine meniscus and the relevance of cell surface microspike. BMC Molecular and Cell Biology. 2022.12; 23(1); 53
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- 11. Hiroki Katagiri, Mikio Shioda, Yusuke Nakagawa, Toshiyuki Ohara, Nobutake Ozeki, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga. Risk Factors Affecting Return to Sports and Patient-Reported Outcomes After Opening-Wedge High Tibial Osteotomy in Active Patients. Orthop J Sports Med. 2022.09; 10(9); 23259671221118836
- 12. Tsukasa Kitahashi, Ryo Kogawa, Kentaro Nakamura, Ichiro Sekiya. Integrin β 1, PDGFR β , and type II collagen are essential for meniscus regeneration by synovial mesenchymal stem cells in rats. Scientific Reports. 2022.08; 12(1); 14148
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- 23. Yugo Miura, Nobutake Ozeki, Hisako Katano, Hayato Aoki, Noriya Okanouchi, Makoto Tomita, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Difference in the joint space of the medial knee compartment between full extension and Rosenberg weight-bearing radiographs. Eur Radiol. 2022.03; 32(3); 1429-1437
- 24. Hisako Katano, Nobutake Ozeki, Hideyuki Koga, Makoto Tomita, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya. Three-dimensional MRI shows cartilage defect extension with no separation from the meniscus in women in their 70s with knee osteoarthritis. Sci Rep.(Scientific Reports). 2022.03; 12(1); 4198
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- 28. Takashi Hoshino, Yusuke Nakagawa, Kei Inomata, Toshiyuki Ohara, Hiroki Katagiri, Koji Otabe, Kanehiro Hiyama, Kenta Katagiri, Mai Katakura, Hiroko Ueki, Masaya Hayashi, Tsuyoshi Nagase, Ichiro Sekiya, Takashi Ogiuchi, Takeshi Muneta, Hideyuki Koga, . Effects of different surgical procedures for meniscus injury on two-year clinical and radiological outcomes after anterior cruciate ligament reconstructions. -TMDU MAKS study. J Orthop Sci. 2022.01; 27(1); 199-206

[Misc]

- 1. Mituru Mizunoi, Nobutake Ozeki, Ichiro Sekiya. Safety of using cultured cells with trisomy 7 in cell therapy for treating osteoarthritis. Regenerative Therapy. 2022.06; 17(21); 81-86
- 2. Yusuke Nakagawa, Nobutake Ozeki, Hideyuki Koga. A narrative review of lateral meniscus root tears and extrusion: techniques and outcomes Annals of Joints. 2022.04; 7(15);

[Conference Activities & Talks]

- 1. Ichiro Sekiya. Fully automatic 3D MRI analysis showed that synovial MSC injections suppressed cartilage loss in patients with progres-sive OA. The 13th Meeting of Asian Cell Therapy Orgnization (ACTO) 2022.09.23 WEB, Taiwan
- 2. Ichiro Sekiya. Is meniscal injury a cause or a consequence in osteoarthritis?. 16th International Workshop on Osteoarthritis Imaging 2022.07.08 Tokyo Japan
- 3. Hisako Katano. Morphological analysis of 3D MRI images of PF joints in asymptomatic subjects. 16th International Workshop on Osteoarthritis Imaging 2022.07.08 Tokyo
- 4. Nobutake Ozeki. IS THERE A ROLE FOR MRI IN REGENERATIVE MEDICINE?. 16th International Workshop on Osteoarthritis Imaging 2022.07.07 Tokyo
- 5. Yugo Miura. Difference in the joint space of the medial knee compartment between full extension and Rosenberg weight-bearing radiographs. 16th International Workshop on Osteoarthritis Imaging 2022.07.07 Tokyo
- 6. Ichiro Sekiya. Medial tibial osteophyte width strongly reflects medial meniscus extrusion distance and medial joint space width moderately reflects cartilage thickness in knee radiographs. MUSCULOSKELETAL WORKSHOP SERIES 2022.02.06 WEB
- 7. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Hiroki Katagiri, Hisako Katano, Makoto Tomita, Jun Masumoto, Ichiro Sekiya. Relationship Between Cartilage Thickness By 3D MRI Analysis And ICRS Arthroscopic Grade In The Knee Joint. Orthopaedic Research Society 2022 Annual Meeting 2022.02.05 Tampa,USA

[Patents]

1. CELL REGION DETERMINATION METHOD, CELL IMAGING SYSTEM, AND CELL IMAGE PROCESSING APPARATUS, Patent Number : CN ZL201611227796.X

JFCR Cancer Biology

Professor Toru HIROTA Professor Noriko SAITOH Akiko TAKAHASHI Professor Professor Kengo TAKEUCHI Professor Akihiro TOMIDA Professor Reo MARUMYAMA Graduate Students Yoshiharu Kusano, Ayumi Fujimoto, Kentaro Narita, Hironobu Sugita, Saho Matsui, Nana Kamakura, Anna Suzuki, Nanami Seshimo, Saki Onodera, Hisamichi Tanaka, Yuxiao Yang

(1) Research

Six research divisions of the Cancer Institute and the Cancer Chemotherapy Center of the Japanese Foundation for Cancer Research (JFCR) pursue a wide series of basic and translational research on cancer, with a profound emphasis on the training of young scientists who will lead the next generation of cancer research.

(2) Education

We are committed to training talented and motivated graduate students, and to help develop their careers in basic and translational cancer research. Our specific aims include: 1. To understand the molecular background and pathological significance of chromosomal instability of cancer cells, and to explore strategies to target chromosomal instability [Hirota Group] 2. To investigate the mechanisms and function of non-coding RNAs for epigenetic regulation in breast cancer [Saitoh Group]

3. To reveal the biological function of senescent cells in the cancer microenvironment [Takahashi Group]

4. To conduct pathological and genetic analysis of human cancer such as malignant lymphoma and lung cancer [Takeuchi Group]

5. To develop strategies for innovative drug therapy based on cancer biology [Tomida Group]

6. To elucidate the mechanisms of intratumoural heterogeneity formation in cancer and its functional

significance through the analysis of patient-derived samples and mouse models. [Maruyama Group]

(3) Publications

[Original Articles]

- *Negoto, T., *Jo, M., Nakayama, I., Morioka, M., Takeuchi, K., Kawachi, H., and Hirota T. (2022) Profiling chromosome-level variations in gastric malignancies. *Cancer Sci.* 113: 3864-3876. doi: 10.1111/cas.15544 (*co-first author)
- Shindo, N., Kumada, K., Iemura, K., Yasuda, J., Fujimori, H., Mochizuki, M., Tamai, K., Tanaka, K., and Hirota, T. (2022) Autocleavage of separase suppresses its premature activation by promoting binding to cyclin B1. *Cell Rep.* 41: 111723.
- Kakui, Y., Barrington, C., Kusano, Y., Thadani, R., Fallesen, T., Hirota, T., and Uhlmann, F. (2022) Chromosome arm length, and a species-specific determinant, define chromosome arm width. *Cell Rep.* 41: 111753.
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- Suzuki, H., Abe, R., Shimada, M., Hirose, T., Hirose, H., Noguchi, K., Ike, Y., Yasui, N., Furugori, K., Yamaguchi, Y., Toyoda, A., Suzuki, Y., Yamamoto, T., Saitoh, N., Sato, S., Tomomori-Sato, C., Conaway, R., Conaway, J., Takahashi, H. (2022) The 3' Pol II pausing at replication-dependent histone genes is regulated by Mediator through Cajal bodies' association with histone locus bodies. *Nat Commun*. 13(1):2905.
- 8. Fukuoka, M., Ichikawa, Y., Osako, T., Fujita, T., Baba, S., Takeuchi, K., Tsunoda, N., Ebata, T., Ueno, T., Ohno, S., *Saitoh, N. (2022) The ELEANOR non-coding RNA

expression contributes to cancer dormancy and predicts late recurrence of ER-positive breast cancer. *Cancer Science*, 113, 2336-2351.

- Matsumori, H., Watanabe, K., Tachiwana, H., Fujita, T., Ito Y., Tokunaga, M., Kumiko Sakata-Sogawa, K., Osakada, H., Haraguchi, T., Awazu, A., Ochiai, H., Sakata, S., Ochiai, K., Toki, T., Ito, Et., Goldberg I., Tokunaga, K., *Nakao, M., *Saitoh, N. (2022) Ribosomal protein L5 facilitates rDNA-bundled condensate and nucleolar assembly. *Life Science Alliance*, 5 (7), e202101045.
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- 20. Suzuki T, Masugi Y, Inoue Y, Hamada T, Tanaka M, Takamatsu M, Arita J, Kato T, Kawaguchi Y, Kunita A, Nakai Y, Nakano Y, Ono Y, Sasahira N, Takeda T, Tateishi K, Uemura S, Koike K, Ushiku T, Takeuchi K, Sakamoto M, Hasegawa K, Kitago M, Takahashi Y, Fujishiro M, Japan GTKPCSGi. KRAS variant allele frequency, but not mutation positivity, associates with survival of patients with pancreatic cancer. *Cancer Sci.* 2022;113:3097-3109.
- 21. Kitajima Y, Yamashina M, Hanamoto M, Shijimaya T, Terai S, Nakamaru S, Makimura K, Inoue N, Takeuchi K, Kiyohara T. Primary cutaneous anaplastic large cell lymphoma with DUSP22-IRF4 rearrangement demonstrating a biphasic histopathologic pattern and a complete natural regression. *J Dermatol.* 2022;49:e309-e310.
- 22. Chen SW, Chang ST, Ho CH, Wang JS, Wang RC, Takeuchi K, Chuang SS. Merkel cell carcinoma in Taiwan: A rare tumour with a better prognosis in those harbouring Merkel cell polyomavirus. *Malays J Pathol*. 2022;44:61-66.
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- 32. Sagawa R, Sakata S, Gong B, Seto Y, Takemoto A, Takagi S, Ninomiya H, Yanagitani N, Nakao M, Mun M, Uchibori K, Nishio M, Miyazaki Y, Shiraishi Y, Ogawa S, Kataoka K, Fujita N, Takeuchi K, Katayama R. Soluble PD-L1 works as a decoy in lung cancer immunotherapy via alternative polyadenylation. *JCI Insight*. 2022;7.
- 33. Kure S, Chiba T, Ebina A, Toda K, Jikuzono T, Motoda N, Mitani H, Sugitani I, Takeuchi K, Ohashi R. Correlation between low expression of protein disulfide isomerase A3 and lymph node metastasis in papillary thyroid carcinoma and poor prognosis: a clinicopathological study of 1,139 cases with long-term follow-up. *Endocr J*. 2022;69:273-281.
- 34. Kogure Y, Kameda T, Koya J, Yoshimitsu M, Nosaka K, Yasunaga JI, Imaizumi Y, Watanabe M, Saito Y, Ito Y, McClure MB, Tabata M, Shingaki S, Yoshifuji K, Chiba K, Okada A, Kakiuchi N, Nannya Y, Kamiunten A, Tahira Y, Akizuki K, Sekine M, Shide K, Hidaka T, Kubuki Y, Kitanaka A, Hidaka M, Nakano N, Utsunomiya A, Sica RA, Acuna-Villaorduna A, Janakiram M, Shah U, Ramos JC, Shibata T, Takeuchi K, Takaori-Kondo A, Miyazaki Y, Matsuoka M, Ishitsuka K, Shiraishi Y, Miyano S, Ogawa S, Ye BH, Shimoda K, Kataoka K. Whole-genome landscape of adult T-cell leukemia/lymphoma. *Blood*. 2022;139:967-982.
- 35. Yamashita K, Funauchi Y, Hayakawa K, Ae K, Matsumoto S, Ikuta K, Nishida Y, Ueno T, Shimoyama Y, Hiruta N, Machinami R, Kawachi H, Takeuchi K. S100-negative epithelioid

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- 37. Osako T, Kurisaki-Arakawa A, Dobashi A, Togashi Y, Baba S, Shiozawa S, Ishigame H, Ishige H, Ohno S, Ishikawa Y, Takeuchi K. Distinct Clinicopathologic Features and Possible Pathogenesis of Localized ALK-positive Histiocytosis of the Breast. *Am J Surg Pathol*. 2022;46:344-352.
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[Review Articles]

- 1. Miyata, K. and *Takahashi, A. Pericentromeric repetitive ncRNA regulates chromatin interaction and inflammatory gene expression. (2022) *Nucleus*, 13(1), 74-78.
- Ebata, H., Loo, T.M., *Takahashi, A., Telomere Maintenance and the cGAS-STING Pathway in Cancer, *Cells* (2022) 11(12), 1958.
- Takeuchi K. Idiopathic plasmacytic lymphadenopathy: A conceptual history along with a translation of the original Japanese article published in 1980. *J Clin Exp Hematop*. 2022;62:79-84.

[Conference Activities & Talks]

- 1. Hirota, T. "The labile control of mitotic chromosome segregation underlies chromosomal instability in cancer cells" 12th AACR-JCA Joint Conference 2022.12, Maui.
- 2. Hirota, T. "Our approaches to chromosomal instability" Mitosis meeting. 2022.07, Mishima.

- Matsui, S., Nozawa, R., Hirota, T. "Structural basis for promoting the localization of HP1-Aurora B complex to centromeres" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Kusano, Y., Nozawa, R., Hirota, T. "Chromosomal instability arising from dysregulation of chromosome structure during DNA replication" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Nozawa, R., Matsui, S., Hirota, T. "Aurora B microenvironment: biomolecular assembly ensuring accurate chromosome segregation" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Kamakura, N., Jo, M., Hirota, T. "Dynamic interplay between kinases and phosphatases in mitotic chromosome segregation" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- 7. Negoto, T., Jo, M., Kawachi, H., Hirota, T. "Chromosome-level abnormalities shape the malignant properties in cancers" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Takahashi, M., Jo, M., Kamakura, N., Kawakita, N., Kato, U., Hirota, T. "Induction of lethal mitotic failure by manipulating the balance between mitotic kinases in cancer cells" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Saitoh, N., Yamamoto, T., Ichikawa, Y., Fukuoka, M., Tachiwana, H. "Chromatin associating long non-coding RNAs involved in dormancy for late recurrence of breast cancer." Cold Spring Harbor Laboratory Meeting, Epigenetics & Chromatin 2022.09, Cold Spring Harbor, NY.
- Saitoh, N., Ichikawa, Y., Fukuoka, M. "Non-coding RNAs in the molecular condensate contribute to chromatin regulation and tumor dormancy in late recurrence of breast cancer." The FASEB Meeting, The Nuclear Bodies Conference: Hubs of Genomic Activity 2022.07, Nova Scotia, Canada.
- Saitoh N. "ELEANOR non-coding RNAs associate with chromatin and regulate the 3D genome structure in breast cancer." The 30th Hot Spring Harbor International Symposium: Chromatin Potential in Development and Differentiation, The 6th Symposium of the Inter-University Research Network for Trans-Omics Medicine, 2022.01, Online Meeting.
- Saitoh N. "Non-coding RNAs regulate the 3D genome architecture in breast cancer." 6th International Anatomical Sciences and Cell Biology Conference 2022.02, Virtual Meeting by National University of Singapore.
- Saitoh N. "ELEANOR non-coding RNAs activate the chromatin domain, balancing cell death and proliferation in the breast cancer dormancy." The 45th Annual meeting of the Molecular Biology Society of Japan. 2022.12, Chiba.
- 14. Yamamoto, T., Ichikawa, Y., Palihati, M., Saitoh, N. "ELEANOR non-coding RNAs associate with chromatin, and contribute to the 3D genome structure in breast cancer." The 81st Annual meeting of the Japanese Cancer Association. 2022.10, Yokohama.

- Tachiwana, H., Saitoh N. "HDAC inhibitors induceH2A.Zaccumulations to gene bodies in specific genes and their transcription suppression" The 81st Annual meeting of the Japanese Cancer Association. 2022.10, Yokohama.
- 16. Akiko Takahashi "Molecular mechanisms of inflammatory gene expression in senescent cells" The 12th BRI International Symposium 2022.2, Niigata
- Akiko Takahashi "Pericentromeric Repetitive ncRNA Regulates Chromatin Interaction and Inflammatory Gene Expression" A3 Symposium "Cellular senescence: from pathophysiology to treatment" 2022.9, Tokyo
- Akiko Takahashi "Biological function of senescent cells in the cancer microenvironment" Woman scientists in cancer research (WSCR), 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Akiko Takahashi "Cellular senescence inhibits cell competition via SASP" The 95th Annual Meeting of the Japanese Biochemical Society, 2022.11, Nagoya
- Akiko Takahashi "Cellular senescence in age-related diseases" MHS2022 Keynote Lecture 2022.11, Nagoya
- 21. Akiko Takahashi "Tumorigenic roles of senescent cells in the cancer microenvironment" International Symposium on Recent Advances in Precision Medicine 2022.12, Korea
- Akiko Takahashi "Epigenetic alteration in senescent cells promotes the inflammatory SASP gene expression" The 45th Annual Meeting of the Molecular Biology Society of Japan 2022.12, Makuhari
- Okamoto, Y., Tomida, A. "Involvement of the integrated stress response in cisplatin sensitization by metabolic inhibitors" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Shirahama, H., Tomida, A. "Omics analyses on density-dependent ferroptosis resistance in melanoma cells" 81st Annual meeting of the Japanese Cancer Association. 2022.09, Yokohama.
- Reo Maruyama R. "Understanding the diversity of breast cancer through single-cell omics analysis." 30th Annual Meeting of the Japan Breast Cancer Society. 2022.7, Yokohama.
- 26. Kumekawa K, Saeki S, Takahashi Y, Yang L, Otsuji K, Takano T, Ohno S, Ueno T, Maruyama E. "Analysis of epigenomic heterogeneity in cancer cells between patients and within tumors in breast cancer." 74th Annual Meeting of the Japanese Society for Cell Biology. 2022.7, Tokyo.

Frontier Biomaterials

Tsuyoshi KIMURA

(1) Research

1) Specific capture of Treg cells

In order to remove Treg cells, which induce immunotolerance, a device of capturing of Treg cells is developed. 2) Decellularization of native tissue for regenerative medicine

In order to obtain a novel scaffold, which can be applied for regenerative tissue, ultra-high pressurization method was developed for the complete elimination of the cells and inactivation of the viruses.

3) Inducing molecular aggregation using ultra-high pressurization

The basic and applied science on molecular aggregation triggered by hydrogen bonding at over 6,000 atm is studied. This technique is being applied for hybridization of DNA with polymer for drug delivery system. 4) Bio-interface

To investigate how the materials interact with biological cues such as phospholipids, proteins, or cells, precisely controlled surface via atomic transfer radical polymerization was prepared. The basic research on physical and biological properties of this surface is being investigated.

(2) Education

In order to develop technology, which may contribute to the advance in the medical science, lectures on functional molecules from basic to advanced knowledge on molecular design for specific purpose, mainly concentrated on medical application would be executed. Theories on functional molecules and overviews on medical system would be lectured in Graduate School of Medical and Dental Sciences. Students would have chances to learn about Genomics and Bio-intelligent system in Graduate School of Biomedical Science.

(3) Publications

[Original Articles]

- 1. Wen-Jin Ho, Mako Kobayashi, Kozue Murata, Yoshihide Hashimoto, Kenji Izumi, Tsuyoshi Kimura, Hideo Kanemitsu, Kazuhiro Yamazaki, Tadashi Ikeda, Kenji Minatoya, Akio Kishida, Hidetoshi Masumoto. A novel approach for the endothelialization of xenogeneic decellularized vascular tissues by human cells utilizing surface modification and dynamic culture. Scientific Reports. 2022.12; 12(1); 22294
- Mika Suzuki, Tsuyoshi Kimura, Yuta Nakano, Mako Kobayashi, Masahiro Okada, Takuya Matsumoto, Yoshihide Hashimoto, Akio Kishida. Preparation of mineralized pericardium by alternative soaking for soft-hard interregional tissue application Journal of Biomedical Materials Research Part A. 2022.09; 1; 1-11
- 3. Anri Koyanagi, Iichiroh Onishi, Karin Muraoka, Ikue Sato, Shingo Sato, Tsuyoshi Kimura, Akio Kishida, Kouhei Yamamoto, Masanobu Kitagawa, Morito Kurata. Identification of the factor that leads human mesenchymal stem cell lines into decellularized bone Bioengineering (Basel). 2022.09; 9(10); 490

- 4. Mako Kobayashi, Naoki Ishida, Yoshihide Hashimoto, Jun Negishi, Hideki Saga, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. Extraction and biological evaluation of atrix-bound nanovesicles (MBVs) from high-hydrostatic pressure-decellularized tissues. International Journal of Molecular Science. 2022.08; 23(16); 8868
- 5. Mika Suzuki, Tsuyoshi Kimura, Yukina Yoshida, Mako Kobayashi, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Shota Anzai, Naoko Nakamura, Akio Kishida. In vitro tissue reconstruction using decellularized pericardium cultured with cells for ligament regeneration Polymers. 2022.06; 14(12); 2351
- 6. Masahiro Yamada, Tsuyoshi Kimura, Naoko Nakamura, Jun Watanabe, Ndia Kartikasari, Xindie He, Watcharaphol Tiskratok, Hayato Yoshioka, Hidenori Shinno, Hiroshi Egusa. The titanium nanosurface with biomimetic physical microenvironment to induce endogenous regeneration of the periodontium ACS Applied Materials & Interfaces. 2022.06; 14(24); 27703-27719
- 7. Yutaro Hayakawa, Masato Furuya, Hironobu Tahara, Yasuhiro Kosuge, Tsuyoshi Kimura, Kosuke Sugawa, Joe Otsuki. Modulation technique of localized surface plasmon resonance of palladium nanospheres by coating with titanium dioxide shell for application to photothermal therapy agent Nanoscale Research Letters. 2022.06; 17; 60
- Yoshihide Hashimoto, Akitatsu Yamashita, Jun Negishi, Tsuyoshi Kimura, Seiichi Funamoto, and Akio Kishida. 4-arm PEG-functionalized decellularized pericardium for effective prevention of postoperative adhesion in cardiac surgery ACS Biomaterials Science & Engineering. 2022.01; 8(1); 261-272
- 9. Hiroki Tsutsumi, Ryota Kurimoto, Ryo Nakamichi, Tomoki Chiba, Takahide Matsushima, Yuta Fujii, Risa Sanada, Tomomi Kato, Kana Shishido, Yuriko Sakamaki, Tsuyoshi Kimura, Akio Kishida, Hiroshi Asahara. Generation of a tendon-like tissue from human iPS cells. J Tissue Eng. 2022.01; 13; 20417314221074018
- Narintadeach Charoensombut, Kinyoshi Kawabata, Jeonghyun Kim, Minki Chang, Tsuyoshi Kimura, Akio Kishida, Takashi Ushida, Katsuko S Furukawa. Internal radial perfusion bioreactor promotes decellularization and recellularization of rat uterine tissue Journal of Bioscience and Bioengineering. 2022.01; 133(1); 83-88

[Conference Activities & Talks]

- 1. Mako Kobayashi, Tsuyoshi Kimura, Akio Kishida, Masaya Yamamoto . The effect of decellularized tissue-derived hydrogels on cancer cell behavior. The 7th International Symposium on Biomedical Engineering (ISBE2022) 2022.11.25 Online
- 2. WenJin Ho, Hidetoshi Masumoto, Mako Kobayashi, Kozue Murata, Tadashi Ikeda, Yoshihide Hashimoto, Tsuyoshi Kimura, Kenji Minatoya, Akio Kishida. A novel approach for pre-implant endothelialization of xenogeneic decellularized vascular tissues by human endothelial cells utilizing tissue surface modification and dynamic culture. American Heart Association 2022 Scientific Sessions 2022.11.04 Chicago, USA
- 3. Yoshihide Hashimoto, Takuya Akizawa, Moeko Hagiwara, Mako Kobayashi, Tsuyoshi Kimura, Akio Kishida. Cellular behaviors of human skeletal muscle satellite cells on tissue specific extracellular matrix coating and hydrogels. Visual-JW 2022 2022.10.25 Osaka, Japan
- 4. Tsuyoshi Kimura, Mika Suzuki, Mako Kobayashi, Masahiro Okada, Takuya Matsumoto, Naoko Nakamura, Yoshihide Hashimoto, Akio Kishida. Development of a mineralized decellularized tissue for soft-hard inter-regional tissue application. TERMIS-AP 2022 2022.10.05 Jeju, South Korea
- 5. Mako Kobayashi, Naoki Ishida, Yoshihide Hashimoto, Jun Negishi, Hideki Saga, Takehiro Iwanaga, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. The effects of matrix-bound nanovesicles(MBVs) derived from high-hydrostatic pressure decellularized tissued on neural regeneration. TERMIS-AP 2022 2022.10.05 Jeju, South Korea

[Patents]

- 1. ANTI-ADHESION MATERIAL AND SUBSTITUTE BIOMEMBRANE USING DECELLULARIZED TISSUE, Patent Number : CA 2978401
- 2. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : KR 2376321

Organogenesis and Neogenesis

Takanori Takebe, MD, PhD, Professor Yosuke Yoneyama, PhD, Assistant Professor Sachiko Sekiya, PhD, Assistant Professor Norikazu Saiki, PhD, Project Assistant Professor Shunsuke Mori, PhD, Project Assistant Professor Ichiro Fukunaga, PhD, Project Assistant Professor Rie Ouchi-Koike, PhD, Project Researcher Yoshihiro Shimada, Part-time Lecturer Takuma Iguchi, Part-time Lecturer Mari Maezawa, Research Assistant Kanae Ohtsu, Research Assistant Naoko Sekinami, Technical Assistant Mayuko Matsushima, Technical Assistant Michiko Mori, Administrative Assistant Noriko Yokota, Administrative Assistant Xu Zeyu, Graduate Student Zhang Jianchun, Graduate Student Hitomi Yamaguchi, Graduate Student Shuntaro Kawamura, Graduate Student Asei Hirai, Graduate Student Harue Chou, Graduate Student Risa Kawauchi, Graduate Student Yasuyuki Kurihara, Graduate Student

(1) Outline

The Takebe Lab enjoys developing new technology and implementing fresh outlooks on discoveries that may be ignored, under-appreciated and overlooked by the traditional scientific community. The Takebe Lab takes a creative lead for the exploitation and dissemination of unpredictable, extraordinary and crazy paradigm by integrating discovery and technology, eventually revolutionizing science, and medico-health-care paradigm. The Takebe Lab is also lending its support to commercial execution to move forward.

The self-organizing tissue-based approach coupled with induced pluripotent stem cell (iPSC) technology has just begun as a promising field for designing a miniature organ, aka an organoid, in culture and is expected to achieve valuable outcomes in '(re-) generative medicine' and 'drug development'. However, how the complex but stereotyped tissue shapes self-organize still remains largely unknown. To understand such complex self-organizing mechanisms, Dr Takebe's lab proposes to take a 'reverse reductionism approach' for a holistic mechanistic understanding of the dynamic nature of a self-developing system. We also seek to translate knowledge of living systems into a revolutionary technology platform towards practical biomedical use in clinics.

(2) Research

Organoids are multicellular structures that can be derived from adult organs or pluripotent stem cells. Early versions of organoids range from simple epithelial structures to complex, disorganized tissues with large cellular diversity. The current challenge is to engineer cellular complexity into organoids in a controlled manner that results in organized assembly and acquisition of tissue function. These efforts have relied on studies of organ assembly during embryonic development and have resulted in development of organoids with multilayer tissue complexity and higher order functions. To advance the field forward, Takebe Lab would like to achieve three interactive and complementary goals:

- 1. The deductive development of a complex human organoid model
- 2. The multidisciplinary dissection of self-driven mechanisms of organogenesis
- 3. The technology prototyping towards biomedical applications

Our early efforts are being made on liver organoid (liver bud or miniature liver) systems using human iPSC. For example, we have demonstrated successful integration of endothelial cells (Nature, 2013), mesenchymal cells (Cell Stem Cell, 2015) and macrophages (Cell Metab, 2019) into human liver organoids, allowing for the study of drug testing and transplant applications. More recently, we showed the inter-coordinated specification and invagination of the human hepato-biliary-pancreatic system from human pluripotent stem cells, thereby, connecting multi-organ systems in a dish (Nature, 2019). Thus we are tackling the questions how the next generation of organoids can be designed by utilizing an engineering-based narrative design, and what promise and impact will be brought towards future biomedical applications (Science, 2019). Our interested expertise includes cell biology, mathematics, bioinformatics, morphogenesis, genomics, bioengineering, chemistry or biomechanics. In a longer term, we seek to realize "organoid medicine" applications through human implementation of extracorporeal device, precision medicine, drug discovery and organ replacement therapy. We are accelerating such biomedical applications of organoids by collaborating with international and diverse industry collaborators, such as the Cincinnati Children's Hospital and the Takeda-CiRA program.

(3) Publications

[Original Articles]

- Kimura M, Iguchi T, Iwasawa K, Dunn A, Thompson W, Yoneyama Y, Chaturvedi P, Zorn A, Wintzinger M, Quattrocelli M, Watanabe-Chailland M, Zhu G, Fujimoto M, Kumbaji M, Kodaka A, Gindin Y, Chung C, Myers R, Subramanian G, Hwa V, Takebe T. En masse organoid phenotyping informs metabolic-associated genetic susceptibility to NASH Cell. 2022.10; 185(22); 4216-4232.e16
- 2. Liu Y, Kimura M, Vijayakumar A, Murakami E, Takebe T, Subramanian M, Auwerx J. ENHANCEMENT OF DE NOVO NAD plus BIOSYNTHESIS BY NOVEL ACMSD INHIBITORS IMPROVES MITOCHONDRIAL FUNCTION IN iPSC-DERIVED HUMAN LIVER ORGANOID Hepatology. 2022.10; 76; S706
- 3. Matsuzaki T, Shimokawa Y, Koike H, Kimura M, Kawano Y, Okuma N, Kawamura R, Yoneyama Y, Furuichi Y, Hakuno F, Takahashi S, Nakabayashi S, Okamoto S, Nakauchi H, Taniguchi H, Takebe T, Yoshikawa H. Mechanical guidance of self-condensation patterns of differentiating progeny iScience. 2022.09; 25(10); 105109
- 4. Wu Y, Oda M, Hayashi Y, Takebe T, Nagata S, Wang C, Mori K. Blood Vessel Segmentation from Low-Contrast and Wide-Field Optical Microscopic Images of Cranial Window by Attention-Gate-Based Network IEEE. 2022.08; 1864-1873
- 5. Lancaster M, Morris S, Takebe T, Qian L, Gao S, Huch M. Anniversary reflections: Inspiring discoveries and the future of the field Cell Stem Cell. 2022.06; 29(66); 879-881
- 6. Mituru Mizuno, Takahisa Matsuzaki, Nobutake Ozeki, Hisako Katano, Hideyuki Koga, Takanori Takebe, Hiroshi Yoshikawa, Ichiro Sekiya. Cell membrane fluidity and ROS resistance define DMSO tolerance of cryopreserved synovial MSCs and HUVECs. Stem Cell Research & Therapy. 2022.05; 13(1); 177

- 7. Jurickova I, Bonkowski E, Angerman E, Novak E, Huron A, Akers G, Iwasawa K, Braun T, Hadar R, Hooker M, Han S, Cutler D, Okou D, Kugathasan S, Jegga A, Wells J, Takebe T, Mollen K, Haberman Y, Denson L. Eicosatetraynoic Acid and Butyrate Regulate Human Intestinal Organoid Mitochondrial and Extracellular Matrix Pathways Implicated in Crohn's Inflammatory Bowel Diseases. 2022.03; 28(7); 988-1003
- 8. Tominaga K, Kechele D, Sanchez G, McCauley H, Enriquez J, Vales S, Jurickova I, Denson L, Takebe T, Helmrath M, Zorn A, Wells J. GENERATION OF HUMAN INTESTINAL ORGANOIDS CONTAINING TISSUE-RESIDENT IMMUNE CELLS Gastroenterology. 2022.02; 62(3); S57

[Conference Activities & Talks]

- 1. Takanori Takebe. From Invention, to Innovation. 日本薬物動態学会 2022.11.08
- 2. Takanori Takebe. Human Organoids Toward Precision Hepatology. AASLD The Liver Meeting 2022 2022.11.07
- 3. Takanori Takebe. Engineering Complex Liver Organoids for Advanced Disease Modeling. 2022 James W. Freston Single Topic Conference 2022.10.07
- 4. Takanori Takebe. Modeling Steatohepatitis in Humans with Liver Organoids. Keystone Symposia 2022.08.09
- 5. 武部貴則. 多能性幹細胞を用いた肝胆膵発生システム. 発生生物学会第55回大会2022.06.01
- 1. Human Organoids For Metabo-flammatory Liver Disease. The 51st Annual Meeting of the Japanese Society for Immunology 2022.12.08
- 2. Regenerative Medicine in Gastroenterology Engaging general public to accelerate reserach. Japan Digestive Disease Week 2022 2022.10.28
- 3. Frontiers of Multi-Organ Engineering. The Japanese Society of Pathology 2022.07.30
- 4. Mammalian enteral ventilation. The 121st Meeting of the Japanese Dermatological Association 2022.06.04
- 5. Organoid based My Medicine for Human Liver Disease. The Japan Society of Hepatology 2022.06.03
- 6. Promise of Street Medical Approach. The Japan Society of Hepatology 2022.06.03
- 7. Takanori Takebe. Promise of Mammalian Enteral Ventilation. Gunma Medical Association 2022.05.27
- 8. Takanori Takebe. My Medicine in Gastroenterology. The Japanese Society of Gastroenterology 2022.04.21
- 9. Takanori Takebe. Engineering Multi-Organs in a Dish. The 126th Annual Meeting of the Japanese Ophthalmological Society 2022.04.15
- Takanori Takebe. Constructing and Deconstructing Human Organogenesis. The 122nd Annual Congress of Japan Surgical Society 2022.04.14
- 11. Takanori Takebe. Hepato-biliary-pancreatic organogenesis in vitro. The 127th Annual Meeting of the Japanese Association of Anatomists 2022.03.28
- 12. Takanori Takebe. Enteral ventilation for ameliorating respiratory failure. The 49th Annual Meeting of the Japanese Society of Intensive Care of Medicine 2022.03.20
- 13. Takanori Takebe. Frontiers of Multi-Organ Engineering. The 21st Congress of the Japanese Society for Regenerative Medicine 2022.03.19
- 14. Takanori Takebe. Pursuing Potential of Organoid Medicine. The 21st Congress of the Japanese Society for Regenerative Medicine 2022.03.17
- 15. Takanori Takebe. Engineering digestive systems in a dish. The 94th Annual Meeting of the Japanese Gastric Cancer Association 2022.03.02

Integrated Data Science

Associate Professor HASEGAWA Takanori Assistant Professor ITO Satoshi Project Professor SATORU Miyano Project Assistant Professor

KAKUTA Masanori Project Assistant Professor OGAWA Miho

(1) Outline

We develop new mathematical methods using bioinformatics and artificial intelligence technologies for integrated analysis of multidimensional and ultra-heterogeneous big data in the medical and biological field. Through the analysis using bioinformatics, statistical science, and machine learning on advanced information processing technologies such as supercomputers and GPUs, we aim to elucidate biological and life systems and immune profiles for cancer, aging, and chronic critical illness for the development of drug discovery and new therapeutic strategies.

Research Topic

1. Knowledge discovery from big data using supercomputers and artificial intelligence technology.

2. Elucidation of biological/life systems and immune profiles of cancer, aging, and chronic critical illness by mathematical modeling.

3. Large-scale data analysis of whole genome/exome sequencing, single-cell transcriptome, proteome data, etc.

4. Systems modeling and simulation of disease states.

(2) Research

Development and application of mathematical methods for biological big data

The pathophysiology of the disease is a situation in which control abnormalities affect each other in a complex manner due to the influence of multiple genes and the environment including the intestine and skin, and in particular, cancer is a state that deviates from integrated control as a system. We integrate ultra-multidimensional and ultra-heterogeneous biological big data such as genome and other omics data, pathological conditions, and environmental data through the development of advanced computational science strategies and information processing technologies such as supercomputers. Our research will elucidate the mechanisms of biological/life system failures, called pathological conditions, and to develop drug discovery and therapeutics.

Joint Research Coronavirus Task Force

As a member of the Collaborative Research Coronavirus Task Force, an emergency project to protect society from novel coronaviruses, we have conducted all preliminary whole genome and transcriptome analyses. Data from this task force is increasing daily, and by FY2022, over 1,000 whole genome samples have been completed;

another 4,000 samples will be analyzed in FY2023, resulting in 10,000 whole genome data including controls.

■ Construction of integrated analysis platform for M & D data and promotion of cooperation system Medical and dental sciences and medical research are entering a new era in terms of both quality and quantity of information. It is common to acquire and use large amounts of biological information, such as genomic information analysis and single cell analysis, which can be integrated to obtain new knowledge and new findings. We will then promote the construction of the necessary information education and infrastructure. The large storage server in our institute has been increased to 2.5PB, and a system that links the hospital's DWH with the Bio-resource center has been constructed.

(3) Education

We joined the following activities:

- [Undergraduate School]
- Introduction to Medical Care and AI / Big Data
- Mathematical/DS/AI Education Literacy Level WG
- Basic Research Physician Program
- Public Health Education Course
- Hosted the "National Medical and AI Contest" for undergraduate students
- Respond to inquiries about data science from undergraduate students

[Graduate School]

- Introduction to Medical Data Science (Master Course)
- Data Science Special Lecture I (English version) (hosted by Professor Kunihiko Takahashi)
- Data Science Special Lecture II (English version) (by Associate Professor Hasegawa)
- Assigned as a secondary supervisor for three doctoral students (Associate Professor Hasegawa).
- Support for research/career inquiries from graduate students

(4) Lectures & Courses

Our education policy is to enable students in clinical/basic research to independently perform data science. Not just for data analysis support, we foster world top-level biomedical data scientists at Tokyo Medical and Dental University.

(5) Clinical Services & Other Works

1. To support COVID-19, Tokyo Medical and Dental University, Keio University School of Medicine, Department of Oncology, Graduate School of Medicine, Kyoto University, Department of Genetic Statistics, Graduate School of Medicine, Osaka University, Human Genome Analysis Center, Institute of Medical Science, University of Tokyo Became the main founder and created a network-type research organization called " the Coronavirus Task Force". About 120 hospitals from all over the country participated, and currently, about 6,000 samples had been collected. Host whole-genome analysis and RNA sequence analysis are performed on more than 1,200 of these samples to search for aggravating factors. These results have been accepted by several international journals, including Nature.

