

ANNUAL PUBLICATIONS

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

CONTENTS

Graduate School of Medical and Dental Sciences

Medical and Dental Sciences

Oral Health Sciences

Oral Pathology	1
Bacterial Pathogenesis, Infection and Host Response	4
Molecular Immunology	6
Advanced Biomaterials	8
Dental Radiology and Radiation Oncology	10
Dental Anesthesiology and Orafacial Pain Management	13
Pediatric Dentistry / Special Needs Dentistry	17
Orthodontic Science	20
Cariology and Operative Dentistry	24
Masticatory Function and Health Science	30
Pulp Biology and Endodontics	35
Advanced Prosthodontics	41
Regenerative and Reconstructive Dental Medicine	51

Maxillofacial and Neck Reconstruction

Plastic and Reconstructive Surgery	54
Head and Neck Surgery	56
Radiation Therapeutics and Oncology	59
Cognitive Neurobiology	61
Molecular Craniofacial Embryology	
→Refer to Molecular Craniofacial Embryology and Oral History (page64)	
Molecular Craniofacial Embryology and Oral History	64
Cellular Physiological Chemistry	67
Maxillofacial Surgery	69
Maxillofacial Orthognathics	72
Reconstructive Plastic Surgery	77

Bio-Matrix

Cell Biology	80
Medical Biochemistry	82
Joint Surgery and Sports Medicine	83
Biochemistry	89
Cell Signaling	93
Periodontology	95
Biosignals and Inheritance	102
Inorganic Biomaterials	103

Public Health

Global Health Promotion	106
Parasitology and Tropical Medicine	111
Forensic Medicine	115
Health Policy and Informatics	117
Life Sciences and Bioethics	126
Forensic Dentistry	128
Dental Education Development	133
Oral Health Promotion	135
Educational Media Development	142
Global Health Entrepreneurship	144

Gerontology and Gerodontology

Gerodontology and Oral Rehabilitation	148
Dysphagia Rehabilitation	153

Comprehensive Patient Care

Laboratory Medicine	161
Intensive Care Medicine	164
Pharmacokinetics and Pharmacodynamics	167
Medical Education Research and Development	168
Acute Critical Care and Disaster Medicine	171
General Dentistry	175
Psychosomatic Dentistry	179
General Medicine	182
Infections Diseases	186

Cognitive and Behavioral Medicine

Neuroanatomy and Cellular Neurobiology	189
Neuropathology	191
Ophthalmology and Visual Science	195
Otorhinolaryngology	202
Neurology and Neurological Science	205
Psychiatry and Behavioral Sciences	211
NCNP Brain Physiology and Pathology	218

Bio-Environmental Response

Biodefense Research	224
Pediatrics and Developmental Biology	227
Dermatology	244
NCCHD Child Health and Development	247
High-risk Infectious Disease Control	254

Systemic Organ Regulation

Human Pathology	255
Physiology and Cell Biology	263
Stem Cell Regulation	267
Respiratory Medicine	269
Gastroenterology and Hepatology	275
Specialized Surgeries	284
Cardiovascular Medicine	286
Cardiovascular Surgery	313
Nephrology	317
Comprehensive Reproductive Medicine	324
Gastrointestinal Surgery	328
Thoracic Surgery	333
Igakuken Disease-oriented Molecular Biology	336

Advanced Therapeutic Sciences

Clinical Anatomy	341
Systems BioMedicine	347
Comprehensive Pathology	350
Molecular Oncology	353
Surgical Pathology	357
Experimental Animal Model for Human Disease →Refor to Center for Experimental Animals (page548)	
Signal Gene Regulation	360
Hematology	362
Molecular Endocrinology and Metabolism	367
Hepatobiliary and Pancreatic Surgery	370
Orthopaedic and Spinal Surgery	378
Diagnostic Radiology and Nuclear Medicine	392
Genomic Function and Diversity	399
Human Genetics and Disease Diversity	401
Applied Regenerative Medicine	403
JFCR Cancer Biology	407

Organogenesis and Neogenesis	416
Biostatistics	420
AI Systems Medicine	424
Life Science and Technology	
Biomedical Engineering	
Biomedical Devices and Instrumentation	426
Biomedical Information	430
Biodesign	432
Material-Based Medical Engineering	433
Chemical Bioscience	437
Medicinal Chemistry	439
Biomechanics	443
Integrative Molecular Biomedicine	
Molecular Cell Biology	445
Advanced Nanomedical Engineering	447
Structural Biology	449
Biomolecular Pathogenesis	451
Functional Genome Informatics	454
Medical Chemistry	455
RIKEN Molecular and Chemical Somatology	456
NCC Cancer Science	459
Cellular and Molecular Medicine	464
Interdisciplinary Sciences	466
Data Science Algorithm Design and Analysis	468
Biomedical Laboratory Sciences	
Pathology and Anatomical Sciences	470
Hematology and Biophysical Systems Analysis	473
Clinical Information and Applied Sciences	477
Clinical and Diagnostic Laboratory Science	481
Clinical Bioanalysis and Molecular Biology	486
Molecular Microbiology and Immunology	491
Division of Oral Health Sciences	
Lifetime Oral Health Care Sciences	495
Oral Care for Systemic Health Support	498
Preventive Oral Health Care Sciences	500
Oral Health Science for Community Welfare	501
Oral Health Care Education	504
Basic Oral Health Engineering	506
Digital Dentistry	509
Oral Biomedical Engineering	514
Endowed Departments	
Cardiovascular Nutrition and Metabolism	517
Lifetime Clinical Immunology	519
Child Health and Development	524
Pulmonary Immunotherapeutics	529
Joint Research Departments	
Advanced Technology in Medicine	
→Refer to Orthopaedic and Spinal Surgery (page378)	
Functional Joint Anatomy	
→Refer to Orthopaedic and Spinal Surgery (page378)	
Nano-Bioscience	
→Refer to Orthopaedic and Spinal Surgery (page378)	

Central Clinical Facilities

(Division of Clinical Meicine)	
Hyperbaric Medical Center	531
(Division of Clinical Dentistry)	
Sports Dentistry	534
(Division of Integrated Facilities)	
Clinical Laboratory	536
Sports Medicine Center	538
Center for Transfusion Medicine and Cell Therapy	540

Sports Science Organization

Clinical Center for Sports Medicine and Sports Dentistry	545

Institute of Research

Center for Experimental Animals	548

Oral Pathology

Professor
Tohru Ikeda

Junior Associate Professor
Kou Kayamori

Assistant Professor
Fukawa Yuki

Graduate Students
HERDIANTOPUTRI RANNY RAHANINGRUM

(1) Research

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

(2) Education

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

(3) Clinical Services & Other Works

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

(4) Publications

[Original Articles]

1. Naoya Kinoshita, Hideaki Hirai, Yuki Fukawa, Yuko Yamagata, Yoshihisa Kashima, Masaru Sato, Tohru Ikeda, Hiroyuki Harada.. A case of dentinogenic ghost cell tumor of the mandible with a review of the literature Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2023.11; 35(6); 545-549

2. Kinoshita N, Tomioka H, Oikawa Y, Fukawa Y, Ikeda T, Harada H.. A case of sclerosing odontogenic carcinoma of the mandible with a review of the literature JOURNAL OF ORAL SCIENCE. 2023.10; 65(4); 281-283
3. Takuma Kugimoto, Naoto Nishii, Yu Oikawa, Takeshi Kuroshima, Hideaki Hirai, Hirofumi Tomioka, Yasuyuki Michi, Kou Kayamori, Junichiro Sakamoto, Joe Iwanaga, R Shane Tubbs, Tohru Ikeda, Masahiko Miura, Hiroyuki Harada. Invasion of the bucco-mandibular space by oral squamous cell carcinoma: histopathological analysis of invasion pattern. Front Oncol. 2023.10; 13; 1168376
4. Kou Kayamori, Ken-Ichi Katsube, Hideaki Hirai, Hiroyuki Harada, Tohru Ikeda.. Role of Stromal Fibroblast-Induced WNT7A Associated with Cancer Cell Migration Through the AKT/CLDN1 Signaling Axis in Oral Squamous Cell Carcinoma. Laboratory investigation; a journal of technical methods and pathology. 2023.08; 103(10); 100228
5. Shiori Watabe, Yukari Aruga, Ryoko Kato, Genji Kawade, Yuki Kubo, Anna Tatsuzawa, Ichiroh Onishi, Yuko Kinowaki, Sachiko Ishibashi, Masumi Ikeda, Yuki Fukawa, Keiichi Akahoshi, Minoru Tanabe, Morito Kurata, Kenichi Ohashi, Masanobu Kitagawa, Kouhei Yamamoto. Regulation of 4-HNE via SMARCA4 Is Associated with Worse Clinical Outcomes in Hepatocellular Carcinoma. Biomedicines. 2023.08; 11(8);
6. Akaike Yu, Morita Kei-ichi, Sakamoto Kei, Tsushima Fumihiko, Kayamori Kou, Maruta Noboru, Yamazaki Kotaro, Anzai Eri, Tonouchi Erina, Harada Hiroyuki, Ikeda Tohru, Yoda Tetsuya. Automatic detection of spongiosis associated with oral lichenoid lesions using machine learning Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2023.07; 35(4); 368-374
7. Cangyou Xie, Fatma Rashed, Yosuke Sasaki, Masud Khan, Jia Qi, Yuri Kubo, Yoshiro Matsumoto, Shinichi Sawada, Yoshihiro Sasaki, Takashi Ono, Tohru Ikeda, Kazunari Akiyoshi and Kazuhiro Aoki. Comparison of Osteoconductive Ability of Two Types of Cholesterol-Bearing Pullulan (CHP) Nanogel-Hydrogels Impregnated with BMP-2 and RANKL-Binding Peptide: Bone Histomorphometric Study in a Murine Calvarial Defect Model 2023.06; 24(11);
8. Pissacha Daroonpan, Ryo Ouchi, Chenyang Zhang, Shigenori Nagai, Naoto Nishii, Yoshihisa Kashima, Fumihiko Tsushima, Hiroyuki Harada, Miwako Hamagaki, Tohru Ikeda, Jun Aida, Ruchadaporn Kaomongkolgit, Miyuki Azuma. Personal immune profiles: Diversity and prognostic value for oral tongue squamous cell carcinoma evaluated by comprehensive immune parameter analyses with multiplex immunofluorescence. Oral Oncol. 2023.06; 143; 106458
9. Herdiantoputri R.R., Komura D., Ikeda T., Ishikawa S. . Head and Neck Tumor Histopathological Image Representation with Pre- Trained Convolutional Neural Network and Vision Transformer Journal of Dentistry Indonesia. 2023.05; 30(1); 41-47
10. Hideaki Hirai, Naoto Nishii, Yu Oikawa, Toshimitsu Ohsako, Takuma Kugimoto, Takeshi Kuroshima, Hirofumi Tomioka, Yasuyuki Michi, Kou Kayamori, Tohru Ikeda, Hiroyuki Harada. Buccinator muscle invasion is a risk factor for cervical lymph node metastasis in squamous cell carcinoma of the buccal mucosa: A retrospective study. Oncol Lett. 2023.04; 25(6); 226
11. Herdiantoputri RR, Komura D, Fujisaka K, Ikeda T, Ishikawa S. Deep texture representation analysis for histopathological images. STAR protocols. 2023.03; 4(2); 102161
12. Natnicha Wamasing, Supasith Yomtako, Hiroshi Watanabe, Junichiro Sakamoto, Kou Kayamori, Tohru Kurabayashi. The magnetic resonance imaging characteristics of radicular cysts and granulomas Dentomaxillofac Radiol. 2023.02; 52(3); 20220336
13. Hata C, Fukawa Y, Motoi T, Kinowaki Y, Akashi T, Ohashi K, Ishikawa Y, Waseda Y, Fujii Y, Kakuta R, Ikeda S, Onishi I. A Primary Kidney Giant Cell Tumor of Soft Tissue Caused Peritoneal Dissemination, Considered to Be Malignant Transformation: A Case Report. Diagnostics (Basel, Switzerland). 2023.02; 13(4);
14. Komura D, Onoyama T, Shinbo K, Odaka H, Hayakawa M, Ochi M, Herdiantoputri RR, Endo H, Katoh H, Ikeda T, Ushiku T, Ishikawa S. Restaining-based annotation for cancer histology segmentation to overcome annotation-related limitations among pathologists. Patterns (New York, N.Y.). 2023.02; 4(2); 100688

15. Tanaka H., Fukawa Y., Yamamoto K., Tanimoto K., Takemoto A., Hasumi H., Hirakawa A., Ishikawa Y., Fukuda S., Waseda Y., Yoshida S., Yokoyama M., Campbell S. C., Fujii Y.. Renal parenchymal infiltration or micronodular spread in non-metastatic clear cell renal cell carcinoma: Prognostic impact and genomic backgrounds EUROPEAN UROLOGY. 2023.02; 83; S668-S669
16. Hirai Hideaki, Kayamori Kou, Noji Rika, Kuroshima Takeshi, Ikeda Tohru, Harada Hiroyuki. A rare case of solitary intraoral superficial angiomyxoma arising in the soft palate Journal of Oral Science. 2023.01; 65(1); 69-71
17. 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. 2023.01; 24(1);
18. M Shibata, H Yoshitake, K Kayamori, T Ikeda, M Seki, T Yoda. Challenges in Diagnosis and Management of Palatal Hemangioma in an Infant: A Case Report Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2023.01; 36; 67-70

[Conference Activities & Talks]

1. ヘルジアントプテリ ランニー、河村 大輔、池田 通、石川 俊平. 深層学習を用いた口腔組織病理診断支援のための大規模な画像検索システム. 第 34 回日本臨床口腔病理学会 2023.08.25
2. 布川 裕規、田中 一、明石 巧、池田 通、大橋 健一、山本 浩平. 淡明細胞型腎細胞癌における腫瘍-腎実質境界部の浸潤様式における臨床病理学的検討. 第 112 回日本病理学会総会 2023.04.15 下関市
3. ヘルジアントプテリ ランニー、河村 大輔、池田 通、石川 俊平. Luigi-Oral: 口腔腫瘍のための類似組織画像検索システム. 第 112 回日本病理学会総会 2023.04.14 下関
4. Tohru Ikeda. The mechanism of bone resorption induced by infiltration of oral squamous cell carcinoma. KPPIKG 2023 2023.02.03 Jakarta
5. Tohru Ikeda. Oral pathology interpretation on odontogenic tumor, OPMD and OSCC cases. KPPIKG 2023 2023.02.03
6. Herdiantoputri R.R., Komura D., Ikeda T., Ishikawa S.. Head and neck tumour histopathological image representation with pre-trained convolutional neural network and vision transformer. KPPIKG 2023 2023.02.02 Jakarta

Bacterial Pathogenesis

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. Doan YH, Dennis FE, Takemae N, Haga K, Shimizu H, Appiah MG, Lartey BL, Damanka SA, Hayashi T, Suzuki T, Kageyama T, Armah GE, Katayama K. Emergence of Intergenogroup Reassortant G9P[4] Strains Following Rotavirus Vaccine Introduction in Ghana. *Viruses*. 2023.12; 15(12);

2. Suzuki, T; Boonyaleka, K; Okano, T; Iida, T; Yoshida, M; Fukano, H; Hoshino, Y; Iwakura, Y; Ablordey, AS; Ashida, H. Inflammasome-triggered IL-18 controls skin inflammation in the progression of Buruli ulcer PLOS Pathogens. 2023.11; 19(11); e1011747
3. Umeda S, Sujino T, Miyamoto K, Yoshimatsu Y, Harada Y, Nishiyama K, Aoto Y, Adachi K, Hayashi N, Amafuji K, Moritoki N, Shibata S, Sasaki N, Mita M, Tanemoto S, Ono K, Mikami Y, Sasabe J, Takabayashi K, Hosoe N, Suzuki T, Sato T, Atarashi K, Teratani T, Ogata H, Nakamoto N, Shiomi D, Ashida H, Kanai T. D-amino Acids Ameliorate Experimental Colitis and Cholangitis by Inhibiting Growth of Proteobacteria: Potential Therapeutic Role in Inflammatory Bowel Disease. Cellular and molecular gastroenterology and hepatology. 2023.08; 16; 1011-1031
4. Miyamoto K, Sujino T, Harada Y, Ashida H, Yoshimatsu Y, Yonemoto Y, Nemoto Y, Tomura M, Melhem H, Niess JH, Suzuki T, Suzuki T, Suzuki S, Koda Y, Okamoto R, Mikami Y, Teratani T, Tanaka K, Yoshimura A, Sato T, Kanai T. The gut microbiota-induced kynurenic acid recruits GPR35-positive macrophages to promote experimental encephalitis. Cell reports. 2023.08; 42(8); 113005
5. Boonyaleka K, Okano T, Iida T, Leewananthawet A, Sasai M, Yamamoto M, Ashida H, Suzuki T. Fusobacterium nucleatum infection activates the noncanonical inflammasome and exacerbates inflammatory response in DSS-induced colitis. European journal of immunology. 2023.07; e2350455
6. Boonyaleka K, Okano T, Iida T, Leewananthawer A, Sasai M, Yamamoto M, Ashida H, Suzuki T. Fusobacterium nucleatum infection activates the noncanonical inflammasome to exacerbate inflammatory response in acute colitis mice Eur. J. Immunol. 2023.07; e2350455;

[Conference Activities & Talks]

1. Toshihiko Suzuki. Advanced collaborative research in infectious diseases in Ghana. Annual Research Meeting 2023 in Noguchi Memorial Institute for Medical Research 2023.11.24 Accra
1. Chenwei Hsu, Tokuju Okano, Toshihiko Suzuki. Tannerella forsythia induces inflammasome activation by triggering both NLRP3 and caspase-4. The 88th Annual Meeting of the Stomatological Society, Japan 2023.12.02
2. Yoshihiko Hoshino, Mitsunori Yoshida, Hanako Fukano, Toshihiko Suzuki. Mycolactone as only exotoxin possessed by mycobacteria and IL-18 as a host factor . The 34th Annual Meeting of Japanese Society for Host Defence Research 2023.09.29 Kyoto
3. Hiroshi Ashida, Toshihiko Suzuki. Regulation of host cell death by bacterial pathogen. The 34th Annual Meeting of Japanese Society for Host Defence Research 2023.09.29 Kyoto
4. Toshihiko Suzuki. Basic research against infectious diseases in Ghana. The 96th Annual Meeting of Japanese Society for Bacteriology 2023.03.16 Himeji
5. Tokuju Okano, Toshihiko Suzuki. Oral infection of P. gingivalis induces exacerbation of neurological manifestation in mice. The 96th Annual Meeting of Japanese Society for Bacteriology 2023.03.16 Himeji

Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Chenyang Zhang
Specially Appointed Assistant Professor	Eri Ikeda (-Mar.)
Adjunct instructor	Emi Nishii
	Shigeru Okuhara (May.-)
Graduate Students (Doctor)	Pissacha Daroonpan(-Sep.)
	Faruzana Sultana
	Ryo Ouchi (University of Toyama)
	Yi Lu
	Yuya Su (Department of Oral and Maxillofacial Surgical Oncology)(Apr.)
(Master)	Yuto Nagatomo(-Mar.)
	Honoka Aoshima(-Mar.)
Research Student	Jin Lu(-Mar.)

(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. Daroonpan P, Ouchi R, Zhang C, Nagai S, Nishii N, Kashima Y, Tsushima F, Harada H, Hamagaki M, Ikeda T, Aida J, Kaomongkolgit R, Azuma M. Personal immune profiles: Diversity and prognostic value for oral tongue squamous cell carcinoma evaluated by comprehensive immune parameter analyses with multiplex immunofluorescence. *Oral oncology*. 2023.08; 143; 106458
2. Yin Y, Sakakibara R, Honda T, Kirimura S, Daroonpan P, Kobayashi M, Ando K, Ujiie H, Kato T, Kichizo Kaga, Mitsumura T, Nakano R, Sakashita H, Matsuge S, Ishibashi H, Akashi T, Hida Y, Morohoshi T, Azuma M, Okubo K, Miyazaki Y. High density and proximity of CD8⁺ T cells to tumor cells are correlated with better response to nivolumab treatment in metastatic pleural mesothelioma. *Thorac Cancer*. 2023.07; 14; 1991-2000
3. Nishi W, Wakamatsu E, Machiyama H, Matsushima R, Saito K, Yoshida Y, Nishikawa T, Takehara T, Toyota H, Furuhashi M, Nishijima H, Takeuchi A, Azuma M, Suzuki M, Yokosuka T. Evaluation of therapeutic PD-1 antibodies by an advanced single-molecule imaging system detecting human PD-1 microclusters. *Nature communications*. 2023.06; 14; 3157
4. Zhang C, Raveney B, Takahashi F, Yeh T, Hohjoh H, Yamamura T, Oki S. Pathogenic microglia orchestrate neurotoxic properties of Eomes-expressing helper T cells. *CELLS*. 2023.03; 12(6); 868
5. Namangkalakul W, Nagai S, Jin C, Nakahama KI, Yoshimoto Y, Ueha S, Akiyoshi K, Matsushima K, Nakashima T, Takechi M, Iseki S. Augmented effect of fibroblast growth factor 18 in bone morphogenetic protein 2-induced calvarial bone healing by activation of CCL2/CCR2 axis on M2 macrophage polarization. *Journal of tissue engineering*. 2023.01; 14; 20417314231187960

[Books etc]

1. Lippincott Illustrated Reviews: Immunology Third Edition. 2023.03 (ISBN : 978-4-621-30801-1)

Advanced Biomaterials

Professor UO Motohiro
 Junior Associate Professor WADA Takahiro
 Assistant Professor MIYAYASU Anna
 Graduate Student WANG Liwei
 Graduate Student HA Roubing
 Graduate Student TSUKADA Saho
 Graduate Student OKAJIMA Natsuki (–2023/3)
 Graduate Student NOGUCHI Shunsuke (2023/4–)
 Graduate Student Saleh Sherif Adel Abdelfattah (Pulp Biology and Endodontics) (–2023/3)

(1) Outline

Dental materials are required to safety, functionality, and esthetics. In our laboratory, we are developing new dental materials made of glass, ceramics, polymers, and their composites, and applying novel analytical techniques to diagnosis and safety evaluation of dental and biomaterials.

(2) 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.

(3) 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.

(4) Publications

[Original Articles]

1. [Advanced Biomaterials : UO Motohiro] Liwei WANG, Tomoya KONISHI, Miki INADA, Takahiro WADA, Motohiro UO. Preparation and properties of the fine ground strontium-based endodontic cements Dental Materials Journal. 2023.12; 42(6); 818-825

2. [Advanced Biomaterials : UO Motohiro] Takahiro Wada, Upendar Kashaboina, Yuta Nishikawa, Yuki Wakisaka, Deling Bao, Satoru Takakusagi, Yuta Inami, Fumiya Kuriyama, Arnoldus Lambertus Dipu, Hitoshi Ogihara, Shoji Iguchi, Ichiro Yamanaka, Daiki Kido, Masao Kimura, Motohiro Uo, Kiyotaka Asakura. The Effect of Structural Change during the Activation Process on the Catalysis of In/SiO₂ Nonoxidative Coupling of Methane: An Operando XAFS Study The Journal of Physical Chemistry C. 2023.12; 127(50); 24211-24222
3. [Gerodontology and Oral Rehabilitation : KOMAGAMINE Yuriko] Komagamine Y, Kanazawa M, Miyayasu A, Uehara Y, Watanabe M, Sahaprom N, Huyen TBN, Iwaki M, Sato D, Minakuchi S. The effect of single-implant overdentures on cognitive function in older adults: A 3-year follow-up report. Journal of dentistry. 2023.09; 136; 104632
4. [Department of Digital Dentistry : TSUCHIDA Yumi] Chaiamornsap P, Katheng A, Ha R, Tsuchida Y, Kanazawa M, Uo M, Minakuchi S, Suzuki T, Takahashi H. Effects of build orientation and bar addition on accuracy of complete denture base fabricated with digital light projection: An in vitro study. J Prosthodont Res. 2023.04;
5. [Advanced Biomaterials : UO Motohiro] Naoaki Mikami, Ikuo Yonemitsu, Hiroshi Takemura, Mark Kondou, Kouhei Soga, Kazuhiro Suga, Zusei Kanno, WeiJen Lai, Motohiro Uo, Takashi Ono. Mechanical analysis of the improved superelastic Ni-Ti alloy wire using the orthodontic simulator with high-precision sensors Journal of the Mechanical Behavior of Biomedical Materials. 2023.04; 142; 105861
6. [Advanced Biomaterials : WADA Takahiro] Daiki Kido, Takahiro Wada, Kiyotaka Asakura. Automatic Collection and Visualization of the Models Given by Thorough Search Analysis and Its Application to the MoO₃ EXAFS Analysis e-Journal of Surface Science and Nanotechnology. 2023.03; 21(3); 231-235

[Conference Activities & Talks]

1. [Advanced Biomaterials : WADA Takahiro] Shunsuke Noguchi, Takahiro Wada, Shogo Matsushita, Motohiro Uo. Fabrication of a Novel 3D Printed Three-Point Bending Jig with a Water Bath for Shape Memory Polymer Measurement. 3rd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture -DEJI2MA 2023- 2023.10.20 Tokyo, Japan
2. [Advanced Biomaterials : WADA Takahiro] K. Asakura, K.Dong, T. Wada, D. Kido, S. Takakusagi. Bent Crystal Laue Analyser Combined with Polarization-dependence Total Reflection Fluorescence X-ray Absorption Fine Structure (BCLA-TRFXAFS) and its Application to Electrode Surface. INTERNATIONAL UNION OF CRYSTALLOGRAPHY (IUCr 2023) 2023.08.22 Melbourne Convention and Exhibition Centre, Australia
3. [Department of Digital Dentistry : TSUCHIDA Yumi] Nakayama M, Li H, Hayashi M, Tsuchida Y, Kanamori Y, Noritake K, Nitta H, Miyayasu A, Iwaki M, Kanazawa M. Quantitative analysis of visual evaluation in abutment tooth for full metal crown. International Summer Program (ISP) 2023, TMDU. 2023.08.02 Tokyo, Japan
4. [Advanced Biomaterials : WADA Takahiro] Wang Liwei, Tomoya Konishi, Miki Inada, Takahiro Wada, Motohiro Uo. Effect of particle size on the mechanical properties of strontium based endodontic cements. The 81st General Session of the Japanese Society for Dental Materials and Devices 2023.04.15 Tokyo, Japan
1. [Masticatory Function and Health Science : HAYASHI Kairi] Li Chenyuan, Takahiro Wada, Yumi Tsuchida, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Retention force comparison of 3D multiple layer mouthguard and conventional mouthguard via cycle-loading durability fatigue test. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
2. [Advanced Biomaterials : WADA Takahiro] Daiki Kido, Takahiro Wada, Genta Ezawa, Wang Qing, Masao Kimura, Kiyotaka Asakura. Design and fabrication of operando XAFS cell for electrochemical reactions using 3D printer. 2022 Quantum Beam Science Festa 2023.03.13 Ibaraki

Department of Dental Radiology and Radiation Oncology

Professor	Masahiko MIURA
Associate Professor	HiroshiI WATANABE
Lecturer	Naoto OHBAYASHI (~Feb)) Atsushi KAIDA (Apr~)
Assistant Professor	Shin NAKAMURA Atsushi KAIDA (~March) Ami KURIBAYASHI Junichiro SAKAMOTO (~Aug) Akiko IMAIZUMU (Apr~)
SA Assistant Professor	Hitomi NOJIMA
Clinical Fellow	Yoshikazu NOMURA Sakurako KAWASHIMA (~March) Miharu TAGUCHI Kohki TOHYAMA (~Apr))
Graduate Students	Esther NG FENG YING (~March) Kohki TOHYAMA (~March) Wamasing NATNICHA (~Sep) Yomtako SUPASITH Arisa OKI
Graduate Research Student	Carulina MESQUITA Sakiko Kume (Dec~)

(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
- Clinical study on the prediction of prognosis after oral cancer treatment using CT diagnosis
- Clinical study on radiotherapy for oral cancer and development of novel therapeutic modalities
- 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]

1. Wamasing N, Nakamura S, Watanabe H, Kuribayashi A, Miura M. Potential of preoperative fluorodeoxyglucose-positron emission tomography/computed tomography to diagnose contralateral lymph node metastases in patients with oral cancer. *Nucl Med Commun.* 2023.12; 44(12); 1168-1175
2. Takuma Kugimoto, Naoto Nishii, Yu Oikawa, Takeshi Kuroshima, Hideaki Hirai, Hirofumi Tomioka, Yasuyuki Michi, Kou Kayamori, Junichiro Sakamoto, Joe Iwanaga, R Shane Tubbs, Tohru Ikeda, Masahiko Miura, Hiroyuki Harada. Invasion of the bucco-mandibular space by oral squamous cell carcinoma: histopathological analysis of invasion pattern. *Front Oncol.* 2023.10; 13; 1168376
3. Atul Ranjan, Elizabeth A Thoenen, Atsushi Kaida, Stephanie Wood, Terry Van Dyke, Tomoo Iwakuma. Hypomorphic Allele in a Diethylnitrosamine-Induced Liver Carcinogenesis Model. *Cancers (Basel).* 2023.09; 15(18);
4. Nakamura S, Watanabe H, Kurabayashi T, Miura M. Risk factors for posttreatment mastoid cellulitis in patients with oral malignancy *Oral Radiology.* 2023.07; 39(3); 528-535
5. Ito K, Tokura S, Takazawa I, Yoshida N, Nakanishi T, Akiyama K, Onuma Y, Adachi T, Harada H, Nojima H, Miura M, Yoshimura R, Kabasawa Y. Clinical investigation of use of Episil® oral solution in oral mucositis during radiotherapy for head and neck cancer. *Heliyon.* 2023.06; 9(6); e15869
6. Yoshikazu Nomura, Hiroshi Watanabe, Hiroshi Tomisato, Sakurako Kawashima, Masahiko Miura. Gumbel distribution-based technique enables quantitative comparison between streak metal artifacts of multidetector row CT and cone-beam CT: a phantom study. *Phys Eng Sci Med.* 2023.06; 46(2); 801-812
7. Natnicha Wamasing, Supasith Yomtako, Hiroshi Watanabe, Junichiro Sakamoto, Kou Kayamori, Tohru Kurabayashi. The magnetic resonance imaging characteristics of radicular cysts and granulomas *Dentomaxillofac Radiol.* 2023.02; 52(3); 20220336

[Conference Activities & Talks]

1. Katarzyna A. Inoue, Kazuki Takahashi, Maki Saito, Shintaro Sakakitani, Keita Iida, Sadahiro Iwabuchi, Daizo Koinuma, Toru Konishi, Susumu Tanaka, Atsushi Kaida, Masahiko Miura, Shinichi Hashimoto, Mariko Okada, Toshihiro Uchihashi, Kohei Miyazono, Tetsuro Watabe. TGF- β confers cancer cells with the high motility and metastatic potential via induction of Slug/HMGA2-independent EMT. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama

2. Wamasing N, Nakamura S,, Watanabe H, Kuribayashi A, Miura M. PET.CT diagnosing contralateral lymph node metastasis in oral cancer patients. Tokyo Medical and Dental University, International Summer Program 2023.08.02 Tokyo
3. Yomtako S, Watamabe H, Kuribayashi A, Miura M. Differentiation of radicular cysts and granulomas by texture analysis on computed tomography images.. Tokyo Medical and Dental University, International Summer Program 2023.08.02 Tokyo
4. Wamasing N, Nakamura S, Watanabe H, Kuribayashi A, Miura M. Interpretation of fluorodeoxyglucose accumulation on contralateral lymph nodes in position emission tomography /computed tomography images for patients with oral cancer. The 63th General assembly and annual scientific congress of Japanese Society for Oral and Maxillofacial Radiology 2023.05.28 Fukuoka
1. Oki A, Nakamura S, Sakamoto J, Taguchi M, Kuribayashi A, Watanabe H, Miura M. Relationship between MRI texture features and neck metastasis in patients with squamous cell carcinoma of the tongue.. The 4th Autumn Conference of Japanese Society for Oral and Maxillofacial Radiology 2023.11.04

Department of Dental Anesthesiology and Orofacial Pain Management

Professor
Shigeru MAEDA

Associate Professor
Ryo WAKITA,

Junior Associate Professor
Tomoka MATSUMURA

Assistant Professors
Yukiko BABA, Yoko YAMAZAKI, Takaya ITO

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

Hospital Staffs
Ken TAKAHASHI, Saki OKABE, Yushi ABE, Yukiko ICHIHASHI, Hiroko KIMURA, Ryoko KURISU,
Maya SAKAMOTO,

Graduate Students
Keiko ABE, Kotomi UCHINUMA, Nozomi UTSUMI, Miki YOKOYAMA, Ayumi NAKAYAMA,
Hikarhi TOMINAGA

Research Students
Hidemasa KUSUNOKI, Satoshi YAMADA, Akihiro KUGA

(1) Outline

Our department is responsible for both dental anesthesiology and orofacial pain control. In addition, orofacial pain control consists of orofacial 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) Etiology and treatment of neuropathic pain in the maxillofacial region
- 2) Development of new local anesthetics
- 3) Management methods to improve satisfaction with sedation
- 4) The pathogenesis of perioperative brain ischemia

(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.

(7) Publications

[Original Articles]

1. Ryo Wakita, Yukiko BaBa, Haruhisa Fukayama, Shigeru Maeda. Factors associated with transient bradycardia during local anesthesia administration to the oral cavity under intravenous sedation: A retrospective cohort study Journal of Dental Sciences. 2023.08;

2. Sumphaongern T, Yamahara E, Wakita R. Sudden Cardiac Arrest in a Dental Patient Awaiting Examination. *Anesthesia progress*. 2023.03; 70(1); 25-30
1. Fumiko HATA, Tatsuki KINOSHITA, Akira OHSHIMA and Shigeru MAEDA. Preoperative Evaluation Using a Lateral Cranial X-ray and Anesthetic Management for Dental Treatment in a Child with Oculodentodigital Dysplasia *JOURNAL OF JAPANESE DENTAL SOCIETY OF ANESTHESIOLOGY*. 2023.04; 51(2); 42-44
2. Toshiaki Fujisawa, Kentaro Mizuta, Tomoka Matsumura, Yasuharu Tachinami, Mitsutaka Sugimura. Recommendations on Emergency Medicines and Equipment that Should be Prepared in Dental Clinics *Journal of Japanese Association for Dental Science*. 2023.03; 42; 51-57

[Misc]

1. Takaya Ito, Nozomi Utsumi, Yukiko Baba, Tomoka Matsumura, Ryo Wakita, Shigeru Maeda. Considerations for Satisfactory Sedation during Dental Implant Surgery *Journal of Personalized Medicine*. 2023.02; 13(3); 461

[Conference Activities & Talks]

1. Takaya Ito, Motoyo Maruyama, Hirotoshi Iwasaki, Yoshitaka Miyagawa, Hidenori Suzuki, Shigeru Maeda, Atsushi Sakai. Involvement of long noncoding RNAs (lncRNAs) containing ultraconserved regions expressed in primary sensory neurons in a rat neuropathic pain model. *Neuroscience 2023* 2023.11.15 Washington DC
2. Ryoko Kurisku, Yoko Yamazaki, Shigeru Maeda. Involvement of Lysophospholipids in trigeminal ganglion in neuropathic pain of orofacial region. *Neuroscience 2023* 2023.11.14 Washington DC
3. Shigeru MAEDA. General anesthesia in dentistry for patients with intellectual disabilities. *General Meeting of Korean Association for Dentistry and Oral Health* 2023.04.16 Seoul
1. Akihiro Kuga, Yushi Abe, Yu Sato, Shigeru Maeda. Satisfaction survey for patients undergoing intravenous sedation in the dental anesthesia department. *The stomatological society, Japan* 2023.12.02
2. Ryoko Kurisu, Yoko Yamazaki, Shigeru Maeda. Involvement of Lysophospholipids in trigeminal ganglion in neuropathic pain of orofacial region. *The 51th Annual Meeting of the Japanese Dental Society of Anesthesiology* 2023.10.08 Nagasaki
3. Ken Takahashi, Yukiko Baba, Naomi Shimada, Chihiro Suzuki, Yu Sato, Takaya Ito, Tomoka Matsumura, Ryo Wakita, Shigeru Maeda. Difference in usage of sugamadex depending on mechano myography or electromyography. *The 51th Annual Meeting of the Japanese Dental Society of Anesthesiology* 2023.10.08 Nagasaki
4. Ayumi Nakayama, Takaya Ito, Masami Hasegawa, Miki Yokoyama, Mako Chiba, Ryo Wakita, Shigeru Maeda. Usefulness of esCCO for intravenous sedation in patient with severe aortic valve retardation and autism spectrum disorder . *The 51th Annual Meeting of the Japanese Dental Society of Anesthesiology* 2023.10.08 Nagasaki
5. Takaya Ito, Atsushi Sakai, Shigeru Maeda. Involvement of H19 lncRNA to neuropathic pain in Schwann cells. *The 51th Annual Meeting of the Japanese Dental Society of Anesthesiology* 2023.10.07 Nagasaki
6. Nozomi Utsumi, Miki Yokoyama, Ryo Wakita, Shigeru Maeda. Changes in esCCO and invasive blood pressure after injection of local anesthetics. *The 51th Annual Meeting of the Japanese Dental Society of Anesthesiology* 2023.10.07 Nagasaki
7. Hikari Tominaga, Takaya Ito, Erika Yamahara, Ryoko Kurisu, Nanako Ikeda, Shigeru Maeda. A case of general anesthesia for oral surgery in patients with EGPA. *The 51th Annual Meeting of the Japanese Dental Society of Anesthesiology* 2023.10.07 Nagasaki
8. Hiroko Kimura, Hiroyuki, Ishiyama, Keisuke Miyazono, Teisuke Akimoto, Akira Nishiyama. A case of comorbid temporomandibular joint disorder and glossodynia successfully treated with Keishikajutsu-buto and Rikkosann . *The 36th Annual Meeting of the Japanese Society for the Temporomandibular Joint* 2023.07.08 Tokyo

9. Akihiro Kuga, Miki Yokoyama, Yu Sato, Takaya Ito, Yukiko Baba, Shigeru Maeda. A case in which a patient was moved to another operating room due to a water leak during general anesthesia. 39th Kanto meeting of Dental Anesthesiology 2023.06.24

Department of 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(-Mar)

Hospital staff

Shigeki Nagahiro(-Mar), Kokoro Iwata, Rika Kurogoushi,
Haruka Naito, Karen Inoue, Kaori Kohi(Apr-),
Gen Takahashi(Apr-), Yuga Toyomura(Apr-),
Chika Hirawada(Apr-), Kanade Yamaki(Apr-)
Takae Aida(-Mar), Kana Hayashi(-Mar), Yusuke Iwabuchi,
Risa Tamenaga, Yuki Shindo(Apr-)

Graduate Student

Cho Li(-Mar), Yujeong Shin(-Mar), Hiroaki Oki, Manami Tanaka,
Yumiko Nakashima, Yuika Yamanaka, Misaki Hamajima(Apr-)

Research Student

Daishi Saito(-Mar), Gen Takahashi(-Mar), Yuga Toyomura(-Mar),
Chika Hirawada(-Mar), Kanade Yamaki(-Mar), Ryo Takenaga,
Ruriko Nitta, Cho Li(Apr-), Yujeong Shin(Apr-)

Special Research Student

Aiko Hoshiai(-Sep)

Adjunct Lecturer

Ryu Matsubara, Shoji Takahashi, Asiri jayawardena,
Yuko Matsumura, Taki Sekiya, Kenichi Miura,
Natsumi Tsuchihashi(Apr-)
Anna Kumakura(-Mar) , Jo Inada, Yosuke Kinoshita, Seiji Sakurai,
Osamu Shinozuka, Tomo Suzuki, Moriyuki Nakamura,
Taiji Hoshiai(Apr-), Takae Aida(Apr-)

(1) Publications

[Original Articles]

1. Sugimoto A, Iwata K, Kurogoushi R, Tanaka M, Nakashima Y, Yamakawa Y, Oishi A, Yoshizaki K, Fukumoto S, Yamamoto A, Ishimaru N, Iwamoto T. C-terminus of PIEZO1 governs Ca(2+) influx and

- intracellular ERK1/2 signaling pathway in mechanotransduction. *Biochemical and biophysical research communications*. 2023.11; 682; 39-45
2. Yuta Chiba, Keigo Yoshizaki, Hiroshi Sato, Tomoko Ikeuchi, Craig Rhodes, Mitsuki Chiba, Kan Saito, Takashi Nakamura, Tsutomu Iwamoto, Aya Yamada, Yoshihiko Yamada, Satoshi Fukumoto. Deficiency of G protein-coupled receptor Gpr111/Adgrf2 causes enamel hypomineralization in mice by alteration of the expression of kallikrein-related peptidase 4 (Klk4) during pH cycling process. *FASEB J*. 2023.04; 37(4); e22861
 3. Wada J, Wada K, Uctasli S, Wakabayashi N, Iwamoto T, Vallittu PK, Lassila L. Effect of splinting material type and location on resistance against deflection force of splinted periodontally compromised teeth with hypermobility. *Journal of the mechanical behavior of biomedical materials*. 2023.04; 142; 105873
 4. Yao Fu, Kanako Miyazaki, Yuta Chiba, Keita Funada, Tomomi Yuta, Tian Tian, Kanji Mizuta, Jumpei Kawahara, Ling Zhang, Daniel Martin, Tsutomu Iwamoto, Ichiro Takahashi, Satoshi Fukumoto, Keigo Yoshizaki. Identification of GPI-anchored protein LYPD1 as an essential factor for odontoblast differentiation in tooth development. *J Biol Chem*. 2023.03; 104638
 5. Junichiro Wada, Kanae Wada, Sufyan Garoushi, Akikazu Shinya, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of 3D printing system and post-curing atmosphere on micro- and nano-wear of additive-manufactured occlusal splint materials *Journal of the Mechanical Behavior of Biomedical Materials*. 2023.03; 142; 105799
 6. Li Zhao, Kakino Satoko, Iwamoto Tsutomu. A Characteristic Analysis of the Pulse Transit Time to Dental Pulp: An Attempt at a New Approach to Dental Pulp Diagnoses Based on the Microcirculatory System *Journal of Oral Health and Biosciences*. 2023.03; 35(2); 61-70
 7. Anrizandy Narwidina, Aya Miyazaki, Kokoro Iwata, Rika Kurogoushi, Asuna Sugimoto, Yasusei Kudo, Keita Kawarabayashi, Yoshihito Yamakawa, Yuki Akazawa, Takamasa Kitamura, Hiroshi Nakagawa, Kimiko Yamaguchi-Ueda, Tomokazu Hasegawa, Keigo Yoshizaki, Satoshi Fukumoto, Akihito Yamamoto, Naozumi Ishimaru, Tomonori Iwasaki, Tsutomu Iwamoto. Iroquois homeobox 3 regulates odontoblast proliferation and differentiation mediated by Wnt5a expression. *Biochem Biophys Res Commun*. 2023.02; 650; 47-54
 8. Fumiya Kano, Noboru Hashimoto, Yao Liu, Linze Xia, Takaaki Nishihara, Wakana Oki, Keita Kawarabayashi, Noriko Mizusawa, Keiko Aota, Takayoshi Sakai, Masayuki Azuma, Hideharu Hibi, Tomonori Iwasaki, Tsutomu Iwamoto, Nobuyasu Horimai, Akihito Yamamoto. Therapeutic benefits of factors derived from stem cells from human exfoliated deciduous teeth for radiation-induced mouse xerostomia. *Sci Rep*. 2023.02; 13(1); 2706
 9. Shin Yujeong, Wada Kanae, Tsuchida Yumi, Ijbara Manhal, Ikeda Masaomi, Takahashi Hidekazu, Iwamoto Tsutomu. Wear behavior of materials for additive manufacturing after simulated occlusion of deciduous dentition *JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS*. 2023.02; 138; 105627
 10. Tomomi Yuta, Tian Tian, Yuta Chiba, Kanako Miyazaki, Keita Funada, Kanji Mizuta, Yao Fu, Jumpei Kawahara, Tsutomu Iwamoto, Ichiro Takahashi, Satoshi Fukumoto, Keigo Yoshizaki. Development of a novel ex vivo organ culture system to improve preservation methods of regenerative tissues. *Sci Rep*. 2023.02; 13(1); 3354
 11. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of Surface Polishing on Physical Properties of an Occlusal Splint Material for Additive Manufacturing under Protection Gas Post-Curing Condition *Polymers*. 2023.01; 15(3); 625
 12. Wada Kanae, Ijbara Manhal, Salim Nesreen A., Wada Junichiro, Iwamoto Tsutomu. Three-dimensional microscopic comparison of wear behavior between immature and mature enamel: an in vitro study *BMC ORAL HEALTH*. 2023.01; 23(1); 40
 13. Zhao LI, Satoko KAKINO, Tsutomu IWAMOTO. A Characteristic Analysis of the Pulse Transit Time to Dental Pulp: An Attempt at a New Approach to Dental Pulp Diagnoses Based on the Microcirculatory System *Journal of Oral Health and Biosciences*. 2023.01; 35(2); 33-42

[Conference Activities & Talks]

1. Kanae Wada. Use of Bioactive Materials in the Paediatric Dentistry Clinic: From Prevention to Rehabilitation. 29 Congresso Brasileiro de Odontopediatria 2023.10.21 Brazil, Rio de Janeiro
2. Merve Uctasli, Mine Betul Uctasli, Kanae Wada, Junichiro Wada, Lippo Lassila. Surface Topography of Different Types of CAD/CAM Restorative Materials. 2023 CED/NOF –IADR Oral Health Research Congress 2023.09.21 Rhodes, Greece
3. Kokoro Iwata, Rika Kurogoushi, Tsutomu Iwamoto. von Willebrand factor D and EGF domains regulates ameloblast differentiation, abnormalities of which result in enamel cracks . International Association of Pediatric Dentistry 2023 2023.06.16
4. Rika Kurogoushi, Kokoro Iwata, Tsutomu Iwamoto. Regulation of cytokine expression by FGF2 in dental pulp-derived mesenchymal stem cells and a consideration on relevance to inflammation and regeneration. IAPD Congress 2023 2023.06.16 Maastricht, The Netherlands
5. Merve Uctasli, Kanae Wada, Junichiro Wada, Lippo Lassila, Mine Betul Uctasli. Surface morphology hybrid ceramic material after different etching protocol. The 7th International Congress on Adhesive Dentistry 2023.06.03 Konya, Turkey
6. Manami Tanaka, Asuna Sugimoto, Yumiko Nakashima, Rei Takenaga, Tsutomu Iwamoto. Odontogenic maxillary sinusitis caused by deciduous molar: A Case Report . 2023.05.18
7. Anrizandy Narwidina, Aya Miyazaki, Kokoro Iwata, Rika Kurogoushi, Tomonori Iwasaki, Tsutomu Iwamoto. Iroquois 3 plays an essential role in odontogenesis. Genome Scientific Conference 2023.02.14 Australia
8. Kanae Wada . Nano-mechanical Properties of Primary Molar Enamel with Enamel Hypoplasia, Early Enamel Demineralized and Sound Enamel. 4th Turku Midwinter Meeting 2023.02.03
1. A case of Hajdu-Cheney Syndrome with submucosal cleft palate. 2023.05.26

[Others]

1. Examination of wear digital dental materials of CAD / CAM suitable for primary tooth restoration., 2023.03
Scandinavia-Japan Sasakawa Foundation, 202204-202303

Orthodontic Science

Professor	Takashi ONO
Associate Professor	Jun HOSOMICHI
Junior Associate Professor	Yoshiro MATSUMOTO
Assistant Professor	Ippei WATARI, Ikuo YONEMITSU, Yuji ISHIDA, Takayoshi ISHIDA Risa USUMI
Project Assistant Professor	Chiho KATO, Hiroko OHMORI, Asuka MANABE
Dental Resident	Seiko ISHIHARA, Aiko ISHIZAKI, Naoaki MIKAMI, Yuka TANAKA
Graduate Students	Thi Kim Uyen DONG Aiko TAKADA, Yoshiyuki HAMADA Ahmad F J M SH ALSULAILI 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, Marin KAWASAKI, Mika KIKUCHI Yuri KINOSHITA, Yu TAKENOUCHI Minami WATANABE, Yaosen CHEN Korkuan JARIYATHEERAWONG
Graduate School Research Students	Chiyo SHIMIZU, Yumi NAKANO, Saori WATAYA Iori SUGITA, Yukari MIZOGUCHI Motoki TAGUCHI, Makoto NAGAKUBO, Mayuka WATANABE Yoshiaki ITO, Sakina MITSUISHI

(1) Outline

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

(2) Research

Research Subjects

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

9) Studies on interrelation between breathing and body function

(3) Education

Subjects of Education:

Orthodontic Science, Pathophysiology for Malocclusion, Biology for Functional Adaptation

(4) Lectures & Courses

Orthodontic Science

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

Pathophysiology for Malocclusion

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

Biology for Functional Adaptation

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

(5) Clinical Services & Other Works

Clinical Services

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

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

(6) Clinical Performances

Highlights of Clinical Services

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

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

(7) Publications

[Original Articles]

1. Haruki Imai, Yosuke Yamashita, Hikaru Takasu, Koichi Fujita, Takashi Ono, Makoto Hirota, Kenji Mitsudo. Accuracy and influencing factors of maxillary and mandibular repositioning using pre-bent locking plates: a prospective study. *Br J Oral Maxillofac Surg*. 2023.12; 61(10); 659-665
2. Eri Misawa-Omori, Hidemasa Okihara, Takuya Ogawa, Yasunori Abe, Chiho Kato, Hideyuki Ishidori, Akiyo Fujita, Satoshi Kokai, Takashi Ono. Reduced mastication during growth inhibits cognitive function by affecting trigeminal ganglia and modulating Wnt signaling pathway and ARHGAP33 molecular transmission Neuropeptides. 2023.08;
3. Hao Guan, Ikuo Yonemitsu, Yuhei Ikeda, Takashi Ono. Reversible Effects of Functional Mandibular Lateral Shift on Masticatory Muscles in Growing Rats. *Biomedicines*. 2023.07; 11(8); 2126
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5. Ruixin Li, Chiho Kato, Akiyo Fujita, Yasunori Abe, Takuya Ogawa, Hideyuki Ishidori, Eri Misawa, Hidemasa Okihara, Satoshi Kokai, Takashi Ono. Effect of Obesity on Masticatory Muscle Activity and Rhythmic Jaw Movements Evoked by Electrical Stimulation of Different Cortical Masticatory Areas. *J Clin Med*. 2023.06; 12(11);
6. Sasin Sritara, Yoshiro Matsumoto, Yixin Lou, Jia Qi, Jun Aida, Takashi Ono. Association between the Temporomandibular Joint Morphology and Chewing Pattern. *Diagnostics (Basel)*. 2023.06; 13(13);
7. Takashi Ono. Pediatric obstructive sleep apnea: Insights and current research *Seminars in Orthodontics*. 2023.06; 29(2); 204-206
8. Wenqian Sun, Hidemasa Okihara, Takuya Ogawa, Hideyuki Ishidori, Eri Misawa, Chiho Kato, Takashi Ono. Pre-Adolescent Diet Normalization Restores Cognitive Function in Young Mice. *J Clin Med*. 2023.05; 12(11);
9. Takumi Suzuki, Jun Hosomichi, Naoyuki Miyasaka, Yasunari Miyazaki, Atsuko Taki, Takashi Zaitzu, Chikako Morioka, Noriko Sato, Manaka Moro, Takashi Ono. Characteristics of obstructive sleep apnea among pregnant Japanese woman and their birth outcomes *SLEEP*. 2023.05; 46; A229
10. Karin Harumi Uchima Koecklin, Chiho Kato, Yasunori Abe, Tadachika Yabushita, Satoshi Kokai, Takashi Ono. Histological and contractile changes in the genioglossus muscle after nasal obstruction in growing rats. *Sci Rep*. 2023.04; 13(1); 6245
11. Naoaki Mikami, Ikuo Yonemitsu, Hiroshi Takemura, Mark Kondou, Kouhei Soga, Kazuhiro Suga, Zusei Kanno, WeiJen Lai, Motohiro Uo, Takashi Ono. Mechanical analysis of the improved superelastic Ni-Ti alloy wire using the orthodontic simulator with high-precision sensors *Journal of the Mechanical Behavior of Biomedical Materials*. 2023.04; 142; 105861
12. Saranya Serirukchutarungsee, Ippei Watari, Masataka Narukawa, Katarzyna Anna Podyma-Inoue, Pornchanok Sangsuriyothai, Takashi Ono. Two-generation exposure to a high-fat diet induces the change of salty taste preference in rats. *Sci Rep*. 2023.04; 13(1); 5742
13. Seiko Ishihara, Risa Usami-Fujita, Yuki Kasahara, Shuji Oishi, Kana Shibata, Yasuhiro Shimizu, Yuji Ishida, Sawa Kaneko, Makoto Sugiura-Nakazato, Makoto J Tabata, Jun Hosomichi, Yoshiaki Taniyama, Takashi Ono. Periostin splice variants affect craniofacial growth by influencing chondrocyte hypertrophy. *J Bone Miner Metab*. 2023.03; 41(2); 171-181
14. Lou Yixin, Matsumoto Yoshiro, Iseki Sachiko, Ono Takashi. Difference in apical resorption activity during rat molar root formation in response to mechanical force *EUROPEAN JOURNAL OF ORTHODONTICS*. 2023.02;

15. Albert Chun-Shuo Huang, Yuji Ishida, Kai Li, Duantawan Rintanalert, Kasumi Hatano-Sato, Shuji Oishi, Jun Hosomichi, Risa Usumi-Fujita, Hiroyuki Yamaguchi, Hiroyuki Tsujimoto, Aiko Sasai, Ayaka Ochi, Hajime Watanabe, Takashi Ono. NF- κ B Decoy ODN-Loaded Poly(Lactic-co-glycolic Acid) Nanospheres Inhibit Alveolar Ridge Resorption. *Int J Mol Sci.* 2023.02; 24(4); 3699
16. Saranya Serirukchutarungsee, Ippei Watari, Pornchanok Sangsuriyothai, Masato Akakura, Takashi Ono. The Effect of Two-Generation Exposure to a High-Fat Diet on Craniofacial Morphology in Rats. *J Clin Med.* 2023.02; 12(5); 1903
17. Wirongrong Wongkitikamjorn, Eiji Wada, Jun Hosomichi, Hideyuki Maeda, Sirichom Satrawaha, Haixin Hong, Ken-Ichi Yoshida, Takashi Ono, Yukiko K Hayashi. Metabolic dysregulation and decreased capillarization in skeletal muscles of male adolescent offspring rats exposed to gestational intermittent hypoxia. *Front Physiol.* 2023.01; 14; 1067683

[Misc]

1. Takashi Ono, Valmy Pangrazio-Kulbersh, Letizia Perillo, Flavia Artese, Ewa Czochrowska, M Ali Darendeliler, Steven Dugoni, William E Fayad Baire, Eric Liou, Jae Hyun Park, David Rice, Abbas Zaher, Athanasios E Athanasiou, Lee W Graber, Nikhilesh R Vaid. World Federation of Orthodontists guidelines for postgraduate orthodontic education. *J World Fed Orthod.* 2023.04; 12(2); 41-49
2. Ikuo Yonemitsu, Shusaku Ozaki, Takashi Ono. The Improved Superelastic Ni-Ti Alloy Wire in Orthodontic Treatment: Characteristics and Clinical Application SEMINARS IN ORTHODONTICS. 2023.03; 29(1); 43-50

[Conference Activities & Talks]

1. Saori Wataya, Takashi Ono. Involvement of maxillary occlusal plane inclination on postoperative relapse in patients with facial asymmetry. The 56th Annual Scientific Congress Of Korean Association Of Orthodontists 2023.10.25 Jeju Island Korea
2. Yuri Kinoshita, Keiko Fukino, Yoshiro Matsumoto, Joe Iwanaga, Takashi Ono, Keiichi Akita. Structure of the muscle layers and direction of the muscle bundles in the soft palate for clarification of the velopharyngeal closure. Joint Congress of European Association of Clinical Anatomy (EACA) and International Symposium of Clinical and Applied Anatomy (ISCAA) 2023.09.14 Carolinum, Prague
3. Jia Qi, Yoshiro Matsumoto, Cangyou Xie, Fatma Rashed, Takashi Ono, Kazuhiro Aoki. Local delivery of bone anabolic agents protects the thin alveolar bone in the murine mechanical orthodontic force model. The 41st Annual Meeting of the Japanese Society for Bone and Mineral Research 2023.07.27 Tokyo
4. Shuntaro Iwaki, Ikuo Yonemitsu, Makoto Tabata, Mirei Keitoku, Takashi Ono. Unilateral nasal obstruction and nitric oxide mediate reversible morphological and phenotypic changes in masticatory muscles in growing rats. 2023 Annual Congress of the European Orthodontic Society 2023.06.11 Oslo, Norway
5. Takumi Suzuki, Jun Hosomichi, Naoyuki Miyasaka, Yasunari Miyazaki, Atsuko Taki, Takashi Zaitu, Manaka Moro, Chikako Morioka, Noriko Sato, Takashi Ono. Characteristics of obstructive sleep apnea among pregnant Japanese woman and their birth outcomes.. SLEEP 2023 2023.06.05 Indiana, USA
6. Moe Tanigawa, Chiho Kato, Takashi Ono, Naofumi Uesaka. Effects of unilateral nasal obstruction during the growth period on cerebellar neural circuit and function. The 100th Anniversary Annual Meeting of The Physiological Society of Japan 2023.05.01 Kyoto, Kyoto

Cariology and Operative Dentistry

Professor: Yasushi Shimada

Associate Professor: Masayuki Otsuki

Junior Associate Professor: Noriko Hiraishi(June~ Research Professor)

Assistant Professor: Takako Yoshikawa, Go Inoue, Rena Takahashi(April~ Junior Associate Professor), Takaaki Sato(~May), Takashi Hatayama(July~)

Specially Appointed Assistant Professor: NHM Khairul Matin, Takashi Hatayama(~June), Tomoko Tabata, Nami Tsuchiyama, Hisaichi Nakagawa(~August)

Hospital Staff: Ayako Nakamoto(~March), Motoi Takahashi(~March), Yousuke Minato,

Keitaro Dohi(April~), Riko Nakamura(April~)

Resident: Shuntaro Abe

Staff Assistant: Rieko Sugiyama(~September), Tomomi Anai(October~)

Graduate Student: Ayaka Sato(~March), Satoshi Akiya(~March), Yuko Ogawa(~March),

Kiyoka Furusawa(~March), Yutaro Motoyama(~March), Ako Yamashita(~March), QI Feng(~March),

Kittisak SANON(~March), TAGHREED ABDULRAHMAN ALREFAIE(~March),

MULTUZA AYED ALI(~March), Soe Kay Thwe Than Naing, Koudai Akabane,

Hiroki Ishihara, Kouta Kibe, Mika Shimojima, CHEN XUEFEI, WEI Diantong,

YANG Yi, Panchanit UBOLSA-ARD, 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,

Azusa Takeuchi, Ryohei Fujimori, Shamima JAHAN, ZENG SIQI,

Kazuhiko Miyagi(April~), FAN LIN(April~), FENG SHUO(April~), HE YUZHENGQIU(April~),

NADER AHMED ABDELAZIZ MAHMOUD ELSEUDY(April~), WANG XINYU(April~)

Research Student: Mineo Kijima, ZHU TIANMAO, FENG Shuo(~March), Riko Nakamura(~March),

ELSEUDY Nadar Ahmed Abdelaziz(~March), HE Yuzhengqiu (~March), FAN Lin(~March),

Keitaro Dohi (~March), WANG Xinyu(~March), Mustafa Ata Cakaloglu(~March),

Rena Hashitani(April~), ABDULQADER HADEEL HUSAM ABDULQADER(April~),

ZHANG JIAMING(April~), NING BOYU(October~), HU QIAO(October~), JIANG JINJUAN(October~),

ZUHRA FATIMA TUJ(October~)

Special Research Student: Nakato Takagi, Asami Yamamoto(October~)

(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]

1. Kouta Kibe, Takashi Hatayama, Yasushi Shimada. In vitro performance of an autocured universal adhesive system in bonding to dentin BMC ORAL HEALTH. 2023.11; 23(1); 933

2. Nami Tsuchiyama, Yukihiro Tamura, Tadamu Gondo, Masaomi Ikeda, Yasushi Shimada. The effect of ions used in bioactive dental materials on proliferation and differentiation of MC3T3-E1 cells Asian Pacific Journal of Dentistry. 2023.10; 23(2); 15-19
3. Tabata T, Nakagawa H, Kobayashi K, Takeuchi A, Fujimori R, Dohi K, Nakamura R, Iwabuchi H, Gondo T, Tsuji Y, Chen X, Sato T, Inoue G, Shimada Y. Diagnosis of occlusal caries using optical coherence tomography in a real clinical situation. Asian Pacific Journal of Dentistry. 2023.10; 23(2); 24-27
4. Takaaki Sato, Tomoko Tabata, Koudai Akabane, Mengtian Zhao, Abu Hasan Mohammad Khaled, Noriko Hiraishi, Yasunori Sumi, Junji Tagami, Yasushi Shimada. Noninvasive diagnostic method using optical coherence tomography detected a vulnerable dentin enamel junction created by phosphoric acid etching. Dental Materials Journal. 2023.08; 42(4); 552-558
5. Seung-Hoon Han, Yasushi Shimada, Alireza Sadr, Tomoko Tabata, Hisaichi Nakagawa, Takaaki Sato, Ji-Eun Byun, Sung-Ho Park. Effect of Attenuated Light Through Translucent Zirconia on the Interfacial Adaptation and Polymerization of Resin Cements. The Journal of Adhesive Dentistry. 2023.08; 25(1); 219-230
6. Mika Shimojima, Noriko Hiraishi, Kodai Akabane, Mohannad Nassar, Masayuki Otsuki, Yasushi Shimada. Effect of an In-Office Bleaching Agent with Surface Pre-Reacted Glass-Ionomer Filler on the Enamel Surface: A In-Vitro Study. J Funct Biomater. 2023.07; 14(7); 386
7. Kodai Akabane, Noriko Hiraishi, Mika Shimojima, Mohannad Nassar, Feng Qi, Masayuki Otsuki, Yasushi Shimada. The bleaching effect of office bleaching agents containing S-PRG filler evaluated by pH value and electron spin resonance. Clin Oral Investig. 2023.07; 27(7); 4051-4059
8. SoeKayThwe ThanNaing, Noriko Hiraishi, Xuefei Chen, Richard Foxton, Yasushi Shimada. In vitro remineralization assessment of enamel subsurface lesions using different percentages of surface reaction-type pre-reacted glass-ionomer containing gum-based material. Journal of dentistry. 2023.06; 135; 104602
9. Ayaka Sato, Takaaki Sato, Masaomi Ikeda, Tomohiro Takagaki, Toru Nikaido, Junji Tagami, Yasushi Shimada. Influence of different tooth etchants on bur-cut and uncut enamel. Dental Materials Journal. 2023.05; 42(3); 311-318
10. Satoshi Akiya, Kento Sato, Kouta Kibe, Antonin Tichy, Noriko Hiraishi, Taweesak Prasansuttiorn, Keiichi Hosaka, Richard M Foxton, Yasushi Shimada, Masatoshi Nakajima. Polymerization shrinkage of light-cured conventional and bulk-fill composites -The effect of cavity depth and post-curing. Dent Mater J. 2023.05; 42(3); 426-432
11. Kiyoka Furusawa, Shun Kobayashi, Ako Yamashita, Antonin Tichy, Keiichi Hosaka, Yasushi Shimada, Masatoshi Nakajima. Effect of filler load on structural coloration and color adjustment potential of resin composites. Dent Mater J. 2023.05; 42(3); 343-350
12. Go Inoue, Yasushi Shimada. Effect of F:Ca:P ratio on fluoride deposition by fluoride-calcium-phosphate complex Asian Pacific Journal of Dentistry. 2023.04; 23(1); 5-8
13. Ako Yamashita, Shun Kobayashi, Kiyoka Furusawa, Antonin Tichy, Rena Oguro, Keiichi Hosaka, Yasushi Shimada, Masatoshi Nakajima. Does the thickness of universal-shade composites affect the ability to reflect the color of background dentin? Dent Mater J. 2023.03; 42(2); 255-265
14. Chen X, Inoue G, Ikeda M, Sadr A, Shimada Y. Time-dependent structural changes and hypermineralisation of artificially demineralised dentine following treatment with silver diammine fluoride and glass ionomer cement. Journal of dentistry. 2023.02; 131; 104452
15. Go Inoue, Xuefei Chen, Yasushi Shimada. Transverse Microradiography Evidence on the Effect of Phosphoryl Oligosaccharides of Calcium (POs-Ca) in Toothpaste on Decalcified Enamel Crystals. 2023.01; 13(2); 206
16. Takaaki Sato, Jirun Sun, Xiaohong Wang, Shozo Takagi, Yoshikazu Teranishi, Go Inoue, Tomohiro Takagaki, Toru Nikaido, Junji Tagami, Yasushi Shimada. Analysis of reaction products on hydroxyapatite created by tooth etchants with different compositions. Journal of Oral Science. 2023.01; 65(1); 53-56

17. Diantong Wei, Ayako Nakamoto, Noriko Hiraishi, Akira Nakane, Gabriel Abuna, Masayuki Otsuki, Yasushi Shimada. Effect of Er: YAG laser irradiation with additional low energy on resin-dentin bonding and morphology of bonded interface. *J Mech Behav Biomed Mater.* 2023.01; 140; 105692
18. Takako Yoshikawa, Alireza Sadr, Yasushi Shimada. Polymerization behavior of bulk-fill and hybrid-type resin composites using different light curing mode *Asian Pacific Journal of Dentistry.* 2023.02; 23(1); 1-4
1. Motoi Takahashi, Rena Takahashi, Yasushi Shimada. Direct Composite Restoration for Esthetic and Functional Disorder of Anterior Teeth with a Digital Workflow: A Case Report *The Japanese Journal of Conservative Dentistry.* 2023.08; 66(4); 224-232
2. Go Inoue, Koji Mizutani, Risako Mikami, Yasushi Shimada, Akira Aoki. Long-term Outcomes of Er: YAG Laser Microsurgery for Melanin Removal in Gingiva: A Case Report *The Japanese Journal of Conservative Dentistry.* 2023.05; 66(2); 147-153

[Books etc]

1. Yasushi Shimada et al. Glossary of Operative Dentistry 2023. 2023.03

[Misc]

1. Tomoko TABATA, Hisaichi NAKAGAWA, Khairul MATIN Masayuki OTSUKI, Akira AOKI and Yasushi SHIMADA. Biofilm Studies Using Optical Coherence Tomography (OCT): Review *Journal of Japanese Society for Laser Dentistry.* 2023.09; 33(1); 11-17

[Conference Activities & Talks]

1. Diantong WEI, Jianfeng CHEN, Noriko HIRAISHI, Masayuki OTSUKI, Masaomi IKEDA, Yasushi SHIMADA. Effect of Er:YAG laser debonding of zirconia restorations on bond strength, temperature increase and surface properties of zirconia and dentin. The 88th meeting of the Stomatological Society 2023.12.01 Tokyo
2. Xuefei Chen, Go Inoue, Yasushi Shimada. Remineralization effect of silver diammine fluoride and glass ionomer cement for artificial caries and natural caries under the combination usage in vitro. The 71st Annual Meeting of Japanese Association for Dental Research 2023.11.25 Sendai, Japan
3. Go Inoue, Masaomi Ikeda, Yasushi Shimada. Composite resin restoration with injection technique on severe eroded teeth. The 71st Annual Meeting of Japanese Association for Dental Research 2023.11.25 Sendai
4. Rena Takahashi, Saki Uchiyama, Yuna Kanamori, Junichi Shinagawa, Toru Nikaido, Yasushi Shimada. Dentin bonding performance of resin cement using resin coating technique and different cleaning protocols. The 25th KACD-JSCD Joint Scientific Meeting 2023.11.04 Seoul, Korea
5. Noriko Hiraishi. Bioactive Effect of S-PRG released ions on mineral precipitation and reaction with enamel and dentin. Academy Dental Materials Meeting 2023.10 USA
6. Xu K, Inokoshi M, Yoshihara K, Kakehata M, Yashiro H, Takahashi R, Yamatomo M, Kamijo S, Ikeda M, Minakuchi S. Bonding efficacy to femtosecond laser irradiated lithium disilicate glass-ceramic. IADR-ANZ Conference 2023 2023.09.29 Sydney
7. Tomoko Tabata, Hisaichi Nakagawa, Takaaki Sato, Go Inoue, Masaomi Ikeda, Yasushi Shimada. Clinical evaluation of optical coherence tomography in the diagnosis of occlusal enamel caries using ICDAS codes. the 2nd General Meeting of Asian-Oceanian Federation of Conservative Dentistry 2023 (ConsAsia 2023) 2023.09.02 Taipei, Taiwan
8. Go Inoue, Hisaichi Nakagawa, Takaaki Sato, Tomoko Tabata, Masaomi Ikeda, Yasushi Shimada. Clinical assessment of diagnosis of enamel caries ICDAS codes using optical coherence tomography. the 2nd General Meeting of Asian-Oceanian Federation of Conservative Dentistry 2023 2023.09.02 Taipei
9. Soe Kay Thwe Than Naing, Noriko Hiraishi, Xuefei Chen, Yasushi Shimada. In vitro remineralization assessment of enamel subsurface lesions using gum-base material containing surface pre-reacted glass-ionomer filler. The 158th Meeting of the Japanese Society of Conservative Dentistry 2023.06.23 Shimane, Japan

10. Mustafa Ata ÇAKALOĞLU, Takaaki SATO, Noriko HIRAISHI, Yasushi SHIMADA. NON-INVASIVE EVALUATION OF MARGINAL ADAPTATION OF DENTIN-GLASS IONOMER CEMENT INTERFACE USING SWEPT SOURCE OPTICAL COHERENCE TOMOGRAPHY . The 7th International Congress on Adhesive Dentistry 2023.06.01 Konya, Turkey
11. Hitoshi Miki, Hirofumi Tashiro, Junji Tagami, Tomohiro Takagaki, Keiichi Hosaka, Takaaki Sato, Takashi Hatayama, Yasushi Shimada. Clinical effectiveness of the mono-block direct composite crown restoration. The 7th International Congress on Adhesive Dentistry 2023.06.01 Konya, Turkey
12. Takako Yoshikawa, Alireza Sadr, Yasushi Shimada. Polymerization Behavior of Various-Composites at Top/Bottom of Cavity using Different-Irradiance-Light. 7th, The International Congress on Adhesive Dentistry 2023.06.02 Konya, TURKEY
1. Rena TAKAHASHI, Yuna KANAMORI, Shunsuke TAKANO, Junichi SHINAGAWA, Yosuke MINATO, Motoi TAKAHASHI, Yuka TSUDA, Yasushi SHIMADA. Evaluation of a novel one-step bonding system on resin coating technique. The 159th Meeting of Japanese Society of Conservative Dentistry 2023.11.11
2. Miyamaoto, Imamura, Adachi, Yamamoto, Noriko Hiraishi, Giuseppe Pezzotti, Kanemura. In vitro evaluation of molecular structural changes of hydroxyapatite induced by Er:YAG laser irradiation by Raman spectroscopic analysis. The 158th Meeting of the Japanese Society of Conservative Dentistry 2023.06.23 Shimane, Japan

[Social Contribution]

1. Materials Guest Editor (Yasushi Shimada), 2021.01 - 2023.03.10

Masticatory Function and Health Science

Professor: Kenji FUEKI

Associate professor: Wataru KOMADA

Junior associate professor: Hiroshi CHUREI

Assistant professor : Shiho OTAKE, Yuka INAMOCHI, Kairi HAYASHI, Hiroyuki ISHIYAMA

Project assistant professor: Mina TAKITA, Mayuko MASTUMURA, Hiroko KIMURA

Clinical staff: Sinya OISHI, Teisuke AKIMOTO, Taisuke OZAKI, Kaito TOGAWA, Keisuke MIYAZONO, Yasuyuki KOWAKA, Tomoyuki MIHARA, Yue YIN, Yayoi OISHI, Taku NEMOTO, Miho OTAWARA

(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 mouth guard and face guard, diagnosis and treatment of TMD

(7) Publications

[Original Articles]

1. Yue Yin, Kosuke Nozaki, Reina Nemoto, Omnia Saleh, Yayoi Oishi, Mayuko Matsumura, Wataru Komada, Hiroyuki Miura, Kenji Fueki. Marginal fit and retention force of zirconia resin-bonded fixed dental prostheses in the posterior region with different designs *Journal of Dental Sciences*. 2023.12;
2. Shinya Oishi, Wataru Komada, Ruri Tsukahara, Shu Yoshimatsu, Daiki Kondo, Satoshi Omori, Kosuke Nozaki, Hiroyuki Miura, Kenji Fueki. 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. *J Prosthodont Res*. 2023.01; 67(1); 70-76
3. 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*. 2023.01; 18(1); 95-104
4. Oishi Shinya, Komada Wataru, Tsukahara Ruri, Yoshimatsu Shu, Kondo Daiki, Omori Satoshi, Nozaki Kosuke, Miura Hiroyuki, Fueki Kenji. 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*. 2023.01; 67(1); 70-76
1. Yuka Inamochi. A case report of occlusal reconstruction by an overdenture for a patient with attrition *The Journal of the Japan Prosthodontic Society*. 2023.04; 15(2); 219-222

[Misc]

1. Tanabe G, Ueno T, Li C, Manka-Malara K, K Janicka J, Togawa K, Hayashi K, Churei H, Gonda T, Suzuki H, Nakajima K, Mizuhashi F, Matsumura H, Maeda Y, Yasui T.. Literature review on the advances and applications of digital dentistry in sports mouthguard fabrication. *International Journal of Sports Dentistry*. 2023.11; 16(1); 15-23
2. Yuka Inamochi, Yoichiro Ogino, Kae Harada, Kenji Fueki, Yasunori Ayukawa, Masahiro Nishimura, Kenji Maekawa, Younghan Kang, Toshihiro Hirai, Takuo Kuboki. Do oral care and rehabilitation improve cognitive function? A systematic review of clinical studies *Journal of Evidence-Based Dental Practice*. 2023.10;
3. Li Yajie, Inamochi Yuka, Wang Zuo, Fueki Kenji. Clinical application of robots in dentistry: A scoping review *JOURNAL OF PROSTHODONTIC RESEARCH*. 2023.06;
1. Are improvements in dental and oral conditions effective in preventing dementia? - Evidence in dental research and future perspectives - *DEMENTIA JAPAN*. 2023.09; 37(3); 401-410
2. Basic literacy for conducting systematic reviews 2023.04; 15(2); 169-174
3. Medical-Dental collaboration: Exploratory research project on the Correlation between Cognitive and Oral function (ECCO): background and research activity 2023.01; 15(1); 72-78

[Conference Activities & Talks]

1. Sentaro Koshida, Takanori Ishii, Hiroshi Churei, Hiroshi Kubota. MEASUREMENT OF HEAD IMPACTS DURING ACTUAL JUDO PRACTICE IN COLLEGE JUDOKAS: A PRELIMINARY STUDY. *International Society of Biomechanics Congress 2023* 2023.07.31 Fukuoka
2. Shimizu S, Hayashi K, Takeuchi Y, Tanabe G, Churei H, Kobayashi H, Ueno T, Fueki K. Effect of Administration of Sonicated P. gingivalis on skeletal muscle injury healing using a rat model. . *ECSS Paris 2023* 2023.07.04 Paris
1. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Hiroshi Churei, Kenji Fueki. The effect of antigen of periodontitis to sports related muscle reaction. *88th congress of Stomatological society Japan* 2023.12.02

2. Yuzuki Komazawa, Gen Tanabe, Tetsuya Hasunuma, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Naoki Moriya, Toshikazu Yasui, Toshiaki Ueno. Assessment of similarity of association between athlete fatigue and subjective oral-maxillofacial symptoms. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
3. Yoko Hotta, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Yumi Takahashi, Shintaro Shimizu, Akihito Kumagai, Norio Hirata, Kazushi Watanabe, Takeshi Negoro, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Questionnaire survey on experiences of maxillofacial trauma during water polo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
4. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
5. Liu Chang, Thida Aung, Kaung Si Thu, Kaito Togawa, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Ryo Sato, Yukio Sasaki, Hiroshi Churei. Effect of CT-slice thickness on defining the maxillofacial fracture area. 2023.11.19
6. Li Chenyuan, Takahiro Wada, Yumi Tsuchida, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Retention force comparison of 3D multiple layer mouthguard and conventional mouthguard via cycle-loading durability fatigue test. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
7. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Zhu Qiushuang, Li Zequn, Gen Tanabe, Hiroshi Churei, Toshiaki Ueno. The effect of P. gingivalis administration to PGC-1 α and TNF α expression in skeletal muscle after endurance training in vivo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
8. Y. Ohara, H. Churei, S. Makino, K. Hayashi, G. Tanabe, G. Kondo, A. Nagai, C. Ichihara, W. Oguchi, T. Ueno. A survey of blind soccer players' attitudes before and after mouthguard use. The 34th Annual Meeting of the Japanese Society of Sports Dentistry 2023.11.19
9. Matsumura M, Matsumura M, Kitazaki H, Baba S, Fueki K. A case report of Pustulosis Palmaris et Plantaris improved by elimination of intraoral metal. The 14th Annual Meeting of Japanese Society of Metal-free Dentistry 2023.11.19
10. Kaito Togawa, Hiroshi Churei, Kairi Hayashi, Yumi Takahashi, Shintaro Shimizu, Yoko Hotta, Takahisa Haraguchi, Tomohiko Tateishi, Kazuyoshi Yagishita, Gen Tanabe, Toshiaki Ueno. A case of a professional futsal player who is able to continue competitive life by using a custom-made faceguard. 34th congress of Japanese society of clinical sports medicine 2023.11.11
11. Hiroyuki Ishiyama. Side effects in OA therapy for obstructive sleep apnea. The Basic Seminar in Sleep Dentistry 2023 2023.10.08 Kyoto, Japan
12. Hiroyuki Ishiyama. The relationship between temporomandibular disorders and sleep disorders. The 45th Annual Meeting of Japanese Society of Sleep Research / The 30th Annual Meeting of Japanese Society for Chronobiology 2023.09.16 Yokohama, Japan
13. Shintaro Shimizu, Gen Tanabe, Tatsuhiko Anzai, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Kunihiro Takahashi, Toshiaki Ueno. Corresponding analysis of sports injury of school life using text mining method. 24th congress of The Japanese Association of Safety Education 2023.09.09
14. Hiroyuki Ishiyama. Responding to complications: the side effects in OA therapy of obstructive sleep apnea. Dental Titration Seminar 2023 2023.09 Online
15. Hiroyuki Ishiyama. A randomized controlled trial on the intensity of jaw opening exercise in the treatment of temporomandibular disorders.. The 36th Annual Meeting of the Japanese Society for Temporomandibular Joint 2023.07.08 Tokyo, Japan
16. Hiroyuki Wake, Tomoaki Shibuya, So Wake, Hiroyuki Ishiyama, Takashi Kaneda. A case of temporomandibular disorders with obstructive sleep apnea who visited the hospital with a complaint of occlusal discomfort. The 36th Annual Meeting of the Japanese Society for Temporomandibular Joint 2023.07.08 Tokyo, Japan

17. Hiroko Kimura, Hiroyuki, Ishiyama, Keisuke Miyazono, Teisuke Akimoto, Akira Nishiyama. A case of comorbid temporomandibular joint disorder and glossodynia successfully treated with Keishikajutsubuto and Rikkosann . The 36th Annual Meeting of the Japanese Society for the Temporomandibular Joint 2023.07.08 Tokyo
18. Matsumura M. Positioning of dental treatment in palmoplantar pustulosis. The meeting of consider team medical care for palmoplantar pustulosis 2023.06.14
19. Hiroyuki Ishiyama. Oral appliance therapy for sleep apnea: treatment effects and side effects. The 132nd Annual Meeting of the Japanese Prosthodontics Society - 90th Anniversary Meeting 2023.05.21 Yokohama, Japan
20. Matsumura M, Yanaka W, Nozaki K, Komada W, Kitazaki H, Baba S, Matsumura M, Fueki K. A case study of treatment methods for patients with resin and metal allergies based on patch test. The 132rd Annual Meeting of the Japan Prosthodontic Society 2023.05.21
21. Daiki Kondo, Wataru Komada, Shinya Oishi, Kenji Fueki. The influence of Zirconia Tube for Stress in Endodontically-Treated Premolar. Commemorative Scientific Meeting of the Japan Prothodontic Society 2023.05.21
22. Yuka Inamochi. Basics of writing clinical research papers; Writing paper of observational study. Japan Prosthodontic Society 132th annual meeting 2023.05.21 Yokohama
23. Fueki K, Inamochi Y, Li Y, Zhang L, Saleh O. Research trends on objective masticatory function: a view of 100 top-cited articles. Japan Prosthodontic Society 132th annual meeting 2023.05.21 Yokohama
24. Hiroyuki Ishiyama. Consideration of Appropriate Mandibular Position from a Risk & Benefit Perspective for Oral appliance for Sleep Apnea. . The 132nd Annual Meeting of the Japanese Prosthodontics Society - 90th Anniversary Meeting 2023.05.20 Yokohama, Japan
25. Matsumoto M, Matsumura M, Saleh O, Yanaka W, Beniya R, Nozaki K, Matsumura M, Wakabayashi N, Fueki K. Colorimetric study of anterior CAD/CAM crowns - Effect of opaque cement on metal abutment teeth. The 132rd Annual Meeting of the Japan Prosthodontic Society 2023.05.20
26. Yuka Inamochi, Kenji Fueki, Li Yajie, Zhang Lingbo. A meta-analysis of randomized controlled trials on oral-health related to quality of life in patients with non-metal clasp dentures. Japan Prosthodontic Society 132th annual meeting 2023.05.20 Yokohama
27. Yuka Abe, Yuka Inamochi, Youhei Hama, Yuriko Kusumoto, Takayuki Ueda, Keiichi Sasaki, Takuo Kuboki, Yuta Manabe, Katsuhiko Kimoto, Kenji Fueki, Kazuyoshi Baba. Correlation between assessment methods of masticatory function and health-related parameters: a scoping review. Japan Prosthodontic Society 132th annual meeting 2023.05.20 Yokohama
28. Matsumura M, Nozaki K, Yanaka W, Saleh O, Matsumura M, Fueki K. Effect of abutment teeth and luting cement on color tone of anterior CAD/CAM crowns. The 14th Annual Meeting of the Japan Academy of Digital Dentistry 2023.04.23
29. C. Liu, K. Hayashi, K. Togawa, Y. Takahashi, S. Shimizu, A. Kumagai, H. Churei. Dental Diseases and Treatments for Patient Education. The 7th Annual Congress of Japanes Society of Medical illustration 2023.03.05
30. C. Liu, K. Hayashi, K. Togawa, Y. Takahashi, S. Shimizu, A. Kumagai, H. Churei. Mouthguards and faceguards for sports. The 7th Annual Congress of Japanes Society of Medical illustration 2023.03.05
31. Kairi Hayashi. Sports Dentistry of Tokyo Medical and Dental University. Seminer of clinical sports dentist course in Aichi Dental Association 2023.03.04
32. Tsuruta Jun, Otake Shiho, Oishi Shinya, Ozaki Taisuke, Komada Wataru, Fueki Kenji. Study for assessment of prepared artificial tooth using the 3D evaluation system for abutment teeth and cavity preparation: A pilot study. The Stomatological Society 2023.03.01
33. Hiroyuki Ishiyama, Masayuki Hidashima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki, Kenji Fueki. The effect of reduction rate of respiratory resistance associated with mandibular advancement on the efficacy of oral appliance for obstructive sleep apnea.. The 22nd Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2023.10.08 Kyoto, Japan

[Awards & Honors]

1. Best Research Award (Kikuchi Award), The 22nd Annual Meeting of the Japanese Academy of Dental Sleep Medicine, 2023.10

[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, Arata EBIHARA (December~)

Assistant Professor:
Arata EBIHARA (~November), Kento TAZAWA, Kentaro HASHIMOTO (~March), Yoshiko IINO (~February),
Keiichiro MAKI (March~), Shunsuke KIMURA (September~)

Specially Appointed Assistant Professor:
Sonoko NODA (~March), Keiichiro MAKI (~February), Shunsuke KIMURA (~August)

Hospital Staff:
Yasuhiro HOSHIHARA, Hiroko SOEDA (~March), Yamato OKADA (April~), Satoshi OOMORI (April~),
Takuya KAWAMURA (April~), Harutaka KOMAKI (April~), Yoko HOSHINO (September~)

Graduate Student:
Hayate UNNO (~March), Satoshi OOMORI (~March), Hiroki OKUDA, Jiayi LIU (~March),
Aseel Alchawoosh (~March), Han Peifeng, Moe Sandar Kyaw (~September), Yuka KASUGA,
Souta MOCHIDUKI, Nyein Chan Ko, Ryota ITO, Keiko HIRANO, Kazuhisa SATAKE, Yu Ziniu, Wang Shihan,
Risako YAMAMOTO, Khaing Nyein Pwint, Ren Chunmei, Kentaro NATORI, Koki TOYODA, Risa OOSHIMA,
Bai Xiyuan, Phu Yadanar Aung Myint, Alghamdi Faisal Turki A, Masaharu ISHIDORI (April~),
Ryuuma SAITO (April~), Kaoru IWAI (April~), Luo Yanshan (April~), Chen Yanyan (April~)

Research Student:
Takuya KAWAMURA (~March), Harutaka KOMAKI (~March), Yoko HOSHINO (~August), Luo Yanshan (~
March), Chen Yanyan (~March), Takayuki SUEYOSHI (April~), Kanami NAKANO (April~), Hiroaki MORI
(April~), Mari YOSHIDA (April~), Wang Xutong (October~)

(1) Outline

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

(2) Research

1. Biology of dentin/pulp complex and dental pulp tissue regeneration
 - Effect of micro RNAs on inflammation and repair of the dental pulp

2. New bioactive endodontic materials

- Properties of new hydraulic calcium silicate-based root canal sealers
- Evaluation of diisotriantimony cerate and trisilicium aluminate as new pulp capping materials

3. Root canal irrigation

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

4. Nickel-titanium (NiTi) rotary instrumentation

- Evaluation of mechanical properties of heat treated NiTi files
- Influence of different kinematics on stationary and dynamic torsional behavior of NiTi files
- Dynamic torque and screw-in force of different glide path instruments
- Effect of preset torque setting on torque/force generation, shaping ability and surface changes of NiTi files in different root canal curvature locations

(3) Education

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

(4) Clinical Services & Other Works

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

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

(5) Clinical Performances

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

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

1. Yahata Y, Handa K, Ohkura N, Okamoto M, Ohshima J, Itoh S, Kawashima N, Tanaka T, Sato N, Noiri Y, Hayashi M, Okiji T, Saito M. Autologous concentrated growth factor mediated accelerated bone healing in root-end microsurgery: A multicenter randomized clinical trial. *Regenerative therapy*. 2023.12; 24; 377-384
2. Kasuga Y, Kimura S, Maki K, Unno H, Omori S, Hirano K, Ebihara A, Okiji T. Phase transformation and mechanical properties of heat-treated nickel-titanium rotary endodontic instruments at room and body temperatures. *BMC Oral Health*. 2023.10; 23(1); 825
3. 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*. 2023.10; 18(4); 1731-1739
4. 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*. 2023.07; 18(3); 1170-1176
5. 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*. 2023.07; 18(3); 1141-1147
6. Han P, Sunada-Nara K, Kawashima N, Fujii M, Wang S, Quoc TQ, Yu Z, Okiji T. MicroRNA-146b-5p Suppresses Pro-Inflammatory Mediator Synthesis via targeting TRAF6, IRAK1, and RELA in lipopolysaccharide-Stimulated human dental pulp cells. *International Journal of Molecular Sciences*. 2023.04; 24(8);
7. Ohkura N, Yoshida K, Yoshida N, Oda Y, Edanami N, Ohshima H, Takenaka S, Okiji T, Noiri Y. Prostaglandin E2-Transporting pathway and its roles via EP2/EP4 in cultured human dental pulp *Journal of Endodontics*. 2023.04; 49(4); 410-418
8. Okihata R, Michi Y, Sunakawa M, Tagashira Y. Pharmacist-led multifaceted intervention in an antimicrobial stewardship program at a university dental hospital in Japan. *Journal of Hospital Infection*. 2023.04; 136; 30-37
9. Thu M, Ebihara A, Maki K, Kimura S, Kyaw MS, Kasuga Y, Nishijo M, Okiji T. Dynamic torque and screw-in force of four different glide path instruments assessed in simulated single- and double-curved canals: An in vitro study *Journal of Dental Sciences*. 2023.10; 18(4); 1598-1603
10. Tazawa K, Sasaki H. Three-dimensional cellular visualization in mouse apical periodontitis using combined whole-mount staining and optical tissue clearing. *Journal of Oral Biosciences*, 2023.05;65(1);132-135
11. Tazawa K, Jadhav R, Azuma MM, Fenno JC, McDonald NJ, Sasaki H. Hypochlorous acid inactivates oral pathogens and a SARS-Cov-2-surrogate *BMC Oral Health*, 2023.02;23(1);111

[Books etc]

1. Kawamura T, Watanabe S, Kouno A, Okiji T. Reconsider endodontic treatment. the Quintessence. 2023.10 120-121

[Misc]

1. Toyoda K, Watanabe S, Okiji T. Taper 0.06 versus taper 0.04: the impact on the danger zone. the Quintessence 2023.11; 42(11);194-195
2. Oshima R, Maki K, Okiji T. Outcome of selective root canal retreatment—a retrospective study. The Nippon DentaReview 2023.09; 83(9); 128-129
3. Watanabe S, OkijiT. Outcome and associated predictors for nonsurgical management of large cyst-like periapical lesions: a CBCT-based prospective cohort study. the Quintessence. 2023.07; 42(7); 204-206
4. Hirano K, Watanabe S, Okiji T. The impact of an enhanced infection on molar root canal treatment outcome - a randomized clinical trial. the Quintessence. 2023.05;41(5); 219-221
5. Toyoda K, Maki K, Okiji T. Comparative evaluation of complete and partial pulpotomy in mature permanent teeth with symptomatic irreversible pulpitis: a randomized clinical trial. The Nippon Dental Review 2023.01; 83(1)122-123
6. Ohshima R, Watanabe S, Okiji T. Prognostic factors and primary healing on root perforation repaired with MTA: a 14-year longitudinal study. the Quintessence 2023.04;42(4); 222-223

[Conference Activities & Talks]

1. Okiji T. Endodontic management of traumatized teeth: Application of MTA. Clinical Workshop, Japan Association of Dental Traumatology 2023.12.03 Tokyo
2. Yu Z, Kawashima N, Wang S, Okiji T. MicroRNA-27a promotes osteo-/odontoblastic differentiation of human dental pulp stem cells by targeting dickkopf homolog 3. The 88 th annual meeting of the Stomatological Society 2023.12.01Tokyo
3. Wang S, Kawashima N, Yu Z, Okiji T. MicroRNA-27a downregulates proinflammatory cytokines expression in LPS-stimulated human dental pulp cells. The 88 th annual meeting of the Stomatological Society 2023.12.01Tokyo
4. Okiji, T. Current trends in endodontics. Special Lecture, Koganei Dental Association 2023.11.28 Koganei
5. Myint P, Watanabe S, Mochizuki S, Natori K, Okiji T. Efficacy of Er:YAG laser-activated irrigation in cleaning root canals with simulated internal resorption cavities. The 35 th annual meeting of Japanese Society for Laser Dentistry 2023.11.25 Tokyo
6. Okiji, T. Vital pulp therapy. Special Lecture, Stomatology College of Dalian Medical University 2023.11.24 Dalian
7. Myint PYA, Watanabe S, Kawamura T, Natori K, Kouno A, Okiji T. Comparative evaluation on the removability of intracanal calcium hydroxide pastes. The 159th Meeting of the Japanese Society of Conservative Dentistry 2023.11.11 Hamamatsu
8. Nyein Chan Ko, Noda S, Okada Y, Tazawa K, Kawashima N, Okiji T. Biocompatibility and pro-mineralization effects of premixed calcium silicate-based materials on human dental pulp stem cells. The 159th Meeting of the Japanese Society of Conservative Dentistry 2023.11.11 Hamamatsu
9. Maki K, Kuroshima Y, Okada Y, Tazawa K, Kawashima N, Okiji T. Pre-Obturation microsurgical management of radicular cyst with persistent intracanal exudation: a case report. The 159th Meeting of the Japanese Society of Conservative Dentistry 2023.11.11 Hamamatsu
10. Mochizuki S, Watanabe S, Liu J, Okiji T. Smear layer removal efficacy of different irrigation techniques in conservatively instrumented root canals. The 25th KACD-JSCD Joint Scientific Meeting 2023.11.04 Seoul, Korea
11. Ito R, Watanabe S, Satake K, Okiji T. Accuracy and efficiency of fiber post removal using surgical guides: An ex vivo study. The 25th KACD-JSCD Joint Scientific Meeting 2023.11.04 Seoul, Korea

12. Ohshima R, Kawashima N, Okiji T. Induction of odontoblasts in MTA-applied exposed molar pulp tissues is disturbed in osteopontin knockout mice. The 25th KACD-JSCD Joint Scientific Meeting 2023.11.04 Seoul, Korea
13. Okiji T. Endodontic management of traumatized teeth. Clinical Workshop, Japan Association of Dental Traumatology 2023.09.10 Tokyo
14. Kawashima N, Okiji T. Effects of hypoxic condition on mineralization and inflammation in the pulp tissue. Asian Pacific Endodontic Confederation (APEC) 2023.08.25 Taipei, Taiwan
15. Okada Y, Kawashima N, Okiji T. Endodontic retreatment of a maxillary first molar with multiple iatrogenic complications. Asian Pacific Endodontic Confederation (APEC) 2023.08.25 Taipei, Taiwan
16. Okiji T. Endodontic management of traumatized immature teeth. 23rd Scientific Meeting, Japan Association of Dental Traumatology 2023.07.23 Takamatsu
17. Okiji T. Diagnosis and management of traumatized teeth: Endodontic considerations. Clinical Workshop, Japan Association of Dental Traumatology 2023.07.16 Tokyo
18. Noritake K, Kabasawa Y, Hama Y, Tonami K, Ebihara A, Hideshima M, Umemori S, Kanamori Y, Miki H, Kido D, Nishiyama A, Nitta H. Newly introduced training contents in the clinical training programs for dental residents at Tokyo Medical and Dental University Hospital. The 42nd Annual Meeting of Japanese Dental Education Association 2023.07.15 Fukuoka
19. Chunmei R, Tazawa K, Kawashima N, Okiji T. Metformin suppresses pro-inflammatory cytokine expression in LPS-stimulated human dental pulp stem cells. The 44th meeting of Japan Endodontic Association 2023.07.09 Tokyo
20. Moe SK, Iino Y, Kimura S, Maki K, Ebihara A, Okiji T. Effect of repetitive pecking motions on torque/force generation and shaping ability of NiTi rotary instruments: An ex vivo study. The 44th meeting of Japan Endodontic Association 2023.07.09 Tokyo
21. Satoshi Watanabe, Sonoko Yabumoto, Nanami Nikaido, Hiroko Soeda, and Takashi Okiji. Cone-beam Computed Tomography Analysis of Root Canal Configuration of All Tooth Types. The 44th Annual Scientific Meeting of Japan Endodontic Association 2023.07.08 Tokyo
22. Okuda H, Kawashima N, Okiji T. Improvement of underwater hardening property of MTA cement by the addition of cellulose nanofibers. The 44th Annual Scientific Meeting of Japan Endodontic Association 2023.07.08 Tokyo
23. Okiji T. Vital Pulp Therapy: The Beginning of a New Era. The 44th Annual Scientific Meeting of Japan Endodontic Association 2023.07.08 Tokyo
24. Ito R, Watanabe S, Kouno A, Yamauchi S, Okiji T. Effect of heating on the physical properties of calcium silicate-based root canal sealers. The 158th Meeting of the Japanese Society of Conservative Dentistry 2023.06.22 Matsue
25. Okiji T. Intracanal medication with calcium hydroxide. The 158th Meeting of the Japanese Society of Conservative Dentistry 2023.06.22 Matsue
26. Tazawa K, Fujimura A, Okiji T, Sasaki H. Histological observation of the presence of lymphatic vessels and extracellular fluid drainage pathways in mouse dental pulp. The 158th Meeting of the Japanese Society of Conservative Dentistry 2023.06.22 Matsue
27. Watanabe S. Root canal irrigation using Er:YAG laser. Momose Dental Clinic Meeting 2023.04.15 Tokyo
28. Okiji T. Trends in vital pulp therapy. Kantoh Endodontic Association 2023.02.05 Tokyo
29. Watanabe S. LAI using Er:YAG laser. E-school Japan Coaching Alumni Meeting 2023.01.29 Tokyo

[Awards & Honors]

1. Watanabe S. The 44th Annual Scientific Meeting of Japan Endodontic Association Excellence Presentation Award, The 44th Annual Scientific Meeting of Japan Endodontic Association, 2023.07
2. Okiji T. Japanese Association for Dental Science President's Award. 2023. 02.
3. Okuda H. The 44th Annual Scientific Meeting of Japan Endodontic Association Wakai Award, The 44th Annual Scientific Meeting of Japan Endodontic Association, 2023.07
4. Myint P. Best Presentation Award, The 35th Annual Meeting of Japanese Society for Laser Dentistry 2023.11

Advanced Prosthodontics

Professor – Noriyuki Wakabayashi

Associate Professor – Takeshi Ueno (～October), Yuka Sumita (～May)

Junior Associate Professor – Atsushi Takaichi (June～), Kousuke Nozaki,
Mariko Hattori (career advancement) (June～), Junichiro Wada (December～)

Assistant Professor – Atsushi Takaichi (～May), Kensuke Takakusaki, Mariko Hattori (～May),
Natsuko Murakami, Mai Murase (June～), Junichiro Wada (～November)

Restart Postdoctoral (RPD) Research Fellowships - Yuka Kajima

Project Assistant Professor - Mihoko Haraguchi, Mai Murase (～May), Toshiki Yamazaki

Hospital Staff – Hisami Okawara (～March), Kim Eung Yeol (～March), Kazuki Sakamoto (～March),
Hirokazu Sato, Shintaro Suzuki, Hiroko Tani, Miyo Tsuji (April～), Tomiharu Nagayama,
Haruka Fujita (～March), Hitomi Matsuno (April～)

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

Graduate Students - Ali Ahmed Sameir Mohamed, Ali Islam Elsayed, Alkrayem Bilal Lukman,
Yurika Ishioka, Yuji Uchida, Miona Utsumi, Qu Wenri, Wu Huaze, Gao Yuan (～March),
Yoshio Kobayashi, Kohei Komine, Shinsuke Koyama, Jiang Mengtian, Zhiwei Zhou, Zou Shiqi,
Huichuan Xu, Satsuki Tanaka, Miyuki Tanimoto, Zhang Yihui, Zhang Fan, Zhang Maorui, Zheng Jingpu,
Ding Zhiyuan, Thida Phyto, Chugh Anshul, Dong Jialin, Towithelertkul Cheewin (～March), Han Xuewei,
Bai Ziyi, Asuka Hirata, Pradhan Nehasha,
Miao Menghan (April～), Yuki Mouri, Yang Shiyi, Yu Hongli, Bin Li, Wang Jiangyu, Wang Yujia (～March)

Part-time Special Student - Arwa Hammam Melhem (October～), Kazuki Nakane, Pang Xinyu,
Miao Menghan (～March), Kazuma Mori, Teruyuki Yoda

Registered Resident - Tetsu Sato

Designated Professor, Tokyo Medical and Dental University - Yuka Sumita (June～)

Clinical Professor - Masaru Yatabe

Part-time Lecturer (Faculty of Dentistry) - Takayuki Arai, Yasuha Ikawa, Keigo Isoshima, Hideaki Inagawa,
Shusuke Inukai, Yuki Iwaki, Takeshi Ueno (November～), Keichiro Uchikura, Hirofumi Uchida,
Elbashti Mahmoud Ellarousi, Hisami Okawara, Takeshi Otsubo, Masahiro Ona, Taihei Kasai,
Ryunosuke Kazama, Kim Eung Yeol, Hayato Kumagai, Masato Kotake, Hirofumi Sato, Natsuki Suzuki,
Yuka Sumita, Takashi Sekinishi, Yuko Teruyama, Yusuke Toyoshima, Yasuo Nakajima,
Koji Nagata, Kazutoshi, Nakamura, Gen Nabeshima, Noriko Hatano, Yoko Hayashi,
Hironari Hayama, Kazuyuki Handa, Shiro Hibi, Masahiro Hirasawa, Kengo Fujiki,
Haruka Fujita (April～), Ichiro Minami, Yesiboli Yeerken (～March), Chie Watanabe

Part-time Lecturer (Graduated School) - Yuki Arai, Ken Inohara, Shogo Ozawa, Chihiro Tanikawa,
Hideharu Hibi, Kazuhiro Hori, Hitoshi Mukohyama

Visiting Researcher - Kweh Ting Jing, Malaysia, 3-14 April 2023.

(1) Outline

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. After the reorganization of prosthodontic departments based on the research fields in 2021 and the acceptance of the staff from the Department of Maxillofacial Prosthetics because of its discontinuation in 2022, as the Department of Advanced 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, Junichiro Wada

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

AMED Translational Research Program: Mihoko Haraguchi

< 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 (Yuka Sumita)

Yamaha Corporation, Yamaha Music Foundation (Yuka Sumita, Mariko Hattori)

The MIKIYA Science And Technology Foundation (Yuka Sumita)

Tokyo metropolitan government (Yuka Sumita)

Innovation Idea Contest (Mariko Hattori)

Innovation Idea Contest (Mariko Hattori)

< WISE Program >

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

(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). 7 April, 14 April, 21 April, 6 October 2023.

(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]

1. 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. 2023.04; 67(2); 196-205

2. Yue Yin, Kosuke Nozaki, Reina Nemoto, Omnia Saleh, Yayoi Oishi, Mayuko Matsumura, Wataru Komada, Hiroyuki Miura, Kenji Fueki. Marginal fit and retention force of zirconia resin-bonded fixed dental prostheses in the posterior region with different designs *Journal of Dental Sciences*. 2023.12;
3. Yurika Ishioka, Junichiro Wada, Eung-Yeol Kim, Kazuki Sakamoto, Yuki Arai, Natsuko Murakami, Toshiaki Yamazaki, Kensuke Takakusaki, Hironari Hayama, Miona Utsumi, Shunsuke Inukai, Noriyuki Wakabayashi. Morphological Comparison of Residual Ridge in Impression for Removable Partial Denture between Digital and Conventional Techniques: A Preliminary In-Vivo Study *Journal of Clinical Medicine*. 2023.11; 12(22); 7103
4. Bai Z, Hattori M, Sumita YI, Wakabayashi N. Case report of a patient with mandibulectomy followed up for 11 years. *Journal of oral science*. 2023.11;
5. Wu, HZ; Ueno, T; Nozaki, K; Xu, HC; Nakano, Y; Chen, P; Wakabayashi, N. Lithium-Modified TiO₂ Surface by Anodization for Enhanced Protein Adsorption and Cell Adhesion *ACS APPLIED MATERIALS & INTERFACES*. 2023.11; 15(48); 55232-55243
6. Gao Y, Hattori M, Sumita YI, Wakabayashi N. Creating and analyzing digital scans of a mandibulectomy cast with simulated trismus. *J Prosthet Dent*. 2023.10;
7. Thant SW, Takaichi A, Kajima Y, Mohamed A, Nozaki K, Takahashi H, Chen P, Hanawa T, Wakabayashi N. Effect of ultraviolet irradiation treatment on shear bond strength between polymethyl methacrylate and cobalt-chromium-molybdenum alloy. *Dental materials journal*. 2023.09; 42(5); 748-755
8. Tanabe G, Towithelertkul C, Fukutome M, Sumita YI, Wakabayashi N. All-in-one-piece type prosthesis combining an obturator, a facial prosthesis, and glasses for the rehabilitation of midfacial defect and its speech evaluation: A clinical report. *Int J Maxillofac Prosthetics*. 2023.09; 6(1); 20-24
9. Amr Mohamed, Atsushi Takaichi, Yuka Kajima, Takao Hanawa, Noriyuki Wakabayashi. Reusing the Co-Cr-Mo support structures of selective laser melted parts: Evaluation of mechanical properties and microstructures *Sustainable Materials and Technologies*. 2023.07; 36; e00608
10. Linn Htat H, Takaichi A, Kajima Y, Kittikundecha N, Kamiyo S, Hanawa T, Wakabayashi N. Influence of stress-relieving heat treatments on the efficacy of Co-Cr-Mo-W alloy copings fabricated using selective laser melting. *Journal of prosthodontic research*. 2023.07;
11. Watanabe C, Wada J, Mizutani K, Nagayama T, Uchida H, Shibata Y, Wakabayashi N. Radiographic predictive factors for 10-year survival of removable partial denture abutment teeth: Alveolar bone level and density *Journal of Prosthodontic Research*. 2023.07; 67(3); 437-443
12. Mohamed, A; Takaichi, A; Kajima, Y; Hanawa, T; Wakabayashi, N. Reusing the Co-Cr-Mo support structures of selective laser melted parts: Evaluation of mechanical properties and microstructures *SUSTAINABLE MATERIALS AND TECHNOLOGIES*. 2023.07; 36;
13. Murase M, Pradhan N, Sumita YI, Wakabayashi N. Use of digital technology in prosthesis fabrication for an elderly patient with a maxillectomy and severe trismus: A clinical report. *J Prosthet Dent*. 2023.06; online.;
14. Ali IE, Enomoto K, Sumita Y, Wakabayashi N. Combined digital-conventional workflow to fabricate a definitive obturator from an interim obturator for a patient with an anterior maxillectomy defect. *J Prosthet Dent*. 2023.06; online.;
15. Wada, J; Wada, K; Garoushi, S; Shinya, A; Wakabayashi, N; Iwamoto, T; Vallittu, PK; Lassila, L. Effect of 3D printing system and post-curing atmosphere on micro- and nano-wear of additive-manufactured occlusal splint materials *JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS*. 2023.06; 142; 105799
16. 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*. 2023.05; 36(3); 366-374
17. Wang Y, Hattori M, Masaki K, Sumita YI. Detailed speech evaluation including formant 3 analysis and voice visualization in maxillofacial rehabilitation: A clinical report. *J Prosthet Dent*. 2023.05; online.;

18. Yu H, Fujita H, Akiyama M, Sumita YI, Wakabayashi N. Prevalence of Possible Dementia in Patients with Maxillofacial Defects and Difficulty of Inserting Obturator in Maxillectomy Patients: Toward Better Provision of Supportive Care. *Journal of clinical medicine*. 2023.04; 12(7);
19. Ali IE, Sumita YI, Hatano N, Kosaka M, Hoshi K, Wakabayashi N. Interdisciplinary management of a patient with medication-related osteonecrosis of the jaw: A clinical report. *Int J Maxillofac Prosthetics*. 2023.04; 6(1); 16-19
20. Mohamed A, Takaichi A, Kajima Y, Takahashi H, Wakabayashi N. Physical Properties of Additively Manufactured Tooth-Colored Material Attached to Denture Base-Colored Material in a Printed Monolithic Unit. *Polymers*. 2023.04; 15(9); 2134
21. Wada J, Wada K, Uctasli S, Wakabayashi N, Iwamoto T, Vallittu PK, Lassila L. Effect of splinting material type and location on resistance against deflection force of splinted periodontally compromised teeth with hypermobility. *Journal of the mechanical behavior of biomedical materials*. 2023.04; 142; 105873
22. Matsushita Y, Liu J, Chu AKY, Tsutsumi-Arai C, Nagata M, Arai Y, Ono W, Yamamoto K, Saunders TL, Welch JD, Ono N. Bone marrow endosteal stem cells dictate active osteogenesis and aggressive tumorigenesis. *Nature communications*. 2023.04; 14(1); 2383
23. Junichiro Wada, Kanae Wada, Sufyan Garoushi, Akikazu Shinya, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of 3D printing system and post-curing atmosphere on micro- and nano-wear of additive-manufactured occlusal splint materials *Journal of the Mechanical Behavior of Biomedical Materials*. 2023.03; 142; 105799
24. Yo Akiyama, Manabu Kanazawa, Maiko Iwaki, Tamaki Hada, Yumika Soeda, Ryosuke Otake, Kenta Kashiwazaki, Yuriko Komagamine, Natsuko Murakami, Atsushi Takaichi, Noriyuki Wakabayashi, Shunsuke Minakuchi. Fabrication of milled removable partial dentures using a custom plate with prefabricated artificial teeth. *J Prosthodont Res*. 2023.02;
25. Kazuki Sakamoto, Junichiro Wada, Yuki Arai, Hironari Hayama, Yurika Ishioka, Eung-Yeol Kim, Ryunosuke Kazama, Yusuke Toyoshima, Noriyuki Wakabayashi. Effect of abutment tooth location on the accuracy of digital impressions obtained using an intraoral scanner for removable partial dentures *Journal of Prosthodontic Research*. 2023.02;
26. Ali IE, Sumita YI, Wakabayashi N. Comparison of Praat and Computerized Speech Lab for formant analysis of five Japanese vowels in maxillectomy patients. *Front Neurosci*. 2023.02; 17; 1098197
27. Hattori M, Patzelt SBM, Itoh M, Sumita YI, Wakabayashi N. Case Report: Dental treatment for an oboist: Post-trauma prosthetic rehabilitation and evaluation of musical performance. *Front Psychol*. 2023.02; 13; 1022205
28. Hitomi Matsuno, Bin Li, Hisami Okawara, Yusuke Toyoshima, Cangyou Xie, Masud Khan, Natsuko Murakami, Kazuhiro Aoki, Noriyuki Wakabayashi. Effect of tension and compression on dynamic alveolar histomorphometry *Journal of the Mechanical Behavior of Biomedical Materials*. 2023.02;
29. Hitomi Matsuno, Bin Li, Hisami Okawara, Yusuke Toyoshima, Cangyou Xie, Masud Khan, Natsuko Murakami, Kazuhiro Aoki, Noriyuki Wakabayashi. Effect of tension and compression on dynamic alveolar histomorphometry *Journal of the Mechanical Behavior of Biomedical Materials*. 2023.02;
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31. 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*. 2023.01; 18(1); 95-104
32. Wang J, Murase M, Towithelertkul C, Tani H, Sumita YI. Custom-made radiotherapy prosthesis for external and internal radiotherapy in a patient with lip cancer. *J Oral Sci*. 2023.01; 65(1); 65-68
33. Kamel A, Yamazaki T, Murakami N, Lyu H, Komine K, Badr A, Fekry G, Takahashi H, Wakabayashi N. Retentive force of a conical crown with CAD/CAM-fabricated PEEK and zirconia secondary crowns on titanium implant abutments. *Dental materials journal*. 2023.01; 42(3); 336-342

34. Junichiro Wada, Kanae Wada, Mona Gibreel, Noriyuki Wakabayashi, Tsutomu Iwamoto, Pekka K. Vallittu, Lippo Lassila. Effect of Surface Polishing on Physical Properties of an Occlusal Splint Material for Additive Manufacturing under Protection Gas Post-Curing Condition Polymers. 2023.01; 15(3); 625
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36. Mohamed A, Takaichi A, Kajima Y, Takahashi H, Wakabayashi N. Bond strength of CAD/CAM denture teeth to a denture base resin in a milled monolithic unit. Journal of prosthodontic research. 2023.01;
37. Towithelertkul C, Sumita YI, Haraguchi M, Murase M, Fujita H, Tanabe G, Kanazaki A, Yoshi S, Kosaka M, Hattori M. A 20-year clinical survey of radiotherapy prostheses at the Clinic for Maxillofacial Prosthetics of Tokyo Medical and Dental University Hospital. J Oral Sci. 2023.01; 65(1); 6-9
38. Yasuyuki Kowaka, Kosuke Nozaki, Tomoyuki Mihara, Kimihiro Yamashita, Hiroyuki Miura, Zhenquan Tan, Satoshi Ohara. Development of Nanosheets with High Dye Degradation Performance by Regulating Crystal Growth. Materials (Basel). 2023.01; 16(3);
39. Ali IE, Otomaru T, Sumita YI. Refabrication of an implant-retained obturator using the denture duplication technique in a bilateral maxillectomy patient with a free fibula osteocutaneous flap. J Prosthodont Res. 2023.01; 67(1); 157-160
40. Liu R, Hattori M, Zhang M, Sumita YI. Use of an occlusal ramp for rehabilitation after a mandibulectomy and its effects on mastication. J Prosthet Dent. 2023.01; 129(1); 234-238
41. 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. 2023;

[Misc]

1. Elbashti ME. Tokyo 2nd edition of the international workshop for Young Maxillofacial Prosthetic Educators (ymPE): Building educators' skills and making impact. Int J Maxillofac Prosthetics. 2023.04; 6(1); 2-7
1. Sumita YI. Fabrication of the maxillofacial prostheses for the patient with mandible defect and future perspectives in maxillofacial prosthetic treatment. Journal of Japanese Dental Science Federation. 2023.12; 2; 44-53
2. Sumita YI. Psychoacoustic analysis of the noise produced by dental cutting equipment. Japanese Journal of Sensory Evaluatio. 2023.04; 27(1); 17-19
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? Part 4. Follow-Up after RPD Placement The Quintessence. 2023.02; 42(2); 66-91

[Conference Activities & Talks]

1. Atsushi Takaichi, Yuka Kajima, San Win Thant, Noriyuki Wakabayashi . Effect of ultraviolet treatment on shear bond strength between polymethyl methacrylate and cobalt–chromium–molybdenum alloy fabricated by selective laser melting . Ninth International Conference on Mechanics of Biomaterials and Tissues 2023.12.17 Waikoloa
2. Yuka Kajima, Atsushi Takaichi, Hein Linn Htat, Noriyuki Wakabayashi. Effect of beam spot size on the microstructural and mechanical properties of selective laser melted Co–Cr–Mo alloys. Ninth International Conference on Mechanics of Biomaterials and Tissues 2023.12.17 Waikoloa
3. Chugh A. Exploring Life Opportunities: A Voyage from India to Japan. International College of Dentistry 2023.12.16 帝国ホテル東京
4. 白子儀, 服部 麻里子, 隅田 由香. 上顎骨切除術と下顎骨切除術を行った患者に対して obturator と occlusal ramp を併用した下顎義歯を使用した 1 例 (A case report of the use of an obturator and a mandibular prosthesis combined with the occlusal ramp for a patient with maxillectomy and mandibulome). 顎顔面補綴 2023.12.01

5. 于 紅莉, 藤田 遥, 隅田 由香. 頭頸部欠損患者における顎顔面補綴物挿入困難の有病率 より良い補綴治療の提供に向けて (Prevalence of the difficulty of inserting maxillofacial prostheses in patients with head and neck defects: toward better provision of supportive care). 顎顔面補綴 2023.12.01
6. Chugh A, Hattori M, Sumita YI, Wakabayashi N. Color stability of two pigmented silicone elastomers for maxillofacial prostheses with exposure to cold beverages: An in vitro study. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
7. Haraguchi M, Ali IE, Takada A, Sumita YI. Prosthetic rehabilitation in a severe case of MRONJ with total sequestration of the entire dentoalveolar segment. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
8. Ali IE, Sumita YI, Wakabayashi N. Advancing maxillofacial prosthodontics using pretrained convolutional neural networks: Image-based classification of the maxilla. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
9. Han X, Hattori M, Sumita YI, Haraguchi M, Wakabayashi N. Factors related to masticatory rhythm in patients with head and neck tumors. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
10. Yu H, Sumita YI, Wakabayashi N. 3D mandibular analysis following iatrogenic mandibular fracture associated with mandibulectomy: case report. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
11. Wang J, Murase M, Sumita YI, Wakabayashi N. Radiological protectivity of conventional heat-cured PMMA and 3D-printed PMMA for radiotherapy prostheses. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
12. Miao M, Sumita YI, Wakabayashi N. Using a convolutional neural network for image-based classification of the mandible in maxillofacial prosthodontics. The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2023.10.21 San Diego (USA)
13. Yoshio Kobayashi, Yuka Kajima, Atsushi Takaichi, and Noriyuki Wakabayashi. The effect of scanning strategies on the fitness accuracy and residual stress of SLM-fabricated 3-unit fixed dental prostheses. The 3rd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA-3) 2023.10.20 Tokyo
14. Jiang Mengtian, Kosuke Nozaki, Takeshi Ueno, Satoshi Ohara, Takayuki Mokudai, Noriyuki Wakabayashi. Influence of three kinds of ionic antibacterial agents on the antibacterial effect of titania. The 3rd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA-3) 2023.10.20
15. Bai Z, Han X, Sumita YI, Hattori M, Maki K, Aboelez MA, Wakabayashi N. Predicting maximum occlusal force and tongue pressure in head and neck cancer patients using decision tree analysis. The 20th Biennial Meeting of the International College of Prosthodontists 2023.10.15 Shanghai (China)
16. Merve Uctasli, Mine Betul Uctasli, Kanane Wada, Junichiro Wada, Lippo Lassila. Surface Topography of Different Types of CAD/CAM Restorative Materials. 2023 CED/NOF –IADR Oral Health Research Congress 2023.09.21 Rhodes, Greece
17. Jiang Mengtian, Kosuke Nozaki, Takeshi Ueno, Noriyuki Wakabayashi. Development of metal nanoparticle-modified titanium dioxide nanosheets through photodeposition. 9th International Summer Program, Tokyo Medical and Dental University 2023.08.01
18. Maorui Zhang, 福島雄大, 野崎浩佑, 中西秀之, 若林則幸, 位高啓史. Enhancement of bone regeneration by coadministration of angiogenic and osteogenic factors using messenger RNA. 第44回日本炎症・再生医学会 2023.07.12
19. Merve Uctasli, Kanane Wada, Junichiro Wada, Lippo Lassila, Mine Betul Uctasli. Surface morphology hybrid ceramic material after different etching protocol. The 7th International Congress on Adhesive Dentistry 2023.06.03 Konya, Turkey
20. Mohamed Ahmed Sameir, 正木 啓太, 服部 麻里子, 隅田 由香, 若林 則幸. 話者非依存型自動音声認識における上顎欠損患者の発話の影響 (The impact of maxillectomy patients' speech on contemporary speaker-independent automatic speech recognition platforms). 日本補綴歯科学会誌 2023.05.01

21. Maorui Zhang, Yuta Fukushima, Kosuke Nozaki, Noriyuki Wakabayashi, Keiji Itaka. Co-delivery of Runx2 and VEGF Messenger RNA by Polyplex Nanomicelles Improves the Process of Mandibular Bone Regeneration. 第 22 回日本再生医療学会総会 2023.03.24
 22. Xu Huichuan, Ueno Takeshi, Wu Haze, Nozaki Kosuke, Wkabayashi Noriyuki. Modified-Glutathione coating immobilized on titanium surface enhances its biocompatibility. . The 2023 AADOCR/CADR Annual Meeting & Exhibition 2023.03.16 Portland, Oregon, USA
 23. Wu Haze, Ueno Takeshi, Xu Huichuan, Nozaki Kosuke, Wkabayashi Noriyuki. Lithium-immobilized titanium surface by anodization with enhanced biological activity . The 2023 AADOCR/CADR Annual Meeting & Exhibition 2023.03.16
 24. Junichiro Wada. Physical properties of additive-manufactured occlusal splints. Turku mid-winter meeting 2023.02.03 Turku, Finland
-
1. Hiroyuki Ishiyama, Masayuki Hidashima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki, Kenji Fueki. The effect of reduction rate of respiratory resistance associated with mandibular advancement on the efficacy of oral appliance for obstructive sleep apnea.. The 22nd Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2023.10.08 Kyoto, Japan
 2. Ishioka Y, Wada J, Kim EY, Sakamoto K, Murakami N, Yamazaki T, Utsumi M, Inukai S, Wakabayashi N. Morphological comparison of residual ridge between digital and conventional impression techniques for removable partial denture. Annual meeting of Tokyo branch of Japan Prosthodontic Society, 2023 2023.12.03 Tokyo
 3. Li B, Murase M, Yamatani Y, Masaki K, Hattori M, Wakabayashi N. Using digital technology in fabricating hollow Palatal augmentation prosthesis for functional recovery to a hemiglossectomy patient: A clinical report. 2023 Annual Scientific Meeting of Japan Prosthodontic Society, Tokyo Branch 2023.12.03 Tokyo (Japan)
 4. Murase M, Tachikawa N, Hasegawa Y, Tomoda T, Marukawa E. A case of bone anchored prosthesis for left side maxillectomy. The 27th Annual Meeting of Japanese Academy of Maxillofacial Implants 2023.12.02 Tokyo (Japan)
 5. Hattori M, Murase M, Mouri Y, Matsui S, Wada J, Wakabayashi N. Retention of a speech-aid prosthesis using a magnetic attachment on a patient with cleft lip and palate: A case report. The 33rd Annual Meeting of the Japanese Society of Magnetic Applications in Dentistry 2023.11.11 Tokyo (Japan)
 6. Matsui S, Murase M, Mouri Y, Li B, Hattori M, Wada J, Wakabayashi N. The case report of maxillofacial prosthesis using a magnetic attachment after maxillary sinus cancer treatment. The 33rd Annual Meeting of the Japanese Society of Magnetic Applications in Dentistry 2023.11.11 Tokyo (Japan)
 7. Shintaro Suzuki, Junichiro Wada, Noriyuki Wakabayashi. A case rehabilitated using overdentures with magnetic attachments for a partially edentulous patient with severe periodontal disease. The 33rd Annual Meeting of the Japanese Society of Magnetic Applications in Dentistry 2023.11.11 Tokyo, Japan
 8. Qu Wenrui, Takaichi Atsushi, Kajima Yuka, Kamiyo Shingo, Wakabayashi Noriyuk. Effect of build orientation on trueness and adaptation of maxillary complete denture frameworks fabricated by selective laser melting. Japan Dental Science and Engineering Society Kinki/Chushikoku Regional Meeting Seminar 2023.10.29 Osaka
 9. Junichiro Wada. Reconsideration of removable partial denture from the viewpoint of the protection of periodontally weakened teeth. The 9th World Dental Meeting in Japan 2023 2023.10.01 Yokohama, Japan
 10. Haraguchi M, Omura K, Kugimoto T, Sumita YI. Prosthetic rehabilitations for patient with mandibular defect caused by BRONJ treatment. The 47th Annual Meeting of Japan Society for Head and Neck Cancer 2023.06.16 Osaka (Japan)
 11. Bai Z, Hattori M, Sumita YI. A case report of the use of an obturator and a mandibular prosthesis combined with the occlusal ramp for a patient with maxillectomy and mandibulectomy. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.03 Nagoya (Japan)

12. Yamatani Y, Kasahara T, Nakamura H, Hattori M, Masaki K, Sumita YI. Fabrication of a palatal augmentation prosthesis using digital technology. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.03 Nagoya (Japan)
13. Higashiyama K, Haraguchi M, Miyamoto Y, Ozawa H, Adachi T, Sumita YI. A case of oral hygiene management for a patient with perforated left buccal mucosa after surgery and proton radiotherapy for oral cancer. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.03 Nagoya (Japan)
14. Otomaru T, Fujita H, Teruyama Y, Sumita YI. Delivery of a CoCr metal based dento-maxillary prosthesis with custom made zirconium artificial teeth in a maxillectomy patient: A case report. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.03 Nagoya (Japan)
15. Haraguchi M, Towithelertkul C, Hattori M, Murase M, Fujita H, Sumita YI. A 20-year clinical survey of radiotherapy prostheses at the Clinic for Maxillofacial Prosthetics of Tokyo Medical and Dental University Hospital. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.02 Nagoya (Japan)
16. Fukutome M, Oki M, Fujita H, Sumita YI. A case of facial prosthesis retained on an exposed mandibular reconstruction plate after mandibulectomy due to osteoradionecrosis. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.02 Nagoya (Japan)
17. Yu H, Fujita H, Sumita YI. Prevalence of the difficulty of inserting maxillofacial prostheses in patients with head and neck defects -toward better provision of supportive care-. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.02 Nagoya (Japan)
18. Murase M, Pradhan N, Sumita YI. A case report on fabrication of denture using digital technology for a medication-related osteonecrosis of the jaw. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.02 Nagoya (Japan)
19. Haraguchi M, Towithelertkul C, Hattori M, Murase M, Fujita H, Sumita YI. A 20-year clinical survey of radiotherapy prostheses at the Clinic for Maxillofacial Prosthetics of Tokyo Medical and Dental University Hospital. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.02
20. Han X, Haraguchi M, Sumita YI. Effect of wearing a denture for masticatory rhythm in mandibulectomy patients. The 40th Annual Meeting of Japanese Academy of Maxillofacial Prosthetics 2023.06.02 Nagoya (Japan)
21. Haraguchi M, Makie A, Han X, Sumita YI. Cr-Br treatment for occlusion and aesthetic restoration in 2 patients with cleft lip and palate. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.26 Tokyo (Japan)
22. Masaki K, Sumita YI, Tonouchi E, Harazono Y, Morita K. A case of articulation therapy and surgery for a child with Tongue-tie with Autism Spectrum Disorder. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.26 Tokyo (Japan)
23. Sumita YI. Seminar: Long-term follow-up of a patient with cleft lip and palate using prosthetic supportive care. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.26 Tokyo (Japan)
24. Otomaru T, Hattori M, Sumita YI. Application of magnetic attachments to upper anterior teeth in a patient with cleft lip and palate. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.26 Tokyo (Japan)
25. Hattori M, Murase M, Haraguchi M, Sumita YI. Use of digital technology in prosthetic treatment on cleft-lip and palate patients: A case report . The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.26 Tokyo (Japan)
26. Murase M, Masaki K, Tamura S, Hattori M, Sumita YI. A case of right cleft lip and palate patient treated with speech-aid removable prostheses. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.26 Tokyo (Japan)
27. Matsumura M, Yanaka W, Nozaki K, Komada W, Kitazaki H, Baba S, Matsumura M, Fueki K. A case study of treatment methods for patients with resin and metal allergies based on patch test. The 132rd Annual Meeting of the Japan Prosthodontic Society 2023.05.21

28. Junichiro Wada. Practical considerations for interventional study -from planning to writing-. The 132rd Annual Meeting of the Japan Prosthodontic Society 2023.05.21 Yokohama, Japan
29. Matsumoto M, Matsumura M, Saleh O, Yanaka W, Beniya R, Nozaki K, Matsumura M, Wakabayashi N, Fueki K. Colorimetric study of anterior CAD/CAM crowns - Effect of opaque cement on metal abutment teeth. The 132rd Annual Meeting of the Japan Prosthodontic Society 2023.05.20
30. Takaichi A, Mohamed A, Kajima Y, Takahashi H, Wakabayashi N. Bond Strength of CAD/CAM Denture Teeth to a Denture Base Resin. 132th annual scientific meeting of Japan Prosthodontic Society 2023.05.20 Yokohama
31. Pradhan N, Murase M, Tani H, Sumita YI. Evaluation of nutritional status by brief type diet history questionnaire among head and neck cancer patients. The 38th Annual Meeting of Japanese Society for Clinical Nutrition and Metabolism 2023.05.09 Kobe (Japan)
32. Matsumura M, Nozaki K, Yanaka W, Saleh O, Matsumura M, Fueki K. Effect of abutment teeth and luting cement on color tone of anterior CAD/CAM crowns. The 14th Annual Meeting of the Japan Academy of Digital Dentistry 2023.04.23
33. Qu W, Kajima Y, Takaichi A, Wakabayashi N. Preliminary research on the trueness of complete denture framework fabricated with contactless support by selective laser melting. The 81th General Session of the Japanese Society for Dental Materials and Devices 2023.04.15 Funabori
34. Komine K, Murakami N, Yamazaki T, Wakabayashi N. Effect of restorative material thickness on thermal stress. The 81st General Session of the Japanese Society for Dental Materials and Devices 2023.04.15 Tower Hall Funabori

[Awards & Honors]

1. The 2023 AAMP Student Poster Competition, Research-2nd Place (Ali IE), The 70th Annual Meeting of the American Academy of Maxillofacial Prosthetics, 2023.10

[Others]

1. 2nd International Workshop for Young Maxillofacial Prosthetics Educators (yMPE), 2023.03
The 2nd International Workshop for Young Maxillofacial Prosthetics Educators (yMPE) was hosted by the International Faculty Development Course (IFDC) and organized by the Maxillofacial Prosthetics team of TMDU, March 7-10, 2023. It was supported by an education grant, funded by the Education and Research Foundation of the International College of Prosthodontists (ICP). This workshop was also sponsored by the International Journal of Maxillofacial Prosthetics (iJMP).
2. Dysphagia Diet Awareness Workshop, 2023.03
Dysphagia Diet Awareness Workshop, was supported by the Female Faculty of Promotion Program (FFPP) of Tokyo Medical and Dental University and the International Faculty Development Course (IFDC) and organized by the Maxillofacial Prosthetics team of TMDU, March 9, 2023. It was sponsored by a grant, funded by the Initiative for Realizing Diversity in the Research Environment.