2. Through this task force, we are participating in the International COVID-19 Consortium.

3. We actively conducted cancer genomics research with a group such as Professor Seishi Ogawa of Kyoto University.

(6) Publications

[Original Articles]

1. Lee H, Chubachi S, Namkoong H, Asakura T, Tanaka H, Otake S, Nakagawara K, Morita A, Fukushima T, Watase M, Kusumoto T, Masaki K, Kamata H, Ishii M, Hasegawa N, Harada N, Ueda T, Ueda S,

Ishiguro T, Arimura K, Saito F, Yoshiyama T, Nakano Y, Mutoh Y, Suzuki Y, Murakami K, Okada Y, Koike R, Kitagawa Y, Kimura A, Imoto S, Miyano S, Ogawa S, Kanai T, Fukunaga K, Japan COVID-19 Task Force. Characteristics of hospitalized patients with COVID-19 during the first to fifth waves of infection: a report from the Japan COVID-19 Task Force. BMC infectious diseases. 2022.12; 22(1); 935

- Park H, Miyano S. Computational Tactics for Precision Cancer Network Biology. International journal of molecular sciences. 2022.11; 23(22);
- 3. Butler-Laporte G, Povysil G, Kosmicki JA, Cirulli ET, Drivas T, Furini S, Saad C, Schmidt A, Olszewski P, Korotko U, Quinodoz M, Celik E, Kundu K, Walter K, Jung J, Stockwell AD, Sloofman LG, Jordan DM, Thompson RC, Del Valle D, Simons N, Cheng E, Sebra R, Schadt EE, Kim-Schulze S, Gnjatic S, Merad M, Buxbaum JD, Beckmann ND, Charney AW, Przychodzen B, Chang T, Pottinger TD, Shang N, Brand F, Fava F, Mari F, Chwialkowska K, Niemira M, Pula S, Baillie JK, Stuckey A, Salas A, Bello X, Pardo-Seco J, Gómez-Carballa A, Rivero-Calle I, Martinón-Torres F, Ganna A, Karczewski KJ, Veerapen K, Bourgey M, Bourque G, Eveleigh RJ, Forgetta V, Morrison D, Langlais D, Lathrop M, Mooser V, Nakanishi T, Frithiof R, Hultström M, Lipcsey M, Marincevic-Zuniga Y, Nordlund J, Schiabor Barrett KM, Lee W, Bolze A, White S, Riffle S, Tanudjaja F, Sandoval E, Neveux I, Dabe S, Casadei N, Motameny S, Alaamery M, Massadeh S, Aljawini N, Almutairi MS, Arabi YM, Algahtani SA, Al Harthi FS, Almutairi A, Algubaishi F, Alotaibi S, Binowayn A, Alsolm EA, El Bardisy H, Fawzy M, Cai F, Soranzo N, Butterworth A, COVID-19 Host Genetics Initiative, DeCOI Host Genetics Group, GEN-COVID Multicenter Study (Italy), Mount Sinai Clinical Intelligence Center, GEN-COVID consortium (Spain), GenOMICC Consortium, Japan COVID-19 Task Force, Regeneron Genetics Center, Geschwind DH, Arteaga S, Stephens A, Butte MJ, Boutros PC, Yamaguchi TN, Tao S, Eng S, Sanders T, Tung PJ, Broudy ME, Pan Y, Gonzalez A, Chavan N, Johnson R, Pasaniuc B, Yaspan B, Smieszek S, Rivolta C, Bibert S, Bochud PY, Dabrowski M, Zawadzki P, Sypniewski M, Kaja E, Chariyavilaskul P, Nilaratanakul V, Hirankarn N, Shotelersuk V, Pongpanich M, Phokaew C, Chetruengchai W, Tokunaga K, Sugiyama M, Kawai Y, Hasegawa T, Naito T, Namkoong H, Edahiro R, Kimura A, Ogawa S, Kanai T, Fukunaga K, Okada Y, Imoto S, Miyano S, Mangul S, Abedalthagafi MS, Zeberg H, Grzymski JJ, Washington NL, Ossowski S, Ludwig KU, Schulte EC, Riess O, Moniuszko M, Kwasniewski M, Mbarek H, Ismail SI, Verma A, Goldstein DB, Kiryluk K, Renieri A, Ferreira MAR, Richards JB. Exome-wide association study to identify rare variants influencing COVID-19 outcomes: Results from the Host Genetics Initiative. PLoS genetics. 2022.11; 18(11); e1010367
- 4. Watanabe K, Kimura S, Seki M, Isobe T, Kubota Y, Sekiguchi M, Sato-Otsubo A, Hiwatari M, Kato M, Oka A, Koh K, Sato Y, Tanaka H, Miyano S, Kawai T, Hata K, Ueno H, Nannya Y, Suzuki H, Yoshida K, Fujii Y, Nagae G, Aburatani H, Ogawa S, Takita J. Identification of the ultrahigh-risk subgroup in neuroblastoma cases through DNA methylation analysis and its treatment exploiting cancer metabolism. Oncogene. 2022.11; 41(46); 4994-5007
- 5. Nakagawara K, Chubachi S, Namkoong H, Tanaka H, Lee H, Azekawa S, Otake S, Fukushima T, Morita A, Watase M, Sakurai K, Kusumoto T, Asakura T, Masaki K, Kamata H, Ishii M, Hasegawa N, Harada N, Ueda T, Ueda S, Ishiguro T, Arimura K, Saito F, Yoshiyama T, Nakano Y, Mutoh Y, Suzuki Y, Edahiro R, Murakami K, Sato Y, Okada Y, Koike R, Kitagawa Y, Tokunaga K, Kimura A, Imoto S, Miyano S, Ogawa S, Kanai T, Fukunaga K. Impact of upper and lower respiratory symptoms on COVID-19 outcomes: a multicenter retrospective cohort study. Respiratory research. 2022.11; 23(1); 315
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- 3. 内御堂亮, 長谷川嵩矩, 若林健二. Longitudinal data analysis for predicting mortality in patients with severe COVID-19 日本集中治療医学会学術集会 (Web). 2022; 49th;

[Books etc]

1. Satoru Miyano, et al.. Integrated understanding and treatment strategies for cancer based on big data analysis. New Science co. ltd., 2022.08

[Conference Activities & Talks]

- 1. 奥田 瑠璃花, 越智 陽太郎, 蝶名林 和久, 眞田 昌, 半田 寛, 白石 友一, 千葉 滋, 石川 隆之, 大屋敷 一馬, 熱田 由 子, 宮野 悟, 牧島 秀樹, 南谷 泰仁, 小川 誠司. がん研究における女性研究者 不均衡転座 der(1;7)(q10;p10) を有する MDS と関連疾患の特徴 (Unbalanced translocation der(1;7)(q10;p10) as a distinct subtype in myelodysplastic syndromes). 日本癌学会総会記事 2022.09.01
- 2. 藤井 陽一, 樋口 誠一郎, 佐藤 悠佑, 白石 友一, 宮野 悟, 久米 春喜, 市川 智彦, 岩間 厚志, 田中 知明, 小川 誠司. コルチゾール産生腺種における CTNNB1 の新規構造異常と分子分類 (Novel structural variants in CTNNB1 and molecular classification cortisol-producing adenoma). 日本癌学会総会記事 2022.09.01
- 3. 山口 貴世志, 中川 沙弥, 高根 希世子, 池上 恒雄, 山口 類, 井元 清哉, 宮野 悟, 古川 洋一. ブロモドメインタン パク質 BRD8 を標的とした新たな大腸がん治療戦略 (Targeting bromodomain protein BRD8 for colorectal cancer treatment). 日本癌学会総会記事 2022.09.01
- 4. 牧島 秀樹, 佐伯 龍之介, 南谷 泰仁, 竹田 淳恵, 桃沢 幸秀, 熱田 由子, 中川 正宏, 宮崎 泰司, 鶴見 寿, 笠原 千嗣, 高折 晃史, 大屋敷 一馬, 木口 亨, 松田 文彦, 宮野 悟, 小川 誠司. 全ゲノム/全エキソーム解析による 生殖細胞系列多型の探索 DDX41 胚細胞変異陽性骨髄腫瘍のリスク定量と臨床的特徴 (Germline DDX41 mutations define a unique subtype of myeloid neoplasms). 日本癌学会総会記事 2022.09.01
- 5. 池上 恒雄, 山口 貴世志, 高根 希世子, 清水 英悟, 笠島 理加, 土方 康基, 片山 琴絵, 渋谷 哲朗, 山口 類, 井元 清哉, 宮野 悟, 古川 洋一. 全ゲノム/全エクソン解析と人工知能を用いた難治がんに対する精密医 療 (Application of whole genome/exome sequencing and artificial intelligence for precision medicine for intractable cancer). 日本癌学会総会記事 2022.09.01

- 6. 平野 智紀, 垣内 伸之, 竹内 康英, 増井 俊彦, 白石 友一, 宮野 悟, 宇座 徳光, 児玉 裕三, 増田 充弘, 田中 雄志. 同時性・異時性多発膵癌の遺伝子解析 (Genetic analysis of synchronous or metachronous multiple pancreatic cancers). 日本癌学会総会記事 2022.09.01
- 7. 井上 善景, 垣内 伸之, 南谷 泰仁, 吉田 健一, 竹内 康英, 藤井 陽一, 千葉 健一, 吉里 哲一, 長山 聡, 宮野 悟, 小濱 和貴, 小川 誠司. 大腸癌におけるトランスレーショナルリサーチの新たな展開 大腸癌の分子分類およ び予後予測リスク分類 (Molecular classification and risk stratification of colorectal cancer). 日本癌学会総 会記事 2022.09.01
- 8. 前田 紘奈, 垣内 伸之, 伊藤 孝司, 小川 絵里, 塩川 雅広, 宇座 徳光, 田中 洋子, 南谷 泰仁, 牧島 秀樹, 保田 宏明, 児玉 裕三, 上本 伸二, 宮野 悟, 小川 誠司. 慢性炎症に伴う胆管上皮におけるクローン拡大 (Clonal expansion in bile duct associated with chronic inflammation). 日本癌学会総会記事 2022.09.01
- 9. 西村 友美, 垣内 伸之, 吉田 健一, 桜井 孝規, 片岡 竜貴, 澤田 守男, 竹内 康英, 前田 紘奈, 馬場 郷子, 滝田 順 子, 宮野 悟, 万代 昌紀, 竹内 賢吾, 羽賀 博典, 戸井 雅和, 小川 誠司. 正常およびがん組織におけるクローン 進化 乳管上皮細胞から乳癌へ至るクローン進化 (Clonal evolution of mammary epithelial cells into breast cancers). 日本癌学会総会記事 2022.09.01
- 10. 渡部 光一, 垣内 伸之, 高松 士朗, 北村 幸子, 滝 真奈, 山ノ井 康二, 村上 隆介, 山口 建, 濱西 潤三, 田中 洋子, 宮野 悟, 万代 昌紀, 小川 誠司. 正常子宮内膜におけるクローン拡大とドライバー遺伝子変異 (Clonal expansion with driver mutations in human normal endometrium.). 日本癌学会総会記事 2022.09.01
- 11. 樋渡 光輝, 関 正史, 松野 良介, 吉田 健一, 長澤 武, 佐藤 亜以子, 山本 将平, 加藤 元博, 渡邉 健太郎, 関口 昌央, 宮野 悟, 小川 誠司, 滝田 順子. 神経芽腫における新規 TENM 3-ALK 融合遺伝子の解析 (Novel ALK fusion in neuroblastoma involving TENM3, a conserved family of transmembrane protein). 日本癌学会総 会記事 2022.09.01
- 12. 末原 泰人, 坂本 佳奈, 藤澤 学, 福本 浩太, 安部 佳亮, 槇島 健一, 須摩 桜子, 末永 孝生, 竹内 賢吾, 中村 直哉, 千葉 健一, 白石 友一, 宮野 悟, 小川 誠司, 千葉 滋, 坂田 麻実子 [柳元]. 血管免疫芽球性 T 細胞リンパ腫 の遺伝子異常に基づく亜分類は予後と関連する (Genetic subtypes of angioimmunoblastic T-cell lymphoma are associated with distinct outcomes.). 日本癌学会総会記事 2022.09.01
- 13. 笠島 理加, 鈴木 理樹, 清水 英悟, 玉田 嘉紀, 新井田 厚司, 廣島 幸彦, 片山 琴絵, 山口 類, 山口 貴世志, 古川 洋一, 宮野 悟, 井元 清哉, 横瀬 智之, 宮城 洋平. 遺伝子ネットワーク解析による高悪性度胎児性肺腺癌のパス ウェイ予測・検討 (Prediction and Investigation of Pathways in High-Grade Fetal Lung Adenocarcinoma by Gene Network Analysis). 日本癌学会総会記事 2022.09.01

[Works]

1. Virtual Grid Engine, Software, IEEE BIBM2018, 2018.12 - Now

Department of Biostatistics

Professor TAKAHASHI Kunihiko Junior Associate Professor ANZAI Tatsuhiko Assistant Professor ITO Tsubasa (- 2022/3) Assistant Professor NISHIDA Yuki (2022/4 -)

(1) Outline

Biostatistics has a central role in medical research. We aim to develop methodologies for data analysis focused on medical, dental and healthcare applications, and will collaborate on practical research.

(2) Research

1) Methodology development for data analysis in M&D field

We are developing biostatistical methodologies for data analysis in the field of M&D. Our focus includes methodologies and applications for spatial epidemiological research with geographic and temporal data, disease surveillance and monitoring, real-world data (RWD) analysis, meta-analysis, dynamic modeling, and their implementation in software.

2) Practical research on M&D field

Another focus is joint research in the field of M&D with medical, dental, and healthcare professionals. Some of our contributions include the design and analysis of any types of medical/clinical, health related studies.

(3) Education

Undergraduate: Introduction to AI and Big Data in Health Sciences, Public Health. Graduate: Medcal Data Science, Data Science I, Biostatistics I, Clinical Biostatistics and Statistical Genetics, Big Data Analytics, Lecture of Biostatistics, Research for Thesis.

(4) Lectures & Courses

The objective of this course is to master methodologies in biostatistics, and will be able to interpret the results of data analysis in medical research.

(5) Publications

[Original Articles]

 Tomoki Nakaya, Kunihiko Takahashi, Hideto Takahashi, Seiji Yasumura, Tetsuya Ohira, Hiroki Shimura, Satoru Suzuki, Satoshi Suzuki, Manabu Iwadate, Susumu Yokoya, Hitoshi Ohto, Kenji Kamiya. Revisiting the Geographical Distribution of Thyroid Cancer Incidence in Fukushima Prefecture: Analysis of Data From the Second- and Third-round Thyroid Ultrasound Examination. J Epidemiol. 2022.12; 32(Suppl_XII); S76-S83

- 2. Hiroyuki Inose, Tsuyoshi Kato, Shoji Tomizawa, Akane Ariga, Takayuki Motoyoshi, Kazuyuki Fukushima, Kunihiko Takahashi, Toshitaka Yoshii, Atsushi Okawa. Impact of romosozumab on serum calcium concentration and factors predicting the fluctuations in calcium concentration upon romosozumab administration: A multicenter retrospective study. Bone Rep. 2022.12; 17; 101635
- 3. Ho Lee, Shotaro Chubachi, Ho Namkoong, Takanori Asakura, Hiromu Tanaka, Shiro Otake, Kensuke Nakagawara, Atsuho Morita, Takahiro Fukushima, Mayuko Watase, Tatsuya Kusumoto, Katsunori Masaki, Hirofumi Kamata, Makoto Ishii, Naoki Hasegawa, Norihiro Harada, Tetsuya Ueda, Soichiro Ueda, Takashi Ishiguro, Ken Arimura, Fukuki Saito, Takashi Yoshiyama, Yasushi Nakano, Yoshikazu Mutoh, Yusuke Suzuki, Koji Murakami, Yukinori Okada, Ryuji Koike, Yuko Kitagawa, Akinori Kimura, Seiya Imoto, Satoru Miyano, Seishi Ogawa, Takanori Kanai, Koichi Fukunaga, . Characteristics of hospitalized patients with COVID-19 during the first to fifth waves of infection: a report from the Japan COVID-19 Task Force. BMC Infect Dis. 2022.12; 22(1); 935
- 4. Noriyuki Takahashi, Takaharu Matsuhisa, Kunihiko Takahashi, Muneyoshi Aomatsu, Stewart W Mercer, Nobutaro Ban. A 2-item version of the Japanese Consultation and Relational Empathy measure: a pilot study using secondary analysis of a cross-sectional survey in primary care. Fam Pract. 2022.11; 39(6); 1169-1175
- 5. Miki Amemiya, Masateru Takigawa, Masahiko Goya, Claire A Martin, Tatsuhiko Anzai, Kunihiko Takahashi, Yuki Shimizu, Takashi Ikenouchi, Tatsuaki Kamata, Tasuku Yamamoto, Takuro Nishimura, Yasuhiro Shirai, Susumu Tao, Shinsuke Miyazaki, Tetsuo Sasano. Comparison of two catheters measuring local impedance: local impedance variation vs lesion characteristics and steam pops. J Interv Card Electrophysiol. 2022.11; 65(2); 419-428
- 6. Tatsuhiko Anzai, Kohtaro Kikuchi, Keisuke Fukui, Yuri Ito, Kunihiko Takahashi. Have restrictions on human mobility impacted suicide rates during the COVID-19 pandemic in Japan? Psychiatry Res. 2022.11; 317; 114898
- 7. Shintaro Shimizu, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tatsuhiko Anzai, Kunihiko Takahashi, Toshiaki Ueno, Kenji Fueki. Quantitative text analysis of the mechanisms of tooth injury: Analysis of accidents in five sports that occurred in 15 years under school control. Dent Traumatol. 2022.11;
- Keibun Liu, Kensuke Nakamura, Sapna R Kudchadkar, Hajime Katsukawa, Peter Nydahl, Eugene Wesley Ely, Kunihiko Takahashi, Shigeaki Inoue, Osamu Nishida. Mobilization and Rehabilitation Practice in ICUs During the COVID-19 Pandemic. J Intensive Care Med. 2022.09; 37(9); 1256-1264
- 9. Takahiro Mitsumura, Tsukasa Okamoto, Mizuho Tosaka, Takashi Yamana, Sho Shimada, Yuki Iijima, Rie Sakakibara, Sho Shibata, Takayuki Honda, Tsuyoshi Shirai, Masahiro Ishizuka, Junichi Aiboshi, Haruhiko Furusawa, Tomoya Tateishi, Meiyo Tamaoka, Hidenobu Shigemitsu, Hirokuni Arai, Yasuhiro Otomo, Shuji Tohda, Tatsuhiko Anzai, Kunihiko Takahashi, Shinsuke Yasuda, Yasunari Miyazaki. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Jpn J Infect Dis. 2022.09; 75(5); 504-510
- Keiji Oi, Hirokuni Arai, Eiki Nagaoka, Tatsuki Fujiwara, Kiyotoshi Oishi, Masashi Takeshita, Tatsuhiko Anzai, Tomohiro Mizuno. Long-term Outcomes of Papillary Muscle Relocation Anteriorly for Functional Mitral Regurgitation Interact Cardiovasc Thorac Surg.. 2022.09; ivac245
- 11. Ayako Morita, Yoshimitsu Takahashi, Kunihiko Takahashi, Takeo Fujiwara. Depressive symptoms homophily among community-dwelling older adults in japan: A social networks analysis. Front Public Health. 2022.09; 10; 965026
- 12. Akira Endo, Kazuma Yamakawa, Takashi Tagami, Yutaka Umemura, Kyosuke Takahashi, Hiroki Nagasawa, Yuichi Araki, Mitsuaki Kojima, Toshiki Sera, Masayuki Yagi, Ryo Yamamoto, Jiro Takahashi, Masaki Nakane, Chikashi Takeda, Chihiro Narita, Satoshi Kazuma, Hiroko Okura, Hiroyuki Takahashi, Takeshi Wada, Shu Tahara, Ayaka Matsuoka, Todani Masaki, Atsushi Shiraishi, Keiichiro Shimoyama, Yuta Yokokawa, Rintaro Nakamura, Hisako Sageshima, Yuichiro Yanagida, Kunihiko Takahashi, Yasuhiro Otomo. Optimal target blood pressure in elderly with septic shock (OPTPRESS) trial: study protocol for a randomized controlled trial. Trials. 2022.09; 23(1); 799
- 13. Toru Shirahata, Hideaki Sato, Sanehiro Yogi, Kaiji Inoue, Mamoru Niitsu, Hitoshi Miyazawa, Tomoe Akagami, Machika Soma, Tomohiko Mio, Makoto Nagata, Yuki Nishida, Shigeho Tanaka, Fuminori

Katsukawa, Hidetoshi Nakamura. Possible association of high-density lipoprotein cholesterol levels with trunk muscle deficits and decrease in energy expenditure in patients with or at risk for COPD: A pilot study. Respir Investig. 2022.09; 60(5); 720-724

- 14. Naho Yakuwa, Kunihiko Takahashi, Tatsuhiko Anzai, Naoki Ito, Mikako Goto, Sachi Koinuma, Chiaki Uno, Tomo Suzuki, Omi Watanabe, Akimasa Yamatani, Atsuko Murashima. Pregnancy Outcomes With Exposure to Second-Generation Antipsychotics During the First Trimester. J Clin Psychiatry. 2022.08; 83(4); 21m14081
- 15. Ho Namkoong, Ryuya Edahiro, Tomomi Takano, Hiroshi Nishihara, Yuya Shirai, Kyuto Sonehara, Hiromu Tanaka, Shuhei Azekawa, Yohei Mikami, Ho Lee, Takanori Hasegawa, Koji Okudela, Daisuke Okuzaki, Daisuke Motooka, Masahiro Kanai, Tatsuhiko Naito, Kenichi Yamamoto, Qingbo S Wang, Ryunosuke Saiki, Rino Ishihara, Yuta Matsubara, Junko Hamamoto, Hiroyuki Hayashi, Yukihiro Yoshimura, Natsuo Tachikawa, Emmy Yanagita, Takayoshi Hyugaji, Eigo Shimizu, Kotoe Katayama, Yasuhiro Kato, Takayoshi Morita, Kazuhisa Takahashi, Norihiro Harada, Toshio Naito, Makoto Hiki, Yasushi Matsushita, Haruhi Takagi, Ryousuke Aoki, Ai Nakamura, Sonoko Harada, Hitoshi Sasano, Hiroki Kabata, Katsunori Masaki, Hirofumi Kamata, Shinnosuke Ikemura, Shotaro Chubachi, Satoshi Okamori, Hideki Terai, Atsuho Morita, Takanori Asakura, Junichi Sasaki, Hiroshi Morisaki, Yoshifumi Uwamino, Kosaku Nanki, Sho Uchida, Shunsuke Uno, Tomoyasu Nishimura, Takashi Ishiguro, Taisuke Isono, Shun Shibata, Yuma Matsui, Chiaki Hosoda, Kenji Takano, Takashi Nishida, Yoichi Kobayashi, Yotaro Takaku, Noboru Takayanagi, Soichiro Ueda, Ai Tada, Masayoshi Miyawaki, Masaomi Yamamoto, Eriko Yoshida, Reina Hayashi, Tomoki Nagasaka, Sawako Arai, Yutaro Kaneko, Kana Sasaki, Etsuko Tagaya, Masatoshi Kawana, Ken Arimura, Kunihiko Takahashi, Tatsuhiko Anzai, Satoshi Ito, Akifumi Endo, Yuji Uchimura, Yasunari Miyazaki, Takayuki Honda, Tomoya Tateishi, Shuji Tohda, Naoya Ichimura, Kazunari Sonobe, Chihiro Tani Sassa, Jun Nakajima, Yasushi Nakano, Yukiko Nakajima, Ryusuke Anan, Ryosuke Arai, Yuko Kurihara, Yuko Harada, Kazumi Nishio, Tetsuya Ueda, Masanori Azuma, Ryuichi Saito, Toshikatsu Sado, Yoshimune Miyazaki, Ryuichi Sato, Yuki Haruta, Tadao Nagasaki, Yoshinori Yasui, Yoshinori Hasegawa, Yoshikazu Mutoh, Tomoki Kimura, Tomonori Sato, Reoto Takei, Satoshi Hagimoto, Yoichiro Noguchi, Yasuhiko Yamano, Hajime Sasano, Sho Ota, Yasushi Nakamori, Kazuhisa Yoshiya, Fukuki Saito, Tomoyuki Yoshihara, Daiki Wada, Hiromu Iwamura, Syuji Kanayama, Shuhei Maruyama, Takashi Yoshiyama, Ken Ohta, Hiroyuki Kokuto, Hideo Ogata, Yoshiaki Tanaka, Kenichi Arakawa, Masafumi Shimoda, Takeshi Osawa, Hiroki Tateno, Isano Hase, Shuichi Yoshida, Shoji Suzuki, Miki Kawada, Hirohisa Horinouchi, Fumitake Saito, Keiko Mitamura, Masao Hagihara, Junichi Ochi, Tomoyuki Uchida, Rie Baba, Daisuke Arai, Takayuki Ogura, Hidenori Takahashi, Shigehiro Hagiwara, Genta Nagao, Shunichiro Konishi, Ichiro Nakachi, Koji Murakami, Mitsuhiro Yamada, Hisatoshi Sugiura, Hirohito Sano, Shuichiro Matsumoto, Nozomu Kimura, Yoshinao Ono, Hiroaki Baba, Yusuke Suzuki, Sohei Nakayama, Keita Masuzawa, Shinichi Namba, Ken Suzuki, Yoko Naito, Yu-Chen Liu, Ayako Takuwa, Fuminori Sugihara, James B Wing, Shuhei Sakakibara, Nobuyuki Hizawa, Takayuki Shiroyama, Satoru Miyawaki, Yusuke Kawamura, Akiyoshi Nakayama, Hirotaka Matsuo, Yuichi Maeda, Takuro Nii, Yoshimi Noda, Takayuki Niitsu, Yuichi Adachi, Takatoshi Enomoto, Saori Amiya, Reina Hara, Yuta Yamaguchi, et al. DOCK2 is involved in the host genetics and biology of severe COVID-19. Nature. 2022.08; 609; 754-760
- 16. Qingbo S Wang, Ryuya Edahiro, Ho Namkoong, Takanori Hasegawa, Yuya Shirai, Kyuto Sonehara, Hiromu Tanaka, Ho Lee, Ryunosuke Saiki, Takayoshi Hyugaji, Eigo Shimizu, Kotoe Katayama, Masahiro Kanai, Tatsuhiko Naito, Noah Sasa, Kenichi Yamamoto, Yasuhiro Kato, Takayoshi Morita, Kazuhisa Takahashi, Norihiro Harada, Toshio Naito, Makoto Hiki, Yasushi Matsushita, Haruhi Takagi, Masako Ichikawa, Ai Nakamura, Sonoko Harada, Yuuki Sandhu, Hiroki Kabata, Katsunori Masaki, Hirofumi Kamata, Shinnosuke Ikemura, Shotaro Chubachi, Satoshi Okamori, Hideki Terai, Atsuho Morita, Takanori Asakura, Junichi Sasaki, Hiroshi Morisaki, Yoshifumi Uwamino, Kosaku Nanki, Sho Uchida, Shunsuke Uno, Tomoyasu Nishimura, Takashri Ishiguro, Taisuke Isono, Shun Shibata, Yuma Matsui, Chiaki Hosoda, Kenji Takano, Takashi Nishida, Yoichi Kobayashi, Yotaro Takaku, Noboru Takayanagi, Soichiro Ueda, Ai Tada, Masayoshi Miyawaki, Masaomi Yamamoto, Eriko Yoshida, Reina Hayashi, Tomoki Nagasaka, Sawako Arai, Yutaro Kaneko, Kana Sasaki, Etsuko Tagaya, Masatoshi Kawana, Ken Arimura, Kunihiko Takahashi, Tatsuhiko Anzai, Satoshi Ito, Kazue Fujita, Yoshinobu Saito, Masahiro Seike, Hiroko Watanabe, Hiroto Matsuse, Norio Kodaka, Chihiro Nakano, Takeshi Oshio, Takatomo Hirouchi, Shohei Makino, Moritoki Egi, Yosuke Omae, Yasuhito Nannya, Takafumi Ueno, Tomomi Takano, Kazuhiko Katayama, Masumi Ai, Atsushi Kumanogoh, Toshiro Sato, Naoki Hasegawa, Katsushi Tokunaga, Makoto Ishii, Ryuji Koike, Yuko Kitagawa, Akinori Kimura, Seiya Imoto, Satoru Miyano, Seishi Ogawa, Takanori

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- 18. Kazuki Nishida, Takuya Usami, Nana Matsumoto, Mitsuaki Nishikimi, Kunihiko Takahashi, Shigeyuki Matsui. The finger-to-nose test improved diagnosis of cerebrovascular events in patients presenting with isolated dizziness in the emergency department. Nagoya J Med Sci. 2022.08; 84(3); 621-629
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- 22. Takako Ishikawa, Sakiko Fukui, Junko Fujita, Aya Fujikawa, Yuka Iwahara, Kunihiko Takahashi. Factors Related to End-of-Life Care Discussions Among Community-Dwelling People in Japan. J Pain Symptom Manage. 2022.04; 63(4); 539-547
- 23. Hiroyuki Inose, Takashi Hirai, Toshitaka Yoshii, Atsushi Kimura, Katsushi Takeshita, Hirokazu Inoue, Asato Maekawa, Kenji Endo, Takuya Miyamoto, Takeo Furuya, Akira Nakamura, Kanji Mori, Shunsuke Kanbara, Shiro Imagama, Shoji Seki, Shunji Matsunaga, Kunihiko Takahashi, Atsushi Okawa. Factors contributing to neck pain in patients with degenerative cervical myelopathy: A prospective multicenter study. J Orthop Surg (Hong Kong). 2022.04; 30(1); 10225536221091848
- 24. Miki Amemiya, Masateru Takigawa, Masahiko Goya, Claire A Martin, Tatsuhiko Anzai, Kunihiko Takahashi, Yuki Shimizu, Takashi Ikenouchi, Tatsuaki Kamata, Tasuku Yamamoto, Takuro Nishimura, Yasuhiro Shirai, Susumu Tao, Shinsuke Miyazaki, Tetsuo Sasano. Comparison of two catheters measuring local impedance: local impedance variation vs lesion characteristics and steam pops. J Interv Card Electrophysiol. 2022.04;
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- Noriyuki Takahashi, Takaharu Matsuhisa, Kunihiko Takahashi, Nobutaro Ban. Diversity of academic general medicine: A cross-sectional bibliometric study of original English-language research articles in general medicine and cardiology in Japan. Medicine (Baltimore). 2022.03; 101(11);
- 28. Keibun Liu, Toru Kotani, Kensuke Nakamura, Takai Chihiro, Yasunari Morita, Kenzo Ishii, Kenji Fujizuka, Daisetsu Yasumura, Daisuke Taniguchi, Tomohiro Hamagami, Nobutake Shimojo, Masakazu Nitta, Takashi Hongo, Kazuki Akieda, Maeda Atsuo, Tadashi Kaneko, Yutaka Sakuda, Kohkichi Andoh, Akiyoshi Nagatomi, Yukiko Tanaka, Yuhei Irie, Hiroshi Kamijo, Manabu Hanazawa, Daisuke Kasugai, Matsuoka Ayaka, Kenji Oike, Alan Kawarai Lefor, Kunihiko Takahashi, Hajime Katsukawa, Takayuki

Ogura. Effects of evidence-based ICU care on long-term outcomes of patients with sepsis or septic shock (ILOSS): protocol for a multicentre prospective observational cohort study in Japan. BMJ Open. 2022.03; 12(3); e054478

- 29. Hidehiro Iwakawa, Masateru Takigawa, Masahiko Goya, Toyoto Iwata, Claire A Martin, Tatsuhiko Anzai, Kunihiko Takahashi, Miki Amemiya, Tasuku Yamamoto, Masahiro Sekigawa, Yasuhiro Shirai, Susumu Tao, Tatsuya Hayashi, Yoshihide Takahashi, Hiroyuki Watanabe, Tetsuo Sasano. Clinical implications of local impedance measurement using the IntellaNav MiFi OI ablation catheter: an ex vivo study. J Interv Card Electrophysiol. 2022.01; 63(1); 185-195
- 30. Toshihiro Sakakibara, Yuichiro Shindo, Daisuke Kobayashi, Masahiro Sano, Junya Okumura, Yasushi Murakami, Kunihiko Takahashi, Shigeyuki Matsui, Tetsuya Yagi, Hideo Saka, Yoshinori Hasegawa. A prediction rule for severe adverse events in all inpatients with community-acquired pneumonia: a multicenter observational study. BMC Pulm Med. 2022.01; 22(1); 34
- 31. Toru Shirahata, Yuki Nishida, Hideaki Sato, Sanehiro Yogi, Tomoe Akagami, Makoto Nagata, Shigeho Tanaka, Hidetoshi Nakamura, Fuminori Katsukawa. Impact of non-exercise activity thermogenesis on physical activity in patients with COPD. Sci Prog. 2022; 105(3); 368504221117064

AI Systems Medicine

Professor: Hideyuki Shimizu, MD, PhD

(1) **Outline**

We are a young team to solve life's mysteries and shape the future of medicine through data-driven biomedical research such as bioinformatics, mathematical modeling, and artificial intelligence. We just started up in February 2022, and motivated students are beginning to join us.

(2) Publications

[Original Articles]

- 1. Hozumi H, Shimizu H. Bayesian network enables interpretable and state-of-the-art prediction of immunotherapy responses in cancer patients medRxiv. 2022.11;
- 2. Habara M, Sato Y, Goshima T, Sakurai M, Imai H, Shimizu H, Katayama Y, Hanaki S, Masaki T, Morimoto M, Nishikawa S, Toyama T, Shimada M. FKBP52 and FKBP51 Differentially Regulate the Stability of Estrogen Receptor in Breast Cancer Proc Natl Acad Sci U S A. 2022.04; 119(15); e2110256119
- 3. Mise S, Matsumoto A, Shimada K, Hosaka T, Takahashi M, Ichihara K, Shimizu H, Shiraishi C, Saito D, Suyama M, Yasuda T, Ide T, Izumi Y, Bamba T, Kimura-Someya T, Shirouzu M, Miyata H, Ikawa M, Nakayama KI. Kastor and Polluks polypeptides encoded by a single gene locus cooperatively regulate VDAC and spermatogenesis. Nature communications. 2022.02; 13(1); 1071

Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi Assistant Professor: Kenta Iitani Lecturer (part-time): Takahiro Arakawa Lecturer (part-time): Koji Toma Lecturer (part-time): Kazuyoshi Yano Lecturer (part-time): Yasuhiko Iwasaki Lecturer (part-time): Naoya Takeda Lecturer (part-time): Tomoko Gessei

(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-continuos (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 Engineering", "Biomedical Device Science and Engineering", "Wearable & IoT Devices and Applications", "Advanced Biomedical Devices", "Integrative Biomedical Sciences for Preemptive Medicine", and "Advanced Medical Device and System"), 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. Tomoko Gessei, Akira Monkawa, Takahiro Arakawa, Kohji Mitsubayashi. Blood sorbitol measurement in diabetic rats treated with an aldose reductase inhibitor using an improved fiber-optic sorbitol biosensor Talanta. 2022.10; 248; 123595
- 2. Koji Toma, Koki Oishi, Kenta Iitani, Arakawa Takahiro, Kohji Mitsubayashi. Surface plasmon-enhanced fluorescence immunosensor for monitoring cardiac troponin I Sensors and Actuators B: Chemical. 2022.10; 368; 132132
- 3. Kenta Iitani, Misa Nakaya, Tsubomi Tomono, Koji Toma, Takahiro Arakawa, Yuji Tsuchido, Kohji Mitsubayashi, Naoya Takeda. Enzyme-embedded electrospun fiber sensor of hydrophilic polymer for fluorometric ethanol gas imaging in vapor phase Biosensors and Bioelectronics. 2022.10; 213; 114453
- 4. Takahiro Arakawa, Riki Ishikawa, Kenta Iitani, Koji Toma, Yasuhiko Iwasaki, Kohji Mitsubayashi. Headset bio-sniffer with wireless CMOS camera for percutaneous ethanol vapor from the ear canal Biosensors and Bioelectronics:X. 2022.09; 11; 100169
- 5. Takahiro Arakawa, Koji Kurihara, Daisuke Mori, Koji Toma, Kazuyoshi Yano, Kohji Mitsubayashi. Glucose-driven Monolithic Polydimethylsiloxane Decompression Unit for Drug Release Device Using Plasma-activated Bonding Technology Sensors and Materials. 2022.04; 34(4); 1501-1514

[Books etc]

1. Takahiro Arakawa, Kenta Iitani, Koji Toma, and Kohji Mitsubayashi. "Encyclopedia of Sensors and Biosensors" - 1st Edition. Elsevier Ltd, 2022.10 (ISBN : 9780128225486)

[Misc]

- 1. Kohji Mitsubayashi, Koji Toma, Kenta Iitani, Takahiro Arakawa. Gas-phase biosensors: a review Sensors and Actuators B: Chemical. 2022.09; 367; 132053
- Takahiro Arakawa, Dzung Viet Dao, Kohji Mitsubayashi. Biosensors and Chemical Sensors for Healthcare Monitoring: A Review IEEJ Transactions on Electrical and Electronic Engineering. 2022.03; 17(5); 626-636
- 1. Kohji Mitsubayashi. Non-Invasive Bio-Photometric Sensing and Imaging for Volatile Makers Japanese journal of optics : publication of the Optical Society of Japan. 2022.11; 51(11); 476-483

[Conference Activities & Talks]

1. Kohji Mitsubayashi. Mouthguard biosensor with Bluetooth module for tele-monitoring in the oral cavity. SFT-22 2022.11.09 Brisbene

- 2. Kenta Iitani, Zhang Geng, Naoki Mizukoshi, Ming Ye, Po-Jen Chien, Kohji Mitsubayashi. Screening diabetes mellitus through monitoring lipid metabolism by measuring and imaging breath acetone using bio-fluorometric gas sensors. Breth biopsy conference 2022 2022.11.01 Online
- 3. Toma K, Oishi K, Iitani K, Arakawa T, Mitsubayashi K. Surface plasmon-enhanced fluorescence immunosensor with a regeneratable surface for monitoring cardiac markers. THE 22ND INTERNATIONAL VACUUM CONGRESS IVC-22 2022.09.14 Sapporo, Japan
- 4. Mitsubayashi K. Gas-phase biosensor for exhaled acetone as an early diagnostic marker for diabetes. ATTD 2022 2022.04.27 Barcelona, Spain and online
- 5. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Enzyme-based biofluorometric gas-imaging system "sniff-cam" for spaciotemporal measurement of human-derived volatile organic compounds. The 11th Advanced Lasers and Photon Sources (ALPS2022) 2022.04.18 Yokohama, Japan and online
- 6. Iitani K, Toma K, Mitsubayashi K. Measuring and imaging of volatile organic compounds emanated via the human skin. The 8th Joint Symposium between IBB/TMDU and Chulalongkorn University on "Biomedical Materials and Engineering" 2022.01.25 online

[Social Contribution]

1. SENSOR EXPO JAPAN, 2022.09.14 - 2022.09.16

Biomedical Information

Professor Yoshikazu NAKAJIMA Associate Professor Shinya ONOGI Assistant Professor Toshihiro KAWASE Takaaki SUGINO Dongbo ZHOU Researcher Pei JIANG Research Assistant Teruyo MORI Graduate Student Misato SHIMIZU Yuya ISHIKAWA Yunaho YONEMITSU Satoshi ISHIDA Jun Feng XUAN Xiaoxi ZHOU Ruiqi ZHANG Longfei ZHAO Hiroyuki HAYASHI Haruka HORIUCHI Azusa MINEMURA Koshiro OKUMOTO Yiqiang XU Yoshiki YASHIMA Yu INAOKA Hengbing GE Kirari SAITO Satoshi TAKAHASHI Tetsutomo YONEYAMA

(1) Research

- 1. Medical data analysis with complex artificial intelligence
- 2. Deep-Learning segmentation and annotation on multi-model medical images
- 3. Surgical navigation system with deformation tracking of soft tissues
- 4. Pneumatic stiffness-tunable mechanism and its application for laparoscopic surgeries

(2) Publications

[Original Articles]

1. Ogawa Takahisa, Yoshii Toshitaka, Oyama Jun, Sugimura Nobuhiro, Akada Takashi, Sugino Takaaki, Hashimoto Motonori, Morishita Shingo, Takahashi Takuya, Motoyoshi Takayuki, Oyaizu Takuya, Yamada
Tsuyoshi, Onuma Hiroaki, Hirai Takashi, Inose Hiroyuki, Nakajima Yoshikazu, Okawa Atsushi. Detecting ossification of the posterior longitudinal ligament on plain radiographs using a deep convolutional neural network: a pilot study SPINE JOURNAL. 2022.06; 22(6); 934-940

2. Fukushima Katsuhiko, Miyazaki Tetsuro, Kawase Toshihiro, Kanno Takahiro, Sogabe Maina, Nakajima Yoshikazu, Kawashima Kenji. A pneumatic rotary actuator for forceps tip rotation SENSORS AND ACTUATORS A-PHYSICAL. 2022.01; 333;

- Sugino T, Ishikawa Y, Okubo K, Nakajima Y. Convolutional neural network-based lesion detection for thoracoscopic lung cancer surgery. The 7th International Symposium on Biomedical Engineering (ISBE 2022) 2022.11.25
- Sugino T, Kin T, Saito N, Nakajima Y. Automatic segmentation of basal ganglia on MRI images using fully convolutional network. The 7th International Symposium on Biomedical Engineering (ISBE 2022) 2022.11.25
- 3. Kasahara D, Iwazaki H, Takei M, Sugino T, Onogi S, Nakajima Y, Masuda K. Automatic extraction of blood vessel network using image processing based on Hessian matrix in ultrasonic volume. The 43rd Symposium on UltraSonic Electronics (USE 2022) 2022.11.08
- 4. Nakajima Y. Current trends of AI healthcare. The 8th International Symposium on the Dialogue for Global Innovation (DFGI 2022) 2022.10.06
- Sugino T, Kin T, Saito N, Nakajima Y. Two-stage convolutional neural network-based approach for improved segmentation of basal ganglia on MR images. 2022 Computer Assisted Radiology and Surgery International Congress (CARS 2022) 2022.06.07

Material-Based Medical Engineering

Professor Akio Kishida Associate Professor Tsuyoshi Kimura Assistant Professor Yoshihide Hashimoto Project Researcher Mako Kobayashi Research Assistant Moeko Hagiwara Secretary Naomi Hiwatari Lecturer(part-time) Hisatoshi Kobayashi Lecturer(part-time) Hisatoshi Kobayashi Lecturer(part-time) Seiichi Funamoto Lecturer(part-time) Akitatsu Yamashita Lecturer(part-time) Masaki Tabuchi Lecturer(part-time) Jun Negishi Lecturer(part-time) Naoko Nakamura Lecturer(part-time) Yongwei Zhang

Doctor Course Student Takuya Konishi Kohei Yabuuchi Shota Toda Say Sreypich Mika Suzuki

(1) **Outline**

Our laboratory has dealt with many research topics from the fundamental study of biomaterials in terms of material engineering to the application study of the medical devices. The keywords 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 systems 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 researches aimed at specific clinical applications using cell engineering and genetic engineering techniques. Target fields are development of novel medical material, regenerative medicine, gene therapy, and treatment engineering.

(1) Regenerative medicine using decellularized biological tissue

For removing immunogenicity, biological tissues are decellularized using a novel processing method, high-hydrostatic pressure (HHP) method. We have demonstrated that decellularized biological tissues are promising materials in tissue engineering and regenerative medicine fields.

(2) Development of processing and high-performance technology for biological materials

This research focuses on developing functional materials with novel functions by processing biological materials. Specifically, we are conducting research on processing into powders, fibers, and hydrogels, and hybrid technology with functional molecules.

(3) Development of inflammatory evaluation method for biomaterials

Macrophages are polarized into an inflammatory type (M1 type) that contributes to inflammation and an anti-inflammatory type (M2 type) that contributes to healing. We are developing an inflammatory evaluation method for biomaterials using macrophage polarization in vitro.

(4) Immune control systems: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulate immune reactions, anti-tumor immune responses can be enhanced. We are developing novel biomaterials and technologies to capture and release Treg using interfacial science.

(3) Education

Our laboratory is in charge of lectures on "Medical Materials Engineering", "Applied Biomaterials", and "Medical, Dental and Pharmaceutical Industrial Engineering" in the graduate school, and "Biomedical Engineering" in the faculty.

Through these lectures, we will explain from the basic knowledge of various materials to the molecular design theory required for device development.