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

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

(2) Research

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

(3) Education

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

(4) Lectures & Courses

Acquire basic knowledge and an attitude of thinking continuously.

(5) Clinical Services & Other Works

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

(6) Clinical Performances

In dental implant clinic in TMDU, the number of clinical cases of dental implant treatments is the most in 29 dental schools in Japan. Difficult cases of dental implant treatments in other hospitals and clinics and problem cases, which have been treated by other dentists, are increasing. We can handle most of these difficult and problem cases.

(7) Publications

[Original Articles]

1. Nasuh S, Balci SO, Bozgeyik I, Ikeda MA, Tekayev M, Saadat KASM. ARID3A and ARID3B exert direct regulatory control over the long non-coding RNAs (lncRNAs) MALAT1 and NORAD within the context of non-small cell lung cancer (NSCLC). *Pathology, research and practice*. 2023.12; 252; 154948
2. Joseph Deering, Dalia Mahmoud, Elyse Rier, Yujing Lin, Anna Cecilia do Nascimento Pereira, Silvia Titotto, Qiyin Fang, Gregory R. Wohl, Feilong Deng, Kathryn Grandfield, Mohamed A. Elbestawi, Jianyu Chen. Osseointegration of functionally graded Ti6Al4V porous implants: Histology of the pore network *Biomaterials Advances*. 2023.11; 155;
3. Shedin Nasuh, Sibel Oguzkan Balci, Ibrahim Bozgeyik, Masa-Aki Ikeda, Muhammetnur Tekayev, Khandakar A.S.M. Saadat. . ARID3A and ARID3B exert direct regulatory control over the long non-coding RNAs (lncRNAs) MALAT1 and NORAD within the context of non-small cell lung cancer (NSCLC) *Pathol. Pathology - Research and Practice*. 2023.11; 252;
4. Karen Kuroyama, Ryuichi Fujikawa, Tomoyo Goto, Tohru Sekino, Fumiya Nakamura, Hiromi Kimura-Suda, Peng Chen, Hiroyasu Kanetaka, Tomoka Hasegawa, Kaname Yoshida, Masaru Murata, Hidemi Nakata, Masaya Shimabukuro, Masakazu Kawashita, Tetsuya Yoda & Taishi Yokoi.. Development of bioinspired damage-tolerant calcium phosphate bulk materials *Science and Technology of Advanced Materials*.. 2023.10; 2261836;
5. Kyaw TT, Abdou A, Arunjaroensuk S, Nakata H, Kanazawa M,. Effect of chemical and electrochemical decontamination protocols on single and multiple-used healing abutments: A comparative analysis of contact surface area, micro-gap, micro-leakage, and surface topography. *Clin Implant Dent Relat Res*.. 2023.09; 25(6); 1207-1215
6. Thiha Tin Kyaw , Ahmed Abdou, Sirida Arunjaroensuk, Hidemi Nakata, Manabu Kanazawa, Atiphan Pimkhaotham.. Effect of chemical and electrochemical decontamination protocols on single and multiple-used healing abutments: A comparative analysis of contact surface area, micro-gap, micro-leakage, and surface topography. *Clin Implant Dent Relat Res*.. 2023.09; 25(6); 1207-1215
7. Reziwanguli Aili, Hidemi Nakata, Munemitsu Miyasaka, Shinji Kuroda, Yukihiro Tamura, Taishi Yokoi, Masakazu Kawashita, Yasushi Shimida, Shohei Kasugai, Eriko Marukawa. Evaluation of a hydroxyapatite-crosslinked fish gelatin membranes. *Journal of Dental Sciences*.. 2023.08;
8. Masahiro Shimogishi, Sawako Kawakami, Noriko Tachikawa. Clinical Evaluation of Short (6 mm) and Longer Implants Placed Side by Side in Posterior Partially Edentulous Area: A 3-Year Observational Study. *International Journal of Dentistry*. 2023.07; 2023; 9086628
9. Yamazaki S, Lin Y, Marukawa E, Ikeda MA. Integrated Bone Formation Through In Vivo Endochondral Ossification Using Mesenchymal Stem Cells. *Journal of visualized experiments : JoVE*. 2023.07; (197);
10. Yamazaki, S; Lin, YJ; Marukawa, E; Ikeda, MA. Integrated bone formation through in vivo endochondral ossification using mesenchymal stem cells JOVE-JOURNAL OF VISUALIZED EXPERIMENTS. 2023.07; (197);
11. Shiba T, Komatsu K, Watanabe T, Takeuchi Y, Nemoto T, Ohsugi Y, Katagiri S, Shimogishi M, Marukawa E, Iwata T. Peri-implantitis management by resective surgery combined with implantoplasty and Er:YAG laser irradiation, accompanied by free gingival graft: a case report. *Therapeutic advances in chronic disease*. 2023.06; 14; 20406223231174816
12. Kang J, Shibasaki M, Terauchi M, Oshibe N, Hyodo K, Marukawa E. Comparative analysis of the in vivo kinetic properties of various bone substitutes filled into a peri-implant canine defect model. *Journal of periodontal & implant science*. 2023.06;
13. Jingyang Kang, Masaki Shibasaki, Masahiko Terauchi, Narumi Oshibe, Katsuya Hyodo, Eriko Marukawa. . Comparative analysis of the in vivo kinetic properties of various bone substitutes filled into a peri-implant canine defect model *J. Periodontal Implant Sci*. . 2023.06; 53;

14. Eskandar Fereiduni, Mohamed Balbaa, Dalia Mahmoud, Mohamed Elbestawi, Guichuan Li, Jianyu Chen, Lin Yujing. Processing of hydroxyapatite (HA)/Ti6Al4V composite powders via laser powder bed fusion (LPBF): effect of HA particle size and content on the microstructure and mechanical properties *Journal of Materials Research and Technology*. 2023.05; 24;
15. Yamazaki S, Hirayama R, Ikeda Y, Iseki S, Yoda T, Ikeda MA. Hyaluronic acid hydrogels support to generate integrated bone formation through endochondral ossification in vivo using mesenchymal stem cells. *PloS one*. 2023.02; 18(2); e0281345
16. Yujing Lin, Mohamed Balbaa, Wenyi Zeng, Yang Yang, Dalia Mahmoud, Mohamed Elbestawi, Feilong Deng, and Jianyu Chen. Osteogenic Properties of Titanium Alloy Ti6Al4V-Hydroxyapatite Composites Fabricated by Selective Laser Melting *Journal of Materials Engineering and Performance*. 2023; 1059-9495;
17. Kang J, Shibasaki M, Meng S, Marukawa E. The kinetics of growth factors secreted from tissue membranes induced in the process of applying Masquelet technique to various aged rats. *Journal of Bio-integration*. 2023; 13;

[Conference Activities & Talks]

1. Yamamoto Maiko, Shibasaki Masaki, Ogura Motohiro, Terauchi Masahiko, Marukawa Eriko. Comparative Study of Bone Grafting Materials Filled in Maxillary Implant-Adjacent Bone Defects. 9th Asian Biomaterials Congress 2023.11.21
2. 佐藤壮将、柴崎真樹、兵頭克也、窪内友也、寺内正彦、丸川恵理子. Clinical application of hydroxyapatite collagen nano composite for sinus augmentation in combination with/without guided bone regeneration. 9th Asian Biomaterial Congress 2023.11.21
3. Development of Amorphous Mg-Ca Coating for Protecting Hydrophilic Dental Implant Surfaces in the Atmosphere. 3rd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture -DEJIMA 2023- 2023.10.20
4. 佐藤壮将、柴崎真樹、兵頭克也、窪内友也、寺内正彦、丸川恵理子. Evaluation of the Efficacy of Applying Hydroxyapatite/Collagen Nano Composite in Sinus Augmentation. 30th annual meeting of European Association for Osseointegration 2023.09.30
5. Masahiko TERAUCHI, Kengo NARITA, Shigeru YAMANAKA, Tetsuya YODA, Eriko MARUKAWA. Surface Hydrophilic Modification of Dental Implant by Amorphous Mg-Ca coating. 25th The International Conference on Oral and Maxillofacial Surgery 2023.06.08
6. Masaki Shibasaki, Katsuya Hyodo, Masahiko Terauchi, Masataka Sato, Lin Yujing, Eriko Marukawa. Efficacy of hydroxyapatite/collagen nano composite in ridge augmentation and guided bone regeneration with/without sinus augmentation :5-year follow-up. International Osteology Symposium 2023.04.27
1. Murase M, Tachikawa N, Hasegawa Y, Tomoda T, Marukawa E. A case of bone anchored prosthesis for left side maxillectomy. The 27th Annual Meeting of Japanese Academy of Maxillofacial Implants 2023.12.02 Tokyo (Japan)

Plastic and Reconstructive Surgery

Professor:Mori Hiroki

Junior Associate Professor:Uemura Noriko

Graduate Student:Yamamoto Mao, Haga Yoshitaka, Kato Sayuri, Kojimahara Tomohiro, 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 using 3D camera
2. Sensory recovery in the nipple-sparing or skin-sparing mastectomy
3. Development of classification and algorithm in blepharoptosis and blepharospasm surgery
4. 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 anomaly (cleft lip and palate, microtia blepharoptosis or polydactyly etc), LASERs, cutaneous malignant tumor, skin ulcer, breast reconstruction, head and neck reconstruction, facial palsy, axillary osmidrosis.

(5) Publications

[Original Articles]

1. Ogiya A, Nagura N, Shimo A, Nogi H, Narui K, Seki H, Mori H, Sasada S, Ishitobi M, Kondo N, Yamauchi C, Akazawa K, Shien T, Collaborative Study Group of Scientific Research of the Japanese Breast Cancer

- Society. ASO Visual Abstract: Long-Term Outcomes of Breast Cancer Patients with Local Recurrence After Mastectomy Undergoing Immediate Breast Reconstruction-A Retrospective, Multi-institutional Study of 4153 Cases. *Annals of surgical oncology*. 2023.10; 30(11); 6543-6544
2. Ishida N, Tanaka K, Homma T, Mori H. Necessity of infraorbital wall reconstruction in patients with residual periosteum after total maxillectomy. *Journal of plastic, reconstructive & aesthetic surgery : JPRAS*. 2023.10; 85; 195-201
 3. Usami S, Kawahara S, Inami K, Hirase Y. Reconstructive Timing of Nail Preserved Fingertip Injury With Reverse Digital Artery Island Flap Hand (N Y). 2023.09; 18(6); 1012-1018
 4. Ogiya A, Nagura N, Shimo A, Nogi H, Narui K, Seki H, Mori H, Sasada S, Ishitobi M, Kondo N, Yamauchi C, Akazawa K, Shien T. ASO Author Reflections: Long Term Outcomes of Breast Cancer Patients with Local Recurrence After Mastectomy Undergoing Immediate Breast Reconstruction. *Annals of surgical oncology*. 2023.07; 30(11); 6541-6542
 5. Ogiya A, Nagura N, Shimo A, Nogi H, Narui K, Seki H, Mori H, Sasada S, Ishitobi M, Kondo N, Yamauchi C, Akazawa K, Shien T, Collaborative Study Group of Scientific Research of the Japanese Breast Cancer Society. Long-Term Outcomes of Breast Cancer Patients with Local Recurrence After Mastectomy Undergoing Immediate Breast Reconstruction: A Retrospective Multi-institutional Study of 4153 Cases. *Annals of surgical oncology*. 2023.07; 30(11); 6532-6540
 6. Haga Y, Yasunaga Y, Araki J, Nakano J, Mori H, Nakagawa M, Mukaigawa T. Perioperative Factors Aggravating Pharyngocutaneous Fistula After Total Laryngectomy HEAD AND NECK SURGERY. 2023.07; 91((1)); 84-89
 7. Hidaka T, Tanaka K, Minami M, Mori H, Okazaki M. Risk Factors for Postoperative Infection After Maxillary Reconstruction Using Skeletal Grafts. *The Journal of craniofacial surgery*. 2023.06; 34(7); e649-e651
 8. Nakagawa T, Mori H, Uemura N, Onishi I, Oda G. A Case of Breast Cancer With Ulceration of a Reconstructed Nipple Due to Local Recurrence. *Cureus*. 2023.05; 15(5); e39563
 9. Takeaki Hidaka, Kentaro Tanaka, Hiroki Mori. An Artificial Intelligence-Based Cosmesis Evaluation for Temporomandibular Joint Reconstruction. *Laryngoscope*. 2023.04; 133(4); 841-848
 10. Usami S, Minamikawa Y, Kinoshita Y, Ohira K, Hamada Y. Intramedullary Insetting of Silicone Implant for Lateral Stability in Distal Interphalangeal Joint Arthroplasty Plast Reconstr Surg Glob Open. 2023.04; 11(4); e4930
 11. Yamakado R, Ishitobi M, Kondo N, Yamauchi C, Sasada S, Nogi H, Saiga M, Ogiya A, Narui K, Seki H, Nagura N, Shimo A, Sakurai T, Niikura N, Mori H, Shien T, . Physicians' perception about the impact of breast reconstruction on patient prognosis: a survey in Japan. *Breast Cancer*. 2023.03; 30(2); 302-308

[Conference Activities & Talks]

1. Usamai S, Minamikawa Y, Hamada Y, Sonoki K. Distal and proximal interphalangeal joint arthroplasty for the symptomatic hand osteoarthritis. Annual meeting of APOA Hand & Upper Limb Society 2023.07.01 Seoul
2. Mori H, Uemura N, Kato S, Kurihara M, Kojimahara T, Tanaka K. Inframammary fold fixation in the DIEP flap breast reconstruction. 15th Japan-Korea Congress of Plastic and Reconstructive Surgery 2023.05.29 Kitakyushu
3. Kojimahara T, Uemura N, Minami M, Kato S, Oda G, Nakagawa T, Mori H. Evaluation of body composition after deep inferior epigastric artery perforator flap breast reconstruction by bioelectrical impedance analysis.. The 15th Japan-Korea Congress of Plastic and Reconstructive Surgery 2023.05.29 小倉市

Head and Neck Surgery

Professor: Takahiro Asakage

Junior Associate Professor: Yosuke Ariizumi, Kazuchika Ohno

Assistant Professor: Akihisa Tasaki

Specially Appointed Assistant Professor: Ryuhei Okada, Yumiko Tateishi, Hiroaki Kawabe

Senior Resident: Ryosuke Takahashi(-2023.3), Takafumi Ohno(2023.4-)

Graduate Student: Toshifumi Tomioka(-2023.3) Sadahiro Kishishita, Ryosuke Takahashi, Masaru Yokomura, Yuta Hoshi, Ai Watanabe, Taisei Nagahisa

(1) Outline

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

(2) Research

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

Surgical anatomy of the skull base.

Establishment of the standard neck dissection.

Treatment of pediatric head and neck tumors.

Chemoradiotherapy for head and neck cancers.

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

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

Human papilloma virus infection and head and neck cancer.

Polymorphisms in alcohol metabolism genes and Head and Neck Cancers.

(3) Education

Education: Undergraduate Course

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

Education :Graduate Course

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

(4) Publications

[Original Articles]

1. Shigeru Kondo, Ryuhei Okada, Yosuke Ariizumi, Takashi Kurita, Hiroshi Shintaku, Takahiro Asakage. A Case of Syphilis Suspected Preoperatively as a Case of Tongue Cancer. *Case Rep Otolaryngol.* 2023.11; 2023; 9469814
2. 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.* 2023.10; 50(5); 816-820
3. Sakihama Naoyuki, Okada Ryuhei, Takahashi Naoto, Fushimi Naoki, Ooka Tomoki, Kawabe Hiroaki, Ariizumi Yosuke, Ohno Kazuchika, Ueki Yutaka, Tayama Niro, Tsutsumi Takeshi, Asakage Takahiro. Post-intubation laryngeal injury after COVID-19 treatment causing dyspnea: A report of six cases(タイトル和訳中) *Auris·Nasus·Larynx.* 2023.10; 50(5); 816-820
4. Yuta Hoshi, Satoshi Shirakura, Masato Yamada, Tomonori Sugiyama, Nobuaki Koide, Satoru Tamii, Kyohei Kamata, Masaru Yokomura, Sotaro Osaki, Takafumi Ohno, Kazuhiro Yagihara, Hiroki Hara, Takeshi Beppu. Site of distant metastasis affects the prognosis with recurrent/metastatic head and neck squamous cell carcinoma patients treated with Nivolumab. *Int J Clin Oncol.* 2023.09; 28(9); 1139-1146
5. Takumi Kumai, Hirotaka Shinomiya, Hirofumi Shibata, Hideaki Takahashi, Toshihiro Kishikawa, Ryuhei Okada, Shigeharu Fujieda, Masafumi Sakashita. Translational research in head and neck cancer: Molecular and immunological updates. *Auris Nasus Larynx.* 2023.08; 51(2); 391-400
6. Ryuhei Okada. [V. Future Prospects of Photoimmunotherapy] . *Gan To Kagaku Ryoho.* 2023.07; 50(7); 794-798
7. 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.* 2023.05; 50(6); 1835-1836
8. Toshifumi Tomioka, Takeshi Beppu, Tetsuro Onitsuka, Yasushi Fujimoto, Kazuyoshi Kawabata, Kazuto Matsuura, Takashi Fujii, Ryuichi Hayashi, Takahiro Asakage. Post-operative progress of arm abduction function and rate of lymph node metastasis around the region of the accessory nerve: a multicentre prospective observational study. *Jpn J Clin Oncol.* 2023.04; 53(5); 401-409
9. Fuyuki F Inagaki, Hiroaki Wakiyama, Aki Furusawa, Ryuhei Okada, Takuya Kato, Daiki Fujimura, Shuhei Okuyama, Hiroshi Fukushima, Seiichiro Takao, Peter L Choyke, Hisataka Kobayashi. Near-infrared photoimmunotherapy (NIR-PIT) of bone metastases. *Biomed Pharmacother.* 2023.04; 160; 114390
10. Takuya Kato, Aki Furusawa, Ryuhei Okada, Fuyuki Inagaki, Hiroaki Wakiyama, Hideyuki Furumoto, Hiroshi Fukushima, Shuhei Okuyama, Peter L Choyke, Hisataka Kobayashi. Near-Infrared Photoimmunotherapy Targeting Podoplanin-Expressing Cancer Cells and Cancer-Associated Fibroblasts. *Mol Cancer Ther.* 2023.01; 22(1); 75-88
11. Shun Kaneko, Yasuhiro Asahina, Mina Nakagawa, Miyako Murakawa, Yasunari Miyazaki, Takahiro Asakage, Shohei Fukuda, Takeshi Namiki, Yoshito Kano, Masashi Nagata, Jun Tsuchiya, Masato Miyoshi, Fukiko Kitahata-Kawai, Sayuri Nitta, Yasuhiro Itsui, Sei Kakinuma, Ryuichi Okamoto. Factors associated with liver injury and prognosis in advanced cancer patients treated with immune checkpoint inhibitors. *Hepatol Res.* 2023.01;
12. Atsumori Hamahata, Takeshi Beppu, Miho Kirita, Hisato Konoeda, Hiroyuki Sakurai. Gemini Anastomosis for Dual Venous Anastomosis in Head and Neck Reconstruction. *Plast Reconstr Surg Glob Open.* 2023.01; 11(1); e4775
13. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol.* 35(3); 402-404

[Conference Activities & Talks]

1. Ryuhei Okada. Near-infrared Photoimmunotherapy: Clinical application and translational research. 16th Taiwan-Japan Conference on Otolaryngology-Head and Neck Surgery 2023.12 Taichung, Taiwan
2. Ryuhei Okada. Near-infrared Photoimmunotherapy: Translational research and clinical application. 23rd National Conference, Foundation for Head & Neck Oncology 2023.12 Daman, India
3. Ryuhei Okada, Hiroaki Kawabe, Takahiro Asakage. Near-infrared Photoimmunotherapy against Head and Neck Cancers. The 8th Conference of the Asian Society of the Head and Neck Oncology 2023.11 Bangkok, Thailand
4. Takahiro Asakage. Chairman : AOS Oral Session 39 Up to Date Head and Neck Cancer/Brain Tumor/Oral Cancer. 3rd Asian Oncology Society 2023.10.23 横浜
5. Ryuhei Okada. Local depletion of immune suppressor cells using near-infrared photoimmunotherapy. 7th World Congress of the International Federation of Head and Neck Oncologic Societies 2023.06 Rome, Italy
6. Takahiro Asakage. Instructional Course Surgical Management of Paraganglioma Diagnosis/Imaging. 7th World congress of the International Federation of Head and Neck Oncologic Societies 2023.06 Rome

Radiation Therapeutics and Oncology

Professor • Ryoichi Yoshimura

Research Associates Hirofumi Kuwabara, Takuya Nagano, Daigoro Matsubara

Hospital Staff members Tomonori Mikitani • Akane Arai

Graduate Students Kazuma Sasamura, Masahiro Yoshida • 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 763 patients, including 233 head and neck cancer patients, 167 urologic cancer patients, 83 breast cancer patients, 67 lung cancer patients, and 51 gynecologic cancer patients, were treated at our hospital in 2022.

(6) Clinical Performances

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

(7) Publications

[Original Articles]

1. Fujiwara M, Tanaka H, Kobayashi M, Nakamura Y, Fan B, Ishikawa Y, Fukuda S, Toda K, Yoshida S, Yokoyama M, Yoshimura R, Fujii Y. Neoadjuvant Chemoradiotherapy Followed by Radical Cystectomy for Muscle-Invasive Bladder Cancer: Analysis of Efficacy and Safety in 119 Patients. *Clinical genitourinary cancer*. 2023.11;
2. Yoshida Soichiro, Takahara Taro, Tanaka Hajime, Yokoyama Minato, Yoshimura Ryoichi, Fujii Yasuhisa. The role of prostate-specific antigen changes in predicting overall survival after progressive-site directed therapy for oligoprogressive castration-resistant prostate cancer *International Journal of Urology*. 2023.07; 30(7); 616-617
3. Ito K, Tokura S, Takazawa I, Yoshida N, Nakanishi T, Akiyama K, Onuma Y, Adachi T, Harada H, Nojima H, Miura M, Yoshimura R, Kabasawa Y. Clinical investigation of use of Episil® oral solution in oral mucositis during radiotherapy for head and neck cancer. *Heliyon*. 2023.06; 9(6); e15869
4. Kimura K, Yoshida S, Tsuchiya J, Kitazume Y, Waseda Y, Tanaka H, Yokoyama M, Toda K, Yoshimura R, Masaya I, Koga F, Tateishi U, Fujii Y. Novel utility of Vesical Imaging-Reporting and Data System in multimodal treatment for muscle-invasive bladder cancer. *European radiology*. 2023.04;
5. Saito AI, Hirai T, Inoue T, Hojo N, Kawai S, Kato Y, Ito K, Kato M, Ozawa Y, Shinjo H, Toda K, Yoshimura RI. Time to Pain Relapse After Palliative Radiotherapy for Bone Metastasis: A Prospective Multi-institutional Study. *Anticancer research*. 2023.02; 43(2); 865-873
6. Yoshida Soichiro, Takahara Taro, Arita Yuki, Toda Kazuma, Kimura Koichiro, Fujiwara Motohiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Patterns of recurrence in genuine and induced oligometastatic castration-resistant prostate cancer treated with progressive sitedirected therapy *International Journal of Urology*. 2023.02; 30(2); 204-210

[Conference Activities & Talks]

1. Yoshida Souichirou, Takahara Taro, Arita Yuki, Toda Kazuma, Kimura Koichiro, Fujiwara Motohiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Patterns of recurrence in genuine and induced oligometastatic castration-resistant prostate cancer treated with progressive site-directed therapy. The 110th Annual Meeting of the Japanese Urological Association 2023.04.01

Cognitive Neurobiology

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

Graduate Students
Moe Tanigawa
Nozomi Utsumi
Midori Wada
Yang Sun
Ibin Han
Shizuki Inaba
XianZhi Shao
Weida Wu
Yongjia Cheng
Kyosuke Goda
Mengke Liu

(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. Shizuki Inaba, Naofumi Uesaka, Daisuke H. Tanaka. Automatic quantification of disgust taste reactivity in mice using machine learning bioRxiv. 2023.04;

[Conference Activities & Talks]

1. 上阪 直史. Developmental oligodendrocytes as a key player in developmental synchrony and the modulation of brain functionality. 第 38 回熊本医学・生物科学国際シンポジウム「機能的脳神経回路システムの構築メカニズム」 2023.12.14
2. 谷川 萌、加藤 千帆、小野 卓史、上阪 直史. 成長期の鼻呼吸障害が小脳の発達と機能に与える影響. 第 14 回三叉神経領域の感覚運動統合機構研究会 抄録_谷川 1026 2023.12.10 千葉、日本
3. 上阪 直史. 神経細胞とシナプスによる脳腫瘍進展メカニズム. 第 4 6 回日本神経組織培養研究会 2023.12.02
4. Naofumi Uesaka, Daisuke Kawauchi. Neuronal and Synaptic Influences on Brain Tumors. シナプス研究会 2023 2023.10.19
5. 上阪 直史. 発達期小脳オリゴデンドロサイトはシナプス刈り込みと脳機能を制御する. 第 46 回日本神経科学大会 2023.08.04
6. Naofumi Uesaka, Daisuke Kawauchi. Conditional expression and activation of DREADDs reveals novel impact of neuron-tumor communications on brain tumor progression. 1st Heidelberg Conference on Cancer Neuroscience 2023.07.18 Germany
7. Uesaka Naofumi, Masumura Ryo, Sekiguchi Mariko. Development of cell-type specific AAV vectors in the mouse brain(タイトル和訳中). The Journal of Physiological Sciences 2023.05.01

8. Masumura Ryo, Uesaka Naofumi. Developmental oligodendrocytes contribute to cerebellar maturation(タイトル和訳中). The Journal of Physiological Sciences 2023.05.01
9. Tanigawa Moe, Kato Chiho, Ono Takashi, Uesaka Naofumi. Effects of unilateral nasal obstruction during the growth period on cerebellar neural circuit and function(タイトル和訳中). The Journal of Physiological Sciences 2023.05.01
10. 上阪 直史、増村 嶺、関口 真理子. 脳における細胞タイプ特異的な AAV ベクターの開発. 日本生理学会 第 100 回記念大会 2023.03.15
11. 増村 嶺、上阪 直史. 発達期オリゴデンドロサイトが小脳の成熟に貢献する. 日本生理学会第 100 回記念大会 2023.03.15
12. 谷川 萌 1、加藤 千帆 1、小野 卓史 1、上阪 直史. 成長期の鼻呼吸障害が小脳の神経回路と機能に及ぼす影響. 日本生理学会 第 100 回記念大会 2023.03.15

Department of Molecular Craniofacial Embryology and Oral Histology

Staffs and Students

Professor Sachiko ISEKI

Associate Professor Makoto TABATA

Junior Associate Professor Yuki YOSHIMOTO

Assistant Professor Noritaka ADACHI

Part-time lecturers Jun TAKEUCHI, Shigeru KURATANI, Masaki TAKECHI, Youichirou NINOMIYA, Daisuke KOYABU

Graduate Students ChengXue JIN, YuYan WANG, HanYang WANG, Aino SASABUCHI

Graduate Students (Others) YaHsuan YU (Maxillofacial Surgery)

Research students

NAMANGKALAKUL Worachat (Chulalongkorn University)

Rika TAKEUCHI (Jichi Medical University), XueYing GAO

(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. Katano W, Mori S, Sasaki S, Tajika Y, Tomita K, Takeuchi JK, Koshiba-Takeuchi K. Sall1 and Sall4 cooperatively interact with Myocd and SRF to promote cardiomyocyte proliferation by regulating CDK and cyclin genes. Development. 2023.12; 150(24); dev201913

2. Takayuki Onai, Noritaka Adachi, Hidetoshi Urakubo, Fumiaki Sugahara, Toshihiro Aramaki, Mami Matsumoto, Nobuhiko Ohno. Ultrastructure of the lamprey head mesoderm reveals evolution of the vertebrate head *iScience*. 2023.11; 26(15); 1-15
3. Hiromu Sato, Noritaka Adachi, Satomi Kondo, Chiyo Kitayama, Masayoshi Tokita. Turtle skull development unveils a molecular basis for amniote cranial diversity *Science Advances*. 2023.11; 9(46); 1-10
4. Mizukami K, Higashiyama H, Arima Y, Ando K, Okada N, Kose K, Yamada S, Takeuchi JK, Koshiba-Takeuchi K, Fukuhara S, Miyagawa-Tomita S, Kurihara H. Coronary artery established through amniote evolution. *Elife*. 2023.08; 12; e83005
5. Fukuma Y, Tokunaga T, Tanimura S, Yoshimoto Y, Mashimo T, Kaneko T, Tian X, Ideo K, Yonemitsu R, Matsushita K, Sugimoto K, Yugami M, Hisanaga S, Nakamura T, Uehara Y, Masuda T, Shukunami C, Karasugi T, Miyamoto T. Potential function of Scx+/Sox9+ cells as progenitor cells in rotator cuff tear repair in rats. *Biochemical and biophysical research communications*. 2023.07; 676; 84-90
6. Hoshino Yukiko, Takechi Masaki, Moazen Mehran, Steacy Miranda, Koyabu Daisuke, Furutera Toshiko, Ninomiya Youichirou, Nuri Takashi, Pauws Erwin, Iseki Sachiko. Synchronodrosis fusion contributes to the progression of postnatal craniofacial dysmorphology in syndromic craniosynostosis *JOURNAL OF ANATOMY*. 2023.03; 242(3); 387-401
7. Fuiten Allison M., Yoshimoto Yuki, Shukunami Chisa, Stadler H. Scott. Digits in a dish: An in vitro system to assess the molecular genetics of hand/foot development at single-cell resolution *FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY*. 2023.03; 11; 1135025
8. Lou Yixin, Matsumoto Yoshiro, Iseki Sachiko, Ono Takashi. Difference in apical resorption activity during rat molar root formation in response to mechanical force *EUROPEAN JOURNAL OF ORTHODONTICS*. 2023.02;
9. Yamazaki S, Hirayama R, Ikeda Y, Iseki S, Yoda T, Ikeda MA. Hyaluronic acid hydrogels support to generate integrated bone formation through endochondral ossification in vivo using mesenchymal stem cells. *PloS one*. 2023.02; 18(2); e0281345
10. Shunya Kuroda, Noritaka Adachi, Shigeru Kuratani. A detailed redescription of the mesoderm/neural crest cell boundary in the murine orbitotemporal region integrates the mammalian cranium into a pan-amniote cranial configuration. *Evolution & Development*. 2023.01; 25(1); 32-53
11. Namangkalakul W, Nagai S, Jin C, Nakahama KI, Yoshimoto Y, Ueha S, Akiyoshi K, Matsushima K, Nakashima T, Takechi M, Iseki S. Augmented effect of fibroblast growth factor 18 in bone morphogenetic protein 2-induced calvarial bone healing by activation of CCL2/CCR2 axis on M2 macrophage polarization. *Journal of tissue engineering*. 2023.01; 14; 20417314231187960
12. Taro Nojiri, Ingmar Werneburg, Vuong Tan Tu, Dai Fukui, Masaki Takechi, Sachiko Iseki, Toshiko Furutera, Daisuke Koyabu. Timing of organogenesis underscores the evolution of neonatal life histories and powered flight in bats *PROCEEDINGS OF THE ROYAL SOCIETY B*. 2023.01; 290; 20221928
13. Kawakami J, Hisanaga S, Yoshimoto Y, Mashimo T, Kaneko T, Yoshimura N, Shimada M, Tateyama M, Matsunaga H, Shibata Y, Tanimura S, Takata K, Arima T, Maeda K, Fukuma Y, Urugami M, Ideo K, Sugimoto K, Yonemitsu R, Matsushita K, Yugami M, Uehara Y, Nakamura T, Tokunaga T, Karasugi T, Sueyoshi T, Shukunami C, Okamoto N, Masuda T, Miyamoto T. Remnant tissue enhances early postoperative biomechanical strength and infiltration of Scleraxis-positive cells within the grafted tendon in a rat anterior cruciate ligament reconstruction model. *PloS one*. 2023; 18(11); e0293944

[Misc]

1. Yuki Yoshimoto, Yumiko Oishi. Mechanisms of skeletal muscle-tendon development and regeneration/healing as potential therapeutic targets. *Pharmacol Ther*. 2023.03; 243; 108357

[Conference Activities & Talks]

1. Chengxue Jin, Noritaka Adachi, Yuki Yoshimoto, Nobuyuki Kawashima, Masato S. Ota, Sachiko Iseki. Fibroblast growth factor signaling regulates the development of tooth root. 第 88 回 口腔病学会学術大会 2023.12.02
1. Chengxue Jin, Noritaka Adachi, Yuki Yoshimoto, Nobuyuki Kawashima, Masato S. Ota, and Sachiko Iseki. FGF18 regulates the development of dental root. The 65th Annual Meeting of Japanese Association for Oral Biology 2023.09.17 Chiyoda, Tokyo
2. Noritaka Adachi, Robert G. Kelly, Sachiko Iseki. Pharyngeal arch and pharynx - mammalian craniofacial development in light of the genetic cell lineage analysis in facial expression muscles. The 63rd Annual Meeting of the Japanese Teratology Society 2023.07.29 Tsukuba, Ibaraki
3. Katano W, Mori S, Sasaki S, Tajika Y, Tomita K, Takeuchi JK, Koshiba-Takeuchi K. Sall1 and Sall4 cooperatively interact with Myocd and SRF to promote cardiomyocyte proliferation by regulating CDK and cyclin genes. . The annual meeting of Society of Developmental Biology 2023.07.19
4. Noritaka Adachi, Robert G. Kelly, Sachiko Iseki. Development and peculiarity of facial expression muscles. The 128th Japanese Association of Anatomists, Annual meeting 2023.03.18 Tohoku University

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Hideto Kameda, Masahiro Shinohara

Research Student : Kei Gouchi

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 first grader.

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

(4) Lectures & Courses

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

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

(5) Publications

[Original Articles]

1. Namangkalakul W, Nagai S, Jin C, Nakahama KI, Yoshimoto Y, Ueha S, Akiyoshi K, Matsushima K, Nakashima T, Takechi M, Iseki S. Augmented effect of fibroblast growth factor 18 in bone morphogenetic

protein 2-induced calvarial bone healing by activation of CCL2/CCR2 axis on M2 macrophage polarization.
Journal of tissue engineering. 2023.01; 14; 20417314231187960

[Conference Activities & Talks]

1. Ken-ichi Nakahama. Visualization of RANK-RANKL binding in living cells. 2023.12.07 Kobe

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, Yasuhiro KURASAWA, Mari Shibata

Special Assistant Professor: Hirokazu KACHI, Erina TONOUCHI, Tomomi SAKUMA, Reiko HOSHI,

Yusoon KIM, (Jul.)Tomoki KANEMARU, (Aug.)Aya KAWAMATA

Hospital Staff: Daisuke YAMAMOTO, Katsuya Hyodo, (Apr.)Hiroki MASUDA, (Sep.)Mako Kubota

Graduate Student: Rina TAJIMA, Karen KUROYAMA, Koutaro YAMAZAKI, Yuka KAKU, Migyuan HSIAO,

Vu Viet Duc,YaXuan YU,THAI THANH HUY

Social Graduate Student: Takuya IWASAKI, Taishi NAKAMURA

Student: Souichi ROKUSHIMA, Yuuko KATSUKI, (Apr.)Yu-uta Atarashi, (Apr.)Makoto ARAKAWA,

(Apr.)Shougo KANN, (Apr.)Shinn MATSUMOTO

Clinical Professor: Fumiaki SATO, Takashi MISHIMAGI

Part-time Lecturer: Masashi YAMASHIRO, Jin SATO, Akiko KOBAYASHI, Kazuhiro YAGIHARA, Yutaka SATO,

Kazuto KUOHARA, Katsuya AIKOU, Yoshio OHYAMA, Junya KUMAGAI, Ryouusuke NAGAOKA,

Toshiyuki YAMADA, Youhei TSUTAKI, Tomohisa KITAMURA, Takasuke INADA, Narumi Oshibe

(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. Iwanaga J, Kitagawa N, Fukino K, Kikuta S, Tubbs RS, Yoda T. Perforation of the temporomandibular joint disc: cadaveric anatomical study. *International journal of oral and maxillofacial surgery*. 2023.11;
2. Ohyama Y, Inaba Y, Kubota M, Kanemaru T, Hasegawa K. CT-assessed sarcopenia and prognostic nutritional index are associated with poor prognosis in oral squamous cell carcinoma. *Oral and Maxillofacial Surgery*. 2023.11;
3. Kuroyama K, Fujikawa R, Goto T, Sekino T, Nakamura F, Kimura-Suda H, Chen P, Kanetaka H, Hasegawa T, Yoshida K, Murata M, Nakata H, Shimabukuro M, Kawashita M, Yoda T, Yokoi T. Development of bioinspired damage-tolerant calcium phosphate bulk materials. *Science and technology of advanced materials*. 2023.10; 24(1); 2261836
4. Shibata M, Takahara N, Kaneko T, Oki M, Sasaki Y, Tomomatsu N, Kurasawa Y, Nakakuki K, Yoda T.. Risk factors for postoperative facial swelling at 1 week after bimaxillary orthognathic surgery in Class III patients. *Journal of Stomatology, Oral and Maxillofacial Surgery*. 2023.10; 124(5); 101516
5. Takahara N, Shibata E, Tonouchi E, Kachi H, Tomomatsu N, Yoda T. Nasolabial soft tissue changes associated with posterior maxillary movement following anterior segmental osteotomy in skeletal Class II patients: A case series *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*. 2023.10;
6. Nobuyoshi Tomomatsu, Taishi Nakamura, Namiaki Takahara, Yasuhiro Kurasawa, Hirokazu Kachi, Tetsuya Yoda. Study of Anatomical Changes of the Inferior Nasal Passage After Le Fort I Osteotomy With Superior Repositioning. *The Journal of Craniofacial Surgery*. 2023.08;
7. Kitamura T, Tsugawa N, Ogasawara H, Matsumoto M, Itaka K, Okubo M, Yoda T, Suda T, Sato T. Vitamin D(3) Promotes Not Motor Coordination but Motor Skill Learning without Influence on Muscle Function. *Journal of nutritional science and vitaminology*. 2023.08; 69(4); 229-236
8. Shi Y, Ren X, Cao S, Xi Chen, Yuan B, Brasil da Costa FH, Rodriguez-Rosario AE, Corona A, Michikawa C, Osman AA, Xie T, Wang W, Sikora SG, Myers JN, Rangel R. TP53 gain-of-function mutation modulates the immunosuppressive microenvironment in non-HPV associated oral squamous cell carcinoma. *Journal for ImmunoTherapy of Cancer*. 2023.08; 11(8); e006666
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10. Chieko Michikawa , Toshiyuki Izumo , Tetsuya Yoda , Narikazu Uzawa . Small tumor invasion of metastatic lymph node can develop extranodal extension in oral cancer *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology Supports open access*. 2023.07;
11. Takahara Namiaki, Nakagawa Satoshi, Sumikura Kanako, Yoda Tetsuya. 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 Radiology*. 2023.07; 39(3); 475-481

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13. Nobuyoshi Tomomatsu, Namiaki Takahara, Yu Akaike, Yudai Sato, Yasuhiro Kurasawa, Tetsuya Yoda. Postoperative stability of bioresorbable plates made of 85:15 poly (L-lactide-co-glycolide) in Le Fort I osteotomy *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2023.05;
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19. Akaike Y, Morita KI, Sakamoto K, Tsushima F, Kayamori K, Maruta N, Yamazaki K, Anzai E, Tonouchi E, Harada H, Ikeda T, Yoda T. Automatic detection of spongiosis associated with oral lichenoid lesions using machine learning *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*. 2023.01; 35(4); 368-374
20. M Shibata, H Yoshitake, K Kayamori, T Ikeda, M Seki, T Yoda. Challenges in Diagnosis and Management of Palatal Hemangioma in an Infant: A Case Report *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*. 2023.01; 36; 67-70

[Conference Activities & Talks]

1. Nobuyoshi Tomomatsu, Namiaki Takahara, Yu Akaike, Yudai Sato, Yasuhiro Kurasawa, and Tetsuya Yoda. Postoperative stability of bioresorbable plate made of 85:15 poly (L-lactide-co-glycolide) in Le Fort I osteotomy. 25th ICOMs 2023.06.08 Vancouver
1. Mari Shibata, Namiaki Takahara, Nobuyoshi Tomomatsu, Yasuhiro Kurasawa, Yoshiyuki Sasaki, Tetsuya Yoda. Contributing factors for postoperative facial swelling one week after orthognathic surgery. 2023.11.10

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 YOSHIKAWA, Takayuki MIYAZAKI

Dental Resident

Hidekazu MATSUMOTO, Yuki NIKI, Atsuhiko INOUE,
Aina OKAWARA

Doctoral Program : Medical and Dental Sciences Track

Yoshiya KAISAKA, Misato SHIMIZU, Ryoto MACHIDA,
Aye Chan Myo, Hanae ARAI, Ayako SUZUKI, Yuri TAKAGIWA,
Satoka TAKEUCHI, Nao UKITA, Suzu CHIDA, Mikiko TERASHIMA,
Daigo YAMAHARA, Yunaho YONEMITSU, Liu Yinan, Lu Yeming
Aung Thet Khine, Ye Thiha, Aoi BEPPU, yae Phyto Htun,
Wang Junyan, Liu Lu, Ayaka KATO, Honoka SAITO, Yusuke SASAKI,
Marina TAKADA

Doctoral Program : Joint Degree Program (Chulalongkorn University)

Nicha Kositkittiwat, Wapol Sodsook, Ploysongsang Kwanrat

Graduate International Research Student Program

Kanako HORI, Mayu Oiwa, Yuichiro OMORI, Ami TSUNASHIMA,
Shintaro ARIKATA, Shiori OKUBO, Konosuke YOSHITANI,
Yuzuki ISHIZEKI, Yoshiki HAYASHI, Yumeno SANO,
Naoki NAGASHIMA, Aoi NOMURA, Hung Chia Yu,
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,
Hiroyuki KAMIMOTO, Yumi INAGAKI, Sakurako KANO,
Yuki SAGAWA

(1) Research

- 1) Basic and clinical studies of cleft lip and/or palate and other congenital craniofacial conditions
- 2) Morphological and physiological studies of facial deformity
- 3) Physiological study about control mechanism of stomatognathic function

- 4) Functional MRI study in the craniofacial region
- 5) Clarify the factors of malocclusion with epidemiological technique

(2) Education

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

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

(3) Clinical Performances

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

(4) Publications

[Original Articles]

1. Takada JI, Higashihori N, Kadota-Watanabe C, Kawamoto T, Toyofuku A, Moriyama K. Case report: Long-term management of occlusion after surgical-orthodontic treatment for a patient with drug-induced open bite developed after the onset of schizophrenia. *Frontiers in Psychiatry*. 2023.12; 14; 1304215
2. Myo AC, Kobayashi Y, Niki Y, Kamimoto H, Moriyama K. Exosome-mediated small interfering RNA delivery inhibits aberrant osteoblast differentiation in Apert syndrome model mice. *Archives of Oral Biology*. 2023.09; 153; 105753
3. Yogi A, Iemura R, Nakatani H, Takasawa K, Gau M, Yamauchi T, Yoshida M, Moriyama K, Ishii T, Hosokawa S, Yamada M, Suzuki H, Kosaki K, Kashimada K, Morio T. BMP2 is a potential causative gene for isolated dextrocardia situs solitus. *European journal of medical genetics*. 2023.08; 66(9); 104820
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6. Faisal A, Yoshizawa H, Matsumoto T, Miyamoto JJ, Moriyama K. Three-dimensional evaluation of orofacial movements during articulation in patients with skeletal Class III malocclusion with mandibular asymmetry clinical and investigative orthodontics. 2023.05; 82(1); 21-31
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9. 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*. 2023.02; 45(1); 20-28

[Conference Activities & Talks]

1. Arai H, Uezono M, Kikuchi M, Moriyama K. Investigation of the factors inducing rapid subperiosteal new bone formation by hydroxyapatite/collagen nanocomposite. The 88th Annual Meeting of Stomatological Society, Japan 2023.12.02 Tokyo
2. Arai H, Uezono M, Kikuchi M, Moriyama K. Investigation of the factors inducing rapid subperiosteal new bone formation by hydroxyapatite/collagen nanocomposite. TMDU-WISE Retreat 2023 2023.11.29 Shizuoka
3. Liu L, Kobayashi Y, Moriyama K. SASP senescent cells induces FGR/FGFR2 binding in coronal suture of Apert syndrome mice. TMDU-WISE Retreat 2023 2023.11.29 Shizuoka
4. Takagiwa Y, Higashihori N, Moriyama K. Roles of the histone methyltransferase SET domain bifurcated 1 in epithelial cells during tooth development. TMDU-WISE Retreat 2023 2023.11.29 Shizuoka
5. Yamahara D, Uezono M, Moriyama K. Biological response to miniscrew-induced bone injury in the surrounding tissue. TMDU-WISE Retreat 2023 2023.11.29 Shizuoka
6. Ukita N, Ogawa T, Moriyama K. Molecular characterization of SATB2 mutations causing SATB2-associated syndrome. TMDU-WISE Retreat 2023 2023.11.29 Shizuoka
7. Chida S, Kurimoto R, Takagi J, Moriyama K, Asahara H. Analyze the function of Mohawk homeobox during Orthodontic Tooth Movement via local control of gene expression. TMDU-WISE Retreat 2023 2023.11.29 Shizuoka
8. Suzuki A, Matsuyama Y, Tani Y, Anzai T, Izumi A, Doi S, Ogawa T, Fujiwara T, Moriyama K. Association between short stature in first grade and permanent teeth caries in sixth grade among elementary school children in Japan: a population-based cohort study. The 71st Annual Meeting of Japanese Association for Dental Research 2023.11.25 Miyagi
9. Moriyama K. management of Residual Alveolar Cleft from An Orthodontic Point of View. 2023 APCA, APCLPC & Chang Gung Forum: the 13th Biennial Congress of Asian Pacific Craniofacial Association (APCA) combined with the 10th Asian Pacific Cleft Lip-Palate & Craniofacial Congress (APCLPC) and the 9th International Workshop on Surgery-First Orthognathic Surgery (Chang Gung Forum) 2023.11.06 Taipei, Taiwan
10. Omori Y, Ogawa T, Kang J, Yokouchi R, Funahashi K, Uezono M, Moriyama K. Association between gender and tooth agenesis patterns in patients with non-syndromic cleft palate. 2023 APCA, APCLPC & Chang Gung Forum: the 13th Biennial Congress of Asian Pacific Craniofacial Association (APCA) combined with the 10th Asian Pacific Cleft Lip-Palate & Craniofacial Congress (APCLPC) and the 9th International Workshop on Surgery-First Orthognathic Surgery (Chang Gung Forum) 2023.11.06 Taipei, Taiwan
11. Jahangir Si S, Kadota-Watanabe C, Eisinger U, Hong C. Investigating p75NTR role in the TMJ Cartilage of Mice using bulk RNA Sequencing. Pacific Coast Orthodontic Society Annual session 2023 2023.11.02 Anaheim, CA, USA
12. Sodsook W, Kobayashi Y, Kamimoto H, Niki Y, Chantarawaratit P, Moriyama K. Roles of B-cell lymphoma 6 (BCL6) in orthodontic tooth movement of rat molars. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
13. Lu Y, Kobayashi Y, Niki Y, Moriyama K. Analysis of SOD3 expression patterns under hypoxia during tooth development in mice. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata

14. Kositkittiwani N, Ogasawara T, Uezono M, techalertpaosarn P, Moriyama K. Biomechanical evaluation of surgical-orthodontic treatment for facial asymmetry with reverse occlusal cant. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
15. Yin E, Kadota C, Hui P, Hong C. Characterizing p75NTR role on osteocytic/chondrogenic function in TMJ using CRISPR-Cas9.. UCSF Research and Clinical Excellence Day 2023 2023.10.11 San Francisco, USA
16. Sagawa Y, Ogawa T, Sudo T, Nagata Y, Moriyama K, Tanaka T. Exome analysis of short root anomaly in Japanese population. 68th Annual Meetings of the Japan Society of Human Genetics 2023.10.11 Tokyo
17. Ogawa T. Basic research on congenital anomalies with abnormal tooth development at Department of Maxillofacial Orthognathics. International Summer Program (ISP) 2023 Symposium 2023.08.01 Tokyo
18. Moriyama K. Epigenetic regulation of palatal development via histone methyltransferase SETDB1. CLEFT SEOUL 2023 2023.06.16 Seoul, Korea
19. Myo AC, Kobayashi Y, Niki Y, Kamimoto H, Moriyama K. Exosome-mediated small interfering RNA delivery inhibits aberrant osteoblast differentiation caused by FGFR2 activation in Apert syndrome model mice. The 98th Congress of the European Orthodontic Society 2023.06.11 Oslo, Norway
20. Myo AC, Kobayashi Y, Niki Y, Kamimoto H, Moriyama K. Exosome-mediated siRNA inhibits aberrant osteoblast differentiation in Apert syndrome model mice. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.25 Tokyo
21. Uezono M, Takakuda K, Moriyama K. New miniscrew-type absolute anchorage device for orthodontic treatment; a case report. AAO 2023 Annual Session 2023.04.21 Chicago, IL
1. Suzuki A, Tani Y, Ogawa T, Fujiwara T, Moriyama K. Frequent toothbrushing boost resilience among children under poverty: Results from A-CHILD, a population-based longitudinal study. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
2. Ogawa T. Establishment of a registry of rare genetic disorders with congenital maxillofacial anomalies. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
3. Ogawa T. Post-graduate education at Department of Maxillofacial Orthodontics, Tokyo Medical and Dental University (TMDU). The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
4. Takagiwa Y, Higashihori N, Moriyama K. The effects of histone methyltransferase SETDB1 in epithelial cells on tooth development. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
5. Yonemitsu Y, Uezono M, Ogasawara T, Shimizu M, Sugino T, Nakajima Y, Moriyama K. A trial to develop an automatic feature point extraction of the mandible using curvature-based registration. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
6. Inoue A, Higashihori N, Moriyama K. Effect of two-jaw surgery on soft tissue thickness in patients with facial asymmetry. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
7. Ishizeki Y, Ogasawara T, Miyazaki T, Hayashi Y, Beppu A, Tsuji M, Moriyama K. Clinical characteristics of orthodontic patients with syndromic oligodontia in our hospital. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
8. Yoshitani K, Ogawa T, Ukita N, Shimizu M, Matsumoto H, Yoshizawa H, FukumotoY, Komaki H, Moriyama K. Clinical survey on orthodontic treatment for patients with muscular diseases in our department. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
9. Miyazaki T, Tsuji M, Arikata S, Kobayashi Y, Moriyama K. Long-term follow-up of occlusion and temporomandibular joints of two orthodontic cases with Stickler syndrome. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
10. Uezono M, Takakuda K, Moriyama K. An orthodontic case treated with a new miniscrew-type absolute anchorage system. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata

11. Kobayashi Y, Yonemitsu Y, Takahara N, Yoda T, Higashihori N, Moriyama K. A retrognathic case with obstructive sleep apnea treated with Le Fort I osteotomy and genioplasty. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
12. Hayashi Y, Ogasawara T, Miyazaki T, Ishizeki Y, Beppu A, Tsuji M, Moriyama K. Maxillofacial characteristics of two cases with incontinentia pigmenti from orthodontic viewpoints. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
13. Omori Y, Ogasawara T, Beppu A, Yamahara D, Sagawa Y, Moriyama K. Non-surgical orthodontic treatment for maxillary protrusion with unilateral scissors bite. The 82nd Annual Meeting of the Japanese Orthodontic Society 2023.11.01 Niigata
14. Yoshizawa H, Niki Y, Inoue A, Hariu K, Oiwa M, Yoshitani K, Aung TK, Higashihori N, Moriyama K. Effect of surgical-orthodontic treatment on condylar movement in skeletal Class II patients. The 33rd Annual Meeting of the Japanese Society for Jaw Deformities 2023.06.08 Tokyo
15. Niki Y, Higashihori N, Inoue A, Hariu K, Ooiwa M, Yoshitani K, Yoshizawa H, Moriyama K. The effect of tongue-jaw bone relationship associated with surgical orthodontic treatment on respiratory function during sleep in Class II patients. The 33rd Annual Meeting of the Japanese Society for Jaw Deformities 2023.06.08 Tokyo
16. Higashihori N. Considering treatment for jaw deformity from the perspective of the jaw function. The 33rd Annual Meeting of the Japanese Society for Jaw Deformities 2023.06.08 Tokyo
17. Tonouchi E, Morita K, Harazono Y, Ogawa T, Moriyama K, Yonemitsu I, Ono T, Yoda T. Study on occlusion after palatoplasty . The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.25 Tokyo
18. Tsuji M, Omori Y, Moriyama K. Long-term outcome of two UCLP cases in which the occlusion was improved by maxillary expansion. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.25 Tokyo
19. Ukita N, Ogawa T, Moriyama K. A case of bilateral cleft lip and palate with de novo variant in AMOTL1. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.25 Tokyo
20. Ogawa T. Efforts to build a registry of genetic disease patients with craniofacial anomalies in orthodontics. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.25 Tokyo
21. Uezono M. Challenging for a novel orthodontic mini screw with high safety. The 47th Annual Meeting of Japanese Cleft Palate Association 2023.05.25 Tokyo

Department of Reconstructive Plastic Surgery

Professor: Kentaro Tanaka

Assistant Professor (Hospital): Naoya Ishida

Graduate students: Naoya Ishida, Kyoichi Murakami, Mayu Ueno

(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. Naoya Ishida, Kentaro Tanaka, Tsutomu Homma, Hiroki Mori. Necessity of infraorbital wall reconstruction in patients with residual periosteum after total maxillectomy. J Plast Reconstr Aesthet Surg. 2023.07; 85; 195-201
2. Hidaka T, Tanaka K, Minami M, Mori H, Okazaki M. Risk Factors for Postoperative Infection After Maxillary Reconstruction Using Skeletal Grafts. The Journal of craniofacial surgery. 2023.06; 34(7); e649-e651
3. Takeaki Hidaka, Kentaro Tanaka, Hiroki Mori. An Artificial Intelligence-Based Cosmesis Evaluation for Temporomandibular Joint Reconstruction. Laryngoscope. 2023.04; 133(4); 841-848
4. Kato S, Mori H, Koga H, Uemura N, Tanaka K. The triangular prism approximation method for volume estimation of deep inferior epigastric artery perforator flap in breast reconstruction Microsurgery. 2023.02; 43(2); 125-130

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

[Conference Activities & Talks]

1. Shogo Yoshihara, Takao Nakata, Naoki Noda, Jun Kashiwazaki, Issei Mabuchi. In vitro reconstruction of contractile rings using schizosaccharomyces pombe cytoplasmic extract. The 46th Annual Meeting of the Molecular Biology Society of Japan 2023.12.07 Kobe Convention Center
2. Aiko Takada, Tomohiro Ishii, Ken-ichi Nakahama, Toshifumi Asano, Takushi Ono, Takao Nakata. Optical control of osteoclast differentiation using optogenetic tools. The 75th Annual Meeting of the Japan Society for Cell Biology 2023.06.30 Nara Prefectural Convention Center

3. Toshifumi Asano, Takao Nakata. Visualization of myotube formation and control of intracellular calcium signal. The 22th Congress of the Japanese Society for Regenerative Medicine 2023.03.24 Kyoto International Conference Center
4. Li Kun, Toshifumi Asano, Takao Nakata. Analysis of skeletal myoblast fusion induced by calcium manipulation using optogenetics. The 128th Annual Meeting of the Japanese Association of Anatomists 2023.03.18 Tohoku University

Medical Biochemistry

Professor OISHI Yumiko
Associate Professor
KOIKE Hiroyuki
Assistant Professor
MATSUZAKI Kyoko

(1) Publications

[Original Articles]

1. Takahisa Matsuzaki, Yuma Kawano, Momoka Horikiri, Yuko Shimokawa, Takashi Yamazaki, Nao Okuma, Hiroyuki Koike, Masaki Kimura, Ryuzo Kawamura, Yosuke Yoneyama, Yasuro Furuichi, Fumihiko Hakuno, Shin-Ichiro Takahashi, Seiichiro Nakabayashi, Satoshi Okamoto, Hiromitsu Nakauchi, Hideki Taniguchi, Takanori Takebe, Hiroshi Y Yoshikawa. Preparation of mechanically patterned hydrogels for controlling the self-condensation of cells. STAR Protocols. 2023.07; 4(3); 102471
2. Aiko Watanabe, Hiroyuki Koike, Naoki Kumagami, Shigeki Shimba, Ichiro Manabe, Yumiko Oishi. Arntl deficiency in myeloid cells reduces neutrophil recruitment and delays skeletal muscle repair. Scientific Reports. 2023.04; 13(1); 6747
3. Caspase-11 contributes to site-1 protease cleavage and SREBP1 activation in the inflammatory response of macrophages 2023.01; 14; 1009973
1. Yosuke Sugita, Yoshimitsu Kuwabara, Akira Katayama, Shigeru Matsuda, Ichiro Manabe, Shunji Suzuki, Yumiko Oishi. Characteristic impairment of progesterone response in cultured cervical fibroblasts obtained from patients with refractory cervical insufficiency Scientific Reports. 2023.07; 13(1);

[Misc]

1. Yuki Yoshimoto, Yumiko Oishi. Mechanisms of skeletal muscle-tendon development and regeneration/healing as potential therapeutic targets. Pharmacol Ther. 2023.03; 243; 108357
2. Rie Ouchi, Hiroyuki Koike. Modeling human liver organ development and diseases with pluripotent stem cell-derived organoids. Frontiers in Cell and Developmental Biology. 2023.02; 11; 1133534

[Conference Activities & Talks]

1. Oishi Yumiko. 健康と疾病における多様な免疫代謝コミュニケーション 日米免疫学プログラム共催セッション 筋肉の修復と再生を制御するマクロファージの新規サブセットの同定 (Diverse immunometabolic communication in health and disease: US-Japan Immunology Program Co-organized Session Identification of a novel subset of macrophage that regulate muscle repair and regeneration). 日本免疫学会総会・学術集会記録 2023.12.01
2. 成 英瀾, 眞鍋 一郎, 早川 清雄, 遠藤 裕介, 大石 由美子. 炎症性カスパーゼ 11 は、マクロファージの炎症応答において、site-1 プロテアーゼの切断と SREBP1 の活性化に寄与する. 日本生化学会大会プログラム・講演要旨集 2023.10.01
3. Cell-cell interactions of post-injury muscle regeneration and tissue repair. 2023.09.14

Joint Surgery and Sports Medicine

Hideyuki Koga
Tomomasa Nakamura, Kazumasa Miyatake, Mai Katakura

Department of Cartilage Regeneration
Yusuke Nakagawa, Ryohei Takada

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
Yasumasa Tokumoto, Rena Hagiwara, Saya Watanabe
Yijie Gao

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. Naoto Watanabe, Takahisa Ogawa, Ryohei Takada, Yusuke Amano, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa, Kazumasa Miyatake. Association of osteoporosis and high serum homocysteine levels with intraoperative periprosthetic fracture during total hip arthroplasty: a propensity-score matching analysis. Arch Orthop Trauma Surg. 2023.12; 143(12); 7219-7227
2. Hao Ding, Hideyuki Koga, Hiroki Katagiri, Shoichi Hasegawa, Tatushiko Anzai, Mai Katakura, Aritoshi Yoshihara, Masaki Amemiya, Takashi Hoshino, Nobutake Ozeki, Tomomasa Nakamura, Yusuke

- Nakagawa. Low central sensitisation inventory score is associated with better post-operative outcomes of osteotomy around the knee. *Knee Surg Sports Traumatol Arthrosc.* 2023.12; 31(12); 5896-5904
3. Tetsuya Tachibana, Hiroki Katagiri, Hideyuki Koga, Takahisa Ogawa, Moe Suzuki, Tetsuya Jinno. Comparison of the cost analysis in total hip arthroplasty of anterior versus posterior approaches: A propensity score-matched cohort study in a single center Comparison of the cost analysis in total hip arthroplasty of anterior versus posterior approaches: A propensity score-matched cohort study in a single center. 2023.12; 1(1); 222-227
 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.* 2023.11; 28(6); 1325-1330
 5. Zhen Qu, Hideyuki Koga, Kunikazu Tsuji, Guo Tang, Yang Yang, Aritoshi Yoshihara, Mai Katakura, Hiroki Katagiri, Kazumasa Miyatake, Tomomasa Nakamura, Ichiro Sekiya, Yusuke Nakagawa. Hyaluronic acid sheet transplantation attenuates infrapatellar fat pad fibrosis and pain in a rat arthritis model. *J Orthop Res.* 2023.11; 41(11); 2442-2454
 6. Ichiro Sekiya, Hisako Katano, Ali Guermazi, Yugo Miura, Noriya Okanouchi, Makoto Tomita, Jun Masumoto, Yoshio Kitazume, Hideyuki Koga, Nobutake Ozeki. Association of AI-determined Kellgren-Lawrence grade with medial meniscus extrusion and cartilage thickness by AI-based 3D MRI analysis in early knee osteoarthritis. *Sci Rep.* 2023.11; 13(1); 20093
 7. Tetsuya Tachibana, Hideyuki Koga, Hiroki Katagiri, Takahisa Ogawa, Ryohei Takada, Kazumasa Miyatake, Tetsuya Jinno. Analysis of survivorship following periacetabular osteotomy for hip dysplasia based on three-dimensional acetabular coverage Analysis of survivorship following periacetabular osteotomy for hip dysplasia based on three-dimensional acetabular coverage. 2023.11; 2023(00); 1-8
 8. Jae-Sung An, Ahmed Mabrouk, Raghibir Khakha, Kristian Kley, Hideyuki Koga, Christophe Jacquet, Matthieu Ollivier. Assessment of return to sport and functional outcomes following distal femoral, double level and high tibial osteotomies for active patients with symptomatic varus malalignment. *Knee Surg Sports Traumatol Arthrosc.* 2023.10; 31(10); 4285-4291
 9. Hisako Katano, Nobutake Ozeki, Mitsuru Mizuno, Kentaro Endo, Noriya Okanouchi, Jo Fujita, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Morphological analysis of three-dimensional MR images of patellofemoral joints in asymptomatic subjects. *Sci Rep.* 2023.10; 13(1); 16750
 10. Zhu Ling, Hailati Aini, Shuhei Kajikawa, Jumpei Shirakawa, Kunikazu Tsuji, Yoshinori Asou, Hideyuki Koga, Ichiro Sekiya, Akira Nifuji, Masaki Noda, Yoichi Ezura. Mutation Are Treatable by Alendronate. *Pharmaceuticals (Basel).* 2023.10; 16(10);
 11. Aritoshi Yoshihara, Renaud Siboni, Yusuke Nakagawa, Caroline Mouton, Christophe Jacquet, Tomomasa Nakamura, Ichiro Sekiya, Romain Seil, Hideyuki Koga. Lateral-medial asymmetry of posterior tibial slope and small lateral tibial plateau articular surface depth are morphological factors of lateral meniscus posterior root tears in ACL-injured patients. *Knee Surg Sports Traumatol Arthrosc.* 2023.09; 31(9); 3594-3603
 12. Shoichi Hasegawa, Yusuke Nakagawa, Aritoshi Yoshihara, Tomomasa Nakamura, Hiroki Katagiri, Masaya Hayashi, Hideya Yoshimura, Tsuyoshi Nagase, Ichiro Sekiya, Hideyuki Koga. Older Age, Poor Preoperative Quadriceps Muscle Strength, and Residual Pain as Risk Factors for Poor Quadriceps Muscle Strength Recovery at 1 Year After ACL Reconstruction: A TMDU MAKs Study of 402 Patients. *Orthop J Sports Med.* 2023.09; 11(9); 23259671231194593
 13. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Kinesiophobia Is Negatively Associated With Psychological Readiness to Return to Sport in Patients Awaiting Anterior Cruciate Ligament Reconstruction. *Arthroscopy.* 2023.09; 39(9); 2048-2055
 14. Hiroki Katagiri, Yusuke Nakagawa, Yusuke Amano, Yoshiko Shirakawa, Nobutake Ozeki, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga. Decision regret following opening wedge high tibial osteotomy: Older age as a risk factor. *Knee.* 2023.06; 43; 62-69