(4) Publications

- 1. Wen-Jin Ho, Mako Kobayashi, Kozue Murata, Yoshihide Hashimoto, Kenji Izumi, Tsuyoshi Kimura, Hideo Kanemitsu, Kazuhiro Yamazaki, Tadashi Ikeda, Kenji Minatoya, Akio Kishida, Hidetoshi Masumoto. A novel approach for the endothelialization of xenogeneic decellularized vascular tissues by human cells utilizing surface modification and dynamic culture. Scientific Reports. 2022.12; 12(1); 22294
- Mika Suzuki, Tsuyoshi Kimura, Yuta Nakano, Mako Kobayashi, Masahiro Okada, Takuya Matsumoto, Yoshihide Hashimoto, Akio Kishida. Preparation of mineralized pericardium by alternative soaking for soft-hard interregional tissue application Journal of Biomedical Materials Research Part A. 2022.09; 1; 1-11
- Anri Koyanagi, Iichiroh Onishi, Karin Muraoka, Ikue Sato, Shingo Sato, Tsuyoshi Kimura, Akio Kishida, Kouhei Yamamoto, Masanobu Kitagawa, Morito Kurata. Identification of the factor that leads human mesenchymal stem cell lines into decellularized bone Bioengineering (Basel). 2022.09; 9(10); 490
- 4. Mako Kobayashi, Naoki Ishida, Yoshihide Hashimoto, Jun Negishi, Hideki Saga, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. Extraction and biological evaluation of atrix-bound nanovesicles (MBVs) from high-hydrostatic pressure-decellularized tissues. International Journal of Molecular Science. 2022.08; 23(16); 8868
- Mika Suzuki, Tsuyoshi Kimura, Yukina Yoshida, Mako Kobayashi, Yoshihide Hashimoto, Hironobu Takahashi, Tatsuya Shimizu, Shota Anzai, Naoko Nakamura, Akio Kishida. In vitro tissue reconstruction using decellularized pericardium cultured with cells for ligament regeneration Polymers. 2022.06; 14(12); 2351
- 6. Masahiro Yamada, Tsuyoshi Kimura, Naoko Nakamura, Jun Watanabe, Ndia Kartikasari, Xindie He, Watcharaphol Tiskratok, Hayato Yoshioka, Hidenori Shinno, Hiroshi Egusa. The titanium nanosurface with biomimetic physical microenvironment to induce endogenous regeneration of the periodontium ACS Applied Materials & Interfaces. 2022.06; 14(24); 27703-27719
- 7. Yutaro Hayakawa, Masato Furuya, Hironobu Tahara, Yasuhiro Kosuge, Tsuyoshi Kimura, Kosuke Sugawa, Joe Otsuki. Modulation technique of localized surface plasmon resonance of palladium nanospheres by coating with titanium dioxide shell for application to photothermal therapy agent Nanoscale Research Letters. 2022.06; 17; 60
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- 9. Hiroki Tsutsumi, Ryota Kurimoto, Ryo Nakamichi, Tomoki Chiba, Takahide Matsushima, Yuta Fujii, Risa Sanada, Tomomi Kato, Kana Shishido, Yuriko Sakamaki, Tsuyoshi Kimura, Akio Kishida, Hiroshi Asahara. Generation of a tendon-like tissue from human iPS cells. J Tissue Eng. 2022.01; 13; 20417314221074018
- Narintadeach Charoensombut, Kinyoshi Kawabata, Jeonghyun Kim, Minki Chang, Tsuyoshi Kimura, Akio Kishida, Takashi Ushida, Katsuko S Furukawa. Internal radial perfusion bioreactor promotes decellularization and recellularization of rat uterine tissue Journal of Bioscience and Bioengineering. 2022.01; 133(1); 83-88

[Conference Activities & Talks]

- 1. Mako Kobayashi, Tsuyoshi Kimura, Akio Kishida, Masaya Yamamoto . The effect of decellularized tissue-derived hydrogels on cancer cell behavior. The 7th International Symposium on Biomedical Engineering (ISBE2022) 2022.11.25 Online
- 2. WenJin Ho, Hidetoshi Masumoto, Mako Kobayashi, Kozue Murata, Tadashi Ikeda, Yoshihide Hashimoto, Tsuyoshi Kimura, Kenji Minatoya, Akio Kishida. A novel approach for pre-implant endothelialization of xenogeneic decellularized vascular tissues by human endothelial cells utilizing tissue surface modification and dynamic culture. American Heart Association 2022 Scientific Sessions 2022.11.04 Chicago, USA
- 3. Yoshihide Hashimoto, Takuya Akizawa, Moeko Hagiwara, Mako Kobayashi, Tsuyoshi Kimura, Akio Kishida. Cellular behaviors of human skeletal muscle satellite cells on tissue specific extracellular matrix coating and hydrogels. Visual-JW 2022 2022.10.25 Osaka, Japan
- 4. Tsuyoshi Kimura, Mika Suzuki, Mako Kobayashi, Masahiro Okada, Takuya Matsumoto, Naoko Nakamura, Yoshihide Hashimoto, Akio Kishida. Development of a mineralized decellularized tissue for soft-hard inter-regional tissue application. TERMIS-AP 2022 2022.10.05 Jeju, South Korea
- 5. Mako Kobayashi, Naoki Ishida, Yoshihide Hashimoto, Jun Negishi, Hideki Saga, Takehiro Iwanaga, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. The effects of matrix-bound nanovesicles(MBVs) derived from high-hydrostatic pressure decellularized tissued on neural regeneration. TERMIS-AP 2022 2022.10.05 Jeju, South Korea

[Patents]

- 1. ANTI-ADHESION MATERIAL AND SUBSTITUTE BIOMEMBRANE USING DECELLULARIZED TISSUE, Patent Number : CA 2978401
- 2. ANTI-ADHESION MATERIAL AND SUBSTITUTE BIOMEMBRANE USING DECELLULARIZED TISSUE, Patent Number : CA 2978401
- 3. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : KR 2376321
- 4. ANTI-ADHESION MATERIAL AND ARTIFICIAL BIOLOGICAL MEMBRANE EACH COMPRISING DECELLULARIZED TISSUE, Patent Number : KR 2376321

Organic and Medicinal Chemistry

Professor Hiroyuki KAGECHIKA Associate Professor Shinya Fujii Assistant Professor Ryosuke ISHIDA Assistant Professor Ma Yue (RCC) Eng. Official Hiroyuki Masuno (RCC) Eng. Official Michiko Nakaishi (RCC)

Graduate Student Yu Miyajima Kotaro Ochiai Nao Namba Zeng Xi Zhang Huize Kanon Nishizono Sae Handa Yuuki Hosaka Ayaka Nakamichi Sheng Jingwen Guo Xiaoyue Tsukasa Saito Undergraduate student Tomoki Ovamada Kaho Fujii Research student Rvo Yonezawa

(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 foe 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]

- Murayama, T.; Kurebayashi, N.; Numaga-Tomita, T.; Kobayashi, T.; Okazaki, S.; Yamashiro, K.; Nakada, T.; Mori, S.; Ishida, R.; Kagechika, H.; Yamada, M.; Sakurai, T.. A reconstituted depolarization-induced Ca2+ release platform for validation of skeletal muscle disease mutations and drug discovery. J. Gen. Physiol.. 2022.12; 154(12); e202213230
- Tsuboi, Y.; Oyama, K.; Kobirumaki-Shimozawa, F.; Murayama, T.; Kurebayashi, N.; Tachibana, T.; Manome, Y.; Kikuchi, E.; Noguchi, S.; Inoue, T.; Inoue, Y. U.; Nishino, I.; Mori, S.; Ishida, R.; Kagechika, H.; Suzuki, M.; Fukuda, N.; Yamazawa, T.. Mice with R2509C-RYR1 mutation exhibit dysfunctional Ca2+ dynamics in primary skeletal myocytes J. Gen. Physiol.. 2022.12; 154; e202213136
- Yamada, S.; Masuno, H.; Kagechika, H.; Tanatani, A.; Kanda, Y. A Novel Lithocholic Acid Derivative Upregulates Detoxification-Related Genes in Human Induced Pluripotent Stem Cell-Derived Intestinal Organoids. Biol. Pharm. Bull. 2022.11; 45(1720); 1724
- 4. Ishida, R.; Mori, S.; Murayama, T.; Nakamichi, A.; Chai, X.; Kurebayashi, N. Iinuma, H.; Kagechika, H.. Development of a water-soluble ryanodine receptor 1 inhibitor. Bioorg. Med. Chem. 2022.09; 74; 117027
- Mori, S.; Tsuemoto, N.; Kawachi, E.; Takubo, C.; Tanatani, A.; Kagechika, H.. Development of retinoic acid receptor antagonists bearing trans-SF4-alkynyl structure as a linear linker. Tetrahedron . 2022.08; 123; 132967
- 6. Hara, Y.; Ando, F.; Oikawa, D.; Ichimura, K.; Yanagawa, H.; Sakamaki, Y.; Nanamatsu, A.; Fujiki, T.; Mori, S.; Suzuki, S.; Yui, N.; Mandai, S.; Susa, K.; Mori, T.; Sohara, E.; Rai, T.; Takahashi, M.; Sasaki, S.; Kagechika, H.; Tokunaga, F.; Uchida, S., LRBA is essential for urinary concentration and body water homeostasis Proc. Natl. Acad. Sci. USA. 2022.07; 119(30); e2202125119
- 7. Oikawa, T.; Fujii, S.; Mori, S.; Masuno, H.; Kawachi, E.; Kagechika, H. . Structural Development of Silicon-Containing Retinoids: Structure–Activity Relationship Study of the Hydrophobic Pharmacophore of Retinobenzoic Acids Using Silyl Functionalities ChemMedChem. 2022.06; e202200176
- 8. Yoshihara, A.; Kawasaki, H.; Masuno, M.; Takada, K.; Numoto, N.; Ito, N.; Hirata, N.; Kanda, Y.; Ishizawa, M.; Makishima, M.; Kagechika, H.; Tanatani, A.. Lithocholic Acid Amides as Potent Vitamin D Receptor Agonists Biomolecules. 2022.01; 12(1); 130

- 1. Ryosuke Ishida, Saki Haraoka, Shuichi Mori, Fumiaki Ando, Shinichi Uchida, Hiroyuki Kagechika. Development of small molecule inducing phosphorylation of perilipin for anti-obesity drug. The 7th International Symposium on Biomedical Engineering 2022.11.25
- 2. Xi Zeng, Ryosuke Ishida, Nagomi Kurebayashi, Murayama Takashi, Yuuga Yamamoto, Shuichi Mori, Hiroyuki Kagechika. Development of novel RyR2 selective inhibitor. The 7th International Symposium on Biomedical Engineering 2022.11.25

- 3. Saki Hatsuzawa, Ryosuke Ishida, Hiroyuki Baba, Tadashi Hosoya, Hiroyuki Kagechika. Development of novel immunosuppressive compounds leading anti-inflammatory effect. The 7th International Symposium on Biomedical Engineering 2022.11.25
- 4. Yoshihiro Tada, Shuto Kawasaki, Hiroyuki Kagechika, Shinya Fujii. Structure-property relationship and PR antagonistic activity of N-phenylphosphinamide derivatives. The 7th International Symposium on Biomedical Engineering 2022.11.25
- 5. Takashi Murayama, Nagomi Kurebayashi, Ryosuke Ishida, Hiroyuki Kagechika. Reconstitution of depolarization-induced Ca2+ release platform for validation of skeletal muscle disease mutations and drug discovery. The 7th International Symposium on Biomedical Engineering 2022.11.25
- 6. Hiroyuki Baba, Tadashi Hosoya, Yuma Kondo, Saki Hatsuzawa, Ryosuke Ishida, Hiroyuki Kagechika, Shinsuke Yasuda. Anti-inflammatory effects of novel NF- κ B inhibitory compounds in two inflammatory animal models. The 7th International Symposium on Biomedical Engineering 2022.11.25
- 7. 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
- 8. 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	Takashi NIWA	
Assistant Professor	Junpei TAGUCHI	
Assistant Professor	Yuki SAKATA	
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	Miho HANYA	
Graduate Students	Akihiro KOBAYASHI, Yohei OHATA,	
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	Kento TOKUNAGA, Takumi OKUYAMA,	
	Kyoko TAKAHASHI, Miho NAKAJIMA	
Collaborators	Ryuji ISODA, Yamato EZOU,	
	Kayato NISHIDA, Daisuke YAMANAKA,	
	Yuting ZHANG, Wenkang ZHAO	

(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 chemical modification methods of biomolecules by strained alkynes.

3. Target protein identification of bioactive compounds based on radioisotope-free (non-RI) photoaffinity labeling based on diazido probe strategy.

4. Development of new methods to efficiently connect multiple molecules based on the characteristic features of azido group.

5. Development of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

(3) Publications

- 1. Katayama A, Jin Y, Nishiyama Y, Hosoya T, Yokoshima S. Substitution of α -Azido Sulfones with Thiolates to Form α -Azido Sulfides. Org Lett. 2022.10; 24(40); 7361-7365
- 2. Inouye S, Sato J, Sahara-Miura Y, Tomabechi Y, Sumida Y, Sekine S, Shirouzu M, Hosoya T. Reverse mutants of the catalytic 19 kDa mutant protein (nanoKAZ/nanoLuc) from *Oplophorus* luciferase with coelenterazine as preferred substrate. PLoS One. 2022.09; 17(9); e0272992
- 3. Watanabe K, Kuratsu A, Hashizume D, Niwa T, Hosoya T. Red light-induced conjugation of amines through amide bond formation triggered via photooxidation of 3-acylindolizines. Commun Chem. 2022.08; 5(1); 91

- 4. Sugiyama K, Sakata Y, Niwa T, Yoshida S, Hosoya T. Azido-type-selective triazole formation by iridium-catalyzed cycloaddition with thioalkynes. Chem Commun. 2022.05; 58(42); 6235-6238
- 5. Fukuchi T, Niwa T, Hosoya T, Watanabe Y. Computational study for amino acid production from carboxylic acid via 14 C β -decay. J Phys Soc Jpn. 2022.04; 91(6); 064301
- 6. Nagai A, Kobayashi A, Sakata Y, Minami Y, Uchida K, Hosoya T, Yoshida S. Synthesis of Multisubstituted Benzenes from Phenols via Multisubstituted Benzynes. Synthesis. 2022.04; 54(22); 5017-5025
- Idogawa R, Kobayashi A, Kim Y, Shimomori K, Hosoya T, Yoshida S. Hydride reduction of o-(fluorosilyl)benzodifluorides for subsequent C-F transformations. Chem Commun. 2022.03; 58(21); 3521-3524
- 8. Kimura N, Saito K, Niwa T, Yamanaka M, Igaue S, Ohkanda J, Hosoya T, Kii I. Expression and purification of DYRK1A kinase domain in complex with its folding intermediate-selective inhibitor FINDY. Protein Expres Purif. 2022.03;
- 9. Nakaoka T, Kaneko K, Irie S, Mawatari A, Igesaka A, Uetake Y, Ochiai H, Niwa T, Yamano E, Wada Y, Tanaka M, Kotani K, Kawahata H, Kawabe J, Miki Y, Doi H, Hosoya T, Maeda K, Kusuhara H, Sugiyama Y, Watanabe Y. Clinical evaluation of [¹⁸F] pitavastatin for quantitative analysis of hepatobiliary transporter activity. Drug Metab Pharmacok. 2022.02;
- 10. Takemura H, Orimoto G, Kobayashi A, Hosoya T, Yoshida S. Modular synthesis of triazoles from 2-azidoacrylamides having a nucleophilic amino group. Org Biomol Chem. 2022.02;
- 11. Miyazaki Y, Kikuchi M, Umezawa K, Descamps A, Nakamura D, Furuie G, Sumida T, Saito K, Kimura N, Niwa T, Sumida Y, Umehara T, Hosoya T, Kii I. Structure-activity relationship for the folding intermediate-selective inhibition of DYRK1A. Eur J Med Chem. 2022.01; 227; 113948
- Inouye S, Nakamura M, Hosoya T. Enzymatic conversion of dehydrocoelenterazine to coelenterazine using FMN-bound flavin reductase of NAD(P)H:FMN oxidoreductase. Biochem Biophys Res Commun. 2022.01; 587; 24-28

- 1. Yang G, Furutani Y, Aoyagi H, Ueda R, Sonobe M, Wakae K, Ogawa K, Niwa T, Kobayashi K, Hosoya T, Kanayama Y, Watanabe Y, Nagoshi S, Matsuura T, Muramatsu M, Wakita T, Aizaki H. Construction of an animal model transplanted with HBV-producing cells for hepatitis B drug discovery. 2022 International HBV Meeting 2022.09.19 France
- Niwa T. Borylation-Based Synthetic Strategies for Expeditious Development of Molecular Probes. Department Seminar Series (Department of Chemistry, National University of Singapore) 2022.09.07 Singapore
- 3. Niwa T. Novel synthetic strategies for molecular probes. RIKEN-NTU Neuroscience Workshop 2022.09.05 Singapore
- 4. Niwa T. Borylation-Based Synthetic Strategies for Expeditious Development of Molecular Probes. CCEB Seminar (School of Chemistry, Chemical Engineering and Biotechnology, Nanyang Technological University) 2022.09.05 Singapore
- 5. Uetake Y, Niwa T, Hosoya T, Sakurai H. Mechanistic study on Lewis acid-mediated Suzuki–Miyaura cross-coupling reaction. 2022.07.27 Fukuoka

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D. Associate Professor Kohei TSUJI, Ph.D. Assistant Professor Takuya KOBAYAKAWA, Ph.D. Research Fellow Kofi Baffour-Awuah Owusu, Ph.D. Technical Assistant Ami MASUDA Technical Assistant Hiroko TAKAGI Technical Assistant Maiko HIRAYAMA Technical Assistant Mamiko HAYAKAWA Assistant Tomoe KAMEI Technical Assistant Tomoe KAMEI

Graduate students

D3 Kofi Baffour-Awuah Owusu, WANG RONGYI D2 Takahiro ISHII D1 Peter Bolah M2 Takato ONISHI, Akane KUDO, Hiroki NAKANO, Miki HORI, Naoya WADA, Shun KAWAKATSU, Yuki KISHIHARA, Yutaro MIURA M1 Koki SHINOHARA, Akito MOCHIZUKI, Kenichi YAMAMOTO, HUANG XUEYUAN

Internal Collaborators LI DONGRUI, HUANG XUEYUAN

External Collaborators Kaito HAYAKAWA

(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 proteins, TALEN and CRISPR-Cas9 for gene therapy and nanotechnology.

Utilizing DNA sequence-specific recognition of zinc finger proteins, TALEN and CRISPR-Cas9, 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. Kaho Matsumoto, Takeo Kuwata, William D Tolbert , Jonathan Richard, Shilei Ding, Jérémie Prévost, Shokichi Takahama, George P Judicate, Takamasa Ueno, Hirotomo Nakata, Takuya Kobayakawa, Kohei Tsuji , Hirokazu Tamamura, Amos B Smith 3rd, Marzena Pazgier, Andrés Finzi, Shuzo Matsushita.

Characterization of a Novel CD4 Mimetic Compound YIR-821 against HIV-1 Clinical Isolates. Journal of virology. 2022.12; e0163822

- Rongyi Wang, Kohei Tsuji, Takuya Kobayakawa, Yishan Liu, Kazuhisa Yoshimura, Shuzo Matsushita, Shigeyoshi Harada, Hirokazu Tamamura. Hybrids of small CD4 mimics and gp41-related peptides as dual-target HIV entry inhibitors Bioorganic & Medicinal Chemistry. 2022.12; 76; 117083
- 3. Kohei Tsuji, Takahiro Ishii, Takuya Kobayakawa, Nobuyo Higashi-Kuwata, Chika Azuma, Miyuki Nakayama, Takato Onishi, Hiroki Nakano, Naoya Wada, Miki Hori, Kouki Shinohara, Yutaro Miura, Takuma Kawada, Hironori Hayashi, Shin-Ichiro Hattori, Haydar Bulut, Debananda Das, Nobutoki Takamune, Naoki Kishimoto, Junji Saruwatari, Tadashi Okamura, Kenta Nakano, Shogo Misumi, Hiroaki Mitsuya, Hirokazu Tamamura. Potent and biostable inhibitors of the main protease of SARS-CoV-2. iScience. 2022.11; 25(11); 105365
- 4. Kohei Tsuji, David Hymel, Buyong Ma, Hirokazu Tamamura, Ruth Nussinov, Terrence R Burke Jr. Development of ultra-high affinity bivalent ligands targeting the polo-like kinase 1. RSC chemical biology. 2022.08; 3(9); 1111-1120
- 5. Kohei Tsuji, Takuya Kobayakawa, Kiju Konno, Ami Masuda, Kohei Takahashi, Nami Ohashi, Kazuhisa Yoshimura, Takeo Kuwata, Shuzo Matsushita, Shigeyoshi Harada, Hirokazu Tamamura. Exploratory studies on soluble small molecule CD4 mimics as HIV entry inhibitors. Bioorganic & Medicinal Chemistry. 2022.02; 56; 116616

- 1. Kofi Baffour-Awuah Owusu , Kohei Tsuji , Takuya Kobayakawa , Youichi Suzuki, Hirokazu Tamamura. Development of SARS-CoV-2 Fusion Inhibitor Peptides Based on SARS-CoV-2 HR-2. The 39th Medicinal Chemistry Symposium 2022.11.23 Online
- 2. Kohei Tsuji, Kofi Baffour-Awuah Owusu, Takuya Kobayakawa, Youichi Suzuki, Hirokazu Tamamura. Development of fusion inhibitor peptides of SARS-CoV-2 learned from anti-HIV-1 agents. The 59th Japanese Peptide Symposium 2022.10.26 Sendai
- 3. Kouki Shinohara, Kohei Tsuji, Takahiro Ishii, Takuya Kobayakawa, Nobuyo Higashi-Kuwata, Yutaro Miura, Hironori Hayashi, Shin-ichiro Hattori, Haydar Bulut, Shogo Misumi, Hiroaki Mitsuya, Hirokazu Tamamura. Structure-activity relationship studies of SARS-CoV-2 main protease inhibitors. The 59th Japanese Peptide Symposium 2022.10.26 Sendai
- 4. Yutaro Miura, Takuya Kobayakawa, Kohei Tsuji, Kiju Konno, Ami Masuda, Nami Ohashi, Takeo Kuwata, Kazuhisa Yoshimura, Tomoyuki Miura, Shigeyoshi Harada, Shuzo Matsushita, Hirokazu Tamamura. Pegylated CD4 mimics as HIV inhibitors. The 59th Japanese Peptide Symposium 2022.10.26 Sendai
- 5. Takahiro Ishii, Kohei Tsuji, Takuya Kobayakawa, Nobuyo Higashi-Kuwata, Chika Azuma, Miyuki Nakayama, Kouki Shinohara, Yutaro Miura, Hironori Hayashi, Shin-ichiro Hattori, Haydar Bulut, Shogo Misumi, Hiroaki Mitsuya, Hirokazu Tamamura. Synthesis of inhibitors targeting the main protease of SARS-CoV-2 for therapeutics of COVID-19. The 59th Japanese Peptide Symposium 2022.10.26 Sendai
- 6. Kohei Tsuji, Rongyi Wang, Kofi Baffour-Awuah Owusu, Takuya Kobayakawa, Tsutomu Murakami, Hirokazu Tamamura. Exploration of novel class anti-HIV-1 agents derived from a viral capsid protein. 36th European and 12th International Peptide Symposium 2022.08.29 Spain
- 7. Hirokazu Tamamura . From HIV to SARS-CoV-2: Fusion Inhibitors Based on Dimerization of HR2 Region Peptides. Frontiers in Peptide Science and Drug Discovery: A Scientific Symposium in Honor of Professor James P. Tam 2022.08.05 Singapore
- 8. Hirokazu Tamamura. Medicinal chemistry based on peptidomimetics. The 8th Joint Symposium between Chulalongkorn University and IBB/TMDU on Biomedical Materials and Engineering 2022.01.25 Online
- Takahiro Ishii, Takuya Kobayakawa, Kouki Matsuda, Kohei Tsuji, Kazuhisa Yoshimura, Hiroaki Mitsuya, Kenji Maeda, Hirokazu Tamamura. Structure optimization of DAG-lactone derivatives toward HIV cure
 The 16th Annual Meeting of Japanese Society for Chemical Biology 2022.05.31 Toyama

Metallic Biomaterials

Takao HANAWA Prof Maki ASHIDA Assist Prof Peng CHEN Assist Prof Akira UMISE Assist Prof Michiko NAKAISHI Technical Support Staff Tomoko SETOGUCHI Secretary

(1) **Outline**

1. Bio-functionalization 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 minimalize 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]

 Matsugaki A, Ito M, Kobayashi Y, Matsuzaka T, Ozasa R, Ishimoto T, Takahashi H, Watanabe R, Inoue T, Yokota K, Nakashima Y, Kaito T, Okada S, Hanawa T, Matsuyama Y, Matsumoto M, Taneichi H, Nakano T. Innovative dsign of bone quality-targeted intervertebral spacer: accelerated functional fusion guiding oriented collagen/apatite microstructure without autologous bone Spine J. 2022.12;

- 2. Zhao Q, Ueno T, Chen P, Nozaki K, Tan T, Hanawa T, Wakabayashi N. Fabrication of micro-/submicro-/nanostructured surfaces on Ti–Zr alloy by varying H₂SO₄/H₂O₂ Surfaces and Interfaces. 2022.11; 34; 102390
- 3. Ishimoto T, Kobayashi Y, Takahata M, Ito M, Matsugaki A, Takahashi H, Watanabe R, Inoue T, Matsuzaka T, Ozasa R, Hanawa T, Yokota K, Nakashima Y, Nakano T. Outstanding in vivo mechanical integrity of additively manufactured spinal cages with a novel "honeycomb tree structure" design via guiding bone matrix orientation Spine J. 2022.10; 22(10); 1742-1757
- 4. Omori S, Ebihara A, Hirano K, Kasuga Y, Unno H, Nakatsukasa T, Kimura S, Maki K, Hanawa T, Okiji T. Effect of rotational modes on torque/force generation and canal centering ability during rotary root canal instrumentation with differently heat-treated nickel-titanium instruments Materials. 2022.10; 15(19); 6850
- Chiu WT, Fuchiwaki K, Umise A, Tahara M, Inamura T, Hosoda H. Promoted mechanical properties and functionalities via Ta-tailored Ti-Au-Cr shape memory alloys towards biomedical applications J Mech Behav Biomed Mater. 2022.09; 133; 105358
- 6. Eda Y, Manaka T, Hanawa T, Chen P, Ashida M, Noda K. X-ray photoelectron spectroscopy-based valence band spectra of passive films on titanium Surf Interface Anal. 2022.08; 54; 892-898
- 7. Hanawa T. Biocompatibility of titanium from the viewpoint of its surface Sci Technol Adv Mate. 2022.08; 23(1); 457-472
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- 2. Chen P, Uruma M, Ashida M, Hanawa T . Electrodeposition of collagen and calcium phosphate on titanium to improve soft tissue adhesion. International Dental Materials Congress 2022(IDMC2022) 2022.11.04 Hybrid/Taipei,Tiwan
- 3. Manaka T, Tsutsumi Y, Chen P, Hanawa T. Electrochemical Surface Treatment to Improve Corrosion Resistance of Type 316L Austenitic Stainless Steel. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA-2) 2022.10.25 Osaka, Japan
- 4. Chen P, Takenaka K, Sato Y, Tsukamoto M, Ashida M, Hanawa T. Promotion of osteoconductivity of titanium with patterned surface groove topographies using femtosecond laser processing. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA-2) 2022.10.25 Osaka, Japan

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- 6. Kajima Y, Takaichi A, Hanawa T, Wakabayashi N. Effect of several heat treatment times on the microstructure and mechanical behavior of selective laser melted Co-Cr-Mo alloys. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA-2) 2022.10.25 Osaka, Japan
- 7. Takazawa Y, Matsuda R, Takenaka K, Sato Y, Heya M, Matsushita N, Chen P, Hanawa T, Tsukamoto M. High-speed formation of pure copper layer by multi-beam laser metal deposition metheod with blue diode lasers. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA-2) 2022.10.25 Osaka, Japan
- 8. Chen P. Regulation of proliferation and differentiation of osteoblast-like cells by titanium with micro/nano-topography designs. The 8th Joint Symposium between IBB/TMDU and Chulalongkorn University 2022.01.25 Online
- 9. Hanawa T, Ashida M, Tsutsumi Y, Chen P, Nomura N. Zirconium alloy with excellent mechanical property to decrease MRI artifact. 2022 Hawaii Joint Symposium SFB + JSB 2022.01.08 Online (Hawaii, USA)
- 10. Chen P, Sato H, Ashida M, Tsutsumi Y, Harada H, Hanawa T . Proliferation, differentiation and calcification of MC3T3-E1 cells on Zr-14Nb-5Ta-1Mo alloy. 2022 Hawaii Joint Symposium SFB + JSB 2022.01.08 Online (Hawaii, USA)

Organic Biomaterials

Professor: Nobuhiko YUI Associate Professor: Atsushi TAMURA Assistant Professor: Yoshinori ARISAKA 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. 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

- 1. Atsushi Tamura, Tae Woong Kang, Asato Tonegawa, Yoshinori Arisaka, Hiroki Masuda, Ryo Mikami, Takanori Iwata, Tetsuya Yoda, Nobuhiko Yui. Supramolecular surface coating with acetylated polyrotaxane-based triblock copolymers for thermal regulation of cell adhesion and fabrication of cell sheets. Biomacromolecules. 2022.11; 23(11); 4860-4871
- Sumio Hayakawa, Atsushi Tamura, Nikita Nikiforov, Hiroyuki Koike, Fujimi Kudo, Yinglan Cheng, Takuro Miyazaki, Marina Kubekina, Tatiana V. Kirichenko, Alexander N. Orekhov, Nobuhiko Yui, Ichiro Manabe, Yumiko Oishi. Activated cholesterol metabolism is integral for innate macrophage responses by amplifying Myd88 signaling. JCI Insight. 2022.11; 7(22); e138539
- 3. Tamura A, Kang TW, Tonegawa A, Arisaka Y, Masuda H, Mikami R, Iwata T, Yoda T, Yui N. Supramolecular Surface Coatings with Acetylated Polyrotaxane-Based Triblock Copolymers for Thermal Regulation of Cell Adhesion and Fabrication of Cell Sheets. Biomacromolecules. 2022.11; 23(11); 4860-4871

- 4. Atsushi Tamura, Tae Woong Kang, Asato Tonegawa, Yoshinori Arisaka, Hiroki Masuda, Ryo Mikami, Takanori Iwata, Tetsuya Yoda, Nobuhiko Yui. Supramolecular surface coating with acetylated polyrotaxane-based triblock copolymers for thermal regulation of cell adhesion and fabrication of cell sheets Biomacromolecules. 2022.10; in press;
- 5. Hongfei Zhu, Atsushi Tamura, Shunyao Zhang, Masahiko Terauchi, Tetsuya Yoda, Nobuhiko Yui. Mitigating RANKL-induced cholesterol overload in macrophages with β -cyclodextrin-threaded polyrotaxanes suppresses osteoclastogenesis. Biomaterials Science. 2022.09; 10(18); 5230-5242
- 6. Yuka Tanaka-Takemura, Yoshinori Arisaka, Masahiro Hakariya, Hiroki Masuda, Ryo Mikami, Ruriko Sekiya-Aoyama, Takanori Iwata, Tetsuya Yoda, Takashi Ono, Nobuhiko Yui. Independent roles of molecular mobility and zeta potential on supramolecular surfaces in the sequence of RAW264.7 macrophage responses Macromolecular bioscience. 2022.09; in press(11); e2200282
- Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Phototethering of collagen onto polyetheretherketone surfaces to enhance osteoblastic and endothelial performance Macromolecular Bioscience. 2022.08; 22(8); 2200115
- 8. Yoshikawa, Atsushi Tamura, Susumu Tsuda, Eisuke Domae, Shunyao Zhang, Nobuhiko Yui, Takashi Ikeo, Tatsuya Yoshizawa. Calcium phosphate-adsorbable and acid-degradable carboxylated polyrotaxane consisting of β -cyclodextrins suppresses osteoclast resorptive activity. Dental Materials Journal. 2022.07; 41(4); 624-632
- 9. Atsushi Tamura, Kei Nishida, Shunyao Zhang, Tae Woong Kang, Asato Tonegawa, Nobuhiko Yui. Cografting of zwitterionic sulfobetaines and cationic amines on β -cyclodextrin-threaded polyrotaxanes facilitates cellular association and tissue accumulation with high biocompatibility. ACS Biomaterials Science & Engineering. 2022.06; 8(6); 2463-2476
- 10. Shunyao Zhang, Atsushi Tamura, Nobuhiko Yui. Coth reading of unmodified and monoazidated β -cyclodextrins in polyrotaxanes for orthogonal modification of cell-penetrating peptides via click chemistry. ACS Applied Polymer Materials. 2022.04; 4(5); 3866-3876
- 11. Tae Woong Kang, Atsushi Tamura, Yoshinori Arisaka, Nobuhiko Yui. Thin-layer photodegradable polyrotaxane gel-immobilized surfaces for photoregulation of surface properties and cell adhesiveness. Journal of Applied Polymer Science. 2022.02; 139(7); 51656
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- 14. Masahiro Hakariya, Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Takanori Iwata, Nobuhiko Yui. Suppressed migration and enhanced cisplatin chemosensitivity in human cancer cell lines by tuning the molecular mobility of supramolecular biomaterials Macromolecular Bioscience. 2022; in press;

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- 3. Atsushi Tamura, Yoshinori Arisaka, Nobuhiko Yui. Development of debondable dental resin cements containing photodegradable polyrotaxane as a cross-linker. SFB/JSB Hawaii Joint Symosium 2022.01.09 オンライン開催

- 4. Moe Ohashi, Atsushi Tamura, Nobuhiko Yui. Influence of terminal structure of triethylene glycol-modified polyrotaxanes on their physicochemical properties and biomaterials functions. SFB/JSB Hawaii Joint Symosium 2022.01.09 オンライン開催
- 5. Yoshinori Arisaka, Ruriko Sekiya-Aoyama, Nobuhiko Yui. Modulation of zeta potential and molecular mobility on polyrotaxane surfaces promotes osteoblastic and adipogenic differentiation of mesenchymal stem cells. 2022 Hawaii Joint Symposium SFB + JSB 2022.01.08

Biomechanics

Hirokazu Kaji, Professor Yuji Nashimoto, Associate Professor Takeshi Hori, Assistant Professor Serge Ostrovidov, Technician Akane Yamamoto, Technician Maki Maejima, Technician

(1) Outline

We are developing micro/nanotechnologies minimally invasive to bio-derived materials and living bodiesbodies for next generation biomedical applications.

(2) Research

- 1. Biofabrication technology
- 2. Drug delivery system
- 3. Cell delivery system
- 4. Micropysiological system (MPS)

(3) Lectures & Courses

Students will learn the latest trends in biomechanics and related research fields, as well as acquire fundamental knowledge and skills. In addition, students will aim to develop the ability to independently promote research in the field.

(4) **Publications**

- 1. Nagai N, Daigaku R, Motoyama R, Kaji H, Abe T. Release of ranibizumab using a porous poly(dimethylsiloxane) capsule suppressed laser-induced choroidal neovascularization via the transscleral route. Journal of materials science. Materials in medicine. 2022.12; 34(1); 5
- 2. Hiramoto Kaoru, Iwase Kazuyuki, Utagawa Yoshinobu, Nashimoto Yuji, Honma Itaru, Ino Kosuke, Shiku Hitoshi. Electrochemical microwell sensor with Fe-N co-doped carbon catalyst to monitor nitric oxide release from endothelial cell spheroids(タイトル和訳中) Analytical Sciences. 2022.10; 38(10); 1297-1304
- 3. Kaoru Hiramoto, Kazuyuki Iwase, Yoshinobu Utagawa, Yuji Nashimoto, Itaru Honma, Kosuke Ino, Hitoshi Shiku. Electrochemical microwell sensor with Fe–N co-doped carbon catalyst to monitor nitric oxide release from endothelial cell spheroids Analytical Sciences. 2022.07; -(-); -
- 4. Yoshinobu Utagawa, Kosuke Ino, Tatsuki Kumagai, Kaoru Hiramoto, Masahiro Takinoue, Yuji Nashimoto, Hitoshi Shiku. Electrochemical glue for binding chitosan/alginate hydrogel fibers for cell culture Micromachines. 2022.03; 13(3); 420

- 5. Kosuke Ino, Keika Komatsu, Kaoru Hiramoto, Yoshinobu Utagawa, Yuji Nashimoto, Hitoshi Shiku. Electrochemiluminescence imaging of cellular adhesion in vascular endothelial cells during tube formation on hydrogel scaffolds Electrochimica Acta. 2022.03; 415; 140240
- Norio Kobayashi, Hiroaki Okae, Hitoshi Hiura, Naoto Kubota, Eri H. Kobayashi, Shun Shibata, Akira Oike, Takeshi Hori, Chie Kikutake, Hirotaka Hamada, Hirokazu Kaji, Mikita Suyama, Marie-Line Bortolin-Cavaillé, Jérôme Cavaillé, Takahiro Arima. The microRNA cluster C19MC confers differentiation potential into trophoblast lineages upon human pluripotent stem cells Nature Communications. 2022.06; 13(1); 3071
- Inês M Gonçalves, Violeta Carvalho, Raquel O Rodrigues, Diana Pinho, Senhorinha F C F Teixeira, Ana Moita, Takeshi Hori, Hirokazu Kaji, Rui Lima, Graça Minas. Organ-on-a-Chip Platforms for Drug Screening and Delivery in Tumor Cells: A Systematic Review. Cancers. 2022.02; 14(4);
- 3. Inês M Gonçalves, Violeta Carvalho, Raquel O Rodrigues, Diana Pinho, Senhorinha F C F Teixeira, Ana Moita, Takeshi Hori, Hirokazu Kaji, Rui Lima, Graça Minas. Organ-on-a-Chip Platforms for Drug Screening and Delivery in Tumor Cells: A Systematic Review. Cancers. 2022.02; 14(4);
- 4. Rise Akasaka, Kosuke Ino, Tomoki Iwama, Kumi Y. Inoue, Yuji Nashimoto, Hitoshi Shiku. Electrochemiluminescence Imaging Based on Bipolar Electrochemistry Using Commercially Available Anisotropic Conductive Films Sensors and Materials. 2022; 34(8); 3113-3122
- 5. 水田太郎, 石原甲平, 梶弘和, 堀武志. Development of artificial human tissues using micromesh sheets 生体 医歯工学共同研究拠点成果報告書. 2022; 2021; 133
- Norio Kobayashi, Hiroaki Okae, Hitoshi Hiura, Naoto Kubota, Eri H. Kobayashi, Shun Shibata, Akira Oike, Takeshi Hori, Chie Kikutake, Hirotaka Hamada, Hirokazu Kaji, Mikita Suyama, Marie-Line Bortolin-Cavaillé, Jérôme Cavaillé, Takahiro Arima. The microRNA cluster C19MC confers differentiation potential into trophoblast lineages upon human pluripotent stem cells Nature Communications. 2022.12; 13(1); 3071
- Inês M. Gonçalves, Raquel O. Rodrigues, Ana S. Moita, Takeshi Hori, Hirokazu Kaji, Rui A. Lima, Graça Minas. Recent trends of biomaterials and biosensors for organ-on-chip platforms Bioprinting. 2022.06; 26; e00202
- Inês M. Gonçalves, Raquel O. Rodrigues, Ana S. Moita, Takeshi Hori, Hirokazu Kaji, Rui A. Lima, Graça Minas. Recent trends of biomaterials and biosensors for organ-on-chip platforms Bioprinting. 2022.06; 26; e00202
- 4. 水田太郎, 石原甲平, 梶弘和, 堀武志. Development of artificial human tissues using micromesh sheets 生体 医歯工学共同研究拠点成果報告書. 2022; 2021;

- 1. Takeshi Hori. Microphysiological systems and 3D cell cultures for accelerating human placenta research. 第7回生体医歯工学共同研究拠点国際シンポジウム (ISBE2022) 2022.11.25
- 2. Yuji Nashimoto. Electrochemical Analysis of Vasculature-on-a-Chip and Vascularized-3D-Model-on-a-Chip. 3D-Bioprinting, Biofabrication, Organoids & Organs-on-Chips Asia 2022 2022.10.07
- 3. Yuji Nashimoto, Yuki Sato, Takeshi Hori, Kosuke Ino, Hitoshi Shiku, Sayaka Katagiri, Hirokazu Kaji. Engineering and analyzing organ microenvironment with a perfusable vascular network and its application in oral pathology. Interface Summer Seminar 2022 2022.08.24
- 4. Takeshi Hori, Sayaka Katagiri, Hiroaki Okae, Takahiro Arima, Yuji Nashimoto, Hirokazu Kaji. Generation of human placental organoids to study the effects of oral dysbiosis on the placental development. The 17th International Workshop on Biomaterials in Interface Science 2022.08.24
- 5. Yuji Nashimoto, Rei Mukomoto, Takuto Imaizumi, Kosuke Ino, Hitoshi Shiku. Electrochemical analysis of a respiration activity for a three-dimensional cultured model with biomimetic vascular flow. 9th World Congress of Biomechanics 2022.07.10

- 6. Takeshi Hori, Hiro
aki Akae, Norio Kobayashi, Takahiro Arima, Hirokazu Kaji. Recapitulating the human placental barrier with trophoblast stem cells and a microfluidic device. 2022 Joint Symposium SFB + JSB 2022.01.08 Honolulu, HI & Online
- 1. Takeshi Hori, Hiroaki Okae, Norio Kobayashi, Takahiro Arima, Hirokazu Kaji. Trophoblast organoids to study xenobiotic transport. 2022.07.11
- 2. Takeshi Hori, Hiroaki Okae, Norio Kobayashi, Takahiro Arima, Hirokazu Kaji. Recapitulating the Human Placental Barrier with Trophoblast Stem Cells and a Microfluidic Device. 2022.01.09

[Awards & Honors]

1. The Young Scientists' Award, The Minister of Education, Culture, Sports, Science and Technology, 2022.04

Molecular Cell Biology

Professor Hiroshi Shibuya Associate Professor Toshiyasu Goto Assistant Professor Masahiro Shimizu

(1) Research

Canonical Wnt signaling is very important in early Xenopus development. During early development before the gastrula stage, high Wnt activity at the dorsal side determines the organizer region. High Wnt activity increases expression of Spemann organizer genes, such as nodal3.1 and sia1, and induces a secondary axis on the ventral side. Conversely, during late development after the gastrula stage, Wnt signaling inhibition at the organizer region by Wnt inhibitors, such as cer1, frzb, and dkk1, is required for head induction.

The key aspect of Wnt signaling is β -catenin protein stability. Dvl is recruited at the cell membrane and prevents β -catenin degradation under the Wnt-on state. Under the Wnt-off state, Axin1, Apc, Gsk3- β and Csnk1a1 form the destruction complex to phosphorylate β -catenin protein. Phosphorylated β -catenin is ubiquitinated by E3 ubiquitin ligases, such as Btrc, and is then degraded by the proteasome system.

The Glucose-Induced degradation Deficient (GID) complex also contributes to β -catenin ubiquitination and destruction. Wdr26, a scaffold protein in the GID complex, degrades β -catenin by binding to Axin1 and is required for head formation in Xenopus. There are two E3 ligases in the GID complex: Maea and Rmnd5a. Both human Maea and Rmnd5a ubiquitinate human β -catenin, and their knockdown increases human β -catenin stability in HEK 293T cells. Moreover, Rmnd5a knockdown in Xenopus reduced expression levels of genes that are necessary for forebrain development. Therefore, Xenopus Maea could also play an important role in β -catenin degradation in Xenopus. However, whether β -catenin protein degradation by Maea occurs in and affects Xenopus development remains unknown. Here, we investigated the effects of Xenopus Maea on early Xenopus development through β -catenin degradation.

1. Maea.S degraded and ubiquitinated ß-catenin protein.

Xenopus laevis is an allotetraploid frog, and their two subgenomes, L (long) and S (short), were identified as sets of homeologous chromosomes with different lengths. The temporal expression patterns of maea.S and maea.L transcripts are almost similar during early development, although the maea.S transcripts are expressed more than those of maea.L. Therefore, we cloned maea.S and investigated its function in all experiments

In Xenopus embryos, maea.S reduced the amount of β -catenin protein. Furthermore, the immunoprecipitation assay revealed that Maea.S also bound to and ubiquitinated β -catenin. Moreover, RT-PCR analysis revealed that maea.S mRNA overexpression did not reduce β -catenin transcripts. These suggest that the decrease in β -catenin protein by Maea.S does not occur at the transcriptional level.

2. Overexpression of maea.S mRNA inhibited the effects of β-catenin

To confirm the effect of β -catenin protein degradation by Maea.S in Xenopus development, we investigated the effects of maea.S mRNA overexpression. Dorsally, maea.S mRNA overexpression decreased Wnt target gene expression at the gastrula stage (st. 10). However, the phenotypes of dorsal maea.S mRNA-injected embryos were similar to those of un-injected control embryos. These findings demonstrate that maea.S mRNA overexpression is sufficient to reduce the expression of Wnt target genes, but insufficient to change phenotypes. When we overexpressed maea.S mRNA into animal dorsal blastomeres of 8-cell embryos, the head structures, including the cement glands, of the injected embryos were enlarged (Figure 1). When we injected with a low dose of β -catenin mRNA into ventral blastomeres of 4-cell embryos, the injected embryos showed a secondary axis formation with complete or partial head structures. Co-injection with maea.S mRNA reduced the appearance rates of embryos that had the secondary axis with complete and partial head structures. Wnt target gene expression in embryos ventrally injected with β -catenin mRNA also decreased by co-injection with maea.S mRNA. These results suggest that maea.S may function as a gene that suppresses excessive Wnt activities through the degradation of β -catenin protein during early development.

3. Maea knockdown interfered with head formation

To investigate the effects of Maea knockdown on early development, we conducted experiments using maea-MO (morpholino oligonucleotides). Injection of maea-MO into animal dorsal blastomeres of 8-cell embryos interfered with head formation in a dose-dependent manner, and the head region phenotypes of the injected embryos were categorized as normal, mild (small eyes), or severe (no eyes) (Figures 2). Anterior development was rescued by co-injection with maea-MO and a MO-resistant form of maea mRNA, 5-mis-maea.S mRNA, which contains five mismatch nucleotides in the MO binding site. These findings reveal that maea might contribute to head formation by inhibiting the Wnt activity through β-catenin protein degradation during early embryogenesis.

4. Maea.S might ubiquitinate unknown lysine residues of β-catenin

In vertebrates, the amino acid sequence of β -catenin involves 26 lysine residues, which are conserved among species. There are four lysine residues known as ubiquitinated sites in β -catenin protein. Both lysine residues 19 and 49 are ubiquitinated by Btrc and Jade1. Additionally, Siah1 ubiquitinates β -catenin at lysine residues 666 and 671. Huwe1 and Shprh are also related to β -catenin protein degradation, but the sites they ubiquitinate have not been identified. To investigate whether Maea.S ubiquitinates novel lysine residues of β -catenin protein, we used a β -catenin-4KRs construct with four lysine to arginine mutations at 19, 49, 666, and 671 lysine residues. In results, maea.S reduced β -catenin-4KRs protein amounts. Moreover, Maea.S also bound to and ubiquitinated β -catenin-4KRs protein. Overexpression of maea.S reduced induction of both secondary axis and Wnt target gene expression by β -catenin-4KRs mRNA. These results demonstrate that β -catenin protein degradation by Maea.S might be due to β -catenin protein ubiquitination at unknown lysine residues.