15. Nobutake Ozeki, Hideyuki Koga, Yusuke Nakagawa, Hiroki Katagiri, Hisako Katano, Makoto Tomita, Jun Masumoto, Ichiro Sekiya. Association between knee cartilage thickness determined by magnetic resonance imaging three-dimensional analysis and the International Cartilage Repair Society (ICRS) arthroscopic grade. *Knee*. 2023.06; 42; 90-98
16. Shoichi Hasegawa, Jae-Sung An, Jun Hino, Yusuke Amano, Yusuke Nakagawa, Kazumasa Miyatake, Hiroki Katagiri, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. Therapeutic effect of C-type natriuretic peptide on persistent pain in a rat knee arthritis model. *J Orthop Surg (Hong Kong)*. 2023.06; 31(2); 10225536231181708
17. Hong CC, Lee JC, Tsuchida A, Katakura M, Jones M, Mitchell AW, Dalmau-Pastor M, Calder J. Individual fascicles of the ankle lateral ligaments and the lateral fibulotalocalcaneal ligament complex can be identified on 3D volumetric MRI. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA*. 2023.06; 31(6); 2192-2198
18. Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Nobutake Ozeki, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga. Comparison of Clinical Outcomes after Revision Anterior Cruciate Ligament Reconstruction using a Bone-patellar Tendon-bone Autograft and that Using a Double-Bundle Hamstring Tendon Autograft. *J Knee Surg*. 2023.05; 36(6); 613-621
19. Amano Y, Ozeki N, Matsuda J, Nakamura T, Nakagawa Y, Sekiya I, Koga H. Augmentation of a Nonanatomical Repair of a Medial Meniscus Posterior Root Tear With Centralization Using Three Knotless Anchors May Be Associated With Less Meniscal Extrusion and Better Compressive Load Distribution in Mid-Flexion Compared With Non-Anatomical Root Repair Alone in a Porcine Knee Model. *Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association*. 2023.05; 39(12); 2487-2498
20. Kei Sato, Atsuko Sato, Naoki Okuda, Matsubara Masaaki, Hideyuki Koga. A propensity score-matched comparison between Mako robotic arm-assisted system and conventional technique in total hip arthroplasty for patients with osteoarthritis secondary to developmental dysplasia of the hip. *Arch Orthop Trauma Surg*. 2023.05; 143(5); 2755-2761
21. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Association between landing biomechanics, knee pain, and kinesiophobia in athletes following anterior cruciate ligament reconstruction: A cross-sectional study. *PMR*. 2023.05; 15(5); 552-562
22. Yusuke Nakagawa, Kunikazu Tsuji, Tomomasa Nakamura, Hiroki Katagiri, Nobutake Ozeki, Mikio Shioda, Jae-Sung An, Ryu Yoshida, Ichiro Sekiya, Hideyuki Koga. Association of Infrapatellar Fat Pad Fibrosis at 3 Months After ACL Reconstruction With Short-term Clinical Outcomes and Inflammatory Cytokine Levels in the Synovial Fluid. *Orthop J Sports Med*. 2023.04; 11(4); 23259671231164122
23. M Isono, H Koga, Y Nakagawa, T Nakamura, I Sekiya, H Katagiri. Inferior Healing Rate in Isolated Meniscal Repair than that in Meniscal Repair with Concomitant ACL Reconstruction Evaluated with MRI. *Malays Orthop J*. 2023.03; 17(1); 61-69
24. Nobutake Ozeki, Mitsuru Mizuno, Shinobu Yanada, Takuya Okada, Rei Kubota, Yoshihisa Kushida, Hideto Furuoka, Kentaro Endo, Hisako Katano, Kentaro Nakamura, Shoji Ohya, Hideyuki Koga, Ichiro Sekiya. Autologous Synovial Mesenchymal Stem Cell Transplantation Suppresses Inflammation Caused by Synovial Harvesting and Promotes Healing in a Micro Minipig Repaired Meniscus Model. *Transplant Proc*. 2023.03; 55(2); 470-480
25. Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. Short-Term Outcomes after High Tibial Osteotomy Aimed at Neutral Alignment Combined with Arthroscopic Centralization of Medial Meniscus in Osteoarthritis Patients. *J Knee Surg*. 2023.02; 36(3); 261-268
26. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. *Orthop Traumatol Surg Res*. 2023.02; 109(1); 103147

27. Mai Katakura, Angela E Kedgley, Joseph W Shaw, Adam M Mattiussi, Shane Kelly, Richard Clark, Nick Allen, James D F Calder. Epidemiological Characteristics of Foot and Ankle Injuries in 2 Professional Ballet Companies: A 3-Season Cohort Study of 588 Medical Attention Injuries and 255 Time-Loss Injuries. *Orthop J Sports Med.* 2023.02; 11(2); 23259671221134131
28. Akane Ariga, Yuji Kohno, Yusuke Nakagawa, Toshifumi Watanabe, Hiroki Katagiri, Toshiyuki Ohara, Mikio Shioda, Nobutake Ozeki, Masaki Amemiya, Atsushi Okawa, Ichiro Sekiya, Hideyuki Koga. Simultaneous bilateral total knee arthroplasty is safe and effective for patients in different ages. *J Orthop Sci.* 2023.01; 28(1); 173-179
29. 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.* 2023.01; 32(1); 76-84
30. Ryuichi Nakamura, Masaki Amemiya, Tomoyuki Shimakawa, Masaki Takahashi, Kazunari Kuroda, Yasuo Katsuki, Akira Okano. Femoral-varus tibial-valgus osteotomy (FVTVO) for neutrally-aligned knee osteoarthritis with severe joint line obliquity enables return to sports activities: A case series study. *Asia Pac J Sports Med Arthrosc Rehabil Technol.* 2023.01; 31; 11-17
31. Koji Murofushi, Daisuke Yamaguchi, Koji Kaneoka, Tomoki Oshikawa, Hiroki Katagiri, Kenji Hirohata, Hidetaka Furuya, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity. *J Med Invest.* 2023; 70(1.2); 208-212

[Conference Activities & Talks]

1. Hideyuki Koga. Innovation of treatment for meniscus injury. 1st Annual Congress of The Japanese Knee Society 2023.12.08 Yokohama, Japan
2. Hideyuki Koga. Meniscal centralization. 67th Korean Orthopaedic Association Annual Meeting 2023.10.12 Seoul, Korea
3. Hideyuki Koga. Management of MMPRT with extrusion using centralization. 1st The Asian Meniscus Summit 2023.10.05 Seoul, Korea
4. Hideyuki Koga. How to improve root repair?. 1st The Asian Meniscus Summit 2023.10.05 Seoul, Korea
5. Yusuke Nakagawa, Aritoshi Yoshihara, Nobutake Ozeki, Hideyuki Koga. How to manage lateral meniscus posterior root tears. 1st The Asian Meniscus Summit 2023.10.05 Seoul, Korea
6. Hideyuki Koga. Medial Meniscus preservation strategies in knee osteotomies. Aix-Marseille university Ground Round 2023.09.14 Marseilles, France
7. Hideyuki Koga. Meniscus centralization -Solution to reduce meniscus extrusion-. 40th AGA Congress 2023.09.14 Berlin, Germany
8. Hideyuki Koga. How do we improve meniscus repair?. 17th International Cartilage Research Society World Congress 2023.09.10 Barcelona, Spain
9. Tetsuya Tachibana, Hiroki Katagiri, Tetsuya Jinno. Femoral Morphology in Developmental Dysplasia of the hip based on three-dimensional analysis with CT. 4th Annual congress of the ASHA 2023.09.09 Taiwan
10. Hideyuki Koga. FiberStitch & Meniscal Centralization. Arthrex Innovation Summit 2023.07.13 Singapore
11. Mai Katakura. MRI findings of the foot and ankle in asymptomatic professional ballet dancers. ISAKOS annual meeting 2023.06.18 Boston
12. Tomomasa Nakamura. Mechanical axis changes and its related factors on the whole leg preoperative planning x-rays under bilateral and unilateral weight-bearing in HTO patients. 2023 ISAKOS annual meeting 2023.06.18 Boston
13. Ryohei Takada, Naoto Watanabe, Kazumasa Miyatake, Naohiko Sugita, Tetsuya Jinno, Toshitaka Yoshii, Hideyuki Koga. Development of non-invasive augmented reality-based navigation system for total hip arthroplasty. The22th Annual Meeting of CAOS 2023.06.07 Pattaya (Thailand)

14. Hideyuki Koga. Meniscal Centralization, Root repair and complex meniscal pathologies. Arthrex Medical Education Program-Knee 2023.05.19 Singapore
15. Yusuke Nakagawa, Nobutake Ozeki, Hideyuki Koga, Ichiro Sekiya. Stem cell therapy using synovial MSCs for knee osteoarthritis. JOA annual meeting 2023.05.10 Yokohama, Japan
16. Hideyuki Koga. ACL injury mechanisms-lessons learned from video analyses. Sports Biomechanics Research Summit 2023.04.15 HongKong
17. Hideyuki Koga. Centralization & ramp lesion repair. Arthrex Knee Cadaver Training 2023.03.26 Singapore
18. Tetsuya Jinno, Gaku Koyano, Masanobu Hirao, Ryota Shinada, Tetsuya Tachibana, Moe Suzuki, Ryohei Takada, Kazumasa Miyatake. Preventive strategies for early and late periprosthetic femoral fracture after cementless total hip arthroplasty. The 53rd Annual Meeting of the Japanese Society for Replacement Arthroplasty 2023.02.17
19. Hideyuki Koga. Patients in Which Lateral Meniscus Repair Contributes to Controlling Pivot Shift Show Low Body Mass Index and Particular Bony Morphologies. ACL Study Group Meeting 2023.01.28 St. Kitts, Saint Christopher and Nevis
20. Hideyuki Koga. How to preserve meniscal function. Santy Center Orthopedique Invited lecture 2023.01.12 Lyon, France
21. Tomomasa Nakamura. Meniscus Functional Preservation using Centralization. Meniscus Centralization International Conference 2023.01.08 Changsha, China

Department of 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, Sinya Yuge
 Collaborative Researcher Kazuki Takahashi, Kazue Terasawa
 Graduate student Maki Saito, Kashio Fujiwara, Hisae Katsumata, Noriko Shibao, Honoka Hirose,
 Qianqian Miao, Lu Jin

(1) Outline

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

(2) Research

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

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

Bio-Matrix

Bio-Matrix

VASH1, which is induced expression by VEGF stimulation in endothelial cells, was re-identified as an enzyme of detyrosination. Detyrosination is one of the post-translational modification of microtubules. It is known that detyrosinated microtubules play a 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 the role as a detyrosination enzyme in the 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 have 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 serve 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. Kazue Terasawa, Tatsuro Seike, Kensaku Sakamoto, Kazumasa Ohtake, Tohru Terada, Takanori Iwata, Tetsuro Watabe, Shigeyuki Yokoyama, Miki Hara-Yokoyama. Site-specific photo-crosslinking/cleavage for protein-protein interface identification reveals oligomeric assembly of lysosomal-associated membrane protein type 2A in mammalian cells. *Protein Sci.* 2023.12; 32(12); e4823
2. Shiori Tokizaki, Katarzyna A Podyma-Inoue, Takehisa Matsumoto, Kazuki Takahashi, Miho Kobayashi, Haruka Ibi, Shizuka Uchida, Sadahiro Iwabuchi, Hiroyuki Harada, Shinichi Hashimoto, Kohei Miyazono, Mikako Shirouzu, Tetsuro Watabe. Inhibition of transforming growth factor- β signals suppresses tumor formation by regulation of tumor microenvironment networks. *Cancer Sci.* 2023.11;
3. Kazuki Takahashi*, Miho Kobayashi*, Hisae Katsumata, Shiori Tokizaki, Tatsuhiko Anzai, Yukinori Ikeda, Daniel M. Alcaide, Kentaro Maeda, Makoto Ishihara, Katsutoshi Tahara, Yoshiaki Kubota, Fumiko Itoh, Jihwan Park, Kunihiro Takahashi, Yukiko T. Matsunaga, Yasuhiro Yoshimatsu, Katarzyna A. Podyma-Inoue, Tetsuro Watabe (*: equally contribution). CD40 is expressed in the subsets of endothelial cells undergoing partial endothelial-mesenchymal transition in tumor microenvironment. *Cancer Science.* 2023.11; 115(2); 490-506
4. Tetsuro Watabe, Kazuki Takahashi, Kristian Pietras, Yasuhiro Yoshimatsu. Roles of TGF- β signals in tumor microenvironment via regulation of the formation and plasticity of vascular system. *Seminars in Cancer Biology.* 2023.07; 92; 130-138
5. Saranya Serirukchutarungsee, Ippei Watari, Masataka Narukawa, Katarzyna Anna Podyma-Inoue, Pornchanok Sangsuriyothai, Takashi Ono. Two-generation exposure to a high-fat diet induces the change of salty taste preference in rats. *Sci Rep.* 2023.04; 13(1); 5742

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1. Endothelial destabilization by tumor-derived exosome 2023.06; 46(1); 7-12

[Conference Activities & Talks]

1. Tetsuro Watabe. Targeting tumor microenvironment networks for developing novel therapeutic strategies. FAOPS 2023 (The 10th Federation of the Asian and Oceanian Physiological Societies Congress) 2023.11.01 Daegu
2. Halder Semanti, Yasuyuki Hanada, Yuka Ozeki, Honami Ogo, Yumi Omine, Katarzyna Inoue, Tetsuro Watabe, Akiyoshi Uemura and Koichi Nishiyama. Endothelial cell-pericyte interaction facilitates the establishment of vascular basement membrane with type-4 collagen deposition via Tgfb2-Alk5 in angiogenesis. The 96th Annual Meeting of the Japanese Biochemical Society 2023.11.01 Fukuoka
3. Katarzyna A. Inoue, Kazuki Takahashi, Maki Saito, Shintaro Sakakitani, Keita Iida, Sadahiro Iwabuchi, Daizo Koinuma, Toru Konishi, Susumu Tanaka, Atsushi Kaida, Masahiko Miura, Shinichi Hashimoto, Mariko Okada, Toshihiro Uchihashi, Kohei Miyazono, Tetsuro Watabe. TGF- β confers cancer cells with the high motility and metastatic potential via induction of Slug/HMGA2-independent EMT. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
4. Miho Kobayashi, Honoka Hirose, Masanori Nakayama, Tetsuro Watabe. Attenuation of the stress response is involved in the age-related reduction of microvascular density. Asia-Australia Vascular Biology Meeting 2023 (AAVBM2023) 2023.09.14 Korea

5. Kazuki Takahashi, Miho Kobayashi, Hisae Katsumata, Yukinori Ikeda, Tatsuhiko Anzai, Katarzyna A. Podyma-Inoue, Daniel M Alcaide, Kentaro Maeda, Jihwan Park, Kunihiro Takahashi, Yukiko Matsunaga, Yasuhiro Yoshimatsu, Tetsuro Watabe. Endothelial-mesenchymal transition (EndoMT) reporter cells visualized multiple groups of cells during progression of TGF- β induced EndoMT. Asia-Australia Vascular Biology Meeting 2023 (AAVBM 2023) 2023.09.14 Seoul, Korea
6. Tetsuro Watabe. Characterization of TGF- β -induced partial endothelial-mesenchymal transition (EndoMT) using EndoMT reporter cells.. TGF β meeting 2023 2023.08.17 Uppsala
7. Katarzyna Inoue. Inhibition of TGF- β signals by a chimeric Fc receptor suppresses tumor formation by regulation of tumor microenvironment networks. TGF β Meeting 2023.08.17 Uppsala, Sweden
1. Miho Kobayashi, Honoka Hirose, Masanori Nakayama, Tetsuro Watabe. Aging and stress in endothelial cells. CVMW2023 2023.12.10
2. Yuma Miyamoto, Shouma Yamaguchi, Tatsuro Seike, Tetsuro Watabe, Miki Yokoyama, Hidemine Torigoe. Development of a new method to artificially degrade target proteins using chaperone-mediated autophagy mechanism. 46th Annual Meeting of the Molecular Biology Society of Japan 2023.12.08
3. Honoka Hirose, Miho Kobayashi, Masanori Nakayama, Tetsuro Watabe. Relationship between aging-related reduction of microvessel density and endothelial stress tolerance. 2023.12.07
4. Miho Kobayashi, Kashio Fujiwara, Honoka Hirose, Yasuhiro Suzuki, Yume Kobayashi, Masanori Nakayama, Yasufumi Sato, Tetsuro Watabe. Physiological function of detyrosination. MBSJ2023 2023.12.06
5. Miho Kobayashi, Kazuki Takahashi, Kashio Fujiwara, Yusuke Yoshioka, Takahiro Ochiya, Katarzyna Anna Inoue, Tetsuro Watabe. Molecular mechanism of vascular destabilization by exosome from oral cancer. JBS2023 2023.11.02
6. Miho Kobayashi. Vascular destabilization by extracellular vesicle derived from oral cancer. 10th Japanese Society for Extracellular Vesicles Meeting 2023.10.23
7. Tetsuro Watabe. Roles of endothelial-mesenchymal transition(EndoMT) during cancer progression.. 2023.09.22
8. Kazuki Takahashi, Hisae Katsumata, Miho Kobayashi, Shiori Tokizaki, Yukinori Ikeda, Kentaro Maeda, Katarzyna A. Inoue, Yukiko Matsunaga, Yasuhiro Yoshimatsu, Tetsuro Watabe. Endothelial-mesenchymal transition (EndoMT) reporter cells visualized multiple groups of cells during progression of TGF- β induced EndoMT. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.21 Yokohama
9. Shiori Tokizaki, Katarzyna A. Inoue, Kazuki Takahashi, Takehisa Matsumoto, Mikako Shirouzu, Shizuka Uchida, Sadahiro Iwabuchi, Shinichi Hashimoto, Hiroyuki Harada, Kohei Miyazono, Tetsuro Watabe. Inhibition of TGF- β signaling suppresses tumorigenesis by regulating tumor microenvironment networks. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.21 Yokohama
10. Sakura Iida, Tetsuro Watabe, Miki Yokoyama. Regulation of a tight junction component, claudin-11, by lactosylceramide. The 65th Annual meeting of the Japanese Association for Oral Biology 2023.09.16 Nihon University School of Dentistry
11. Miho Kobayashi, Honoka Hirose, Yume Kobayashi, Tetsuro Watabe. Dynamics of post-translational modification of α -tubulin and intracellular trafficking. The 75th Annual Meeting of the Japan Society for Cell Biology 2023.06.28
12. Miho Kobayashi. Vessel reduction with aging. The 47th Meeting of the Japanese Society of Lymphology 2023.06.10
13. Miho Kobayashi. Relationship between vascular and microtubules in healthy longevity. 8th Young investigator meeting of vascular biology 2023.05.27
14. Kazue Terasawa, Tatsuro Seike, Kensaku Sakamoto, Kazumasa Ohtake, Tohru Terada, Takanori Iwata, Tetsuro Watabe, Shigeyuki Yokoyama, and Miki Hara-Yokoyama. Structure of a complex formed by LAMP2A molecules, an essential factor for chaperone-dependent autophagy, on the lysosomal membrane. The 96th Annual Meeting of the Japanese Biochemical Society 2023.11.02 Fukuoka International Congress Center

Cell Signaling

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

(1) Research

Research Subjects

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

(2) Education

Purpose of Education

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

(3) Publications

[Original Articles]

1. Naomi Toyama, Takehito Ono, Takashi Ono, Tomoki Nakashima. The interleukin-6 signal regulates orthodontic tooth movement and pain. *Biochem Biophys Res Commun.* 2023.12; 684; 149068

[Conference Activities & Talks]

1. Takehito Ono, Naomi Toyama, Takashi Ono, Tomoki Nakashima. IL-6 regulates orthodontic tooth movement and pain. The 71st Annual Meeting of Japanese Association for Dental Research 2023.11.26 Sendai
2. Takehito Ono. Augmentation of musculoskeletal tissues by locomimeticism. The 19th Bone Biology Forum 2023.08.18 Makuhari
1. Takehito Ono. Elucidation of the mechanisms of how the bone protect the mind. The 41st Annual Meeting of the Japanese Society for Bone and Mineral Research 2023.07.29 Tokyo

2. Takehito Ono. Can Strengthening bone and muscle improve health of the whole body?. The 41st Annual Meeting of the Japanese Society for Bone and Mineral Research 2023.07.28 Tokyo

Periodontology

From January. 2023

【Professor】 Takanori Iwata

【Photoperiodontics Professor】 Akira Aoki

【Associate Professor】 Sayaka Katagiri

【Junior Associate Professor】 Yasuo Takeuchi(～Mar), Koji Mizutani(Apr～)

【Specially Appointed Junior Associate Professor】 Daisuke Shimura(Jul～)

【Assistant Professor】 Shogo Maekawa, Risako Mikami(Apr～), Yujin Ohsugi

【Specially appointed Assistant Professor】 Yosuke Tsuchiya, Munehiro Okada(～Mar)

【Clinical Fellow】

Natsumi Saito, Hiromi Niimi(～Mar), Kazuki Miyata (～Mar), Yuri Ito (～Mar), Aiko Fujino (～Mar),

Tsuyoshi Shimohira(Apr～), Masahiro Hakariya(Apr～), Yumine Kiuchi Yuya Hamada,

Sakurako Kawamoto(Apr～), Hiroe Nakashima(Apr～), Yugo Itoh(Apr～), Saki Goto(Apr～)

【Research Fellowship for Young Scientists PD】

Sumiko Yoshida(Apr～)

【Graduate Students】 Ryo Mikami(～Mar), Shunsuke Takeuchi(～Mar), Masahiro Hatasa(～Mar), Anhao Liu,

Shu Takemura, Keita Nakagawa, Takahiko Nagai, Mako Yokose, Kazuki Morita(～Mar), Lisa Yagasaki,

Sakura Hayashi, Jiacheng Wang, Peiya Lin, Shiwei Sun, Ryota Kobayashi, Eri Sakaniwa, Tatsuro Seike,

Kanji Tabata, Keita Toyoshima, Daichi Yamaki, Chihiro Imai, Junya Watanabe, Naoki Toyoda(～Mar),

Hua Wenrui(Apr～), Azusa Shimizu(Apr～), Shunsuke Matsumura(Apr～), Chen Lu, Akinaga Moreira Bruna,

Mingran Zhang, Jingyi Gao, Ye Yint Kaung Myint, Wang Wenli (Oct～) , Jiang Hui (Oct～)

【Adult graduate student】 Fumihiko Kimura, Ito Hirasawa

【Postdoctoral Fellowship for Foreign Researchers】 Taichen Lin

【Graduate Research Student】

Akane Ochiai, Takahiro Naito(Apr～), Mari Sugimoto(Apr～), Huang Chun Yang(Apr～), Ai Watanabe(Apr～)

【Clinical Professor】 Hiroaki Kobayashi, Shigenari Kikuchi, Hiroaki Tsutioka

【Adjunct Lecturer】 47

【Registered dentist】 74

【Assistant Administrative Staff】 Keiko Odaka (～Mar), Jun Suga (Jul～)

【Technical Assistant】 Lisa Takeshita (Apr～)

(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

[Original Articles]

1. Strauss FJ, Fukuba S, Naenni N, Jung R, Jonker B, Wolvius E, Pijpe J. Alveolar ridge changes 1-year after early implant placement, with or without alveolar ridge preservation at single-implant sites in the aesthetic region: A secondary analysis of radiographic and profilometric outcomes from a randomized controlled trial. *Clinical Implant Dentistry Related Research*. 2023.12;
2. Fukuba S, Okada M, Iwata T. Clinical outcomes of periodontal regenerative therapy with carbonate apatite granules for treatments of intrabony defects, Class II and Class III furcation involvements: A 9-month prospective pilot clinical study. *Regenerative Therapy*. 2023.12; 24; 343-350
3. Matsuura, T; Mikami, R; Mizutani, K; Shioyama, H; Aoyama, N; Suda, T; Kusunoki, Y; Takeda, K; Izumi, Y; Aida, J; Aoki, A; Iwata, T. Assessment of bone defect morphology for the adjunctive use of bone grafting combined with enamel matrix derivative: A 3-year cohort study *JOURNAL OF PERIODONTOLOGY*. 2023.11;
4. Takemura S, Mizutani K, Mikami R, Nakagawa K, Hakariya M, Sakaniwa E, Saito N, Kominato H, Kido D, Takeda K, Aoki A, Iwata T. Enhanced periodontal tissue healing via vascular endothelial growth factor expression following low-level erbium-doped: yttrium, aluminum, and garnet laser irradiation: In vitro and in vivo studies. *Journal of periodontology*. 2023.11;
5. Lin P, Niimi H, Hirota T, Ohsugi Y, Shimohira T, Toyoshima K, Katagiri S, Iwata T, Aoki A. Effects of low-level Er:YAG laser irradiation on proliferation and gene expression in primary gingival fibroblasts isolated from mouse maxilla *Journal of biophotonics*. 2023.11; e202300166
6. Tokuda K, Tanaka A, Tobe A, Shirai Y, Kurobe M, Kubota Y, Kunieda T, Miyazaki T, Mizutani K, Furusawa K, Ishii H, Murohara T. Impact of C-Reactive Protein on Long-Term Cardiac Events in Stable Coronary Artery Disease Patients with Chronic Kidney Disease *Journal of Atherosclerosis and Thrombosis*. 2023.11; 30(11); 1635-1643
7. Aoki A, Mizutani K, Mikami R, Ohsugi Y, Kobayashi H, Akizuki T, Taniguchi Y, Takeuchi Y, Katagiri S, Sasaki Y, Komaki M, Meinzer W, Izumi Y, Iwata T. Er:YAG laser-assisted comprehensive periodontal pocket therapy for residual periodontal pocket treatment: A randomized controlled clinical trial *Journal of Periodontology*. 2023.10; 94(10); 1187-1199
8. Toyoshima K, Ohsugi Y, Lin P, Komatsu K, Shiba T, Takeuchi Y, Hirota T, Shimohira T, Tsuchiya Y, Katagiri S, Iwata T, Aoki A. Blue LED irradiation without a photosensitizer alters oral microbiome composition of ligature-induced periodontitis in mice *Photobiomodulation, Photomedicine, and Laser Surgery*. 2023.10;

9. Hayashi S, Takeuchi Y, Hiratsuka K, Kitanaka Y, Toyoshima K, Nemoto T, Aung N, Hakariya M, Ikeda Y, Iwata T, Aoki A. Effects of various light-emitting diode wavelengths on periodontopathic bacteria and gingival fibroblasts: An in vitro study. *Photodiagnosis and Photodynamic Therapy*. 2023.10; 44;
10. Mikami R, Komagamine Y, Aoyama N, Mizutani K, Sasaki Y, Iwata T, Minakuchi S, Kanazawa M. Association between occlusal supports and nutritional status in older adults: A systematic review *Journal of Dental Sciences*. 2023.09;
11. Katagiri S, Ohsugi Y, Shiba T, Yoshimi K, Nakagawa K, Nagasawa Y, Uchida A, Liu A, Lin P, Tsukahara Y, Iwata T, Tohara H. Homemade blenderized tube feeding improves gut microbiome communities in children with enteral nutrition *Frontiers in Microbiology*. 2023.08; 14; 1215236
12. Takeuchi Y, Nemoto T, Kitanaka Y, Aoki A, Izumi Y, Iwata T, Arakawa S. Antibacterial activity of lysozyme-chitosan oligosaccharide conjugates on two periodontal bacteria *Oral diseases*. 2023.08;
13. Takeda K, Mizutani K, Mikami R, Fujino A, Ito Y, Takeuchi S, Saito N, Iwata T. Morphological analysis of the impact of diabetes on gingival capillaries with non-invasive blood flow scope - A preliminary study. *Journal of dental sciences*. 2023.07; 18(3); 1134-1140
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15. Watanabe C, Wada J, Mizutani K, Nagayama T, Uchida H, Shibata Y, Wakabayashi N. Radiographic predictive factors for 10-year survival of removable partial denture abutment teeth: Alveolar bone level and density *Journal of Prosthetic Research*. 2023.07; 67(3); 437-443
16. Shiba T, Komatsu K, Watanabe T, Takeuchi Y, Nemoto T, Ohsugi Y, Katagiri S, Shimogishi M, Marukawa E, Iwata T. Peri-implantitis management by resective surgery combined with implantoplasty and Er:YAG laser irradiation, accompanied by free gingival graft: a case report. *Therapeutic advances in chronic disease*. 2023.06; 14; 20406223231174816
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20. Takeuchi S, Fukuba S, Okada M, Nohara K, Sato R, Yamaki D, Matsuura T, Hoshi S, Aoki K, Iwata T. Preclinical evaluation of the effect of periodontal regeneration by carbonate apatite in a canine one-wall intrabony defect model. *Regenerative Therapy*. 2023.03; 22; 128-135
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1. Tomoko TABATA, Hisaichi NAKAGAWA, Khairul MATIN Masayuki OTSUKI, Akira AOKI and Yasushi SHIMADA. Biofilm Studies Using Optical Coherence Tomography (OCT): Review *Journal of Japanese Society for Laser Dentistry*. 2023.09; 33(1); 11-17
2. Aoki A. Comprehensive periodontal pocket therapy using scaler and Er:YAG laser *The Japanese journal of conservative dentistry*. 2023.04; 66(2); 105-113
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? Part 4. Follow-Up after RPD Placement *The Quintessence*. 2023.02; 42(2); 66-91

4. Ohsugi Y, Toyoshima K, Hatasa M, Shimohira T, Shiba T, Komatsu K, Tsuchiya Y, Fukuba S, Niimi H, Katagiri S, Iwata T, Aoki A. Cytological responses in periodontal tissue to photobiomodulation by low-level diode laser irradiation *Journal of Japan Society for Laser Dentistry*. 2023.02; 32(3); 33-38

[Conference Activities & Talks]

1. Aoki A. Development of flapless periodontal surgery using Er:YAG laser. The 22nd congress of Iranian Academy of Periodontology (IAP) 2023.11 Virtual
2. Shimizu S, Hayashi K, Takeuchi Y, Tanabe G, Churei H, Kobayashi H, Ueno T, Fueki K. Effect of Administration of Sonicated *P. gingivalis* on skeletal muscle injury healing using a rat model. . ECSS Paris 2023 2023.07.04 Paris
3. Aoki A. The State of the Art of Lasers in Periodontology. Master of Laser in Dentistry of Sapienza University of Rome in partnership with the EMDOLA Project 2023.06.14 Sapienza University of Rome, Vertial
4. Franz J. Strauss, Shunsuke Fukuba, Nadja Naenni, Eppo Wolfius, Justin Pijpe, Ronald Jung, Brend Jonker. Alveolar ridge changes after early implant placement with or without alveolar ridge preservation at single implant sites in the aesthetic region: a one-year radiographic and profilometric analysis of a randomized controlled trial. International Osteology Symposium Barcelona 2023.04.28 Barcelona, Spain
5. Fukuba S. Pushing the limit of periodontal regeneration -Give the hope to the hopeless tooth-. International Osteology Symposium 2023.04.28 Barcelona, Spain
6. Lin P, Niimi H, Hirota T, Ohsugi Y, Shimohira T, Toyoshima K, Katagiri K, Iwata T, Aoki A. Effect of low-level Er:YAG laser irradiation on proliferation and gene expression changes of primary gingival fibroblasts isolated from mouse maxilla. The 17th Congress of WFLD, Faculty of Pharmacy 2023.04.16 Wrocław Medical University, Wrocław
7. Aoki A. Er:YAG laser-assisted comprehensive periodontal pocket therapy (Er-LCPT). The 17th Congress of WFLD, Faculty of Pharmacy 2023.04.15 Wrocław Medical University, Wrocław
8. Aoki A (Chair). Grzech-Lesniak K, Shibli J, Dominiak M, Romanos G, Vescovi P, Romeo U, Arnabat J, Nammour S, Zeinoun T. Round Table on Periodontal and Peri-Implant Therapy Using Lasers. The 17th Congress of WFLD, Faculty of Pharmacy 2023.04.15
9. Aoki A. Periodontal and peri-implant therapy using Er:YAG laser. Morita corporation forum. The 17th Congress of WFLD, Faculty of Pharmacy 2023.04.14 Wrocław Medical University, Wrocław
10. Aoki A. Esthetic soft tissue management with Er:YAG Laser. The 17th Congress of WFLD, Faculty of Pharmacy 2023.04
11. Kunieda T, Tanaka A, Shirai Y, Kurobe M, Tokuda K, Tobe A, Mizutani K, Miyazaki T, Kubota Y, Furusawa K, Ishii H, Murohara T. Incidence of Cardiac Events Following Non-cardiac Surgery among the Patients with or without Coronary Artery Stenosis by Pre-operative Coronary Angiography. The 87th Annual Scientific Meeting of the Japanese Circulation Society 2023.03.11
1. Shimura D. Promote Gap junction formation by GJA1-20k for Arrhythmogenic Cardiomyopathy. Cardiovascular and Metabolic Week 2023 2023.12.09 Kobe
2. Aoki A. Fundamental knowledge regarding Er:YAG laser. 2023.12.06
3. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Hiroshi Churei, Kenji Fueki. The effect of antigen of periodontitis to sports related muscle reaction. 88th congress of Stomatological society Japan 2023.12.02
4. Maalouf M, Gonzalez JJ, Hong TT, Shaw RM, Shimura D. GJA1-20k is a mediator between mitochondria and phosphoinositides for mitochondrial morphological regulation. 2023.12
5. Hayashi S, Takeuchi Y, Hiratsuka K, Kitanaka Y, Toyoshima K, Hakariya M, wata T, Aoki A.. Effects of various light-emitting diode wavelengths on *Porphyromonas gingivalis* and gingival fibroblasts. Laser Week IV in Tokyo, Academy of Laser Dentistry 35th Annual Conference 2023.11.26

6. Miyata K, Mizutani K, Ohsugi Y, Mikami R, Takagi T, Oda S, Iwata T, Aoki A. Characterization of Er:YAG laser-irradiated root surfaces and histological analysis of periodontal tissue attachment. 2023.11.25
7. Aoki A. Application of Er:YAG laser in the treatment of peri-implantitis. 2023.11.25
8. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Zhu Qiushuang, Li Zequn, Gen Tanabe, Hiroshi Churei, Toshiaki Ueno. The effect of P. gingivalis administration to PGC-1 α and TNF α expression in skeletal muscle after endurance training in vivo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
9. Shimura D, Maalouf M, Nguyen VD, Hunter J, Shaw RM. GJA1-20k mediates mitochondrial contact and actin sheet formation to achieve mitochondrial protection. 2023.11.14
10. Aoki A. Application of Er:YAG laser in minimally invasive flapless pocket surgery. China-Japan Oral Medicine Forum 2023.10.30 China Japan Friendship Hospital
11. Aoki A. Treatment of peri-implantitis and application of Er:YAG laser. 2023.10.21
12. Hayashi S, Takeuchi Y, Hiratsuka K, Kitanaka Y, Toyoshima K, Nemoto T, Hakariya M, Ikeda Y, Iwata T, Aoki A.. Effects of various light-emitting diode wavelengths on Porphyromonas gingivalis. The 66th Autumn Meeting of Japanese Society of Periodontology 2023.10.14
13. Ohsugi Y, Imai C, Katagiri S, Hirota T, Shiba T, Toyoshima K, Uesaka N, Iwata T. Oral-gut-brain axis in ligature-induced periodontitis in mice. The 66th Autumn Meeting of Japanese Society of Periodontology 2023.10.13 Nagasaki
14. Aoki A. Application of Er:YAG laser in minimally invasive flapless pocket surgery. The 9th Japan International Dental Congress 2023 2023.09.30 Yokohama
15. LIU ANHAO, Mikihiro Hayashi, Sayaka Katagiri, Yujin Ohsugi, Takanori Iwata, Tomoki Nakashima. Spatio-temporal analysis of the pathogenesis of periodontitis: application of the novel mouse ligature model. The 41st Annual Meeting of the Japanese Society for Bone and Mineral Research 2023.07.27
16. Aoki A. Application of Er:YAG laser in periodontitis and peri-implantitis and the latest periodontal treatment. Kyushu Ochanomizu meeting 2023.07.23
17. Aoki A. Application of laser for periodontal disease treatment. 2023 Tokyo Dental Association post-graduation seminar 2023.06.29
18. Ohsugi Y. Biological effects of laser expand possibility with Bioinformatics. The 34th Annual Meeting of Japan Laser Therapy 2023.06.18 Utsunomiya
19. Aoki A. Advances in the treatment of periodontitis and peri-implantitis. Japan Implant Clinical Research Association, 2023 certification workshop. Implant 100 Hour Course 2023.06.18 B.BRAUN AESCULAP, 6th floor, training room
20. Katagiri S. Effect of glucose and lipid metabolic disorder in oral microbiota disruption. The 66th Spring Meeting of Japanese Society of Periodontology 2023.05.27 Takamatsu
21. Matsuda S, Sugaya T, Kato S, Nemoto E, Takeuchi Y, Yamashita K, Numabe Y, Nishida T, Ogata Y, Shin K, Nagano T, Morozumi T, Komatsu Y, Dewake N, Goto R, 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 2nd report. 2023.05.27
22. The effect of low-level Er:YAG laser irradiation on endothelial cells. 2023.05.26
23. Nakagawa K, Mizutani K, Watanabe K, Saito N, Takemura S, Sakaniwa E, Mikami R, Kido D, Takeda K, Kominato H, Hattori A, Iwata T. Comprehensive gene expression analysis during the healing phase of ligature-induced experimental periodontitis in diabetic rats. 2023.05.26
24. Miyata K, Mizutani K, Ohsugi Y, Mikami R, Takagi T, Kawakatsu N, Shirkata Y, Tsuchioka H, Oda S, Kinoshita A, Iwata T, Aoki A. Histological analysis of periodontal tissue attachment on Er:YAG Laser Irradiated root surfaces in beagle dogs. The 66th Spring Meeting of the Japanese Society of Periodontology 2023.05.26 Rexam Hall, Kagawa

25. Daichi Y, Shunsuke F, Munehiro O, Shunsuke T, Shu H, Takanori M, Takanori I. Effects of Octacalcium Phosphate and Collagen Composite for periodontal regeneration in a canine 1-wall defect model. The 66th Spring meeting of the Japanese Society of Periodontology 2023.05.26
26. Aoki A. Photo-periodontics, [New periodontology from periodontal department in TMDU] - State-of-the-art insights and technology. 2023.02.05 Tokyo Medical and Dental University

[Awards & Honors]

1. Scholarship students of Kobayashi scholarship association, Kobayashi scholarship association, 2023.03
2. JSP Research Encouragement Award (Ohsugi Y), Japanese Society of Periodontology, 2023.05
3. Japanese Society of Periodontology (JSP) Young Investigator Research Fund (Fukuba S), Japanese Society of Periodontology, 2023.05
4. Best Poster Award (Lisa Yagasaki), The Japanese Society for Bone and Mineral Research, 2023.07
5. The 35th Annual Meeting of the Japanese Society for Laser Dentistry (Miyata K), The Japanese Society for Laser Dentistry, 2023.11

Department of Biosignals and Inheritance

(1) Publications

[Original Articles]

1. Xu Y, Kusuyama J, Osana S, Matsushashi S, Li L, Takada H, Inada H, Nagatomi R. Lactate promotes neuronal differentiation of SH-SY5Y cells by lactate-responsive gene sets through NDRG3-dependent and -independent manners. *The Journal of biological chemistry*. 2023.05; 299(6); 104802
1. Chang - Hwan Seong, Norika Chiba, Mardiyantoro Fredy, Joji Kusuyama, Kiyohide Ishihata, Toshiro Kibe, Muhammad Subhan Amir, Ryohei Tada, Tomokazu Ohnishi, Norifumi Nakamura, Tetsuya Matsuguchi. Early induction of Hes1 by bone morphogenetic protein 9 plays a regulatory role in osteoblastic differentiation of a mesenchymal stem cell line *Journal of Cellular Biochemistry*. 2023.08; 124(9); 1366-1378

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 μ m in diameter are useful for the radiotherapy of cancers, especially for tumors located deep inside the body. Also, ferromagnetic microspheres 20-30 μ 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 important 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

[Original Articles]

1. Aoki S, Shimabukuro M, Kishida R, Kyuno K, Noda K, Yokoi T, Kawashita M. Electrochemical Deposition of Copper on Bioactive Porous Titanium Dioxide Layer: Antibacterial and Pro-Osteogenic Activities. *ACS applied bio materials*. 2023.11; 6(12); 5759-5767
2. Kuroyama K, Fujikawa R, Goto T, Sekino T, Nakamura F, Kimura-Suda H, Chen P, Kanetaka H, Hasegawa T, Yoshida K, Murata M, Nakata H, Shimabukuro M, Kawashita M, Yoda T, Yokoi T. Development of bioinspired damage-tolerant calcium phosphate bulk materials. *Science and technology of advanced materials*. 2023.10; 24(1); 2261836
3. Kubota, M; Furuya, M; Yokota, K; Kanetaka, H; Ogawa, T; Saito, S; Jeyadevan, B; Shimabukuro, M; Yokoi, T; Kawashita, M. Proliferation and differentiation of MC3T3-E1 cells on polymethyl methacrylate cements containing Fe₃O₄ and TiO₂ for hyperthermic treatment of metastatic bone tumors *JOURNAL OF BIOMATERIALS APPLICATIONS*. 2023.10; 38(5); 605-613
4. Taishi Yokoi, Masahiro Watanabe, Yuejun Wang, Tomoyo Goto, Tohru Sekino, Masaya Shimabukuro, Masakazu Kawashita. Synthesis and fluorescence properties of octacalcium phosphate with incorporated pyridinedicarboxylate ions *Journal of the Ceramic Society of Japan*. 2023.10; 131(10); 701-707
5. Tan, JLT; Shimabukuro, M; Kobayashi, M; Kishida, R; Kawashita, M; Ishikawa, K. Ant - nest type porous scaffold with micro - struts consisting of carbonate apatite for promoting bone formation and scaffold resorption *Journal of biomedical materials research. Part A*. 2023.09; 112(1); 31-43
6. Masaya Shimabukuro, Mamiko Kobayashi, Masakazu Kawashita. Metallic Substrate Influences on the Osteogenic Cell Compatibility and Antibacterial Activity of Silver-Incorporated Porous Oxide Layers Formed by Micro-Arc Oxidation 2023.08; 1(8); 2288-2294
7. K. Suzuki, M. Iwatsu, T. Mokudai, H. Kanetaka, M. Shimabukuro, T. Yokoi, M. Kawashita. Visible-light-enhanced antibacterial activity of silver and copper co-doped titania formed on titanium via chemical and thermal treatments *Molecules*. 2023.01; 28(2); 650
8. Yokoi T, Watanabe M, Nakamura F, Kimura-Suda H, Shimabukuro M, Kawashita M. Formation of octacalcium phosphate with incorporated dicarboxylate ions containing disulfide bonds. *Dalton transactions (Cambridge, England : 2003)*. 2023; 52(45); 16586-16590

[Conference Activities & Talks]

1. L. Chang, P. Chen, T. Mokudai, M. Kawashita, H. Kanetaka, I. Mizoguchi. Enhancing osteoconductivity of titanium by alkali-hot-water pretreatment. 第6回日本金属学会第7分野講演会 2023.12.23
2. S. Usuki, T. Ogawa, M. Shimabukuro, T. Yokoi, M. Kawashita. ϵ -Fe₂₋₃N nanoparticles for magnetic hyperthermia. The 21st Asian BioCeramics Symposium (ABC2023) 2023.12.17
3. Y. Tsutsumi, H. Tsutsumi, M. Shimabukuro, P. Chen, M. Kawashita, H. Katayama, T. Hanawa. Development of novel titanium surface with both long-term antibacterial property and hard-tissue compatibility by two-step micro arc oxidation process. 11th Pacific Rim International Conference on Advanced Materials and Processing (PRICM11) 2023.11.20
4. T. Yokoi, K. Kuroyama, T. Goto, T. Sekino, P. Chen, H. Kanetaka, M. Shimabukuro, M. Kawashita, T. Yoda. Development of bioinspired highly damage-tolerant calcium phosphate-based bulk ceramic materials for biomedical applications. the 37th International Korea-Japan Seminar on Ceramics 2023.11.16
5. L. Chang, P. Cheng, T. Mokudai, M. Kawashita, H. Kanetaka, I. Mizoguchi. Evaluation of osteogenic properties of bioactive porous titanium for orthodontic applications. TACT 2023 International Thin Films Conference 2023.11.13

6. S. Usuki, T. Ogawa, M. Shimbukuro, T. Yokoi, M. Kawashita. Magnetic and heat-generation properties of ϵ -Fe₂-₃N nanoparticles for magnetic hyperthermia therapy. The 3rd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA 2023) 2023.10.20
7. T. Yokoi, K. Kuroyama, T. Goto, T. Sekino, P. Chen, H. Kanetaka, M. Shimabukuro, M. Kawashita, T. Yoda. Development of bioinspired damage tolerant calcium phosphate/pyrolytic carbon composite materials. The 3rd International Symposium on Design & Engineering by Joint Inverse Innovation for Materials Architecture (DEJI2MA 2023) 2023.10.20
8. P.-C. Sung, M. Shimabukuro, T. Yokoi, M. Kawashita. Preparation of bioactive titanium with visible light-enhanced antibacterial activity by hydrogen peroxide, copper acetate, and heat treatments. Biomaterials International 2023 2023.08.01
9. M. Shimabukuro, M. Kawashita, K. Ishikawa. ANTIBACTERIAL CARBONATE APATITE ARTIFICIAL BONE FOR BONE REGENERATION AND INFECTION PREVENTION. Biomaterial international 2023 (BMI2023) 2023.07.31

[Awards & Honors]

1. Best Poster Paper Award, Biomaterials International 2023 (BMI2023), 2023.08

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: Hisaaki Nishimura, MD
 Project Assistant Professor: Yui Yamaoka, PhD
 Project Assistant Professor : Yuna Koyama, MD, PhD

(1) Outline

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases.

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

(2) Research

The main focus of the department is as follows:

1. Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
2. Life-course epidemiology (impact of child poverty and adverse childhood experiences on health) and international comparison study
3. Prevention on child abuse and neglect
4. Mental health (antenatal and postnatal mental health, mental health after a disaster, and child mental health)
5. Nutritional epidemiology (childhood nutrition from prenatal to early school-years and the food environment)
6. Environmental health (the physical environment and climate change)
7. Occupational health (harassment and work-place social capital)
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 determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

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

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

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

(4) Publications

[Original Articles]

1. Akaishi Y, Nawa N, Kashimada A, Itsui Y, Okada E, Yamawaki M. Association between Grit and depressive symptoms at the timing of job start among medical residents during the COVID-19 pandemic in Japan: a cross-sectional study. *Medical education online*. 2023.12; 28(1); 2225886
2. Morita A*, Fujiwara T, Murayama H, Machida M, Inoue S, Shobugawa Y. Association between trajectory of socioeconomic position and regional brain volumes related to dementia: Results from the NEIGE study. *J Gerontol A Biol Sci Med Sci*. 2023.12;
3. Segawa Y*, Jinno T, Matsubara M, Mastuyama Y, Fujiwara T, Okawa A. A cross-sectional study evaluating patients' preferences for Salter innominate osteotomy. *J Orthop Sci*. 2023.11; 28(6); 1298-1302
4. Morimoto M, Nawa N, Okada E, Itsui Y, Kashimada A, Yamamoto K, Akaishi Y, Yamawaki M. Elucidation of the needs for telecritical care services in Japan: A qualitative study. *BMJ Open*. 2023.11; 13(11); e072065
5. Sadachi R, Sato H, Fujiwara T, Hirakawa A. Enhancement of Bayesian optimal interval design by accounting for overdose and underdose errors trade-offs. *J Biopharm Stat*. 2023.11; 1-20
6. Tani Y*, Fujiwara T, Anzai T, Kondo K. Cooking skills, living alone, and mortality: JAGES cohort study. *Int J Behav Nutr Phys Act*. 2023.11; 20(1); 131
7. Matsukura H, Yamaoka Y, Matsuyama Y, Kondo K, Fujiwara T*. Association between adverse childhood experiences and marital status among Japanese older adults. *Child Abuse Negl*. 2023.10; 144; 106340
8. Matsuyama Y, Isumi A, Doi S, Fujiwara T*. Persistent poverty and child dental caries: time-varying exposure analysis. *J Epidemiol Community Health*. 2023.10; 77(10); 670-675
9. Terada S, Fujiwara T*, Sugawara J, Maeda K, Satoh S, Mitsuda N. Association of severe maternal morbidity with bonding impairment and self-harm ideation: A multicenter prospective cohort study. *J Affect Disord*. 2023.10; 338; 561-568
10. Nawa N, Nishimura H, Matsuyama Y, Doi S, Isumi A and Fujiwara T*. Association between the number of convenience stores and caries status in permanent teeth among elementary school children: results from the A-CHILD population-based longitudinal cohort study. 2023.10; 11; 1228197
11. Tani Y, Isumi A, Doi S, Fujiwara T*. Number of siblings and social capital among parents rearing schoolchildren: Results from the A-CHILD study. *J Epidemiol*. 2023.09; 33(9); 478-483
12. Tani Y*, Matsuyama Y, Yamaoka Y, Matsukura H, Kawahara T, Fujiwara T. Change of human flourishing during the COVID-19 pandemic in Japan: Results from population-based U-CORONA study. *SSM Popul Health*. 2023.09; 23; 101430
13. Mizusawa J, Sato H, Rubinstein LV, Fujiwara T, Yonemori K*, Hirakawa A*. Racial differences in longitudinal toxicities of anticancer agents in early phase cancer clinical trials. *Cancer Med*. 2023.09; 12(17); 18098-18109
14. Ishii T, Nawa N, Doi S, Morio T, Fujiwara T*. Association between the initiation of insurance coverage for fetal echocardiography and mortality from congenital heart disease in infants: An interrupted time series analysis. *Paediatr Perinat Epidemiol*. 2023.09; 37(7); 607-617
15. Tani Y*, Yamamoto T, Kusama T, Kinugawa A, Aida J, Fujiwara T, Kondo K. Cooking skills modify the association between oral health and mortality. *Age Ageing*. 2023.09; 52(9); afad180

16. Ogawa T, Onuma R, Kristensen MT, Yoshii T, Fujiwara T, Fushimi K, Okawa A, Jinno T. Association between additional weekend rehabilitation and in-hospital mortality in patients with hip fractures. *Bone Joint J.* 2023.08; 105-B(8); 872-879
17. Nishimura H, Nawa N, Yamaoka Y, Koyama Y, Kuramochi J, Fujiwara T. Association between residential greenness and severe psychological distress and the moderating role of ‘stay-at-home’ status: a population-based cross-sectional study during the COVID-19 pandemic in Japan. *BMJ Public Health.* 2023.08; e000093
18. Kanda K, Nishimura H, Koiso T, Takemoto K, Nakagoe K, Yamada T, Takahashi M, Hanafusa M, Kawahara T, Yanagida Y, Kuramochi J, Fujiwara T. Applying negative ions and an electric field to countermeasure droplets/aerosol transmission without hindering communication. *Scientific reports.* 2023.08; 13(1); 13965
19. Sasaki N, Tabuchi T, Fujiwara T, Nishi D*. Adverse childhood experiences and living in the socially deprived areas in adulthood: a cross-sectional study of the nationwide data in Japan. *BMC Public Health.* 2023.08; 23(1); 1616
20. Fujiwara T*, Koyama Y, Isumi A, Matsuyama Y, Tani Y, Ichida Y, Kondo K, Kawachi I. “What did you do in the War, Daddy?” : Paternal military conscription during WWII, economic hardship and family violence in childhood and health in late life in Japan. *J Interpers Violence.* 2023.07; 38(13-14); 8114-8135
21. Doi SK, Isumi A, Yamaoka Y, Shakagori S, Yamazaki J, Ito K, Shiomi M, Sumioka H, Fujiwara T*. The effect of breathing relaxation to improve poor sleep quality in adults using a huggable human-shaped device: a randomized controlled trial. *Sleep Breath.* 2023.07;
22. Ito Y, Okamoto K*, Mizuno Y, Ogino K, Fujiwara T, Nakagawa T, Ishikawa T, Kubo T, Uetake H. Double-lumen catheter is a risk factor for complications of peripherally inserted central venous catheters in children *Journal of Pediatric Surgery Open.* 2023.07; 2; 100023
23. Mizoguchi M, Kizuki M, Iwata N, Tokunaga M, Fushimi K, Kinugasa Y, Fujiwara T*. Comparison of short-term outcomes between robot-assisted and laparoscopic rectal surgery for rectal cancer: A propensity score-matched analysis using the Japanese Nationwide diagnosis procedure combination database. *Annals of Gastroenterological Surgery.* 2023.07;
24. Fukuya Y, Nawa N, Morita A, Fujiwara T*. Association of revision of Money Lending Business Act and suicide rate in Japan: An interrupted time series analysis. *Suicide Life Threat Behav.* 2023.06; 53(3); 372-384
25. Soma T, Fukuda S*, Matsuyama Y, Ikeda R, Inoue M, Waseda Y, Tanaka H, Yoshida S, Yokoyama M, Matsuoka Y, Fujiwara T, Kageyama Y, Fujii Y. Peritoneal closure and the processus vaginalis transection method to prevent inguinal hernia after robot-assisted radical prostatectomy. *Int J Urol.* 2023.06; 30(6); 532-538
26. Ashida T*, Fujiwara T, Kondo K. Association between adverse childhood experiences and social integration among older people in Japan: Results from the JAGES study. *Arch Gerontol Geriatr.* 2023.06; 114; 105099
27. Abe E*, Kobayashi M, Horikawa R, Morisaki N, Tanaka H, Sago H, Ogawa K, Fujiwara T. The Association Between Eating Quickly and Excessive Gestational Weight Gain. *Womens Health Rep (New Rochelle).* 2023.06; 4(1); 280-287
28. Zeng Z, Nawa N, Hirama C, Fujiwara T*. Hedonic Risk Preference Associated with High-Risk Behaviors under COVID-19 Pandemic among Medical Students in Japan. *Int J Environ Res Public Health.* 2023.06; 20(12);
29. Khin YP, Yamaoka Y, Abe A, Fujiwara T*. Association of child-specific and household material deprivation with depression among elementary and middle school students in Japan. *Soc Psychiatry Psychiatr Epidemiol.* 2023.06; 1-11
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[Conference Activities & Talks]

1. 藤原 武男. 四大学連合によるポストコロナ社会コンソーシアムの取組等について. 第7回社会科学の発展を考える円卓会議 2023.01.26 オンライン

Department of Parasitology & Tropical Medicine

Professor ISHINO Tomoko
Assistant Professor KUMAGAI Takashi
Lecturer SHINZAWA Naoaki
Project Lecturer NAGAOKA Hikaru
Assistant Professor Minami Baba
Visiting Lecturer Motomi Torii
Visiting Lecturer Shoji Yamaoka
Visiting Lecturer Fukumi Nakamura
Visiting Lecturer Rieko Shimogawara
Visiting Lecturer KOBAYASHI Daisuke
Visiting Lecturer Suganuma Masumi
Graduate Student ARIMOTO Shou
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 Issahaqu
Graduate Student SEKINE Takashi
Graduate Student Peter Bolah
Graduate Student Frederick Ofosu Appiah
Graduate Student Amanor Ivy Brago
Graduate Student Eric Coffie
Graduate Student SHINOZAKI Momoka
Graduate Student OKADA Rena
Technical Assistant MURAYAMA Hisako
Technical Assistant Tokiko Okamura

(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

[Original Articles]

1. Kunkeaw, N; Nguitragool, W; Takashima, E; Kangwanrangsan, N; Muramatsu, H; Tachibana, M; Ishino, T; Lin, PJC; Tam, YK; Pichyangkul, S; Tsuboi, T; Pardi, N; Sattabongkot, J. A Pvs25 mRNA vaccine induces complete and durable transmission-blocking immunity to *Plasmodium vivax* NPJ VACCINES. 2023.12; 8(1); 187
2. Maartje R Inklaar, Roos M de Jong, Ezra T Bekkering, Hikaru Nagaoka, Felix L Fennemann, Karina Teelen, Marga van de Vegte-Bolmer, Geert-Jan van Gemert, Rianne Stoter, C Richter King, Nicholas I Proelochs, Teun Bousema, Eizo Takashima, Takafumi Tsuboi, Matthijs M Jore. Pfs230 Domain 7 is targeted by a potent malaria transmission-blocking monoclonal antibody. NPJ Vaccines. 2023.12; 8(1); 186
3. Thongpoon, S; Roobsoong, W; Nguitragool, W; Chotirat, S; Tsuboi, T; Takashima, E; Cui, LW; Ishino, T; Tachibana, M; Miura, K; Sattabongkot, J. Naturally Acquired Transmission-Blocking Immunity Against Different Strains of *Plasmodium vivax* in a Malaria-Endemic Area in Thailand JOURNAL OF INFECTIOUS DISEASES. 2023.11; 229(2); 567-575
4. Occurrence and prevalence of third-stage larvae of the Anisakidae family in Macrouridae species captured from bathyal depths of Sagami Bay, Japan 2023.10;

5. Ladzekpo Danielle, Kwofie Kofi Dadzie, Kawada Hayato, Mikami Fusako, Tsuji Naotoshi, Iwanaga Shiroh, Dadzie Samuel Kweku, Hatta Takeshi, Ishino Tomoko. A possible circulation of a dominant *Dibothriocephalus nihonkaiensis* haplotype in Japan revealed by molecular analysis of clinical tapeworm samples *Parasitology International*. 2023.10; 96; 1-9
6. Nishida T, Hiramatsu Y, Shinzawa N, Horino A, Mori S, Horiguchi Y. Complete genome sequences of nine *Burkholderia pseudomallei* strains. *Microbiology resource announcements*. 2023.09; 12(9); e0040023
7. Ifra Hassan, Bernard N Kanoi, Hikaru Nagaoka, Jetsumon Sattabongkot, Rachanee Udomsangpetch, Takafumi Tsuboi, Eizo Takashima. High-Throughput Antibody Profiling Identifies Targets of Protective Immunity against *P. falciparum* Malaria in Thailand *Biomolecules*. 2023.08; 13(8);
8. Somphou Sayasone, Phonepadith Khattignavong, Sengdeuane Keomalaphet, Phoyphaylinh Prasayasith, Pheovaly Soundala, Sonesimmaly Sannikone, Takashi Kumagai, Souk Phomhaksa, Phouth Inthavong, Emilie Louise Akiko Matsumoto-Takahashi, Bouasy Hongvanthong, Paul T Brey, Shigeyuki Kano, Moritoshi Iwagami. Low Prevalence of *Schistosoma mekongi* Infection and High Prevalence of Other Helminth Infections among Domestic Animals in Southern Lao People's Democratic Republic *Trop Med Infect Dis*. 2023.07; 8(7); 372
9. Matsumoto-Takahashi ELA, Kumagai T, Oyoshi K, Sasaki Y, Mizukami Y, Hongvanthong B, Brey PT, Kano S, Iwagami M. Impact of precipitation on the prevalence of schistosomiasis mekongi in Lao PDR: Structural equation modelling using Earth observation satellite data *One health (Amsterdam, Netherlands)*. 2023.06; 16; 100563
10. Baba M, Nozaki M, Tachibana M, Tsuboi T, Torii M, Ishino T. Rhoptry neck protein 4 plays important roles during *Plasmodium* sporozoite infection of the mammalian liver. *mSphere*. 2023.06; 8(4); e0058722
11. Baba Minami, Nozaki Mamoru, Tachibana Mayumi, Tsuboi Takafumi, Torii Motomi, Ishino Tomoko. Rhoptry neck protein 4 plays important roles during *Plasmodium* sporozoite infection of the mammalian liver *MSPHERE*. 2023.06; 8(4); e0058722
12. Kohdai Yamada, Fumiya Soga, Soh Tokunaga, Hikaru Nagaoka, Tatsuhiko Ozawa, Hiroyuki Kishi, Eizo Takashima, Tatsuya Sawasaki. GATS tag system is compatible with biotin labelling methods for protein analysis. *Sci Rep*. 2023.06; 13(1); 10243
13. Otsuki H, Kaneko O, Ito D, Kondo Y, Iriko H, Ishino T, Tachibana M, Tsuboi T, Torii M. Cysteine Residues in Region 6 of the *Plasmodium yoelii* Erythrocyte-Binding-like Ligand That Are Related to Its Localization and the Course of Infection. *Biomolecules*. 2023.03; 13(3);
14. Azerigyik FA, Faizah AN, Kobayashi D, Amoa-Bosompem M, Matsumura R, Kai I, Sasaki T, Higa Y, Isawa H, Iwanaga S, Ishino T. Evaluating the mosquito host range of Getah virus and the vector competence of selected medically important mosquitoes in Getah virus transmission. *Parasites & vectors*. 2023.03; 16(1); 99
15. Kumagai Takashi, Shiozaki Akira, Tajima Yuko. Molecular characterization of the parasitic nematode genus *Crassicauda*; larvae parasitic on the firefly squid and adults on beaked whales off the coast of Japan *INTERNATIONAL JOURNAL FOR PARASITOLOGY-PARASITES AND WILDLIFE*. 2023.01; 20; 56-62
16. Ramin Mazhari, Eizo Takashima, Rhea J Longley, Shazia Ruybal-Pesantez, Michael T White, Bernard N Kanoi, Hikaru Nagaoka, Benson Kiniboro, Peter Siba, Takafumi Tsuboi, Ivo Mueller. Identification of novel *Plasmodium vivax* proteins associated with protection against clinical malaria. *Front Cell Infect Microbiol*. 2023; 13; 1076150

Forensic Medicine

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Shutaro NAGANO
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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

[Original Articles]

1. Moeka Nomura, Shuheng Wen, Kana Unuma, Takeshi Funakoshi, Toshihiko Aki, Koichi Uemura. Increased fatty acid synthesis and disturbed lipid metabolism in Neuro2a cells after repeated cocaine exposure: A preliminary study. *Biochem Biophys Res Commun.* 2023.12; 695; 149438
2. Kana Unuma, Shuheng Wen, Toshihiko Aki, Koichi Uemura. Ectopic myogenesis and fibrosis accompany adipogenesis during thymic involution induced by repeated cocaine administration. *Biochem Biophys Res Commun.* 2023.12; 686; 149201
3. Shuheng Wen, Kana Unuma, Ryoichi Hanazawa, Shutaro Nagano, Ryo Watanabe, Akihiro Hirakawa, Koichi Uemura. Alcohol and toxicological factors influencing fatal falls from height in the Greater Tokyo Area: a retrospective study. *Int J Legal Med.* 2023.11;
4. Shuheng Wen, Kana Unuma, Koichi Uemura, Kazuki Harada. Revisiting the canonical definition of heat hematoma: A rare case of postmortem subdural heat hematoma. *J Forensic Leg Med.* 2023.07; 98; 102563
5. Shuheng Wen, Kana Unuma, Takeshi Funakoshi, Toshihiko Aki, Koichi Uemura. Cocaine induces vascular smooth muscle cells proliferation via DRP1-mediated mitochondrial fission and PI3K/HIF-1 α signaling. *Biochem Biophys Res Commun.* 2023.07; 676; 30-35
6. Toshihiko Aki, Hiroki Tanaka, Takeshi Funakoshi, Kana Unuma, Koichi Uemura. Excessive N-acetylcysteine exaggerates glutathione redox homeostasis and apoptosis during acetaminophen exposure in Huh-7 human hepatoma cells. *Biochem Biophys Res Commun.* 2023.07; 676; 66-72
7. Kana Unuma, Hiroyuki Sato, Shuheng Wen, Yohsuke Makino, Akihiro Hirakawa, Koichi Uemura. The proportion of false-positives in positive Seratec® prostate-specific antigen SemiQuant test results in postmortem screening for seminal fluid. *Leg Med (Tokyo).* 2023.05; 62; 102243
8. Toshihiko Aki, Mitsuki Kukita, Mao Takata, Takeshi Funakoshi, Kana Unuma, Koichi Uemura. Induction of filamin-C and its involvement in the regulation of cellular senescence and apoptosis in Huh-7 hepatoma cells during arsenic trioxide exposure. *Biochem Biophys Res Commun.* 2023.04; 651; 92-97
9. Kana Unuma, Dan Tomomasa, Kosuke Noma, Kouhei Yamamoto, Taka-Aki Matsuyama, Yohsuke Makino, Atsushi Hijikata, Shuheng Wen, Tsutomu Ogata, Nobuhiko Okamoto, Satoshi Okada, Kenichi Ohashi, Koichi Uemura, Hirokazu Kanegane. Case Report: Molecular autopsy underlie COVID-19-associated sudden, unexplained child mortality. *Front Immunol.* 2023.04; 14; 1121059
10. Miyu Komatsu, Takeshi Funakoshi, Toshihiko Aki, Kana Unuma, Koichi Uemura. Aristolochic acid induces an inflammatory response with prostaglandin E2 production and apoptosis in NRK-52E proximal tubular cells. *Toxicol Lett.* 2023.03; 378; 39-50
11. Shuheng Wen, Kana Unuma, Motoki Inaji, Yohsuke Makino, Shutaro Nagano, Kazuki Harada, Nobutaka Arai, Koichi Uemura. Case report: Fatal ischemic stroke induced by unruptured traumatic intracranial vertebral artery dissection. *Front Neurol.* 2023; 14; 1202698

Health Policy and Informatics

Professor:Kiyohide FUSHIMI

Associate Professor:Daisuke SHINJO

Graduate Student:Akira HOMMA, Mihoko OTA, 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:Kazushige ENDO

(1) Research

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

(2) Education

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

(3) Publications

[Original Articles]

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101. Hayato Yamana, Seyune Lee, Yi-Chieh Lin, Nan-He Yoon, Kiyohide Fushimi, Hideo Yasunaga, Shou-Hsia Cheng, Hongsoo Kim. Institutional Variance in Mortality after Percutaneous Coronary Intervention for Acute Myocardial Infarction in Korea, Japan, and Taiwan. *Int J Health Policy Manag*. 2023.01; 12; 6796
102. Nozomu Sugimoto, Ryutaro Matsugaki, Satoshi Kuhara, Hanaka Imamura, Hideaki Itoh, Masaru Araki, Kiyohide Fushimi, Shinya Matsuda, Satoru Saeki. The Relationship Between Preoperative Frailty Risk as Assessed by the Hospital Frailty Risk Score and the Outcome at Discharge in Coronary Artery Bypass Grafting (CABG) Patients: A Retrospective Observational Study Using the Diagnosis Procedure Combination Database. *J UOEH*. 2023.01; 45(4); 209-216

Life Sciences and Bioethics

Masayuki Yoshida
Yusuke Ebana
Hiroko Kohbata
Naki Gau

(1) Outline

The purpose of our center is to contribute to advancing medical research at TMDU by establishing an efficient support system for the development of education, research, and clinical services in the field of bioethics. While advising on the regulatory authorities of research ethics guidelines, we also provide support to the university's internal review board and also serve as the headquarter of research ethics committees at domestic medical universities nationwide.