(2) 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.

(3) Publications

- 1. Masahiro Shimizu, Hiroshi Shibuya. WNK1/HSN2 mediates neurite outgrowth and differentiation via a OSR1/GSK3 β -LHX8 pathway. Sci Rep. 2022.09; 12(1);
- 2. Goto T, Michiue T, Shibuya H. ccr7 affects both morphogenesis and differentiation during early Xenopus embryogenesis. Development, growth & differentiation. 2022.05; 64(5); 254-260
- 3. Shimizu M, Shibuya H, Tanaka N. Enhanced O-GlcNAc modification induced by the RAS/MAPK/CDK1 pathway is required for SOX2 protein expression and generation of cancer stem cells. Scientific reports. 2022.02; 12(1); 2910

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D. Lecturer Satoshi Kofuji, Ph.D. Assistant Professor Yoshimi Okamoto, Ph.D. Project Assistant Professor Jing Pu, Ph.D. Project Assistant Professor Keiko Kanayama, Ph.D. Technical Assistant Mizuki Kusaba Secretary Kaori Kofuji

(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

- Oda C, Kamimura K, Shibata O, Morita S, Tanaka Y, Setsu T, Abe H, Yokoo T, Sakamaki A, Kamimura H, Kofuji S, Wakai T, Nishina H, Terai S. HBx and YAP expression could promote tumor development and progression in HBV-related hepatocellular carcinoma. Biochemistry and biophysics reports. 2022.12; 32; 101352
- 2. Kobayashi S, Ogasawara N, Watanabe S, Yoneyama Y, Kirino S, Hiraguri Y, Inoue M, Nagata S, Okamoto-Uchida Y, Kofuji S, Shimizu H, Ito G, Mizutani T, Yamauchi S, Kinugasa Y, Kano Y, Nemoto Y, Watanabe M, Tsuchiya K, Nishina H, Okamoto R, Yui S. Collagen type I-mediated mechanotransduction controls epithelial cell fate conversion during intestinal inflammation. Inflammation and regeneration. 2022.11; 42(1); 49

- 3. Kobayashi Sakurako, Ogasawara Nobuhiko, Watanabe Satoshi, Yoneyama Yosuke, Kirino Sakura, Hiraguri Yui, Inoue Masami, Nagata Sayaka, Okamoto-Uchida Yoshimi, Kofuji Satoshi, Shimizu Hiromichi, Ito Go, Mizutani Tomohiro, Yamauchi Shinichi, Kinugasa Yusuke, Kano Yoshihito, Nemoto Yasuhiro, Watanabe Mamoru, Tsuchiya Kiichiro, Nishina Hiroshi, Okamoto Ryuichi, Yui Shiro. Collagen type I-mediated mechanotransduction controls epithelial cell fate conversion during intestinal inflammation(タイトル和訳 中) Inflammation and Regeneration. 2022.11; 42; 1 of 18-18 of 18
- 4. Hiroshi Nishina. Physiological and pathological roles of the Hippo-YAP/TAZ signaling pathway in liver formation, homeostasis, and tumorigenesis. Cancer Sci. 2022.06; 113(6); 1900-1908
- 5. Takeaki Shibata, Hiroki Kawana, Yuri Nishino, Yoshiko Ito, Hiroyasu Sato, Hirofumi Onishi, Kuniyuki Kano, Asuka Inoue, Yoshitaka Taketomi, Makoto Murakami, Satoshi Kofuji, Hiroshi Nishina, Atsuo Miyazawa, Nozomu Kono, Junken Aoki. Abnormal male reproduction and embryonic development induced by downregulation of a phospholipid fatty acid-introducing enzyme Lpgat1 in zebrafish. Sci Rep. 2022.05; 12(1); 7312
- 6. Sinclear Caleb Kwame, Maruyama Junichi, Nagashima Shunta, Arimoto-Matsuzaki Kyoko, Kuleape Joshua Agbemefa, Iwasa Hiroaki, Nishina Hiroshi, Hata Yutaka. Protein kinase C α activation switches YAP1 from TEAD-mediated signaling to p73-mediated signaling(和訳中) Cancer Science. 2022.04; 113(4); 1305-1320
- 7. Shoko Miyata, Noriaki Saku, Saeko Akiyama, Palaksha Kanive Javaregowda, Kenta Ite, Nagisa Takashima, Masashi Toyoda, Kei Yura, Tohru Kimura, Hiroshi Nishina, Atsuko Nakazawa, Mureo Kasahara, Hidenori Nonaka, Tohru Kiyono, Akihiro Umezawa. Puromycin-based purification of cells with high expression of the cytochrome P450 CYP3A4 gene from a patient with drug-induced liver injury (DILI). Stem Cell Res Ther. 2022.01; 13(1); 6
- Yazan Alwarawrah, Keiko Danzaki, Amanda G Nichols, Brian E Fee, Cheryl Bock, Gary Kucera, Laura P Hale, Gregory A Taylor, Nancie J MacIver. Irgm1 regulates metabolism and function in T cell subsets. Scientific Reports. 2022.01; 12(1); 850
- 9. Hirotoshi Soyama, Miki Nishio, Junji Otani, Toshiko Sakuma, Shintaro Takao, Shigeo Hara, Takaaki Masuda, Koshi Mimori, Shinya Toyokuni, John P Lydon, Kazuwa Nakao, Hiroshi Nishina, Takumi Fukumoto, Tomohiko Maehama, Akira Suzuki. Hippo-TAZ signaling is the master regulator of the onset of triple-negative basal-like breast cancers. Proc Natl Acad Sci U S A. 2022.07; 119(29); e2123134119
- 10. Joshua Agbemefa Kuleape, Shakhawoat Hossain, Caleb Kwame Sinclear, Takanobu Shimizu, Hiroaki Iwasa, Junichi Maruyama, Kyoko Arimoto-Matsuzaki, Hiroshi Nishina, Yutaka Hata. DNA Damage Triggers the Nuclear Accumulation of RASSF6 Tumor Suppressor Protein via CDK9 and BAF53 To Regulate p53 Target Gene Transcription. Mol Cell Biol. 2022.02; 42(2); e0031021
- 11. Caleb Kwame Sinclear, Junichi Maruyama, Shunta Nagashima, Kyoko Arimoto-Matsuzaki, Joshua Agbemefa Kuleape, Hiroaki Iwasa, Hiroshi Nishina, Yutaka Hata. Protein kinase C α activation switches YAP1 from TEAD-mediated signaling to p73-mediated signaling. Cancer Sci. 2022.04; 113(4); 1305-1320

- 1. Jing Pu,Satoshi Kofuji,Hiroshi Nishina. Identification of ceramide as a negative regulator of primitive streak formation. 2022 年度日本生化学会関東支部例会 2022.06.18
- 1. Satoshi Kofuji, Jing Pu, Hiroshi Nishina. Sphingolipid metabolism regulates primitive streak formation essential for mesendoderm-derived organogenesis. 2022.12.02

Structural Biology

Professor Nobutoshi ITO Associate Professor Nobutaka NUMOTO Assistant Professor Yuya HANAZONO

(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) Rational design of PDZ domain inhibitors involved in regulation of intracellular signaling
- 5) Structural basis of giant hemoglobins
- 6) Molecular basis of suppression of HIV-1
- 7) Structure based drug design for protein kinases
- 8) Structural analysis including hydrogen atoms by ultra-high resolution crystallography
- 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. Hall D, Basu G, Ito N. Computational biophysics and structural biology of proteins-a Special Issue in honor of Prof. Haruki Nakamura's 70th birthday. Biophysical reviews. 2022.12; 14(6); 1211-1222
- 2. Hanazono Yuya, Hirano Yu, Takeda Kazuki, Kusaka Katsuhiro, Tamada Taro, Miki Kunio. Revisiting the concept of peptide bond planarity in an iron-sulfur protein by neutron structure analysis SCIENCE ADVANCES. 2022.05; 8(20); eabn2276
- 3. Nobutaka Numoto, Seiko Onoda, Yoshiaki Kawano, Hideo Okumura, Seiki Baba, Yoshihiro Fukumori, Kunio Miki, Nobutoshi Ito. Structures of oxygen dissociation intermediates of 400 kDa V2 hemoglobin provide coarse snapshots of the protein allostery. Biophys Physicobiol. 2022.05; 19; 1-10
- 4. Oda Masayuki, Sano Tomoki, Kamatari Yuji O., Abe Yoshito, Ikura Teikichi, Ito Nobutoshi. Structural Analysis of Hen Egg Lysozyme Refolded after Denaturation at Acidic pH PROTEIN JOURNAL. 2022.02; 41(1); 71-78
- 5. Basu G, Hall D, Ito N. Special Issue call: Computational biophysics and structural biology of proteins-A Special Issue in honor of Prof. Haruki Nakamura's 70th birthday. Biophysical reviews. 2022.02; 14(1); 21-22
- 6. Yoshihara Ayana, Kawasaki Haru, Masuno Hiroyuki, Takada Koki, Numoto Nobutaka, Ito Nobutoshi, Hirata Naoya, Kanda Yasunari, Ishizawa Michiyasu, Makishima Makoto, Kagechika Hiroyuki, Tanatani Aya. Lithocholic Acid Amides as Potent Vitamin D Receptor Agonists BIOMOLECULES. 2022.01; 12(1);
- Fujioka Toshifumi, Numoto Nobutaka, Akama Hiroyuki, Shilpa Kola, Oka Michiko, Roy Prodip K., Krishna Yarkali, Ito Nobutoshi, Baker David, Oda Masayuki, Tanaka Fujie. Varying the Directionality of Protein Catalysts for Aldol and Retro-Aldol Reactions CHEMBIOCHEM. 2022.01; 23(2); e202100435
- 1. Hanazono Yuya, Hirano Yu, Tamada Taro, Miki Kunio. New Description of the Peptide Bond in Proteins Revealed by High-Resolution Neutron Crystallography Journal of the Crystallographic Society of Japan. 2022.08; 64(3);

- 1. Xibin Quan, Nobutaka Numoto, Takeshi Tsubata, Nobutoshi Ito. Structure analysis of human B cell inhibitory co-receptor CD72. The 60th Annual Meeting of the Biophysical Society of Japan 2022.09.28 Hakodate
- 2. Nobutaka Numoto, Narutoshi Kamiya, Masayuki Oda. Improvement of thermostability and activity of PET-degrading enzyme Cut190 towards a detailed understanding and application of the enzymatic reaction mechanism. ACS Fall 2022 2022.08.25 Chicago (USA)
- 1. Yuya Hanazono. Ultra-high resolution X-ray crystallography and high-resolution neutron crystallography. Biomolecular Interaction Research Association 19th workshop of 2022.12.12 Tokyo
- 2. Natsuko Goda, Shotaro Yasukochi, Kiminori Hori, Yuki Kamiya, Nobutaka Numoto, Nobutoshi Ito, Takeshi Tenno, Hidekazu Hiroaki. Analysis of pharmacological activity of novel compounds binding to Wnt signaling-related protein Dishevelled. The 45th Annual Meeting of the Molecular Biology Society of Japan 2022.12.02
- 3. Shota Suzuki, Yoko hiroaki, Kotaro Tanaka, Koki Nishikawa, Nobutaka Numoto, Daisuke Sasaki, Akiko Kamegawa, Hiroshi Suzuki, Atsunori Oshima, Yoshinori Fujiyoshi. Structural insight into the activation mechanism of lipid-mediated G-protein-coupled receptors. The 45th Annual Meeting of the Molecular Biology Society of Japan 2022.12.01
- 4. Daisuke Kozai, Nobutaka Numoto, Kouki Nishikawa, Akiko Kamegawa, Shohei Kawasaki, Yoko Hiroaki, Katsumasa Irie, Atsunori Oshima, Hiroyuki Hanzawa, Kousei Shimada, Yutaka Kitano, Yoshinori Fujiyoshi. The recognition mechanism of the analgesic drug mirogabalin by recombinant human α_2 δ 1 protein. The 96th Annual Meeting of the Japanese Pharmacological Society 2022.11.30

- 5. Yuya Hanazono, Yu Hirano, Kazuki Takeda, Katsuhiro Kusaka, Taro Tamada, Kunio Miki. Non-planarity of the peptide bond revealed by high-resolution neutron structure. CrSJ Annual Meeting and General Assembly 2022 2022.11.26 Nishinomiya
- 6. Nobutaka Numoto, Gert-Jan Bekker, Narutoshi Kamiya, Masayuki Oda, Nobutoshi Ito. Enzymatic reaction cycle revealed by substrate analog binding structure of PET degrading enzyme Cut190. CrSJ Annual Meeting and General Assembly 2022 2022.11.26
- 7. Nobutaka Numoto, Xibin Quan, Takeshi Tsubata, Nobutoshi Ito. Ligand recognition mechanism of B cell inhibitory co-receptor CD72. The 95th Annual Meeting of the Japanese Biochemical Society 2022.11.11
- 8. Yu Hirano, Yuya Hanazono, Kazuki Takeda, Katsuhiro Kusaka, Taro Tamada, Kunio Miki. Revisiting the peptide bond planarity by high-resolution neutron crystallography. The 22nd Annual Meeting of the Japanese Society for Neutron Science 2022.10.27 Chiba
- 9. Nobutaka Numoto. Allosteric regulation of PET-degrading enzyme Cut190 through the weakly bound Ca²⁺ ion. The 60th Annual Meeting of the Biophysical Society of Japan 2022.09.29 Hakodate
- 10. Yuya Hanazono, Yu Hirano, Kazuki Takeda, Katsuhiro Kusaka, Taro Tamada, Kunio Miki. Revisiting the peptide bond planarity by high-resolution neutron structure. The 60th Annual Meeting of the Biophysical Society of Japan 2022.09.28 Hakodate
- 11. Yuya Hanazono, Yu Hirano, Kazuki Takeda, Katsuhiro Kusaka, Taro Tamada, Kunio Miki. A high-resolution neutron structure reveals the nonplanarity of the peptide bond. The 22nd Annual Meeting of the Protein Science Society of Japan 2022.06.08 Tsukuba
- 12. Yuya Hanazono, Yu Hirano, Kazuki Takeda, Katsuhiro Kusaka, Taro Tamada, Kunio Miki. New description of the peptide bond in proteins revealed by the high-resolution structure analysis. The 4th Annual Meeting of the Quantum Life Science Society 2022.05.26 Kobe
- 13. Shotaro Yasukochi, Nobutaka Numoto, Yuki Kamiya, Emi Hibino, Kiminori Hori, Natsuko Goda, Takeshi Tenno, Nobutoshi Ito, Hidekazu Hiroaki. Rational design of non-peptidic PDZ domain inhibitors of human Dvl1 based on the crystal structure of the target-inhibitor complex. 143rd Annual Meeting of the Pharmaceutical Society of Japan 2022.03.25 Sapporo, Japan

[Awards & Honors]

- 1. Early Career Presentation Award (Yuya Hanazono), Biophysical Society of Japan, 2022.09
- 2. Travel Fellowship Awards (Yuya Hanazono), IUPAB/NanoLSI Workshop on Computational Biophysics of Atomic Force Microscopy, 2022.09

Department of Biomolecular Pathogenesis

Noriyuki Matsuda Koji Yamano Fumika komatsuya (Koyano) Waka Kojima Aiko Watanabe Reika Yamagishi (Kikuchi)

Shizuka Ogiwara Ryu Endo Momoha Sawada Tomoyuki Hoshina

Kai Kanematsu

Tomoya Ito Saya Osozawa Hiroki Kinefuchi

Hisako Hirano

(1) Outline

Note: Biomolecular Pathogenesis Laboratory was launched in 2022 and thus is a newly established young lab. Various functional biomolecules and organelles exist in cells. However, many of them are suffered from damage during their functional processes, and finally they are accumulated as the damaged form. To maintain normal cellular functions, it is crucial to selectively eliminate such "damaged biomolecules and organelles."

On the other hand, degradation of essential biomolecules and organelles is an extremely dangerous process. To make this process beneficial, it is imperative to correctly recognize and identify the targets for degradation under stringent control.

In recent years, factors involved in this process have been well understood, and their relevance to human diseases (i.e., pathophysiological significance) has become evident. Thus, we have been studying on (1) the molecular mechanisms for the selective recognition and degradation of damaged proteins and organelles within cells, and (2) the mechanisms underlying how the failure of this process leads to neurodegenerative disorders, with focusing on ubiquitin, autophagy, and Parkinson disease.

(2) Research

The main research themes of our laboratory (Biomolecular Pathogenesis Lab) are as follows:

1. Elucidation of the molecular mechanisms by which PINK1 and Parkin, the causative genes for hereditary recessive Parkinson's disease, collaborate and ubiquitylate damaged mitochondria.

2. Elucidation of the molecular mechanisms by which ubiquitylated damaged mitochondria are directed to selective autophagic degradation (called mitophagy), and how this mitophagy process suppresses the onset of hereditary Parkinson's disease.

3. Elucidation of the molecular mechanisms of DJ-1, causative gene product of hereditary recessive Parkinson's disease, with focusing on post-translational modifications of amino groups.

4. Understanding the molecular mechanisms how the dysfunction of newly discovered autophagy-related factor, BCAS3-C16orf70 complex, leads to human hereditary neurodevelopmental disease.

5. Elucidation of the molecular mechanisms by which organelles other than damaged mitochondria (e.g., peroxisomes) are directed to autophagic degradation.

6. Identifying and characterization of novel factors involved in membrane trafficking process during the selective degradation of damaged organelles.

(3) Education

I am in charge of the following lectures for the undergraduate and graduate students.

Undergraduate Class/Faculty Lecture: Elective Subjects I/II - Life Science and Technology.

Graduate School Lecture: Introduction to Biomedical Sciences and Engineering, Biochemistry, and Biomedical Science.

(4) Lectures & Courses

Our goal in this lab is elucidation of the molecular mechanisms by which damaged biomolecules and damaged organelles are selectively recognized and degraded in cells. In pursuit of this goal, we utilize a wide range of research methodologies, such as cell biology, biochemistry, molecular biology, and developmental engineering. Additionally, by revealing the pathophysiological significances of this process, we aim to uncover the pathogenic mechanisms of several neurodegenerative diseases including hereditary Parkinson's disease.

(5) Publications

- 1. Noriyuki Matsuda. Novel autophagy-relevant hereditary disease HEMARS (BCAS3-associated disease) and pexophagy suppression by FAF2-p97/VCP complex. The 10th international symposium on autophagy 2022.10.25 Chateraise Gateaux Kingdom Sapporo, Hokkaido
- 2. Noriyuki Matsuda. Mitophagy dysfunction relevant to the hereditary Parkinson's disease and muerodevelopmental disorder HEMARS. NEURO2022 2022.06.30 Okinawa Convention Center

Department of Functional Genome Informatics

Professor NIKAIDO Itoshi Graduate Student WAKITA Maiko

(1) **Outline**

We will develop human resources capable of development at an advanced level in molecular biology and data science technologies to measure genome function information at an unprecedented scale and accuracy and produce human resources that can promote the next generation of medicine creatively and proactively.

(2) Publications

[Conference Activities & Talks]

1. Morita Ritsuko, Sanzen Noriko, Sasaki Hiroko, Hayashi Tetsutaro, Umeda Mana, Yoshimura Mika, Yamamoto Takaki, Shibata Tatsuo, Abe Takaya, Kiyonari Hiroshi, Furuta Yasuhide, Nikaido Itoshi, Fujiwara Hironobu. Tracing the origin of hair follicle stem cells(タイトル和訳中). 日本研究皮膚科学会年 次学術大会・総会プログラム 2022.10.01

RIKEN Molecular and Chemical Somatology

Visiting Professor	Ichiro Taniuchi	
Visiting Professor	Mikiko Sodeoka	
Visiting Professor	Nobumoto Watanabe	
Visiting Professor	Shinya Hagihara	
Visiting Professor	Motomasa Tanaka	
Visiting Professor	Rikiya Watanabe	
Visiting Lecturer	Nobuhiko Miyasaka	
Visiting Lecturer	Hiromasa Yoshioka	
Visiting Lecturer	Masanori Izumi	
Visiting Lecturer	Kosuke Dodo	
Visiting Lecturer	Ryo Endo	
Visiting Lecturer	Hideyuki Yoshida	
Visiting Lecturer	Nicolas Gailhouste	
Visiting Lecturer	Kazuyoshi Ishigaki	
Visiting Lecturer	Shunsuke Tagami	
Visiting Lecturer	Krzyzanowski Marek	
Graduate Students	D3	Xintong Liu
	D3	Nayan Suryawanshi
	D3	Chang Jingjie
	D2	Shingo Tamai

(1) Research

Molecular and Chemical Somatology is an interdisciplinary field for understanding of the basis of Bio-organic Chemistry, Chemical Biology, Structural Biology, Molecular Immunology and Molecular Neuroscience as well as interdiciplenary study for developping a new technology to measure bio-molecules at singe molecular level. Our studies will also aim to apply our findngs 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 immune cell development
- 5) Molecular Neuropathology

 \cdot Molecular basis of neurodegenerative disorders and psychiatric diseases

- 6) Digital Biology
 - Development of new technology to detecte bio-molecules at single moclecular level and its application for rapid disease diagnosis.

(3) Publications

- Nakagawa Y., Shen C-h., Komi Y., Sugiyama S., Kurinomaru T., Tomabechi Y., Krayukhina E., Okamoto K., Yokoyama T., Shirouzu M., Uchiyama S., Inaba M., Niwa T., Sako Y., Taguchi H., Tanaka M. Amyloid conformation-dependent disaggregation in a reconstituted yeast prion system. *Nat. Chem. Biol.*, 18, 321-331 (2022).
- Shinoda, H., Iida, T., Makino, A., Yoshimura, M., Ishikawa, J., Ando, J., Murai, K., Sugiyama, K., Muramoto, Y., Nakano, M., Kiga, K., Cui, L., Nureki, O., Takaeuchi, H., Noda, T., *Nishimasu, H., & *Watanabe, R. Automated amplification-free digital RNA detection platform for rapid and sensitive SARS-CoV-2 diagnosis. *Commun Biology* 5: 473 (2022).
- 3. Shinoda, H., Taguchi, Y., Nakagawa, R., Makino, A., Okazaki, S., Nakano, M., Muramoto, Y., Takahashi, C., Takahashi, I., Ando, J., Noda, T., *Nureki, O.,

*Nishimasu, H., & *Watanabe, R. Amplification-free RNA detection with CRISPR-Cas13. *Commun Biology* 4, 476 (2021).

- Toh, K., Nishio, K., Nakagawa, R., Egoshi, S., Abo, M., Perron, A., Sato, S., Okumura, N., Koizumi, N., Dodo, K., Sodeoka, M., Uesugi, M. Chemoproteomic Identification of Blue Light-Damaged Proteins. J. Am. Chem. Soc. 144, 20171 (2022).
- Chen, B., Zhou, J., Mao, T., Cao, T., Hu, S., Zhang, W., Li, X., Qin, X., Liu, X., Watanabe, N., Li, J. The Critical Biomarkers Identification of Insulin Signaling Involved in Initiating cAMP Signaling Mediated Salivary Secretion in Sjogren Syndrome: Transcriptome Sequencing in NOD Mice Model. *Biol. Proc.* Online 24: 26 (2022)
- Wei, W., Cao, T., Pathak, J. L., LIU, X., Mao, T., Watanabe, N., Li, X., Zhang, M., and Li, J.: Apigenin, a single active component of herbal extract, alleviates xerostomia via ERα-mediated upregulation of AQP5 activation. *Front. Pharmacol.* 13: 818116 (2022)

7.

[Review Articles]

- Yamashita M., Taniuchi I. Fine-tuning Notch1 by the stage-specific enhancer. Nat. Immunol, 23: 1509 (2022).
- Okuyama K., Taniuchi I. Three residues in the BTB domain promote a good partnership between NuRD and Thpok. *Sci. Immunol*, 7: eabq1408 (2022).
- Hui K.K., Chater T.E., Goda Y., Tanaka M. How Staying Negative Is Good for the (Adult) Brain: Maintaining Chloride Homeostasis and the GABA-Shift in Neurological Disorders. Front. Mol. Neurosci., 15, 893111 (2022).
- Dodo, K., Fujita, K., Sodeoka, M. Raman Spectroscopy for Chemical Biology Research. J. Am. Chem. Soc. 144, 19651 (2022).

[Books]

[Conference Activities & Talks]

1. Taniuchi, I."Phosphorylation of Runx proteins controls thymocyte fate" 1CSHL meeting. Nov 1, 2022. NY, USA.

- Chang Jingjie. "Mechanisms of impaired hematopoiesis caused by the IKZF1^{N159S} variant" The 51th Annual Meeting of the Japanese Society for Immunology, Dec 8, 2022, Kumamoto, Japan.
- Motomasa Tanaka, Cross-scale analysis of yeast prion propagation in cells, The 60th Annual Meeting of the Biophysical Society of Japan, Hakodate Arena, September 28, 2022
- Motomasa Tanaka, Deciphering proteostasis regulation mechanism through understanding of disaggregation process for amyloid fibrils, The 74th, Japanese Cell Biology Conference, Tower Hall Funabor, June 29, 2022
- 5. Motomasa Tanaka, Deciphering amyloid disaggregation mechanism by a novel in vitro reconstitution system, The 63rd Japanese Neuropathology Conference, Kyoto Institute, Library and Archives, June 25, 2022.
- 6. Liu, X., Sanada, E., Osada, H., Watanabe, N. "High-throughput screening system for ligands of β -TrCP and analyses of hit compounds." The International Symposium in Tokyo 2022, "Ubiquitin New Frontier from Neo-Biology to Targeted Protein Degradation" Dec 3, 2022. , Ito International Research Center, Tokyo, Japan.
- Liu, Z., Sanada, E., Ishikawa, K., Semba, K., Osada, H., Watanabe, N. "High-throughput screening identified antimycin A as an accelerator of ubiquitin-proteasome dependent degradation of c-Myc protein." The International Symposium in Tokyo 2022, "Ubiquitin New Frontier from Neo-Biology to Targeted Protein Degradation" Dec 3, 2022. , Ito International Research Center, Tokyo, Japan.

NCC Cancer Science

Visiting Professor Hirofumi ARAKAWA Visiting Professor Kenkichi MASUTOMI Visiting Professor Ryuji HAMAMOTO Visiting Professor Masahiro YASUNAGA Visiting Associate Professor Yasushi UEMURA Visiting Associate Professor Yoshikatsu KOGA Visiting Lecturer Kazunori AOKI Naoto TSUCHIYA Visiting Lecturer Visiting Lecturer Issay KITABAYASHI Tadashi KONDO Visiting Lecturer Visiting Lecturer Ken-ichi YOSHIOKA Visiting Lecturer **Bunsyo SHIOTANI** Visiting Lecturer Keisuke SEKINE Visiting Lecturer Akihide YOSHIMI Eri HASHIMOTO Graduate Students D3 Yamato OGIWARA Akira SAKAI Norio SHINKAI Takahiro SHIRAI Yuri YAMASU D1 M2Yuma TAKAMOTO Rie SAWADO Tomomasa TANIYAMA Haruka ASAI M1Yuya MANAKA Megumi KATO Shoju ENDO Ta-Chun LIN Takumi YAMADA

(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]

- Hamada K, Kurashige T, Shimamura M, Arakawa H, Nakamura Y, Nagayama Y. MIEAP and ATG5 are tumor suppressors in a mouse model of BRAFV600E-positive thyroid cancer. *Frontiers in Endocrinology*. 13: 932754, 2022.
- Machitani M, Takei J, Kaneko MK, Ueki S, Ohashi H, Watashi K, Kato Y, Masutomi K. Development of novel monoclonal antibodies against nsp12 of SARS-CoV-2. Virology J. 19: 213, 2022.
- 3. Matsuda Y, Yamashita T, Ye J, Yasukawa M, Yamakawa K, Mukai Y, Machitani M, Daigo Y, Miyagi Y, Yokose T, Oshima T, Ito H, Morinaga S, Kishida T, Minamoto T, Yamada S, Takei J, Kaneko MK, Kojima M, Kaneko S, Masaki T, Hirata M, Haba R, Kontani K, Kanaji N, Miyatake N, Okano K, Kato Y, Masutomi K. Phosphorylation of hTERT at threonine 249 is a novel tumor biomarker of aggressive cancer with poor prognosis in multiple organs. *J Pathol.* 257: 172-185, 2022.

- 4. Sakai A, Komatsu M, Komatsu R, Matsuoka R, Yasutomi S, Dozen A, Shozu K, Arakaki T, Machino H, Asada K, Kaneko S, Sekizawa A, Hamamoto R. Medical Professional Enhancement Using Explainable Artificial Intelligence in Fetal Cardiac Ultrasound Screening. *Biomedicines*. 10(3): 551, 2022.
- 5. Yamada M, Shino R, Kondo H, Yamada S, Takamaru H, Sakamoto T, Bhandari P, Imaoka H, Kuchiba A, Shibata T, Saito Y, Hamamoto R. Robust automated prediction of the revised Vienna Classification in colonoscopy using deep learning: development and initial external validation. *J Gastroenterol.* 57(11): 879-889, 2022.
- 6. Shozu K, Kaneko S, Shinkai N, Dozen A, Kosuge H, Nakakido M, Machino H, Takasawa K, Asada K, Komatsu M, Tsumoto K, Ohnuma SI, Hamamoto R. Repression of the PRELP gene is relieved by histone deacetylase inhibitors through acetylation of histone H2B lysine 5 in bladder cancer. *Clin Epigenetics*. 14(1): 147, 2022.
- Koganemaru S, Kawai T, Fuchigami H, Maeda N, Koyama K, Kuboki Y, Mukohara T, Doi T, Yasunaga M. Quantitative analysis of drug distribution in heterogeneous tissues using dual-stacking capillary electrophoresis-mass spectrometry. Br J Pharmacol. 180(6):762-774, 2022.
- Takashima H, Ohnuki K, Manabe S, Koga Y, Tsumura R, Anzai T, Wang Y, Yin X, Sato N, Shigekawa Y, Nambu A, Usuda S, Haba H, Fujii H, Yasunaga M. Tumor Targeting of 211At-Labeled Antibody under Sodium Ascorbate Protection against Radiolysis. *Mol Pharm.* 20(2):1156-1167, 2022.
- Anzai T, Saijou S, Takashima H, Hara M, Hanaoka S, Matsumura Y, Yasunaga M. Identification of CD73 as the Antigen of an Antigen-Unknown Monoclonal Antibody Established by Exosome Immunization, and Its Antibody-Drug Conjugate Exerts an Antitumor Effect on Glioblastoma Cell Lines. *Pharmaceuticals (Basel)*. 15(7):837, 2022.
- Ogiwara Y, Nakagawa M, Nakatani F, Uemura Y, Zhang R, Kudo-Saito C. Blocking FSTL1 boosts NK immunity in treatment of osteosarcoma. *Cancer Letters.* 537: 215690, 2022.

 Matsuno Y, Kusumoto-Matsuo R, Asai H, Manaka Y, and Yoshioka K. Echoed Induction of Nucleotide Variants and Chromosomal Structural Variants in Cancer Cells. *Scientific Reports*, 12, 20964, 2022.

[Book]

 Arakawa H. MLOs and control of metabolic pathways. Uversky V. Droplets of life. Elsevier. Chapter 14. 431-446, 2022.

[Reviews Articles]

- Hamamoto R, Takasawa K, Machino H, Kobayashi K, Takahashi S, Bolatkan A, Shinkai N, Sakai A, Aoyama R, Yamada M, Asada K, Komatsu M, Okamoto K, Kameoka H, Kaneko S. Application of non-negative matrix factorization in oncology: one approach for establishing precision medicine. *Brief Bioinform.* 23(4): bbac246, 2022.
- 2. Hamamoto R, Koyama T, Kouno N, Yasuda T, Yui S, Sudo K, Hirata M, Sunami K, Kubo T, Takasawa K, Takahashi S, Machino H, Kobayashi K, Asada K, Komatsu M, Kaneko S, Yatabe Y, Yamamoto N. Introducing AI to the molecular tumor board: one direction toward the establishment of precision medicine using large-scale cancer clinical and biological information. *Exp Hematol Oncol.* 11(1): 82, 2022.

- 1. Naoki Ikari, Yasuyuki Nakamura, Hirofumi Arakawa. Mieap forms membraneless oragenelles to compartmentalize and facilitate cardiolipin metabolism. AACR Annual Meeting 2022, April 2022.
- 2. Yasunaga M. Development of next-generation antibody therapeutics against refractory cancer utilizing DDS and molecular imaging. 18th PEGS Boston, May 2022.

Cellular and Molecular Medicine

Associate Professor Junko Sasaki

(1) Outline

Phosphoinositides (PIPs) are the molecules that contain phosphatidylinositol, which has a glycerol backbone, two long-chain fatty acids, and an inositol head group. As a result of combinatorial phosphorylation of the hydroxyls of inositol ring, seven other PIPs classes can be generated. Each PIPs exhibits a unique stereochemistry and can bind to distinct cellular protein targets, thereby regulating a wide variety of cellular activities and responses. In terms of PIPs acyl chains, our knowledge about how much importance these hydrocarbon chains have is only limited, in contrast to the phosphorylation patterns. Our goal is to reveal the functions of each PIPs molecular species.

(2) Research

Recently, we revealed that the acyl profiles of phosphoinositides are altered in human prostate cancer tissues. Therefore we are currently studying the physiological and pathophysiological functions of each PIPs molecular species by three approaches.

1. Cellular analyses: We examine changes in PIPs molecular species regulating cellular responses, including cell migration, proliferation, and differentiation.

2. In vivo analyses: We examine changes in PIPs molecular species of diseased tissues from gene-targeted mice lacking PIPs metabolizing enzymes.

3. Molecular analyses: We find the binding proteins of each PIPs molecular species by developing new methods for studying lipid-protein interaction.

(3) Education

Topics of research for graduate student

- 1. Cancers and PIPs molecular species
- 2. Inflammations and PIPs molecular species
- 3. Disorders of sex development and PIPs molecular species

(4) Lectures & Courses

Each student has an independent research theme. Students are expected to have experimental science knowledge and skills.

The goal is to be able to plan, execute, and present original research in cooperation with other researchers.

(5) Publications

[Original Articles]

- Tomonori Ayukawa, Masakazu Akiyama, Yasukazu Hozumi, Kenta Ishimoto, Junko Sasaki, Haruki Senoo, Takehiko Sasaki, Masakazu Yamazaki. Tissue flow regulates planar cell polarity independently of the Frizzled core pathway. Cell Rep. 2022.09; 40(12); 111388
- 2. Kaori Kanemaru, Makoto Shimozawa, Manabu Kitamata, Rikuto Furuishi, Hinako Kayano, Yui Sukawa, Yuuki Chiba, Takatsugu Fukuyama, Junya Hasegawa, Hiroki Nakanishi, Takuma Kishimoto, Kazuya Tsujita, Kazuma Tanaka, Toshiki Itoh, Junko Sasaki, Takehiko Sasaki, Kiyoko Fukami, Yoshikazu Nakamura. Plasma membrane phosphatidylinositol (4,5)-bisphosphate is critical for determination of epithelial characteristics. Nat Commun. 2022.05; 13(1); 2347
- 3. Asami Kawasaki, Akiko Sakai, Hiroki Nakanishi, Junya Hasegawa, Tomohiko Taguchi, Junko Sasaki, Hiroyuki Arai, Takehiko Sasaki, Michihiro Igarashi, Fubito Nakatsu. PI4P/PS countertransport by ORP10 at ER-endosome membrane contact sites regulates endosome fission. J Cell Biol. 2022.01; 221(1);
- 4. Shin Morioka, Hiroki Nakanishi, Toshiyoshi Yamamoto, Junya Hasegawa, Emi Tokuda, Tomoya Hikita, Tomoko Sakihara, Yuuki Kugii, Chitose Oneyama, Masakazu Yamazaki, Akira Suzuki, Junko Sasaki, Takehiko Sasaki. A mass spectrometric method for in-depth profiling of phosphoinositide regioisomers and their disease-associated regulation. Nat Commun. 2022.01; 13(1); 83

[Conference Activities & Talks]

- 1. Takehiko Sasaki, Junko Sasaki. Phosphoinositide phosphatases in cancer. EMBO WORKSHOP 2022.12.11 Palm Springs, CA, USA
- 2. Takehiko Sasaki, Junko Sasaki. High resolution phosphoinositide profile in pathological samples. FASEB science research conference 2022.11.14 Bangalore, India
- 3. Junko Sasaki, Shogo Yanai, Junjie Huang, Junya Hasegawa, Takehiko Sasaki. Premature ovarian insufficiency in mice lacking phosphoinositide-metabolizing enzymes.. The 17th International Symposium of the Institute Network for Biomedical Sciences 2022.10.14 Kanazawa
- 4. Takehiko Sasaki, Junko Sasaki. Phosphoinositide dynamics in cancer, Symposium on World Cancer Research. Symposium on World Cancer Research 2022 (SWCR) 2022.05.06 Web (Singapore)

[Others]

1. Seeing lipids more deeply with mass spectrometry, 2022.03 AAAS EurekAlert! The Global Source for Science News

Interdisciplinary Sciences

Prof. Mitsunori Hieda (Physics) Prof. Atsuhiko Hattori (Biology) Prof. Masayuki Nara (Chemistry) Assoc. Prof. Shinichi Tokunaga (Mathematics)

(1) **Outline**

Our research group conducts interdisciplinary studies relating to medical science using biology, chemistry, physics and mathematics.

(2) Publications

[Original Articles]

- 1. Tatsuki Yamamoto, Mika Ikegame, Yukihiro Furusawa, Yoshiaki Tabuchi, Kaito Hatano, Kazuki Watanabe, Umi Kawago, Jun Hirayama, Sachiko Yano, Toshio Sekiguchi, Kei-ichiro Kitamura, Masato Endo, Arata Nagami, Hajime Matsubara, Yusuke Maruyama, Atsuhiko Hattori, and Nobuo Suzuki. Osteoclastic and Osteoblastic Responses to Hypergravity and Microgravity: Analysis Using Goldfish Scales as a Bone Model ZOOLOGICAL SCIENCE. 2022.08; 39; 388-396
- 2. Aika Sekimoto, Tsuyoshi Ohira, Atsushi Shigematsu, Takuji Okumura, Miyuki Mekuchi, Kenji Toyota, Hiroyuki Mishima, Ryoya Kawamura, Kaito Hatano, Umi Kawago, Yoichiro Kitani, Toshio Sekiguchi, Thumronk Amornsakun, Jun Hirayama, Atsuhiko Hattori, Hajime Matsubara, Nobuo Suzuki. Functional analysis of a matrix peptide involved in calcification of the exoskeleton of the kuruma prawn, Marsupenaeus japonicus Aquaculture. 2022.06; 559; 738437
- 3. Tatsuki Yamamoto, Mika Ikegame, Kohei Kuroda, Jingjing Kobayashi-Sun, Jun Hirayama, Isao Kobayashi, Ryoya Kawamura, Masato Endo, Yoshiaki Tabuchi, Yukihiro Furusawa, Koji Yachiguchi, Toshio Sekiguchi, Hajime Matsubara, Sachiko Yano, Atsuhiko Hattori, and Nobuo Suzuki. Activation of RANKL-producing cells under simulated microgravity with a three-dimensional clinostat in regenerating goldfish scale Biological Sciences in Space. 2022.06; 36; 9-14
- 4. Hassan El-Sayed Embaby, Takuya Miyakawa, Satoshi Hachimura, Tomonari Muramatsu, Masayuki Nara, Masaru Tanokura. Study on physical and chemical properties of Nabak (Zizyphus spina-christi) seed kernel and sweet pepper (Capsicum annuum L.) seed oils Journal of the Science of Food and Agriculture. 2022.05; 102(7); 2660-2666
- 5. Suzuki, N., Honda, M., Sato, M., Yoshitake, S., Kawabe, K., Tabuchi, Y., Omote, T., Sekiguchi, T., Furusawa, Y., Toriba, A., Tang, N., Shimasaki, Y., Nagato, E.G., Zhang, L., Srivastav, A.K., Amornsakun, T., Kitani, Y., Matsubara, H., Yazawa, T., Hirayama, J., Hattori, A., Oshima, Y. and Hayakawa, K.. Hydroxylated benzo[c] phenanthrene metabolites cause osteoblast apoptosis and skeletal abnormalities in fish. Ecotoxicology and Environmental Safety. 2022.03; 234; 113401
- 6. Hisayuki Morii, Masayuki Nara. Fragment-matching survey for amyloid-core region of amyloid beta (1-42) Peptide Science 2021. 2022.03; 58; 151-154

- 7. Masayuki Nara, Hisayuki Morii, Akira Sakamoto, Takuya Miyakawa, Masaru Tanokura. ATR-FTIR study of synthetic peptide analogs of the calcium-binding site III of rabbit skeletal muscle troponin C: Effects of amino-acid replacement Peptide Science 2021. 2022.03; 58; 161-162
- 8. Hassan El-Sayed Embaby, Takuya Miyakawa, Satoshi Hachimura, Tomonari Muramatsu, Masayuki Nara, Masaru Tanokura. Crystallization and melting properties studied by DSC and FTIR spectroscopy of goldenberry (Physalis peruviana) oil Food Chemistry. 2022.01; 366(3);

- 1. Ryoya Kawamura, Miyuki Mekuchi, Kenji Toyota, Shouzo Ogiso, Yukina Watabe, Arata Nagami, Yusuke Maruyama, Atsuhiko Hattori, Seiji Yanai, Jun Hirayama, Hajime Matsubara, and Nobuo Suzuki. Changes in osmoregulatory function during growth of red-clawed crab larvae. The 6th International Exchange Seminar of Zoology 2022.09.17
- 2. Junko Taniguchi, Airi Kaneko, Masato Kuribara, Masaru Suzuki, and Mitsunori Hieda. Superfluid measurements of 4He confined in a nanochannel by a 100 kHz tuning fork. International Conference on Ultra Low Temperature Physics (ULT2022) 2022.08.25
- 3. Taku Matsushita, Azimjon A. Temurjonov, Ryosuke Shibatsuji, Yasuhiro Shimizu1, Yoshiaki Kobayashi, Masayuki Itoh, Mitsunori Hieda, and Nobuo Wada. NMR study of 1D 3He in nanochannels. International Conference on Ultra Low Temperature Physics (ULT2022) 2022.08.25
- 4. Nobuo Wada, Taku Matsushita, Mitsunori Hieda. Heat Flow Resistance of Compact Nanopore Heat Exchanger. 29th International Conference on Low Temperature Physics (LT29) 2022.08.18
- Azimjon A. Temurjonov, Taku Matsushita, Kazunori Amaike, Ryoichi Inagaki, Mitsunori Hieda, Nobuo Wada, Yasuhiro Shimizu, Yoshiaki Kobayashi, Masayuki Itoh. Influence of Precoated 4He layer on the 3He Dimerization in Nanopores. 29th International Conference on Low Temperature Physics (LT29) 2022.08.18
- 6. Airi Kaneko, Yamato Ota, Junko Taniguchi, Masaru Suzuki, Mitsunori Hieda. Simultaneous measurements of 4He confined in an oriented porous membrane by 32- and 100-kHz tuning forks. 29th International Conference on Low Temperature Physics (LT29) 2022.08.18
- 7. Taku Matsushita, Azimjon A. Temurjonov, Ryosuke Shibatsuji, Yasuhiro Shimizu, Yoshiaki Kobayashi, Masayuki Itoh, Mitsunori Hieda, and Nobuo Wada. Examination of Possible Tomonaga-Luttinger Liquid Behavior for 1D 3He Formed in Nanochannels. 29th International Conference on Low Temperature Physics (LT29) 2022.08.18

Division of Data Science Algorithm Design and Analysis

Professor BANNAI Hideo Assistant Professor KOEPPL Dominik

(1) Outline

The department of Data Science Algorithm Design and Analysis studies algorithms, which are an essential component of data science, especially for handling large data sets. Our aim is to design algorithms and data structures that are both effective and efficient, in order to help manage and analyze various types of medical data.