Moreover, we organize research ethics seminars for medical professionals and researchers throughout the university to ensure scientific and ethical integrity. In the clinical field, we are in charge of the Department of Medical Genetics which provides genetic diagnosis and treatment for hereditary cancers and rare diseases with a system to provide genetic counseling to clients, including patients and their families.

(2) Publications

[Original Articles]

1. Okamura T, Tsukamoto K, Arai H, Fujioka Y, Ishigaki Y, Koba S, Ohmura H, Shoji T, Yokote K, Yoshida H, Yoshida M, Deguchi J, Dobashi K, Fujiyoshi A, Hamaguchi H, Hara M, Harada-Shiba M, Hirata T, Iida M, Ikeda Y, Ishibashi S, Kanda H, Kihara S, Kitagawa K, Kodama S, Koseki M, Maezawa Y, Masuda D, Miida T, Miyamoto Y, Nishimura R, Node K, Noguchi M, Ohishi M, Saito I, Sawada S, Sone H, Takemoto M, Wakatsuki A, Yanai H. Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2022. *Journal of atherosclerosis and thrombosis*. 2023.12;
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3. Yusuke Ebana, Lian Liu, Kensuke Ihara, Keiko Abe, Chikashi Terao, Yoichiro Kamatani, Tetsuo Sasano, Tetsushi Furukawa. Genetic risk score of cerebral infarction in atrial fibrillation genome-wide association study. *Eur J Clin Invest*. 2023.08; e14084
4. 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*. 2023.02; 30(2); 131-137
5. Egawa M, Kanda E, Ohtsu H, Nakamura T, Yoshida M. Hypertensive Disorders of Pregnancy are Associated with Cardiovascular Disease in Middle- and Older-Aged Japanese Women. *Journal of atherosclerosis and thrombosis*. 2023.01; 30(10); 1420-1426
6. Shizuka Kirino, Analia Yogi, Eriko Adachi, Hisae Nakatani, Maki Gau, Ryosei Iemura, Haruki Yamano, Toru Kanamori, Takayasu Mori, Eisei Sohara, Shinichi Uchida, Kentaro Okamoto, Tomohiro Udagawa,

Kei Takasawa, Tomohiro Morio, Kenichi Kashimada. Phenotypic Variation in 46,XX Disorders of Sex Development due to the Fourth Zinc Finger Domain Variant of WT1: A Familial Case Report. Sex Dev. 2023; 17(1); 51-55

[Books etc]

1. Genetic counseling standard text. 2023.10 (ISBN : 978-4-7878-2596-4)

[Conference Activities & Talks]

1. Eriko Adachi, Ryuichi Nakagawa, Atsumi Tsuji-Hosokawa, Maki Gau, Shizuka Kirino, Analia Yogi, Hikase Nakatani, Tomomi Yamaguchi, Masanori Murakami, Toshihiro Tajima, Tomonobu Hasegawa, Tetsuya Yamada, Tomohiro Morino, Osamu Ohara, Kenichi Kashimada. Development of a clinically applicable one-step PCR-based CYP21A2 analysis using long read sequences.. Human Genetics Asia 2023(68th Annual Meeting of Japan Society of Human Genetics/ 14th Asia Pacific Conference on Human Genetics/ 22nd Annual meeting of East Asian Union of human Genetics Societies) 2023.10.14 Tokyo Japan
2. Suzuka Kato, Yusuke Ebana. Exploratory study for patient and public involvement in genomic researchers. 14th Asia Pacific Conference on Human Genetics (APCHG) 2023.10.11 Tokyo
3. Shizuka Kirino, Ryuichi Nakagawa, Kei Takasawa, Maki Gau, Atsumi Tsuji-Hosokawa, Liang Zhao, Josephine Bowles, Peter Koopman, Tomohiro Morio, Kenichi Kashimada.. Application of Cap analysis of gene expression (CAGE) in genetic analysis of mouse sex differentiation. Ninth International Symposium on the Biology of Vertebrate Sex Determination 2023.04.19 Kailua-Kona, HAWAII
4. Yusuke Ebana. How to solve research ethics issues? -Role of Certified Research Ethics Professionals (CReP) as an Ethical Review Expert-. ENRIO2023 (European Network of Research Integrity Offices) 2023.09.07
5. Mariko Komine, Yusuke Ebana. The current status and issues of genetic counseling and testing with inherited cardiac arrhythmia at our hospital. 14th Asia Pacific Conference on Human Genetics (APCHG) 2023.10.11 Tokyo
6. Yusuke Ebana. Role of Certified Research Ethics Professionals (CReP) as an Ethical Review Expert. Asia Pacific Research Integrity Network Meeting 2023.03.21 Tokyo
1. Hiyori Ueda, Hiroko Terui-Kohbata, Masayuki Yoshida. Ethical Issues in Pediatric Genomic Data Sharing: Current Status and Opinions of Biobanks on Reconsent. The 35th Annual Meeting of the Japan Society for Bioethics 2023.12.09 Tokyo
2. Eiko Ishihara, Hiroko Terui-Kohbata, Masayuki Yoshida. Survey on Ethical Issues in Informed Consent for the Treatment of COVID-19. The 35th Annual Meeting of the Japan Society for Bioethics 2023.12.09 Tokyo
3. Hiroko Terui-Kohbata. How to use the "Standard Text of Genetic Counseling" in the Genetic Counselor Training Course. The 68th Annual Meeting of the Japan Society of Human Genetics, the 14th Annual Meeting of the Asia-Pacific Society of Human Genetics, and the 21st Annual Meeting of the East Asian Society of Human Genetics 2023.10.12 Tokyo

Forensic Dentistry

Professor Koichi SAKURADA
 Associate Professor Hisako SAITOH
 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
 Graduate Student Nanami AOKI
 Graduate Student Sayaka YAMADA

(1) Outline

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

(2) Research

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

(3) Education

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

(6) Publications

[Original Articles]

1. Hajime Utsuno, Yohsuke Makino, Shuuji Namiki, Saki Minegishi, Maiko Toya, Hirotaro Iwase, Koichi Sakurada. Morphological Observation of the Alar Region between the Piriform Aperture and the Alar Soft Tissue for Facial Approximation (Reconstruction) Forensic Anthropology. 2023.11;
2. Saitoh H, Takeyama M, Moriya T, Yusa K, Minegishi S, Torimitsu S, Chiba F, Hoshioka Y, Nagasawa S, Iino M, Sakurada K, Iwase H, Tokanai F. Usefulness of powdered crown of mandibular first premolars in birth year estimation by radiocarbon dating. Journal of forensic and legal medicine. 2023.10; 100; 102607
3. Namiki S, Utsuno H, Makino Y, Minegishi S, Toya M, Iwase H, Sakurada K. Estimation of missing mandible from the skull using postmortem CT images. Legal medicine (Tokyo, Japan). 2023.09; 65; 102321
4. Sumi N, Minegishi S, Ohta J, Utsuno H, Sakurada K. Study on the Mechanism of the Pink Tooth Phenomenon Using Bovine Teeth: A Pilot Study. Diagnostics (Basel, Switzerland). 2023.08; 13(16);
5. Ohta J, Minegishi S, Noda N, Sakurada K. Estimating the way of deposition of saliva stains using quantitative analysis of forensic salivary biomarkers. Legal medicine (Tokyo, Japan). 2023.06; 64; 102277
6. Mirei Takeyama, Toru Moriya, Hisako Saitoh, Hiroko Miyahara, Fusa Miyake, Motonari Ohyama, Rimi Sato, Rie Shitara, Hirohisa Sakurai, Fuyuki Tokanai. Present status of the YU-AMS system and its operation over the past 10 years Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms. 2023.05; 538; 30-35
7. Saki Minegishi, Hajime Utsuno, Jun Ohta, Shuuji Namiki, Maiko Toya, Nozomi Sumi, Hisako Saitoh, Koichi Sakurada. Comparison of racemization rates between vital and endodontically treated teeth for age estimation. Leg Med (Tokyo). 2023.03; 61; 102189
8. Kei Kira, Fumiko Chiba, Yohsuke Makino, Suguru Torimitsu, Rutsuko Yamaguchi, Shigeki Tsuneya, Ayumi Motomura, Maiko Yoshida, Naoki Saitoh, Go Inokuchi, Yumi Hoshioka, Hisako Saitoh, Daisuke Yajima, Hirotaro Iwase. Stature estimation by semi-automatic measurements of 3D CT images of the femur International journal of legal medicine. 2023.03; 137(2); 359-377
9. Hisako Saitoh, Yuko Sakai-Tagawa, Sayaka Nagasawa, Suguru Torimitsu, Kazumi Kubota, Yuichiro Hirata, Kiyoko Iwatsuki-Horimoto, Ayumi Motomura, Namiko Ishii, Keisuke Okaba, Kie Horioka, Hiroyuki Abe, Masako Ikemura, Hirofumi Rokutan, Munetoshi Hinata, Akiko Iwasaki, Yoichi Yasunaga, Makoto Nakajima, Rutsuko Yamaguchi, Shigeki Tsuneya, Kei Kira, Susumu Kobayashi, Go Inokuchi, Fumiko Chiba, Yumi Hoshioka, Aika Mori, Isao Yamamoto, Kimiko Nakagawa, Harutaka Katano, Shun Iida, Tadaki Suzuki, Shinji Akitomi, Iwao Hasegawa, Tetsuo Ushiku, Daisuke Yajima, Hirotaro Iwase, Yohsuke Makino, Yoshihiro Kawaoka. High titers of infectious SARS-CoV-2 in COVID-19 corpses. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2023.02; 129; 103-109
10. Kiyoko Iwatsuki-Horimoto, Hiroshi Ueki, Mutsumi Ito, Sayaka Nagasawa, Yuichiro Hirata, Kenichiro Hashizume, Kazuho Ushiwata, Hirotaro Iwase, Yohsuke Makino, Tetsuo Ushiku, Shinji Akitomi, Masaki Imai, Hisako Saitoh, Yoshihiro Kawaoka. SARS-CoV-2 Transmission from Virus-Infected Dead Hamsters mSphere. 2023.01; e0041122

11. Yuichiro Hirata, Shun Iida, Takeshi Arashiro, Sayaka Nagasawa, Hisako Saitoh, Hiroyuki Abe, Masako Ikemura, Yohsuke Makino, Rintaro Sawa, Hirotaro Iwase, Tetsuo Ushiku, Tadaki Suzuki, Shinji Akitomi. Impact of the COVID-19 pandemic on pathological autopsy practices in Japan Pathology international. 2023.01; 73(3); 120-126
1. Hisako Saitoh, Koichi Nakakuki, Namiko Ishii, Tetsuya Iida, Yoshihiro Yamada, Hirotaro Iwase.. Study of usefulness of scanning images in dental findings from Corpses -Utilization of intraoral scanners for Disaster Victim Identification- Japanese Journal of Disaster Medicine. 2023.12; 28(3); 124-127
2. Koichi Sakurada. Dental Education White Paper 2021 Forensic Dentistry Education 2023.02; 別冊; 77-78

[Misc]

1. Koichi Sakurada. Effects on oral tissues of asphyxiation caused by cervical compression: The pink teeth phenomenon in Kato's studies (1941). Leg Med (Tokyo). 2023.06; 64; 102284

[Conference Activities & Talks]

1. Shuuji Namiki, Hjime Utusno, Yosuke Makino, Saki Minegishi, Maiko Toya, Nozomi Sumi, Hirotaro Iwase, Koichi Sakurada. Method for estimating missing mandible from the skull using postmortem CT images . The 107th Congress of the Japanese Society of Legal Medicine 2023.06.08 Odawara City
2. Hanafi Muhammad Garry Syahrizal, Hajime Utsuno, Saki Minegishi, Koichi Sakurada . Forensic Odontology in Indonesia. 17th Annual Meeting of Japanese Society of Forensic Dental Science 2023.05.14 Tokyo Medical and Dental University
1. Saki Minegishi, Kana Unuma, Koichi Uemura, Koichi Sakurada. Comparison between dental findings of unidentified cadavers and Ministry of Health, Labor and Welfare dental disease survey. The 60th Annual Meeting of the Japanese Association of Criminology 2023.11.26 Bunkyo-ku, Tokyo
2. Jun Ohta, Saki Minegishi, Kosuke Tanimoto, Hajime Utsuno, Hisako Saitoh, Koichi Sakurada. Search for bacterial DNA markers that is useful for identifying saliva from degraded samples through bacterial flora analysis. The 32nd Annual Meeting of the Japanese society for DNA Polymorphism Research 2023.11.17 Shimonoseki city
3. Nozomi Sumi, Saki Minegishi, Hajime Utsuno, Shuuji Namiki, Maiko Toya, Jun Ohta, Hisako Saitoh, Koichi sakurada. Pilot study on the mechanism of pink tooth phenomenon using bovine teeth. The 92nd Kanto District Meeting of the Japanese Society of Legal Medicine 2023.10.14 Kawasaki city
4. Maiko Toya, Saki Minegishi, Hajime Utsuno, Jun Ohta, Syuuji Namiki, Nozomi Toya, Hisako Saitoh, Kana Unuma, Koichi Uemura, Koichi Sakurada. Research on trauma findings of physical abuse of the elderly in day care facilities and collaboration with related organizations. The 92nd Kanto District Meeting of the Japanese Society of Legal Medicine 2023.10.14 Kawasaki city
5. Hisako Saitoh. Grief care effect for bereaved families by embalming. The 65th Annual Meeting of Japanese Association for Oral Biology 2023.09.18 Tokyo
6. Hisako Saitoh. DNA typing using FFPE samples. The 65th Annual Meeting of Japanese Association for Oral Biology 2023.09.17 Tokyo
7. Hisako Saitoh, Seiko Katsumura, Hiroko Oka, Eiko Kosuge, Rie Yamaguchi, Akiko Kumagai.. Digital Educational Materials on Identification Work with Dental Findings. The 42nd Annual Meeting of Japanese Dental Education Association 2023.07.15 WEB
8. Hiroko Oka, Hisako Saitoh, Saki Minegishi, Masataka Nagao.. Verification of materials used in dental treatment in Vietnam. The 107th Congress of the Japanese Society of Legal Medicine 2023.06.09 Odawara City
9. Sayaka Nagasawa, Yuichiro Hirata, Shigeki Tsuneya, Kei Kira, Susumu Kobayashi, Shinji Akitomi, Tadaki Suzuki, Hirotaro Iwase, Yohsuke Makino, Hisako Saitoh.. Investigation of changes over time in viral titers in SARS-CoV-2-infected cadavers. The 107th Congress of the Japanese Society of Legal Medicine 2023.06.08 Odawara City

10. Namiko Ishii, Naoki Saito, Satomi Mizuno, Susumu Kobayashi, Ayaka Sakuma, Ayumi Motomura, Go Inokuchi, Daisuke Yajima, Hirotaro Iwase, Hisako Saitoh.. Dental evaluation in child abuse cases. The 107th Congress of the Japanese Society of Legal Medicine 2023.06.08
11. Hajime Utsuno, Syuuji Namiki, Yosuke Makino, Hisako Saitoh, Saki Minegishi, Maiko Toya, Nozomi Sumi, Jun Ohta, Hirotaro Iwase, Koichi Sakurada . Study on the morphological estimation of the auricle in facial reconstruction of the Japanese skull. The 107th Congress of the Japanese Society of Legal Medicine 2023.06.08 Odawara City
12. Tomoko Akutsu, Saki Minegishi, Ken Watanabe, Koichi Sakurada. Exploration and evaluation of menstrual blood markers for the development of menstrual blood test methods. The 107th Congress of the Japanese Society of Legal Medicine 2023.06.08 Odawara City
13. Nozomi Sumi, Saki Minegishi, Hajime Utsuno, Maiko Toya, Jun Ohta, Hisako Saitoh, Koichi sakurada. Study on color development mechanism in pink teeth phenomenon -examination of involvement with hemoglobin, degradation products, and red pigment-producing bacteria-. 17th Annual Meeting of Japanese Society of Forensic Dental Science 2023.05.14 Tokyo Medical and Dental University
14. Hisako Saitoh, Sayaka Nagasawa, Yuichiro Hirata, Yohsuke Makino, Suguru Torimitsu, Susumu Kobayashi, Namiko Ishii, Isao Yamamoto, Kimiko Nakagawai, Iwao Hasegawa, Daisuke Yajima, Hirotaro Iwase, Yoshihiro Kawaoka.. Evaluation of the infectivity of SARS-CoV-2 remaining in cadavers. 17th Annual Meeting of Japanese Society of Forensic Dental Science 2023.05.14 Tokyo
15. Akiko Kumagai, Yumiko Ohbayashi, Hiroko Oka, Yuka Hatano, Seiko Katsumura, Eiko Kosuge, Rie Yamaguchi, Hisako Saitoh, . Introducing digital teaching materials for identity verification training, including support for bereaved families, provided by JUMP (Japan Unidentified and Missing Persons Response Team). 17th Annual Meeting of Japanese Society of Forensic Dental Science 2023.05.14 Tokyo
16. Susumu Kobayashi. Rutusko Yamaguchi, Yohsuke Makino, Suguru Torimitsu, Fumiko Chiba, Sayaka Nagasawa, Maiko Yoshida, Hisako Saitoh, Hirotaro Iwase.. Age estimation using teeth of infant remains buried in plaster 50 years ago. 17th Annual Meeting of Japanese Society of Forensic Dental Science 2023.05.14 Tokyo
17. Hisako Saitoh, Koichi Nakakuki, Namiko Ishii, Kimiko Nakagawa, Saeko Fujita, Hiroshi Ohira, Isao Yamamoto, Hirotaro Iwase, Iwao Hasegawa, Yoshihiro Yamada, Keiko Shimizu.. Examination of dental chartings using an intraoral scanner on unidentified corpses. The 28th Annual Meeting of Japanese Association of Disaster Medicine 2023.03.10 Iwate
18. Saeko Fujita, Isao Yamamoto, Kimiko Nakagawa, Hiroshi Ohira, Masanori Ikeno, Iwao Hasegawa, Hisako Saitoh, Yohsuke Maikono, Hirotaro Iwase, Yoshihiro Yamada.. Investigation of work efficiency by PPE (personal protective equipment) in dental chartings. The 28th Annual Meeting of Japanese Association of Disaster Medicine 2023.03.10 Iwate

[Others]

1. The 17th Annual Meeting of Japanese Society of Forensic Dental Science (Koichi Sakurada), 2023.05
A sponsor of the 17th Annual Meeting of Japanese Society of Forensic Dental Science

[Social Contribution]

1. Personal identification using dental findings and others (101 cases) , 2023.01.01 - 2023.12.31
2. 2022 Personal identification training program (Second) (Koichi Sakurada) , Tokyo Dental Association, Japan Dental Association Building, 2023.03.12
3. Thinking about the multidisciplinary collaboration required in the field of forensic medicine and forensic dentistry, Miyazaki Dental Association Police Dental and Disaster Countermeasures Conference (Hisako Saitoh), Miyazaki Dental Association Building, 2023.08.19
4. Tokyo/Higashimurayama City Joint Comprehensive Disaster Prevention Drill (Koichi Sakurada, Shuuji Namiki), Tokyo/Higashimurayama City, Higashimurayama City, 2023.09.03
5. 2023 Personal identification training program (First) (Koichi Sakurada) , Tokyo Metropolitan Government Bureau of Public Health and Medical Care, Dental Association Building, 2023.10.15

6. 2023 Personal identification training program in Kanagawa (Koichi Sakurada, Hisako Saitoh) , Kanagawa Dental Association , Tsurumi University , 2023.11.19
7. Disaster victim Identification system required in future mass disasters, Yamagata Dental Association (Hisako Saitoh), Yamagata Dental Association Building, 2023.12.03
8. Arakawa Dental Association Lecture (Koichi Sakurada) , Arakawa Dental Association , Workshop for the Police Cooperating Medical Association , Arakawa Dental Association Building , 2023.12.06
9. Forensic Odontology seminar of Iwate Dental Association (Koichi Sakurada), Iwate Dental Association, seminar, Iwate Dental Association Building , 2023.12.09

Dental Education Development

Associate Professor: Naoko SEKI

(1) Research

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

(2) Education

The educational goal of this section as part of the graduate school, is to help students training to deliver health care learn the basics of medical/dental curricula: educational objectives, strategies and evaluation. This section is currently involved in the following education as the coordinators of multiple modules: the students' research projects, courses for global competencies including various English courses; courses for international exchange/global-mindset for both undergraduate and postgraduate students; and courses for clinical skill acquisition as a part of life-long learning.

(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. Collaborative Continuing Education Course Provision between Melbourne Dental School and Tokyo Medical and Dental University (TMDU)

(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*. 2023.07; 18(3); 1094-1102
2. 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*. 2023.02; 45(1); 20-28
3. 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*. 2023.01; 18(1); 95-104

4. 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*. 2023.01; 18(1); 443-447

Oral Health Promotion

Professor Jun Aida
 Associate Professor Yusuke Matsuyama
 Junior Associate Professor Shiho Kino
 Assistant Professor Takashi Zaito
 Medical staff Risa Aritomi
 Project researcher Yuko Inoue
 Collaborative researcher Sakura Kiuchi
 Office administrator Sumi Ito
 Graduate Student Tomoya Saito
 Akiko Okuda
 Ho Sy Minh Duc
 Satomi Shimada
 Masuko Sayo
 Sharmin Farzana
 Kewei Wang
 Syunya Masuko
 Aishwarya Gaikwad

(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

[Original Articles]

1. Kinumi Yamamoto-Kuramoto, Taro Kusama, Sakura Kiuchi, Katsunori Kondo, Ken Osaka, Kenji Takeuchi, Jun Aida. Lower socio-economic status in adolescence is associated with poor oral health at an older age: Mediation by social and behavioural factors. *Gerodontology*. 2023.12; 40(4); 509-517
2. Taro Kusama, Kenji Takeuchi, Sakura Kiuchi, Jun Aida, Ken Osaka. Poor oral health and dementia risk under time-varying confounding: A cohort study based on marginal structural models. *J Am Geriatr Soc*. 2023.12;
3. Anna Kinugawa, Taro Kusama, Kenji Takeuchi, Jun Aida, Sakura Kiuchi, Ryoko Katagiri, Hiroyuki Hikichi, Satoshi Sasaki, Katsunori Kondo, Ken Osaka. Association between dietary pattern and insomnia symptoms among independent older adults: A cross-sectional study based on JAGES. *Sleep Med*. 2023.12; 112; 70-76
4. 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*. 2023.11; 28(6); 1298-1302
5. Ishimaru, M; Zaitzu, T; Kino, S; Inoue, Y; Taira, K; Takahashi, H; Tamiya, N. Recent dental visits and family caregiving among individuals with dental symptoms: A nationwide cross-sectional study in Japan *COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY*. 2023.11;
6. Shuji Hibiya, Takashi Fujii, Toshimitsu Fujii, Shinji Suzuki, Mayumi Kondo, Shinya Ooka, Yohei Furumoto, Seishin Azuma, Kei Tanaka, Hitoshi Kurata, Shohei Tanaka, Masayuki Kurosaki, Kazuyoshi Nagayama, Fumihiko Kusano, Yasuhiro Iizuka, Takahiro Kawamura, Hidekazu Ikemiyagi, Shinya Sakita, Tsunehito Yauchi, Hideki Watanabe, Ami Kawamoto, Yusuke Matsuyama, Kazuo Ohtsuka, Ryuichi Okamoto. COVID-19 severity is associated with the risk of gastrointestinal bleeding. *BMJ Open Gastroenterol*. 2023.11; 10(1);
7. Yusuke Matsuyama, Takahiro Tabuchi. Does Tobacco Smoking Increase Social Isolation? A Mendelian Randomization Study. *Am J Epidemiol*. 2023.11;
8. Matsuura, T; Mikami, R; Mizutani, K; Shioyama, H; Aoyama, N; Suda, T; Kusunoki, Y; Takeda, K; Izumi, Y; Aida, J; Aoki, A; Iwata, T. Assessment of bone defect morphology for the adjunctive use of bone grafting combined with enamel matrix derivative: A 3-year cohort study *JOURNAL OF PERIODONTOLOGY*. 2023.11;
9. Shiho Kino, Jun Aida J, Katsunori Kondo, Ichiro Kawachi. Do disasters exacerbate socioeconomic inequalities in health among older people? *International Journal of Disaster Risk Reduction*. 2023.11; 98(104071);

10. Matsukura H, Yamaoka Y, Matsuyama Y, Kondo K, Fujiwara T*. Association between adverse childhood experiences and marital status among Japanese older adults. *Child Abuse Negl.* 2023.10; 144; 106340
11. Yoshinaka S, Yamaguchi K, Yanagida R, Ishii M, Nakagawa K, Yoshimi K, Nakane A, Matsuyama Y, Aida J, Tohara H . Tongue Strength of Older Adults Requiring Long-Term Care Varies throughout the Day Geriatrics. 2023.10;
12. Yudai Tamada, Kenji Takeuchi, Taro Kusama, Masashige Saito, Tetsuya Ohira, Kokoro Shirai, Chikae Yamaguchi, Katsunori Kondo, Jun Aida, Ken Osaka. Reduced number of teeth with and without dental prostheses and low frequency of laughter in older adults: Mediation by poor oral function. *J Prosthodont Res.* 2023.10;
13. Tani Y*, Matsuyama Y, Yamaoka Y, Matsukura H, Kawahara T, Fujiwara T. Change of human flourishing during the COVID-19 pandemic in Japan: Results from population-based U-CORONA study. *SSM Popul Health.* 2023.09; 23; 101430
14. Hiroyuki Hikichi, Koichiro Shiba, Jun Aida, Katsunori Kondo, Ichiro Kawachi. Association between sense of coherence and health and well-being among older survivors of a natural disaster: a prospective outcome-wide study. *Sci Rep.* 2023.09; 13(1); 16385
15. Yukako Tani, Takafumi Yamamoto, Taro Kusama, Anna Kinugawa, Jun Aida, Takeo Fujiwara, Katsunori Kondo. Cooking skills modify the association between oral health and mortality. *Age Ageing.* 2023.09; 52(9);
16. Kinumi Yamamoto-Kuramoto, Sakura Kiuchi, Kenji Takeuchi, Taro Kusama, Noriko Nakazawa, Yudai Tamada, Jun Aida, Katsunori Kondo, Ken Osaka. Oral status and incident functional disability: A 9-year prospective cohort study from the JAGES. *Arch Gerontol Geriatr.* 2023.08; 111; 105009
17. Sakura Kiuchi, Jun Aida, Upul Cooray, Ken Osaka, Angelique Chan, Rahul Malhotra, Marco A Peres. Education-related inequalities in oral health among older adults: Comparing Singapore and Japan. *Community Dent Oral Epidemiol.* 2023.08; 51(4); 671-679
18. Hiroyuki Hikichi, Yasuyuki Sawada, Jun Aida, Katsunori Kondo, Ichiro Kawachi. Association between housing damage, present bias and delayed-onset post-traumatic stress symptoms among older adults 9 years after a natural disaster. *J Epidemiol Community Health.* 2023.08; 77(8); 494-500
19. Shiho Kino, Keiko Ueno, Daisuke Nishioka, Naoki Kondo, Jun Aida. Prevalence of dental visits in older Japanese adults receiving public assistance. *Community Dent Oral Epidemiol.* 2023.08;
20. Shiho Kino, Yudai Tamada, Kenji Takeuchi, Atsushi Nakagomi, Koichiro Shiba, Taro Kusama, Takafumi Yamamoto, Jun Aida. Exploring the relationship between oral health and multiple health conditions: An outcome-wide approach. *J Prosthodont Res.* 2023.08;
21. L. H. Matsunaga, D. Aldrich, C. Faiad, T. Aoki, P.-H. Tseng, J. Aida. The Psychological Determinants of Avoiding Crowded Areas: An International and Political Investigation *Journal of Social and Political Psychology.* 2023.08; 11(2); 458-477
22. Keiko Ueno, Daisuke Nishioka, Junko Saito, Shiho Kino, Naoki Kondo. Identifying meaningful subpopulation segments among older public assistance recipients: a mixed methods study to develop tailor-made health and welfare interventions *International Journal for Equity in Health.* 2023.08; 22(1);
23. Shiho Kino, Yudai Tamada, Kenji Takeuchi, Atsushi Nakagomi, Koichiro Shiba, Taro Kusama, Takafumi Yamamoto, Jun Aida. Exploring the relationship between oral health and multiple health conditions: An outcome-wide approach *Journal of prosthodontic research.* 2023.08;
24. Takeo Fujiwara, Yuna Koyama, Aya Isumi, Yusuke Matsuyama, Yukako Tani, Yukinobu Ichida, Katsunori Kondo, Ichiro Kawachi. "What Did You Do in the War, Daddy?": Paternal Military Conscription During WWII, Economic Hardship and Family Violence in Childhood, and Health in Late Life in Japan *J Interpers Violence.* 2023.07; 38(13-14); 8114-8135
25. Risako Mikami, Koji Mizutani, Tomohito Gohda, Yusuke Matsuyama, Hiromichi Gotoh, Keita Nakagawa, Shu Takemura, Norio Aoyama, Takanori Matsuura, Daisuke Kido, Kohei Takeda, Natsumi Saito, Yuichi Izumi, Takanori Iwata. Malnutrition- inflammation- atherosclerosis (MIA) syndrome associates with periodontitis in end-stage renal disease patients undergoing hemodialysis: a cross-sectional study. *Sci Rep.* 2023.07; 13(1); 11805

26. Yusuke Matsuyama, Aya Isumi, Satomi Doi, Takeo Fujiwara. Persistent poverty and child dental caries: time-varying exposure analysis. *J Epidemiol Community Health*. 2023.07;
27. T Yamamoto, M Hanazato, H Hikichi, K Kondo, K Osaka, I Kawachi, J Aida. Change in Geographic Accessibility to Dental Clinics Affects Access to Care. *J Dent Res*. 2023.07; 102(7); 719-726
28. Satomi Shimada, Takashi Zaitzu, Akiko Oshiro, Shiho Kino, Jun Aida. Association of oral health with various work problems: a cross-sectional study of Japanese workers. *BMC Oral Health*. 2023.07; 23(1); 488
29. Taro Kusama, Kenji Takeuchi, Sakura Kiuchi, Jun Aida, Hiroyuki Hikichi, Satoshi Sasaki, Katsunori Kondo, Ken Osaka. Dental prosthesis use is associated with higher protein intake among older adults with tooth loss. *J Oral Rehabil*. 2023.07;
30. S Kiuchi, U Cooray, J Aida, K Osaka, A Chan, R Malhotra, M A Peres. Effect of Tooth Loss on Cognitive Function among Older Adults in Singapore. *J Dent Res*. 2023.07; 102(8); 871-878
31. U Cooray, G Tsakos, A Heilmann, R G Watt, K Takeuchi, K Kondo, K Osaka, J Aida. Impact of Teeth on Social Participation: Modified Treatment Policy Approach. *J Dent Res*. 2023.07; 102(8); 887-894
32. Miho Ishimaru, Takashi Zaitzu, Shiho Kino, Kento Taira, Yuko Inoue, Hideto Takahashi, Nanako Tamiya. Dental Utilization Stratified by the Purpose of Visit: A Population-Based Study in Japan. *International dental journal*. 2023.07;
33. Satomi Shimada, Takashi Zaitzu, Akiko Oshiro, Shiho Kino, Jun Aida. Association of oral health with various work problems: a cross-sectional study of Japanese workers *BMC Oral Health*. 2023.07;
34. Manami Hoshi-Harada, Jun Aida, Upul Cooray, Noriko Nakazawa, Katsunori Kondo, Ken Osaka. Difference of income inequalities of denture use by co-payment rates: A JAGES cross-sectional study. *Community Dent Oral Epidemiol*. 2023.06; 51(3); 557-564
35. Yusuke Matsuyama. Time-varying exposure analysis of the relationship between sustained natural dentition and cognitive decline. *J Clin Periodontol*. 2023.06; 50(6); 727-735
36. Pissacha Daroonpan, Ryo Ouchi, Chenyang Zhang, Shigenori Nagai, Naoto Nishii, Yoshihisa Kashima, Fumihiko Tsushima, Hiroyuki Harada, Miwako Hamagaki, Tohru Ikeda, Jun Aida, Ruchadaporn Kaomongkolgit, Miyuki Azuma. Personal immune profiles: Diversity and prognostic value for oral tongue squamous cell carcinoma evaluated by comprehensive immune parameter analyses with multiplex immunofluorescence. *Oral Oncol*. 2023.06; 143; 106458
37. Sasin Sritara, Yoshiro Matsumoto, Yixin Lou, Jia Qi, Jun Aida, Takashi Ono. Association between the Temporomandibular Joint Morphology and Chewing Pattern. *Diagnostics (Basel)*. 2023.06; 13(13);
38. Keiko Murakami, Jun Aida, Shinichi Kuriyama, Hideki Hashimoto. Associations of health literacy with dental care use and oral health status in Japan. *BMC Public Health*. 2023.06; 23(1); 1074
39. Yuki Arakawa, Maho Haseda, Kosuke Inoue, Daisuke Nishioka, Shiho Kino, Daisuke Nishi, Hideki Hashimoto, Naoki Kondo. Effectiveness of mHealth consultation services for preventing postpartum depressive symptoms: a randomized clinical trial *BMC Medicine*. 2023.06; 21(1);
40. Maki Nii, Nobuhiro Yoda, Ramadhan Hardani Putra, Jun Aida, Keiichi Sasaki. Evaluation of the optimal hardness and thickness of music splints for wind instrument players. *J Prosthet Dent*. 2023.05; 129(5); 754-762
41. Suzuki Takumi, Hosomichi Jun, Miyasaka Naoyuki, Miyazaki Yasunari, Taki Atsuko, Zaitzu Takashi, Morioka Chikako, Sato Noriko, Moro Manaka, Ono Takashi. CHARACTERISTICS OF OBSTRUCTIVE SLEEP APNEA AMONG PREGNANT JAPANESE WOMAN AND THEIR BIRTH OUTCOMES SLEEP. 2023.05; 46; A229
42. Hazem Abbas, Jun Aida, Sakura Kiuchi, Katsunori Kondo, Ken Osaka. Oral status and homebound status: A 6-year bidirectional exploratory prospective cohort study. *Oral Dis*. 2023.04; 29(3); 1291-1298
43. Hazem Abbas, Jun Aida, Upul Cooray, Takaaki Ikeda, Shihoko Koyama, Katsunori Kondo, Ken Osaka. Does remaining teeth and dental prosthesis associate with social isolation? A six-year longitudinal study from the Japan Gerontological Evaluation Study (JAGES). *Community Dent Oral Epidemiol*. 2023.04; 51(2); 345-354

44. Takaaki Ikeda, Yoshimune Hiratsuka, Natsuyo Yanagi, Yasunori Komaki, Masayasu Murakami, Jun Aida, Katsunori Kondo, Ken Osaka. Health-related quality of life in various health conditions: two consecutive surveys of older Japanese adults. *Qual Life Res.* 2023.04; 32(4); 1209-1219
45. Lucas Heiki Matsunaga, Toshiaki Aoki, Cristiane Faiad, Daniel P Aldrich, Po-Hsing Tseng, Jun Aida. Why People Stayed Home During the COVID-19 Pandemic: Implications for Health Communication Across Four Countries. *J Health Commun.* 2023.04; 28(4); 218-230
46. Kousuke Iwai-Saito, Koryu Sato, Jun Aida, Katsunori Kondo. Association of frailty with influenza and hospitalization due to influenza among independent older adults: a longitudinal study of Japan Gerontological Evaluation Study (JAGES). *BMC Geriatr.* 2023.04; 23(1); 249
47. Masanori Iwasaki, Akihiro Yoshihara, Kana Suwama, Takashi Zaitzu, Seitaro Suzuki, Hikaru Ihira, Norie Sawada, Jun Aida. A cross-sectional study of the association between periodontitis and physical activity in the Japanese population. *J Periodontal Res.* 2023.04; 58(2); 350-359
48. Yusuke Matsuyama, Takahiro Tabuchi. Stepwise Tobacco Price Increase and Smoking Behavioral Changes in Japan: The Japan "Society and New Tobacco" Internet Survey 2017-2021 Longitudinal Study. *Nicotine Tob Res.* 2023.03; 25(4); 657-664
49. Shiho Kino, Andrew Stickley, Yuki Arakawa, Masashige Saito, Tami Saito, Naoki Kondo. Social isolation, loneliness, and their correlates in older Japanese adults. *Psychogeriatrics.* 2023.03;
50. Takaaki Ikeda, Yusuke Matsuyama, Masayasu Murakami, Ken Osaka. Duration of Education and Back Pain: Lessons From English Schooling Reforms. *Am J Epidemiol.* 2023.02; 192(2); 195-204
51. Yusuke Matsuyama, Takeo Fujiwara, Jun Aida. Tap water natural fluoride and parent-reported experience of child dental caries in Japan: Evidence from a nationwide birth cohort survey. *Community Dent Oral Epidemiol.* 2023.02;
52. Koichiro Shiba, Adel Daoud, Hiroyuki Hikichi, Aki Yazawa, Jun Aida, Katsunori Kondo, Ichiro Kawachi. Uncovering Heterogeneous Associations Between Disaster-Related Trauma and Subsequent Functional Limitations: A Machine-Learning Approach. *Am J Epidemiol.* 2023.02; 192(2); 217-229
53. Noriko Nakazawa, Taro Kusama, Upul Cooray, Takafumi Yamamoto, Sakura Kiuchi, Hazem Abbas, Tatsuo Yamamoto, Katsunori Kondo, Ken Osaka, Jun Aida. Large Contribution of Oral Status for Death Among Modifiable Risk Factors in Older Adults: The Japan Gerontological Evaluation Study (JAGES) Prospective Cohort Study. *J Gerontol A Biol Sci Med Sci.* 2023.01; 78(1); 167-173
54. Y Matsuyama, H Jürges, S Listl. Causal Effect of Tooth Loss on Cardiovascular Diseases. *J Dent Res.* 2023.01; 102(1); 37-44
55. T Kusama, K Takeuchi, S Kiuchi, J Aida, K Kondo, K Osaka. Weight Loss Mediated the Relationship between Tooth Loss and Mortality Risk. *J Dent Res.* 2023.01; 102(1); 45-52
56. Noriko Nakazawa, Taro Kusama, Kenji Takeuchi, Sakura Kiuchi, Tatsuo Yamamoto, Katsunori Kondo, Ken Osaka, Jun Aida. Co-Payments and Inequality in Gingival Bleeding and Dental Visits. *Int Dent J.* 2023.01; 73(5); 628-635
57. Tanemura Takashi, Zaitzu Takashi, Oshiro Akiko, Inoue Yuko, Kawaguchi Yoko, Aida Jun. Association of overtime work duration with oral health-related quality of life in Japanese workers *JOURNAL OF ORAL SCIENCE.* 2023.01; 65(1); 44-47
58. Rikuya Hosokawa, Toshiyuki Ojima, Tomoya Myojin, Jun Aida, Katsunori Kondo, Naoki Kondo. Association between the Standardized Mortality Ratio and Healthy Life Expectancy in Japan. *JMA J.* 2023.01; 6(1); 27-35
59. Jin Aoki, Takashi Zaitzu, Akiko Ohshiro, Jun Aida. Association of Stressful Life Events with Oral Health Among Japanese Workers. *J Epidemiol.* 2023.01;
60. A Yazawa, K Shiba, H Hikichi, S S Okuzono, J Aida, K Kondo, S Sasaki, I Kawachi. Post-Disaster Mental Health and Dietary Patterns among Older Survivors of an Earthquake and Tsunami. *J Nutr Health Aging.* 2023; 27(2); 124-133

61. Sayo Masuko, Takashi Zaitzu, Akiko Oshiro, Miho Ishimaru, Jun Aida. Association between place of dental check-ups and work absenteeism among Japanese workers. *J Occup Health*. 2023; 65(1); e12415
62. Association between the number of convenience stores and caries status in permanent teeth among elementary school children: results from the A-CHILD population-based longitudinal cohort study. 2023; 11; 1228197
63. Inoue Y, Cooray U, Ishimaru M, Saito K, Takeuchi K, Kondo K, Aida J. Oral self-care, pneumococcal vaccination, and pneumonia among Japanese older people, assessed with machine learning. *The journals of gerontology. Series A, Biological sciences and medical sciences*. 2023.07;
1. Risako Mikami, Koji Mizutani, Norio Aoyama, Takanori Matsuura, Tomonari Suda, Kohei Takeda, Natsumi Saito, Shinichi Arakawa, Yuichi Izumi, Takanori Iwata, Jun Aida. Income-related inequalities in the association of smoking with periodontitis: a cross-sectional analysis in Tokyo Metropolitan Districts Clinical Oral Investigations. 2023.02; 27(2); 519-528

[Misc]

1. Jun Aida, Miho Ishimaru, Shiho Kino. Reconsidering economic interventions to reduce oral health inequalities. *Community Dent Oral Epidemiol*. 2023.08; 51(4); 600-605

[Conference Activities & Talks]

1. Wang K, Kino S, Matsuyama Y, Shiba K, Nakagomi A, Shirai K, Fueki K, Aida J. Association between oral condition and multidimensional flourishing: A cross-sectional study from the Japan Gerontological Evaluation Study (JAGES). 第 88 回 口腔病学会学術大会 2023.12
2. 相田潤. Oral and cognitive function in the real world: evidence from the JAGES project. The 71st Annual Meeting of Japanese Association for Dental Research 2023.11.25 Sendai
3. Suzuki A, Matsuyama Y, Tani Y, Anzai T, Izumi A, Doi S, Ogawa T, Fujiwara T, Moriyama K. Association between short stature in first grade and permanent teeth caries in sixth grade among elementary school children in Japan: a population-based cohort study. 2023.11.25
4. 相田潤. PDCA を PdCa にせず、pDcA ですすめる健康日本 21（第三次）. 第 82 回日本公衆衛生学会総会 2023.11.02 筑波
5. 木野志保、相田潤. 社会ネットワークの多様性と死亡との関連：前向きコホートをを用いた 9 年間の縦断研究. 第 82 回日本公衆衛生学会総会 2023.11.02
6. 島田怜実、松山祐輔、木野志保、木内桜、近藤克則、相田潤. 所得と認知症の関連における喫煙の媒介効果 JAGES 2010-2019 縦断研究. 第 82 回日本公衆衛生学会総会 2023.11.02
7. 財津崇、井上祐子、相田潤. 労働者の口腔保健状況と EQ-5D との関連について. 第 82 回日本公衆衛生学会総会 2023.11.02
8. 島田怜実、松山祐輔、木野志保、木内桜、近藤克則、相田潤. 所得と認知症の関連における喫煙の媒介効果 JAGES 2010-2019 縦断研究. 第 82 回日本公衆衛生学会総会 2023.11.02
9. Keiko Ueno, Daisuke Nishioka, Shiho Kino, Naoki Kondo. Identifying segments of support for children in households on public assistance: An explanatory sequential mixed methods research design. 5th Regional Mixed Methods Conference 2023.09
10. Takashi Zaitzu. Oral Health Promotion in Space and Antarctic Environment. Stovit Summer Course 2023 2023.08.08 Airlangga University
11. 相田潤. Oral health, general health, and social relations. International Social Capital Conference 2023.06.30 Spain

Educational Media Development

Professor KINOSHITA Atsuhiko
 Assistant Professor SUNAGA Masayo
 Graduate Student AKIYAMA Kyoko(～ March)

(1) Research

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

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

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

At our university, we executed the Integration of Information and Communication Technologies into Clinical Training project, which was adopted as part of the Support Program for the Contemporary Educational Needs in 2007. 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.

4) Development of Analytical Software for Distinguishing Dental Formulas and Conditions from Intraoral Photographs

In collaboration with corporations, we are researching to develop and verify the effectiveness of a deep-learning

model that can identify the dental formula and distinguish conditions such as caries and implants from intraoral photographs.

(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.

The courses "Introduction to AI and Big Data in Health Sciences" and "Advanced AI and Big Data in Health Sciences," targeted at students from all schools and majors, equip students with a foundational understanding of data science. In these courses, students are taught cutting-edge research examples in a lecture format and participate in programming exercises using Python and machine learning exercises with various data types.

(3) Publications

[Original Articles]

1. Kyoko Akiyama, Masayo Sunaga, Ridan Cao, Megumi Arai, Atsuhiko Kinoshita. Development, application, and evaluation of interactive simulation materials for learning the dental hygiene process of care Journal of Medical and Dental Sciences. 2023.03; 70(0); 1-9

Department of Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD
Junior Associate Professor: Kaoruko Seino, PhD
Specially Appointed Assistant Professor: Alemi Sharifullah, MD, PhD
Research Fellow: Yuri Tashiro, MPharm, MPH, PhD;
AL-SOBAlHI Saber, RN, MPH, PhD;

Graduate Student:
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;
Prangkhwan Jiaranaisilawong, MD;

(1) Outline

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

(2) Research

Major Research Topics:

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

(3) Education

PhD programs

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

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

Master Programs

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

(4) Lectures & Courses

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

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

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

(5) Publications

[Original Articles]

1. Tran XMT, Nakamura K, Al-Sobaihi S, Seino K. Parental engagement in caregiving activities and its association with socioeconomic and child-rearing environment at home in Vietnam. *Early Child Development and Care*. 2023.12;
2. Hemat S, Almei S, Ahmady S, Nakamura K. Increase in institutional delivery and child immunisation coverage through an appreciative inquiry-based community dialogue intervention in Afghanistan. *Public Health in Practice*. 2023.10; 6; 100436
3. Vo MTH, Nakamura K, Seino K, Moncatar TRT, Han TDT, Siongco KLL, Tashiro Y, Vo TV. Can collaboration among health and social care workers play a role in addressing geriatric care challenges? A qualitative case study in Central Vietnam *International Health*. 2023.09;
4. Sato F, Nakamura K. Exploration of the relationships between men' s healthy life expectancy in Japan and regional variables by integrating statistical learning methods *Int. J. Environ. Res. Public Health* . 2023.09; 20(18); 6782

5. Latorre AAE, Nakamura K, Seino K, Hasegawa T.. Vector autoregression for forecasting the number of COVID-19 cases and analyzing behavioral indicators in the Philippines: an ecologic time-trend study, *JMIR Form Res* . 2023.06; 7; e46357
6. Akahoshi K, Nakamura K, Kondo H, Wakai A, Koido Y. Containment of COVID-19 outbreaks with lower incidence and case fatality rates in long-term care facilities by early intervention of emergency response teams. *Plos ONE*. 2023.06; 18(6); e0287675
7. Latorre AAE, Nakamura K, Seino K, Hasegawa T. Vector Autoregression for Forecasting the Number of COVID-19 Cases and Analyzing Behavioral Indicators in the Philippines: Ecologic Time-Trend Study. *JMIR formative research*. 2023.06; 7; e46357
8. Sato H, Nakamura K, Kibusi S, Seino K, Maro II, Tashiro Y, Bintabara D, Shayo FK, Miyashita A, Ohnishi M. Patient trust and positive attitudes maximize non-communicable diseases management in rural Tanzania. *Health promotion international*. 2023.04; 38(2);
9. Rivera AKB, Latorre AAE, Nakamura K, Seino K.. Using complete blood count parameters in the diagnosis of iron deficiency and iron deficiency anemia in Filipino women. *Journal of Rural Medicine*. 2023.04; 18(2); 79-86
10. Rivera AKB, Latorre AAE, Nakamura K, Seino K. Using complete blood count parameters in the diagnosis of iron deficiency and iron deficiency anemia in Filipino women. *Journal of rural medicine : JRM*. 2023.04; 18(2); 79-86
11. Rivera Ana Kriselda B., Latorre Angelica Anne E., Nakamura Keiko, Seino Kaoruko. フィリピン人女性での鉄欠乏症および鉄欠乏性貧血の診断における全血球計算測定値の使用 (Using complete blood count parameters in the diagnosis of iron deficiency and iron deficiency anemia in Filipino women) *Journal of Rural Medicine*. 2023.04; 18(2); 79-86
12. Sato H, Nakamura K, Kibusi S, Seino K, Maro II, Tashiro Y, Bintabara D, Shayo FK, Miyashita A, Ohnishi M.. Patient trust and positive attitudes maximize noncommunicable diseases management in rural Tanzania. *Health Promotion International*. 2023.03; 38(2); daad007
13. Alemi S, Nakamura K, Arab AS, Mashal MO, Tashiro Y, Seino K, Hemat S.. Prevalence, determinants, and association of overweight/obesity with non-communicable disease-related biomedical indicators: a cross-sectional study in schoolteachers in Kabul, Afghanistan. *PLOS Glob Public Health*. 2023.03; 3(3); e0001676
14. Sharifullah Alemi,Keiko Nakamura, Ahmad Shekib Arab,Mohammad Omar Mashal,Yuri Tashiro,Kaoruko Seino,Shafiqullah Hemat. Prevalence, determinants, and association of overweight/obesity with non-communicable disease-related biomedical indicators: A cross-sectional study in schoolteachers in Kabul, Afghanistan *PLOS Global Public Health*. 2023.03;
15. Alemi S, Nakamura K, Arab AS, Mashal MO, Tashiro Y, Seino K, Hemat S. Prevalence, determinants, and association of overweight/obesity with non-communicable disease-related biomedical indicators: A cross-sectional study in schoolteachers in Kabul, Afghanistan. *PLOS global public health*. 2023; 3(3); e0001676
1. Sato F, Nakamura K, Akahoshi K. Exploration of a value-based method to multidimensionally evaluate and integrate citizens' standards of health. 2023.05; 46(2); 54-61

[Misc]

1. Vo MTH, Thonglor R, Moncatar TR, Han TDT, Tejavaddhana P, Nakamura K. Fear of falling and associated factors among older adults in Southeast Asia: a systematic review. *Public Health*. 2023.08; 222; 215-228

[Conference Activities & Talks]

1. Nakamura K. Healthy Cities around the world. WHO European Healthy Cities Annual Conference 2023 2023.11.22 Utrecht, Netherlands
2. Nakamura K. The Alliance for Healthy Cities: agenda for the future: Sustainable Health City: Health in all Policy.. WORLD HEALTH CITY FORUM 2023.11.20 Incheon, Republic of Korea

3. Nakamura K.. Healthy Cities in Blue and Green Zones.. Building Healthy Cities Together: Study Tour For Healthy Cities Mayors of EURO to WPRO 2023.11.08 Tokyo
4. Nakamura K.. Community mHealth Integrated Care (ComHIC) to manage hypertension/diabetes in Tanzania' s overburdened health system.. ComHIC Third Stakeholders Meeting 2023.10.23 Dodoma, Tanzania
5. 中村桂子、赤星昂己、佐藤文哉. 持続可能な健康都市の展開のための指標の活用に関する研究：総合指標の開発. 2023 年健康都市連合日本支部総会 2023.07.15
6. Nakamura K. Promoting the Health of Urban Populations: Healthy Cities. Young Leaders Program Special Lecture, Nagoya University 2023.06.12
7. Nakamura K. Global efforts in planetary health education for transdisciplinary research. The University Panel Symposium on Planetary Health for the G7 Hiroshima Summit 2023.04.21 Hiroshima

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, ONUMA Hiraku,

Dental Resident

UEDA Kaori, SHIMIZU Kento, YAMAGUCHI Kohei, AKIYAMA Yo,
UEDA Kaori, OKADA Mitsuzumi, KASHIWAZAKI Kenta, FUKASE Madoka,
HAYAKAWA Wakako,

Graduate Student

KATADA Haruko, YANAGIHARA Yuiko, NAMANO Sahaprom, KHIN Pyae Sone, QI Keyu, XU Kaiqi,
FUTATSUYA Ryota, KIKUTA Miho, SUNAMI Akiho, SEKIMOTO Yu, CHANG Chun Wei, WU Shanglin, OKKAR Ky,
IWASE Risa, MATSUZAKI Mayuko, MUKAI Mariko, BA Htoo Chit, NGUYEN Thi Khanh An, WANG Bohua, ZHOU

Research Student

KUNISAWA Kiko, WU Di, CHIHARA Miyuki, OSADA Yuya, SHIMOKUBO Mako, ISHIGAKI Yuri, LI Chengze,
LU Yibing, THEIN Soe, KHIN Moe Thu, INOUE Yuki, YOSHIDA Ryo, HIROSE Miho,

Staff

TERADA Mito

Adjunct lecturer

IKEBE Kazunori, CHO Fuizu, NAKANODA Shinichi, SHIMIZUBATA Makoto,
KAWAI Yasuhiko, ANDO Kazuo, OWATARI Tsuneto, KOMATSU Yoshihiko,
SAKAGUCHI Hideo, TOBITA Ayako, HIRANO Shigezo, ITO Junji,
INOUE Minoru, UEHARA Yoko, U Chi Da Tatsuro, OTAKE Ryosuke,
OSADA Eiji, KOBAYASHI Shoji, SATO Yusuke, TAKAHASHI Noboru,
TAKEUCHI Satoshi, TAKEUCHI Shuhei, TANOUE Mariko, TERANAKA Satoshi,
TOMIOKA Eiji, HADA Tamaki, HATANO Keita, BABA Yuya, HIRATSUKA Tomohiro,
HIRANO Yasuyoshi, HIRAYAMA Daisuke, YAMAGA Eijiro, YAMAMOTO Mao,
YOSHIZAKI Taro,
YONEYAMA Takeyoshi, WATANABE Ikki, WATANABE Masataka, OGAWA Takahiko,
KAWAI Yosuke,

(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
- 16) The effects of denture adhesives by the differences of the denture fitting

(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

[Original Articles]

1. Liu H, Inokoshi M, Xu K, Tonprasong W, Minakuchi S, Van Meerbeek B, Vleugels J, Zhang F. Does speed-sintering affect the optical and mechanical properties of yttria-stabilized zirconia? A systematic review and meta-analysis of in-vitro studies. *Jpn Dent Sci Rev.* 2023.12; 59; 312-328
2. Ueda K, Inokoshi M, Kubota K, Yamaga E, Minakuchi S. Factors influencing postoperative bleeding after dental extraction in older adult patients receiving anticoagulation therapy. *Clin Oral Investig.* 2023.12; 28(1); 22
3. Akiyama Y, Iwaki M, Komagamine Y, Minakuchi S, Kanazawa M. Effect of spindle speed and feed rate on surface roughness and milling duration in the fabrication of milled complete dentures: an in vitro study. *Appl Sci.* 2023.12; 13(24); 13338
4. Okada M, Hama Y, Futatsuya R, Sasaki Y, Noritake K, Yamaguchi K, Matsuzaki M, Kubota C, Hosoda A, Minakuchi S. Association between Masticatory Performance, Nutritional Intake, and Frailty in Japanese Older Adults. *Nutrients.* 2023.12; 15(24);
5. Kashiwazaki K, Komagamine Y, Namano S, Park JM, Iwaki M, Minakuchi S, Kanazawa M. Prediction accuracy of incisal points in determining occlusal plane of digital complete dentures. *J Adv Prosthodont.* 2023.12; 15(6); 281-289
6. Yanagihara Y, Suzuki H, Furuya J, Nakagawa K, Yoshimi K, Seto S, Shimizu K, Tohara H, Minakuchi S. Usefulness of oral health assessment performed by multiple professionals using a short video recording acquired with a tablet device *Journal of Dental Sciences .* 2023.11;

7. Yoshinaka S, Yamaguchi K, Yanagida R, Ishii M, Nakagawa K, Yoshimi K, Nakane A, Matsuyama Y, Aida J, Tohara H . Tongue Strength of Older Adults Requiring Long-Term Care Varies throughout the Day Geriatrics. 2023.10;
8. Kashiwazaki K, Komagamine Y, Shanglin W, Ren X, Hayashi N, Nakayama M, Namano S, Kanazawa M, Minakuchi S. Improvements in Maximum Bite Force with Gum-Chewing Training in Older Adults: A Randomized Controlled Trial. J Clin Med. 2023.10; 12(20);
9. Komagamine Y, Kanazawa M, Miyayasu A, Uehara Y, Watanabe M, Sahaprom N, Huyen TBN, Iwaki M, Sato D, Minakuchi S. The effect of single-implant overdentures on cognitive function in older adults: A 3-year follow-up report. Journal of dentistry. 2023.09; 136; 104632
10. Risako Mikami, Yuriko Komagamine, Norio Aoyama, Koji Mizutani, Yoshiyuki Sasaki, Takanori Iwata, Shunsuke . Association between occlusal supports and nutritional status in older adults: A systematic review Journal of Dental Sciences. 2023.09;
11. Suzuki H, Furuya J, Nakagawa K, Hidaka R, Nakane A, Yoshimi K, Shimizu Y, Saito K, Itsui Y, Tohara H, Minakuchi S. Factors influencing the selection of oral healthcare providers in multidisciplinary Nutrition Support Team for malnourished inpatients: A cross-sectional study. Journal of oral rehabilitation. 2023.08; 50(12); 1446-1455
12. Komagamine, Y; Suzuki, H; Iwaki, M; Minakuchi, S; Kanazawa, M. Effect of New Complete Dentures and Simple Dietary Advice on Cognitive Screening Test among Edentulous Older Adults: A Randomized Controlled Trial JOURNAL OF CLINICAL MEDICINE. 2023.07; 12(14);
13. Kashiwazaki K, Komagamine Y, Uehara Y, Yamamoto M, Nakai H, Trang BNH, Liu H, Namano S, Tonprasong W, Kanazawa M, Minakuchi S. Effect of gum-chewing exercise on maintaining and improving oral function in older adults: A pilot randomized controlled trial. J Dent Sci. 2023.07;
14. 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. J Prosthodont Res. 2023.07; 67(3); 430-436
15. Shimizu K, Suzuki H, Isoyama N, Yanagihara Y, Minakuchi S. Influence of wearing complete dentures on control of head position during walking in edentulous older adults. J Oral Rehabil. 2023.05;
16. Inokoshi M, Liu H, Yoshihara K, Yamamoto M, Tonprasong W, Benino Y, Minakuchi S, Vleugels J, Van Meerbeek B, Zhang F. Layer characteristics in strength-gradient multilayered yttria-stabilized zirconia. Dent Mater. 2023.03; 39(4); 430-441
17. Tonprasong W, Inokoshi M, Tamura M, Hatano K, Minakuchi S. Impact of surface pre-reacted glass ionomer filler eluate on lipase gene expression in *Candida albicans*: An in vitro study. Dent Mater J. 2023.01; 42(1); 49-54
18. 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. 2023.01; 18(1); 95-104
19. Kohei Yamaguchi, Yohei Hama, Hitomi Soeda, Keita Hatano, Mitsuzumi Okada, Ryota Futatsuya, Shunsuke Minakuchi. Factors Associated with Selection of Denture Adhesive Type: A Cross-Sectional Survey. J Clin Med. 2023.01; 12(3); 873
20. Akiyama Y, Kanazawa M, Iwaki M, Hada T, Soeda Y, Otake R, Kashiwazaki K, Komagamine Y, Murakami N, Takaichi A, Wakabayashi N, Minakuchi S. Fabrication of milled removable partial dentures using a custom plate with prefabricated artificial teeth. J Prosthodont Res. 2023.10; 67(4); 647-651
1. Inokoshi M, Minakuchi S. Learning from cases: Mandatory knowledge regarding systemic diseases on home-visit dental treatment. Ann Jpn Prosthodont Soc. 2023.04; 15(2); 189-194

[Misc]

1. Onuma H, Inokoshi M, Minakuchi S. Smoothed particle hydrodynamics method applied to oral region: A narrative review. Dent Mater J. 2023.11; 42(6); 759-765

[Conference Activities & Talks]

1. Inokoshi M. Contemporary dental ceramics – Recent topics based on material research. 51st Indian Prosthodontic Society Conference 2023.12.09 Goa
2. Yohei Hama, Yuriko Komagamine, Kohei Yamaguchi, Mitsuzumi Okada, Y, Ryota Futatsuya, Mayuko Matsuzaki, Shunsuke Minakuchi. Utility of the chewing gum method to evaluate the masticatory performance and general health in older adults. IAGG-AOR 2023 Satellite symposium 2023.10.26 Kyoto
3. Onuma H, Inokoshi M, Minakuchi S. Introduction and application of the smoothed particle hydrodynamics method in dentistry. Andaman Dental Congress 2023 2023.10.19 Phuket
4. Sunami A, Inokoshi M, Tamura M, Hatano K, Minakuchi S. Flexural Strength of Novel Hard Relining Material Containing S-PRG filler. IADR-ANZ Conference 2023 2023.09.29 Sydney
5. Xu K, Inokoshi M, Yoshihara K, Kakehata M, Yashiro H, Takahashi R, Yamatomo M, Kamiyo S, Ikeda M, Minakuchi S. Bonding efficacy to femtosecond laser irradiated lithium disilicate glass-ceramic. IADR-ANZ Conference 2023 2023.09.29 Sydney
6. Inokoshi M. Recent updates of dental zirconia ceramics. IADR-ANZ Conference 2023 2023.09.27 Sydney
7. Ueda K, Inokoshi M, Kubota K, Yamaga E, Minakuchi S. Factors affecting postoperative bleeding in older adults on anticoagulation therapy. IADR-ANZ Conference 2023 2023.09.27 Sydney
8. Watanabe I. Digital Consideration in Prosthesis .. The 2023 Ministry of Health and Welfare - Curriculum for Advanced Digital Dentistry at Taipei 2023.09.21 Taipei
9. Hada T, Kanazawa M, Iwaki M, Minakuchi S. Effects of printed layer thickness and infill rate on mechanical properties of shape memory materials used in 4D-printed sports mouthguard. International College of Prosthodontists (ICP) 2023, London Symposium. 2023.08.31 London
10. Wang B, Inokoshi M, Liu H, Minakuchi S. Influence of surface treatments on the low-temperature degradation behavior of speed-sintered zirconia. The 38th Annual Meeting of Japanese Society for Dental Product/2023 Kanto Regional Meeting of the Japanese Society for Dental Materials and Devices 2023.08.05 Tokyo
11. Qi K, Kanazawa M, Hada T, Sahaprom N, Ren X, Akiyama Y, Minakuchi S. Effect of silanization on SLA resin enhanced by 3Y-TZP nanoparticles. The 101st General Session & Exhibition of the IADR 2023.06.23 Bogota
12. Hayashi N, Akiyama Y, Kashiwazaki K, Komagamine Y, Iwaki M, Minakuchi S, Kanazawa M. Effects of the offset values of fixed part of metal framework on accuracy in milled removable partial denture using custom plate. IAGG Asia/Oceania Regional Congress 2023. 2023.06.14 Yokohama
13. Yohei Hama. Impact of masticatory performance on general health in older adults. IAGG Asia/Oceania Regional Congress 2023 2023.06.14 Yokohama
14. Hitomi Soeda, Yohei Hama, Kohei Yamaguchi, Mitsuzumi Okada, Ryota Futatsuya, Tomokazu Yoshida, Kazumi Yamaguchi, Shunsuke Minakuchi.. Differences in Tongue Coating Index and Masticatory Performance by Denture Adhesive Type: Investigation using Propensity Score Matching. IAGG Asia/Oceania Regional Congress 2023 2023.06.14 Pacifico Yokohama North, Yokohama, Japan
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2. Inokoshi M. Bonding strategy for dental zirconia ceramics: stories about ceramic material research. The 42nd Annual Meeting of Japan Society for Adhesive Dentistry 2023.10.01 Tokyo
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[Awards & Honors]

1. Inokoshi M. Science Award of the Japanese Society for Dental Materials and Devices, The Japanese Society for Dental Materials and Devices, 2023.04

[Social Contribution]

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

Department of Dysphagia Rehabilitation

(1) Outline

The Department of Dysphagia Rehabilitation has been established in 2020. In the context of Japan's super-aged society, our goal is to cultivate professionals capable of practicing dysphagia patients. Our clinical targets are not limited to the older patients but also include adults and children, offering treatment modalities for outpatients, home and facility care visits, as well as support for inpatients at TMDU hospitals. Recently, we have also initiated telemedicine. Our research encompasses not only the swallowing functions and its training methods but also investigates the aging changes in the perioral muscles (tongue, masticatory muscles, and swallowing-related muscles), the connection between these changes and overall health, the impacts of oral intake on the body.