(2) Research

We research is mainly on the following topics

- 1. Algorithms and data structures for pattern matching, pattern discovery
- 2. Algorithms and data structures for data compression and processing of compressed data
- 3. Combinatorics on words

(3) Publications

[Original Articles]

- 1. Laurentius Leonard, Shunsuke Inenaga, Hideo Bannai, Takuya Mieno. Online algorithms for finding distinct substrings with length and multiple prefix and suffix conditions String Processing and Information Retrieval. 2022.11; 24-37
- Katsuhito Nakashima, Noriki Fujisato, Diptarama Hendrian, Yuto Nakashima, Ryo Yoshinaka, Shunsuke Inenaga, Hideo Bannai, Ayumi Shinohara, Masayuki Takeda. Parameterized DAWGs: Efficient constructions and bidirectional pattern searches Theoretical Computer Science. 2022.10; 933; 21-42
- 3. Hideo Bannai, Keisuke Goto, Masakazu Ishihata, Shunsuke Kanda, Dominik Köppl, Takaaki Nishimoto. Computing NP-hard Repetitiveness Measures via MAX-SAT Proc. The 30th Annual European Symposium on Algorithms. 2022.09; 244; 12:1-12:16
- 4. Tooru Akagi, Yuki Kuhara, Takuya Mieno, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Combinatorics of minimal absent words for a sliding window Theoretical Computer Science. 2022.08; 927; 109-119
- Hideo Bannai, Tomohiro I, Tomasz Kociumaka, Dominik Köppl, Simon J. Puglisi. Computing Longest (Common) Lyndon Subsequences Proc. International Workshop on Combinatorial Algorithms (IWOCA 2022). 2022.06; 13270; 128-142
- 6. Paolo Ferragina, Giovanni Manzini, Travis Gagie, Dominik Köppl, Gonzalo Navarro, Manuel Striani, Francesco Tosoni. Improving matrix-vector multiplication via lossless grammar-compressed matrices Proceedings of the VLDB Endowment. 2022.06; 15(10); 2175-2187

- 7. Tomohiro I, Dominik Köppl. Space-Efficient B Trees via Load-Balancing. Combinatorial Algorithms 33rd International Workshop(IWOCA). 2022.06; 327-340
- 8. Kazuya Tsuruta, Dominik Köppl, Shunsuke Kanda, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. c-trie++: A Dynamic Trie Tailored for Fast Prefix Searches Information and Computation. 2022.05; 104794
- 9. Alexandre P. Francisco, Travis Gagie, Dominik Köppl, Susana Ladra, Gonzalo Navarro. Graph Compression for Adjacency-Matrix Multiplication SN Computer Science. 2022.05; 3(3);
- 10. Hiroe Inoue, Yoshiaki Matsuoka, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Factorizing Strings into Repetitions Theory of Computing Systems. 2022.04;
- 11. Takuya Mieno, Yuta Fujishige, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Computing Minimal Unique Substrings for a Sliding Window Algorithmica. 2022.03;
- 12. Dominik Köppl. Computing Lexicographic Parsings Proc. Data Compression Conference 2022 (DCC 2022). 2022.03; 232-241
- 13. Jin Jie Deng, Wing-Kai Hon, Dominik Köppl, Kunihiko Sadakane. FM-Indexing Grammars Induced by Suffix Sorting for Long Patterns Proc. Data Compression Conference 2022 (DCC 2022). 2022.03; 63-73
- 14. Dominik Köppl, Gonzalo Navarro, Nicola Prezza. HOLZ: High-Order Entropy Encoding of Lempel-Ziv Factor Distances Proc. Data Compression Conference 2022 (DCC 2022). 2022.03; 83-92
- 15. Dominik Köppl. Inferring Spatial Distance Rankings with Partial Knowledge on Routing Networks Information. 2022.03; 13(4); 1-28
- Takuya Mieno, Kiichi Watanabe, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Palindromic Trees for a Sliding Window and Its Applications Information Processing Letters. 2022.01; 173; 106174
- 17. Dominik Köppl, Simon J. Puglisi, Rajeev Raman. Fast and Simple Compact Hashing via Bucketing. Algorithmica. 2022; 84(9); 2735-2766
- 18. Dominik Köppl. Linking Off-Road Points to Routing Networks. Algorithms. 2022; 15(5); 163
- 19. Luís M.S. Russo, Diogo Costa, Rui Henriques, Hideo Bannai, Alexandre P. Francisco. Order-preserving pattern matching indeterminate strings Information and Computation. 2022; 289(A); 104924

[Conference Activities & Talks]

1. Computing Lexicographic Parsings. 2022.03.01

[Awards & Honors]

1. IWOCA 2022 Best Paper Award, 33rd International Workshop on Combinatorial Algorithms (IWOCA 2022), 2022.06

Department of Anatomical and Physiological Science

Professor Osamu Hoshi Assistant Professor Hitomi Fujishiro (Master's Programs)Ryusuke Kobayashi, Miki Azumaya, Nanami Seshimo, Maki Tejima, Mayu Funabashi, Yuho Shishido

(1) Outline

Anatomy and physiology are the primary disciplines taught in the field of anatomy and physiological sciences. Anatomy explores the morphology and structure of the human body from the organ to cellular and molecular levels. It is the most fundamental area of medical science. Physiology investigates what kind of mechanism is needed for each structural component of the human body to function, and how such components are integrated into the whole human body. Anatomy and physiology function like two wheels of a cart for the scientific understanding of the human body. These two subjects lay down the foundation required to study advanced subjects. The teaching team is committed to providing students with education that helps them master the basics of the subjects and successfully transition to the clinic.

(2) Research

Morphology and biological information analysis uses various microscopic techniques including electron microscopy for observing the microstructure of the living tissue, with the primary aim of gaining new scientific knowledge. Cutting-edge research has been conducted in this area, such as the development of new imaging technologies and applying atomic force microscopy to biomedicine.

(3) Education

Examination for Technology Stream: Human Anatomy Lecture, Human Anatomy Practicum, Physiological Examination Lecture I, Physiological Examination Practicum I, Theory of Advanced Medical Technology, General Lecture, Graduate Research Project

Examination for Nursing Stream: Anatomy, Physiology, Joint Practicum with Advanced and Basic Students (anatomy practicum)

Examination for Science Stream: Morphology and Biological Information Analysis Special Lecture A, Morphology and Biological Information Analysis Experiment A, Morphology and Biological Information Analysis Special Lecture

(4) Lectures & Courses

The teaching team provides students with education and research instructions that help them grow their interest to study and research in the field of medicine. The team simultaneously reviews feedback from students to improve the method of conducting lectures and practicums.

(5) Publications

[Original Articles]

 Atsuhiro Fukai, Akimoto Nimura, Masahiro Tsutsumi, Hitomi Fujishiro, Koji Fujita, Junya Imatani, Keiichi Akita. Lateral Ulnar Collateral Ligament of the Elbow Joint: Reconsideration of Anatomy in Terms of Connection with Surrounding Fibrous Structures. J Bone Joint Surg Am. 2022.08; 104(15); 1370-1379

- 1. Hoshi O, Takaei N. The relationship between ribosomes and actin filament associated with local protein synthesis in axonal growth cones. NEURO2022 2022.07.01 Okinawa
- 2. Hoshi O, Takaei N. Changes in the relationship between ribosomal protein S6 and actin during local protein synthesis in growth cones. 第 127 回日本解剖学会総会 · 全国学術集会 2022.03.28 Web 方式

Molecular and Cellular Biology

Nobuharu Suzuki, Associate Professor

(1) Outline

In 2022, the 5th year for our department, Assoc. Prof. Suzuki and 4 graduate students were the members and performed various activities in research and education. Regarding our research, our main project was the elucidation of the molecular mechanism of myelination in the central nervous system. In 2022 particularly, we created and prepared 5 different lines of genetically engineered mice to develop new models of related neurological and mental disorders. In terms of education, we taught graduate and undergraduate students at many lectures and laboratory classes of basic biochemistry/molecular biology, particularly related to medical technologies. In addition, Suzuki was a member of the administrative offices of Lab Safety and a representative or a member of other committees and contributed to their activities.

(2) Research

In the central nervous system, myelin is formed by oligodendrocytes and is essential for the rapid propagation of neuronal signal. Therefore, defects in the functions of myelin cause neurological disorders, such as multiple sclerosis and leukodystrophy. In addition, it has been recently revealed that the myelin functions are critically associated with mental disorders and dementia. Thus, the study regarding myelin functions will give new insights in brain science and better understanding of the mechanisms and new strategies of the treatments for the diseases. In our department, we investigate its cellular and molecular mechanisms using the mutant mouse line that develops hypomyelination in the central nervous system and try to expand our research to application studies. In 2022, we created and prepared 5 different lines of genetically engineered mice to develop new models of related diseases. In addition, we proceeded to elucidate the molecular mechanisms of functions of a cell adhesion protein teneurin-4 and extracellular matrix proteins, fibulin-7 and laminins. Further, we revealed that the mechanism of axon degeneration after the myelin defect in the mutant mice, indicating that this mouse line is useful for understanding the mechanism and for developing the treatment for axonal loss in the related diseases. We reported the summary of these results in a review (Yamada et al, 2022, Front Cell Dev Biol) and in presentations at expertise meetings [Society for Neuroscience (SfN), The Japanese Society for Neurochemistry (JSN), The Molecular Biology Society of Japan (MBSJ), and The Japanese Society for myelin study] .

(3) Education

In 2022, for undergraduate students, Suzuki was a responsible organizer for "Biochemistry", "Biochemistry, Lecture", "Medical Genetics and Human Genome Science, Lecture", "Biochemistry, Laboratory", "Medical Genetics, Laboratory", "Medical Ethics, Laws and Regulations", "Global Communication I", "Global Communication II", "English for Health Care Science I", and English for Health Care Science II", and taught parts of the lectures of "Practice of Medical Science" and "General Medical Technology". Total number of the classes that Suzuki took care of is more than 100. For graduate students, Suzuki taught parts of "Medical Technology I" and "Biomedical Laboratory Science Seminar I" for master course students, and "Development of Novel Technologies for Clinical Tests" and "Biomedical Laboratory Science Seminar II" for students in the laboratory/department.

(4) Lectures & Courses

As until 2021, we have had the concept for education to explain well about 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

scientific editor in 2international journals. In In 2022.Suzuki worked as a topic of them. Frontiers Cell and Developmental Biology, Suzuki released article one inan collection together with co-editors of famous investigators in US and Germany ("Dynamic Diverse Functions of Oligodendrocytes and Myelin in the Central Nervous System": and https://www.frontiersin.org/research-topics/26968/dynamic-and-diverse-functions-of-oligodendrocytes-andmyelin-in-the-central-n

Suzuki was Special Volunteer at National Institutes of Health (NIH) and contributed to international relationships between the research institutes and universities. 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 Japanese Society for Neurochemistry (JSN), The Japanese Society for Matrix Biology and Medicine (JSMBM), and the Japanese Society for Myelin Study and contributed to their activities.

(6) Publications

[Misc]

1. Momona Yamada, Miho Iwase, Binri Sasaki, Nobuharu Suzuki. The molecular regulation of oligodendrocyte development and CNS myelination by ECM proteins Frontiers in Cell and Developmental Biology. 2022.09; 10; 952135

- 1. Momona Yamada, Miho Iwase, Chikako Hayashi, de Vega Susana, Nobuharu Suzuki. An extracellular matrix protein Fibulin-7 positively regulates oligodendrocyte differentiation through the N-terminal active sequence. 第 45 回日本分子生物学会年会 2022.12.01
- Miho Iwase, Chikako Hayashi, Binri Sasaki, Momona Yamada, Nobuharu Suzuki. Teneurin-4 promotes CNS myelin formation through a molecular interaction with actin-regulating proteins in oligodendrocytes. 第 45 回日本分子生物学会年会 2022.11.30
- 3. Momona Yamada, Miho Iwase, Chikako Hayashi, Susana de Vega, Nobuharu Suzuki. The extracellular matrix protein fibulin-7 positively regulates oligodendrocyte differentiation through the interaction between myelin and neuronal axons. Neuroscience 2022 2022.11.13 San Diego Convention Center, San Diego, CA, USA
- 4. Miho Iwase, Chikako Hayashi, Binri Sasaki, Momona Yamada, Nobuharu Suzuki. Teneurin-4 forms a molecular complex with actin-regulating proteins in oligodendrocytes and promotes myelin sheath formation in the CNS. Neuroscience 2022 2022.11.13 San Diego Convention Center, San Diego, CA, USA
- 5. Nobuharu Suzuki, Riko Takahashi, Hinako Saito, Yukina Hosoda, Chikako Hayashi. The Maintenance of Small Caliber Axons in Teneurin-4 Deficient Mice with the Congenital Hypomyelination in the CNS. 第 65 回日本神経化学会大会 2022.07.02
- 6. Miho Iwase, Momona Yamada, Chikako Hayashi, Nobuharu Suzuki. The molecular function of the actin cytoskeletal regulator Arpc1a in proliferation and morphogenesis of oligodendrocyte-lineage cells. 第 65 回日本神経化学会大会 2022.07.01
- 7. Momona Yamada, Miho Iwase, Chikako Hayashi, Susana de Vega, Nobuharu Suzuki. Fibulin-7, an extracellular matrix protein, positively regulates oligodendrocyte differentiation and attachment to neuronal axons. 第 65 回日本神経化学会大会 2022.07.01

1. Nobuharu Suzuki, Miho Iwase, and Momona Yamada . Axon diameter-dependent myelination by specific subpopulations of oligodendrocytes. The 6th Annual Meeting of the Japan Myelin Society 2022.02.12

Molecular Pathology

Professor: Motoji Sawabe(Retired in March 2022) Junior Associate Professor(Career Track): Yurie Soejima

Graduate student Doctoral Program Graduated in 2022: Mizuho Sato, Minami Kikuchi Enrolled in 2022: Mayumi Kinoshita, Akiya Tatsumi, HATTHAKONE THAVISOUK

Graduate student Master's Program Graduated in 2022: Shiori Watabe, OUNDAVONG SUNTI

Staff Assistant: Hitomi Sasaki Technical Assistant: Momoka Sakai

(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 higher quality diagnoses by various examinations and methods such as histology, cytology, immunohistochemistry, genetic analysis, and electron microscopy. We explore the essence of the diseases in both aspects 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 the diagnosis.

- 1. Immunohistochemical analysis of human and mouse cardiac conduction system
- 2. Proteomic analysis of human cardiac aging
- 3. Molecular epidemiologic and clinicopathological study of Lipoprotein(a)
- 4. Molecular pathological study of cholangiocarcinoma and development of a novel therapy
- 5. Creation of digital content using cytological images, AI imaging diagnosis
- 6. Development of pathological diagnosis and pathological technology in developing countries

(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 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, precious humanity and high ethical values, the ability of self-problem raising and solution, life-long-thinking, the following education are providing.

1) Undergraduate education

 \cdot In the 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 the second grade of Medical Technology, practical training of pathological examination is organized to contributes to the diagnosis of diseases and elucidation the pathogenesis, such as various special staining methods, immunohistochemistry, cytology, and frozen section, in addition to visual inspection of organs, basic preparation of specimens and observation.

 \cdot In the second grade of Nursing science, we have pathological anatomical observation as a part of the Practice of Medical Sciences.

 \cdot In the third grade of Medical Technology, pathological examination practice is carried out at the Department of Pathology in TMDU hospital as Clinical Practice.

• In the fourth grade of Medical Technology, we provide the education of the basics of research, such as how to proceed with the study and how to write the research paper as the Undergraduate Research

2) Graduate education

· In the Master's Program, we discuss essentials of diseases, with the 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, gene analysis, image analysis, etc.), which useful for elucidation 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.

 \cdot In the 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

 \cdot In the Pathology department of the TMDU hospital, Sawabe participates in the pathological diagnosis of autopsy cases. Soejima participates in the cytological diagnosis and supervises graduate students.

 \cdot Soejima provided education on practical training of pathological examination as a part-time instructor at Bunkyo Gakuin University.

(6) Publications

[Original Articles]

- Mayumi Kinoshita, Motoji Sawabe, Yurie Soejima, Makiko Naka Mieno, Tomio Arai, Naoko Honma. Gross Cystic Disease Fluid Protein-15 (GCDFP-15) Expression Characterizes Breast Mucinous Carcinomas in Older Women. Diagnostics (Basel). 2022.12; 12(12);
- 2. Thavisouk Hatthakone, Sunti Oundavong, Yurie Soejima, Motoji Sawabe. Development of a new histological identification method of human sinoatrial node suitable for immunohistochemical study. Anat Sci Int. 2022.11;

[Conference Activities & Talks]

1. 木下真由美、新井冨生、副島友莉恵、沢辺元司、本間尚子. 高齢女性における乳腺粘液癌の特徴. 第111回日本病理学会総会 2022.04.14 神戸

Biofunctional System Engineering

Professor ITO Minami Assistant Professor HONMA Satoru Visiting Lecturer AKAZAWA Kouhei Visiting Lecturer SATO Tomoaki

(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, electrophysiological 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 a method of psychophysics and electrophysiological recordings mainly from a single cell in an animal, we may reveal causal relationships between them.

So far, we have trained three Japanese monkeys to conduct our material discrimination tasks. Five materials (metal, fabric, gel sheet, wood bark, fur) were used as reference stimuli, which represent categories of material discrimination. Then, the second task was introduced, combining haptic inspection of material cues and visual inspection of correct response levers. Under the covid19 situation, the training was continued to keep animals' performance. This year, we have conducted a searching task, in which human subjects search objects by a cue of material property or material category, in order to examine the impact of paying attention to a particular material cue.

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. Now, we started more realistic simulations by using a simulation head model that assumes occurrence of local inflammation and circulatory disorders and examined several control programs.

(3) Education

1) Undergraduate school

Under the covid19 situation, remote lectures were carried out via on-line programs or tutoring via an e-mail. The practices were carried out with sever precaution against the covid19, separating students into two classes. 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 programing rules and programing 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 Baysian 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. Biomedical Laboratory Sciences Seminar: 4 joint seminar with all members of the biomedical laboratory science track. In a part of special lectures, we discussed the system neuroscience, visual information processing in the brain, and relationships with the artificial intelligence.

(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]

 Katsudal T, Sato N, Mogushi K, Hase T & Muramatsu M. Sub-GOFA: A tool for Sub-Gene Ontology function analysis in clonal mosaicism using semantic (logical) similarity Bioinformation. 2022; 18(1); 53-60

[Conference Activities & Talks]

1. Minami Ito, Kanako Koyama, Rio Hayashida, Risa Sugawara. Material perception associating haptic and visual inspections in non-human primate subjects. 第45回日本神経科学学会 2022.07.03 Ginowan,

Okinawa

Department of Respiratory and Nervous System Science

Professor: Yuki Sumi, MD, PHD.
Assistant Professor: Miho Akaza, MD, PHD.
Part-time: Keiko Hara, MD, PHD, Sayaka Aritake, MT, PHD,
Mina Ako, MT, PHD, Osamu Takahashi, MT, PHD,
Yoko Soroida, MT, PHD, Akihiko Tajima, MT, PHD,
Jyunji Endo, MD, PHD, Yuri Ichikawa, MT, PHD,
Yoshiaki Adachi, PHD, Yuko Kato, MT, PHD,
Yoshiaki Adachi, PHD, Luna Okubo, MT.
Master's: Yuka Hosoya MT, Chiune Funaita MT, Gengen Ko MT,
Maina Oshige.
Students: Eri Ota, Maiko Kawahara, Yusuke Komabashiri ,Yukina Higasiguchi,
Sakura Shimooki, Kouki Kawamura, Hiyori Tarui, Satomi Tozato,
Jun Ninomiya.

(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.

Previously, 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 diagnosis 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 Department of Clinical and Physiological Laboratory Science 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 given on the research methods and minds, focusing on the research theme assigned to each person. 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.

In addition, the educational effort equal to or higher than the lecture training in our Department is given to the 1st to 6th grade medical students and residents. (Details omitted)

The Ministry of Education, Culture, Sports, Science and Technology (MEXT) has set 2025 as the target year in its "AI Strategy 2019" for (1) all university and technical college students, regardless of their background, to acquire elementary level skills and (2) university and technical college students to acquire basic skills for application in their own specialized fields. The University has developed a model curriculum and teaching materials for mathematics, Data Science, and Artifical Intelligence education in the fields of medicine and dentistry, and has newly established "Introduction to AI and Big Data with Medicine," as a university-wide common subject, "Applied AI and Big Data with Medicine" to medical and dental students, aiming to incorporate it into the University's curriculum and disseminate it to medical and dental schools across the country. In addition, "AI Practical Exercise" was offered to those who wished to take it. (Details are omitted.)

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 educates 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 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 Pharmaco-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.

(6) Clinical Performances

Dr. Sumi is a specialist in general internal medicine from the Japanese Society of Internal Medicine, an advisor and specialist in respiratory medicine from the Japanese Society of Respiratory Medicine, and a specialist in allergy from the Japanese Society of Allergy.

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. Toru Sasaki, Shigenori Kawabata, Jun Hashimoto, Yuko Hoshino, Kensuke Sekihara, Yoshiaki Adachi, Miho Akaza, Koji Fujita, Akimoto Nimura, Toshitaka Yoshii, Yuki Miyano, Yuki Mitani, Taishi Watanabe, Shinji Sato, Sukchan Kim, Atsushi Okawa. Assessing carpal tunnel syndrome with magnetoneurography. Clin Neurophysiol. 2022.07; 139; 1-8
- 2. Sasaki Y, Nakakuki K, Ikeda M, Sumi Y, Miura H, Imazu Y, Otomo Y. Undergraduate medical and dental science students' interest and support needs in medical volunteer activities during times of disasters Japanese Journal of Disaster Medicine. 2022.04; 27; 102-109
- 3. Matsubayashi T, Akaza M, Hayashi Y, Hamaguchi T, Satoh K, Kosami K, Ae R, Kitamoto T, Yamada M, Shimohata T, Yokota T, Sanjo N. Specific electroencephalogram features in the very early phases of sporadic Creutzfeldt-Jakob disease. J Neurol Sci. 2022.04; 437; 120265

Clinical and Diagnostic Laboratory Science

Professor Sei Kakinuma, M.D., Ph.D.

Assistant Professor Junji Yamaguchi, M.D., Ph.D.

Graduate Students, Doctoral Program. Jun Tsuchiya, M.D., Taro Shimizu, M.D., Keiya Watakabe, M.D., Tomohiro Mochida, M.D., Kento Inada, M.D. (Apr. 2022-). (in collaboration with Department of Gastroenterology and Hepatology, Medical and Dental Science Track)

Graduate Students, Master Program. Rion Kamimae.

Undergraduate Students. 4th grade, Nana Shibayama, Ayaka Suga, Kai Suzuki, Kyoko Chino, Momoko Furue. 3rd grade, Minori Kurata, Minori Sato, Hoshie Hirayama, Kaho Yamada

(1) Outline

Patients died from 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 liver diseases, and the development of effective treatment for progressive liver diseases has been quite essential. Moreover, patients died from biliary and pancreatic cancer are more than 50,000 persons per a year in Japan. It is still difficult to detect such diseases at early stages and to establish the standard therapeutic strategy for them. It is urgently needed to address this issue as well as that of chronic liver diseases.

We believe that an essential role of departments in the Graduate school in Principles in Division of Biomedical Laboratory Sciences, TMDU, is to provide a basis for the innovative medical examination and to establish the treatment in next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel laboratory and therapeutic strategy established upon basic research are required.

Our department is founded in 2020 under pandemic infection, which is standing by such principles. Our research projects focus on hepato-biliary diseases (by Dr. Kakinuma) and cardiovascular diseases (by Dr. Yamaguchi). The goal of our education is to promote students to become a well-developed scientist, and also leading experts in the field of hepato-biliary or cardiac diseases and medical technology.

(2) Research

Our principle of research is to achieve studies evoked from various clinical problems, and also directs to launch innovative diagnostic and therapeutic procedures. Prof. Kakinuma focuses on the basic studies of novel disease models using human iPS cells to elucidate the pathophysiology. We also focus on analysis of cell-to-cell interaction regulating development and progression of hepatobiliary diseases. We focus other projects described as below, and promote them using molecular and cellular biologic approaches. We are collaborating with Department of Gastroenterology and Hepatology (Medical and Dental Science Track, Graduate school, TMDU), a lot of departments in TMDU, and several departments in other universities in Japan.

Dr. Yamaguchi is collaborating with Department of Cardiovascular Medicine, and is researching in the field of basic and clinical cardiology. We are currently researching on the development of novel absorbable biomaterials for ischemic diseases, and the role of extracellular vesicles in the myocardial remodeling. We also research on the low-/non-invasive health monitoring devices, including the screening of sleep apnea syndrome (SAS) with infrared camera and the detection of early-stage heart failure and arrhythmia using a single lead electrocardiogram. We are focusing on the cardiovascular research from broad perspectives, aiming for a clinical application in the future.

Research Projects:

(1) Development of novel disease models using human iPS cells to elucidate the pathophysiology

(2) Analysis of cell-to-cell interaction regulating development and progression of hepatobiliary diseases

(3) Development of hepatobiliary and pancreatic disease models using organoid culture system

(4) Molecular mechanisms regulating homeostasis of stem/progenitor cells in gastrointestinal, hepatobiliary, and pancreatic tissue

(5) Research on molecular mechanisms regulating liver regeneration and hepatic fibrosis

(6) Development of a novel treatment for cardiac/limb ischemia using biocompatible and bioabsorbable materials

(7) Analysis on cell communication and signaling in the process of myocardial remodeling.

(8) Development of low-/non-invasive health monitoring devices

(3) Education

Undergraduate students.

We are teaching the courses of physiological function tests and clinical pathophysiology for undergraduate students of medical technologists in School of Medicine, TMDU. We also teach about basic techniques and scientific thinking necessary to advance the scientific research of undergraduate students in TMDU.

Graduate students

The goal of our education is to promote students to become a well-developed scientist, and also leading experts in the field of hepato-biliary or cardiac diseases and medical technology.

Primary goal for education of graduate students is to train highly educated and experienced clinical and technological scientists in the field of hepato-biliary diseases or cardiovascular diseases. Our goal for education of graduate students is to produce clinical and technological scientists thinking from a wide perspective and to bring up leaders of scientists in next generation.

(4) Lectures & Courses

Undergraduate students.

- # Clinical Medicine (II)
- # Physiological Laboratory Science
- # Advanced physiological function
- # Analysis of Electrocardiogram

Graduate students.

Clinical and Diagnostic Laboratory Science

Our lectures and courses are collaboration with Department of Respiratory and Nervous System Science in undergraduate course, and with Department of Gastroenterology and Hepatology and Department of Cardiovascular Medicinein graduate course. We also educate residents and medical technologist in Medical Hospital of TMDU.

Goals for education in scientific research

#1. Students should master the strategy of research for molecular, regenerative, and stem cell biology to reveal

the pathophysiology of Hepato-Biliary-Pancreatic diseases.

#2. Students should master the theory and techniques about physiological laboratory and diagnostic imaging in the field of Hepato-Biliary-Pancreatic diseases.

#3. Students should learn about the research strategy to develop a novel diagnostic and therapeutic methods.

(5) Clinical Services & Other Works

We pursue development 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 clinical study collaborating with the Department of Gastroenterology and Hepatology in TMDU.

We participate in eight research projects for treatment and eradiation of hepatitis virus and one for cancer research and clinical evolution, 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. 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 contribute to the management of the activities and academic meetings held by the American Association for the Study of Liver Disease, the Japanese Society of Gastroenterology, the Japanese Society of Hepatology, the Japanese Society for Regenerative Medicine, and the Japanese Society for the Research of Hepatic cells.

(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 established the outpatient section specialized for chronic hepatitis, cirrhosis, and HCC. We are operating several multicenter studies about hepatitis and liver cancer, including one named as "Ochyanomizu Liver Conference". More than 2000 patients with viral hepatitis were enrolled in such studies, and they 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 biomarkers, and dynamic contrast-enhanced ultrasonography.

Dr. Yamaguchi also research on the low-/non-invasive health monitoring devices, including the screening of sleep apnea syndrome (SAS) with infrared camera and the detection of early-stage heart failure and arrhythmia using a single lead electrocardiogram.

(7) **Publications**

[Original Articles]

- Nakagawa M, Asahina Y, Kakinuma S, Okamoto R. Impact of eradication of hepatitis C virus on liver-related and -unrelated diseases: morbidity and mortality of chronic hepatitis C after SVR. J Gastroenterol. 2022.12;
- Takahashi J, Mizutani T, Sugihara HY, Nagata S, Kato S, Hiraguri Y, Takeoka S, Tsuchiya M, Kuno R, Kakinuma S, Watanabe M, Okamoto R. Suspension culture in a rotating bioreactor for efficient generation of human intestinal organoids. Cell Reports Methods. 2022.11; 2(11); 100337
- 3. Yamaguchi J, Takigawa M, Goya M, Martin C, Amemiya M, Yamamoto T, Nishimura T, Nakamura R, Shirai Y, Tao S, Miyazaki S, Takahashi Y, Sasano T. Impact of tip design and thermocouple location on the efficacy and safety of radiofrequency application. Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing. 2022.04;
- 4. Yamaguchi J, Chiba R, Komuro H, Ihara K, Nozaki K, Nagai A, Furukawa T, Sasano T. Local Injection of Hydroxyapatite Electret Ameliorated Infarct Size After Myocardial Infarction. Circulation reports. 2022.01; 4(1); 38-47

- 1. Junji Yamaguchi, Masateru Takigawa, Miki Amemiya, Tasuku Yamamoto, Takashi Ikenouchi, Tatsuaki Kamata, Rena Nakamura, Takuro Nishimura, Susumu Tao, Shinsuke Miyazaki, Masahiko Goya, and Tetsuo Sasano. Impact of the Different Contact Force on Lesion Characteristics in Very High-power and Short-duration Ablation. The 86th Annual Scientific Meeting of the Japanese Circulation Society (JCS2022) 2022.03.13
- 2. Junji Yamaguchi, Masateru Takigawa, Miki Amemiya, Tasuku Yamamoto, Takashi Ikenouchi, Tatsuaki Kamata, Rena Nakamura, Takuro Nishimura, Susumu Tao, Shinsuke Miyazaki, Masahiko Goya, and Tetsuo Sasano. Comparison of Three Different Approaches of Very High-power Short-duration Ablation using QDOT MICRO Catheter. The 86th Annual Scientific Meeting of the Japanese Circulation Society (JCS2022) 2022.03.13

Analytical Laboratory Chemistry

Professor: • 2022.1-12 : Ryunosuke Ohkawa

Assistant Professor: • 2022.1-12 : Takahiro Kameda

Contract Lecturer · 2022.4-12 : Yuna Horiuchi

Graduate Students:

(Master students)

· 2022.1-3 : Ayuko Hara, Yume Mutsuda, Mei Ogino, Rina Kawaguchi, Marino Shibuya, Takako Yamada · 2022.4-12 : Mei Ogino, Rina Kawaguchi, Marino Shibuya, Motoki Nakamura, Takako Yamada, Wakana Okabayashi, Riho Shimizu, Sun Chengman, Motoki Nakamura, Yuna Hakii, Tsunehiro Miyakoshi

(Doctoral Students)

Adult Graduate Students:

· 2022.1-3 : Azusa Yamazaki, Masamichi Mikame

· 2022.4-12 : Azusa Yamazaki, Masamichi Mikame, Takuya Shimura

Research Students: • 2022.1-3 : Sun Chengman, Motoki Nakamura

Under Graduate Students:

(Senior)

· 2022.4-12 : Sayaka Okuma, Yuto Kikuchi, Honoka Sedutu, Yuwa Someya, Taichi Hasimoto (Junior)

 \cdot 2022.1-3 : Sayaka Okuma, Yuto Kikuchi, Honoka Sedutu, Yuwa Someya, Taichi Hasimoto

 \cdot 2022.11-12 : Hanae Akiyama, Nao Igarashi, Mizuki Tanaka, Kotoko Matayoshi

(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), antioxidant ability and anti-inflammatory effect of high-density lipoprotein (HDL) 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). Moreover, it is known that HDL is not structurally homogeneous but heterogeneous in size, density and chemical composition. We are investigating the mechanism of the HDL diversification through the interactions with other lipoproteins and tissue, and its effect on the HDL character and functions. We are further studying the red blood cell-related lipids metabolism.

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 above mechanisms 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
- · Mechanism of HDL diversification and its effect on the character and function
- \cdot Molecular mechanism of red blood cell-related lipids metabolism

(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. Out 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. Ogino M, Kameda T, Mutsuda Y, Tanaka H, Takahashi J, Okazaki M, Ai M, Ohkawa R. Development of internal standard for lipoprotein subclass analysis using dual detection gel-permeation high-performance liquid chromatography system. Bioscience reports. 2022.05; 42(6);
- 2. Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Minoru Tozuka, Ryunosuke Ohkawa. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: Confirmation and improvement for application in clinical laboratory. Ann Clin Biochem. 2022.03; 59(2); 134-143

- Yamazaki A., Kameda T., Ichimura N., Tohda S., and Ohkawa R. Investigation of Assays for Cholesterol Content of Erythrocytes. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine (ASCPaLM) 2022.10.09 神戸
- 2. Kawaguchi R., Kameda T., Yoshimoto A., and Ohkawa R. The effect of high-density lipoprotein N-homocysteinylation on paraoxnase1 activities and distribution. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine (ASCPaLM) 2022.10.09 神戸
- 3. Ogino M., Kameda T., and Ohkawa R. Improvement of serum antioxidant capacity assay using 1,1-diphenyl-2-picrylhydrazyl. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine (ASCPaLM) 2022.10.09 神戸

- 4. Yamada T., Kameda T., and Ohkawa R.. Investigation of very low-density lipoprotein-triglyceride hydrolysis assessment. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.27 Chicago
- 5. Ikenaga A., Kameda T. and Ohkawa R.. Chymase truncation of apolipoprotein E in high-density lipoprotein is further promoted under myeloperoxidase oxidation. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 6. Ogino M., Kameda, Mutsuda Y., Tanaka H., Takahashi J., Okazaki M., Ai M., and Ohkawa R. Development of internal standard for lipoprotein subclass analysis using dual detection gel-permeation HPLC system. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 7. Kawaguchi R., Kameda T., Yoshimoto A., and Ohkawa R.. The effect of sampling procedure and substrate type for activity assay on PON1 assessment. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 8. Sun C., Kameda T., Ikenaga A., and Ohkawa R.. Improved method for quantification of apoA-I/apoA-II heterodimer in high-density lipoprotein. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- Yamazaki A., Fujii Y., Kameda T., Ichimura N., Tohda S., and Ohkawa R.. Investigation of Assays for Cholesterol Content of Erythrocytes Membrane. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- Kameda T., Ogino M., Kawaguchi R., Shibuya M., Yamada T., Ikenaga A., Sun C., and Ohkawa R.. Effects of serum amyloid A on the structure and antioxidant ability of low-density lipoprotein. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 11. Ohkawa R., Mutsuda Y., Horiuchi Y., Kameda T., and Tozuka M.. Development and validation of novel automatable assay for cholesterol efflux capacity. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 12. Kameda T., Ogino M., Kawaguchi R., Shibuya M., Yamada T., Ikenaga A., Sun C., and Ohkawa R... Effects of serum amyloid A on the structure and antioxidant ability of low-density lipoprotein. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago

Department of Laboratory Molecular Genetics of Hematology

Associate professor : Miwako NISHIO Researcher: Mayumi YOSHIMORI

Adjunct Lecturer : Ayako Arai, Kumiko SAEKI, Ken-ichi IMADOME, Yoichi NAKAYAMA

Graduate Student : Minori SAITO, Kaoru KOIKE, Eri Susaki, Airi MINAMIKAWA

(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

4.Development of new treatment methods using regenerative medicine technology

5.Functional Analysis of human iPS cells derived Brown Adipocytes

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. 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.

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. 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

Research:

Our research group 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. We analyze the blood sample in CAEBV patients.

(7) Publications

[Original Articles]

- Masahide Yamamoto, Maho Sato, Yasushi Onishi, Yoji Sasahara, Hideki Sano, Masayoshi Masuko, Hirohisa Nakamae, Ken-Ichi Matsuoka, Takahide Ara, Kana Washio, Makoto Onizuka, Kenichiro Watanabe, Yoshiyuki Takahashi, Tsuneaki Hirakawa, Miwako Nishio, Chizuko Sakashita, Tohru Kobayashi, Akihisa Sawada, Tatsuo Ichinohe, Takahiro Fukuda, Yoshiko Hashii, Yoshiko Atsuta, Ayako Arai. Registry data analysis of hematopoietic stem cell transplantation on systemic chronic active Epstein-Barr virus infection patients in Japan. Am J Hematol. 2022.06; 97(6); 780-790
- 2. Ohashi Ayaka, Uemura Yu, Yoshimori Mayumi, Wada Naomi, Imadome Ken-Ichi, Yudo Kazuo, Koyama Takatoshi, Nishio Miwako, Arai Ayako. The Plasma Level of IL-1 beta As a Biomarker of Angiopathy in Systemic Chronic Active EBV Infection Front Microbiol. 2022.04; 13; 874998
- Oshima Kumi, Yoshimori Mayumi, Ohashi Ayaka, Nishio Miwako, Shimizu Norio, Arai Ayako. Simvastatin Induces Anti-Tumor Effects on Systemic CAEBV In Vitro and In Vivo Journal of St. Marianna University. 2022; 13(2); 59-68

- 1. Ayaka Ohashi, Mayumi Yoshimori, Miwako Nishio, Kaoru Koike, Norio Shimizu, Kazuo Yudo, Morito Kurata, and Ayako Arai. Will BCL2 be a Potent Therapeutic Target for Systemic Chronic Active Epstein-Barr Virus Disease?. 12th AACR-JCA joint conference 2022.12.10
- 2. 加藤 久詞, Fu Bin, 田中 都, 西尾 美和子, 菅波 孝祥, 浅原 哲子. 植物由来フラボノイド · タキシフォリンの 肥満と脂肪肝/NASH/肝癌の進展抑制作用 -褐色脂肪細胞活性化と FGF21 の関与. 第 96 回日本内分泌学会 学術総会 2022.06.01

Molecular Microbiology

Professor: Ryoichi Saito Associate Professor: Yukie Tanaka Assistant Professor: Yusuke Ota Graduate Student (doctor's course): Samiratu Mahazu, Mika Nagata, Shu Hagiwara Graduate Student (master's course): Runa Furuya, Kei Yasunaga, Kayo Yamada, Taira Kawamura, Miho Matsuba, Yikeshan Yalikun Research Assistant: Isaac Prah

(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. Research on the resistance mechanism of multidrug-resistant bacteria with whole-genome sequencing

2. Research on the regulation system of virulence in Neisseria meningitidis, Clostridioides difficile, and Clostridium perfringens

3. Research on clarifying the interaction between microorganisms and environments with metagenomics and transcriptomics

4. Development of rapid assay methods for detecting globally important bacteria

(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. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Yoko Nukui, Masato Suzuki, Yoshihiko Hoshino, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Klebsiella species and Enterobacter cloacae isolates harboring blaOXA-181 and blaOXA-48: resistome, fitness cost, and plasmid stability. Microbiol Spectr. 2022.12; e0332022
- 2. Yusuke Ota, Reina Okada, Hideyuki Takahashi, Ryoichi Saito. Molecular detection of fluoroquinolone-resistant Neisseria meningitidis by using mismatched PCR-restriction fragment length polymorphism technique. Front Cell Infect Microbiol. 2022.08; 12; 911911

- 3. Yusuke Ota, Chihiro Tani Sassa, Masayo Kashiwagi, Chikako Okawara, Shuji Tohda, Ryoichi Saito. Complete genome sequence of an Enterobacter roggenkampii strain with reduced carbapenem susceptibility isolated from a home-visit nursing agency Microbiology Resource Announcements. 2022.08; e0035322
- 4. Yusuke Ota, Chihiro Tani Sassa, Masayo Kashiwagi, Chikako Okawara, Shuji Tohda, Ryoichi Saito. Complete Genome Sequence of an Enterobacter roggenkampii Strain with Reduced Carbapenem Susceptibility Isolated from a Home-Visit Nursing Agency. Microbiol Resour Announc. 2022.08; e0035322
- 5. Tanaka Y, Sato T, Yagishita N, Yamauchi J, Araya N, Aratani S, Takahashi K, Kunitomo Y, Nagasaka M, Kanda Y, Uchimaru K, Morio T, Yamano Y.. Potential role of HTLV-1 Tax-specific cytotoxic t lymphocytes expressing a unique t-cell receptor to promote inflammation of the central nervous system in myelopathy associated with HTLV-1. Front Immunol. 2022.08; 13; 993025
- 6. Yusuke Ota, Reina Okada, Hideyuki Takahashi, Ryoichi Saito. Molecular detection of fluoroquinolone-resistant Neisseria meningitidis by using Mismatched PCR-restriction fragment length polymorphism technique Frontiers in Cellular and Infection Microbiology . 2022.07; 12; 911911
- 7. Yuasa S, Nakajima J, Takatsuki Y, Takahashi Y, Tani-Sassa C, Iwasaki Y, Nagano K, Sonobe K, Yoshimoto T, Nukui Y, Takeuchi H, Tanimoto K, Tanaka Y, Kimura A, Ichimura N, Tohda S.. Viral load of SARS-CoV-2 Omicron is not high despite its high infectivity Journal of Medical Virology. 2022.07; 94(11); 5543-5546
- 8. Isaac Prah, Yoko Nukui, Shoji Yamaoka, Ryoichi Saito. Emergence of a high-risk Klebsiella michiganensis clone disseminating carbapenemase genes. Front Microbiol. 2022.05; 13; 880248
- 9. Chihiro Tani-Sassa, Yumi Iwasaki, Naoya Ichimura, Katsutoshi Nagano, Yuna Takatsuki, Sonoka Yuasa, Yuta Takahashi, Jun Nakajima, Kazunari Sonobe, Yoko Nukui, Hiroaki Takeuchi, Kousuke Tanimoto, Yukie Tanaka, Akinori Kimura, Shuji Tohda. Viral loads and profile of the patients infected with SARS-CoV-2 Delta, Alpha, or R.1 variants in Tokyo. J Med Virol. 2022.04; 94(4); 1707-1710
- 10. Yusuke Ota, Isaac Prah, Yoko Nukui, Ryuji Koike, Ryoichi Saito. blaKPC-2-Encoding IncP-6 Plasmids in Citrobacter freundii and Klebsiella variicola Strains from Hospital Sewage in Japan. Appl Environ Microbiol. 2022.04; e0001922
- 11. Ryoichi Saito, Jun Nakajima, Isaac Prah, Masatomo Morita, Samiratu Mahazu, Yusuke Ota, Ayuka Kobayashi, Shuji Tohda, Hajime Kamiya, Hideyuki Takahashi, Makoto Ohnishi. Penicillin- and Ciprofloxacin-Resistant Invasive Neisseria meningitidis Isolates from Japan. Microbiol Spectr. 2022.04; e0062722
- 12. Samiratu Mahazu, Wakana Sato, Alafate Ayibieke, Isaac Prah, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Insights and genetic features of extended-spectrum beta-lactamase producing Escherichia coli isolates from two hospitals in Ghana. Sci Rep. 2022.02; 12(1); 1843
- Akane NATSUKI, Masayuki HORI, Kousaku MATSUBARA, Yusuke OTA, Ryoichi SAITO, Kenichi ISOME, Aya IWATA, Mami IKEMACHI, Hiroshi TAKEGAWA, Go YAMAMOTO, Misako OHKUSU, Naruhiko ISHIWADA. Moraxella catarrhalis bacteremia in a 3-year-old child without underlying disease. The Journal of the Japanese Association for Infectious Diseases. 2022;

- 1. Yusuke Ota, Reina Okada, Hideyuki Takahashi, Ryoichi Saito. Rapid and simple PCR-RFLP assay for detecting a mutation at codon 91 of gyrA in Neisseria meningitidis. The 17th Congress of Asian Society of Clinical Pathology and Laboratory Medicine (ASCPaLM) 2022.10.09
- 2. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Yoko Nukui, Masato Suzuki, Yoshihiko Hoshino, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Klebsiella species and Enterobacter cloacae isolates harbouring blaOXA-181 and blaOXA-48: resistome, fitness cost, and plasmid stability.. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09 Hyogo, Japan

- 3. Yikeshan Yalikun, Isaac Prah, Samiratu Mahazu, Yusuke Ota, Anthony Ablordey, Ryoichi Saito. Characterization of extended-spectrum β -lactamase producing Klebsiella pneumoniae from Ghana.. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09 Hyogo, Japan
- 4. Kayo Yamada, Alafate Ayibieke, Samiratu Mahazu, Isaac Prah, Yusuke Ota, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Genetic and phenotypic features of Staphylococcus epidermidis ST2 bloodstream isolates from Tokyo.. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09 Hyogo, Japan
- 5. Taira Kawamura, Akari Samejima, Yukino Usui, Issac Prah, Samiratu Mahazu, Yusuke Ota, Ryoichi Saito. Role of cyclic-di-AMP phosphodiesterase on vancomycin susceptibility and growth in Clostridioides difficile.. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09 Hyogo, Japan
- 6. Yusuke Ota, Reina Okada, Hideyuki Takahashi, Ryoichi Saito. Rapid and simple PCR-RFLP assay for detecting a mutation at codon 91 of gyrA in Neisseria meningitidis.. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09 Hyogo, Japan
- 7. Yikeshan Yalikun, Isaac Prah, Samiratu Mahazu, Yusuke Ota, Anthony Ablordey, Ryoichi Saito. Characterization of extended-spectrum β -lactamase producing Klebsiella pneumoniae from Ghana. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09
- 8. Kayo Yamada, Alafate Ayibieke, Samiratu Mahazu, Isaac Prah, Yusuke Ota, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Genetic and phenotypic features of Staphylococcus epidermidis ST2 bloodstream isolates from Tokyo. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09
- 9. Taira Kawamura, Akari Samejima, Yukino Usui, Issac Prah, Samiratu Mahazu, Yusuke Ota, Ryoichi Saito. Role of cyclic-di-AMP phosphodiesterase on vancomycin susceptibility and growth in Clostridioides difficile. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09
- 10. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Yoko Nukui, Masato Suzuki, Yoshihiko Hoshino, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Klebsiella species and Enterobacter cloacae isolates harbouring blaOXA-181 and blaOXA-48: resistome, fitness cost, and plasmid stability. The 17th Congress of Asian Society for Clinical Pathology and Laboratory Medicine 2022.10.09
- 11. Isaac Prah, Yoko Nukui, Ryoichi Saito. Molecular Profiling of New Delhi Metallo- β -lactamase 5 producing Klebsiella oxytoca strain in Japan. AMS Microbe 2022 2022.06.11 Washington, DC
- 12. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Yoko Nukui, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Molecular characterization of Klebsiella pneumoniae and Enterobacter cloacae isolates harboring blaOXA-181 and blaOXA-48. AMS Microbe 2022 2022.06.11 Washington, DC
- 13. Kayo Yamada, Alafate Ayibieke, Samiratu Mahazu, Isaac Prah, Yusuke Ota, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Novel insights and genetic features of Staphylococcus epidermidis bloodstream isolates from Tokyo. AMS Microbe 2022 2022.06.11 Washington, DC
- 14. Y Nukui, Y Ota, I Prah, R Saito, Y Aiso, M Sugii, S Kanehira, J Nakajima, K Sonobe, S Tohda, R Koike, Y Gu. Molecular Epidemiological Analysis of Third Generation Cephalosporin and Piperacillin/Tazobactam-Resistant Klebsiella oxytoca, Which Caused an Outbreak in a COVID-19 Intensive Care Unit. AMS Microbe 2022 2022.06.10 Washington, DC
- 15. Y Nukui, Y Ota, I Prah, R Saito, Y Aiso, M Sugii, S Kanehira, J Nakajima, K Sonobe, S Tohda, R Koike, Y Gu. Molecular Epidemiological Analysis of Third Generation Cephalosporin and Piperacillin/Tazobactam-Resistant Klebsiella oxytoca, Which Caused an Outbreak in a COVID-19 Intensive Care Unit. ASM Microbe 2022.06.10 Washington, DC
- 16. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Yoko Nukui, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Molecular characterization of Klebsiella pneumoniae and Enterobacter cloacae isolates harboring blaOXA-181 and blaOXA-48. ASM Microbe 2022.06.10

- 17. Kayo Yamada, Alafate Ayibieke, Samiratu Mahazu, Isaac Prah, Yusuke Ota, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Novel insights and genetic features of Staphylococcus epidermidis bloodstream isolates from Tokyo. ASM Microbe 2022.06.10
- 1. Biological function of pneumococci-derived hydrogen peroxide on host cells. The 95th Annual Meeting of Japanese society for bacteriology 2022.03.29 Online
- 2. Yusuke Ota, Yoko Nukui, Shuji Tohda, Ryoichi Saito. Polymerase chain reaction-based open reading frame typing method for the clonality investigation of Clostridioides difficile isolates. The 33th Annual Meeting of the Japanese society for clinical microbiology 2022.01.29 Miyagi, Japan
- 3. Miho Ohto, Yusuke Ota, Ryoichi Saito. A case report of Moraxella catarrhalis isolated from blood culture in a pediatric patient with acute otitis media. The 33rd Annual Meeting of the Japanese society for clinical microbiology 2022.01.29 Miyagi, Japan
- 4. Ryoichi Saito. Seminar for how to write a scientific maniscript. The 33rd Annual Meeting of the Japanese society for clinical microbiology 2022.01.29 Miyagi, Japan
- 5. Ryoichi Saito. A good lecture to get students interested in Microbiology.. The 33rd Annual Meeting of the Japanese society for clinical microbiology 2022.01.29 Miyagi, Japan

[Awards & Honors]

1. Usui Yukino, scientific paper award on Japanese association for anaerobic infection research, Japanese association for anaerobic infection research, 2022.03
Department of Lifetime Clinical Immunology

MORI Masaaki KIMURA Naoki SASAKI Hirokazu IRABU Hitoshi

(1) Outline

(Overview)

In response to the rapid rise of social interest, the importance of medical care throughout lifelong, including the development of transitional medical care, has been reviewed. In addition, since 2015, the intractable disease policy in Ministry of Health, Labour and Welfare has been enriched as a national policy. However, the university courses in Japan have not successfully departed from the traditional framework of internal medicine and pediatrics so far. Especially in intractable immune diseases, pediatric rheumatology has developed mainly in a limited number of university hospitals, but rather than integrating with internal medicine, the stable succession of this field has even become a challenge. In addition, there is a shortage of providers who can treat pediatric patients with primary immunodeficiency after they reach adulthood. Therefore, the cooperation between the Departments of Pediatrics and Rheumatology is essential in dealing with autoimmune diseases complicated by primary immunodeficiency.

Therefore, it is now required to establish a system for seamless research and education on intractable immune diseases such as rheumatic diseases from children to adults, succeeding the pediatric rheumatology in Japan. In response to this demand, the Lifelong Intractable Immunological Diseases Lecture (hereafter referred to as "this course") was established as a donation course at the Graduate School of Medical and Dental Sciences of our university in April, 2016. With the cooperation of the Departments of Rheumatology and Pediatrics, under the concept of "There is no framework of pediatrics/internal medicine in intractable diseases," we are confident that the new course has become a pioneer in the reform and enhancement of medical care and academics for all intractable diseases by building a research and educational system for intractable immune diseases, which could not be achieved in the existing courses. Thanks to these efforts, the "transitional medicine" research being conducted in this course has become widely accepted by society and is now being taken up as part of national policy. By renewing this course, we need and have an obligation to respond to the needs of society. Since 2022, we have been planning to renew the course with the aim of further pursuing and expanding the course to meet the needs for the medical care of autoimmune diseases complicated with PID and transitional care for PID patients diagnosed in childhood, while applying the achievements made so far in actual clinical practice.

(2) Research

(Research activities)

1) Establishment of a research and educational system through cooperation between the Departments of Pediatrics and Rheumatology

This course clarifies the differences and similarities of rheumatic diseases between children and adults and

develops and embodies a universal approach to "countermeasures for intractable diseases throughout life course". Although various treatment strategies have been proposed for rheumatic diseases, no detailed strategy that takes into account patient background, especially age, has yet been proposed. Especially in the transitional phase from pediatric to adult, there may be many transition-specific problems such as changes in the department/physician in charge from pediatrics to internal medicine and changes in the required amount of medication due to changes in drug metabolism and physique.

In addition, we will continue to propose treatment strategies that consider the needs and issues of those who wish to have children and are restricted from various treatments, such as with methotrexate, and the elderly, for whom complications and compliance may be a concern.

2) Construction and analysis of a database for pediatric rheumatic diseases and comparative study with adult cases

With this course playing a central role, we aim to complete the construction of a nationwide database on pediatric rheumatic diseases, which has not yet been developed in Japan.

In particular, for juvenile idiopathic arthritis (JIA), we aim to enroll 500 cases and monitor their long-term course through continuous observation, in cooperation with the Pediatric Rheumatology Association of Japan, in a design linked to the existing adult rheumatoid arthritis (RA) database: National Database of Rheumatic Disease by iR-net in Japan (NinJa). We will grasp the current status and extract problems in JIA, establish evaluation indices that can be commonly used in JIA and RA, and examine the validity of existing RA disease activity indices in JIA. Since approximately 30% of patients with joint-type JIA, including those with severely active disease in childhood, are drug-free, we will analyze these cases to determine the possibility of drug-free diseases in adult patients. Adult-onset Still's disease has been considered to be the adult onset of systemic JIA, but differences exist. In systemic JIA, on the other hand, genetic abnormalities are now considered to be the underlying cause. In this course, we will perform the pathological analysis of various types of JIA as well as adult-onset Still's disease and RA using cohort studies, systematic genetic analysis, and microbiome analysis in order to redefine these diseases.

In other rheumatic diseases, polymyositis and dermatomyositis, especially dermatomyositis, have two peaks of onset in childhood and adulthood, and there are also differences in symptoms such as cutaneous calcification, drawing attention to the dissimilarities in the pathophysiology. Cohort studies in Japan have been conducted independently in children and adults for the purpose of certification for "designated intractable diseases" and "specific pediatric chronic diseases" by the Ministry of Health, Labour and Welfare. Internationally, Euromyositis is constructing a multinational database. In this course, we will construct a database of patients from childhood to adulthood that will be linked to international databases to clarify the current situation of the medical care of patients with myositis in Japan.

3) Epidemiological studies on pediatric patients with rheumatic diseases in Japan and database studies for proper evaluation and formulation of evidence-based diagnostic criteria and severity classifications

In this course, we will initiate the "epidemiological studies on pediatric and adult patients in transitional phase of rheumatic diseases in Japan and database studies for proper evaluation and formulation of evidence-based diagnostic criteria and severity classifications", especially for pediatric rheumatic diseases, as a joint research project with the Pediatric Rheumatology Association of Japan, Research Group for "Research contributing to the proper use of biological agents and other drugs based on patient stratification in rheumatic diseases centering on JIA in the transition phase" (Principal Investigator: Masaaki Mori), Ministry of Health, Labour and Welfare Scientific Research Project on Intractable Diseases (Policy Research Project on Allergic and Immunological Diseases, etc.). We will utilize the NinJa system described above in 2) to make clinical use of data from the disease registry system of the Pediatric Rheumatology Association of Japan, as well as data on pediatric chronic diseases and designated intractable diseases. In particular, we will prioritize epidemiological studies on patients receiving biological agents for JIA, the most common pediatric rheumatic disease, and continue to evaluate their efficacy and safety in Japan. In juvenile dermatomyositis, the diagnostic criteria for inflammatory muscle diseases proposed by the International Myositis Classification Criteria Project (IMCCP) have been validated in a multicenter survey of a population of Japanese pediatric patients with dermatomyositis, and it is now at the stage of reporting its results to the world.

4) Elucidation of the pathophysiology of all intractable immune diseases observed in children and adults by whole exome sequencing, next-generation sequence analysis, and immunomarker research using the Bioresource Research Center

In this course, we will utilize the Bioresource Research Center, which has the latest technologies such as whole exome sequencing, next-generation sequence analysis, and immunomarker research, to elucidate the pathophysiology of all intractable immune diseases (primary immunodeficiency, autoinflammatory diseases, rheumatic diseases, and vasculitis syndrome) in children and adults and to perform comprehensive analysis of childhood-onset cases, cases transitioning from childhood to adulthood, and adult-onset cases. More than 300 responsible genes have been identified in primary immunodeficiency, and genetic abnormalities have also been identified mainly in disease symptoms such as systemic lupus erythematosus (SLE) symptoms, arthritis, and vasculitis. Based on these findings, we will conduct research that sheds light on the genetic background and expression modifications in rheumatic diseases in adults. In addition, we will make efforts to develop and introduce advanced early diagnostic methods, such as neonatal mass screening for primary immunodeficiency, and examine their relevance to rheumatic diseases in adulthood. Expected applications of the research results include: 1) determination of the efficacy of cytokine inhibitors for JIA; 2) determination of the efficacy of anti-IL-1 β monoclonal antibody therapy for "cryopyrin-associated periodic syndrome with a background of genetic mutation"; 3) establishment of universal early diagnosis based on the cause and onset mechanism of hypercytokinemia; 4) analysis of the involvement of immunodeficiency genes in adult patients with rheumatic diseases; and 5) efficacy of IVIg in autoimmune diseases with a background of immunodeficiency.

5) Implementation of transitional care for patients with primary immunodeficiency and medical care for complicated autoimmune phenomena and autoimmune diseases

Most primary immunodeficiency occurs in children and often requires continuous replacement therapy with immunoglobulin products, however, there is a shortage of providers who can continue to treat these patients after they reach adulthood. Furthermore, primary immunodeficiency and complicated autoimmune phenomena and autoimmune diseases found in adulthood are not rare, and a cross-departmental system of medical care is required. Our institution is actively involved in the transitional care of patients with primary immunodeficiency, and we will take advantage of being able to provide seamless care between the Departments of Pediatrics and Rheumatology to meet these unmet needs.

(3) Education

(Educational activities)

Fostering a "hybrid physician" who can provide consistent medical care from children to adults

The clinical system so far has been separated for children and adults. From the perspective of patients, many feel confused and anxious about the change of the department in charge and the attending physician once they reach a certain age when they grow up despite the same disease. The adult physicians also often struggle with how those patients have progressed the diseases, what problems or worries of patients have had other than medical concerns while growing up, and whether those patients in carry-over case can be treated in the same manner as adults. For this purpose, this course plays a central role in providing an educational system for fostering "hybrid physicians" who are specialists in rheumatism treatment, are well familiar with treatment for both children and adults, and transcend the boundaries between children and adults.

(4) Lectures & Courses

(Education policy)

In this course, with the cooperation of Department of Rhewumatology and Pediatrics, we will promote the integration of research, education, and clinical systems for intractable immune diseases throughout the life of patients, and further aim to be a pioneer of renovation and enhancement of medical treatment and academics for intractable diseases. And this course is intending to foster pediatricians and adult physicians who can solve various problems for patients in the transition from childhood to adulthood and from adulthood to the elderly.

(5) Clinical Performances

(Clinical features)

The Lifelong Intractable Immunological Diseases Lecture, "is a unique university course that cannot be found elsewhere in the world, which aims to integrate research, education, and treatment systems for "immune intractable diseases", such as collagen and rheumatic diseases, for a lifetime from children to adults and the elderly". This course in our University has assessed various problems for patients with intractable diseases in the transitional phase from pediatric to adult or adult to elderly, which have not been solved by conventional medical system of Pediatrics and Internal medicine.

(6) **Publications**

- Shuya Kaneko, Masaki Shimizu, Asami Shimbo, Hitoshi Irabu, Susumu Yamazaki, Toru Kanamori, Tomohiro Udagawa, Tomohiro Morio, Masaaki Mori. A girl with hearing loss, dizziness, hypertension, and pyelonephritis with ureteral edema: Answers Pediatr Nephrol. 2022.12; 37(12); 3059-3061
- 2. Kaneko Shuya, Shimizu Masaki, Shimbo Asami, Irabu Hitoshi, Yamazaki Susumu, Kanamori Toru, Udagawa Tomohiro, Morio Tomohiro, Mori Masaaki. A girl with hearing loss, dizziness, hypertension, and pyelonephritis with ureteral edema: Questions PEDIATRIC NEPHROLOGY. 2022.12; 37(12); 3057-3058
- Kosei Yamashita, Takeru Kanazawa, Yoshifusa Abe, Takuya Naruto, Masaaki Mori. Kawasaki disease without changes in inflammatory biomarkers: A case report. World J Clin Cases. 2022.12; 10(35); 13038-13043
- 4. Mariko Mouri, Toru Kanamori, Eriko Tanaka, Kanako Hiratoko, Mariko Okubo, Michio Inoue, Tomohiro Morio, Masaki Shimizu, Ichizo Nishino, Naoko Okiyama, Masaaki Mori. Hepatic veno-occlusive disease accompanied by thrombotic microangiopathy developing during treatment of juvenile dermatomyositis and macrophage activation syndrome: A case report Mod Rheumatol Case Rep. 2022.11;
- 5. Mariko Mouri, Mitsuru Imamura, Shotaro Suzuki, Tatsuya Kawasaki, Yoshiki Ishizaki, Keiichi Sakurai, Hiroko Nagafuchi, Norihiro Matsumura, Marina Uchida, Takayasu Ando, Kohei Yoshioka, Seido Ooka, Takahiko Sugihara, Hiroshi Miyoshi, Masaaki Mori, Tomoyuki Okada, Masao Yamaguchi, Hiroyuki Kunishima, Motohiro Kato, Kimito Kawahata. Serum polyethylene glycol-specific IgE and IgG in patients with hypersensitivity to COVID-19 mRNA vaccines. Allergol Int. 2022.10; 71(4); 512-519
- 6. Hermine I Brunner, Carlos Abud-Mendoza, Masaaki Mori, Clarissa A Pilkington, Reema Syed, Syuji Takei, Diego O Viola, Richard A Furie, Sandra Navarra, Fengchun Zhang, Damon L Bass, Gina Eriksson, Anne E Hammer, Beulah N Ji, Mohamed Okily, David A Roth, Holly Quasny, Nicolino Ruperto. Efficacy and safety of belimumab in paediatric and adult patients with systemic lupus erythematosus: an across-study comparison. RMD Open. 2022.09; 7(3); e001747
- Shimizu Masaki, Takei Syuji, Mori Masaaki, Yachie Akihiro. Pathogenic roles and diagnostic utility of interleukin-18 in autoinflammatory diseases FRONTIERS IN IMMUNOLOGY. 2022.09; 13; 951535
- 8. Hidehiko Narazaki, Shinji Akioka, Yuko Akutsu, Mariko Araki, Mikiya Fujieda, Daisuke Fukuhara, Ryoki Hara, Kunio Hashimoto, Seira Hattori, Ren Hayashibe, Tomoyuki Imagawa, Yuzaburo Inoue, Hiroyuki Ishida, Shuici Ito, Yasuhiko Itoh, Tomohiro Kawabe, Toshiyuki Kitoh, Ichiro Kobayashi, Tadashi Matsubayashi, Takako Miyamae, Mao Mizuta, Masaaki Mori, Ayako Murase, Yasuo Nakagishi, Koji Nagatani, Naoko Nakano, Toyoki Nishimura, Tomo Nozawa, Nami Okamoto, Yuka Okura, Hiromi Sawada, Emi Sawanobori, Yuko Sugita, Yujiro Tanabe, Minako Tomiita, Ken-Ichi Yamaguchi, Ryuhei Yasuoka, Koji Yokoyama. Epidemiology conduction of paediatric rheumatic diseases based on the registry database of the Pediatric Rheumatology Association of Japan. Mod Rheumatol. 2022.09;
- 9. Susumu Yamazaki, Masaki Shimizu, Yuko Akutsu, Asami Shimbo, Masaaki Mori. Tacrolimus as an alternative treatment for patients with juvenile idiopathic arthritis. Mod Rheumatol. 2022.07; 32(4); 783-791

- Ryosuke Wakatsuki, Masaki Shimizu, Shimbo Asami, Eriko Adachi, Toru Kanamori, Susumu Yamazaki, Tomohiro Udagawa, Kei Takasawa, Kenichi Kashimada, Tomohiro Morio, Masaaki Mori. Atrophic Autoimmune Thyroiditis Complicated with Systemic Lupus Erythematosus. Mod Rheumatol Case Rep. 2022.07;
- 11. Yamaguchi Y, Takasawa K, Irabu H, Hiratoko K, Ichigi Y, Hirata K, Tamura Y, Murakoshi M, Yamashita M, Nakatani H, Shimoda M, Ishii T, Udagawa T, Shimizu M, Kanegane H, Morio T. Infliximab treatment for refractory COVID-19-associated multisystem inflammatory syndrome in a Japanese child. Journal of infection and chemotherapy. 2022.06; 28(6); 814-818
- 12. Yuki Ichimura, Risa Konishi, Miwako Shobo, Sae Inoue, Mari Okune, Akemi Maeda, Ryota Tanaka, Noriko Kubota, Isao Matsumoto, Akiko Ishii, Akira Tamaoka, Asami Shimbo, Masaaki Mori, Tomohiro Morio, Takayuki Kishi, Takako Miyamae, Jantima Tanboon, Michio Inoue, Ichizo Nishino, Manabu Fujimoto, Toshifumi Nomura, Naoko Okiyama. Reliability of antinuclear matrix protein 2 antibody assays in idiopathic inflammatory myopathies is dependent on target protein properties J Dermatol. 2022.04; 49(4); 441-447
- 13. Fumiaki Kondo, Takahiko Sugihara, Natsuka Umezawa, Hisanori Hasegawa, Tadashi Hosoya, Naoki Kimura, Masaaki Mori, Shinsuke Yasuda. Associated factors with poor treatment response to initial glucocorticoid therapy in patients with adult-onset Still's disease. Arthritis Res Ther. 2022.04; 24(1); 92
- 14. Yuki Ichimura, Risa Konishi, Miwako Shobo, Sae Inoue, Mari Okune, Akemi Maeda, Ryota Tanaka, Noriko Kubota, Isao Matsumoto, Akiko Ishii, Akira Tamaoka, Asami Shimbo, Masaaki Mori, Tomohiro Morio, Takayuki Kishi, Takako Miyamae, Jantima Tanboon, Michio Inoue, Ichizo Nishino, Manabu Fujimoto, Toshifumi Nomura, Naoko Okiyama. Anti-nuclear matrix protein 2 antibody-positive inflammatory myopathies represent extensive myositis without dermatomyositis-specific rash. Rheumatology (Oxford). 2022.03; 61(3); 1222-1227
- 15. Yutaka Kawahito, Akio Morinobu, Yuko Kaneko, Masataka Kohno, Shintaro Hirata, Mitsumasa Kishimoto, Yohei Seto, Takahiko Sugihara, Eiichi Tanaka, Hiromu Ito, Toshihisa Kojima, Isao Matsushita, Keiichiro Nishida, Masaaki Mori, Atsuko Murashima, Hisashi Yamanaka, Takeo Nakayama, Masayo Kojima, Masayoshi Harigai. Drug Treatment Algorithm and Recommendations from the 2020 update of the Japan College of Rheumatology Clinical Practice Guidelines for the Management of Rheumatoid Arthritis-Secondary Publication. Mod Rheumatol. 2022.03;
- 16. Masayo Kojima, Mieko Hasegawa, Shintaro Hirata, Hiromu Ito, Yuko Kaneko, Mitsumasa Kishimoto, Masataka Kohno, Toshihisa Kojima, Isao Matsushita, Masaaki Mori, Akio Morinobu, Atsuko Murashima, Keiichiro Nishida, Yohei Seto, Yasumori Sobue, Takahiko Sugihara, Eiichi Tanaka, Takeo Nakayama, Yutaka Kawahito, Masayoshi Harigai. Patients' perspectives of rheumatoid arthritis treatment: a questionnaire survey for the 2020 update of the Japan college of rheumatology clinical practice guidelines. Mod Rheumatol. 2022.02; 32(2); 307-312
- 17. Takahiko Sugihara, Yutaka Kawahito, Akio Morinobu, Yuko Kaneko, Yohei Seto, Toshihisa Kojima, Hiromu Ito, Masataka Kohno, Takeo Nakayama, Yasumori Sobue, Keiichiro Nishida, Isao Matsushita, Atsuko Murashima, Masaaki Mori, Eiichi Tanaka, Shintaro Hirata, Mitsumasa Kishimoto, Hisashi Yamanaka, Masayo Kojima, Masayoshi Harigai. Systematic review for the treatment of older rheumatoid arthritis patients informing the 2020 update of the Japan College of Rheumatology clinical practice guidelines for the management of rheumatoid arthritis. Mod Rheumatol. 2022.02; 32(2); 313-322
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- 19. Masaaki Mori, Shinji Akioka, Toru Igarashi, Yuzaburo Inoue, Hiroaki Umebayashi, Shiro Ohshima, Susumu Nishiyama, Motomu Hashimoto, Toshihiro Matsui, Takako Miyamae, Takahiro Yasumi. Transitioning from paediatric to adult rheumatological healthcare: English summary of the Japanese Transition Support Guide. Mod Rheumatol. 2022.02; 32(2); 248-255
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- 21. Kimura Naoki, Kawahara Takuya, Uemura Yukari, Atsumi Tatsuya, Sumida Takayuki, Mimura Toshihide, Kawaguchi Yasushi, Amano Hirofumi, Iwasaki Yukiko, Kaneko Yuko, Matsui Toshihiro, Muro Yoshinao, Imura Yoshitaka, Kanda Takashi, Tanaka Yoshiya, Kawakami Atsushi, Jinnin Masatoshi, Ishii Tomonori, Hiromura Keiju, Miwa Yusuke, Nakajima Hiroshi, Kuwana Masataka, Nishioka Yasuhiko, Morinobu Akio, Kameda Hideto, Kohsaka Hitoshi. Branched chain amino acids in the treatment of polymyositis and dermatomyositis: a phase II/III, multi-centre, randomized controlled trial RHEUMATOLOGY. 2022.02; 61(11); 4445-4454
- 22. Masaki Shimizu, Asami Shimbo, Susumu Yamazaki, Yuko Segawa, Masaaki Mori. Septic arthritis of the pubic symphysis in a patient with SLE. Pediatr Int. 2022.01; 64(1); e14875
- 23. Eiichi Tanaka, Yutaka Kawahito, Masataka Kohno, Shintaro Hirata, Mitsumasa Kishimoto, Yuko Kaneko, Hiroya Tamai, Yohei Seto, Akio Morinobu, Takahiko Sugihara, Atsuko Murashima, Masayo Kojima, Masaaki Mori, Hiromu Ito, Toshihisa Kojima, Yasumori Sobue, Keiichiro Nishida, Isao Matsushita, Takeo Nakayama, Hisashi Yamanaka, Masayoshi Harigai. Systematic review and meta-analysis of biosimilar for the treatment of rheumatoid arthritis informing the 2020 update of the Japan College of Rheumatology clinical practice guidelines for the management of rheumatoid arthritis. Mod Rheumatol. 2022.01; 32(1); 74-86
- 24. Susumu Yamazaki, Asami Shimbo, Takahiro Kamiya, Masaki Shimizu, Masaaki Mori. Ankylosing spondylitis, Crohn's disease, and myelodysplasia in an adolescent. Pediatr Int. 2022.01; 64(1); e15215
- 25. Hoshi Yurika, Shimizu Masaki, Shimbo Asami, Yamazaki Susumu, Mori Masaaki. Overt myösitis in a girl with systemic lupus erythematosus PEDIATRICS INTERNATIONAL. 2022.01; 64(1); e15338

- 1. Yamazaki S. Mori M. Unmet Medical Needs in Rheumatic Diseases in Japan: A literture Review.. the 24th Asia-Pacific League of Associations for Rheumatology Congress (APLAR 2022). 2022.10.31 Hong Kong
- 2. Mori M. Safety of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease in Immunocompromised Children: The Phase 2 MUSIC Study.. the 10th Asian Congress of Pediatric Infectious Diseases (ACPID 2022) 2022.10.26 Seoul, Korea
- 3. 星合 愛子, 楠本 康香, 星合 泰治, 木村 直樹, 伊藤 由希子, 吉田 直美, 篠塚 修, 岩本 勉. 関節リウマチ患者の 口腔衛生管理に影響を及ぼす要因の検討 (Factors Influencing Oral Hygiene Management in Patients with Rheumatoid Arthritis). 障害者歯科 2022.02.01

Pediatrics, Perinatal and Maternal Medicine (Ibaraki)

Professor Masakazu Terauchi MD PhD Assistant Professor Tamami Odai MD PhD

(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 serton in 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 insomina 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]

- Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. Body weight and body fat are negatively associated with severe dyspareunia in postmenopausal women. J Obstet Gynaecol Res. 2022.12; 48(12); 3279-3285
- 2. Terauchi M, Kimura T. Response: The introduction of 21st century abortion methods in Japan-Policy based on all WHO recommendations is needed. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2022.08;
- 3. Masakazu Terauchi, Tsuyoshi Higuchi. Women's Health Care Committee, Japan Society of Obstetrics and Gynecology: Annual report-2022. Journal of Obstetrics and Gynaecology Research. 2022.07;
- 4. Tamami Odai, Masakazu Terauchi, Hidenori Umeki, Naoyuki Miyasaka, Yoshiaki Somekawa. Sleep apnea in postmenopausal women is associated with joint pain severity and fatigability: a cross-sectional study. Menopause. 2022.06; 29(6); 680-686
- 5. Toba M, Terauchi M, Moriwaki M, Obayashi S, Miyasaka N, Fushimi K. Fractures within 2 years of an obstetric hospitalization: analysis of nationwide administrative data in Japan. Journal of bone and mineral metabolism. 2022.06;
- 6. Terauchi M, Kimura T. Letter to the editor: Japan foresees early-stage medical abortion approval: Will this reduce barriers to access safe abortion? International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2022.04; 158(1); 227
- 7. Mayuko Kazama, Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. The Inverse Correlation of Isoflavone Dietary Intake and Headache in Peri- and Post-Menopausal Women Nutrients. 2022.03; 14; 1226
- 8. Odai T, Terauchi M, Umeki H, Miyasaka N, Somekawa Y. Sleep apnea in postmenopausal women is associated with joint pain severity and fatigability: a cross-sectional study. Menopause (New York, N.Y.). 2022.02;

[Books etc]

1. Masakazu Terauchi. Nutrition Challenges for Middle-Aged and Older Women. MDPI, 2022.10

[Conference Activities & Talks]

1. Masakazu Terauchi, Yuki Ideno, Kunihiko Hayashi. The effect of shift work on daytime sleepiness in middle-aged female nurses: results from the Japan Nurses' Health Study. The 18th World Congress on Menopause 2022.10.28 Lisbon, Portugal

- 2. Masakazu Terauchi. APMF Panel Discussion: Overview, Challenges and Solutions for Midlife Women' s Health in Asia Pacific "S-Equol: a novel therapeutic option from Asian perspective". The 18th World Congress on Menopause 2022.10.27 Lisbon, Portugal
- 3. Masakazu Terauchi. The current practice of menopause management and the role of S-Equol in Japan. Equol Advisory Meeting 2022.10.27 Lisbon, Portugal
- 4. Odai Tamami, Ohno Haruko, Nakamura Reiko, Tsukada Takafumi, Oshima Noriko, Wakana Kimio, Miyasaka Naoyuki. 組織病理学的および遺伝子学的検査により診断された原発性肺絨毛癌 (Primary pulmonary choriocarcinoma diagnosed by histopathologic and genetic examination). 日本産科婦人科学会 雑誌 2022.02.01

Pulmonary Immunotherapeutics

Associate Professor Tsukasa Okamoto

(1) **Outline**

Lung has well-developed immune system. To discover the pathology and treatment for the refractory lung diseases including novel corona virus infection, severe bronchial asthma, hypersensitivity pneumonitis, lung fibrosis, and lung cancer, we need to control the immune system in the lung. Our aim is to find the treatment for these lung diseases with department of respiratory medicine.

(2) Research

Clarify the pathology and discover the treatment for 1) novel corona virus infection, 2) severe asthma, 3) pulmonary fibrosis, especially hypersensitivity pneumonitis, 4) lung cancer with/without pulmonary fibrosis.

(3) Education

We have classes of respiratory medicine for students and residents. We are doing researches with graduated students in department of respiratory medicine.

(4) Clinical Services & Other Works

We practice respiratory medicine for the patients with novel corona virus infection, severe asthma, pulmonary fibrosis, and lung cancer.

(5) Publications

- Okamoto T, Dobrinskikh E, Hennessy CE, Liu N, Schwarz MI, Evans CM, Fontenot AP, Yang IV, Schwartz DA. Muc5b plays a role in the development of inflammation and fibrosis in hypersensitivity pneumonitis induced by < i> Saccharopolyspora rectivirgula< /i> . American journal of physiology. Lung cellular and molecular physiology. 2022.09; 323(3); L329-L337
- 2. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Japanese journal of infectious diseases. 2022.09; 75(5); 504-510
- 3. Mitsumura Takahiro, Okamoto Tsukasa, Tosaka Mizuho, Yamana Takashi, Shimada Sho, Iijima Yuki, Sakakibara Rie, Shibata Sho, Honda Takayuki, Shirai Tsuyoshi, Ishizuka Masahiro, Aiboshi Junichi, Furusawa Haruhiko, Tateishi Tomoya, Tamaoka Meiyo, Shigemitsu Hidenobu, Arai Hirokuni, Otomo Yasuhiro, Tohda Shuji, Anzai Tatsuhiko, Takahashi Kunihiko, Yasuda Shinsuke, Miyazaki Yasunari.

Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases(タイトル和訳中) Japanese Journal of Infectious Diseases. 2022.09; 75(5); 504-510

- 4. Ikeda Tokuji, Ichiba Shingo, Sasaki Takashi, Sato Masaaki, Konoeda Chihiro, Okamoto Tsukasa, Miyazaki Yasunari, Nakajima Jun, Sakamoto Atsuhiro. A case of severe respiratory failure due to interstitial pneumonia successfully bridged to lung transplantation from a brain-dead donor using 109-day veno-arterial extracorporeal membrane oxygenation JOURNAL OF ARTIFICIAL ORGANS. 2022.06;
- 5. Ejima M, Okamoto T, Suzuki T, Miyazaki Y. Role of serum surfactant protein-D as a prognostic predictor in fibrotic hypersensitivity pneumonitis. Respiratory investigation. 2022.05; 60(3); 369-378
- 6. Mitsumura T, Okamoto T, Tosaka M, Yamana T, Shimada S, Iijima Y, Sakakibara R, Shibata S, Honda T, Shirai T, Ishizuka M, Aiboshi J, Furusawa H, Tateishi T, Tamaoka M, Shigemitsu H, Arai H, Otomo Y, Tohda S, Anzai T, Takahashi K, Yasuda S, Miyazaki Y. SARS-CoV-2 RNA copy number is a factor associated with the mortality of COVID-19 and improves the predictive performance of mortality in severe cases. Japanese journal of infectious diseases. 2022.05; 75(5); 504-510
- 7. Endo S, Honda T, Kawahara T, Sakakibara R, Mitsumura T, Okamoto T, Miyazaki Y. Profile of metastatic lung cancer patients susceptible to development of thromboembolism during immunotherapy. Cancer treatment and research communications. 2022; 31; 100547
- Murakami T, Iijima Y, Ando T, Ejima M, Shirai T, Furusawa H, Okamoto T, Tateishi T, Tamaoka M, Miyazaki Y. Successful diagnosis of humidifier lung by individual provocation test to a responsible environment, a case report. Respiratory medicine case reports. 2022; 37; 101639
- 9. Endo S, Honda T, Kawahara T, Sakakibara R, Mitsumura T, Okamoto T, Miyazaki Y. Profile of metastatic lung cancer patients susceptible to development of thromboembolism during immunotherapy. Cancer treatment and research communications. 2022; 31; 100547

[Conference Activities & Talks]

1. Yin Yuting, Sakakibara Rie, Honda Takayuki, Mitsumura Takahiro, Kirimura Susumu, Okubo Kenichi, Azuma Miyuki, Miyazaki Yasunari. 悪性胸膜中皮腫の腫瘍免疫微小環境の解明 (Elucidation of Tumor Immune Microenvironment in Malignant Pleural Mesothelioma). 日本呼吸器学会誌 2022.04.01

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA Junior Associate Professor Yuhei Matsuda Specially Appointed Assistant Professor Masayuki TOI Specially Appointed Assistant Professor Risako MIKAKMI Research Student ZHONG HUI

(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 oralpathology 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) :antimicrobila activity and effects to eukaryotic cells (induction of anti-oxydant capacities and wound healing activities etc.)

Preservation of oral health with of Ozone ultrafine bubble water that contributes to medical care and prevents adverse effects caused by cancer treatment.

2) Probing pocket depth could be associated with HbA1c more than periodontal inflamed surface area in controlled periodontitis patients

Diabetes and periodontitis are the most prevalent chronic diseases, influencing each other's progression. Only a few studies have shown the correlation between diabetes and mild periodontitis. We aimed to investigate the relationship between well-controlled periodontitis and glycated hemoglobin (HbA1c) in patients with diabetes. 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 oralpathology 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 oralpathology and oral health promotion, and are trained to master the modality of oral health care Medical and Dental Science and Technology

(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. Risako Mikami, Koji Mizutani, Shinichi Arakawa, Yuichi Izumi, Takanori Iwata, Jun Asida. Income-related inequalities in the association of smoking with periodontitis: a cross-sectional analysis in Tokyo Metropolitan Districts Clinical Oral Investigation. 2022.11;
- 2. Yuhei Matsuda, Ruriko Mizuno, Saki Miyajima, Shinichi Arakawa and Yuji Kabasawa. A Case of Oral Health Management for a Patient with Extensive Ulceration of the Oral Mucosa Due to Herpes Zoster Healthcare. 2022.11; 10(11);
- 3. Risako Mikami, Takeaki Sudo, Shunsuke Fukuba, Kohei Takeda, Takanori Matsuura, Tomoaki Kariya, Shunsuke Takeuchi, Akane Ochiai, Sakurako Kawamoto, Keita Toyoshima, Koji Mizutani, Shinichi Arakawa, Akira Aoki, Takanori Iwata. Prognostic factors affecting periodontal regenerative therapy using recombinant human fibroblast growth factor-2: A 3-year cohort study Regenerative Therapy. 2022.08;
- 4. Matsuda Y, Jayasinghe RD, Zhong H, Arakawa S, Kanno T. Oral Health Management and Rehabilitation for Patients with Oral Cancer: A Narrative Review. Healthcare (Basel, Switzerland). 2022.05; 10(5);
- Akira Kato, Yuhei Matsuda, Reon Morioka, Tatsuo Okui, Satoe Okuma, Hiroto Tatsumi, Takahiro Kanno. Discrepancy between subjective and objective postoperative oral dysfunction assessment after oral cancer treatment: a single-center cross-sectional study Oral Oncology. 2022.04; 129; 105879
- 6. Kondo Keiko, Kanenaga Ryoko, Tanaka Yoshinori, Hotta Kunimoto, Arakawa Shinichi. The neutralizing effect of mouth rinsing with alkaline electrolyzed water on different regions of the oral cavity acidified by acidic beverages(和訳中) Journal of Oral Science. 2022.01; 64(1); 17-21

[Books etc]

1. Nozaki K, Saleh O, Arakawa S, Miura H. Water-Formed Deposits Fundamentals and Mitigation Strategies. 2022.03

[Misc]

1. Yuhei Matsuda, Ruwan D. Jayasinghe, Hui Zhong, Shinichi Arakawa and Takahiro Kanno. Oral Health Management and Rehabilitation for Patients with Oral Cancer: A Narrative Review Healthcare. 2022.05; 10(5); 1-19

- 1. Shinichi Arakawa. Basic property and clinical application of the ozone ultrafine bubble water (OUFBW). International Session of KSTU 2022 2022.10.29 Kore (Web)
- 2. 杉澤 満、荒川真一. オゾンウルトラファインバブル水 を用いて改善した歯性上顎洞炎(症例報告). 日本 有病者歯科医療学会学術大会 2022.04.30
- 1. Tooi M, Kondo M, Shinichi A, Hirofumi A. Search for neural systems of feeding behavior in Drosophila. The 44th Annual Meeting of the Molecular Biology Society of Japan 2022.12.01 Yokohama

Oral Care for Systemic Health Support

Professor Yuhji Kabasawa Assistant Professor Kanade Ito Postgraduate student(Master's course) Shiori Tokura

(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, 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

- 1. Yuhei Matsuda, Ruriko Mizuno, Saki Miyajima, Shinichi Arakawa and Yuji Kabasawa. A Case of Oral Health Management for a Patient with Extensive Ulceration of the Oral Mucosa Due to Herpes Zoster Healthcare. 2022.11; 10(11);
- Chen MA, Liu CK, Yang YH, Huang ST, Yen CW, Kabasawa Y, Huang HL. Clinical-based oral rehabilitation programme improved the oral diadochokinesis and swallowing function of older patients with dementia: A randomized controlled trial. Journal of oral rehabilitation. 2022.09; 49(12); 1163-1172
- 3. Furuya J, Suzuki H, Hidaka R, Matsubara C, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Miyake S, Minakuchi S. Association between oral health and advisability of oral feeding in advanced cancer patients receiving palliative care: a cross-sectional study. Support Care Cancer. 2022.07; 30(7); 5779-5788
- 4. Shen KL, Huang CL, Lin YC, Du JK, Chen FL, Kabasawa Y, Chen CC, Huang HL. Effects of Artificial Intelligence (AI)-Assisted Dental Monitoring Intervention in Patients with Periodontitis: A Randomized Controlled Trial. Journal of clinical periodontology. 2022.06; 49(10); 988-998
- 5. Sakamoto Yujiro. Characterization of the pterygomeningeal artery based on branching pattern and muscular distribution. SURGICAL AND RADIOLOGIC ANATOMY. 2022.04; 44(4); 543-550
- Lin YC, Huang SS, Yen CW, Kabasawa Y, Lee CH, Huang HL. Physical Frailty and Oral Frailty Associated with Late-Life Depression in Community-Dwelling Older Adults. Journal of personalized medicine. 2022.03; 12(3);
- Furuya J, Suzuki H, Hidaka R, Koshitani N, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Minakuchi S, Miyake S. Factors affecting the oral health of inpatients with advanced cancer in palliative care. Support Care Cancer. 2022.02; 30(2); 1463-1471
- Chang Ai-Hua, Lin Pei-Chen, Lin Pei-Chao, Lin Yi-Ching, Kabasawa Yuji, Lin Cheng-Yu, Huang Hsiao-Ling. Effectiveness of Virtual Reality-Based Training on Oral Healthcare for Disabled Elderly Persons: A Randomized Controlled Trial JOURNAL OF PERSONALIZED MEDICINE. 2022.02; 12(2);
- 9. Ai Ohsato, Naoko Seki, Tam Thi Thanh Nguyen, Janelle Moross, Masayo Sunaga, Yuji Kabasawa, Atsuhiro Kinoshita, Ikuko Morio. Evaluating e-learning on an international scale: An audit of computer simulation learning materials in the field of dentistry. J Dent Sci. 2022.01; 17(1); 535-544

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1. Jun Aida, Kenji Takeuchi, Michiko Furuta, Kanade Ito, Yuji Kabasawa, Georgios Tsakos. Burden of Oral Diseases and Access to Oral Care in an Ageing Society. Int Dent J. 2022.08; 72(4S); S5-S11

- 1. YUKI SAKAGUCHI,MASAYUKI TOI,TOSHIKO ADACHI,YUJI KABASAWA,TSUTOMU IWAMOTO. A case report of long-term oral health management to prevent the risk of chronic oral GVHD in a patient with HLA-DRB1 mismatched unrelated bone marrow transplantation.. The 39th Annual Meeting of the Japanese Society for Disability and Oral Health 2022.11.04
- 2. Remote interprofessional learning for younger undergraduate students' early exposure. 2022.08.05

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA Assistant Professor Naoko ADACHI

Part-time lecturer Atsushi OHYAMA, Kenichi TANAKA, Kanako TODA, Chie YOSHIZU, Yuka SHIZUMA

Graduate Students Master Course WANG LIYANG(-March), Yuko HIROTA, WANG RAN(April-), Kyoko KAZITANI(April-) Graduate Students(research) WANG RAN (-March)

(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. Liao SR, Seki N, Akiyama M, Shinada K, Morio I. Perceived stress and career planning awareness of Japanese and Taiwanese undergraduate dental hygiene students Journal of Dental Sciences. 2022.11;

- Naito M, Shinada K, Seki N, Akiyama M, Yamamoto R, Onishi T, Taniyama K, Morio I. Effects of two-year oral health information provision on changes in gingival crevicular fluid in male day-night shift workers Journal of Dental Sciences. 2022.05; 17(4); 1463-1470
- 3. Suzuki H, Sugimoto K, Kubota-Miyazawa A, Noritake K, Umemori S, Araki K, Adachi N, Otsuka H, Yoshida N. A survey of oral health status, subjective oral symptoms and oral health behaviors among first-year dental students at a Japanese university. Journal of oral science. 2022.01; 64(1); 85-90

- 1. 鈴木瞳,杉本久美子,安達奈穂子,吉田直美. 口腔保健衛生学専攻・看護学専攻合同の口腔ケアに関する連携教育の試み. 第 87 回 口腔病学会学術大会 2022.12.03
- 2. 廣田優子,安達奈穂子,品田佳世子.コロナ禍における食生活の意識とリテラシーとの関連について.第87 回 口腔病学会学術大会 2022.12.03

Oral Hearth Sciences for Community Welfare

Professor Koichiro MATSUO Assistant Professor Rena HIDAKA Graduate Student Misaki TANAKA Tomoka MARUYAMA

(1) Outline

The Vision of department of Oral Health Sciences for Community Welfare is:

To establish the basis of human resource development where dental professionals can manage the needs of older adults who have various characteristics.