(2) Research

1. Development of Devices for Assessing Dysphagia, Oral Function Decline, and Oral Frailty

We are developing an advanced device for quantitatively assessing swallowing functions and their clinical applications. Previously, we developed a mouth-opening force gauge aimed at simplifying the assessment of swallowing function and oral function decline, for which we have obtained a patent. Currently, we are developing devices to measure aspects that were previously difficult to assess, such as jaw movement during chewing, biting force, and the strength of muscles involved in eating and swallowing. Additionally, these devices can be applied not only for dysphagia but also for evaluating oral frailty and oral function decline, which have gained importance in recent years.

2. Nutritional Studies Using a Gastrotomy Model in Rats

In older adults and patients with dysphagia, enteral nutrition methods like gastrostomy are chosen to prevent aspiration pneumonia and malnutrition. While gastrostomy is a nutrition intake method with many advantages, it can also lead to chronic gastrointestinal disorders. Therefore, we have created a gastrotomy model in rats, raising them on various types of nutrition to explore changes in nutritional value and gut microbiota.

3. Image Analysis of Swallowing Function in Patients with Cervical Spine Diseases

There have been several studies on postoperative dysphagia in patients with cervical spine diseases. However, few such patients have kinematically analyzed the causes of dysphagia. In collaboration with the Department of Orthopedic Surgery at our medical school, we analyze the hyoid bone movement before and after surgery in patients with cervical spine diseases based on videofluoroscopic swallow studies to investigate the causes of postoperative dysphagia.

4. Comprehensive Research on the Collaboration between Medical and Dental Care for Stroke Patients

For stroke patients, the effects of interventions and methods for managing oral functions through medical-dental collaboration have not been established. Thus, we introduced early oral function management interventions for stroke patients admitted to our university hospital to reduce the incidence of acute pneumonia. We have also completed a care manual and a medical-dental collaboration guidebook for acute phase stroke patients and are currently verifying the intervention effects in multi-institutional cooperative research, aiming to establish methods for managing oral functions through medical-dental collaboration across Japan.

5. Development of an Innovative Intraoral Device for Alternative Voice Production in Total Laryngectomy Patients

Total laryngectomy patients significantly impair their quality of life due to the loss of speaking function. Although alternative voice methods such as electronic larynxes and esophageal speech have been used, they come with issues like the need for surgery and high costs. We are advancing the development and effectiveness verification of a completely different, removable intraoral alternative voice method.

6. Unraveling Frailty in the Older Adults Focused on Perioral Muscles and Establishing a New Functional Evaluation Method

Frailty and sarcopenia in older adults are widely recognized globally. Although evaluations of frailty focus on muscle mass, strength, and physical function, similar considerations for the perioral muscles have not progressed. We aim to clarify frailty occurring in the perioral muscles using ultrasound diagnostic devices for muscle mass evaluation and dedicated measuring devices for muscle strength and function, establishing a simple, clinically applicable method for assessing oral and swallowing functions.

7. Verification of the Effectiveness of Carbonated Thickened Beverages and Development of a Two-Stage Angle Endoscope for Patients with Dysphagia

Patients with dysphagia often cannot consume carbonated drinks due to the risk of aspiration. While carbonation has been reported to have beneficial effects on swallowing, no studies have been reported on the intake of carbonated drinks thickened to reduce this risk. We are verifying the effects of carbonation on swallowing dynamics with thickened carbonated beverages. Additionally, the design of endoscopes used for evaluating swallowing function has not changed for nearly 30 years. We have developed a two-stage bending endoscope, improving the traditional single-bend shaft, and are verifying its effectiveness. This allows observation of the posterior tracheal wall, potentially improving the detection accuracy of aspiration.

8. Development of a Non-Invasive Swallowing Function Evaluation Device Using Fluorescent Substances

Swallowing endoscopy and videofluoroscopic swallow studies are performed in various clinical settings, but both are invasive and require a high level of operator skill, affecting the accuracy of the examination and diagnosis. Therefore, a practical, non-invasive, and repeatable new examination method is sought. We are developing a non-invasive aspiration risk detection system that applies fluorescence measurement of food-grade fluorescent substances in collaboration with other universities.

9. Research on the Digitalization of Dysphagia Rehabilitation, Including Online Consultations and Intraoral Scanners

Digitalization is steadily progressing in dentistry. The utility of digital technology, including for dysphagia rehabilitation and dental home visit services is increasing, yet its widespread use is currently limited. We are engaged in verifying the usefulness of online consultations and digital devices (especially intraoral scanners) in dysphagia rehabilitation and home visit services, as well as developing new devices suitable for clinical use.

(3) Education

In anticipation of an increasingly aging society, we are dedicated to developing professionals who can contribute to healthcare, nursing care, and society at large through dysphagia rehabilitation and other means. Our undergraduate education not only covers lectures related to dysphagia but also provides opportunities to learn about multidisciplinary collaboration in the field through accompanying home visits, facility visits, or hospital consultations.

(4) Clinical Services & Other Works

We are conducting evaluations of swallowing functions using videoendoscopic and videofluoroscopic evaluation of swallowing, as well as implementing rehabilitation based on these assessments. Our department places a strong emphasis on home healthcare through home visits, striving not only to evaluate the feasibility of oral intake but also to ensure patients can enjoy their lives to the fullest, without losing the joy of eating, by adjusting the consistency of food, posture, and the patient's environment. In outpatient care, we primarily focus on the rehabilitation of patients after oral cancer surgery but also cater to patients with swallowing disorders caused by a variety of diseases, unique to a university hospital setting. Additionally, we have established an environment capable of telemedicine, targeting patients with dysphagia living in medically underserved areas. Telemedicine

have also proven to be effective in situations where face-to-face interactions are impossible due to measures against COVID-19.

(5) Clinical Performances

Our department specializes in providing dysphagia rehabilitation in home healthcare settings. Therefore, we are fully capable of effective collaboration with primary care dentists responsible for oral hygiene and oral function management in dental home visit services. Additionally, telemedicine can be offered not only to patients within the country but also to those abroad.

(6) Publications

[Original Articles]

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[Conference Activities & Talks]

1. Rieko Moritoyo, Kazuharu Nakagawa, Kohei Yamaguchi, Kanako Yoshimi, Ryosuke Yanagida, Chizuru Namiki, Haruka Tohara. Effects of Telemedicine in Dysphagia Rehabilitation in the Period of Discontinued of Home-Visit Medical Care during the COVID-19 Pandemic. ESSD 2023 13th Annual Congress 2023.12.01 Toulouse, France
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11. Kazuharu Nakagawa, Sirinthip Amornsuradech. Role of dentists in dysphagia management :Exchanges between Thailand and Japan. 第29回日本摂食嚥下リハビリテーション学会学術大会 2023.09.03 横浜
12. 住吉幸子, 吉見佳那子, 中川量晴, 山口浩平, 雨宮輝美, 有本正子, 戸原 玄. 訪問診療での胃ろう患者への食支援から、外出支援に繋がれた症例. 第29回日本摂食嚥下リハビリテーション学会学術大会 2023.09.02 横浜
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16. Ryosuke Yanagida, Kohei Yamaguchi, Kazuharu Nakagawa, Chantaramanee Ariya, Patcharaphol Samnieng, Sirinthip Amornsuradech, Kanako Yoshimi, Ayako Nakane, Haruka Tohara. Investigations and activities on Oral Hypofunction in Thailand. IAGG Asia/Oceania Regional Congress 2023 2023.06.14
17. Ryosuke Yanagida, Kohei Yamaguchi, Kazuharu Nakagawa, Chantaramanee Ariya, Patcharaphol Samnieng, Rieko Moritoyo, Sirinthip Amornsuradech, Kanako Yoshimi, Haruka Tohara. International comparison of oral function among community-dwelling older adults between Thailand and Japan.. FDCU International Symposium 2023 2023.05.23 Bangkok, Thailand
18. Ryosuke Yanagida;Kohei Yamaguchi;Kazuharu Nakagawa;Kanakano Yoshimi;Ayako Nakane;Haruka Tohara. Association between sleep-disordered breathing and oral problem in post-stroke patients with dysphagia. The 3rd Annual Meeting of the International Society of Oral Care 2023.04.21 Tokyo, Japan
19. Yanagida Ryosuke, Yamaguchi Kohei, Nakagawa Kazuharu, Yoshimi Kanako, Nakane Ayako, Tohara Haruka. 脳卒中後の嚥下障害患者における睡眠呼吸障害と口腔内問題の関連性 (Association between sleep-disordered breathing and oral problem in post-stroke patients with dysphagia). 日本口腔ケア学会雑誌 2023.04.01
20. Yanagida Ryosuke, Yamaguchi Kohei, Nakagawa Kazuharu, Yoshimi Kanako, Nakane Ayako, Tohara Haruka. 脳卒中後の嚥下障害患者における睡眠呼吸障害と口腔内問題の関連性 (Association between sleep-disordered breathing and oral problem in post-stroke patients with dysphagia). 日本口腔ケア学会雑誌 2023.04.01
21. Yamada Taishi, Yamaguchi Kohei, Nakagawa Kazuharu, Horike Ayane, Hasegawa Shohei, Ishii Miki, Tohara Haruka. 新規のマウスピース型電気式人工喉頭である「ボイスリトリーバー」は発声に関連した生活の質を改善する (A novel mouthpiece-shaped electrolarynx "Voice Retriever" improves voice-related quality of life). 口腔病学会雑誌 2023.03.01
22. Yamada Taishi, Yamaguchi Kohei, Nakagawa Kazuharu, Horike Ayane, Hasegawa Shohei, Ishii Miki, Tohara Haruka. 新規のマウスピース型電気式人工喉頭である「ボイスリトリーバー」は発声に関連した生活の質を改善する (A novel mouthpiece-shaped electrolarynx "Voice Retriever" improves voice-related quality of life). 口腔病学会雑誌 2023.03.01
1. Analysis of changes in gut microbiota by fermented pickles in adults. 2023.12.02
2. Analysis of gut microbiota using fermented pickles easily consumed for patients with disabilities. 2023.11.11
3. MAI MIYACHI. Cutting-edge dental treatment using oral devices to improve sleep-disordered breathing. the 9th world dental meeting in japan 2023.09.23 Pacifico Yokohama
4. MAI MIYACHI. Clinical practice and practice of sleep dentistry telemedicine in hands-on dentistry. Joint Congress of the 45th Annual Meeting of Japanese Society of Sleep Research, the 30th Annual Meeting of Japanese Society for Chronobiology 2023.09.15 Pacifico Yokohama North
5. Ryota Kanai ,Kohei Yamaguchi, Kosuke Motoki, Rieko Moritoyo, Kanako Yoshimi, Kazuharu Nakagawa, Haruka Tohara. Visual-Taste Sensory cross-modal correspondence in Healthy Older People.. The Japanese Society of Dysphagia Rehabilitation 2023.09.03
6. Aritoshi Uchida,Kazuharu Nakagawa, Yuuki Nagasawa,Kanakano Yoshimi,Kohei Yamaguchi,Haruka Tohara. Examination of factors affecting activity and muscle mass changes in socially isolated model animals. The Japanese Society of Dysphagia Rehabilitation 2023.09.03 Pacifico Yokohama North
7. Analysis of changes in gut microbiota by fermented pickles in adults. 2023.09.02

8. Akino Saiki, Kanako Yoshimi, Yuki Nagasawa, Taishi Yamada, Aritoshi Uchida, Ryota Kanai, Sachiko Sumiyoshi, Kazuharu Nakagawa, Haruka Tohara. A case of improved health-related quality of life after dysphagia rehabilitation intervention for a postoperative patient with upper lip cancer. The 29th Annual Meeting of the Japanese Society of Dysphagia Rehabilitation 2023.09.02
9. Aritoshi Uchida, Kazuharu Nakagawa, Yuuki Nagasawa, Kanako Yoshimi, Kohei Yamaguchi, Haruka Tohara. Examination of factors affecting activity and muscle mass changes in socially isolated model animals. 2023.06.18 Pacifico Yokohama North
10. Rieko Moritoyo, Kazuharu Nakagawa, Kohei Yamaguchi, Shohei Hasegawa, Kanako Yoshimi, Miki Ishii, Ryosuke Yanagida, Haruka Tohara. Relationship between Jaw -Closing Force and Dietary Form in Older Adults Requiring Care without Functional Occlusal Support.. 2023.06.17
11. Ayane Horike, Ayako Nakane, Taishi Yamada, Kohei Yamaguchi, Kanako Yoshimi, Kazuharu Nakagawa, Haruka Tohara. Case report on changes in V-RQOL before and after use of the app version of Voice Retriever and its usability. 2023.06.17
12. Hara Yoshiko. A case of an elderly person with a history of choking on multiple occasions who was able to take oral intake safely through dysphagia rehabilitation and multidisciplinary collaboration. The 34th Annual Meeting of the Japanese Society of Geriatric Dentistry 2023.06.16 Pacifico Yokohama
13. MAI MIYACHI. Overview of obstructive sleep apnea treatment using oral appliances in clinical dentistry. Society of Japan Clinical Dentistry 2023.06.04 Ochanomizu Sola City Conference Center Hall WEST
14. Rieko Moritoyo, Kazuharu Nakagawa, Shohei Hasegawa, Miki Ishii, Kohei Yamaguchi, Kanako Yoshimi, Ayako Nakane, Haruka Tohara. Is Jaw-closing force useful in determining dietary form for older adults requiring nursing care without functional Occlusal Support?. The 38th Annual Meeting of Japanese Society for Clinical Nutrition and Metabolism 2023.05.09

[Awards & Honors]

1. Oral Presentation Award, Asian Dysphagia Society, 2023.11
2. Travel Award, Asian Dysphagia Society, 2023.11

Laboratory Medicine

Professor Shuji TOHDA
Junior Associate Professor Tadashi KANOUCHI
Junior Associate Professor Mai ITOH
Assistant Professor Ayako NOGAMI
Graduate Students Toshihisa SATTA, Haruka KUMADA, Honoka SEZUTSU

(1) Outline

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

(2) Research

Our research subjects are as follows:

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

(3) Education

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

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

(7) Publications

[Original Articles]

1. Azusa Yamazaki, Yoko Nukui, Takahiro Kameda, Ryoichi Saito, Yuki Koda, Naoya Ichimura, Shuji Tohda, Ryunosuke Ohkawa. Variation in presepsin and thrombomodulin levels for predicting COVID-19 mortality. *Sci Rep.* 2023.12; 13(1); 21493
2. Motomura, Y; Yoshifuji, K; Tachibana, T; Takase, H; Arai, A; Tanaka, K; Okada, K; Nogami, A; Umezawa, Y; Sakashita, C; Yamamoto, M; Mori, T; Nagao, T. Clinical factors for central nervous system progression and survival in primary vitreoretinal lymphoma *BRITISH JOURNAL OF HAEMATOLOGY.* 2023.12;
3. Keisuke Tanaka, Ayako Ichikawa, Natsuka Umezawa, Kouhei Yamamoto, Kota Yoshifuji, Keigo Okada, Ayako Nogami, Yoshihiro Umezawa, Toshikage Nagao, Chizuko Sakashita, Takehiko Mori, Shuji Tohda, Ryuji Koike, Shinsuke Yasuda, Masahide Yamamoto. Lymphoproliferative disorder risk after methotrexate treatment for rheumatoid arthritis. *Cancer Sci.* 2023.09; 114(9); 3719-3727
4. Kotomi Noguchi, Mai Itoh, Chisuzu Ito, Shuji Tohda. Effects of MYC Inhibitors on the Growth of Acute Leukaemia Cells. *Anticancer Res.* 2023.07; 43(7); 3023-3028
5. Noguchi K, Itoh M, Ito C, Tohda S. Effects of MYC Inhibitors on the Growth of Acute Leukaemia Cells. *Anticancer research.* 2023.07; 43(7); 3023-3028

[Conference Activities & Talks]

1. Miyakoshi T., Horiuchi Y., Araki M., Yonetsu T., Watanabe M., Nakamura M., Kameda T., Yoshimoto A., Ichimura N., Tohda S., Tozuka M., Sasano T., Ohkawa R. Association between CEC measured by immobilized liposome-bound gel beads method and the size of lipid-rich coronary artery plaque. Scientific Session of the American Heart Association 2023.11.09
2. Haruka Kumada, Mai Itoh, and Shuji Tohda. Effects of ferroptosis inducers and inhibitors on growth of acute leukemia cells. 52nd annual scientific meeting, International Society of Experimental Hematology 2023.08.19
3. Mai Itoh, Shuji Tohda. Renin-angiotensin system inhibitors suppress the growth of leukemia cells. 52nd annual scientific meeting, International Society of Experimental Hematology 2023.08.19 New York
4. Haruka Kumada, Mai Itoh, Shuji Tohda. Effects of ferroptosis inducers and inhibitors on the growth of acute leukemia cells.. 52nd Annual Science meeting, International Society for Experimental Hematology 2023.08.18 New York, USA
5. Miyakoshi T., Mutsuda Y., Horiuchi Y., Kameda T., Tozuka M., Ohkawa R. Application of bilirubin oxidase for improvement of false positive error caused by bilirubin on cholesterol efflux capacity assay by immobilize liposome-bound gel beads method. American Association for Clinical Chemistry (AACC) 2023 AACC Annual Scientific Meeting & Clinical Lab Expo 2023.07.24 Anaheim
6. Satoru Aoyama, Ayako Nogami, Sadakatsu Ikeda, Takehiko Mori. Novel protease-mediated double antigen recognizing Chimeric Antigen Receptor (CAR) enhances the directionality of CAR-T cell activity and improves target cell specificity.. Keystone symposia A4: Emerging Cellular Therapies at the Forefront of Cancer Immunotherapy 2023.01.31
7. Mai Itoh, Shuji Tohda. Renin-angiotensin system inhibitors suppress the growth of leukemia cells.. 52nd Annual Science meeting, International Society for Experimental Hematology 2023.08.19 New York, USA
1. Ayako Nogami, Morito Kurata, Towako Taguchi, Shomi Koyama, Katsutoshi Nagano, Keisuke Tanaka, Kota Yoshifuji, Yoshihiro Umezawa, Naoya Ichimura, Shuji Tohda, and Takehiko Mori. Efficacy of pathological method of identifying causative virus of hemorrhagic cystitis by cell block. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo

2. Keigo Okada, Makiko Saito, Yotaro Motomura, Kota Yoshifuji, Satoru Aoyama, Toshikage Nagao, and Ayako Nogami. FLT3-ITD activates PDK1 which phosphorylates N-Rsk and inhibits Bim to enhance survival in AML cells. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo
3. Keisuke Tanaka, Hikari Kanai, Hiroya Kuwahara, Kota Yoshifuji, keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Toshikage Nagao, Chizuko Sakashita, Takehiko Mori, Masahide Yamamoto. Diffuse large B-cell lymphoma developed under the treatment of fingolimod. The Japanese Society for Lymphoreticular Tissue Reserch 2023.06.24
4. Yotaro Motomura, Kota Yoshifuji, Daichi Sadato , Ayako Nogami, Makiko Saito, Keigo Okada, Satoru Aoyama, Takehiko Mori, and Toshikage Nagao. Establishment and characterization of TMD13. a novel GCB-type DLBCL cell line. The 63th Annual Meeting of the Japanese Society for Lymphoreticular Tissue Research 2023.06.22 Saitama
5. Momoko Chiba, Keisuke Tanaka, Fumihiko Ouchi, Marie Yagi, Hikari Kanai, Takuma Harada, Hiroki Hatsuzawa, Kota Yoshifuji, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Chizuko Sakashita, Toshikage Nagao, Takehiko Mori, Masahide Yamamoto. Evaluation of autologous stem cell transplantation using busulfan-containing conditioning for central nervous system lymphoma. 5th JSTCT Annual Meeting Japanese Society for Transplantation and Cellular Therapy 2023.02.11 Nagoya

Intensive Care Medicine

Professor and Chairman

Kenji Wakabayashi (2021.10.1 -)

Specially Appointed Professor

Hideo Takahashi (2017.4.1 -)

Associate Professor

Hideo Yamanouchi (2023.4.1 -)

Specially Appointed Associate Professor

Toyomu Ugawa (2021.4.1~2023.1.31)

Junior Associate Professor

Hideo Yamanouchi (2019.4.1 -2023.3.31)

Nobuyuki Nosaka (2022.4.1 -)

Ayako Noguchi (2023.4.1 -)

Assistant Professor

Takahiro Masuda (Intensive Care Unit) (2014.4.1 -)

Fumi Maruyama (Intensive Care Unit) (2017.2.1 -)

Yuka Mishima (2023.4.1 -)

Specially Appointed Assistant Professor

Nobuhiro Shiota (Intensive Care Unit) (2017.4.1 -)

Ryo Uchimido (Intensive Care Unit) (2020.4.1 -)

Yoichi Iki (Intensive Care Unit) (2023.10.1-)

Yuka Mishima (Intensive Care Unit) (2017.4.1 -2023.3.31)

Yusuke Kuwahara (Intensive Care Unit) (2023.4.1-)

Toshihiro Kubo (Intensive Care Unit) (2019.10.1 -)

Fellow:

Kouki Kiyama (2022.4.1 -)

Tomoki Hongo (2023.4.1 -)

Postgraduate students:

Nobuhiro Shiota (2017.4.1 -)

Yoichi Iki (2018.4.1 -)

Michiko Abe (2019.4.1 -)

Yuka Mishima (2019.4.1 -2023.3.31)

Ryo Uchimido (2020.4.1 -)

Toshihiro Kubo (2021.4.1-)

Ichiro Osawa (2021.4.1-)

Adjunct lecturer

Yoshito Ujike (2017.4.1 -)

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 and 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. Nakanishi, N; Liu, KB; Kawauchi, A; Okamura, M; Tanaka, K; Katayama, S; Mitani, Y; Ota, K; Taito, S; Fudeyasu, K; Masuka, Y; Yoshihiro, S; Utsumi, S; Nishikimi, M; Masuda, M; Iida, Y; Kawai, Y; Hatakeyama, J; Hifumi, T; Unoki, T; Kawakami, D; Obata, K; Katsukawa, H; Sumita, H; Morisawa, T; Takahashi, M; Tsuboi, N; Kozu, R; Takaki, S; Haruna, J; Fujinami, Y; Nosaka, N; Miyamoto, K; Nakamura, K; Kondo, Y; Inoue, S; Nishida, O. Instruments to assess post-intensive care syndrome assessment: a scoping review and modified Delphi method study CRITICAL CARE. 2023.11; 27(1); 430
2. Mishima Y, Saito K, Nosaka N. "Stuffy nose" in a case of Guillain-Barré syndrome with an esophageal bezoar under enteral nutrition. The American journal of the medical sciences. 2023.05;

3. Hosoya T, Oba S, Komiya Y, Kawata D, Kamiya M, Iwai H, Miyamoto S, Kataoka M, Tobiume M, Kanno T, Ainai A, Sato H, Hirakawa A, Mitsui Y, Satoh T, Wakabayashi K, Yamada T, Otomo Y, Miyazaki Y, Hasegawa H, Suzuki T, Yasuda S. Apple-shaped obesity: A risky soil for cytokine-accelerated severity in COVID-19. *Proceedings of the National Academy of Sciences of the United States of America*. 2023.05; 120(22); e2300155120
4. Nosaka N, Anzai T, Uchimido R, Mishima Y, Takahashi K, Wakabayashi K. An anthropometric evidence against the use of age-based estimation of bodyweight in pediatric patients admitted to intensive care units. *Scientific reports*. 2023.03; 13(1); 3574
5. Mishima Y, Nawa N, Asada M, Nagashima M, Aiso Y, Nukui Y, Fujiwara T, Shigemitsu H. 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*. 2023.01; 5(1); e0837

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata

Postgraduate student 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

[Original Articles]

1. Yokoyama K, Yakuo T, Mamada M, Nagata M. Olanzapine Overdose in a Two-Year-Old Girl Resulting in Both High Serum and Plasma Levels. *Cureus*. 2023.08; 15(8); e43002
2. Shun Kaneko, Yasuhiro Asahina, Mina Nakagawa, Miyako Murakawa, Yasunari Miyazaki, Takahiro Asakage, Shohei Fukuda, Takeshi Namiki, Yoshito Kano, Masashi Nagata, Jun Tsuchiya, Masato Miyoshi, Fukiko Kitahata-Kawai, Sayuri Nitta, Yasuhiro Itsui, Sei Kakinuma, Ryuichi Okamoto. Factors associated with liver injury and prognosis in advanced cancer patients treated with immune checkpoint inhibitors. *Hepatol Res*. 2023.01;

[Conference Activities & Talks]

1. Noda T., Mizuno S., Hase T., Mogushi K., Iida Y., Ishiwata Y., Nagata M.. Using machine learning algorithm to predict the occurrence of nephrotoxicity with tacrolimus. 81st FIP World Congress of Pharmacy and Pharmaceutical Sciences 2023.09.27
2. Kawano Y., Kawasumi K., Mano Y., Matsui R., Maeda-Minami A., Yamamoto Y., Negishi K., Shimada S., Nagata M., Aoyama T.. Risk factors associated with unplanned acute care in outpatient chemotherapy with oral anticancer drugs as monotherapy or combination therapy with injectable anticancer drugs. 81st FIP World Congress of Pharmacy and Pharmaceutical Sciences 2023.09.26
1. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19

Medical Education Research and Development

Professor Masanaga YAMAWAKI
 Associate Professor Eriko OKADA
 Assistant Professor Yu AKAISHI
 Assistant Professor 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.

- 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.

- Research on career education

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

- 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.

- Research on team medical care and multidisciplinary education

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

- 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.

- 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

[Original Articles]

1. Akaishi Y, Nawa N, Kashimada A, Itsui Y, Okada E, Yamawaki M. Association between Grit and depressive symptoms at the timing of job start among medical residents during the COVID-19 pandemic in Japan: a cross-sectional study. Medical education online. 2023.12; 28(1); 2225886
2. Akaishi Y, Nawa N, Kashimada A, Itsui Y, Okada E, Yamawaki M. Association between Grit and depressive symptoms at the timing of job start among medical residents during the COVID-19 pandemic in Japan: a cross-sectional study. Medical education online. 2023.12; 28(1); 2225886

3. Morimoto M, Nawa N, Okada E, Itsui Y, Kashimada A, Yamamoto K, Akaishi Y, Yamawaki M. Elucidation of the needs for telecritical care services in Japan: A qualitative study. *BMJ Open*. 2023.11; 13(11); e072065
4. Morimoto M, Nawa N, Okada E, Itsui Y, Kashimada A, Yamamoto K, Akaishi Y, Yamawaki M. Elucidation of the needs for telecritical care services in Japan: a qualitative study. *BMJ open*. 2023.11; 13(11); e072065
5. Morimoto M, Nawa N, Okada E, Itsui Y, Kashimada A, Yamamoto K, Akaishi Y, Yamawaki M. Elucidation of the needs for telecritical care services in Japan: a qualitative study. *BMJ open*. 2023.11; 13(11); e072065
6. Morimoto M, Nawa N, Okada E, Itsui Y, Kashimada A, Yamamoto K, Akaishi Y, Yamawaki M. Elucidation of the needs for telecritical care services in Japan: a qualitative study. *BMJ open*. 2023.11; 13(11); e072065
7. Suzuki H, Furuya J, Nakagawa K, Hidaka R, Nakane A, Yoshimi K, Shimizu Y, Saito K, Itsui Y, Tohara H, Minakuchi S. Factors influencing the selection of oral healthcare providers in multidisciplinary Nutrition Support Team for malnourished inpatients: A cross-sectional study. *J Oral Rehabil*. 2023.08;
8. Akaishi Y, Nawa N, Kashimada A, Itsui Y, Okada E, Yamawaki M. Association between Grit and depressive symptoms at the timing of job start among medical residents during the COVID-19 pandemic in Japan: a cross-sectional study. *Medical education online*. 2023.06; 28(1); 2225886
9. Shun Kaneko, Yasuhiro Asahina, Mina Nakagawa, Miyako Murakawa, Yasunari Miyazaki, Takahiro Asakage, Shohei Fukuda, Takeshi Namiki, Yoshito Kano, Masashi Nagata, Jun Tsuchiya, Masato Miyoshi, Fukiko Kitahata-Kawai, Sayuri Nitta, Yasuhiro Itsui, Sei Kakinuma, Ryuichi Okamoto. Factors associated with liver injury and prognosis in advanced cancer patients treated with immune checkpoint inhibitors. *Hepatol Res*. 2023.01;

[Conference Activities & Talks]

1. Manabu Sugie, Yusuke Noguchi, Nobutoshi Nawa, Ayako Kashimada, Kazuyuki Ito, Tsutomu Kondo, Satoshi Kusuda, Chikako Morioka, Tomohiro Morio, Kenichi Kashimada. Implication of Acquiring Oxidative Stress Resistance in Chorioamnionitis Leading to Reduced Risk of Severe Retinopathy of Prematurity. *FAOPS 2023; The 22nd Congress of the Federation of Asia and Oceania Perinatal Societies* 2023.10.09 Tokyo
 2. Masanaga Yamawaki, Eriko Okada, Nobutoshi Nawa, Makoto Takahashi, Ayako Kashimada, Yu Akaishi, Shouko Yoshida, Yujiro Tanaka. Development of evaluation system from undergraduate to postgraduate clinical training : a nation wide EPOC (E PORTfolio of Clinical training) in Japan. *AMEE(the International association for Health Professions Education)2023* 2023.08.28 Glasgow
 3. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Eriko Okada, Eiji Kaneko, Janelle Moross, Jun Tsuruta, Keiichi Akita, Masanaga Yamawaki. Patients as teachers: a novel IPE curriculum . *AMEE2023* 2023.08.28
1. A novel RNF213 gene de novo variant is involved in systemic vasculopathy. 2023.05.27

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
Emergency Life-saving Technician Mizuki Harashima

(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

- Analysis of inflammatory mediators in septic patients
- Analysis of lipid mediators with mass spectrometry
- Interventional research of concentrated fibrinogen and blood transfusion in patients with massive blood loss
- Investigation of neutrophil function in severely septic patients
- 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

[Original Articles]

1. Keita Nakatsutsumi, Koji Morishita, Todd W Costantini, Tomohiro Adachi, Akira Suekane, Keisuke Suzuki, Mitsuaki Kojima, Makoto Arita, Yasuhiro Otomo. Analysis of lipid metabolites derived from gut microbiota in ischemia-reperfusion model. *J Trauma Acute Care Surg.* 2023.12;
2. Yáñez Benítez C, Lorente-Aznar T, Labaka I, Soteras I, Baselga M, Morishita K, Ribeiro M, Güemes A.. EXTREMITY TOURNIQUET SELF-APPLICATION BY ANTARCTICA ZODIAC CREW MEMBERS. *Disaster Med Public Health Prep.* 2023.11; 8; 1-22
3. Suekane A, Takayama W, Hashimoto R, Morishita K, Otomo Y. Risk factors for recurrence of suicide attempt via overdose: A prospective observational study. *The American journal of emergency medicine.* 2023.10; 75; 1-6
4. Hatakeyama T, Kiguchi T, Sera T, Nachi S, Urushibata N, Ochiai K, Kitamura T, Ogura S, Otomo Y, Iwami T. Pre-hospital airway management and neurological status of patients with out-of-hospital cardiac arrest: A retrospective cohort study. *Resuscitation plus.* 2023.09; 15; 100422
5. Akutsu T, Endo A, Sonobe H, Suzuki K, Murata K, Otomo Y. A case of fulminant myocarditis with full recovery after a 38-h sustained asystole. *Clinical case reports.* 2023.08; 11(8); e7722
6. Morishita K, Coimbra R, Ito K, Otomo Y. The American Association for the Surgery of Trauma-European Society of Trauma and Emergency Surgery Emergency Surgery Course: Initial experience in Japan. *The journal of trauma and acute care surgery.* 2023.08; 95(2); e3-e5
7. Nakatsutsumi K, Endo A, Todd W C, Takayama W, Morishita K, Otomo Y, Inoue A, Hifumi T, Sakamoto T, Kuroda Y, Save-J II study group. Time-saving effect of real-time ultrasound-guided cannulation for extracorporeal cardiopulmonary resuscitation: A multicenter retrospective cohort study. *Resuscitation.* 2023.08; 109927
8. Carlos Yáñez Benítez, Teófilo Lorente-Aznar, Idurre Labaka, Marcelo A. F. Ribeiro Jr, Yosu Viteri, Koji Morishita, Marta Baselga, Antonio Güemes. Tourniquet self-application assessment in cold weather conditions 2023.08; 23(101);
9. Takayama W, Endo A, Morishita K, Otomo Y. Manual Chest Compression versus Automated Chest Compression Device during Day-Time and Night-Time Resuscitation Following Out-of-Hospital Cardiac Arrest: A Retrospective Historical Control Study. *Journal of personalized medicine.* 2023.07; 13(8);
10. Hosoya T, Oba S, Komiya Y, Kawata D, Kamiya M, Iwai H, Miyamoto S, Kataoka M, Tobiume M, Kanno T, Aina A, Sato H, Hirakawa A, Mitsui Y, Satoh T, Wakabayashi K, Yamada T, Otomo Y, Miyazaki Y, Hasegawa H, Suzuki T, Yasuda S. Apple-shaped obesity: A risky soil for cytokine-accelerated severity in COVID-19. *Proceedings of the National Academy of Sciences of the United States of America.* 2023.05; 120(22); e2300155120
11. Nakatsutsumi Keita, Endo Akira, Asano Hiroshi, Shinohara Shoichi, Kurosaki Ryo, Kawashima Shuji, Ishii Wataru, Nozawa Masashi, Tagaya Nobumi, Otomo Yasuhiro. Prophylactic effect of negative-pressure wound therapy and delayed sutures against incisional-surgical site infection after

- emergency laparotomy for colorectal perforation: A multicenter retrospective cohort study(タイトル和訳中) *Annals of Gastroenterological Surgery*. 2023.05; 7(3); 441-449
12. Wada Takeshi, Yamakawa Kazuma, Kabata Daijiro, Abe Toshikazu, Fujishima Seitaro, Kushimoto Shigeki, Mayumi Toshihiko, Ogura Hiroshi, Saitoh Daizoh, Shiraishi Atsushi, Otomo Yasuhiro, Gando Satoshi. Sepsis-related coagulopathy treatment based on the disseminated intravascular coagulation diagnostic criteria: a post-hoc analysis of a prospective multicenter observational study(タイトル和訳中) *Journal of Intensive Care*. 2023.03; 11; 1 of 11-11 of 11
 13. Haruta Koichi, Endo Akira, Shiraishi Atsushi, Otomo Yasuhiro. Usefulness of resuscitative endovascular balloon occlusion of the aorta compared to aortic cross-clamping in severely injured trauma patients: Analysis from the Japan Trauma Data Bank(タイトル和訳中) *Acute Medicine & Surgery*. 2023.03; 10(1); 1 of 8-8 of 8
 14. Mori Shusuke, Ai Tomohiko, Taguchi Towako, Negi Mariko, Otomo Yasuhiro. Aggressive diffuse large B-cell lymphoma manifested by splenic rupture progressed 2 months after transverse myelitis: an autopsy case report(タイトル和訳中) *Acute Medicine & Surgery*. 2023.02; 10(1); 1 of 5-5 of 5
 15. Mori S, Ai T, Taguchi T, Negi M, Otomo Y. Aggressive diffuse large B-cell lymphoma manifested by splenic rupture progressed 2 months after transverse myelitis: an autopsy case report. *Acute medicine & surgery*. 2023.01; 10(1); e822
 16. Akutsu T, Endo A, Okuzawa H, Suzuki K, Yonekawa C, Hoshi H, Otomo Y. Gastric tube perforation penetrating the pericardium after esophagectomy that needed surgical repair. *Acute medicine & surgery*. 2023.01; 10(1); e861
 17. Asada S, Mori S, Takemoto A, Tamura K, Ito G, Otomo Y. Spontaneous splenic rupture due to occult signet-ring cell gastric cancer accompanied by a bulky splenic vein thrombosis and postoperative brain infarction: A case report. *Acute medicine & surgery*. 2023.01; 10(1); e879
 18. Akutsu T, Endo A, Sonobe H, Saida F, Miyakawa K, Takedatsu F, Suzuki K, Murata K, Otomo Y. Surgical strategy for airway management and bleeding control in penetrating neck injury in zone II: A case report. *Clinical case reports*. 2023.01; 11(1); e6862
 19. Haruta K, Endo A, Shiraishi A, Otomo Y. Usefulness of resuscitative endovascular balloon occlusion of the aorta compared to aortic cross-clamping in severely injured trauma patients: Analysis from the Japan Trauma Data Bank. *Acute medicine & surgery*. 2023.01; 10(1); e830
 20. Inoue H, Tanaka H, Sakanashi S, Kinoshi T, Numata H, Yokota H, Otomo Y, Masuno T, Nakano K, Sugita M, Tokunaga T, Sugimoto K, Inoue J, Kato N, Nakagawa K, Tanaka S, Sagisaka R, Miyamoto T, Akama T. Incidence and factor analysis for the heat-related illness on the Tokyo 2020 Olympic and Paralympic Games. *BMJ open sport & exercise medicine*. 2023; 9(2); e001467
 1. Koji Morishita, Yasuhiro Otomo. Experience of managements of severe COVID-19 patients at Tokyo Medical and Dental University *Japanese Journal of Intensive Care Medicine*. 2023.12; 47; S102-S105
 2. Akira Endo, Atsushi Shiraishi, Shigeki Kushimoto, Yasuhiro 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. Japan Trauma System and Education System. Trauma System Development Exchange Meeting & Trauma Core Technology Training Course The 3rd National Center for Trauma Medicine Life Trauma Care Training Course 2023.11.04 Shenzhen, China
2. Koji Morishita. Real Action!! Trauma Ultrasound!!!. Annual Congress of KSS 2023, 75th Congress of The Korean Surgical Society 2023.11.04 Seoul, Korea
3. Kosuke Sekiya, Keisuke Suzuki, Keita Nakatsutsumi, Wataru Takayama, Koji Morishita, Junichi Aiboshi, Masahito Kaji, Yasuhiro Otomo. Challenges and Issues at the Closing Abdomen in Japan. World Trauma Congress 2023 2023.08.12 Tokyo

4. Yohei Iwasaki, Akira Endo, Koji Morishita¹, Atsushi Shiraishi, Yasuhiro Otomo . Gunshot Wounds Experiences and Protocols in Japan - A Nationwide Web-based Survey for Tertiary Emergency Medical Centers. World Trauma Congress 2023 2023.08.12 Tokyo
5. Koji Morishita, Yasuhiro Otomo, Kazuhide Matsuhima, Tomohisa Shoko, Junichi Inoue, Eiji Hira, Takaaki Nakada, Yasumitsu Mizobata, Hiroaki Watanabe, Satoshi Hirano, Hirohisa Matsubara . The current problems related to the institutional trauma care system in Japan and potential solutions: A survey. World Trauma Congress 2023 2023.08.11 Tokyo
6. Wataru Takayama, Koji Morishita, Yasuhiro Otomo. The impact of blood type on the mortality of patients with severe ABdOminal trauma: A multicenter observational study . World Trauma Congress 2023 2023.08.11 Tokyo
7. Hazuki Koguchi, Wataru Takayama, Koji Morishita, Yasuhiro Otomo. Age-related differences in the impact of coagulopathy in patients with traumatic brain injury. World Trauma Congress 2023 2023.08.10 Tokyo

Department of General Dentistry

Professor Hiroshi NITTA
Associate Professor Akira NISHIYAMA
Junior Associate Professor Masayuki HIDEISHIMA
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 Hitan SOU
Project Assistant Professor Naoko HARADA
Hospital Staff Shoko KAIDA
Hospital Staff Yutaro KITANAKA
Hospital Staff Hideyuki TAKAMATSU
Hospital Staff Shoko TOBE
Hospital Staff Akitaka HATTORI
Hospital Staff Hirohito MIKI
Hospital Staff Yuko MITSUMA
Graduate student/Hospital Staff Ayako SEKIGUCHI
Graduate student Mei HARDA

(1) Outline

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

(2) Research

Recent research themes are listed below.

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

(3) Education

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

(4) Lectures & Courses

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

(5) Clinical Services & Other Works

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

(6) Clinical Performances

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

(7) Publications

[Original Articles]

1. Okada M, Hama Y, Futatsuya R, Sasaki Y, Noritake K, Yamaguchi K, Matsuzaki M, Kubota C, Hosoda A, Minakuchi S. Association between Masticatory Performance, Nutritional Intake, and Frailty in Japanese Older Adults. *Nutrients*. 2023.12; 15(24);
2. Shu Takemura, Koji Mizutani, Risako Mikami, Keita Nakagawa, Masahiro Hakariya, Eri Sakaniwa, Natsumi Saito, Hiromi Kominato, Daisuke Kido, Kohei Takeda, Akira Aoki, Takanori Iwata. Enhanced periodontal tissue healing via vascular endothelial growth factor expression following low-level erbium-doped: yttrium, aluminum, and garnet laser irradiation: In vitro and in vivo studies. *J Periodontol*. 2023.11;
3. Hayashi S, Takeuchi Y, Hiratsuka K, Kitanaka Y, Toyoshima K, Nemoto T, Aung N, Hakariya M, Ikeda Y, Iwata T, Aoki A. Effects of various light-emitting diode wavelengths on periodontopathic bacteria and gingival fibroblasts: An in vitro study. *Photodiagnosis and Photodynamic Therapy*. 2023.10; 44;
4. Komagamine Y, Kanazawa M, Miyayasu A, Uehara Y, Watanabe M, Sahaprom N, Huyen TBN, Iwaki M, Sato D, Minakuchi S. The effect of single-implant overdentures on cognitive function in older adults: A 3-year follow-up report. *Journal of dentistry*. 2023.09; 136; 104632
5. Takeuchi Y, Nemoto T, Kitanaka Y, Aoki A, Izumi Y, Iwata T, Arakawa S. Antibacterial activity of lysozyme-chitosan oligosaccharide conjugates on two periodontal bacteria. *Oral diseases*. 2023.08;
6. Nakamura S, Watanabe H, Kurabayashi T, Miura M. Risk factors for posttreatment mastoid cellulitis in patients with oral malignancy *Oral Radiology*. 2023.07; 39(3); 528-535

7. Kimura-Ono Aya, Maekawa Kenji, Kuboki Takuo, Nawachi Kumiko, Fujisawa Masanori, Sato Hironobu, Aita Hideki, Koyama Shigeto, Hideshima Masayuki, Sato Yuji, Wake Hiroyuki, Nagao Kan, Kodaira-Ueda Yorika, Tamaki Katsushi, Sadamori Shinsuke, Tsuga Kazuhiro, Nishi Yasuhiro, Sawase Takashi, Koshino Hisashi, Masumi Shin-ichi, Sakurai Kaoru, Ishibashi Kanji, Ohyama Takashi, Akagawa Yasumasa, Hirai Toshihiro, Sasaki Keiichi, Koyano Kiyoshi, Yatani Hirofumi, Matsumura Hideo, Ichikawa Tetsuo, Ohkawa Shuji, Baba Kazuyoshi. Prosthodontic treatment can improve the ingestible food profile in Japanese adult outpatients Journal of Prosthodontic Research. 2023.04; 67(2); 189-195
8. Okihata R, Michi Y, Sunakawa M, Tagashira Y. Pharmacist-led multifaceted intervention in an antimicrobial stewardship programme at a university dental hospital in Japan. Journal of Hospital Infection . 2023.04; 136; 30-37
9. Natnicha Wamasing, Supasith Yomtako, Hiroshi Watanabe, Junichiro Sakamoto, Kou Kayamori, Tohru Kurabayashi. The magnetic resonance imaging characteristics of radicular cysts and granulomas Dentomaxillofac Radiol. 2023.02; 52(3); 20220336
10. 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. 2023.01; 18(1); 95-104
11. Akiyama Kyoko, Sunaga Masayo, Cao Ridan, Arai Megumi, Kinoshita Atsuhiko. 歯科衛生ケアのプロセスを学ぶためのインタラクティブシミュレーション教材の開発、適用、評価 (Development, application, and evaluation of interactive simulation materials for learning the dental hygiene process of care) Journal of Medical and Dental Sciences. 2023; 70; 1-9
12. Daisuke Kido, Keiji Komatsu, Toshikatsu Suzumura, Takanori Matsuura, James Cheng, Jeong Kim, Wonhee Park, Takahiro Ogawa. Influence of Surface Contaminants and Hydrocarbon Pellicle on the Results of Wettability Measurements of Titanium International Journal of Molecular Sciences. 2023.09; 24(19);

[Misc]

1. Lin P, Liu A, Tsuchiya Y, Noritake K, Ohsugi Y, Toyoshima K, Tsukahara Y, Shiba T, Nitta H, Aoki A, Iwata T, Katagiri S. Association between periodontal disease and chronic obstructive pulmonary disease Japanese Dental Science Review. 2023.12; 59; 389-402
2. Takeuchi Y, Aoki A, Hiratsuka K, Chui C, Ichinose A, Aung N, Kitanaka Y, Hayashi S, Toyoshima K, Iwata T, Arakawa S. Application of different wavelengths of LED lights in antimicrobial photodynamic therapy for the treatment of periodontal disease. Antibiotics (Basel, Switzerland). 2023.11; 12(12);
1. TONAMI Ken-ichi. Accurate and efficient comprehensive diagnoses in dentistry 2023.01; 75(10); 33-40

[Conference Activities & Talks]

1. 関口絢子, 曹 日丹, 礪波健一, 梅森 幸, 則武加奈子, 須永昌代, 木下淳博, 新田 浩. スマートグラスを用いた遠隔歯科臨床指導の教育効果 -概形印象採得-. 第 88 回口腔病学会学術大会 2023.12.02
2. 岡田大和, 川島伸之, 野田園子, Nyein Chan Ko, 村野浩気, 砂川光宏, 興地隆史. ラット臼歯歯髄への MO 貼付に伴う視床における Sostdc1 mRNA 発現の低下. 日本歯科保存学会 2023 年度秋季学術大会 (第 159 回) 2023.11.11 浜松
3. Rena Takahashi, Saki Uchiyama, Yuna Kanamori, Junichi Shinagawa, Toru Nikaido, Yasushi Shimada. Dentin bonding performance of resin cement using resin coating technique and different cleaning protocols. The 25th KACD-JSCD Joint Scientific Meeting 2023.11.04 Seoul, Korea
4. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Eriko Okada, Eiji Kaneko, Janelle Moross, Jun Tsuruta, Keiichi Akita, Masanaga Yamawaki. Patients as teachers: a novel IPE curriculum . AMEE2023 2023.08.28
5. Nakayama M, Li H, Hayashi M, Tsuchida Y, Kanamori Y, Noritake K, Nitta H, Miyayasu A, Iwaki M, Kanazawa M. Quantitative analysis of visual evaluation in abutment tooth for full metal crown. International Summer Program (ISP) 2023, TMDU 2023.08.02 Tokyo, Japan

6. Daisuke Kido, Keiji Komatsu, Toshikatsu Suzumura, Takanori Matsuura, Takahiro Ogawa. Clinical Determinants of Hydrophilic State of Titanium Surfaces. the 2023 IADR/LAR General Session & Exhibition with WCPD 2023.06.24 Bogota Colombia
1. Rena TAKAHASHI, Yuna KANAMORI, Shunsuke TAKANO, Junichi SHINAGAWA, Yosuke MINATO, Motoi TAKAHASHI, Yuka TSUDA, Yasushi SHIMADA. Evaluation of a novel one-step bonding system on resin coating technique. The 159th Meeting of Japanese Society of Conservative Dentistry 2023.11.11
2. Kazuhiro Nagata¹, Masayuki Hideshima, Chikahiro Ohkubo, Yasunori Suzuki, Daisuke Kurihara, Kenta Sorimachi. Survey on the usage of magnetic attachments after the introduction of the National Health Insurance. The 33rd Annual Meeting of the Japanese Society of Magnetic Dentistry 2023.11.11 Tokyo
3. Hiroaki Yamamoto¹, Masayuki Hideshima. Progress report on the implant-assisted removable partial denture units using a new method for attaching magnetic assemblies. The 33rd Annual Meeting of the Japanese Society of Magnetic Dentistry 2023.11.11 Tokyo
4. Characteristics of change in perception of human relationship during “Introduction of behavioral dentistry” online class. 2023.07.28
5. Kanako Noritake, Kumiko Yamaguchi, Makoto Kikukawa, Yuna Kanamori, Hiroshi Nitta. The characteristics of a good clinical teacher for dental trainees in Japan.. 2023.07.27
6. Yuna Kanamori, Kanako Noritake, Yumi Tsuchida, Maiko Iwaki, Manabu Kanazawa, Hiroshi Nitta. Comparison of quantitative evaluation and self-evaluation by trainee residents at Tokyo Medical and Dental University (TMDU) Hospital in abutment tooth preparation. The 42nd Annual Meeting of Japanese Dental Education Association 2023.07.17 Web
7. Hirohito Miki, Kanako Noritake, Sachi Umemori, Ken-ichi Tonami, Hiroshi Nitta.. Changes in medical interview competencies at the first visit during comprehensive clinical practice of dental students at Tokyo Medical and Dental University. . The 42nd Annual Meeting of Japanese Dental Education Association. 2023.07.15
8. Kanako Noritake, Yuji Kabasawa, Yohei Hama, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Sachi Umemori, Yuna Kanamori, Hirohito Miki, Daisuke Kido, Akira Nishiyama, Hiroshi Nitta.. Newly introduced training contents in the clinical training programs for dental residents at Tokyo Medical and Dental University Hospital. 2023.07.15
9. The effect of low-level Er:YAG laser irradiation on endothelial cells. 2023.05.26
10. Keita Nakagawa, Koji Mizutani, Kazuki Watanabe, Natsumi Saito, Shu Takemura, Eri Sakaniwa, Risako Mikami, Daisuke Kido, Kohei Takeda, Hiromi Kominato, Atsuhiko Hattori, Takanori Iwata. Comprehensive gene expression analysis during the healing phase of ligature-induced experimental periodontitis in diabetic rats. 2023.05.26
11. Miyata K, Mizutani K, Ohsugi Y, Mikami R, Takagi T, Kawakatsu N, Shirkata Y, Tsuchioka H, Oda S, Kinoshita A, Iwata T, Aoki A. Histological analysis of periodontal tissue attachment on Er:YAG Laser Irradiated root surfaces in beagle dogs. The 66th Spring Meeting of the Japanese Society of Periodontology 2023.05.26 Rexam Hall, Kagawa

[Others]

1. Prognosis of treatment effect for sleep apnea with oral appliance therapy - videoendoscopic evaluation for the predicting model -, 2023.04
Masayuki HIDEISHIMA
Grant-in-Aid for Scientific Research(C) 2022
Research No. 22K10051
Research Period 2012-2024
Principal Investigator Masayuki HIDEISHIMA
Research Fund \3,200,000

[Social Contribution]

1. Kanako Noritake, Pediatric and Adult Gum Oral Hygiene, Shinjuku Public Health Center, Dental Seminar for Parents and Children 2023, Web, 2023.11.08 - 2023.11.30

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 Atsushi Ito
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 through clinical training. We have comprehensive medical teaching for fifth and sixth-year students. Students can listen to patient’s complaints directly and deepen their understanding. Actually

they can see patients with dental psychosomatic disorders, and they know that these disorders are treatable. Moreover, they can learn negative effects of wrong ideas as a psychogenic disorder, and they can understand serious distress in patients and family members.

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

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

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

(4) Clinical Services & Other Works

We take charge of “Psychosomatic Dentistry clinic” in Tokyo Medical and Dental University Hospital. 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(Phantom bite syndrome).

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

[Original Articles]

1. Chihiro Takao, Motoko Watanabe, Gayatri Nayanar, Trang Tu, Yojiro Umezaki, Miho Takenoshita, Haruhiko Motomura, Takahiko Nagamine, Akira Toyofuku. Clinical Features and Variations of Pain Expressions in 834 Burning Mouth Syndrome Patients With or Without Psychiatric Comorbidities. *Cureus*. 2023.12; 15(12); e51139
2. Chizuko Maeda, Motoko Watanebe, Trang Thi Huyen Tu, Chihiro Takao, Gayatri Krishnakumar Nayanar, Risa Tominaga, Yasuyuki Kimura, Takahiko Nagamine, Akira Toyofuku . Psychiatric comorbidities in chronic orofacial pain during COVID-19 pandemic *Journal of psychosomatic research*. 2023.09;
3. Satoshi Kasahara, Yuichi Kato, Kaori Takahashi, Ko Matsudaira, Naoko Sato, Ken-Ichi Fukuda, Akira Toyofuku, Shin-Ichi Niwa, Kanji Uchida. Improvement in persistent idiopathic facial pain with comorbid

ADHD using the combination of a dopamine system stabilizer and psychostimulant: A case report. Clin Case Rep. 2023.06; 11(6); e7552

4. Chizuko Maeda, Motoko Watanabe, Trang Thi Huyen Tu, Chihiro Takao, Gayatri Krishnakumar Nayanar, Risa Tominaga, Yasuyuki Kimura, Takahiko Nagamine, Akira Toyofuku. Psychiatric comorbidities in chronic orofacial pain during COVID-19 pandemic. J Psychosom Res. 2023.06; 172; 111420
5. Motoko Watanabe, Trang Thi Huyen Tu, Chihiro Takao, Chizuko Maeda, Gayatri Krishnakumar Nayanar, Risa Tominaga, Yasuyuki Kimura, Miho Takenoshita, Tatsuya Yoshikawa, Koji Sumi, Satoko Sumi, Haruhiko Motomura, Takahiko Nagamine, Akira Toyofuku. Case series of drug-induced open bite: Extrapyramidal symptoms related to psychotropic medications. Front Psychiatry. 2023.04; 14; 1137917
6. Yojiro Umezaki, Haruhiko Motomura, Rui Egashira, Akira Toyofuku, Toru Naito. A Case of Oral Cenesthopathy Treated With the Combination of Brexpiprazole and Mirtazapine. Clin Neuropharmacol. 2023.03;
7. Mitsuhiro Asami, Yasuyuki Kimura, Miho Takenoshita, Risa Tominaga, Chizuko Maeda, Chihiro Takao, Motoko Watanabe, Trang Thi Huyen Tu, Takahiko Nagamine, Akira Toyofuku. Dental conditions in patients with medically unexplained oral symptoms Journal of Dental Sciences. 2023.01;
8. Ayano Katagiri, Kazuo Tsubota, Lou Mikuzuki, Shigeru Nakamura, Akira Toyofuku, Takafumi Kato, David A Bereiter, Koichi Iwata. Tear secretion by Diquafosol suppresses the excitability of trigeminal brainstem nuclear complex neurons by reducing excessive P2Y2 expression in the trigeminal ganglion in dry eye rats Neurosci Res. 2023.01;
9. Satoshi Kasahara, Kaori Takahashi, Ko Matsudaira, Naoko Sato, Ken-Ichi Fukuda, Akira Toyofuku, Tatsuya Yoshikawa, Yuichi Kato, Shin-Ichi Niwa, Kanji Uchida. Diagnosis and treatment of intractable idiopathic orofacial pain with attention-deficit/hyperactivity disorder. Sci Rep. 2023.01; 13(1); 1678
10. Maeda C, Nagamine T, Takao C, Tominaga R, Kimura Y, Watanabe M, Toyofuku A.. Are the Effects of Amitriptyline and Aripiprazole on Pain Catastrophizing in Patients with Burning Mouth Syndrome Associated with Changes in QTc and Prolactin Levels? Int Med J.. 2023; 30(4); 178-182
11. Jun-Ichi Takada, Norihisa Higashihori, Chiho Kadota-Watanabe, Tatsuo Kawamoto, Akira Toyofuku, Keiji Moriyama. Case report: Long-term management of occlusion after surgical-orthodontic treatment for a patient with drug-induced open bite developed after the onset of schizophrenia. Front Psychiatry. 2023; 14; 1304215

[Misc]

1. M Watanabe, R Tominaga, A Toyofuku, T T H Tu. Pandemic OPSD woes. Br Dent J. 2023.12; 235(12); 914
2. G K Nayanar, T Thi Huyen Tu, T Nagamine, A Toyofuku. The assessment of the long-term prognosis of burning mouth syndrome following treatment necessitates a reappraisal. Int J Oral Maxillofac Surg. 2023.02;

[Conference Activities & Talks]

1. Akira Toyofuku. Psychosomatic Dentistry: Treatment Approach and Research. The 3rd Indonesia dental exhibition and conference 2023.09.17 Jakarta, Indonesia,
2. Motoko Watanabe, Chihiro Takao, Chizuko Maeda, Risa Tominaga, Yasuyuki Kimura, Akira Toyofuku. Careful multidisciplinary consideration for psychiatric comorbidities in the patients with jaw deformities. The 3rd Annual Congress of Korean Society of Psychosomatic Dentistry 2023.08.19 Soul, Korea,
3. Motoko Watanabe, Trang Thi Huyen Tu, Chihiro Takao, Chizuko Maeda, Gayatri Krishnakumar Nayanar, Risa Tominaga, Yasuyuki Kimura, Miho Takenoshita, Tatsuya Yoshikawa, Koji Sumi, Satoko Sumi, Haruhiko Motomura, Takahiko Nagamine, Akira Toyofuku. Case series of drug-induced open bite; extrapyramidal symptoms related to psychotropic medications. The 3rd Annual Congress of Korean Society of Psychosomatic Dentistry 2023.08.19 Soul, Korea,
4. 松岡紘史、宇都宮雅史、Paudel Durga、吉田光希、渡邊素子、森谷満、三浦宏子、豊福明、安彦善裕. 舌痛症患者の労働状態に、痛みの重症度、気分状態、破局的思考が及ぼす影響. 第38回日本歯科心身医学会総会・学術大会 2023.07.01

Department of General Medicine

Professor HASHIMOTO MASAYOSHI

Professor ISHIDA TAKESHI

Professor KIMURA Takuma

Junior Associate Professor

BEPPU Masashi

Junior Associate Professor

YAMADA Toru

Assistant Professor

HADANO Yoshirou

Assistant Professor

MABUCHI Suguru

Project Assistant Professor

SAKAI Kazuhisa

Project Assistant Professor

SASAKI Mari

Visiting Lecturer

ABE Yasuko

Visiting Lecturer

BEPPU Masashi

Visiting Lecturer

SHIMOZONO Hisashi

Visiting Lecturer

SUZUKI Risa

Graduate Student

ANDO Yuuya

Graduate Student

DATEOKA Kaname

Graduate Student

FUTAMI Akane

Graduate Student

HADA Kouta

Graduate Student

KOIKE Hiroshi

Graduate Student

OUCHI Shuji

Graduate Student

SHINOHARA Takahiro

Graduate Student

SUGIHARA Masako

Graduate Student

YAMADA Hironori

Senior Resident

NIN Hiroki

Senior Resident

(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

[Original Articles]

1. Yuya Ando, Atit Suwannathot. Melioidosis in a 38-year-old Thai Woman Caused by *Burkholderia pseudomallei*. *Intern Med.* 2023.12;
2. Yamada T, Minami T, Yoshino S, Emoto K, Mabuchi S, Hanazawa R, Hirakawa A, Hashimoto M. Diaphragm Ultrasonography: Reference Values and Influencing Factors for Thickness, Thickening Fraction, and Excursion in the Seated Position. *Lung.* 2023.11;
3. Toru Yamada, Taro Minami, Yuka Kitano, Shunpei Yoshino, Suguru Mabuchi, Nilam Soni. Development of a national point-of-care ultrasound training course for physicians in Japan: A 3-year evaluation *MedEdPublish.* 2023.10; 13; 223
4. Ando Y, Ono Y, Ono S, Tanaka Y. Restrictive Ventilatory Impairment Due to Severe Scoliosis with a Large Cobb Angle. *JMA journal.* 2023.10; 6(4); 539-540
5. Miyagami T, Shimizu T, Kosugi S, Kanzawa Y, Nagasaki K, Nagano H, Yamada T, Fujibayashi K, Deshpande GA, Flora Kisuule, Tazuma S, Naito T. Roles considered important for hospitalist and non-hospitalist generalist practice in Japan: a survey study. *BMC primary care.* 2023.07; 24(1); 139
6. Yamada T, Ehara J, Funakoshi H, Endo K, Kitano Y. Effectiveness of point of care ultrasound (POCUS) simulation course and skills retention for Japanese nurse practitioners. *BMC nursing.* 2023.01; 22(1); 21
7. Hayashi Toshiyuki, Ai Masumi, Goto Satoshi, Nakamura Marie, Nagaike Hiroe, Suzuki Risa, Abe Yasuko, Ohta Motoko, Ito Yasuki, Hirano Tsutomu. Circadian Rhythm of Subspecies of Low-Density Lipoprotein-Cholesterol and High-Density Lipoprotein-Cholesterol in Healthy Subjects and Patients with Type 2 Diabetes(タイトル和訳中) *Journal of Atherosclerosis and Thrombosis.* 2023.01; 30(1); 3-14
8. Yuya Ando, Masato Kadoya, Tsutomu Kodera. Involuntary Movements During Treatment for Hyperglycemia. *AACE Clin Case Rep.* 2023; 9(1); 21-22

9. the Japanese Circulation Society/ the Japanese Association of Cardiac Rehabilitation Joint Working Group. JCS/JACR 2021 Guideline on Rehabilitation in Patients With Cardiovascular Disease Circulation Journal. 2023; 87; 155-235

[Misc]

1. Nanako Hashido, Masanori Kobayashi, Ami Kawamoto, Suguru Mabuchi, Hiromune Katsuda, Kazuo Ohtsuka, Yasuhiro Asahina, Masayoshi Hashimoto, Ryuichi Okamoto. Sphincter of Oddi dysfunction that could not be diagnosed with Rome IV: a case report. Clin J Gastroenterol. 2023.12; 16(6); 913-918

[Conference Activities & Talks]

1. Kanako Yoshimi, Kazuharu Nakagawa, Toru Yamada, Takahiro Shinohara, Shuji Ouchi, Mitsuko Saito, Ayane Horike, Haruka Tohara. Relationship between respiratory and swallowing function in older patients with dysphagia . ESSD 2023 13th Annual Congress 2023.11.30 Toulouse, France
2. 黒木平、木村琢磨、石田哲久、鶴若莉央、関口大樹、大内修司、山田徹、馬渕卓、橋本正良. 両側多発深部静脈血栓を契機に横行結腸癌が発見された一例。 . 2023.09.30 関東甲信越地方会
3. Dr. Risa Suzuki, Ms. Ayuko Umezawa, Dr. Chieko Sumiya , Dr. Yamato Hoshino, Dr. Yoshiyuki Numasawa, Dr. Shohei Kawagoe. Survey of nutritional management of patients receiving tube feeding in home medical care. IAGG Asia/Oceania Regional Congress 2023 2023.06.13 Yokohama

Department of Infectious Diseases

Professor GU Yoshiaki
Associate professor OKAMOTO Koh
Associate professor / lecturer TAGASHIRA Yasuaki
Assistant professor KURITA Takashi
Assistant professor (Division of Infection Control and Prevention) IDE Satoshi
Assistant professor (Division of Infection Control and Prevention) SATO Lubna
Medical staff OOI Marina
Project researcher AGATA Chikako
Project researcher SAKAGUCHI Mikiyo
Doctoral student HORIUCHI Kouji
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. Our department is responsible for the Division of Clinical Medicine of the TMDU Center for Infectious Diseases (TCIDEA), which was established in 2023

(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.