We engage in the activities with the Mission below:

To conduct practice, research and education to nurture human resources who act vigorously as oral health professional, working together with the other health professionals in acute care to community welfare

Please contact us if you are interested in the graduate school or collaborative research (matsuo.ohcw at tmd.ac.jp)

(2) Research

1. Invention of oral frail preventive program for community dwelling older adults

- 2. Invention of monitoring system for eating behavior in dependent older adults
- 3. Innovative food technology systems for independent senior living
- 4. Establishment of oral management system during stroke recovery
- 5. Invention of peri-operative oral management system for cancer patients
- 6. Multidisciplinary Oral management system

(3) Education

Under-graduate course

Gerodontology/Welfare for older adults/Nursing-care for older adults/Prosthodontics/Home visiting dentistry/Community dental care/ Social work

Post-graduate course Welfare and Oral Health Care for older adults

(4) Lectures & Courses

The education policy of our department is:

To educate dental professionals who will acquire the competency below: Knowledge, skill and experience to work in medical and health care fields Communication skill to educate the other health professionals Activities with self-intent Interest in international academic activities with positive research mind

(5) Clinical Services & Other Works

Japanese Society of Gerodontology: Specialist, Instructor, Executive Board Member (International Affair) Japanese Association of Dentistry and Oral Health: Specialist, Instructor, Board Member (International Affair) Japanese Society of Dysphagia Rehabilitation Japanese Society for Clinical Nutrition and Metabolism

Japanese Society for Chinical Nutrition and Metabolishi

Asian Association of Dentistry and Oral Health: Board member International Association of Dentistry and Oral Health: Councilor,International Advisory Committee

(6) Publications

[Original Articles]

- Suzuki H, Furuya J, Nakagawa K, Hidaka R, Nakane A, Yoshimi K, Shimizu Y, Saito K, Itsui Y, Tohara H, Sato Y, Minakuchi S. Changes in Nutrition-Intake Method and Oral Health through a Multidisciplinary Team Approach in Malnourished Older Patients Admitted to an Acute Care Hospital. Int J Environ Res Public Health. 2022.08; 19(16);
- Furuya J, Suzuki H, Hidaka R, Matsubara C, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Miyake S, Minakuchi S. Association between oral health and advisability of oral feeding in advanced cancer patients receiving palliative care: a cross-sectional study. Support Care Cancer. 2022.07; 30(7); 5779-5788
- Furuya J, Suzuki H, Hidaka R, Koshitani N, Motomatsu Y, Kabasawa Y, Tohara H, Sato Y, Minakuchi S, Miyake S. Factors affecting the oral health of inpatients with advanced cancer in palliative care. Support Care Cancer. 2022.02; 30(2); 1463-1471

- 1. 松尾 浩一郎. 口腔機能に関する知見を国際的に共有する 高齢者の口腔機能低下 · 障害に対する介入効果 (Intervention effects on oral hypofunction and oral dysfunction in older adults). 日本老年歯科医学会総会 · 学術大会プログラム · 抄録集 2022.06.01
- 2. Rena Hidaka, Koichiro Matsuo. Questionnaire survey on aspiration pneumonia and oral care. The 2nd Annual Meeting of the International Society of Oral Care 2022.04.24
- 3. Hidaka Rena, Matsuo Koichiro. 誤嚥性肺炎と口腔ケアに関するアンケート調査 (Questionnaire Survey on Aspiration Pneumonia and Oral Care). 日本口腔ケア学会雑誌 2022.04.01

Oral Health Care Education

Professor Naomi Yoshida Assistant Professor Graduate Students Nana Yoshida

Hitomi Suzuki Itsuki Takazawa

(1) Research

- 1) Research on oral health behabior
- 2) Research on oral health management
- 3) Research on interprofessional education and work
- 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 theoretid 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 the their oral and general health in the entire lifetime.

(4) **Publications**

- 1. Ayako Kubota-Miyazawa, Kumiko Sugimoto, Yasunari Miyazaki, Yoshimi Sakurai, Meiko Oki, Hitomi Suzuki, Naomi Yoshida. A cross-sectional survey on the status of oral health administration for students in Japanese universities 2022.11;
- 2. Hoshiai Aiko, Kusumoto Yasuka, Hoshiai Taiji, Kimura Naoki, Ito Yukiko, Yoshida Naomi, Shinozuka Osamu, Iwamoto Tsutomu. Factors Influencing Oral Hygiene Management in Patients with Rheumatoid Arthritis 障害者歯科. 2022.02; 43(1); 7-16
- 3. Suzuki H, Sugimoto K, Kubota-Miyazawa A, Noritake K, Umemori S, Araki K, Adachi N, Otsuka H, Yoshida N. A survey of oral health status, subjective oral symptoms and oral health behaviors among firstyear dental students at a Japanese university. Journal of oral science. 2022.01; 64(1); 85-90
- 4. Kubota-Miyazawa Ayako, Sugimoto Kumiko, Miyazaki Yasunari, Sakurai Yoshimi, Oki Meiko, Suzuki Hitomi, Yoshida Naomi. A cross-sectional survey on the status of oral health administration for students in Japanese universities. Journal of Medical and Dental Sciences. 2022; 69; 21-28

[Misc]

1. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 1), Dental Hygienists 2022.04; 46(4); 2. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 2), Dental Hygienists 2022.05; 46(5); 3. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 3), Dental Hygienists 2022.06; 46(6); 4. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 4), Dental Hygienists 2022.07; 46(7); 5. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 5), Dental Hygienists 2022.08; 46(8); 6. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 1), Dental Hygienists 2022.09; 46(9); 7. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 1), Dental Hygienists 2022.10; 46(10); 8. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 1), Dental Hygienists 2022.11 46(11); 9. Naomi Yoshida, Hiroshi Nitta, Usappa, Tsuyoshi Isomura Let's start learning with cartoons MI (Vol. 1), Dental Hygienists 2022.12 46(12);

- 1. Hitomi Suzuki, Kumiko Sugimoto, Naoko Adachi, Naomi Yoshida. An Attempt at Joint Cooperative Education on Oral Health Care by the Department of Oral Health Sciences and the Department of Nursing. 第87回口腔病学会学術大会 2022.12.04 Tokyo
- 2. Itsuki Takasawa, Hitomi Suzuki, Kumiko Sugimoto, Yuji Kabasawa, Naomi Yoshida. Examination of the status of oral care implementation and factors related to the practice in the university's hospital wards. 第 87 回 口腔病学会学術大会 2022.12.04
- 3. Itsuki Takasawa, Hitomi Suzuki, Kumiko Sugimoto, Akiko Hashizume, Takako Yano, Kanade Ito, Nahoko Andachi, Rena Hidaoka, Naomi Yoshida. A Survey of Newly-hired Nurses' Understanding of Oral Health Care Knowledge and the Effectiveness of Oral Health Care Training The 28th Japanese Society for Ingestion and Swallowing Rehabilitation 2022.09.23 Chiba

Basic Oral Health Engineering

Professor Kazuhiro Aoki Associate Professor Meiko Oki Assistant Professor Shingo Kamijo Technical Assistant Masud Khan

(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 novel bone anabolic reagents targeting RANKL (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 objective evaluation methods for tooth carving
- 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

 \cdot Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects

 \cdot Making dental and maxillofacial prostheses

(5) Publications

[Original Articles]

- 1. Ayako Kubota-Miyazawa, Kumiko Sugimoto, Yasunari Miyazaki, Yoshimi Sakurai, Meiko Oki, Hitomi Suzuki, Naomi Yoshida. A cross-sectional survey on the status of oral health administration for students in Japanese universities Journal of Medical and Dental Sciences. 2022.11; 69; 21-28
- Xie Cangyou, Satake-Ozawa Michiko, Rashed Fatma, Khan Masud, Ikeda Masaomi, Hayashi Shunya, Sawada Shinichi, Sasaki Yoshihiro, Ikeda Tohru, Mori Yoshiyuki, Akiyoshi Kazunari, Aoki Kazuhiro. Perforated Hydrogels Consisting of Cholesterol-Bearing Pullulan (CHP) Nanogels: A Newly Designed Scaffold for Bone Regeneration Induced by RANKL-Binding Peptides and BMP-2 INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES. 2022.07; 23(14); 7768 (1)-7768 (15)

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1. Kazuhiro Aoki. The Role of Bone Histomorphometry in the Oral Biological Study Journal of Japanese Society for Bone Morphometry. 2022.11; 32(2); 58-59

- 1. Nanaka Imaguma, Kaito Sugano, Masaomi Ikeda, and Kazuhiro Aoki. Investigation Of Cancer Markers In Saliva Considering The Level Of Happiness. The 87th Annual meeting of the Stomatological Society 2022.12.03 Bunkyo-ku
- 2. Sugano K, Imaguma N, Aoki K. Identification of well-being parameters in saliva and analysis of the association between oral flora and cancer risk.. The 44th Annual meeting of Japanese Academy of Dental Technology 2022.11.19 Online web
- 3. Kazuhiro Aoki. Present and Future Perspectives of Bone Morphometry- From the Oral Biological Point of View. The 42nd Annual meeting of Japanese Society for Bone Morphometry 2022.06.30 Yonago city, Tottori

Digital Dentistry

Professor: Manabu Kanazawa (May-) Associate Professor: Maiko Iwaki (Apr-) Assistant Professor: Naohiko Iwasaki (-Mar) Assistant Professor: Yumi Tsuchida RPD: Tamaki Hada

Graduate Student (Master) Ha Rou Bing (-Mar) Mirai Nakayama (Apr-) Nanaka Hayashi(Apr-)

(1) Outline

Department of Digital Dentistry was founded on May 1, 2021, and is responsible for digital dentistry research, clinical practice, and teaching. "Digital dentistry" is an interdisciplinary field consisting of dentistry and engineering. This department provides a smooth connection between clinical dentistry and digital devices (hardware and software) in the field of engineering, and educates and trains individuals in research, clinical practice, and education.

(2) Research

1) Milled Complete Base Denture

Traditional complete denture manufacturing entails a high number of visits, varying treatment quality due to dentist competence variances, and contamination resistance issues due to the use of acrylic resin. To address these issues, we developed a denture fabrication process based on CAD/CAM technology that reduces the number of visits, improves treatment quality uniformity, and improves the physical qualities of dentures. In the traditional milled denture, only the denture base was milled and the artificial teeth were connected thereafter, resulting in issues such as the adhesive surface of the artificial teeth deteriorating. As a result, we invented the TMDU custom disk method, in which a personalized disk is generated for each patient and the denture base is milled as a single piece with artificial teeth. This custom disk is patented, as well as an application for an overseas patent with the help of the Industry-University Collaboration Office. In a prospective clinical study of complete dentures with CAD/CAM technology, which began in 2019, the findings of employing the TMDU custom disk method revealed better cost-effectiveness compared to fabricating complete dentures using the conventional method. The digital denture fabrication process we've developed incorporates a workflow that starts with an intraoral scanner optical impression of the edentulous jaw crest, then denture design and fabrication on a computer. To further digitalize the process, we intend to integrate AI-assist in denture design in the future. In addition, the company collaborates with manufacturer of milling machine and cutting tool on the creation of milling discs, which are required for milling digital dentures, as well as the verification of acceptable milling machine settings.

2) Digital partial denture

The digital partial denture has not been applied in clinical practice compared to the digital complete denture, because there are few research reports. One reason for this could be that partial dentures must accept a wide range of defect and support methods, and are made comprised of metal and resin materials in a variety of forms to do so. While it is possible to fabricate metal frames using the Selective Laser Melting (SLM), subsequent fabrication processes such as artificial teeth placement and polymerization are still carried out using traditional partial denture fabrication procedures, making it difficult to say that all processes have been digitized. As a result, we developed a method for fabricating a custom plate for partial dentures in which a metal frame created using the SLM method and ready-made artificial tooth is embedded for each patient by adapting the TMDU custom disc method for complete dentures. This allowed for the milling of the artificial tooth, metal frame, and denture base all in one piece, overcoming the issues with traditional digital partial dentures. Dry milling machine is used to create this digital partial denture, but a wet milling machine might be utilized to create partial dentures of any size in the future. In the future, appropriate designs for custom plates will be considered, and fabrication of partial dentures for various defect configurations is assessed.

3) Implant overdenture

For a long period, implant overdentures (IOD) for edentulous mandible patients have been explored. Many research were undertaken in Europe and the United States in the 1980s and 1990s, and many evidence has been amassed in this field since a consensus statement was issued in 2002. We began our clinical research in 2008 at Tokyo Medical and Dental University Hospital, and we now have over 100 patients, with the longest case being followed for over ten years. To date, the following IOD studies have been conducted.

- 1) Prospective clinical study of 2-IOD using ball attachment (2008-)
- 2) RCT comparing normal and immediate loading of 2-IOD using magnetic attachments (2011-)
- 3) Prospective clinical study of mini-IODs using mini-implants (2013-2014 McGill University)
- 4) Prospective clinical studies of 1-IOD (2015-)
- 5) Joint clinical research with Showa University on implant-assisted partial denture (IARPD) (2017-)
- 6) Model experiments on IOD implant placement location and denture movement

On the other hand, only a few clinical trials on maxillary IOD have been conducted worldwide. Based on the evidence of mandibular 2-IOD and our knowledge of edentulous prosthodontics, we believe that if the jaw crest conditions are selected, maxillary IOD can be maintained with two implants, and that this will be an effective treatment choice in the super-aging society. To demonstrate proof, we plan to conduct clinical research of 2-IOD employing two implants as the maintenance source in the maxilla as well as in the mandible to establish evidence.

4) Medical device program

Software intended for illness diagnosis and treatment can now be sold on a stand-alone basis and is regulated as a "medical device program," thanks to the passage of legislation in 2014. This has resulted in the development of medical device programs in a variety of fields. We are currently developing applications (medical device programs) to support oral myofunctional therapy for patients with malocclusion and periodontal disease treatment in our department, and we intend to test their clinical effectiveness, including synergistic effects, with face-to-face examinations.

(3) Education

Under graduate: In charge of the following lectures and practical training, focusing on the basics of dental technology, complete denture fabrication methods, and digital dentistry.

Basic Technology of Manufacturing, Teeth Morphological Carving, Advanced Teeth Morphological Carving, Complete Denture Prosthodontic Practice, Removable Partial Prosthodontic Practice 1, Basic Fixed Prosthodontic Practice, Advanced Fixed Prosthodontics Practice, Aesthetic Dentistry Practice, CAD/CAM System Technology Practice, Process Device Engineering, Graduation Reseach 1, CAD/CAM System Technology Practice, Oral and Maxillofacial Radiology, Graduation Reseach 2.

Graduate: In charge of research guidance and lectures "Oral Health Engineering" for the master's program of the graduate school.

(4) Lectures & Courses

Undergraduate: Provide education on cutting-edge technology, particularly in the field of digital dentistry, in order to create digital dental technicians and scientists.

Graduate: Provide professional education in clinical and cutting-edge technologies in the field of digital dentistry, as well as build research skills.

(5) Clinical Performances

Center for Advanced Interdisciplinary Dentistry: Charge of digital dentistry and prosthetic dentistry as a specialist of denture.

Prosthodontics: A unique intraoral assessment and denture design must be conducted in order to repair the morphological and functional alterations induced by the unique intraoral condition of the edentulous jaw and retention with a complete denture. Complete dentures, in particular, cannot rely on teeth to keep them in oral cavity, instead relying on saliva-mediated adhesion between the oral mucosa and the denture base surface. The subfloor mucosa supports the occlusal stresses on a complete denture through the denture base. It is necessary to retention the denture base, take into account the opposing relationship between the upper and lower jaw crests, and organize the artificial teeth and occlusal style in accordance with jaw movement. The denture should be in a form that harmonizes with the morphology and dynamics of the surrounding muscles and associated soft tissues and improves denture retention in order to restore the significant changes in the facial appearance of edentulous individuals due to missing teeth and tooth-supporting tissues. In addition, when dealing with patients, the psychological impact of tooth loss and the installation of massive prostheses in the mouth should be considered. These alterations in general health, including mental status, are likely to cause changes in the oral mucosa, which will affect denture retention, stability, and function. As a result, periodic recalls are conducted, and the patient's subjective evaluation of the denture and function gained by interview and VAS is continually studied to verify that the recovered function is maintained and enhanced over time. Furthermore, we have created our own evaluation standards to objectively assess the efficacy of prosthetic procedures based on EBM as well as patient subjective opinions.

(6) **Publications**

- 1. Soeda Y, Komagamine Y, Kanazawa M, Hada T, Iwaki M, Minakuchi S. Trueness and precision of artificial teeth in CAD-CAM milled complete dentures from custom disks with a milled recess. The Journal of prosthetic dentistry. 2022.12;
- 2. Masataka Watanabe, Manabu Kanazawa, Daisuke Sato, Yoko Uehara, Anna Miyayasu, Maiko Iwaki, Yuriko Komagamine, Sai Tun Naing, Awutsadaporn Katheng, Yuriko Kusumoto, Kazuyoshi Baba, Shunsuke Minakuchi. Oral function of implant-assisted removable partial dentures with magnetic attachments using short implants: A prospective study Tokyo Medical and Dental University. 2022.12;
- Shiozawa M, Tsuchida Y, Suzuki T, Takahashi H. Discoloration of fiber-reinforced composite resin disc for computer-aided design/computer-aided manufacturing after immersion in coffee and curry solutions. Dental materials journal. 2022.10; 42(1); 64-71
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- 11. Komagamine Yuriko, Kanazawa Manabu, Sato Daisuke, Iwaki Maiko, Miyayasu Anna, Minakuchi Shunsuke. Patient-reported outcomes for the immediate loading of mandibular overdentures supported by two implants soon after implant surgery. JOURNAL OF DENTAL SCIENCES. 2022.01; 17(1); 560-567
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- 2. Tamaki HADA, Manabu KANAZAWA, Maiko IWAKI, Anna MIYAYASU, Motohiro UO, Shunsuke MINAKUCHI. Evaluation of mechanical properties of custom blocks for digital dentures fabricated using a new polymerization method. International Dental Materials Congress 2022 (IDMC2022) 2022.11.04 Taipei
- 3. Manabu Kanazawa. Treatment planning. TMDU-CU Geriatric course 2022.10.27
- 4. Manabu Kanazawa. The cutting edge of digital dentures. TMDU-CU Geriatric course 2022.10.24
- 5. Sahaprom Namano, Manabu Kanazawa, Awutsadaporn Katheng, Bui Ngoc Huyen Trang, Tamaki Hada, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. Trueness and eco-efficiency analysis of the support structure reduction for SLA printed maxillary denture.. PER-IADR Oral Health Research Congress 2022.09.17 Marseille, France
- 6. Manabu Kanazawa. The cutting edge of digital dentures. the 1st Indonesian Prosthodontic Society Meeting 2022.09.09
- 7. Manabu Kanazawa. Scan in digital dentures. The 13th Asian Academy of Prosthodontics Biennial Congress 2022.08.26
- 8. Manabu Kanazawa, Yuriko Komagamine. Bolder molding for mandibular complete dentures. Essential Expertise for Clinical Dentistry (EECD) 2022.08.22
- 9. Manabu Kanazawa. Roundtable. Align education 2022.07.19
- 10. Manabu Kanazawa. One day direct denture restorations using hard and soft relining materials. International Faculty Development Course (IFDC) AY2022. 2022.07.15

- 11. Manabu Kanazawa. Digital milled denture with artificial teeth-embedded custom disc. DGSHAPE 2022.07.02
- 12. BUI Ngoc Huyen Trang, Manabu Kanazawa, Daisuke Sato, Masataka Watanabe, Yoko Uehara, Maiko Iwaki, Yuriko Komagamine, Sai Tun Naing, Yuriko Kusumoto, Yuka Abe, Kazuyoshi Baba, Shunsuke Minakuchi. Masticatory Function With Implant-assisted Removable Partial Dentures Using Short Implants. 2022 IADR/APR General Session 2022.06.22 Web
- 13. Sahaprom Namano, Manabu Kanazawa, Awutsadaporn Katheng, Bui Ngoc Huyen Trang, Tamaki Hada, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. The effect of support structures on the precision of SLA 3D printing dentures: an in vitro study. FDCU International Symposium 2022: Artificial Intelligence and Personalized Dental Medicine- the Future Dentistry. 2022.05.18
- 14. Manabu Kanazawa. Let's start digital denture. Master course, Chulalongkorn University 2022.05.11
- 1. Development of new sports mouth guards using 4D printing technology. The 33rd Annual Meeting of Japanese Academy of Sports Dentistry 2022.12.04
- 2. The influence of wearing a complete denture on control of head position during walking exercise in edentulous older adults. 2022.07.16
- 3. Effect of different filler contents on the mechanical properties for photopolymer resins for 3D printing. 2022.07.16

Oral Prosthetic Engineering

Professor Noriyuki WAKABAYASHI Junior Associate Professor Masaomi IKEDA Assistant Professor 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) Advanced technology which utilized a CAD/CAM system.
- 2) 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, Teeth Morphological Curving, Advanced Teeth Morphological Curving, Conservative Dentistry, Science of Occlusion, Advanced Science of Occlusion, Communication Theory, Health Promotion, Basic Fixed Prosthodontics, Advanced Fixed Prosthodontics, Complete Denture Prosthodontics, Removable Partial Prosthodontics, Globalization for Oral Health Engineering, Gerodontology, Laws for Dental Technologists, CAD/CAM System Technology, CAD/CAM System Technology Practice, Special Lectures for Advanced Technology, Management and Regulation for Dental Technologists, Oral Appliances, Aesthetic Dentistry Practice, Orthodontic Dentistry, Comprehensive Oral Rehabilitation Engineering Practice, Graduation Research

(4) Publications

[Original Articles]

1. Shiozawa M, Tsuchida Y, Suzuki T, Takahashi H. Discoloration of fiber-reinforced composite resin disc for computer-aided design/computer-aided manufacturing after immersion in coffee and curry solutions.

Dental materials journal. 2022.10; 42(1); 64-71

- Shiho Otake, Shinya Oishi, Taisuke Ozaki, Masaomi Ikeda, Wataru Komada. Effect of Method of Removing Caries-Affected Dentin on the Bond Strength of Composite Resin to Root Canal Dentin. Healthcare (Basel). 2022.10; 10(11);
- 3. Sanon Kittisak, Hatayama Takashi, Tichy Antonin, Thanatvarakorn Ornnicha, Prasansuttiporn Taweesak, Wada Takahiro, Ikeda Masaomi, Hosaka Keiichi, Nakajima Masatoshi. Smear layer deproteinization with NaOCl and HOCl:Do application/wash-out times affect dentin bonding of one-step self-etch adhesives?(和 訳中) Dental Materials Journal. 2022.05; 41(3); 353-362
- 4. Sasaki Y, Nakakuki K, Ikeda M, Sumi Y, Miura H, Imazu Y, Otomo Y. Undergraduate medical and dental science students' interest and support needs in medical volunteer activities during times of disasters Japanese Journal of Disaster Medicine. 2022.04; 27; 102-109
- 5. Khanlar LN, Takagaki T, Abdou A, Inokoshi M, Ikeda M, Takahashi A, Yoshihara K, Nagaoka N, Nikaido T, Blatz MB, Tagami J. Effect of Air-Particle Abrasion Protocol and Primer on The Topography and Bond Strength of a High-Translucent Zirconia Ceramic. J Prosthodont. 2022.03; 31(3); 228-238
- 6. Sanon K, Hatayama T, Tichy A, Thanatvarakorn O, Prasansuttiporn T, Wada T, Ikeda M, Hosaka K, Nakajima M. Smear layer deproteinization with NaOCl and HOCl: Do application/wash-out times affect dentin bonding of one-step self-etch adhesives? Dental Materials Journal. 2022.01;
- 7. Roubing Ha, Yumi Tsuchida, Maho Shiozawa, Hidekazu Takahashi. Effect of thickness on color appearance of multilayer CAD/CAM composite resin blocks Odontology. 2022;
- 8. Mori S, Onda K, Fujita S, Suzuki T, Ikeda M, Zay Yar Myint K, Hikage J, Abe O, Tomimoto H, Oishi K, Taguchi J. Brain atrophy in middle age using magnetic resonance imaging scans from Japan's health screening programme. Brain communications. 2022; 4(4); fcac211

- Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Mechanical evaluation of face guards fabricated by stereolithographic three- dimensional printing. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 (IDMC2022) 2022.11.04 Taipei, Taiwan
- 2. Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Ayumu Murata, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Evaluation of core and cushion materials of face guards made by stereolithography additive manufacturing. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA) 2022.10.25 Osaka, Japan
- 3. Xuefei Chen, Go Inoue, Hidenori Hamba, Masaomi Ikeda, Yasushi Shimada . Remineralization Enhancement of Dentin Lesion Using the Combination of SDF+GIC.. The International Association for Dental Research 100th General Session & Exhibition 2022.06.23 ChengDu, China (Web)
- 4. Yi Yang, Go Inoue, Keiichi Hosaka, Masaomi Ikeda, Yasushi Shimada. The effect of deproteinizing pretreatment on bonding performance and acid resistance to eroded dentin. IAD 2022@Sapporo The International Congress on Adhesive Dentistry 2022.06.03 Hokkaido University Conference Hall
- 1. Hirotoshi Iwabuchi,Go Inoue,Masaomi Ikeda,Yasushi Shimada. The evaluation of acid-resistance and bond strength of an experimental calcium-containing adhesive system on enamel. The 157th Meeting of the Japanese Society of Conservative Dentistry 2022.11.10 Okayama,Japan

Hyperbaric Medical Center

Director and Professor; Kazuyoshi YAGISHITA Assistant Professor ; Takashi HOSHINO Specially Appointed Assistant Professor ; Masaki AMEMIYA (2022.4 ~) , Etsuko MATSUMURA (~ 2022.3) Senior Resident ; Tatsunobu IKEDA (2022.4 ~) Adjunct Lecturer; Yasushi KOJIMA, Yumi NIIZEKI, Takuya OYAIZU, Toshiyuki OHHARA Researcher; Masaki HORIE, Toshihiro KONDOH, Naohiro MITSUMOTO Staff Assistant; Kiyomi ITOH

(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 arterior 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 2022, 2,224 times hyperbaric oxygen therapy (HBO) in 228 patients were performed in the university hospital.

(5) Publications

- 1. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Changes in subjective knee function and psychological status from preoperation to 6 months post anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2022.12; 9(1); 114
- 2. Derman W, Runciman P, Eken M, Boer PH, Blauwet C, Bogdos M, Idrisova G, Jordaan E, Kissick J, LeVan P, Lexell J, Mohammadi F, Patricio M, Schwellnus M, Webborn N, Willick SE, Yagishita K. Incidence and burden of illness at the Tokyo 2020 Paralympic Games held during the COVID-19 pandemic: a prospective cohort study of 66 045 athlete days. British journal of sports medicine. 2022.12; 57(1); 55-62
- 3. Derman W, Runciman P, Eken M, Boer PH, Blauwet C, Bogdos M, Idrisova G, Jordaan E, Kissick J, LeVan P, Lexell J, Mohammadi F, Patricio M, Schwellnus M, Webborn N, Willick SE, Yagishita K. Incidence and burden of injury at the Tokyo 2020 Paralympic Games held during the COVID-19 pandemic: a prospective cohort study of 66 045 athlete days. British journal of sports medicine. 2022.12; 57(1); 63-70
- 4. Mitomo S, Aizawa J, Hirohata K, Ohji S, Ohmi T, Ohara T, Koga H, Yagishita K. Association Between Knee Extension Strength at 3 and 6 Months After Anterior Cruciate Ligament Reconstruction. Journal of sport rehabilitation. 2022.08; 1-9
- Murofushi K, Oshikawa T, Kaneoka K, Akuzawa H, Yamaguchi D, Mitomo S, Furuya H, Hirohata K, Yagishita K. Differences in trunk and lower extremity muscle activity during squatting exercise with and without hammer swing. Scientific reports. 2022.08; 12(1); 13387
- 6. Hirohata K, Aizawa J, Ohmi T, Ohji S, Mitomo S, Ohara T, Koga H, Yagishita K, Jinno T, Okawa A. Reactive strength index during single-limb vertical continuous jumps after anterior cruciate ligament reconstruction: cross-sectional study. BMC sports science, medicine & rehabilitation. 2022.08; 14(1); 150
- Adachi T, Katagiri H, An JS, Engebretsen L, Tateishi U, Saida Y, Koga H, Yagishita K, Onishi K, Forster BB. Imaging-detected bone stress injuries at the Tokyo 2020 summer Olympics: epidemiology, injury onset, and competition withdrawal rate. BMC musculoskeletal disorders. 2022.08; 23(1); 763
- 8. Miyamoto Reina, Hirai Takashi, Yoshii Toshitaka, Onuma Hiroaki, Inose Hiroyuki, Yuasa Masato, Matsukura Yu, Morishita Shingo, Yamamoto Kouhei, Koyanagi Hirotaka, Sato Shingo, Yagishita Kazuyoshi, Okawa Atsushi. Surgical Strategy for Osteoid Osteoma Localized in Anterior Lumbar Vertebral Body: A Case Report(和訳中) Spine Surgery and Related Research. 2022.07; 6(4); 408-411
- Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Association between landing biomechanics, knee pain, and kinesiophobia in athletes following anterior cruciate ligament reconstruction: A cross-sectional study PM&R. 2022.07;
- Aizawa J, Hirohata K, Ohji S, Ohmi T, Mitomo S, Koga H, Yagishita K. Cross-sectional study on relationships between physical function and psychological readiness to return to sport after anterior cruciate ligament reconstruction. BMC sports science, medicine & rehabilitation. 2022.06; 14(1); 97
- 11. Guo Tang, Yoshinori Asou, Etsuko Matsumura, Yusuke Nakagawa, Kazumasa Miyatake, Hiroki Katagiri, Tomomasa Nakamura, Hideyuki Koga, Keiichiro Komori, Ichiro Sekiya, Yoich Ezura, Kunikazu Tsuji. Short cytoplasmic isoform of IL1R1/CD121a mediates IL1 β induced proliferation of synovium-derived mesenchymal stem/stromal cells through ERK1/2 pathway. Heliyon. 2022.05; 8(5); e09476
- Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Jae-Sung An, Ichiro Sekiya. Ultrasound-assisted arthroscopic all-inside repair technique for posterior lateral meniscus tear. Arthroscopy Techniques. 2022.04; 11(5); e929-e935
- 13. Miyamoto R, Hirai T, Yoshii T, Onuma H, Inose H, Yuasa M, Matsukura Y, Morishita S, Yamamoto K, Koyanagi H, Sato S, Yagishita K, Okawa A. Surgical Strategy for Osteoid Osteoma Localized in Anterior Lumbar Vertebral Body: A Case Report. Spine surgery and related research. 2022; 6(4); 408-411
- 14. Murofushi Koji, Oshikawa Tomoki, Kaneoka Koji, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Akuzawa Hiroshi, Yagishita Kazuyoshi. The effect of external-focus using a paper balloon on the activity of upper limb and trunk muscles during static and dynamic tasks ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(4); 345-355

15. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Strength normalized to muscle volume rather than body weight is more accurate for assessing knee strength following anterior cruciate ligament reconstruction ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(1); 7-13

Neurosurgery

(1) Publications

- Noda Mariko, Inaji Motoki, Karakama Jun, Arai Yukika, Kuroha Masae, Tamura Kaoru, Tanaka Yoji, Maehara Taketoshi. ベバシズマブ治療下で多発性脳動脈狭窄を伴う虚血性脳卒中を発症した退形成星細胞腫 患者 1症例報告 (Ischemic Stroke with Multiple Cerebral Artery Stenosis in a Patient with an Anaplastic Astrocytoma during Bevacizumab Treatment: A Case Report) NMC Case Report Journal. 2022.12; 9(1); 13-17
- Fujino A, Tanaka Y, Abe D, Ariizumi Y, Inaji M, Maehara T. A New Technique for the Endoscopic Reconstruction of Skull Base Defects Using Multiple-balloon Catheters. Neurologia medico-chirurgica. 2022.09;
- 3. Sabari JK, Velcheti V, Shimizu K, Strickland MR, Heist RS, Singh M, Nayyar N, Giobbie-Hurder A, Digumarthy SR, Gainor JF, Rajan AP, Nieblas-Bedolla E, Burns AC, Hallin J, Olson P, Christensen JG, Kurz SC, Brastianos PK, Wakimoto H. Activity of Adagrasib (MRTX849) in Brain Metastases: Preclinical Models and Clinical Data from Patients with KRASG12C-Mutant Non-Small Cell Lung Cancer. Clinical cancer research : an official journal of the American Association for Cancer Research. 2022.08; 28(15); 3318-3328
- 4. RNF213 Gene Variants in Moyamoya Disease: Questions Remain Unanswered. 2022.06; 162; 18-20
- 5. Kuroda N, Kubota T, Horinouchi T, Ikegaya N, Kitazawa Y, Kodama S, Kuramochi I, Matsubara T, Nagino N, Neshige S, Soga T, Takayama Y, Sone D, IMPACT-J EPILEPSY (In-depth Multicenter analysis during Pandemic of Covid19 Throughout Japan for Epilepsy practice) study group., Kanemoto K, Ikeda A, Terada K, Goji H, Ohara S, Hagiwara K, Kamada T, Iida K, Ishikawa N, Shiraishi H, Iwata O, Sugano H, Iimura Y, Higashi T, Hosoyama H, Hanaya R, Shimotake A, Kikuchi T, Yoshida T, Shigeto H, Yokoyama J, Mukaino T, Kato M, Sekimoto M, Mizobuchi M, Aburakawa Y, Iwasaki M, Nakagawa E, Iwata T, Tokumoto K, Nishida T, Takahashi Y, Kikuchi K, Matsuura R, Hamano SI, Fujimoto A, Enoki H, Tomoto K, Watanabe M, Takubo Y, Fukuchi T, Nakamoto H, Kubota Y, Kunii N, Shirota Y, Ishikawa E, Nakasato N, Maehara T, Inaji M, Takagi S, Enokizono T, Masuda Y, Hayashi T. Impact of COVID-19 pandemic on epilepsy care in Japan: A national-level multicenter retrospective cohort study. Epilepsia open. 2022.05;
- Kota Yokoyama, Jun Oyama, Junichi Tsuchiya, Jun Karakama, Kaoru Tamura, Motoki Inaji, Yoji Tanaka, Daisuke Kobayashi, Taketoshi Maehara, Ukihide Tateishi . Branch - like enhancement on contrast enhanced MRI is a specific finding of cerebellar lymphoma compared with other pathologies Scientific Reports. 2022.03;
- 7. Shimizu K, Tamura K, Hara S, Inaji M, Tanaka Y, Kobayashi D, Sugawara T, Wakimoto H, Nariai T, Ishii K, Sakuma I, Maehara T. Correlation of Intraoperative 5-ALA-Induced Fluorescence Intensity and Preoperative < sup> 11< /sup> C-Methionine PET Uptake in Glioma Surgery. Cancers. 2022.03; 14(6);
- 8. Takamura T, Hara S, Nariai T, Ikenouchi Y, Suzuki M, Taoka T, Ida M, Ishigame K, Hori M, Sato K, Kamagata K, Kumamaru K, Oishi H, Okamoto S, Araki Y, Uda K, Miyajima M, Maehara T, Inaji M, Tanaka Y, Naganawa S, Kawai H, Nakane T, Tsurushima Y, Onodera T, Nojiri S, Aoki S. Effect of Temporal Sampling Rate on Estimates of the Perfusion Parameters for Patients with Moyamoya Disease

Assessed with Simultaneous Multislice Dynamic Susceptibility Contrast-enhanced MR Imaging. Magnetic resonance in medical sciences : MRMS : an official journal of Japan Society of Magnetic Resonance in Medicine. 2022.03;

- 9. Takamura T, Hara S, Nariai T, Ikenouchi Y, Suzuki M, Taoka T, Ida M, Ishigame K, Hori M, Sato K, Kamagata K, Kumamaru K, Oishi H, Okamoto S, Araki Y, Uda K, Miyajima M, Maehara T, Inaji M, Tanaka Y, Naganawa S, Kawai H, Nakane T, Tsurushima Y, Onodera T, Nojiri S, Aoki S. Effect of Temporal Sampling Rate on Estimates of the Perfusion Parameters for Patients with Moyamoya Disease Assessed with Simultaneous Multislice Dynamic Susceptibility Contrast-enhanced MR Imaging. Magnetic resonance in medical sciences : MRMS : an official journal of Japan Society of Magnetic Resonance in Medicine. 2022.03;
- Shimizu K, Tamura K, Hara S, Inaji M, Tanaka Y, Kobayashi D, Sugawara T, Wakimoto H, Nariai T, Ishii K, Sakuma I, Maehara T. Correlation of Intraoperative 5-ALA-Induced Fluorescence Intensity and Preoperative (11)C-Methionine PET Uptake in Glioma Surgery. Cancers. 2022.03; 14(6);
- 11. Mariko NODA, Motoki INAJI, Jun KARAKAMA, Yukika ARAI, Masae KUROHA, Kaoru TAMURA, Yoji TANAKA, Taketoshi MAEHARA. Ischemic Stroke with Multiple Cerebral Artery Stenosis in a Patient with an Anaplastic Astrocytoma during Bevacizumab Treatment: A Case Report NMC Case Report Journal. 2022.02;
- Kobayashi T, Nitta M, Shimizu K, Saito T, Tsuzuki S, Fukui A, Koriyama S, Kuwano A, Komori T, Masui K, Maehara T, Kawamata T, Muragaki Y. Therapeutic Options for Recurrent Glioblastoma-Efficacy of Talaporfin Sodium Mediated Photodynamic Therapy. Pharmaceutics. 2022.02; 14(2);
- Hara S, Mukawa M, Akagawa H, Thamamongood T, Inaji M, Tanaka Y, Maehara T, Kasuya H, Nariai T. Absence of the RNF213 p.R4810K variant may indicate a severe form of pediatric moyamoya disease in Japanese patients. Journal of neurosurgery. Pediatrics. 2022.01; 29(1); 48-56
- 14. Ueda Y, Tanaka Y, Hara S, Inaji M, Ishii K, Maehara T, Nariai T. Differences in cerebral blood flow measurement using arterial spin labeling MRI between patients with moyamoya disease and patients with arteriosclerotic cerebrovascular disease. Acta radiologica (Stockholm, Sweden : 1987). 2022.01; 2841851211069245
- 15. Noda M, Inaji M, Karakama J, Arai Y, Kuroha M, Tamura K, Tanaka Y, Maehara T. Ischemic Stroke with Multiple Cerebral Artery Stenosis in a Patient with an Anaplastic Astrocytoma during Bevacizumab Treatment: A Case Report. NMC case report journal. 2022; 9; 13-17
- 1. Shoko Hara, Tadashi Nariai. [Indirect Revascularization Surgery for Chronic Ischemia in Moyamoya Disease] . No shinkei geka. Neurological surgery. 2022.07; 50(4); 826-838

- 1. Shoko Hara. Disrupted cerebral microstructural integrity revealed by diffusion MRI in adult moyamoya disease. ICMRI 2022 (10th International Congress on MRI) & 27th Annual Scientific Meeting of KSMRM (the Korean Society of Magnetic Resonance in Medicine) 2022.11.05
- 2. Shoko Hara, Junko Kikuta, Kaito Takabayashi, Koji Kamagata, Shihori Hayashi, Motoki Inaji, Yoji Tanaka, Masaaki Hori, Kenji Ishii, Tadashi Nariai, Toshiaki Taoka, Shinji Naganawa, Shigeki Aoki, Taketoshi Maehara. Glymphatic system activity may be disrupted in moyamoya disease: the diffusion tensor image analysis along the perivascular space (DTI-ALPS) study. ICMRI 2022 (10th International Congress on MRI) & 27th Annual Scientific Meeting of KSMRM (the Korean Society of Magnetic Resonance in Medicine) 2022.11.04
- 3. Shoko Hara, Tadashi Nariai, Mai Fujioka, Toshihiko Hayashi, Motoki Inaji, Yoji Tanaka, Taketoshi Maehara. Indirect revascularization for pediatric moyamoya disease: a single center experience over 40 years. World Internet Conference on Moyamoya Disease 2022 2022.10.12
- 1. Shoko Hara, Yoji Tanaka, Motoki Inaji, Shihori Hayashi, Kenji Ishii, Tadashi Nariai, Taketoshi Maehara. Detecting misery perfusion using spatial coefficient of variation of ASL-MRI in moyamoya disease. 2022.03.17
- 2. Evaluation of glymphatic system activity using diffusion tensor image analysis along the perivascular space (DTI-ALPS) in patients with Moyamoya disease. 2022.02.18
[Awards & Honors]

1. President award, first prize in clinical competition, JSMRM2022, 2022.09 $\,$

Sports Dentistry

(1) Publications

[Original Articles]

- 1. Shintaro Shimizu, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tatsuhiko Anzai, Kunihiko Takahashi, Toshiaki Ueno, Kenji Fueki. Quantitative text analysis of the mechanisms of tooth injury: Analysis of accidents in five sports that occurred in 15 years under school control. Dent Traumatol. 2022.11;
- Kairi Hayashi, Yasuo Takeuchi, Shintaro Shimizu, Gen Tanabe, Hiroshi Churei, Hiroaki Kobayashi, Toshiaki Ueno. Continuous Oral Administration of Sonicated P. gingivalis Delays Rat Skeletal Muscle Healing Post-Treadmill Training. International Journal of Environmental Research and Public Health. 2022.10; 19(20);
- 3. Towithelertkul C, Haraguchi M, Tanabe G, Fujita H, Ali IE, Han X, Sumita YI. Two-piece detachable interlocking mold for low-dose-rate brachytherapy: A dental technique for radiotherapy prosthesis fabrication. J Prosthet Dent. 2022.08; online.;
- 4. Tanabe G, Hattori M, Obata S, Takahashi Y, Churei H, Nishiyama A, Ueno T, Sumita YI. Case report: Psychoacoustic analysis of a clarinet performance with a custom-made soft lip shield worn to prevent mucosal erosion of lower lip. Front Psychol. 2022.04; 13; 852866
- 5. Ruman Uddin Chowdhury, Hiroshi Churei, Gen Tanabe, Yuriko Yoshida, Kairi Hayashi, Hidekazu Takahashi, Takahiro Wada, Motohiro Uo, Takahiro Mizobuchi, Nafees Uddin Chowdhury, Toshiaki Ueno. Useful design of custom-made mouthguard for athletes undergoing orthodontic treatment with brackets and wires. J Dent Sci. 2022.01; 17(1); 308-315
- 6. Chowdhury RU, Churei H, Tanabe G, Yoshida Y, Hayashi K, Takahashi H, Wada T, Uo M, Mizobuchi T, Chowdhury NU, Ueno T. Useful design of custom-made mouthguard for athletes undergoing orthodontic treatment with brackets and wires. J Dent Sci. 2022.01; 17(1); 308-315

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 Toshikazu Yasui, Yoshinobu Maeda, Anthony Clough, Melvin Choy, Kazunori Nakajima, Rieko Koushi, Kazunori Ikebe, Paul Picciniinni, Hiroshi Suzuki, Hidehisa Matsumura, Yuto Tanaka, Masashi Yoshida, Tsung-Chieh Yang, David Kumamoto, Kung Rock Kwon, Tomotaka Takeda, Kairi Hayashi, Sylvaine Goupy, Ashraf Samy Ghanem, Naoki Tsukimura, Hiroshi Churei, Gen Tanabe, Siegfried Marquardt, Richard Lee Sungbok, Tomoyo Gonda, Kazunari Kimoto, Nanaho Katsutani. Statements from the 2019 Second International Workshop on Sports Dentistry in Osaka Japan. International Journal of Sports Dentistry. 2022.11; 15(1); 7-16

[Conference Activities & Talks]

 Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Mechanical evaluation of face guards fabricated by stereolithographic three- dimensional printing. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 (IDMC2022) 2022.11.04 Taipei, Taiwan

- 2. Hiroshi Churei, Kairi Hayashi, Gen Tanabe, Yuumi Takahashi, Kairi Togawa, Shintaro Shimizu, Chenyuan Li, Chang Liu, Thida Aung, Qiushuang Zhu, Zequn Li, Yunchia Lian, Akihito Kumagai, Toshiaki Ueno.. Relationship between appropriate heating temperature and drooping distance of poly-olefin sheet materials for mouthguard. INTERNATIONAL DENTAL MATERIALS CONGRESS 2022 2022.11.04 HYBRID ACADEMIC CONFERENCE, Taiwan
- 3. Takahiro WADA, Aya TAKAMURA, Momoko ADACHI, Ayumu Murata, Maho SHIOZAWA, Hiroshi CHUREI, Motohiro UO. Evaluation of core and cushion materials of face guards made by stereolithography additive manufacturing. The 2nd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA) 2022.10.25 Osaka, Japan
- 4. Tanabe G, Hattori M, Mizuguchi D, Masaki K, Wang Y, Hasegawa S, Tohara H, Sumita YI. Effect of voice training on maxillofacial function; a preliminary survey. Musicians' and Performing Artists' Health and Performance Conference 2022 (MHPC22) 2022.09.23 Oslo (Norway)+Web
- 5. Hattori M, Tanabe G, Patzelt SBM, Schulze D, Sumita YI. Visualization of oral function during playing a wind instrument by a lateral dental impression: a proof-of-concept investigation. Musicians' and Performing Artists' Health and Performance Conference 2022 (MHPC22) 2022.09.22 Oslo (Norway)+Web
- 6. Hattori M, Tanabe G, Sumita YI, Obata S, Churei H, Ueno T. Does playing music influence the rehabilitation of a maxillofacial defect patient?. 40th Annual PAMA International Symposium 2022.06.25 Chicago (USA)+Web
- 7. Chenyuan Li, Hiroshi Churei, Chang Liu, Qiushuang Zhu, Zequn Li, Gen Tanabe, Toshiaki Ueno. . Questionnaire survey on safety awareness for boxers in China. 2022 IADR (100th)/IADR APR(5th) 2022.06.20 web/ China
- 1. Nishiyama A, Tanabe G, Hattori M, Churei H, Sumita YI, Ueno T. Dental problems that the person teaching the instrumentalist believes affect the performance. The 1st Annual Meeting of Japanese Performing Arts Medicine Association 2022.07.18 Tokyo (Japan)
- 2. Tanabe G, Obata S, Hattori M, Churei H, Nishiyama A, Ueno T, Mori T, Sumita YI. Exploring the relation between Musical Instrument Performance and Oral Sciences -Current state and policy for a massive questionnaire survey of instrumentalists through academia-industry collaboration-. The 1st Annual Meeting of Japanese Performing Arts Medicine Association 2022.07.18 Tokyo (Japan)
- 3. Haraguchi M, Towithelertkul C, Tanabe G, Fujita H, Han X, Sumita YI. Two-piece detachable interlocking mold for low-dose-rate brachytherapy: A dental technique for radiotherapy prosthesis fabrication. The 39th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2022.06.24 Miyazaki (Japan)+Web
- 4. Tanabe G, Hattori M, Tani H, Sumita YI. Two case reports of speech aid repair support for patients with cleft lip and palate. The 46th Annual Meeting of Japanese Cleft Palate Association 2022.05.27 Kagoshima (Japan)+Web

Dental Clinic for Sleep Disorders (Apnea and Snoring)

Junior Associate Professor (Clinic Chief) Masayuki HIDESHIMA Hospital Staff Mai MIYACHI Hospital Staff Akitake HATTORI Nanami SAITOH Adjunct Assistant Professor Adjunct Assistant Professor Haruyuki YANAGISAWA Adjunct Assistant Professor Mai MIYACHI Adjunct Assistant Professor Shuichiro YOSHIZAWA Project Assistant Professor Hiroyuki ISHIYAMA (concurrently with TMJ Clinic) Hospital Staff Yuko MITSUMA (concurrently with Oral Diagnosis and General Dentistry) Dental technician Hisashi MATSUBARA (concurrently with Dental Laboratory) Dental technician Tatsu SUZUKI (concurrently with Dental Laboratory) Dental technician Koichi ENOMOTO (concurrently with Dental Laboratory) Assistant Clerk Naoko OBATA

(1) **Outline**

his clinic was established in October 2012 and provides dental treatment for relatively mild patients with obstructive sleep apnea who repeats apnea and snoring during sleep. Currently, about 230,000 people are diagnosed with OSA and are being treated in Japan, and the number of potential patients is said to be as high as 2 million. Since OSA patients sleep lightly, they do not only interfere with their daily lives such as strong drowsiness during the day and lack of concentration, but also have a high risk of diseases such as hypertension, diabetes, myocardial infarction, and cerebrovascular accident.

For OSA with apnea and hypopnea frequency (Apnea Hypopnea Index: AHI) of 20 or more per hour during sleep, wear a nasal mask called CPAP (Continuous Positive Airway Pressure) at the medical hospital to support breathing. The treatment is covered by social medical insurance in Japan. On the other hand, if AHI is less than 20, CPAP cannot be covered by social insurance, so in dentistry, a mouthpiece (sleep sprint) called Oral Appliance (OA) is delivered to protrude the lower jaw, preventing from the tongue sinking, enlarge the pharyngeal airway and make it easier to breathe. Therefore, CPAP is usually applied to relatively severe OSA, and OA is usually applied to mild OSA.

However, even if OA is not as effective as CPAP, it has the advantages of excellent portability and less discomfort during sleep. It is often used in patients who cannot continue to use CPAP even if AHI is 20 or more. Also, it is often used in patients with severe OSA who has pollinosis or business trips.

In this way, in order to treat diseases in the medical field across multiple fields of medicine and dentistry, cooperation with many clinical departments is indispensable. In Tokyo medical and dental university, the sleep apnea center cooperates with the department of respiratory, psychiatry, and otorhinolaryngology cooperates with dental clinic for sleep disorder which cooperate with dental prosthetics department, general dentistry, TMD department, and engineering department work together. We provide collaborative medical care with outpatients, hold regular conferences, and consider more effective treatment methods.

(2) Research

At the conference with sleep apnea medical center, we are planning and discussing research, making presentations at specialized academic societies, planning symposiums, formulating clinical practice guidelines, and conducting activities such as applying for research funds. The outline of the research is as follows.

• Transition of outpatient SAS cases and clinical usefulness of OA therapy.

 \bullet Effects of Nursing Home on Temporomandibular Joint Pain for Obstructive Sleep Apnea Syndrome Using OA. — Double-Blind Randomized Comparative Study

- Effects of long-term use of upper and lower integrated OA on the orofacial in OSA patients
- Development of a system for determining the therapeutic effect of OA on OSA patients
- Development and application of OA treatment prediction model for OSA patients
- Effects of lifestyle factors on the rapeutic effect in her OA therapy for OSA patients
- Development of non-contact screening methods for OSA patients
- An open study of the effects of hyperbaric oxygen therapy on sleep

(3) Clinical Services & Other Works

In order to provide OA treatment by insurance for OSA patients in a dental clinic for sleep disorder, it is necessary to perform a sleep test at a medical hospital and diagnose sleep apnea syndrome by physician. No insurance treatment is available in dentistry without a referral letter and a summary of sleep test.

To fabricate OA, the maxillary and mandibular impressions are taken, the bite registration with mandibular anterior positions taken, and the upper and lower OA are prepared separately, and trial fitting and adjustment are performed in the oral. If OA covered by insurance, it is necessary to glue the upper and lower OA pieces with an immediate polymerization resin and attach them together. On the other hand, in OA that is not covered by insurance, the maxilla and mandibulae are separated, and there is a freedom in the range of movement without retracting the lower jaw, so there is less burden on the TMJ, snoring and apnea are reduced, and patient can be obtained more comfortable sleep.

If dentist adjust OA, and a patient can wear it every night, it is necessary to refer a patient to medical hospital to take sleep study test.

Medical treatments are coordinated in both medical and dental clinic, and conferences are held regularly to consider more effective treatment methods. In addition, dental clinic for sleep disorder accepts patient requests from off-campus medical sleep clinics, and proceed with OA treatment, requesting referrals to primary physician, and provide regular examinations.

(4) Clinical Performances

Taking advantage of the characteristics of our university, which has both medical and dentistry, we carry out close collaborative medical treatment and information exchange between the sleep apnea center and dental clinic for sleep disorder, and practice tailor-made treatment suitable for each case.

In dental clinic for sleep disorder, the staff of the dental prosthetics department, general dentistry, TMD department, and engineering department, which specialize in dental prosthodontics, oral diagnosis, orofacial pain control, and dental engineering, cooperate to OA treatment of OSA patients.

Although it is difficult to fabricate OA for edentulous or partial missing teeth dentition even in dentistry, OA can be applied to these cases because the specialist of the prosthesis department and engineering department handles it, and it is possible to improve general health and QOL of OSA patient.

In addition, OA therapy, in which the mandibula is fixed forward during bed time, may cause side effect such as temporomandibular joint pain. However Specialized staff in TMD department provide treatment for pain and preventive therapy to maintain OA compliance.

(5) Publications

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- 2. Kimura-Ono A, Maekawa K, Kuboki T, Nawachi K, Fujisawa M, Sato H, Aita H, Koyama S, Hideshima M, Sato Y, Wake H, Nagao K, Kodaira-Ueda Y, Tamaki K, Sadamori S, Tsuga K, Nishi Y, Sawase T, Koshino

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- 1. Hiroyuki Ishiyama, Masayuki Hideshima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki. Evaluation of Respiratory Resistance as a Predictor for Oral Appliance Treatment Response in Obstructive Sleep Apnea: A Pilot Study Journal of oral and sleep medicine. 2022.05; 8(3); 64-72

[Books etc]

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[Misc]

- 1. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part15 The Introduction of Sleep Dentistry into General Dentists and the Prospect of the OSA Treatment. the Quintessence. 2022.03; 41(3); 172-179
- 2. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part14 Case Study:Treatment of Obstructive Sleep Apnea the Quintessence. 2022.02; 41(2); 166-178
- 3. Mai Miyachi. Progressive Acquisition of Practical Skills on Dental Sleep Medicine. Part13 The Screening and Clinical Diagnosis of Pediatric Obstructive Sleep Apnea and Its Treatment Options. the Quintessence. 2022.01; 4(1); 202-207

[Conference Activities & Talks]

- 1. Ken-ichi Tonami, Sachi Umemori, Kanako Noritake, Masayuki Hideshima, Arata Ebihara, Cao Ridan, Masayo Sunaga, Atsuhiro Kinoshita, Hiroshi Nitta. Development of an insurance claim training application using Microsoft Excel macro. The 87th Annual Meeting of The Stomatological Society 2022.12.03 Tokyo
- 2. MAI MIYACHI. Airway Analysis and A Fully Digital Workflow of Oral Appliance for the Treatment of Obstructive Sleep Apnea. The 21st Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2022.11.21 Okinawa Bankoku Shinryokan
- 3. Masayuki HIDESHIMA. Adoption to the social insurance system and clinical practice guidelines for magnetic attachment. The 131st Annual Meeting of the japan Prosthodontic Society, Clinical Lecture Series 4,Knowledge and skills of magnetic attachment for prosthodontists 2022.07.17 Osaka
- 4. Miyachi Mai. Medical-dental collaboration in sleep-disordered breathing treatment Let's ask each other
 What we want to ask the medical department about CPAP treatment. The 47th annual meeting of Japanese society of sleep research 2022.06.30

[Others]

 Prognosis of treatment effect for sleep apnea with oral appliance therapy - videoendoscopic evaluation for the predicting model -, 2022.04 Masayuki HIDESHIMA Grant-in-Aid for Scientific Research(C) 2022 Research No. 22K10051 Research Period 2012-2024 Principal Investigator Masayuki HIDESHIMA Research Fund \3,200,000

Clinical Laboratory

General Manager -Professor : Shuji Tohda Associate Manager -Junior Associate Professor : Tadashi Kanouchi Assistant Professor : Ayako Nogami Assistant Professor : Sayuri Nitta Assistant Professor : Mie Ochida 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.
- 9) Typing of SARS-CoV-2 variants by PCR.

(3) Education

We lecture on clinical laboratory medicine and give technical training on clinical laboratory tests and physiolosical 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 14 junior residents of university hospital in 2021.

(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

- Takahiro Mitsumura, Tsukasa Okamoto, Mizuho Tosaka, Takashi Yamana, Sho Shimada, Yuki Iijima, Rie Sakakibara, Sho Shibata, Takayuki Honda, Tsuyoshi Shirai, Masahiro Ishizuka, Junichi Aiboshi, Haruhiko Furusawa, Tomoya Tateishi, Meiyo Tamaoka, Hidenobu Shigemitsu, Hirokuni Arai, Yasuhiro Otomo, Shuji Tohda, Tatsuhiko Anzai, Kunihiko Takahashi, Shinsuke Yasuda, Yasunari Miyazaki. Association of SARS-CoV-2 RNA Copy Number with the COVID-19 Mortality Rate and Its Effect on the Predictive Performance of Mortality in Severe Cases. Jpn J Infect Dis. 2022.09; 75(5); 504-510
- 2. Yusuke Ota, Chihiro Tani Sassa, Masayo Kashiwagi, Chikako Okawara, Shuji Tohda, Ryoichi Saito. Complete Genome Sequence of an Enterobacter roggenkampii Strain with Reduced Carbapenem Susceptibility Isolated from a Home-Visit Nursing Agency. Microbiol Resour Announc. 2022.08; e0035322
- 3. Yuasa S, Nakajima J, Takatsuki Y, Takahashi Y, Tani-Sassa C, Iwasaki Y, Nagano K, Sonobe K, Yoshimoto T, Nukui Y, Takeuchi H, Tanimoto K, Tanaka Y, Kimura A, Ichimura N, Tohda S.. Viral load of SARS-CoV-2 Omicron is not high despite its high infectivity Journal of Medical Virology. 2022.07; 94(11); 5543-5546
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- 7. Ryoichi Saito, Jun Nakajima, Isaac Prah, Masatomo Morita, Samiratu Mahazu, Yusuke Ota, Ayuka Kobayashi, Shuji Tohda, Hajime Kamiya, Hideyuki Takahashi, Makoto Ohnishi. Penicillin- and Ciprofloxacin-Resistant Invasive Neisseria meningitidis Isolates from Japan. Microbiol Spectr. 2022.04; e0062722
- 8. Saito T, Itoh M, Tohda S. TYRO3 knockdown suppresses the growth of myeloid leukaemia cells. Anticancer Research. 2022.04; 42(4); 1757-1761

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- Kameda Takahiro, Horiuchi Yuna, Shimano Shitsuko, Yano Kouji, Lai Shao-Jui, Ichimura Naoya, Tohda Shuji, Kurihara Yuriko, Tozuka Minoru, Ohkawa Ryunosuke. Effect of myeloperoxidase oxidation and N-homocysteinylation of high-density lipoprotein on endothelial repair function BIOLOGICAL CHEMISTRY. 2022.02; 403(3); 265-277
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- 1. Kimura M, Nishiyama Y, Ueda H, Kitajo A, Arimatsu T, Kuboki M, Takahata A, Saito M, Sakashita C, Okada K, Umezawa Y, Nagao T, Yamamoto M, Tohda S, Tanabe M, Mori T, Nogami A. Perioperative management of laparoscopic cholecystectomy in a patient with paroxysmal nocturnal haemoglobinuria undergoing ravulizumab treatment 2022; 63(4); 260-264

- Yamazaki A., Fujii Y., Kameda T., Ichimura N., Tohda S., and Ohkawa R.. Investigation of Assays for Cholesterol Content of Erythrocytes Membrane. American Association for Clinical Chemistry (AACC) 2022 AACC Annual Scientific Meeting & Clinical Lab Expo 2022.07.26 Chicago
- 1. Makiko Saito, Satoshi Koi, Kana Bando, Hiroki Fujiwara, Yuki Osada, Kota Yoshifuji, Keisuke Tanaka, Keigo Okada, Ayako Nogami, Yoshihiro Umezawa, Toshikage Nagao, Chizuko Sakashita, Masahide Yamamoto, Shuji Tohda, Takehiko Mori. Clostridioides difficile infection among patients with hematological disorders. The 84th Annual Meeting of the Japanese Society of Hematology 2022.10.15 Fukuoka International Congress Center

Sports Medicine Center

Director and Professor; Kazuyoshi YAGISHITA Head Physical Therapist; Kenji HIROHATA Assistant Professor; Takashi HOSHINO, Toshiyuki OHHARA (~ 2022.3) Specially Appointed Assistant Professor; Masaki AMEMIYA (2022.4~) Physical Therapist; Takehiro OHMI, Shunsuke OHJI, Sho MITOMO (~ 2022.9) Adjunct Lecturer; Tomohiko TATEISHI Staff Assistant; Kiyomi ITOH

Etsuko MATSUMURA (~ 2022.3)

(1) **Publications**

- 1. Ryuichi Nakamura, Masaki Amemiya, Fumiyoshi Kawashima, Akira Okano. Ankle-Angle-Adjusting Fibular Osteotomy in Closed Wedge High Tibial Osteotomy. Arthroscopy Techniques. 2022.12; 11(12); e2169-e2175
- 2. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Changes in subjective knee function and psychological status from preoperation to 6 months post anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2022.12; 9(1); 114
- 3. Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Nobutake Ozeki, Takashi Hoshino, Masaki Amemiya, Ichiro Sekiya. Simultaneous Correction of Varus Deformity and Posterior Tibial Slope by Modified Hybrid Closed-Wedge High Tibial Osteotomy. Arthrosc Tech. 2022.11; 11(11); e2081-e2089
- 4. Masaki Amemiya, Ryuichi Nakamura, Mitsuo Yoshimura, Tomoharu Takagi. Proximal tibiofibular joint (PTFJ) dislocation due to Ehlers-Danlos syndrome: posterolateral open-wedge high tibial osteotomy combined with medial closed-wedge distal femoral osteotomy can correct the severe valgus deformity with a markedly increased tibial posterior slope. BMJ Case Reports. 2022.11; 15(11);
- Takehiro Ohmi, Takumi Yamada, Sadaya Misaki, Tomohiro Tazawa, Ryota Shimamura, Junpei Kato, Kazutaka Sugimoto. Differences in gait kinetics and kinematics between patients with rotating hinge knee and cruciate-retaining prostheses: a cross-sectional study Journal of Physical Therapy Science. 2022.09; 34; 635-641
- 6. Mitomo S, Aizawa J, Hirohata K, Ohji S, Ohmi T, Ohara T, Koga H, Yagishita K. Association Between Knee Extension Strength at 3 and 6 Months After Anterior Cruciate Ligament Reconstruction. Journal of sport rehabilitation. 2022.08; 1-9
- Murofushi K, Oshikawa T, Kaneoka K, Akuzawa H, Yamaguchi D, Mitomo S, Furuya H, Hirohata K, Yagishita K. Differences in trunk and lower extremity muscle activity during squatting exercise with and without hammer swing. Scientific reports. 2022.08; 12(1); 13387
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- Murofushi Koji, Yamaguchi Daisuke, Katagiri Hiroki, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Oshikawa Tomoki, Kaneoka Koji, Koga Hideyuki. The relationship between movement self-screening scores and pain intensity during daily training The Journal of Medical Investigation. 2022.08; 69(3-4); 204-216
- Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Association between landing biomechanics, knee pain, and kinesiophobia in athletes following anterior cruciate ligament reconstruction: A cross-sectional study PM&R. 2022.07;
- 11. Aizawa J, Hirohata K, Ohji S, Ohmi T, Mitomo S, Koga H, Yagishita K. Cross-sectional study on relationships between physical function and psychological readiness to return to sport after anterior cruciate ligament reconstruction. BMC sports science, medicine & rehabilitation. 2022.06; 14(1); 97
- Tomoko Kawasaki, Shunsuke Ohji, Junya Aizawa, Tomoko Sakai, Kenji Hirohata, Hironobu Kuruma, Hirohisa Koseki, Atsushi Okawa, Tetsuya Jinno. Correlation between the Photographic Cranial Angles and Radiographic Cervical Spine Alignment. Int J Environ Res Public Health. 2022.05; 19(10);
- Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Jae-Sung An, Ichiro Sekiya. Ultrasound-assisted arthroscopic all-inside repair technique for posterior lateral meniscus tear. Arthroscopy Techniques. 2022.04; 11(5); e929-e935
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- 17. Murofushi Koji, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho. Variations in upper limb and trunk muscles activation during isometric exercises with or without exertion of control ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(3); 251-258
- 18. Murofushi Koji, Oshikawa Tomoki, Kaneoka Koji, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Akuzawa Hiroshi, Yagishita Kazuyoshi. The effect of external-focus using a paper balloon on the activity of upper limb and trunk muscles during static and dynamic tasks ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(4); 345-355
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- 21. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Strength normalized to muscle volume rather than body weight is more accurate for assessing knee strength following anterior cruciate ligament reconstruction ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(1); 7-13

Center for Transfusion Medicine and Cell Therapy

Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine/Professor)

Vise Director: Michiko Kajiwara (Center for Transfusion Medicine and Cell Therapy/Junior Associate Professor) Vise Director: Hisako Katano (Center for Stem Cell and Regenerative Medicine/Junior Associate 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: Takahiro Tomoda(Center for Transfusion Medicine and Cell Therapy) Head Medical Technologist: Naoki Ohtomo

Section Chief Medical Technologist: Keiko Aikawa, Yukari Usui

Assisitant Section Chief Medical Technologist: Yukiko Ohishi, Chihiro Itoh

Medical Technologist: Tomoko Kamiyama, Misaki Chiba, Akiko Shiraishi,

Mei Tanaka, Yukiko Kuroki, Sumire Fujiki, Akemi Fukuoka, Nozomi Oda

Technician: Ayako Tsuji, Yuri Kohno

Clerical Assistant: Jun Kusano

(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

 \cdot 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

 \cdot 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 organoid-based therapy for inflammatory bowel disease

(Department of Gastroenterology & Hepatology, Advanced Research Institute)

6) Promote the development of infrastructure for cell culture processing support

(3) Education

 \cdot 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.

 \cdot 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

 \cdot Blood Transfusion services (The result of 2022)

 The number of blood products used Red cell component products 9,125Units (4,658 bags) Platelet concentration 19,185 Units (1,719 bags) Fresh frozen plasma 5,703 Units (2,785 bags) Allogenic cryoprecipitate 432 Units (108 bags)

- 2) Autologous blood collection and transfusion
 Autologous blood collection 244 cases (314 times, 622Units)
 Autologous blood transfusion 216 cases (529 Units)
- 3) The number of clinical tests of transfusion Blood typing 8,813 Anti-red blood cell antibody test 6,202 Crossmatch tests 6,092
- \cdot Cell Therapy services (The result of 2022)
- 1) Hematopoietic stem cell harvest

Autologous peripheral blood stem cell harvest 15cases 19 times

Allogenic peripheral blood stem cell harvest 7 cases 7 times

Allogenic bone marrow harvest 10 cases 10 times

- (Including Japan Marrow Donor Program donors)
- 2) Cryopreservation of hematopoietic stem cells 39 times
- 3) Hematopoietic stem cell transplantation
- (The evaluation and preservation of the stem cells were done in our department) Autologous peripheral blood stem cell transplantation 14 cases 14 times Allogenic peripheral blood stem cell transplantation 9 cases 10 times Allogenic bone marrow transplantation 11 cases 11 times Allogenic umbilical cord blood transplantation 0 case 0 time
- 4) Donor lymphocyte infusion 3 cases 8 times
- 5) CAR-T therapy

Obtained Kymriah facility certification at the end of October 2019

2022 Autologous peripheral blood mononuclear cell collection 14 cases 14 times Tisagen Recleucell administration 11 cases 11 times

The cell products currently prepared in our center include

- #1 Synovium-derived mesenchymal stem cells
- #2 HeartSheet®: 2 cases 2 times

#3 Autologous Protein Solution (APS: concentrated Platelet-Rich Plasma) for the knees: 15 cases 23 times

#4 Autologous Protein Solution (APS: concentrated Platelet-Rich Plasma) for the hips: 3 cases 3 times #5 GPS III Platelet Concentration System (PRP for the extraarticular tissues): 3 cases 3 times #6 Organoid-based therapy for inflammatory bowel disease 2 cases 2 times

(5) Clinical Performances

\cdot 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 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

- 1. Yusuke Nakagawa, Hideyuki Koga, Tomomasa Nakamura, Masafumi Horie, Hiroki Katagiri, Nobutake Ozeki, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta, Toshifumi Watanabe. Mid-term clinical outcomes of a posterior stabilized total knee prosthesis for Japanese patients: A minimum follow-up of 5 years. J Orthop Sci. 2022.12;
- Mitsuru Mizuno, Kouichirou Yori, Toshikazu Takeuchi, Tetsuya Yamaguchi, Ken Watanabe, Yasuhiro Tomaru, Norio Shimizu, Ichiro Sekiya. Cross-contamination risk and decontamination during changeover after cell-product processing. Regenerative Therapy. 2022.12; 22; 30-38
- 3. Shunichi Fujii, Kentaro Endo, Nobutake Ozeki, Yuriko Sakamaki, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Comparison of adhesion of thawed and cultured synovial mesenchymal stem cells to the porcine meniscus and the relevance of cell surface microspike. BMC Molecular and Cell Biology. 2022.12; 23(1); 53
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- 5. Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Nobutake Ozeki, Takashi Hoshino, Masaki Amemiya, Ichiro Sekiya. Simultaneous Correction of Varus Deformity and Posterior Tibial Slope by Modified Hybrid Closed-Wedge High Tibial Osteotomy. Arthrosc Tech. 2022.11; 11(11); e2081-e2089
- 6. Shunichi Fujii, Kentaro Endo, Seiya Matsuta, Keiichiro Komori, Ichiro Sekiya. Comparison of the yields and properties of dedifferentiated fat cells and mesenchymal stem cells derived from infrapatellar fat pads. Regenerative Therapy. 2022.11; 21; 611-619
- Takahiro Tanimoto, Kentaro Endo, Yuriko Sakamaki, Nobutake Ozeki, Hisako Katano, Mitsuru Mizuno, Hideyuki Koga, Ichiro Sekiya. Human synovial mesenchymal stem cells show time-dependent morphological changes and increased adhesion to degenerated porcine cartilage. Scientific Reports. 2022.10; 12(1); 16619
- Ichiro Sekiya, Nobutake Ozeki. The 16th International Workshop on Osteoarthritis Imaging: "New insightson treatment and imaging: A :couple that belongs together" Osteoarthritis Imaging. 2022.10; Volume 2(Supplement 1);
- 9. Masaaki Isono, Jun Takeuchi, Ami Maehara, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga, Yoshinori Asou, Kunikazu Tsuji. Effect of CD44 signal axis in the gain of mesenchymal stem cell surface antigens from synovial fibroblasts in vitro Heliyon. 2022.10; 8(10); e10739

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- 11. Hiroki Katagiri, Mikio Shioda, Yusuke Nakagawa, Toshiyuki Ohara, Nobutake Ozeki, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga. Risk Factors Affecting Return to Sports and Patient-Reported Outcomes After Opening-Wedge High Tibial Osteotomy in Active Patients. Orthop J Sports Med. 2022.09; 10(9); 23259671221118836
- 12. Tsukasa Kitahashi, Ryo Kogawa, Kentaro Nakamura, Ichiro Sekiya. Integrin β 1, PDGFR β , and type II collagen are essential for meniscus regeneration by synovial mesenchymal stem cells in rats. Scientific Reports. 2022.08; 12(1); 14148
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- 14. Yugo Miura, Kentaro Endo, Keiichiro Komori, Ichiro Sekiya. Clearance of senescent cells with ABT-263 improves biological functions of synovial mesenchymal stem cells from osteoarthritis patients. Stem Cell Research & Therapy. 2022.06; 3(1); 222
- 15. Mituru Mizuno, Takahisa Matsuzaki, Nobutake Ozeki, Hisako Katano, Hideyuki Koga, Takanori Takebe, Hiroshi Yoshikawa, Ichiro Sekiya. Cell membrane fluidity and ROS resistance define DMSO tolerance of cryopreserved synovial MSCs and HUVECs. Stem Cell Research & Therapy. 2022.05; 13(1); 177
- 16. Hirotaka Nakashima, Soshi Uchida, Akihisa Hatakeyama, Yoichi Murata, Yoshiaki Yamanaka, Manabu Tsukamoto, Ichiro Sekiya, Akinori Sakai. Isolation and Characterization of Synovial Mesenchymal Stem Cells Derived From Patients With Chronic Lateral Ankle Instability: A Comparative Analysis of Synovial Fluid, Adipose Synovium, and Fibrous Synovium of the Ankle Joint. Orthop J Sports Med. 2022.05; 10(5);
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- Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Toshiyuki Ohara, Jae-Sung An, Ichiro Sekiya. Ultrasound-assisted arthroscopic all-inside repair technique for posterior lateral meniscus tear. Arthroscopy Techniques. 2022.04; 11(5); e929-e935
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- 23. Hisako Katano, Nobutake Ozeki, Hideyuki Koga, Makoto Tomita, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya. Three-dimensional MRI shows cartilage defect extension with no separation from the meniscus in women in their 70s with knee osteoarthritis. Sci Rep.(Scientific Reports). 2022.03; 12(1); 4198

- 24. Hisako Katano, Nobutake Ozeki, Hideyuki Koga, Kenji Suzuki, Jun Masumoto, Makoto Tomita, Ichiro Sekiya. Interscan measurement error in measurements of the meniscus, including the meniscal roots, by fully automatic three-dimensional MRI analysis. Osteoarthritis Imaging. 2022.03; 2(1);
- 25. Seiji Noda, Tadashi Hosoya, Yoji Komiya, Yasuhiro Tagawa, Kentaro Endo, Keiichiro Komori, Hideyuki Koga, Yasuhiro Takahara, Kazutaka Sugimoto, Ichiro Sekiya, Tetsuya Saito, Fumitaka Mizoguchi, Shinsuke Yasuda. synovial fibroblast subset in arthritic joints has high osteoblastic and chondrogenic potentials in vitro. Arthritis Res Ther. 2022.02; 24(1); 45
- 26. Takashi Hoshino, Yusuke Nakagawa, Kei Inomata, Toshiyuki Ohara, Hiroki Katagiri, Koji Otabe, Kanehiro Hiyama, Kenta Katagiri, Mai Katakura, Hiroko Ueki, Masaya Hayashi, Tsuyoshi Nagase, Ichiro Sekiya, Takashi Ogiuchi, Takeshi Muneta, Hideyuki Koga, . Effects of different surgical procedures for meniscus injury on two-year clinical and radiological outcomes after anterior cruciate ligament reconstructions. -TMDU MAKS study. J Orthop Sci. 2022.01; 27(1); 199-206

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1. Mituru Mizuno, Nobutake Ozeki, Ichiro Sekiya. Safety of using cultured cells with trisomy 7 in cell therapy for treating osteoarthritis. Regenerative Therapy. 2022.06; 17(21); 81-86

[Conference Activities & Talks]

- 1. Ichiro Sekiya. Fully automatic 3D MRI analysis showed that synovial MSC injections suppressed cartilage loss in patients with progres-sive OA. The 13th Meeting of Asian Cell Therapy Orgnization (ACTO) 2022.09.23 WEB, Taiwan
- 2. Ichiro Sekiya. Is meniscal injury a cause or a consequence in osteoarthritis?. 16th International Workshop on Osteoarthritis Imaging 2022.07.08 Tokyo Japan
- 3. Hisako Katano. Morphological analysis of 3D MRI images of PF joints in asymptomatic subjects. 16th International Workshop on Osteoarthritis Imaging 2022.07.08 Tokyo
- 4. Ichiro Sekiya. Medial tibial osteophyte width strongly reflects medial meniscus extrusion distance and medial joint space width moderately reflects cartilage thickness in knee radiographs. MUSCULOSKELETAL WORKSHOP SERIES 2022.02.06 WEB
- 5. Nobutake Ozeki, Hideyuki Koga, Tomomasa Nakamura, Yusuke Nakagawa, Hiroki Katagiri, Hisako Katano, Makoto Tomita, Jun Masumoto, Ichiro Sekiya. Relationship Between Cartilage Thickness By 3D MRI Analysis And ICRS Arthroscopic Grade In The Knee Joint. Orthopaedic Research Society 2022 Annual Meeting 2022.02.05 Tampa,USA

[Patents]

1. CELL REGION DETERMINATION METHOD, CELL IMAGING SYSTEM, AND CELL IMAGE PROCESSING APPARATUS, Patent Number : CN ZL201611227796.X

Clinical Center for Sports Medicine and Sports Dentistry

Clinical Center of Sports Medicine Director and Professor ; Kazuyoshi YAGISHITA Assistant Professor; Takashi HOSHINO Chief Physiotherapist; Kenji HIROHATA Physiotherapist; Takehiro OHMI,Shunsuke OHJI,Sho MITOMO(~ 2022.9) Staff Assistant; Rento HAYASHI,Kiyomi ITOH

Sports Medicine/Dentistry Junior Associate Professor; Hiroshi CHUREI Assistant Professor ; Kairi HAYASHI Dental Resident ;Kaito TOGAWA

(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

 \bigcirc Clinical Center of Sports Medicine

- 1) Sports Physiotherapy Department 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
- \bigcirc 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 2022 to December 2022)
 Section of out-patient clinic: 3,242
 Section of physiotherapy: 4,018

○ 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 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.

(4) Publications

- 1. Ohji S, Aizawa J, Hirohata K, Ohmi T, Mitomo S, Koga H, Yagishita K. Changes in subjective knee function and psychological status from preoperation to 6 months post anterior cruciate ligament reconstruction. Journal of experimental orthopaedics. 2022.12; 9(1); 114
- 2. Derman W, Runciman P, Eken M, Boer PH, Blauwet C, Bogdos M, Idrisova G, Jordaan E, Kissick J, LeVan P, Lexell J, Mohammadi F, Patricio M, Schwellnus M, Webborn N, Willick SE, Yagishita K. Incidence and burden of illness at the Tokyo 2020 Paralympic Games held during the COVID-19 pandemic: a prospective cohort study of 66 045 athlete days. British journal of sports medicine. 2022.12; 57(1); 55-62
- 3. Derman W, Runciman P, Eken M, Boer PH, Blauwet C, Bogdos M, Idrisova G, Jordaan E, Kissick J, LeVan P, Lexell J, Mohammadi F, Patricio M, Schwellnus M, Webborn N, Willick SE, Yagishita K. Incidence and burden of injury at the Tokyo 2020 Paralympic Games held during the COVID-19 pandemic: a prospective cohort study of 66 045 athlete days. British journal of sports medicine. 2022.12; 57(1); 63-70
- 4. Kairi Hayashi, Yasuo Takeuchi, Shintaro Shimizu, Gen Tanabe, Hiroshi Churei, Hiroaki Kobayashi, Toshiaki Ueno. Continuous Oral Administration of Sonicated P. gingivalis Delays Rat Skeletal Muscle Healing Post-Treadmill Training. International Journal of Environmental Research and Public Health. 2022.10; 19(20);
- 5. Takehiro Ohmi, Takumi Yamada, Sadaya Misaki, Tomohiro Tazawa, Ryota Shimamura, Junpei Kato, Kazutaka Sugimoto. Differences in gait kinetics and kinematics between patients with rotating hinge knee and cruciate-retaining prostheses: a cross-sectional study Journal of Physical Therapy Science. 2022.09; 34; 635-641
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- 8. Hirohata K, Aizawa J, Ohmi T, Ohji S, Mitomo S, Ohara T, Koga H, Yagishita K, Jinno T, Okawa A. Reactive strength index during single-limb vertical continuous jumps after anterior cruciate ligament reconstruction: cross-sectional study. BMC sports science, medicine & rehabilitation. 2022.08; 14(1); 150
- Adachi T, Katagiri H, An JS, Engebretsen L, Tateishi U, Saida Y, Koga H, Yagishita K, Onishi K, Forster BB. Imaging-detected bone stress injuries at the Tokyo 2020 summer Olympics: epidemiology, injury onset, and competition withdrawal rate. BMC musculoskeletal disorders. 2022.08; 23(1); 763
- Murofushi Koji, Yamaguchi Daisuke, Katagiri Hiroki, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Oshikawa Tomoki, Kaneoka Koji, Koga Hideyuki. The relationship between movement self-screening scores and pain intensity during daily training The Journal of Medical Investigation. 2022.08; 69(3-4); 204-216
- Miyamoto Reina, Hirai Takashi, Yoshii Toshitaka, Onuma Hiroaki, Inose Hiroyuki, Yuasa Masato, Matsukura Yu, Morishita Shingo, Yamamoto Kouhei, Koyanagi Hirotaka, Sato Shingo, Yagishita Kazuyoshi, Okawa Atsushi. Surgical Strategy for Osteoid Osteoma Localized in Anterior Lumbar Vertebral Body: A Case Report(和訳中) Spine Surgery and Related Research. 2022.07; 6(4); 408-411
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- Aizawa J, Hirohata K, Ohji S, Ohmi T, Mitomo S, Koga H, Yagishita K. Cross-sectional study on relationships between physical function and psychological readiness to return to sport after anterior cruciate ligament reconstruction. BMC sports science, medicine & rehabilitation. 2022.06; 14(1); 97
- Tomoko Kawasaki, Shunsuke Ohji, Junya Aizawa, Tomoko Sakai, Kenji Hirohata, Hironobu Kuruma, Hirohisa Koseki, Atsushi Okawa, Tetsuya Jinno. Correlation between the Photographic Cranial Angles and Radiographic Cervical Spine Alignment. Int J Environ Res Public Health. 2022.05; 19(10);
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- 22. Murofushi Koji, Oshikawa Tomoki, Kaneoka Koji, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Akuzawa Hiroshi, Yagishita Kazuyoshi. The effect of external-focus using a paper balloon on the activity of upper limb and trunk muscles during static and dynamic tasks ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(4); 345-355

- 23. Murofushi K, Yamaguchi D, Katagiri H, Hirohata K, Furuya H, Mitomo S, Oshikawa T, Kaneoka K, Koga H. The relationship between movement self-screening scores and pain intensity during daily training. The journal of medical investigation : JMI. 2022; 69(3.4); 204-216
- 24. Murofushi K, Yamaguchi D, Katagiri H, Hirohata K, Furuya H, Mitomo S, Oshikawa T, Kaneoka K, Koga H, Yagishita K. Validity of the KOJI AWARENESS self-screening test for body movement and comparison with functional movement screening. PloS one. 2022; 17(12); e0277167
- 25. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. Strength normalized to muscle volume rather than body weight is more accurate for assessing knee strength following anterior cruciate ligament reconstruction ISOKINETICS AND EXERCISE SCIENCE. 2022; 30(1); 7-13

[Misc]

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- 4. Hattori M, Tanabe G, Sumita YI, Obata S, Churei H, Ueno T. Does playing music influence the rehabilitation of a maxillofacial defect patient?. 40th Annual PAMA International Symposium 2022.06.25 Chicago (USA)+Web
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Center for Experimental Animals

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- 2. Uchida A, Imaimatsu K, Suzuki H, Han X, Ushioda H, Uemura M, Imura-Kishi K, Hiramatsu R, Takase HM, Hirate Y, Ogura A, Kanai-Azuma M, Kudo A, Kanai Y. SOX17-positive rete testis epithelium is required for Sertoli valve formation and normal spermiogenesis in the male mouse. Nature communications. 2022.12; 13(1); 7860
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- 2. Gerel Melig, Ikuo Nobuhisa, Kiyoka Saito, Ryota Tsukahara, Ayumi Itabashi, Yoshiakira Kanai, Masami Kanai, Tetsuya Taga. Investigating the function of Rasip1 in HSC-containing IAHCs of midgestation mouse embryos. 19th Stem Cell Symposium 2022.05.27 Awaji Yumebutai International Conference Center
- 1. Effects of granulosa cell removal on ovarian function in mice. 2022.09.11

Life Science and Bioethics Research Center

Masayuki Yoshida Yusuke Ebana Hiroko Kohbata Mizuko Osaka

(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.

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