Outpatient services include medical care for infectious diseases, including HIV infection, and vaccination to prevent infectious diseases.

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

1. Haruki Mito, Ryota Hase, Hideki Ueda, Nobuaki Tsuyama, Motoki Fujii, Naoya Matsuda, Emiri Muranaka, Takashi Kurita, Yudai Yano. A pitfall of cognitive bias during the pandemic: Two cases of *Plasmodium falciparum* malaria coinfecting or misdiagnosed with COVID-19. *J Infect Chemother.* 2023.09; 29(9); 916-918
2. Noguchi Atsushi, Kurita Takashi, Matsuzawa Katsura. Clinical features of atlantoaxial involvement in patients with rheumatoid arthritis using F-18-fluorodeoxyglucose-positron emission tomography with computed tomography *CLINICAL RHEUMATOLOGY.* 2023.07; 42(7); 1875-1884
3. Ide Satoshi, Ishikane Masahiro, Aoyagi Kensuke, Ono Akane, Asai Yusuke, Tsuzuki Shinya, Kusama Yoshiki, Gu Yoshiaki, Kodama Eiichi, Ohmagari Norio. Investigation of oral macrolide prescriptions in Japan using a retrospective claims database, 2013-2018 *PLOS ONE.* 2023.06; 18(6); e0287297
4. Abe Keishi, Abe Sarah Krull, Fujita Takanori, Gu Yoshiaki, Hashizume Masahiro, Ikeda Chieko, Inaba Masaki, Jindai Kazuaki, Kondo Naoki, Kunii Osamu, Matsuo Makiko, Nakatani Hiroki, Nishino Yoshitaka, Nomura Shuhei, Sakamoto Haruka, Shiroyama Hideaki, Suzuki Tomoko, Takemi Ayako, Takuma Kayo. Promote global solidarity to advance health-system resilience: proposals for the G7 meetings in Japan *LANCET.* 2023.04; 401(10385); 1319-1321
5. Nomoto Hidetoshi, Ishikane Masahiro, Gu Yoshiaki, Yamamuro Ryosuke, Osawa Ryosuke, Hosokawa Naoto, Sahara Toshinori, Nakamura-Uchiyama Fukumi, Fukushima Kazuaki, Sekiya Noritaka, Imamura Akifumi, Fujikura Yuji, Kawana Akihiko, Nagata Kaoru, Tamura Kaku, Kutsuna Satoshi, Ohmagari Norio. 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.* 2023.01; 76(1); 20-26
6. Ota Y, Prah I, Mahazu S, Gu Y, Nukui Y, Koike R, Saito R. Novel insights into genetic characteristics of bla(GES)-encoding plasmids from hospital sewage. *Frontiers in microbiology.* 2023; 14; 1209195
7. Sako A, Gu Y, Masui Y, Yoshimura K, Yanai H, Ohmagari N. Prescription of anti-influenza drugs in Japan, 2014-2020: A retrospective study using open data from the national claims database. *PloS one.* 2023; 18(10); e0291673

[Conference Activities & Talks]

1. 具芳明. 日本の AMR 対策. 国立国際医療研究センター国際医療協力局 2023 年度 JICA 課題別研修「薬剤耐性 (AMR)・医療関連感染管理」 2023.11.06

[Social Contribution]

1. Promoting Global Solidarity to Advance Health System Resilience: Recommendations for the G7 Meetings in Japan, Hiroshima G7 Global Health Task Force, 2023.04

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio
Lecturer : SAITO Kenta
Assistant Professor: KAWAGISHI Masahiko
Assistant Professor: SATO Keisuke
Graduate Student : HANAOKA Miho
Affiliated Researcher: SUGIZAKI AYANA
Affiliated Researcher: IKETAKI YOSHINORI

(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

[Conference Activities & Talks]

1. 佐藤 啓介, 杉崎 綾奈, 鎌田 勝彦, 久野 玉雄, 桂 一茂, 白水 美香子, 寺田 純雄. F-actin 配向プローブ POLArISact と F-actin 複合体のクライオ電子顕微鏡解析と、それに基づく改良型 POLArISact の開発. 第 128 回日本解剖学会総会・全国学術集会 2023.03.20

Department of Neuropathology

Professor: Hitoshi Okazawa

Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone, Kyota Fujita

Project Associate Professor: Hidenori Homma

Lecturer: Hikari Tanaka

Assistant Professor : Maiko Inotsume

Assistant Administrative Staff: Xuemei Zhang, Shigemi Sato

Secretary: Marie Tanaka

Graduate Student : Yuki Yoshioka, Huang Yong, Sumire Takayama, Jin Meihua(∼2023.3), Jin Xiaocen(∼2023.3),

(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]

1. A secret passage for mutant protein to invade the brain

In a study published recently in Cell Reports, we have shown that a mutated version of a protein called α -synuclein propagates to various cerebral regions through the lymphatic system and then aggregates. Although the function of α -synuclein is not fully understood, it participates in neurotransmission. However, in some neurodegenerative diseases including Parkinson' s disease, α -synuclein changes shape and forms pathological clumps. Most experiments conducted so far only used fibrils, which are the clumps formed when monomeric α -synuclein aggregates. The fibrils are transmitted from neurons to neurons, but it remains unclear whether monomers act in the same way.

To further investigate how monomers and fibrils of α -synuclein move around in the brain, we injected small amounts of viral particles into the orbital cortex of mice to produce fluorescent monomeric mutant α -synuclein.

Because any cell type can contribute to α -synuclein propagation, we used viral particles to enable the synthesis of α -synuclein monomers in all cell types present in the injection area. This method ensured that all modes of propagation were accounted for.

Twelve months after the injection, although the fluorescent signal was lower in the injected region, signals were detected in other brain areas. Interestingly, fluorescent α -synuclein was detected in remote regions two weeks after injection, indicating an early spreading of mutant α -synuclein in the brain.

But how did α -synuclein propagate? We followed the three-dimensional distribution of α -synuclein in the brain and found fluorescent α -synuclein in the glymphatic system, which is the lymphatic system of the brain. The glymphatic system is involved in draining and renewing fluid from the brain and eliminating toxins, but it could also distribute toxic substances throughout the brain. We also observed the presence of fluorescent α -synuclein in the matrix surrounding neurons and in the cytosol of neurons. This finding suggested that fluorescent α -synuclein was taken up by the extracellular matrix and, subsequently, by neurons.

We also investigated the aggregation state of α -synuclein in the remote brain regions. Fibrils of α -synuclein formed after the monomers had propagated, specifically, we observed α -synuclein monomer in the glymphatic system and remote regions as early as two weeks after injection, while we found α -synuclein fibrils 12 months after injection.

This study shows how monomeric α -synuclein propagates through the glymphatic system in a different way from the fibrils. Thus, targeting these early events, α -synuclein monomer and brain lymphatic system, may limit the progression of Parkinson's disease.

2. Antagonistic roles of canonical and Alternative-RPA in disease-associated tandem CAG repeat instability

Seventy neurodegenerative diseases are caused by expansions of gene-specific tandem repeat sequences, several of which are associated with (CAG),(CTG) expansions, including Huntington disease (HD) and multiple spinocerebellar ataxias (SCAs). Inherited expansions continue to somatically expand with age in affected tissues, suggesting that ongoing expansions drive disease age of onset (AOO), progression, and severity.

Screens for repeat disease modifiers validated three AOO modifiers, strengthening a connection of somatic expansions to disease. Slipped-CAG DNA structures form from misaligned base-pairing as single-stranded DNA (ssDNA) re-anneals following transcription, replication, repair, or recombination.

The main SSB in humans is canonical RPA (replication protein A), a complex of RPA1, RPA2, and RPA3 (Figure 1A). RPA is essential for life, ubiquitously expressed, and mediates virtually every process involving ssDNA, including DNA duplex destabilization, melting of unusual DNA structures, reannealing of DNAs, protection of ssDNA, and protein recruitment to DNA.

We assess the role of RPA and Alt-RPA in somatic CAG repeat instability. We observe that RPA and Alt-RPA are upregulated 2- and 10-fold, respectively, in HD and SCA type 1 (SCA1) patient brains relative to age- and sex-matched controls. Our data show RPA enhances in vitro slipped-CAG repair, while high levels of Alt-RPA block slipped-DNA repair. Both SSBs bind slipped-DNAs, but only RPA efficiently melts them. FAN1-nuclease-mediated slipped-CAG cleavage is enhanced by RPA but inhibited by Alt-RPA. BioID of each RPA subunit reveals unique and shared associations with proteins important for somatic repeat instability. Expression of RPA inhibits while Alt-RPA expression enhances repeat expansions in human cells. Over-expressing murine Rpa1 ablates spontaneous somatic CAG expansions in SCA1 mouse brains, reduces disease biomarkers, and improves motor functions. These results indicate that RPA/Alt-RPA modulate CAG repeat instability.

3. Promising new treatment for a common hereditary nerve disease

In a study published last month in Communications Medicine, we have unveiled a groundbreaking genome-editing technique. This innovation holds promise for treating Charcot-Marie-Tooth (CMT), a relatively common hereditary nerve disease that affects the nerves and currently has no clinical treatments.

CMT is characterized by altered sensation and muscle weakness in the limbs and affects 10 to 80 people per 100,000. The most common CMT subtype is known as CMT1A and is caused by a duplication of the gene encoding peripheral myelin protein 22 (PMP22), leading to high levels of this protein in affected individuals. PMP22 is important for forming myelin structural unit, the fatty insulation that allows signals to rapidly travel from the limbs to the brain and back.

We have tried to reduce PMP22 in animal models of CMT1A using different techniques, but its translation to human patients has been unsuccessful. This may be because existing animal models do not have human-like PMP22 gene duplication. This study aimed to solve this problem.

We created a cell model by taking cells from a patient with CMT1A and growing them into Schwann cells,

which are the cells that make myelin. We then used a specialized genome-editing technique, known as AAV vectors, to decrease the amount of PMP22 protein that was produced by the cells.

Because both higher and lower PMP22 levels can lead to different types of nerve diseases (known as neuropathies), we had to be very careful about how much we reduced PMP22. We created and trialed different AAV vectors, and eventually chose one that removed 20% to 40% of PMP22 gene copies from the genome. This was enough to reverse many CMT-related changes in Schwann cell cultures and to improve the myelination abilities of these cells, thus highlighting the potential of this treatment as a clinical therapy for the disease.

We are cautiously optimistic because similar AAV-based gene therapies are beginning to be approved by the FDA for the treatment of hematological diseases. We believe that our therapeutic approach has low risks for human applications and may be relatively simple to translate into a clinical therapy. Given that there are currently no treatments for CMT beyond physiotherapy, occupational therapy, and pain management, the development of this genome-editing technique for PMP22 is an important breakthrough and may reduce symptoms and improve quality of life in CMT patients.

(3) Education

As educational tasks, we have lecture and experiment classes of neuropathology for medical/dental graduate school program and medical school program. We also have general pathology and neuropathology classes for graduate school for health sciences, and clinical anatomical and therapeutic pathology classes for research students.

(4) Lectures & Courses

We provide students with opportunities to learn practical research techniques on neuropathology, especially neurodegenerative diseases.

(5) Publications

[Original Articles]

1. Yoshioka Y, Taniguchi JB, Homma H, Tamura T, Fujita K, Inotsume M, Tagawa K, Misawa K, Matsumoto N, Nakagawa M, Inoue H, Tanaka H, Okazawa H. AAV-mediated editing of PMP22 rescues Charcot-Marie-Tooth disease type 1A features in patient-derived iPS Schwann cells. *Commun Med (Lond)*. 2023.11; 3(1); 170
2. Gall-Duncan T, Luo J, Jurkovic CM, Fischer LA, Fujita K, Deshmukh AL, Harding RJ, Tran S, Mehkary M, Li V, Leib DE, Chen R, Tanaka H, Mason AG, Lévesque D, Khan M, Razzaghi M, Prasolava T, Lanni S, Sato N, Caron MC, Panigrahi GB, Wang P, Lau R, Castel AL, Masson JY, Tippet L, Turner C, Spies M, La Spada AR, Campos EI, Curtis MA, Boisvert FM, Faull RLM, Davidson BL, Nakamori M, Okazawa H, Wold MS, Pearson CE. Antagonistic roles of canonical and Alternative-RPA in disease-associated tandem CAG repeat instability. *Cell*. 2023.10; 186(22); 4898-4919.e25
3. Fujita K, Homma H, Jin M, Yoshioka Y, Jin X, Saito Y, Tanaka H, Okazawa H. Mutant α -synuclein propagates via the lymphatic system of the brain in the monomeric state. *Cell Rep*. 2023.08; 42(8); 112962
4. Shiwaku H, Katayama S, Gao M, Kondo K, Nakano Y, Motokawa Y, Toyoda S, Yoshida F, Hori H, Kubota T, Ishikawa K, Kunugi H, Ikegaya Y, Okazawa H, Takahashi H. Analyzing schizophrenia-related phenotypes in mice caused by autoantibodies against NRXN1 α in schizophrenia. *Brain Behav Immun*. 2023.07; 111; 32-45
5. Jin X, Tanaka H, Jin M, Fujita K, Homma H, Inotsume M, Yong H, Umeda K, Kodera N, Ando T, Okazawa H. PQBP5/NOL10 maintains and anchors the nucleolus under physiological and osmotic stress conditions. *Nat Commun*. 2023.01; 14(1); 9

[Conference Activities & Talks]

1. Hitoshi Okazawa. Development of HMGB1 antibody therapy against neurodegenerative dementias. The 42nd Annual Meeting of Japan Society for Dementia Research 2023.11.24 Nara Prefectural Convention Center(Nara)
2. Hikari Tanaka, Xiaocen Jin, Meihua Jin, Kyota Fujita, Hidenori Homma, Miako Inotsume, Huang Yong, Kenichi Umeda, Noriyuki Koderu, Toshio Ando, Hitoshi Okazawa. PQBP5/NOL10 maintains and anchors the nucleolus under physiological and osmotic stress conditions. 2023.08.04 Sendai International Center (Miyagi Sendai)
3. Kyota Fujita, Hitoshi Okazawa. DNA damage repair and neurodegeneration. 64th Annual Meeting of the Japanese Society of Neurology 2023.06.02 MakuhariMesse(Chiba)
4. Hitoshi Okazawa. Neuroinflammation and neurodegeneration. 64th Annual Meeting of the Japanese Society of Neurology 2023.06.02 MakuhariMesse(Chiba)
5. Xiaocen Jin, Hikari Tanaka, Meihua Jin, Kyota Fujita, Hidenori Homma, Maiko Inotsume, Huang Yong, Kenichi Umeda, Noriyuki Koderu, Toshio Ando, Hitoshi Okazawa. PQBP5/NOL10 maintains and anchors the nucleolus under physiological and osmotic stress conditions. The 15th CBIR Symposium Inspiring the Next Generation (online) 2023.02.17

[Patents]

1. Diagnosis methods, diagnostic agents, and therapeutic agents against alzheimer's disease and frontotemporal lobar degeneration, and screening methods for these agents, Patent Number : 11623946

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, Tomonari Takahashi, Keigo Sugisawa

Graduate student; Zong Yuan, Xiong Jianping, Chen Changyu, Lu Hongshuang, Zhou Nan, Wang Yining, Zhang Jing, Yang Mingming, Wang Ziyue

(1) Outline

Our department was established in 1944. Prof. Jin Ohtsuka initiated research on myopia in 1946, and Emeritus Prof. Takashi Tokoro established high myopia clinic in 1974 as the world only clinic specific to pathologic myopia. To date, clinical practice as well as basic research on myopia have continuously been performed in our department. Uveitis clinic was established by Emeritus Prof. Manabu Mochizuki in 1988. Since Prof. Kyoko Ohno-Matsui was appointed to a professorship in our department, clinical practice and basic research on wide variety of fields such as glaucoma, cataract, diabetic retinopathy, vitreoretinal disorder, and macular diseases in addition to myopia and uveitis have been actively performed.

(2) Research

1. High myopia

- 1) Analysis of retinochoroidal complications in high myopia (choroidal neovascularization, myopic tractional retinopathy)
- 2) Evaluation of the molecular mechanism of choroidal angiogenesis using the cultured cells as well as experimental animals (collaboratory project with Department of Cellular Physiological Chemistry)
- 3) Gene analysis of highly myopic patients (collaborator project with Kyoto University)
- 4) Establishment of a novel therapy to prevent an axial elongation or the formation of posterior staphyloma

2. Ocular immunology and inflammation

- 1) Evaluation of the molecular mechanism of immunoregulation in intraocular inflammation
- 2) Pathogenic mechanism of intraocular inflammatory diseases
- 3) Development of novel treatments of intraocular inflammation
- 4) Molecular diagnosis of virus-infected uveitis and intraocular lymphomas.

3. Neuro-ophthalmology

- 1) Evaluation of the change of the circulation as well as the glucose metabolism in the visual cortex using positron emission tomography (PET) in various ocular disorders
- 2) Mechanism of visual pathway in normal conditions as well as in the patients with amblyopia.

4. Vitreoretinal disorder

- 1) Development of a novel treatment for vitreoretinal disorders like retinal detachment, diabetic retinopathy, and macular holes.

5. Strabismus and amblyopia clinic

- 1) Effect of the visual background on binocular vision as well as the influence of strabismus on dynamic visual

acuity.

(3) Education

Undergraduate education of ophthalmology is composed of 1) classes on histology and physiology of the eye, and on diagnosis and treatment of ocular disorders, 2) combination block in which clinical examination is trained, and the diagnostic process is actively learned through group discussion using case series, 3) pre-clerkship and clerkship in which the medical students practically learn the major ocular disorders by seeing the patients and discussing in the conference.

After the initial residency of the first two years, the residency in ophthalmology is programmed for four years according to the educational program on diploma of ophthalmology by Japanese ophthalmological society.

The graduate students are expected to be academic doctors who develop and perform highly-qualified ophthalmologists, as well as become scientists who can perform basic research focusing on their clinical interest.

(4) Lectures & Courses

Main objective of ophthalmology and visual science in the graduate course is to obtain the highly-advanced knowledge in the diagnosis and the treatment of various ocular disorders and to perform the basic research based on clinical experience.

(5) Clinical Services & Other Works

Clinical practice is organized by the general ophthalmology clinic as well as the several subspecialty clinics. When the patients visited our department, they are screened in the general clinic, and then the final decision of the diagnosis and treatment is made in cooperation with each subspecialty clinic. Subspecialty clinics include high myopia clinic, uveitis clinic, glaucoma clinic, vitreoretinal disorder clinic, diabetic retinopathy clinic, neuro-ophthalmology clinic, and medical retina clinic. Approximately, 1,300 surgeries are performed per year (e.g., cataract surgery, vitreoretinal surgery, glaucoma surgery, strabismus surgery).

(6) Publications

[Original Articles]

1. Tomonari Takahashi, Tae Igarashi-Yokoi, Noriko Nakao, Kengo Uramoto, Takeshi Yoshida, Kyoko Ohno-Matsui. Dome-shaped macula with protrusion of inner part of sclera. *Am J Ophthalmol Case Rep.* 2023.12; 32; 101926
2. Motomura, Y; Yoshifuji, K; Tachibana, T; Takase, H; Arai, A; Tanaka, K; Okada, K; Nogami, A; Umezawa, Y; Sakashita, C; Yamamoto, M; Mori, T; Nagao, T. Clinical factors for central nervous system progression and survival in primary vitreoretinal lymphoma *BRITISH JOURNAL OF HAEMATOLOGY.* 2023.12;
3. Mingming Yang, Koju Kamoi, Yuan Zong, Jing Zhang, Yaru Zou, Kyoko Ohno-Matsui. Ocular Manifestations of Human Immunodeficiency Virus Infection in the Combination Antiretroviral Therapy Era. *Pathogens.* 2023.12; 12(12);
4. Takeshi Yoshida, Sota Yoshimoto, Takuhei Nomura, Taiju Ito, Motohisa Ohno, Shintaro Yasuda, Yuto Shiotani, Kyoko Ohno-Matsui. Intraocular pressure-lowering effects of ripasudil on open-angle glaucoma in eyes with high myopia and pathological myopia. *Sci Rep.* 2023.12; 13(1); 22888
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6. Hongshuang Lu, Changyu Chen, Jianping Xiong, Yining Wang, Ziyue Wang, Muka Moriyama, Koju Kamoi, Kengo Uramoto, Tomonari Takahashi, Takeshi Yoshida, Kyoko Ohno-Matsui. Longitudinal Changes of Posterior Vortex Veins in Highly Myopic Eyes determined by Retrospective Analyses of Indocyanine Green Angiograms. *Retina.* 2023.11;

7. Shiqi Xie, Hongshuang Lu, Changyu Chen, Jianping Xiong, Yining Wang, Kengo Uramoto, Koju Kamoi, Yuka Onishi, Kyoko Ohno-Matsui. MORPHOLOGIC CHARACTERISTICS AND PROGRESSION PATTERNS OF MACULAR NEOVASCULARIZATION-RELATED ATROPHY IN EYES WITH PATHOLOGIC MYOPIA. *Retina*. 2023.10; 43(10); 1662-1672
8. Yining Wang, Ran Du, Shiqi Xie, Changyu Chen, Hongshuang Lu, Jianping Xiong, Daniel S W Ting, Kengo Uramoto, Koju Kamoi, Kyoko Ohno-Matsui. Machine Learning Models for Predicting Long-Term Visual Acuity in Highly Myopic Eyes. *JAMA Ophthalmol*. 2023.10;
9. Jingwen Jiang, Yunhe Song, Kangjie Kong, Peiyuan Wang, Fengbin Lin, Xinbo Gao, Zhenyu Wang, Ling Jin, Meiling Chen, Dennis S C Lam, Robert N Weinreb, Jost B Jonas, Kyoko Ohno-Matsui, Shida Chen, Xiulan Zhang, . Optic Nerve Head Abnormalities in Nonpathologic High Myopia and the Relationship With Visual Field. *Asia Pac J Ophthalmol (Phila)*. 2023.10; 12(5); 460-467
10. Kyoko Ohno-Matsui, Masahiro Akiba, Tatsuro Ishibashi, Akito Hirakata. EVALUATION OF MORNING GLORY SYNDROME BY SWEEP SOURCE OPTICAL COHERENCE TOMOGRAPHY. *Retin Cases Brief Rep*. 2023.09; 17(5); 542-547
11. Cherng-Ru Hsu, Tae Igarashi-Yokoi, I-Chia Liang, Kyoko Ohno-Matsui. Ten-year longitudinal morphological changes in dome-shaped maculas in highly myopic eyes. *Retina*. 2023.09;
12. Izabela P Klaska, Tian Yu, Rosie Fordyce, Koju Kamoi, Richard J Cornall, Cristina Martin-Granados, Lucia Kuffova, John V Forrester. Targeted delivery of autoantigen to dendritic cells prevents development of spontaneous uveitis. *Front Immunol*. 2023.09; 14; 1227633
13. Kyoko Ohno-Matsui. Evaluating the Entire Shape of the Eye With Pathologic Myopia. *JAMA Ophthalmol*. 2023.08; 141(8); 774-775
14. Yunhe Song, Fei Li, Rachel S Chong, Wei Wang, An Ran Ran, Fengbin Lin, Peiyuan Wang, Zhenyu Wang, Jingwen Jiang, Kangjie Kong, Ling Jin, Meiling Chen, Jian Sun, Deming Wang, Clement C Tham, Dennis S C Lam, Linda M Zangwill, Robert N Weinreb, Tin Aung, Jost B Jonas, Kyoko Ohno-Matsui, Ching-Yu Cheng, Neil M Bressler, Xiaodong Sun, Carol Y Cheung, Shida Chen, Xiulan Zhang, . High Myopia Normative Database of Peripapillary Retinal Nerve Fiber Layer Thickness to Detect Myopic Glaucoma in a Chinese Population. *Ophthalmology*. 2023.07;
15. Takeshi Yoshida, Takuhei Nomura, Sota Yoshimoto, Motohisa Ohno, Taiju Ito, Shintaro Horie, Kyoko Ohno-Matsui. Outcomes of standalone ab interno trabeculotomy in the treatment of open-angle glaucoma in eyes with high myopia. *BMC Ophthalmol*. 2023.06; 23(1); 261
16. Kyoko Ohno-Matsui, Hiroyuki Takahashi, Zaixing Mao, Noriko Nakao. Determining posterior vitreous structure by analysis of images obtained by AI-based 3D segmentation and ultrawidefield optical coherence tomography. *Br J Ophthalmol*. 2023.05; 107(5); 732-737
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18. Rosie Clark, Samantha Sze-Yee Lee, Ran Du, Yining Wang, Sander C M Kneepkens, Jason Charng, Yu Huang, Michael L Hunter, Chen Jiang, J Willem L Tideman, Ronald B Melles, Caroline C W Klaver, David A Mackey, Cathy Williams, Hélène Choquet, Kyoko Ohno-Matsui, Jeremy A Guggenheim, . A new polygenic score for refractive error improves detection of children at risk of high myopia but not the prediction of those at risk of myopic macular degeneration. *EBioMedicine*. 2023.05; 91; 104551
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21. Xiu Juan Zhang, Duncan Ka Shun Chau, Yu Meng Wang, Cynthia Sze Hang Cheung, Hei-Nga Chan, Jian Shi, Ka Ming Nip, Shumin Tang, Ryan C F Chan, Alistair Lau, Sit Hui Kei, Ka Wai Kam, Alvin L Young, Li Jia Chen, Clement C Tham, Kyoko Ohno-Matsui, Chi Pui Pang, Jason C Yam. Prevalence and Characteristics of Peripapillary Gamma Zone in Children With Different Refractive Status: The Hong Kong Children Eye Study. *Invest Ophthalmol Vis Sci*. 2023.04; 64(4); 4
22. Changyu Chen, Ran Du, Shiqi Xie, Hongshuang Lu, Jianping Xiong, Yining Wang, Noriko Nakao, Hiroyuki Takahashi, Tae Igarashi-Yokoi, Koju Kamoi, Kengo Uramoto, Kyoko Ohno-Matsui. LONGITUDINAL STUDY OF CHANGES IN INNER SCLERAL CURVATURE PATTERNS AND DEVELOPMENT OF POSTERIOR STAPHYLOMAS IN HIGHLY MYOPIC EYES OF CHILDREN AND ADOLESCENTS. *Retina*. 2023.03; 43(3); 454-463
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25. Shintaro Horie, Corradetti Giulia, Houri Esmaeilkhanian, Srimivas R Sadda, Chui Ming Gemmy Cheung, Yeji Ham, Andrew Chang, Tomonari Takahashi, Kyoko Ohno-Matsui. Microperimetry in Retinal Diseases. *Asia Pac J Ophthalmol (Phila)*. 2023.03; 12(2); 211-227
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27. Hongshuang Lu, Shiqi Xie, Jianping Xiong, Changyu Chen, Yining Wang, Muka Moriyama, Koju Kamoi, Kengo Uramoto, Kyoko Ohno-Matsui. Complex hemodynamics of intervortex vein anastomoses in highly myopic eyes. *Retina*. 2023.01;
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30. Yuta Yasaka, Eiichi Hasegawa, Hiroshi Keino, Yoshihiko Usui, Kazuichi Maruyama, Yuki Yamamoto, Toshikatsu Kaburaki, Daiju Iwata, Masaru Takeuchi, Sentaro Kusuhara, Hiroshi Takase, Kenji Nagata, Ryoji Yanai, Yutaka Kaneko, Chiharu Iwahashi, Atsuki Fukushima, Nobuyuki Ohguro, Koh-Hei Sonoda, . A multicenter study of ocular inflammation after COVID-19 vaccination. *Jpn J Ophthalmol*. 2023.01; 67(1); 14-21
1. A case with inflammatory choroidal neovascularizations that was difficult to differentiate from myopic choroidal neovascularizations in pathologic myopia 2023.01; (16); 12-17

[Misc]

1. Sunao Sugita, Hiroshi Takase, Satoko Nakano. Role of Recent PCR Tests for Infectious Ocular Diseases: From Laboratory-Based Studies to the Clinic. *Int J Mol Sci*. 2023.05; 24(9);
2. Tetsuaya Muto, Shinichiro Imaizumi, Koju Kamoi. Viral Conjunctivitis. *Viruses*. 2023.03; 15(3);
3. Mingming Yang, Koju Kamoi, Yuan Zong, Jing Zhang, Kyoko Ohno-Matsui. Human Immunodeficiency Virus and Uveitis. *Viruses*. 2023.02; 15(2);

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7. Yaru Zou, Koju Kamoi, Yuan Zong, Jing Zhang, Mingming Yang, Kyoko Ohno-Matsui. Ocular Inflammation Post-Vaccination. *Vaccines (Basel)*. 2023.10; 11(10);

[Conference Activities & Talks]

1. Ohno-Matsui K. Pathologic myopia. International Summit on High Myopia & Complications 2023 2023.12.23 web
2. Tae Igarashi-Yokoi . Scleral Imaging of DSM. APVRS DSM 発表 2023.12.09 香港
3. Ohno-Matsui K. Imaging of pathologic myopia. Johns Hopkins University Wilmer Eye Institute, Fourth Annual Retinal Festival 2023.12.02 web
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9. Ohno-Matsui K. Vitreous-macular-choroidal and peripheral OCT imaging: Cross-sectional, angiographic, widefield, navigated, en face, 3-D and intraoperative. AAO 2023 2023.11.06 San Francisco, USA
10. Ohno-Matsui K. Myopia Management: Global perspectives, digital innovation and AI. AAO 2023 2023.11.05 San Francisco, USA
11. Yasuda S, Shiotani Y, Yoshimoto S, Ito T, Xiong J, Yoshida T, Ohno-Matsui K. Retromode imaging of the optic nerve changes in patients with myopic and glaucomatous optic neuropathy. AAO 2023 2023.11.05 San Francisco, USA
12. Ohno-Matsui K. Polarization-sensitive imaging of scleral abnormalities in myopia and dome-shaped macula. AAO 2023 2023.11.04 San Francisco, USA
13. Kyoko Ohno-Matsui, Tae Igarashi-Yokoi (equally contributing first author), Takeshi Azuma, Keigo Sugisawa, Jiang Xiong, Tomonari Takahashi, Kengo Uramoto, Koju Kamoi, Michiaki Okamoto, Suchandra Banerjee, Masahiro Yamanari. Polarization-Sensitive Imaging of Scleral Abnormalities in Myopia and Dome-Shaped Macula. アメリカ眼科学会 網膜サブスペシャルティデイ 2023.11.03 サンフランシスコ

14. Nan Zhou, Takeshi Yoshida, Kyoko Ohno-Matsui. The association of lamina cribrosa defects and γ -zone parapapillary atrophy with the central visual field in patients with high myopia. 第 77 回臨床眼科学会 2023.10.08 東京都千代田区 (国際フォーラム)
15. Ohno-Matsui K. High myopia and how to avoid it in 2023. High myopia and its complications. EURETINA 2023 2023.10.06 Amsterdam, Nederland
16. Ohno-Matsui K. When and how staphylomas develop? Myopia. EURETINA 2023 2023.10.06 Amsterdam, Nederland
17. Hiroshi Takase. Usage of biologics in the management of non-infectious uveitis. TMS 2023 Taiwan Macula Society Annual Meeting 2023.09.24 台湾 台北市
18. Hiroshi Takase. Molecular diagnosis of vitreoretinal lymphoma. TMS 2023 Taiwan Macula Society Annual Meeting 2023.09.24 台湾 台北市
19. Takahashi H, Tanaka N, Shinohara K, Uramoto K, Yokoi T, Yoshida T, Ohno-Matsui K. Importance of paravascular vitreal adhesions for development of myopic macular retinoschisis detected by ultra-widefield OCT. 37 回東京医科歯科大学眼科学教室同門会集談会プログラム 2023.07.17 東京都文京区 (東京医科歯科大学、web)
20. Takahashi H, Tanaka N, Shinohara K, Uramoto K, Yokoi T, Yoshida T, Ohno-Matsui K. Importance of Paravascular Vitreal Adhesions for Development of Myopic Macular Retinoschisis Detected by Ultra-Widefield OCT. Ophthalmology. 37 回東京医科歯科大学眼科学教室同門会集談会プログラム 2023.07.15 東京都文京区 (東京医科歯科大学、web)
21. Ohno-Matsui K. Novel paravascular lesions with abnormal autofluorescence in eyes with pathologic myopia. Asia Pacific Retinal Imaging Society (APVRS) 2023.06.30 Korea, Seoul、web
22. Ohno-Matsui K. Pathologic Myopia. シンガポール国立大学 web 講演会 2023.06.13 web
23. Ohno-Matsui K. Pathologic Myopia. RCOphth Congress 2023 2023.05.23 Birmingham, England (Royal College of London)
24. Wang Y, Ohno-Matsui K, Du R, Xie S, Xiong J, Chen C, Lu H. A nomogram predicting the risk of visual impairment in high myopic eyes. 第 5 回日本近視学会総会 2023.05.14 福岡県福岡市 (九州大学医学部百年講堂)
25. Lu H, Xie S, Xiong J, Chen C, Wang Y, Moriyama M, Kamoi K, Uramoto K, Ohno-Matsui K. Analysis of long-term changes of posterior vortex vein in highly myopic eyes. 第 5 回日本近視学会総会 2023.05.13 福岡県福岡市 (九州大学医学部百年講堂)
26. Chen C, Xie S, Lu H, Xiong J, Wang Y, Nakao N, Uramoto K, Igarashi-Yokoi T, Kamoi K, Takahashi H, Ohno-Matsui K. The Development of posterior staphyloma and changes of scleral shape in pathologic myopia. 第 5 回日本近視学会総会 2023.05.13 福岡県福岡市 (九州大学医学部百年講堂)
27. Hsu C, Igarashi-Yokoi T, Liang I, Ohno-Matsui K. Ten-year follow-up of dome-shaped macula in Highly Myopic Eyes. 第 5 回日本近視学会総会 2023.05.13 福岡県福岡市 (九州大学医学部百年講堂)
28. Changyu Chen, Shiqi Xie, Hongshuang Lu, Jianping Xiong, Yining Wang, Noriko Nakao, Hiroyuki Takahashi, Tae Igarashi-Yokoi, Koju Kamoi, Kengo Uramoto, Kyoko Ohno-Matsui.. The development of posterior staphyloma and changes of scleral shape in pathologic myopia.. 第 5 回日本近視学会総会 2023.05.13 東京国際フォーラム,webinar
29. Ohno-Matsui K. Intervortex vein anastomoses in pathologic myopia. 30th Anniversary of The Retina Center at Pali Momi & Hawaii Macula and Retina Institute 2023.04.29 Hawaii, USA
30. Tae Igarashi-Yokoi . International Symposium 5 Optimal and timely vision care for children.” Optimal and timely vision care for children Myopia control.”. 第 127 回日本眼科学会 2023.04.08 東京国際フォーラム,webinar
31. Xiong J, Xie S, Lu H, Chen C, Wang Y, Yoshida T, Ohno-Matsui K.. Retro-mode scanning laser ophthalmoscopy of optic disc abnormalities.. 第 127 回日本眼科学会 2023.04.07 東京都千代田区 (国際フォーラム)、web

32. Wang Y, Du R, Xie S, Lu H, Chen C, Xiong J, Ohno-Matsui K.. Prediction Models for Vision Outcome with Machine Learning in Highly Myopic Eyes. 第 127 回日本眼科学会 2023.04.07 東京都千代田区 (国際フォーラム)、web
33. Chen C, Xie S, Lu H, Xiong J, Wang Y, Nakao N, Takahashi H, Igarashi-Yokoi T, Kamoi K, Uramoto K, Ohno-Matsui K.. The Development of posterior staphyloma and changes of scleral shape in pathologic myopia. 第 127 回日本眼科学会 2023.04.06 東京都千代田区 (国際フォーラム)、web
1. Kota Yoshifuji, Daichi Sadato, Takashi Toya, Yotaro Motomura, Hiroshi Takase, Yuka Harada, Takehiko Mori, Toshikage Nagao. Genetic alterations of primary vitreoretinal lymphoma are associated with CNS progression. 85th Congress of the Japanese Society of Hematology 2023.10.14 Tokyo

[Awards & Honors]

1. The 2023 APAO Jose Rizal Medal, Asia-Pacific Academy of Ophthalmology, 2023.02
2. The 1st Asia-Pacific Eye 100 Most Influential Ophthalmologists 2022, Asia-Pacific Journal of Ophthalmology, 2023.02
3. The Power List 2023, The Ophthalmologist, 2023.04
4. Senior Achievement Award, AAO, 2023.07

Otorhinolaryngology

Professor: Takeshi Tsutsumi

Associate Professor: Yoshiyuki Kawashima

Junior Associate Professor: Taku Ito

Assistant Professor: Tarou Fujikawa, Keiji Honda, Ayako Nishio

Hospital Staff: Takamori Takeda, Ayako Maruyama, Keisuke Kondo

Graduate Student: Ayako Maruyama, Bai Jing, Ayame Yamazaki, Hiroki Watanabe, Natsuki Aoki, Tomoki Ooka, Kaori Mohri

(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 clerkship III, students also attend a "micro-conference" on teaching. Finally, students are assigned to patients throughout their treatment, consistently dealing with the same individuals before, during, and after surgery; this allows the students to become familiar with the course of clinical care.

(3) Clinical Performances

Otorhinolaryngology clinic provides full examinations and treatment for diseases in ear, nose, throat, head, and neck, including dizziness, sudden deafness, facial palsy, infectious disease and benign as well as malignant disease in the otorhinolaryngeal area. We have performed the first implementation of bone anchored hearing aid implant in Japan and since then we have experienced many patients for this surgery. We also have performed surgery for patients with malignant disease as well as skull base lesions in collaboration with the Department of

the Head and Neck Surgery. Our outpatient clinic includes general ear, nose and throat clinic as well as allergy, sinusitis, dizziness, otitis media, tumor, deafness, and tinnitus clinic.

(4) Publications

[Original Articles]

1. Sakihama Naoyuki, Okada Ryuhei, Takahashi Naoto, Fushimi Naoki, Ooka Tomoki, Kawabe Hiroaki, Ariizumi Yosuke, Ohno Kazuchika, Ueki Yutaka, Tayama Niro, Tsutsumi Takeshi, Asakage Takahiro. Post-intubation laryngeal injury after COVID-19 treatment causing dyspnea: A report of six cases(タイトル和訳中) *Auris·Nasus·Larynx*. 2023.10; 50(5); 816-820
2. Yamazaki A, Aoki N, Ooka T, Takeda T, Honda K, Yabunaka S, Tsutsumi T. Sustained deviation of torsional eye position associated with transient semicircular canal stimulation. *Acta oto-laryngologica*. 2023.10; 143(10); 849-855
3. Kurata N, Kawashima Y, Ito T, Fujikawa T, Nishio A, Honda K, Kanai Y, Terasaki M, Endo I, Tsutsumi T. Advanced Magnetic Resonance Imaging Sheds Light on the Distinct Pathophysiology of Various Types of Acute Sensorineural Hearing Loss. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*. 2023.08; 44(7); 656-663
4. Kurata N, Kawashima Y, Ito T, Fujikawa T, Nishio A, Honda K, Kanai Y, Terasaki M, Endo I, Tsutsumi T. Advanced Magnetic Resonance Imaging Sheds Light on the Distinct Pathophysiology of Various Types of Acute Sensorineural Hearing Loss. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*. 2023.08; 44(7); 656-663
5. Kurata N, Kawashima Y, Ito T, Fujikawa T, Nishio A, Honda K, Kanai Y, Terasaki M, Endo I, Tsutsumi T. Advanced Magnetic Resonance Imaging Sheds Light on the Distinct Pathophysiology of Various Types of Acute Sensorineural Hearing Loss. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*. 2023.08; 44(7); 656-663
6. Kurata, N; Kawashima, Y; Ito, T; Fujikawa, T; Nishio, A; Honda, K; Kanai, Y; Terasaki, M; Endo, I; Tsutsumi, T. Advanced Magnetic Resonance Imaging Sheds Light on the Distinct Pathophysiology of Various Types of Acute Sensorineural Hearing Loss *OTOLOGY & NEUROTOLOGY*. 2023.08; 44(7); 656-663
7. Watanabe H, Ito T, Aoki N, Bai J, Honda K, Kawashima Y, Fujikawa T, Ikeda T, Tsutsumi T. Quantitative analysis and correlative evaluation of video-oculography, micro-computed tomography, and histopathology in Pendrin-null mice. *Neurobiology of disease*. 2023.07; 183; 106194
8. Watanabe H, Ito T, Aoki N, Bai J, Honda K, Kawashima Y, Fujikawa T, Ikeda T, Tsutsumi T. Quantitative analysis and correlative evaluation of video-oculography, micro-computed tomography, and histopathology in Pendrin-null mice. *Neurobiology of disease*. 2023.07; 183; 106194
9. Watanabe H, Ito T, Aoki N, Bai J, Honda K, Kawashima Y, Fujikawa T, Ikeda T, Tsutsumi T. Quantitative analysis and correlative evaluation of video-oculography, micro-computed tomography, and histopathology in Pendrin-null mice. *Neurobiology of disease*. 2023.07; 183; 106194
10. Quantitative analysis and correlative evaluation of video-oculography, micro-computed tomography, and histopathology in Pendrin-null mice 2023.07; 183;
11. Watanabe H, Ito T, Aoki N, Bai J, Honda K, Kawashima Y, Fujikawa T, Ikeda T, Tsutsumi T. Quantitative analysis and correlative evaluation of video-oculography, micro-computed tomography, and histopathology in Pendrin-null mice. *Neurobiology of disease*. 2023.07; 183; 106194
12. Quantitative analysis and correlative evaluation of video-oculography, micro-computed tomography, and histopathology in Pendrin-null mice. 2023.07; 183; 106194

13. Bai Jing, Ito Taku, Fujikawa Taro, Honda Keiji, Kawashima Yoshiyuki, Watanabe Hiroki, Kurata Natsuko, Tsutsumi Takeshi. Three-dimensionally visualized ossification and mineralization process of the otic capsule in a postnatal developmental mouse LARYNGOSCOPE INVESTIGATIVE OTOLARYNGOLOGY. 2023.06; 8(4); 1036-1043
14. 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
1. Jing Bai, Taku Ito, Taro Fujikawa, Keiji Honda, Yoshiyuki Kawashima, Hiroki Watanabe, Natsuko Kurata, Takeshi Tsutsumi. Three-dimensionally visualized ossification and mineralization process of the otic capsule in a postnatal developmental mouse Laryngoscope Investigative Otolaryngology. 2023; 8(4); 1036-1043

[Conference Activities & Talks]

1. Tsutsumi Takeshi, Aoki Natsuki, Yamazaki Ayame, Takeda Takamori, Honda Keiji. ヘッドマウントディスプレイをベースとした VOG 装置の開発 (Development of head mounted display-based VOG device). Equilibrium Research 2023.10.01
2. Takeshi Tsutsumi. Short-term outcome of 98 external auditory canal cancer treated at a single institution . 7th World Congress of the International Federation of Head and Neck Oncologic Societies (IFHNOS) 2023.06.23

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]

1. Kawai H, Matsubayashi T, Yokota T, Sanjo N. Serial changes in regional cerebral blood flow in Gerstmann-Sträussler-Scheinker disease caused by a Pro-to-Leu mutation at codon 105 in the prion protein gene. *Prion*. 2023.12; 17(1); 138-140
2. Hirata K, Matsuoka K, Tagai K, Endo H, Tatebe H, Ono M, Kokubo N, Oyama A, Shinotoh H, Takahata K, Obata T, Dehghani M, Near J, Kawamura K, Zhang MR, Shimada H, Yokota T, Tokuda T, Higuchi M, Takado Y. Altered Brain Energy Metabolism Related to Astrocytes in Alzheimer’s Disease. *Annals of neurology*. 2023.09;
3. Noda K, Hattori Y, Hori M, Nakaoku Y, Tanaka A, Yoshimoto T, Nishimura K, Yokota T, Harada-Shiba M, Ihara M. Amplified Risk of Intracranial Artery Stenosis/Occlusion Associated With RNF213 p.R4810K in Familial Hypercholesterolemia. *JACC. Asia*. 2023.08; 3(4); 625-633
4. Iida S, Kanouchi T, Hattori T, Kanai K, Nakazato T, Hattori N, Yokota T. Verification of propagation hypothesis in patients with sporadic hand onset amyotrophic lateral sclerosis. *Acta neurologica Belgica*. 2023.08; 123(4); 1511-1517
5. Yuhei Takahashi, Kiyoshi Kakuta, Yukichi Namioka, Ayumi Igarashi, Taiichi Sakamoto, Rintaro Iwata Hara, Kazuki Sato, Takeshi Wada. Synthesis of P-Modified DNA from Boranophosphate DNA as a Precursor via Acyl Phosphite Intermediates *The Journal of Organic Chemistry*. 2023.07; 88(15); 10617-10631
6. Motoki Miura, Fumika Sakaue, Hirokazu Matsuno, Kento Morita, Akiko Yoshida, Rintaro Iwata Hara, Ren Nishimura, Yurika Nishida, Mariko Yokogawa, Masanori Osawa, Takanori Yokota. TDP - 43 N - terminal domain dimerisation or spatial separation by RNA binding decreases its propensity to aggregate *FEBS Letters*. 2023.06; 597(12); 1667-1676
7. Nakamura R, Tohnai G, Nakatochi M, Atsuta N, Watanabe H, Ito D, Katsuno M, Hirakawa A, Izumi Y, Morita M, Hirayama T, Kano O, Kanai K, Hattori N, Taniguchi A, Suzuki N, Aoki M, Iwata I, Yabe I, Shibuya K, Kuwabara S, Oda M, Hashimoto R, Aiba I, Ishihara T, Onodera O, Yamashita T, Abe K, Mizoguchi K, Shimizu T, Ikeda Y, Yokota T, Hasegawa K, Tanaka F, Nakashima K, Kaji R, Niwa JI, Doyu M, Terao C, Ikegawa S, Fujimori K, Nakamura S, Ozawa F, Morimoto S, Onodera K, Ito T, Okada Y, Okano H, Sobue G, Japanese Consortium for Amyotrophic Lateral Sclerosis research (JaCALS) study group. Genetic factors affecting survival in Japanese patients with sporadic amyotrophic lateral sclerosis:

- a genome-wide association study and verification in iPSC-derived motor neurons from patients. *Journal of neurology, neurosurgery, and psychiatry*. 2023.05; 94(10); 816-824
8. Kazuki Sato, Kazumasa Muramoto, Tomoya Hagio, Rintaro I. Hara, Takeshi Wada. Solid-Phase Synthesis of Glycosyl Phosphate Repeating Units via Glycosyl Boranophosphates as Stable Intermediates *Organic Letters*. 2023.05; 25(21); 3927-3931
 9. Mitsui J, Matsukawa T, Uemura Y, Kawahara T, Chikada A, Porto KJL, Naruse H, Tanaka M, Ishiura H, Toda T, Kuzuyama H, Hirano M, Wada I, Ga T, Moritoyo T, Takahashi Y, Mizusawa H, Ishikawa K, Yokota T, Kuwabara S, Sawamoto N, Takahashi R, Abe K, Ishihara T, Onodera O, Matsuse D, Yamasaki R, Kira JI, Katsuno M, Hanajima R, Ogata K, Takashima H, Matsushima M, Yabe I, Sasaki H, Tsuji S. High-dose ubiquinol supplementation in multiple-system atrophy: a multicentre, randomised, double-blinded, placebo-controlled phase 2 trial. *EClinicalMedicine*. 2023.05; 59; 101920
 10. Yanagidaira M, Yoshioka K, Nagata T, Nakao S, Miyata K, Yokota T. Effects of combinations of gapmer antisense oligonucleotides on the target reduction. *Molecular biology reports*. 2023.04; 50(4); 3539-3546
 11. Li F, Ichinose K, Ishibashi S, Yamamoto S, Iwasawa E, Suzuki M, Yoshida-Tanaka K, Yoshioka K, Nagata T, Hirabayashi H, Mogushi K, Yokota T. Preferential delivery of lipid-ligand conjugated DNA/RNA heteroduplex oligonucleotide to ischemic brain in hyperacute stage. *Molecular therapy : the journal of the American Society of Gene Therapy*. 2023.04; 31(4); 1106-1122
 12. Honda T, Matsumura K, Hashimoto Y, Yokota T, Mizusawa H, Nagao S, Ishikawa K. Temporal Relationship between Impairment of Cerebellar Motor Learning and Deterioration of Ataxia in Patients with Cerebellar Degeneration. *Cerebellum (London, England)*. 2023.04;
 13. Ohara M, Hirata K, Hallett M, Matsubayashi T, Chen Q, Kina S, Shimano K, Hirakawa A, Yokota T, Hattori T. Long-term levodopa ameliorates sequence effect in simple, but not complex walking in early Parkinson's disease patients. *Parkinsonism & related disorders*. 2023.03; 108; 105322
 14. Jia C, Lei Mon SS, Yang Y, Katsuyama M, Yoshida-Tanaka K, Nagata T, Yoshioka K, Yokota T. Change of intracellular calcium level causes acute neurotoxicity by antisense oligonucleotides via CSF route. *Molecular therapy. Nucleic acids*. 2023.03; 31; 182-196
 15. Miyashita A, Kobayashi M, Yokota T, Zochodne DW. Diabetic Polyneuropathy: New Strategies to Target Sensory Neurons in Dorsal Root Ganglia. *International journal of molecular sciences*. 2023.03; 24(6);
 16. Tomomi Shiraishi, Kazuki Sato, Rintaro Iwata Hara, Takeshi Wada. Properties of artificial cationic oligodiaminosaccharides and oligopeptides that bind to A-type oligonucleotide duplexes *Nucleosides, Nucleotides & Nucleic Acids*. 2023.02; 619-636
 17. Hattori T, Ohara M, Yuasa T, Azuma R, Chen Q, Hanazawa R, Hirakawa A, Orimo S, Yokota T. Correlation of callosal angle at the splenium with gait and cognition in normal pressure hydrocephalus. *Journal of neurosurgery*. 2023.01; 139(2); 1-11
 18. Amano A, Sanjo N, Araki W, Anraku Y, Nakakido M, Matsubara E, Tomiyama T, Nagata T, Tsumoto K, Kataoka K, Yokota T. Peripheral administration of nanomicelle-encapsulated anti-A β oligomer fragment antibody reduces various toxic A β species in the brain. *Journal of nanobiotechnology*. 2023.01; 21(1); 36
 19. Aiba I, Hayashi Y, Shimohata T, Yoshida M, Saito Y, Wakabayashi K, Komori T, Hasegawa M, Ikeuchi T, Tokumaru AM, Sakurai K, Murayama S, Hasegawa K, Uchihara T, Toyoshima Y, Saito Y, Yabe I, Tanikawa S, Sugaya K, Hayashi K, Sano T, Takao M, Sakai M, Fujimura H, Takigawa H, Adachi T, Hanajima R, Yokota O, Miki T, Iwasaki Y, Kobayashi M, Arai N, Ohkubo T, Yokota T, Mori K, Ito M, Ishida C, Tanaka M, Idezuka J, Kanazawa M, Aoki K, Aoki M, Hasegawa T, Watanabe H, Hashizume A, Niwa H, Yasui K, Ito K, Washimi Y, Mukai E, Kubota A, Toda T, Nakashima K, J-VAC study group. Clinical course of pathologically confirmed corticobasal degeneration and corticobasal syndrome. *Brain communications*. 2023; 5(6); fcad296
 20. Takaaki Koide, Shintaro Mandai*, Reo Kitaoka, Hisazumi Matsuki, Motoko Chiga, Kouhei Yamamoto, Kotaro Yoshioka, Yohsuke Yagi, Soichiro Suzuki, Tamami Fujiki, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Tatemitsu Rai, Takanori Yokota, Shinichi Uchida. Circulating Extracellular Vesicle-Propagated microRNA Signature as a Vascular Calcification Factor in Chronic Kidney Disease. *Circ Res*. 2023.01;

[Conference Activities & Talks]

1. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. Clinicopathological analysis in prion disease with PRNP P105L mutation(タイトル和訳中). Dementia Japan 2023.10.01
2. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. PRNP 遺伝子に P105L 変異を認めるプリオン病の臨床病理学的解析 (Clinicopathological analysis in prion disease with PRNP P105L mutation). Dementia Japan 2023.10.01
3. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. PRNP 遺伝子に P105L 変異を認めるプリオン病の臨床病理学的解析 (Clinicopathological analysis in prion disease with PRNP P105L mutation). Dementia Japan 2023.10.01
4. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. PRNP 遺伝子に P105L 変異を認めるプリオン病の臨床病理学的解析 (Clinicopathological analysis in prion disease with PRNP P105L mutation). Dementia Japan 2023.10.01
5. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. PRNP 遺伝子に P105L 変異を認めるプリオン病の臨床病理学的解析 (Clinicopathological analysis in prion disease with PRNP P105L mutation). Dementia Japan 2023.10.01
6. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. PRNP 遺伝子に P105L 変異を認めるプリオン病の臨床病理学的解析 (Clinicopathological analysis in prion disease with PRNP P105L mutation). Dementia Japan 2023.10.01
7. Matsubayashi Taiki, Ae Ryusuke, Kosami Koki, Tsukamoto Tadashi, Satoh Katsuya, Hamaguchi Tsuyoshi, Furukawa Fumiko, Takao Masaki, Kitamoto Tetsuyuki, Nakamura Yosikazu, Mizusawa Hidehiro, Yamada Masahito, Yokota Takanori, Sanjo Nobuo. PRNP 遺伝子に P105L 変異を認めるプリオン病の臨床病理学的解析 (Clinicopathological analysis in prion disease with PRNP P105L mutation). Dementia Japan 2023.10.01
8. Ishihara Tomohiko, Ikenaka Kensuke, Takahashi Yuji, Yokota Takanori, Ishikawa Kinya, Hirano Makito, Nagai Yoshitaka, Onodera Osamu. AJA030-002 ポリグルタミン病に対するタンパク質凝集阻害剤の第 II 相試験 (AJA030-002:Phase II Study of a Protein Aggregation Inhibitor for Polyglutamine Disease). 臨床神経学 2023.09.01
9. Amano Eiichiro, Raveney Ben, Yokota Takanori, Yamamura Takashi, Oki Shinji. NRP-1+Th 細胞は CD11c+B 細胞を増殖させ脳反応性自己抗体の強力な供給源となる (NRP-1+Th cells expand CD11c+B cells that are potent source of brain reactive autoantibodies). 臨床神経学 2023.09.01
10. Yanagidaira Mitsugu, Nagata Testuya, Hasegawa Juri, Ishii Satoshi, Ebihara Satoe, Yokota Takanori. PMO/RNA ヘテロ 2 本鎖を用いた CNS におけるスプライス制御の新規技術 (Novel technology for splice modulation in CNS by PMO/RNA heteroduplex). 臨床神経学 2023.09.01
11. Iwase Ryo, Ishiguro Taro, Hasegawa Juri, Iwata Hara Rintaro, Nagata Tetsuya, Yokota Takanori. RNA-DNA ヘテロ G4 構造誘導 ASO を用いた DMD エクソンスキッピングに対する新戦略 (A new strategy for DMD exon skipping with RNA-DNA hetero-G4 structure inducing ASOs). 臨床神経学 2023.09.01
12. Kuroda Takayuki, Yoshioka Kotaro, Su Su Lei Mon , Sakamoto Toshihiro, Katsuyama Maho, Yoshida-Tanaka Kie, Iwata-Hara Rintaro, Yamaguchi Takao, Nagata Tetsuya, Obika Satoshi, Yokota Takanori. アンチセンスオリゴヌクレオチドの神経毒性を克服するための化学的改良の開発 (Development of chemical modifications to overcome neurotoxicity of antisense oligonucleotide). 臨床神経学 2023.09.01

13. Yokote Hiroaki, Miyazaki Yusei, Toru Shuta, Nishida Yoichiro, Hattori Takaaki, Niino Masaaki, Sanjo Nobuo, Yokota Takanori. 日本人多発性硬化症患者の脳容積減少を抑制する有効性の高い治療法 (High-efficacy therapy reduces brain volume loss in Japanese patients with multiple sclerosis). 臨床神経学 2023.09.01
14. Miura Motoki, Sakaue Fumika, Matsuno Hirokazu, Morita Kento, Hara Rintaro, Yokota Takanori. 核酸結合による TDP-43 の空間分布を介した溶解性の制御 (Regulation of TDP-43 solubility via its spatial organization by nucleic acid binding). 臨床神経学 2023.09.01
15. Ono Daisuke, Kawai Honami, Kuwahara Hiroya, Yokota Takanori. 機械学習アプリケーションによる腓腹神経生検の自動 whole slide 解析 (Automated Whole Slide Analysis of Sural Nerve Biopsy by Machine Learning Application). 臨床神経学 2023.09.01
16. Hattori Takaaki, Kitsuka Narumi, Sanjo Nobuo, Oyama Jun, Yoshii Toshitaka, Okawa Atsushi, Yokota Takanori. 硬膜閉鎖後の表在性シデロースにおける前側頭葉の逆説的な MRI 増悪 (Paradoxical MRI exacerbation in anterior temporal lobe in superficial siderosis after dural closure). 臨床神経学 2023.09.01
17. Yokota Takanori. 神経疾患に関する遺伝子治療と細胞療法 神経疾患を標的とした DNA/RNA ヘテロ 2 本鎖オリゴヌクレオチド (Gene and cell therapy for neurological diseases DNA/RNA heteroduplex oligonucleotides for neurological diseases). 臨床神経学 2023.09.01
18. 常 詩晨, 田中 敏博, 稲澤 譲治, 水澤 英洋, 三條 伸夫, 横田 隆徳, 石川 欽也. 神経疾患の遺伝的リスク評価. 臨床神経学 2023.09.01
19. Ichinose Keiko, Li Fuying, Ishibashi Satoru, Iwasawa Eri, Suzuki Motohiro, Yoshida Kie, Yoshioka Kotaro, Nagata Tetsuya, Mogushi Kaoru, Yokota Takanori. 脂質結合 DNA/RNA ヘテロ 2 本鎖オリゴヌクレオチドの急性虚血脳への効果的な送達 (Effective delivery of lipid conjugated DNA/RNA heteroduplex oligonucleotide to acute ischemic brain). 臨床神経学 2023.09.01
20. Miura Motoki, Sakaue Fumika, Matsuno Hirokazu, Morita Kento, Hara Rintaro, Yokota Takanori. 核酸結合による TDP-43 の空間分布を介した溶解性の制御 (Regulation of TDP-43 solubility via its spatial organization by nucleic acid binding). 臨床神経学 2023.09.01
21. Yokote Hiroaki, Miyazaki Yusei, Toru Shuta, Nishida Yoichiro, Hattori Takaaki, Niino Masaaki, Sanjo Nobuo, Yokota Takanori. 日本人多発性硬化症患者の脳容積減少を抑制する有効性の高い治療法 (High-efficacy therapy reduces brain volume loss in Japanese patients with multiple sclerosis). 臨床神経学 2023.09.01
22. Motoki Miura. Nucleic acid binding regulates TDP-43 solubility via its spacial arrangement. 2023.09 Malaysia
23. Motoki Miura. Regulation of TDP-43 solubility via its spatial organization by nucleic acid binding.. 2023.06.01
1. Keisuke Tanaka, Hikari Kanai, Hiroya Kuwahara, Kota Yoshifuji, keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Toshikage Nagao, Chizuko Sakashita, Takehiko Mori, Masahide Yamamoto. Diffuse large B-cell lymphoma developed under the treatment of fingolimod. The Japanese Society for Lymphoreticular Tissue Reserch 2023.06.24

[Patents]

1. CARRIER FOR USE IN DELIVERING DRUG, CONJUGATE, COMPOSITION COMPRISING SAME, AND METHOD FOR ADMINISTRATING SAME, Patent Number : 2931056
2. CARRIER FOR USE IN DELIVERING DRUG, CONJUGATE, COMPOSITION COMPRISING SAME, AND METHOD FOR ADMINISTRATING SAME, Patent Number : 2931056
3. ISCHEMIC-LESION-SITE-SPECIFIC GENE THERAPY, Patent Number : 11674141
4. ISCHEMIC-LESION-SITE-SPECIFIC GENE THERAPY, Patent Number : 11674141
5. NUCLEIC ACID COMPLEX, Patent Number : 11597928
6. NUCLEIC ACID WITH REDUCED TOXICITY, Patent Number : US11851654
7. NUCLEIC ACID WITH REDUCED TOXICITY, Patent Number : US11851654

8. NUCLEIC ACID WITH REDUCED TOXICITY, Patent Number : 特許第 7333079 号
9. NUCLEIC ACID WITH REDUCED TOXICITY, Patent Number : 特許第 7333079 号
10. ISCHEMIC-LESION-SITE-SPECIFIC GENE THERAPY, Patent Number : EP 3760209

Psychiatry and Behavioral Sciences

Professor, Chair

Hidehiko TAKAHASHI

Professor (forensic psychiatry)

Takayuki OKADA

Associate Professor

Genichi SUGIHARA

Associate Professor (liaison psychiatry and psycho-oncology)

Takashi TAKEUCHI

Associate Professor (tenure track)

Hiroki SHIWAKU

Associate Professor (specially appointed; joint research: cyber psychiatry)

Daisuke JITOKU

Junior Associate Professor

Junya FUJINO, Shunsuke TAKAGI

Junior Associate Professor (carrier up)

Miho MIYAJIMA

Assistant Professor

Takehiro TAMURA, Hironobu NAKAMURA, Yoshionori SASAKI, Yuuki SHIDEI

Assistant Professor (specially appointed; joint research: cyber psychiatry)

Nanase KOBAYASHI

Assistant Professor (project)

Takehisa HANDA

Senior Resident

Reina MORITA, Haruka NISHIOKA, Keita KANAZAWA

Resident

Koki ONDA, Kosei KAINUMA, Yosuke MATSUNO, Kotoe ISOBE, Mariko IMADA, Sakura MURATA, Tomohiro MORI, Yukari NARITA, Kyoshiro ISHIDA

Clinical Psychologist

Kazunori MURAKAMI, Ryoko MOCHIMATSU, Ayako KUSANO, Aki HATTORI, Sayuri YAMAZAKI

Psychiatric Social Worker

Yoshifumi KANEKO, Akinori MONTA, Mai KUDO, Masae NAKANISHI

Occupational Therapist

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Graduate Students (Doctoral Course)

Masaki OHYA, Hironobu NAKAMURA, Marino KAWAMOTO, Kazushige HIRAKAKAWA, Takao KANAI, Yuuki SHIDEI, Mariko SUNAHARA, Kouichi TABATA, Takashi MARUO, Kentaro NAGAO, Shiori NOGUCHI, Yoritsugu IIDA, Chenyu QIAN, Masaaki SHIMIZU, Masanori ICHIIHASHI, Yukiko MOTOKAWA, Saori TOYODA, Yukiaki KOIZUMI, Ryuta GOSHIMA, Yusei YAMAMOTO, Mao OTAKE, Mitsuhito UEDA, Shuhei ABE, Ikuko ARAKAWA, Takehiro IBARAKI, Marika OKAMURA, Wataru NAKAGAWA, Saiko KUBO, Sayaka OZAKA, Hiroyuki TANAKA, Yukari BANDO, Hitomi MATSUI

(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 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.

5) Research on cyber-psychiatry

Research on behavioral addictions such as gaming disorder and smartphone/internet dependency is being conducted in collaboration with KDDI Corporation and KDDI Research, Inc. For patients with behavioral addictions like gaming disorder and smartphone/internet dependency, we are conducting behavioral analysis based on log apps, comparing behavioral logs with medical information to advance the understanding of the pathophysiology of behavioral addictions. Furthermore, based on these insights, we are advancing clinical research aimed at the practical application as diagnostic and treatment support apps for patients with gaming disorder.

(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 team consists of a physician and two nurses, as well as a psychosocial worker or clinical psychologist. 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. Kawamoto M, Takagishi H, Ishihara T, Takagi S, Kanai R, Sugihara G, Takahashi H, Matsuda T. Hippocampal volume mediates the relationship of parental rejection in childhood with social cognition in healthy adults. *Scientific reports*. 2023.11; 13(1); 19167
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9. Oya M, Matsuoka K, Kubota M, Fujino J, Tei S, Takahata K, Tagai K, Yamamoto Y, Shimada H, Seki C, Itahashi T, Aoki YY, Ohta H, Hashimoto RI, Sugihara G, Obata T, Zhang MR, Suhara T, Nakamura M, Kato N, Takado Y, Takahashi H, Higuchi M. Increased glutamate and glutamine levels and their relationship to astrocytes and dopaminergic transmissions in the brains of adults with autism. *Scientific reports*. 2023.07; 13(1); 11655
10. Kota Kanda, Shisei Tei, Hidehiko Takahashi, Junya Fujino. Neural basis underlying the sense of coherence in medical professionals revealed by the fractional amplitude of low-frequency fluctuations. *PLoS One*. 2023.06; 18(6); e0288042

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1. Shunsuke Takagi. Sports and epilepsy: A comprehensive review in the Japanese context 2023.11;
1. Takashi Takeuchi. Liaison psychiatry in the perinatal period Japanese Journal of Psychiatric Treatment. 2023.12; 38(12); 1393-1397
2. Takayuki Okada. Psychiatric expert testimony of victims of rape and sexual assault- four key points for effective forensic psychiatry evaluation Japanese Journal of Forensic Mental Health. 2023.03; 18(1); 61-64
3. Takashi Takeuchi, Keiko Yoshida. Basic knowledge of postpartum depression Pain Clinic. 2023.02; 44(2); 162-168
4. Takashi Takeuchi, Eisuke Matsushima. Depression in liaison psychiatry -recent trends- Japanese Journal of Clinical Psychiatry. 2023.01; 52(1); 97-102
5. Takayuki Okada. Methodology of legal comprehension of crime mechanism for judgment of criminal responsibility- Beyond the eight steps structure model. The hanreijiho. 2023.01; (2537); 74-92

[Conference Activities & Talks]

1. Nanase Kobayashi, Daisuke Jitoku, Toshitaka Hamamura, Akio Yoneyama, Masaru Honjo, Genichi Sugihara, Hidehiko Takahashi.. Difficulty in switching attention and its neural basis in problematic smartphone use; validation using a smartphone log application and brain MRI.. International Behavioral Neuroscience Society 2023 2023.06.27 Niagara
2. Kiwamu Matsuoka, Masaki Oya, Manabu Kubota, Junya Fujino, Shisei Tei, Keisuke Takahata, Kenji Tagai, Yasuharu Yamamoto, Hitoshi Shimada, Chie Seki, Takashi Itahashi, Yuta Y. Aoki, Haruhisa Ohta, Ryu-ichiro Hashimoto, Genichi Sugihara, Takayuki Obata, Ming-Rong Zhang, Tetsuya Suhara, Motoaki Nakamura, Nobumasa Kato, Yuhei Takado, Hidehiko Takahashi, Makoto Higuchi. Elevated glutamine levels and activation of astrocytes involved in excessive excitatory neurotransmissions in autism spectrum disorder. ISMRM & ISMRT Annual Meeting & Exhibition 2023.06
3. Furusawa S, Hamamura T, Yoneyama A, Honjo M, Kobayashi N, Jitoku D, Uchida M.. Visualization Methods to Support the Medical Treatment of the Problematic Use of Smartphones.. The 7th International Conference on Medical and Health Informatics 2023.05.12 Kyoto
4. Yoshinori Sasaki. Current status of juvenile delinquency and Treatment of juvenile delinquents in Japan. The Program for International Promotion of Japan 's Healthcare Technologies and Services in 2022 2023.02.14 Manila, Philippines

NCNP Brain Physiology and Pathology

1. Staffs

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Tadafumi HASHIMOTO
Collaborative Professor	Noritaka ICHINOHE
Collaborative Professor	Yoshitsugu AOKI
Collaborative Associate Professor	Yuichi YAMASHITA
Collaborative Associate Professor	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. This year, we found that DSCAM, which is associated with Down syndrome psychiatric symptoms, schizophrenia, and autism spectrum disorders, promotes the retrieval of excess glutamate at the synaptic cleft for proper synaptic development and function (published on Feb 1st, Nat Commun 15(1), 458).

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. *APOE ϵ 4* is a strong genetic risk factor for the development of Alzheimer's disease. This year, we used a co-culture system between primary cultured neurons and human iPS-derived astrocytes, and found that the spine density of neurons

co-cultured with astrocyte carrying *APOEε4* was significantly reduced compared to that of astrocytes carrying *APOEε3*, suggesting that the novel deleterious effect of human *APOEε4* astrocytes on synaptic architecture (Watanabe et al, 2023, Stem Cell Reports).

3) Autism research using a primate model marmoset

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, NCNP)

Autism is a developmental disorder characterized by social impairments and rigidity. While research on autism has been conducted using rodent models, no treatment has been developed yet. The New World monkey, the marmoset, is evolutionarily closer to humans and is expected to be suitable for autism research due to its high level of sociality and well-developed prefrontal cortex. We have developed an autism model in New World marmosets through maternal administration of valproic acid and are working on elucidating the pathophysiology of autism and developing treatments. In particular, we are analyzing the autism model marmosets from multiple perspectives using molecular and cellular biological methods, systems neuroscience approaches (electrophysiology, structural MRI, etc.), and behavioral methods. This fiscal year, we have established a database of structural MRI and functional MRI essential for elucidating the brain pathology of marmosets (Hata et al., 2023, Scientific Data; Okuno et al., 2023, Front NeuroImaging), and conducted studies on the anatomical connections of the marmoset's prefrontal cortex (Watakabe et al., 2023, Neuron). A comparison of the transcriptome results of human autism with those of marmosets administered maternal valproic acid revealed that one subtype, accounting for a quarter of human autism, is identical to the valproic acid marmoset. This suggests that the valproic acid marmoset is expected to make a significant contribution to the elucidation of the pathophysiology of human autism and the development of biomarkers in the future.

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)

Duchenne Muscular Dystrophy (DMD) is an intractable disease caused by mutations in the DMD gene. Our department has successfully developed "Viltolarsen," an exon 53 skipping drug using antisense oligonucleotides to treat DMD. This drug received conditional approval in March 2020 and can potentially treat 8% of DMD patients. Additionally, we are developing "Brogidirsen," the world's first antisense

oligonucleotide (ASO) drug, potentially treating 6% of DMD patients amenable to exon 44 skipping. We are preparing for Phase 2 global trials for this drug, published in *Mol Ther Nucleic Acids* 2023.

We recently reported that administering an mRNA drug that replenishes dystrophin in mice was found to normalize the E/I balance in the amygdala, which could potentially alleviate symptoms in 30% of DMD patients with autism spectrum disorders (*Prog Neurobiol.* 2022;216:102288).

We previously faced difficulties in predicting the optimal sequence design of therapeutic ASO, which required significant time and effort. To address this issue, we have developed a machine learning model that predicts exon skipping efficiency. We have released this model worldwide through eSkip-Finder (*Nucleic Acids Res.* 2021;49:W193-W198.), enabling us to efficiently design optimal ASO sequences for various neuromuscular disorders, including DMD.

Moreover, we have developed 3D tissue models (organoids) of muscle and brain using urinary-derived cells obtained from DMD patients (*Sci Rep.* 2024;14:2329). These models replicate the disease pathophysiology, allowing us to test the efficacy of novel therapies, such as exon skipping.

These research achievements are expected to serve as a crucial foundation for stratified medicine to overcome neuromuscular disorders.

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 2023, we investigated the interplay between stochasticity in neural networks, the acquisition of hierarchical representations, and the behavioral and cognitive flexibility through neuro-robotic simulations that emulate predictive information processing. This study elucidated the underlying mechanisms contributing to neuro-diversity in cognitive development (Soda et al., *Front Psych*, 2023). Furthermore, the hypothesis that delayed predictive signals in information processing may lead to the aberrant sense of agency in schizophrenia was tested by

combining simulations with actual behavioral data obtained from patients with schizophrenia (Okimura et al., npj Schizophrenia, 2023).

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 functional subset of helper T cells. After demonstrating that Eomes⁺ Th cells, a neurotoxic subset of novel functional helper T cell accumulated in the CNS of mouse models of neurodegenerative diseases, induce granzyme B-dependent neuronal cell death, we investigated the behavior of Eomes⁺ Th cells in patients of amyotrophic lateral sclerosis (ALS) and Alzheimer's diseases (AD). We revealed that frequency of Eomes⁺ Th cells in the peripheral blood of patients (Eomes frequency) is significantly increased in the patients of ALS and AD. In addition, we demonstrated that Eomes frequency is inversely correlated with HDS-R score of AD patients and a notable increase of Eomes frequency was observed in rapidly-progressing ALS patient within 5 year after disease onset (Kanazawa et al. Ann Neurol in press) . As significant pathogenic correlation between Eomes⁺ Th cells and neurodegenerative diseases are confirmed, we are now trying to draw the molecular landscape of the immune-mediated neurodegeneration and the pathogenesis of neurodegenerative 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]

1. Tran DM, Yoshioka N, Bizen N, Mori-Ochiai Y, Yano M, Yanai S, Hasegawa J, Miyashita S, Hoshino M, Sasaki J, Sasaki T, Takebayashi H. Attenuated cerebellar phenotypes in Inpp4a truncation mutants with preserved phosphatase activity. Dis Model Mech. 2023 Jul 1;16(7): dmm050169
2. Watanabe H, Murakami R, Tsumagari K, Morimoto S, Hashimoto T, Imaizumi K, Sonn I,

- Yamada K, Saito Y, Murayama S, Iwatsubo T, Okuno H. Astrocytic *APOE4* genotype-mediated negative impacts on synaptic architecture in human pluripotent stem cell mode. *Stem Cell Rep.* 2023 Sep 12; 18(9): 1854-1869.
3. Okuno, T., Ichinohe N., & Woodward, A. (2024). A reappraisal of the default mode and frontoparietal networks in the common marmoset brain. *Frontiers in neuroimaging*, 2, 1345643. <https://doi.org/10.3389/fnimg.2023.1345643>
 4. Hata, J., Nakae, K., Tsukada, H., Woodward, A., Haga, Y., Iida, M., Uematsu, A., Seki, F., Ichinohe N., Gong, R., Kaneko, T., Yoshimaru, D., Watakabe, A., Abe, H., Tani, T., Hamda, H. T., Gutierrez, C. E., Skibbe, H., Maeda, M., Papazian, F., ... Okano, H. (2023). Multi-modal brain magnetic resonance imaging database covering marmosets with a wide age range. *Scientific data*, 10(1), 221. <https://doi.org/10.1038/s41597-023-02121-2>
 5. Watakabe, A., Skibbe, H., Nakae, K., Abe, H., Ichinohe N., Rachmadi, M. F., Wang, J., Takaji, M., Mizukami, H., Woodward, A., Gong, R., Hata, J., Van Essen, D. C., Okano, H., Ishii, S., & Yamamori, T. (2023). Local and long-distance organization of prefrontal cortex circuits in the marmoset brain. *Neuron*, 111(14), 2258–2273.e10. <https://doi.org/10.1016/j.neuron.2023.04.028>
 6. Yamauchi N, Tamai K, Kimura I, Naito A, Tokuda N, Ashida Y, Motohashi N, Aoki Y, Yamada T. High-intensity interval training in the form of isometric contraction improves fatigue resistance in dystrophin-deficient muscle. *J Physiol.* 2023 Jul;601(14):2917-2933.
 7. Watanabe N, Tone Y, Nagata T, Masuda S, Saito T, Motohashi N, Takagaki K, Aoki Y, Takeda S. Exon 44 skipping in Duchenne muscular dystrophy: NS-089/NCNP-02, a dual-targeting antisense oligonucleotide. *Mol Ther Nucleic Acids.* 2023 Sep 20;34:102034.
 8. Motohashi N, Minegishi K, Aoki Y. Inherited myogenic abilities in muscle precursor cells defined by the mitochondrial complex I-encoding protein. *Cell Death Dis.* 2023 Oct 19;14(10):689.
 9. Zhu A, Chiba S, Shimizu Y, Kunitake K, Okuno Y, Aoki Y, Yokota T. Ensemble-Learning and Feature Selection Techniques for Enhanced Antisense Oligonucleotide Efficacy Prediction in Exon Skipping. *Pharmaceutics.* 2023 Jun 24;15(7):1808.
 10. Tominari T, Takatoya M, Matsubara T, Matsunobe M, Arai D, Matsumoto C, Hirata M, Yoshinouchi S, Miyaura C, Itoh Y, Komaki H, Takeda S, Aoki Y, Inada M. Establishment of a Triple Quadrupole HPLC-MS Quantitation Method for Dystrophin Protein in Mouse and Human Skeletal Muscle. *Int J Mol Sci.* 2023 Dec 25;25(1):303.
 11. Sakai-Takemura F, Saito F, Nogami K, Maruyama Y, Elhussieny A, Matsumura K, Takeda S, Aoki Y, Miyagoe-Suzuki Y. Antioxidants restore store-operated Ca²⁺ entry in patient-iPSC-derived myotubes with tubular aggregate myopathy-associated Ile484ArgfsX21 STIM1 mutation via upregulation of binding immunoglobulin protein. *FASEB Bioadv.* 2023

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12. Preethy S, Aoki Y, Minegishi K, Iwasaki M, Senthilkumar R, Abraham SJK. Resolution of fibrosis in mdx dystrophic mouse after oral consumption of N-163 strain of *Aureobasidium pullulans* produced β -glucan. *Sci Rep*. 2023 Oct 9;13(1):17008.
13. Takahashi Y, Murata S, Ueki M, Tomita H, Yamashita Y. Interaction between Functional Connectivity and Neural Excitability in Autism: A Novel Framework for Computational Shinji Oki 10.5334/cpsy.93
14. Soda T, Ahmadi A, Tani J, Honda M, Hanakawa T, Yamashita Y. Simulating developmental diversity: Impact of neural stochasticity on atypical flexibility and hierarchy. *Front Psychiatry*. 2023;14:1080668. doi: 10.3389/fpsy.2023.1080668
15. Okimura T, Maeda T, Mimura M, Yamashita Y. Aberrant sense of agency induced by delayed prediction signals in schizophrenia: a computational modeling study. *npj Schizophr*. 2023;9:72. <https://doi.org/10.1038/s41537-023-00403-7>
16. Pathogenic Microglia Orchestrate Neurotoxic Properties of Eomes-Expressing Helper T Cells. Chenyang Zhang, Ben JE Raveney, Fumio Takahashi, Tu-wen Yeh, Hirohiko Hohjoh, Takashi Yamamura, Shinji Oki. *Cells*. 2023 12(6): 868. doi: 10.3390/cells12060868.

[Review Articles • Books]

1. Ishizuka T, Komaki H, Asahina Y, Nakamura H, Motohashi N, Takeshita E, Shimizu-Motohashi Y, Ishiyama A, Yonee C, Maruyama S, Hida E, Aoki Y. Systemic administration of the antisense oligonucleotide NS-089/NCNP-02 for skipping of exon 44 in patients with Duchenne muscular dystrophy: Study protocol for a phase I/II clinical trial. *Neuropsychopharmacol Rep*. 2023 Jun;43(2):277-286.
2. Motohashi N, Minegishi K, Imamura M, Aoki Y. Techniques for Injury, Cell Transplantation, and Histological Analysis in Skeletal Muscle. *Methods Mol Biol*. 2023;2640:193-205.
3. Motohashi N, Minegishi K, Imamura M, Aoki Y. Techniques for Injury, Cell Transplantation, and Histological Analysis in Skeletal Muscle. *Methods Mol Biol*. 2023;2640:193-205.
4. Aoki Y. Mr. Takashi Onaka Memorial Oration: I. Updates on solutions to DMD. *J Stem Cells Regen Med*. 2023 Apr 30;19(1):19-21.

Department of Biodefense Research

Professor Toshiaki Ohteki
Associate Professor Taku Sato(to Sep.30)
Adjunct Lecturer Nobuyuki Onai
Assistant Professor Masashi Kanayama(to Sep. 30)(from Oct.1 Associate Professor)
Graduate Student Megumi Akiyama
Graduate Student Hajime Sato
Graduate Student Joe Tonai
Graduate Student Yuki Yamada
Graduate Student Shun Ishikawa
Graduate Student Yuta Izumi(to March 31)
Graduate Student Mai Nakagawa(to March 31)
Graduate Student Eriko Ohashi(to March 31)
Research Technician Kisho Shiseki(to Oct. 31)
Research Technician Tomiki Hayashi(to March 31)
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. Shinya Abe, Takuma Asahi, Takahiro Hara, Guangwei Cui, Akihiro Shimba, Shizue Tani-Ichi, Kohei Yamada, Kazuko Miyazaki, Hitoshi Miyachi, Satsuki Kitano, Naotoshi Nakamura, Junichi Kikuta, Alexis Vandenbon, Masaki Miyazaki, Ryo Yamada, Toshiaki Ohteki, Masaru Ishii, Veronika Sexl, Takashi Nagasawa, Koichi Ikuta. Hematopoietic cell-derived IL-15 supports NK cell development in scattered and clustered localization within the bone marrow. *Cell Rep.* 2023.09; 42(9); 113127
2. Masashi Kanayama, Yuta Izumi, Megumi Akiyama, Toyoki Hayashi, Koji Atarashi, Axel Roers, Taku Sato, Toshiaki Ohteki. Myeloid-like B cells boost emergency myelopoiesis through IL-10 production during infection. *J Exp Med.* 2023.04; 220(4); e20221221

[Misc]

1. Ziegler-Heitbrock L, Ohteki T, Ginhoux F, Shortman K, Spits H.. Reply to 'Reclassifying plasmacytoid dendritic cells as innate lymphocytes is premature'. *Nat Rev Immunol.* 2023.05; 23(5); 338-339

[Conference Activities & Talks]

1. Masashi Kanayama, Toshiaki Ohteki. A novel B cell subset boosts myelopoiesis during infection. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo
2. Masashi Kanayama, Toshiaki Ohteki. Myeloid-like B cells protect the host by boosting myelopoiesis during infection. JSICR/MMCB 2023 Joint Symposium 2023.05.25 Wakayama
1. Masashi Kanayama, Toshiaki Ohteki. B cell enhances innate immunity during systemic infection. KTCC 2023 2023.06.16 Kyoto University

Pediatrics and Developmental Biology

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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, metabolism, nephrology, rheumatology, neonatology, and allergy. On the other hand, our scientific and academic activities encompass a wide spectrum, from basic to clinical research. By focusing on innovative strategies for clarifying pathogenesis, diagnostic tests, and therapeutic interventions, we are looking at comprehensive resolution of the child's health problems, improving their future.

(2) Research

Our research covers many specialties of pediatric diseases, and the research spans from bench to bedside. Our current main projects are

1. Identification of responsible genes for inborn errors of immunity (IEI).
2. Development of therapeutic 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. Establishment of a patient registry, treatment markers, and a simple genetic test method for 21-hydroxylase deficiency
11. Establishing novel therapeutic approach to congenital hyperinsulinemia
12. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
13. Study of autoimmunity in Opsoclonus Myoclonus Syndrom
14. Development of gene therapy for Ataxia Telangiectasia
15. Study of molecular biology in systemic vascular stenosis
16. Genetic background of leukemia development
17. Study using single cell sequencing analysis in pediatric leukemia
18. Development of novel CAR-NK cell therapy for child cancer
19. Identifying the molecular pathology of metabolic syndrome in 21 hydroxylase deficiency
20. 3D genome structure and molecular mechanism in leukemia
21. Mechanistic insight into activation of super-enhancer in T cell commitment
22. Genetic analysis and development of therapeutic approach for epilepsy syndrome
23. Clarifying immunological profiles of the patients with autoimmune diseases
24. Developing a methodology for the diagnosis of cytokine storm syndrome by exploiting a novel biomarker
25. Development of newborn screening for treatable childhood diseases including spinal muscular atrophy
26. Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease
27. Research in pathophysiology and prognostic predictor of nephritis /nephrotic syndrome
28. 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 Science, 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. We reported that compound heterozygosity for two variants in the RAD50 gene is associated with bone marrow failure and B-cell immunodeficiency (Takagi, Hoshino, Kanakane). Also, we are working with domestic and overseas researchers to analyze the pathogenesis of IEI and to develop therapeutic methods. An international investigation reported that hematopoietic stem cell transplantation could serve as an alternative curative treatment for X-linked agammaglobulinemia (XLA), for which immunoglobulin replacement therapy has been the conventional treatment (Nishimura, Kanegane). 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 (Isoda). 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

A study conducted multi-omics analysis using single-cell technologies to elucidate the origin of Myeloid/NK precursor acute leukemia, revealing it as a distinct independent disease concept. (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))”

“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).

< Clinical research >

“Genetic analysis and development of therapeutic approach for epilepsy syndrome” (collaboration with Showa University)

“Research for rare epilepsy syndrome” (collaboration with Institute of Epilepsy and Neurological Disorders)

“Systematic measurement and functional analysis of autoantibody in immunologic neurological diseases” (collaboration with Tokyo Metropolitan Institute of Medical Science)

“Evaluation of adrenocortical function in the patients with West syndrome treated with ACTH therapy”

“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

Our current research focuses 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. The study will lead to the development of a novel approach to diagnosis and a therapeutic approach to differences in sex development. Another 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 analyzing 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 establishing a registry system of 21-OHD patients to develop a novel approach for preventing comorbidities in adulthood.

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 cow's milk, hen eggs, wheat, tree nuts and so on. 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. One third of the lectures “were performed using an active-learning” style. Nineteen asynchronous lectures for students to review, nine 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 ranked national medical universities in Japan, and achieving cutting edge research is another social responsibility. For students, we provide educational programs to learn primary pediatric care, management of the diseases in every organ during neonatal period childhood, and basic science. For residents, our educational program is mainly focused on producing physician scientists who possess the skills of pediatrics for primary care, of physician specialist and of basic researcher.

(5) Clinical Services & Other Works

● Hematology/Oncology/Immunology Group

Treating children with 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 FY2023, we performed HCT for 8 cases (6 allo-HCT, 2 auto-HCT). In addition, Two HCTs were performed in collaboration with the hematology department.

For a relapsed ALL case, CAR-T was 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 sirolimus 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 2023, the number of inpatients was 103, which consisted of 42 congenital heart disease, 17 pulmonary hypertension, 8 Kawasaki Disease (acute treatment), 11 coronary aneurysm with Kawasaki disease (follow up) 7 arrhythmia, and so on. Cardiac catheterizations were performed in 56 patients and cardiac surgery was performed in 16 patients (open-heart surgery).

● Neurology Group

We provide medical care in a wide range of pediatric neurologic diseases.

In particular, collaborating with the department of neurosurgery, we run an epilepsy center, providing advanced medical care for pediatric patients with intractable epilepsy.

The medical services in our department are long-term video EEG monitoring, high magnetic field MRI/PET, ACTH therapy, ketogenic diet, vagus nerve stimulation and surgical operation, such as focal brain resection and callosotomy. 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 diabetes, such as disorders of growth, pubertal development, Ca/P metabolism. (including skeletal dysplasia), gonadal development and adrenal cortex function. We are especially focusing on providing advanced medical services 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 babies born from mothers with complication.

● Allergy Group

The qualified allergists of the group attend both inpatient and outpatient care units for allergic diseases in the allergy medical center of our university and extramural, affiliated hospitals, where not only the standard medical services following clinical guidelines for allergic diseases are provided, but also highly advanced treatment such as oral immunotherapy for food allergy as well.

(6) Clinical Performances

● Hematology-Oncology/ Immunology Group

Hematology-Oncology/ Immunology Group provides diagnosis, treatment and pathological analysis of hematological malignancies and inborn errors of immunity. We perform hematopoietic stem cell transplantation for refractory diseases. Specifically, we treat the largest number of primary immunodeficiency disease patients in Japan. We participate in multi-center cooperative clinical research to establish both standard and novel therapies for childhood cancers, and also participate in the approval of industry-based clinical trials for drugs (such as anticancer drugs).

● Cardiology 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 intractable 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 screen-

ing in Tokyo. We treat substantial number of CAH (21-OHD) patients and performed couples of clinical studies. We also focus on differences in 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 a 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-Schönlein 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 severe persistent asthma patients.

(7) Publications

[Original Articles]

1. Kunihiko Moriya, Kanako Mitsui-Sekinaka, Yujin Sekinaka, Akifumi Endo, Hirokazu Kanegane, Tomohiro Morio, Kohsuke Imai, Shigeaki Nonoyama. Clinical practice guideline for activated phosphatidyl inositol 3-kinase-delta syndrome in Japan. *Immunol Med.* 2023.12; 46(4); 153-157
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14. Analía Yogi, Kenichi Kashimada. Current and future perspectives on clinical management of classic 21-hydroxylase deficiency. *Endocr J.* 2023.10; 70(10); 945-957
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2. Holm H Uhlig, Claire Booth, Judy Cho, Marla Dubinsky, Anne M Griffiths, Bodo Grimbacher, Sophie Hambleton, Ying Huang, Kelsey Jones, Jochen Kammermeier, Hirokazu Kanegane, Sibylle Koletzko, Daniel Kotlarz, Christoph Klein, Michael J Lenardo, Bernice Lo, Dermot P B McGovern, Ahmet Özen, Lissy de Ridder, Frank Ruemmele, Dror S Shouval, Scott B Snapper, Simon P Travis, Dan Turner, David C Wilson, Aleixo M Muise. Precision medicine in monogenic inflammatory bowel disease: proposed mIBD REPORT standards. *Nat Rev Gastroenterol Hepatol*. 2023.12; 20(12); 810-828
3. Motoi Yamashita, Tomohiro Morio. Germline STAT6 gain-of-function variants cause severe allergy. *J Allergy Clin Immunol*. 2023.05; 151(5); 1252-1254
4. Hirokazu Kanegane, Atsuko Noguchi, Yuki Yamada, Takahiro Yasumi. Rare diseases presenting with hemophagocytic lymphohistiocytosis. *Pediatr Int*. 2023; 65(1); e15516

[Conference Activities & Talks]

1. Kenichi Kashimada. Faculty Presentation: Nuances in the management of different types of CAH. ISPAE 2023 (Indian Society for Pediatric and Adolescent Endocrinology) 2023.11.17 Bengaluru, India
2. Hirokazu Kanegane. Flow cytometry use in Primary Immunodeficiency disorders. Mini-symposium: Inborn errors of immunity 2023.10.27 Bangkok
3. Hirokazu Kanegane. NK cell assays. APSID 2023 2023.10.26 Singapore
4. Hirokazu Kanegane. Diagnosis and Management of Primary Atopic Disorder. APAAACI 2023 2023.10.25 Singapore
5. Morio T. Dissection of the molecular pathogenesis of transcription factor defects using model mice/cell systems. Chang Gung University 2023.10.20 Taipei
6. Masatoshi Takagi, Motoi Yamashita, Takahiro Tomoda, Takeshi Isoda, Makiko Egawa, Masayuki Yoshida, Tsutomu Toki, Ko Kudou, Kiminori Terui, Etsuro Ito, Tomohiro Morio. Transient erythroblastopenia by GATA1 variant in female. . Human Genetics Asia 2023 2023.10.14 Tokyo
7. Eriko Adachi, Ryuichi Nakagawa, Atsumi Tsuji-Hosokawa, Maki Gau, Shizuka Kirino, Analia Yogi, Hikase Nakatani, Tomomi Yamaguchi, Masanori Murakami, Toshihiro Tajima, Tomonobu Hasegawa, Tetsuya Yamada, Tomohiro Morino, Osamu Ohara, Kenichi Kashimada . Development of a clinically applicable one-step PCR-based CYP21A2 analysis using long read sequences. Human Genetics Asia 2023(68th Annual Meeting of Japan Society of Human Genetics/ 14th Asia Pacific Conference on Human Genetics/ 22nd Annual meeting of East Asian Union of human Genetics Societies) 2023.10.14 Tokyo, Japan
8. Manabu Sugie, Yusuke Noguchi, Nobutoshi Nawa, Ayako Kashimada, Kazuyuki Ito, Tsutomu Kondo, Satoshi Kusuda, Chikako Morioka, Tomohiro Morio, Kenichi Kashimada. Implication of Acquiring Oxidative Stress Resistance in Chorioamnionitis Leading to Reduced Risk of Severe Retinopathy of Prematurity. FAOPS 2023; The 22nd Congress of the Federation of Asia and Oceania Perinatal Societies 2023.10.09 Tokyo

9. Ryo Aoki, Chikako Morioka, Kikuko Oku, Shigeru Takishima, Yoshihiro Minosaki, Tomonori Ichikawa. Pressure Evaluation of Nasal Continuous Positive Airway Pressure Cannula Using a New Connector and Respiratory Simulator. FAOPS 2023; The 22nd Congress of the Federation of Asia and Oceania Perinatal Societies 2023.10.09 Tokyo
10. Hirokazu Kanegane. Rare diseases presenting with hemophagocytic lymphohistiocytosis. IEI SCAC 2023 2023.09.15 重慶
11. Satoshi Miyamoto, Daiki Niizato, Takahiro Kamiya, Takeshi Isoda, Masatoshi Takagi, Shohei Azumi, Shinsuke Hirabayashi, Kenichi Sakamoto, Kenji Kishimoto, Takako Miyamura, Katsutsugu Umeda, Masakatsu Yanagimachi, Kaori Kanda, Yasuhiro Ikawa, Kenichiro Watanabe, Tatsuo Ichinohe, Hirotochi Sakaguchi, Tomohiro Morio, Hirokazu Kanegane. Allogenic hematopoietic cell transplantation with alemtuzumab in Asian patients with inborn errors of immunity. ICBMT2023 2023.09.01 Busan
12. Taku Ishii, Keiko Uchida, Susumu Hosokawa, Hidekazu Ishida, Shinichi Takatsuki, Shigetoyo Kogaki, Kei Inai, Hiroyuki Fukushima, Hiroyuki Yamagishi, Shozaburo Doi. Baseline characteristic of pulmonary hypertension patients with congenital heart disease in Japan: Insights from Japanese association of congenital heart disease with pulmonary hypertension registry (JACPHR). PH Korea 2023 with 3rd EASOPH 2023.07.14 Incheon, Korea
13. Kenichi Kashimada, Taninee Sahakitrungruang. 21OHD/CAH (clinical management, molecular biology, neonatal screening) . APPES-TSPE CME MEETING 2023 2023.06.06 Bangkok, THAILAND
14. Kenichi Kashimada. Neonatal screening of 21-hydroxylase deficiency using LC-MS/MS. The 52nd Korean Society of Pediatric Endocrinology 2023.05.19 Soul, Korea
15. Dan Tomomasa, Tasuku Suzuki, Ichiro Takeuchi, Kimitoshi Goto, Shin-Ichiro Hagiwara, Dai Keino, Satoshi Saida, Takashi Ishige, Takahiro Kudo, Masataka Ishimura, Motohiro Kato, Yoji Sasahara, Tomohiro Morio, Katsuhiko Arai, Hirokazu Kanegane. Clinical and genetic characteristics of IL10RA deficiency patients in Japan. The 2nd International Symposium of Clinical Immunology 2023.05.19 神奈川
16. Kaneko S, Shimbo A, Irabu H, Shimizu M, Mori M, Morio T. Clinical significance of serum cytokine profiling for the differentiation of underlying diseases in cytokine storm syndrome. The 2nd International Symposium of Clinical Immunology 2023.05.19 Kanagawa
17. Hirokazu Kanegane. HLH associated with inborn errors of metabolism and familial hemophagocytic lymphohistiocytosis in adult. 2nd National Congress of Inborn Errors of Immunity and National Forum on Pediatric Immunology (IEI China 2023 and FOPI) 2023.04.26 Web 開催
18. Tomohiro Morio. Novel Gene Discovery. Asia Pacific Society for Immunodeficiencies (APSID) 2023.04.23 Hong Kong
19. Mahnaz Jamee, Hirokazu Kanegane. Lung Surgery in STAT3 loss-of-function mutation: is it advisable?. APSID 2023 2023.04.22 香港
20. Shizuka Kirino, Ryuichi Nakagawa, Kei Takasawa, Maki Gau, Atsumi Tsuji-Hosokawa, Liang Zhao, Josephine Bowles, Peter Koopman, Tomohiro Morio, Kenichi Kashimada. Application of Cap analysis of gene expression (CAGE) in genetic analysis of mouse sex differentiation. Ninth International Symposium on the Biology of Vertebrate Sex Determination 2023.04.19 Kailua-Kona, HAWAII
1. Kenichi Kashimada. Preconception Care for Pediatric Patients with Endocrine Diseases. The 56th JSPE Saitama 2023.10.19
2. Eriko Adachi, Ryuichi Nakagawa, Atsumi Tsuji, Maki Gau, Shizuka Kirino, Analia Yogi, Hisae Nakatani, Kei Takasawa, Tomomi Yamaguchi, Tomoki Kosho, Masanori Murakami, Toshihiro Tajima, Tomonobu Hasegawa, Tetsuya Yamada, Tomohiro Morio, Osamu Ohara, Kenichi Kashimada . Development of a clinically applicable one-step PCR-based CYP21A2 analysis using long read sequences, identifying a novel structural abnormality. The 56th JSPE Saitama 2023.10.19 Saitama
3. Kenichi Kashimada, Ichiro Miyata, Takuo Kubota, Jun Mori, Kayo Ozaki, Yosuke Nonaka, Yoshikazu Nakamura, Toya Ohashi, Keiichi Ohzono . Designing early phase II study of anti-FGF2 RNA aptamer in children with achondroplasia. The 56th JSPE Saitama 2023.10.19 Saitama

4. Haruki Yamano, Ryosei Iemura, Shizuka Kirino, Kumi Shuno, Yoko Saitou, Eriko Adachi, Hanako Tajima, Tomohiro Morio, Kenichi Kashimada, Kei Takazawa . A new treatment strategy for congenital hyperinsulinism using lanreotide and continuous glucose monitoring. The 56th JSPE Saitama 2023.10.19 Saitama
5. Shizuka Kirino, Ryuichi Nakagawa, Kei Takazawa, Maki Gau, Kenichi Kashimada . Sequencing of Functionally Active Enhancers Reveals a Novel Transcriptional Regulatory Mechanism in Gonadogenesis . The 56th JSPE Saitama 2023.10.19 Saitama
6. Hideyuki Iwayama, Saiki Sugimoto, Makoto Ono, Sachiko Kitagawa, Kohei Kawahara, Kiyoshi Yamakawa, Ryosuke Miyamoto, Kenichiro Kaneko, Shogo Nakano, Yasushi Fujimoto, Junko Takagi, Akihisa Okumura, Chiyo Shirota, Takahisa Tainaka, Hiroo Uchida, Shigeru Takishima, Kei Takazawa, Misako Nagatsuma, Kenichi Kashimada. Pathogenic bacteria and their antibiotic resistance in uncomplicated acute suppurative thyroiditis in Japan. The 56th JSPE Saitama 2023.10.19 Saitama
7. Yoko Miyoshi, Makiko Tachibana, Naoko Nagai, Tadashi Akao, Masanori Adachi, Junko Ito, Kenichi Kashimada, Junko Kanno, Takeshi Sato, Shizuyo Nagai, Tomohiro Hori, Reiko Horikawa, Koji Muroya, Shuntaro Morikawa, Satoshi Okada, . Questionnaire survey for pediatric endocrinologists regarding nutritional management in childhood and AYA cancer patients. The 56th JSPE Saitama 2023.10.19 Saitama
8. Shogo Akahoshi, Tomohiro Nagata, Masako Tomotsune, Hiroaki Zukeran, Kento Ikegawa, Marie Konno, Yoshihiko Morikawa, Shigeru Takishima, Yukihiro Hasegawa. Feedback Sheet for Type 1 Diabetes Care: Interim Report(Derivation Study) and Invitation to Collaborate(Validation Study) . The 56th JSPE Saitama 2023.10.19 Saitama
9. Kanshi Minamitani, Kentaro Shiga, Asako Tajima, Kenichi Kashimada, Yasusada Kawada, Ken Fukuda, Yumiko Kotani, Miyuki Kitamura, Junnosuke Miura, Ikuko Takahashi, Hanako Tajima, Ichiro Yokota, Shigetaka Sugihara, Toru Kikuchi . Thyroid function in pediatric fulminant type 1 diabetes mellitus. The 56th JSPE Saitama 2023.10.19 Saitama
10. Nozomi Matsuda, Shigeru Takishima, Kaoru Sato, Kenichi Kashimada, Takeshi Hasegawa. A study of central precocious puberty before and after the COVID-19 pandemic.. The 56th JSPE Saitama 2023.10.19 Saitama
11. Ryosei Iemura, Haruki Yamano, Haruka Iwata, Kazuyuki Itou, Manabu Sugie, Chikako Morioka, Kei Takasawa, Kenichi Kashimada, Tomohiro Morio . A neonate with chromosome Xp21 deletion syndrome presenting as severe adrenal insufficiency. The 56th JSPE Saitama 2023.10.19 Saitama
12. Lessons from CAH Newborn Screening by LC-MS/MS assay. Japanese Journal of Neonatal Screening 2023.08.26
13. A novel RNF213 gene de novo variant is involved in systemic vasculopathy. 2023.05.27
14. Allogenic HCT with alemtuzumab in pediatric patients with inborn errors of immunity. 2023.02.12
15. A case of A20 haploinsufficiency diagnosed by recurrent fever and vomiting attacks during follow-up as initial diagnosis of oligoarticular juvenile idiopathic arthritis . 2023.02.12
16. Two cases of late-onset familial hemophagocytic lymphohistiocytosis type 3 presenting with CLIPPERS-like syndrome. 2023.02.12
17. Wiskott-Aldrich syndrome due to chromosomal structural abnormalities. 2023.02.12
18. Investigation of calprotectin suppressive therapy using disease-specific iPS cells in a pathological model of PAMI syndrome. 2023.02.12
19. A case of relapsed AML maintained complete remission by re-transplantation using clofarabine. 2023.02.11
20. Support for adolescent patients and their families by HSC coordinators in fertility preservation. 2023.02.11
21. Comparison of adult and pediatric cases with hyper-IgE syndrome caused by function in STAT3. 2023.02.11

22. Efficacy of JAK inhibitors for patients with gain-of-function mutation of STAT3. 2023.02.11
23. The potential of baricitinib as a treatment for Aicardi-Goutières syndrome type 7. 2023.02.11
24. Hematopoietic cell transplantation for patients with inborn errors of immunity. 2023.02.11

Dermatology

Professor: Naoko OKIYAMA

Associate Professor: Takeshi NAMIKI

Head of medical office: Hana TAKESHITA

Assistant Professor: Tadatsune IIDA, Yuutaro IWAMOTO, Azusa KANAZAWA, Atsushi ODA

Senior Resident: Mituki YAMAMOTO, Hideki SHIMA, Mika FUJIWARA

Resident: Yua HARIMOTO, Ittiki SUGITA, Kenta MORIMOTO

Adjunct Doctor: Yuuki ICHIMURA, Risa KONISHI,

Tomoko FUJIMOTO, Makiko NISHIDA, Minako INAZAWA

Doctoral Student: Taku NAMATAME, Chie UCHIDA

Research fellow : Yu Lei

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 therapies (STAT6 decoy ODN) for severe atopic dermatitis in the clinic.

(3) Publications

[Original Articles]

1. Takahashi Y, Takamiya M, Ichimura Y, Okiyama N, Nishino I, Morimoto N.. [Two cases of anti-nuclear matrix protein 2 antibody-positive dermatomyositis sine dermatitis with severe diffuse subcutaneous edema and dysphagia] Rinsho Shinkeigaku. 2023.11; 63(11); 737-742
2. Ebisawa Yuka(Department of General Medicine and Primary Care, Faculty of Medicine, University of Tsukuba), Masumoto Shoichi, Okiyama Naoko, Yoshimoto Hisashi, Maeno Tetsuhiro. 高齢患者における食物依存性運動誘発アナフィラキシーの発症 (The Onset of Food-dependent Exercise-induced Anaphylaxis in an Elderly Patient)(原著論文/英語) Internal Medicine. 2023.10; 62(19); 2907-2909
3. Oyama M, Ohnuki Y, Uruha A, Saito Y, Nishimori Y, Suzuki S, Inoue M, Tanboon J, Okiyama N, Shiina T, Nishino I, Suzuki S.. Association Between HLA Alleles and Autoantibodies in Dermatomyositis Defined

- by Sarcoplasmic Expression of Myxovirus Resistance Protein A. *Journal of Rheumatology*. 2023.09; 50(9); 1159-1164
4. Namiki Takeshi, Makiguchi Moe, Wada Shogo, Al-Busani Hind, Nishida Makiko, Ugajin Tsukasa, Miura Keiko, Yokoyama Kota, Okiyama Naoko. The potential value of thallium-201 scintigraphy in the diagnosis of squamous cell carcinoma arising from extensive pyoderma(タイトル和訳中) *The Journal of Dermatology*. 2023.07; 50(7); 942-945
5. Tanboon J, Inoue M, Hirakawa S, Tachimori H, Hayashi S, Noguchi S, Okiyama N, Fujimoto M, Suzuki S, Nishino I.. Muscle pathology of antisynthetase syndrome according to antibody subtypes. *Brain Pathology*. 2023.07; 33(4); e13155
6. Inaba M, Fukushima H, Hara M, Hosaka S, Fujiyama S, Maruo K, Nomura T, Okiyama N, Takada H.. Antigen-specific T cell balance reveals Why patients with atopic dermatitis fail to achieve immune tolerance. *Clinical Immunology*. 2023.07; 252; 109649
7. 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 developed during treatment of juvenile dermatomyositis and macrophage activation syndrome: A case report. *Mod Rheumatol Case Rep*. 2023.06; 7(2); 404-409
8. Ichimura Y, Ikei H, Konishi R, Zeniya M, Okai T, Nomura T, Negishi K, Okiyama N.. Relevance of leukaemia inhibitory factor to anti-melanoma differentiation-associated gene 5 antibody-positive interstitial lung disease *Rheumatology (Oxford)*. 2023.06; 62(6); 2267-2271
9. Oya K, Nakamura Y, Watanabe R, Tanaka R, Ichimura Y, Kubota N, Matsumura Y, Tahara H, Okiyama N, Fujimoto M, Nomura T, Fujisawa Y.. Eribulin mesylate exerts antitumor effects via CD103. *Oncoimmunology*. 2023.05; 12(1); 2218782
10. Iwata Masahiro, Ogawa Tatsuya, Anju Keisuke, Okiyama Naoko, Nomura Toshifumi. Adult-onset Still's disease following mRNA-1273 Moderna COVID-19 vaccination: A case report(タイトル和訳中) *Journal of Cutaneous Immunology and Allergy*. 2023.04; 6(2); 66-67
11. Iwata Masahiro(Department of Dermatology, Faculty of Medicine, University of Tsukuba), Ogawa Tatsuya, Anju Keisuke, Okiyama Naoko, Nomura Toshifumi. mRNA-1273 モデルナによる COVID-19 ワクチン接種後にみられた成人発症型 Still 病 1 症例報告 (Adult-onset Still's disease following mRNA-1273 Moderna COVID-19 vaccination: A case report)(レター/英語) *Journal of Cutaneous Immunology and Allergy*. 2023.04; 6(2); 66-67
12. Konishi Risa, Ichimura Yuki, Okiyama Naoko. Murine models of idiopathic inflammatory myopathy(タイトル和訳中) *Immunological Medicine*. 2023.03; 46(1); 9-14
13. Kubota N, Tanaka R, Ichimura Y, Konishi R, Tso JY, Tsurushita N, Nomura T, Okiyama N.. Blockade of CD122 on memory T cells in the skin suppresses sclerodermatous graft-versus-host disease. *Journal of Dermatological Science*. 2023.03; 109(3); 127-135
1. Tadatsune IIDA, Shizuka OZASA, Shogo WADA, Taku NAMATAME, Takuya WAKASA, Masahiro KATAGIRI, Minako INAZAWA, Tomoko FUJIMOTO, Takeshi NAMIKI, Hiroo YOKOZEKI, Naoko OKIYAMA. Acquired Idiopathic Generalized Anhidrosis with repeated anaphylaxis rinsho derma (Tokyo). 2023.12; 65(13); 2062-2065

[Misc]

1. Ebisawa Yuka, Masumoto Shoichi, Okiyama Naoko, Yoshimoto Hisashi, Maeno Tetsuhiro. The Onset of Food-dependent Exercise-induced Anaphylaxis in an Elderly Patient(タイトル和訳中) *Internal Medicine*. 2023.10; 62(19); 2907-2909
2. Mouri Mariko, Kanamori Toru, Tanaka Eriko, Hiratoko Kanako, Okubo Mariko, Inoue Michio, Morio Tomohiro, Shimizu Masaki, Nishino Ichizo, Okiyama Naoko, Mori Masaaki. Hepatic veno-occlusive disease accompanied by thrombotic microangiopathy developed during treatment of juvenile dermatomyositis and macrophage activation syndrome: A case report(タイトル和訳中) *Modern Rheumatology Case Reports*. 2023.07; 7(2); 404-409

3. Konishi R, Ichimura Y, Okiyama N. Murine models of idiopathic inflammatory myopathy. Immunological medicine. 2023.03; 46(1); 9-14
4. Kubota Noriko, Tanaka Ryota, Ichimura Yuki, Konishi Risa, Tso J.Yun, Tsurushita Naoya, Nomura Toshifumi, Okiyama Naoko. Blockade of CD122 on memory T cells in the skin suppresses sclerodermatous graft-versus-host disease(タイトル和訳中) Journal of Dermatological Science. 2023.03; 109(3); 127-135

[Conference Activities & Talks]

1. Oyama Munenori, Ohnuki Yuko, Uruha Akinori, Saito Yoshihiko, Nihimori Yukako, Suzuki Shingo, Inoue Michio, Tanboon Jantima, Okiyama Naoko, Shiina Takashi, Nishino Ichizo, Suzuki Shigeaki. 皮膚筋炎における HLA 対立遺伝子と自己抗体の密接な関連性 (Tight association between HLA alleles and autoantibodies in dermatomyositis). 臨床神経学 2023.09.01

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

multifactorial disorder.

4) Elucidating for molecular mechanism of perinatal abnormality using system biology (Hata, Kenichiro; Dept. of Maternal-Fetal Biology, National Institute for Child Health and Development)

We aim to clarify mechanisms underlying abnormalities in fetal development and placentation, and/or perinatal diseases with developmental defects. To identify the underlying mechanisms of perinatal diseases, we take advantage of post-genomic technologies and investigate etiologies using an integrated genomic and epigenomic approach.

5) Identification of target molecules in severe diseases and establishment of disease model mice by studying molecular mechanisms of genomic imprinting, gametogenesis and sexual differentiation

(Takada, Shuji; Dept. of Systems Biomedicine, National Institute for Child Health and Development)

Our aim is to reveal the molecular mechanisms underlying embryonic development, cell differentiation and tissue formation and apply our findings to understand the causes of developmental diseases.

6) Elucidation for allergic disease mechanism and target molecules using molecular biology and 'omics' technology

(Matsumoto, Kenji; Dept. of Allergy and Clinical Immunology, National Institute for Child Health and Development)

Our mission is to clarify the precise pathogenic mechanisms of various immunological and allergic diseases, such as Kawasaki disease, various allergic diseases, allogeneic immune tolerance, congenital viral infections and severe infectious diseases. To achieve this, we employ various experimental approaches, including epidemiology, clinical and basic research. Our ultimate aim is to develop better means of preventing, diagnosing and treating allergic and immunological and infectious diseases based on our research findings and cumulative knowledge.

(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]

1. Isono W, Kawasaki T, Ichida JK, Nagasaka K, Hiraike O, Umezawa A, Akutsu H*. Transcriptomic analysis of feeder-free culture system for maintaining naïve-state pluripotency in human pluripotent stem cells. *Stem Cell Investig.* 2023 Apr 19;10:10.
2. Ite K, Toyoda M, Akiyama S, Enosawa S, Yoshioka S, Yukitake T, Yamazaki-Inoue M, Tatsumi K, Akutsu H, Nishina H, Kimura T, Otani N, Nakazawa A, Fukuda A, Kasahara M, Umezawa A. Stem cell challenges and opportunities. *Prog Mol Biol Transl Sci.* 2023; 199: 379-395.
3. Takeuchi I, Tanase-Nakao K, Ogawa A, Sugawara T, Migita O, Kashima M, Yamazaki T, Iguchi A, Naiki Y, Uchiyama T, Tamaoki J, Maeda H, Shimizu H, Kawai T, Taniguchi K, Hirata H, Kobayashi M, Matsumoto K, Naruse K, Hata K, Akutsu H, Kato T, Narumi S, Arai K, Ishiguro A. Congenital anaemia associated with loss-of-function variants in DNA polymerase epsilon 1. *J Med Genet.* 2023 Oct 13:jmg-2023-109444.
4. Tanuma-Takahashi A, Inoue M, Kajiwaru K, Takagi R, Yamaguchi A, Samura O, Akutsu H, Sago H, Kiyono T, Okamoto A, Umezawa A. Restoration of keratinocytic phenotypes in autonomous trisomy-rescued cells. *Stem Cell Res Ther.* 2021 Aug 25;12(1):476.
5. Ogawa Y, Terao M, Tsuji-Hosokawa A, Tsuchiya I, Hasegawa M, Takada S: SOX9 and SRY binding sites on mouse mXYSRa/Enh13 enhancer redundantly regulate Sox9 expression to varying degrees. *Human Molecular Genetics*, 32(1):55-64 (2023).
6. Richard Albert J, Kobayashi T, Inoue A, Monteagudo-Sánchez A, Kumamoto S, Takashima T, Miura A, Oikawa M, Miura F, Takada S, Hirabayashi M, Korthauer K, Kurimoto K, Greenberg MVC, Lorincz M, Kobayashi H: Conservation and divergence of canonical and non-canonical imprinting in murids. *Genome Biology*, 24(1):48 (2023).
7. Azuma N, Yokoi T, Tanaka T, Matsuzaka E, Saida Y, Nishina S, Terao M, Takada S, Fukami M, Okamura K, Maehara K, Yamasaki T, Hirayama J, Nishina H, Handa H, Yamaguchi Y: Integrator complex subunit 15 controls mRNA splicing and is critical for eye development. *Human Molecular Genetics*, 32(12):2032-2045 (2023).
8. Yamada S, Ko T, Ito M, Sassa T, Nomura S, Okuma H, Sato M, Imasaki T, Kikkawa S, Zhang B, Yamada T, Seki Y, Fujita K, Katoh M, Kubota M, Hatsuse S, Katagiri M, Hayashi H, Hamano M, Takeda N, Morita H, Takada S, Toyoda M, Uchiyama M, Ikeuchi M, Toyooka K, Umezawa A, Yamanishi Y, Nitta R, Aburatani H, Komuro I: TEAD1 trapping by the Q353R-Lamin A/C causes dilated cardiomyopathy. *Science Advances*, 9(15):eade7047 (2023).
9. Katoh-Fukui Y, Hattori A, Zhang R, Terao M, Takada S, Nakabayashi K, Hata K, Yamada Y, Matsuura N, Fukami M: Chromosomal microdeletion leading to pituitary gigantism through hormone-gene overexpression. *Human Molecular Genetics*, 32(14):2318-2325 (2023).
10. Mashima R, Ohira M, Okuyama T, Onodera M, Takada S: A novel mucopolysaccharidosis type

- II mouse model with an iduronate-2-sulfatase-P88L mutation. *Scientific Reports*, 13(1):7865 (2023).
11. Abe T, Kanno S, Niihori T, Terao M, Takada S, Aoki Y: LZTR1 deficiency exerts high metastatic potential by enhancing sensitivity to EMT induction and controlling KLHL12-mediated collagen secretion. *Cell Death & Disease*, 14(8):556 (2023).
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Department of High-risk Infectious Disease Control

(1) Publications

[Original Articles]

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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 (logos + 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

1. About human cancer:

There are three main purposes.

(1) Carcinogenesis and histogenesis of cancers: For the understanding 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.

2. 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. Novel cell death-focused pathological analysis and cancer treatment strategies:

Cells are genetically designed to undergo apoptosis, a process that is closely related to various phenomena such as human development and lymphocyte differentiation. Radiotherapy and chemotherapy in cancer induce apoptosis by inducing apoptotic signals, however, various inhibitory mechanisms are activated in some cancer cells, causing cancer resistance and recurrence, which in turn leads to a poor prognosis. Recently, a novel form of cell death called 'ferroptosis' has been discovered. This cell death is an iron ion-dependent, lipid peroxidation-induced cell death that can be induced in apoptosis-resistant cancer cells and is attracting attention as a new therapeutic strategy for refractory cancers that are resistant to various existing treatments. GPX4, FSP1 and GCH1 are known as the main genes that regulate ferroptosis, and all of them are known as negative regulators of ferroptosis. The laboratory has investigated the expression of these genes and the accumulation of 4-HNE, a lipid peroxidation marker, in human cancer tissues. The results varied according to the type of cancer and reported that over-expression or accumulation of these factors, or reduced expression or accumulation, is a predictor of poor prognosis in cancer. We will further integrate these findings with data from different cancers and establish the molecular basis for new therapeutic strategies by molecular biological methods using cultured cells, etc.

(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 therapeutic effect. If a patient has unfortunately joined the majority, morbid anatomy is done by the pathologists along with the patient's attending physician. They study the resulting effects of laboratory findings and choice of treatment, and improve the future diagnosis and treatments. The department of Human Pathology and Surgical Pathology technically work as one although they are separated in this university's organizational structure. Human Pathology does not directly work with the patients; however, it is involved directly with the diagnosis as well as the treatments. Strong cooperation between clinicians and pathologists is essential for the best practice, and is required for the university hospital as an "advanced treatment hospital." Therefore, doctors of Human Pathology study, research and practice pathology to be the great pathologists so-called the "doctor of doctors."

(7) Publications

[Original Articles]

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[Conference Activities & Talks]

1. Keiko Miura, Junichi Shiraishi, Yuriko Yukino, Takayuki Fusumae, Mika Fujiwara, Atsushi Oda, Takeshi Namiki. Two cases of heavily pigmented melanocytic neoplasm mimicking pigmented epithelioid melanocytoma. 39th Japanese Society of Dermatopathology and Histology 2023.04.15 Ryogoku,Tokyo

[Social Contribution]

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

6. Fiber Photometry Using Viral Vector Approach for Neuronal Activity and Neurotransmitter Release Measurement

This method involves the use of a viral vector approach for the targeted expression of genetically encoded indicators within specific neuronal populations. For assessing population-level neuronal activity, we employ calcium indicators such as GCaMP, providing a real-time measure of neuronal activity. Additionally, we utilize dLight, a dopamine-sensitive fluorescent probe, to measure local dopamine release. This probe enables the precise quantification of dopamine levels change in targeted brain regions. The viral vector method ensures that these indicators are selectively expressed in neurons of interest, allowing for the specific and localized measurement of neuronal activity or neurotransmitter release.

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. Koji Ikezoe, Naoki Hidaka, Satoshi Manita, Masayoshi Murakami, Shinichiro Tsutsumi, Yoshikazu Isomura, Masanobu Kano, Kazuo Kitamura. Cerebellar climbing fibers multiplex movement and reward signals during a voluntary movement task in mice. *Commun Biol.* 2023.09; 6(1); 924
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3. Riichiro Hira, Leah B. Townsend, Ikuko T. Smith, Che-Hang Yu, Jeffrey N. Stirman, Yiyi Yu, Spencer LaVere Smith. Mesoscale functional architecture in medial posterior parietal cortex. *bioRxiv* (preprint). 2023.08;
4. Shogo Soma, Shinya Ohara, Satoshi Nonomura, Naofumi Suematsu, Junichi Yoshida, Eva Pastalkova, Yutaka Sakai, Ken-Ichiro Tsutsui, Yoshikazu Isomura. Rat hippocampal CA1 region represents learning-related action and reward events with shorter latency than the lateral entorhinal cortex. *Commun Biol.* 2023.05; 6(1); 584
5. Tomohiko Yoshizawa, Yuuto Miyamura, Yuta Ochi, Riichiro Hira, Makoto Funahashi, Yutaka Sakai, Yilong Cui, Yoshikazu Isomura. Working memory-based and -free reward prediction in a dual dopamine system in the basal ganglia. *bioRxiv* (preprint). 2023.03;

[Conference Activities & Talks]

1. Hikaru Sugino, Tatsumi Yoshida, Yoshikazu Isomura, Riichiro Hira. Layer specific temporal activity patterns in superior colliculus in response to cortical input. 253rd Physiology Tokyo Danwakai 2023.12.09 Teikyo Univ., Tokyo
2. Airi Mochimasu, Masanori Kawabata, Yoshikazu Isomura. Alterations of higher cognitive functions in psychotic model rats explored in waiting time task. The 83rd the Japanese Society for Animal Psychology 2023.10.08 Teikyo Univ. of Sciences, Tokyo
3. Masanori Kawabata, Yuka Hirayama, Teppei Ebina, Yoshikazu Isomura, Masanori Matsuzaki. Establishing cognitive behavioral tasks with dexterity movements for marmoset. The 83rd the Japanese Society for Animal Psychology 2023.10.08 Teikyo Univ. of Sciences, Tokyo
4. Yoshikazu Isomura. Action-outcome signaling in hippocampus and entorhinal cortex. Diverse approaches to understanding learning and memory 2023.09.26 NIPS, Okazaki
5. Riichiro Hira. Holism in neuroscience: Large-scale recording and simulation. 6TH JP-EU WORKSHOP ON NEUROROBOTICS 2023.09.15 Univ. of Tokyo, Tokyo
6. Yuuto Miyamura, Tomohiko Yoshizawa, Riichiro Hira, Yoshikazu Isomura. A hierarchical structure of reservoir model enables flexible behavior based on the presence of regularity without synaptic plasticity. JNNS2023 2023.09.05 Univ. of Tokyo, Tokyo
7. Yoshizawa T, Miyamura Y, Ochi Y, Hira R, Funahashi M, Sakai Y, Cui Y, Isomura Y. Parallel processing of working memory-based and -free reward prediction in dual dopamine system of the basal ganglia. The 46th annual meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center

8. Sakairi T, Kawabata M, Alain R, Kaneko S, Sakai Y, Isomura Y. Hippocampal sharp-wave ripples disappear during consummatory licking in head-fixed rodents . The 46th annual meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center
9. Fukabori R, Isomura Y, Kobayashi K. Intermanual transfer between both forelimbs of lever-push motion procedural memory in rodents . The 46th annual meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center
10. Alain Rios, Satoshi Nonomura, Shigeki Kato, Junichi Yoshida, Natsuki Matsushida, Atsushi Nambu, Masahiko Takada, Riichiro Hira, Kazuto Kobayashi, Yutaka Sakai, Minoru Kimura, Yoshikazu Isomura. Integration of Reward Expectation and Action Selection in the Nigrostriatal System. The 46th annual meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center
11. Sunahara M, Rios A, Kawabata M, Takahashi H, Isomura Y. The functional role of thalamic reticular nucleus in motor execution. The 46th annual meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center
12. Masanori Kawabata, Yoshikazu Isomura. Wide-area electrophysiological analysis on distribution of sensory and motor-related information in the rodent cerebral cortex. The 46th annual meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center
13. Yoshikazu Isomura. The basal ganglia predicting and responding to action outcome . NIPS Research Meeting: Multi disciplinary approach to understand neuronal network architecture to control motor actions 2023.03.18 NIPS, Okazaki, Aichi
14. Yoshikazu Isomura. Adaptive circuit dynamics for operant learning of optimal behavior. ACC International Symposium 2023 2023.02.22 Riken, Wako, Saitama

Department of 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 aim to improve student's understanding of stem cells from multiple viewpoints.

(5) Publications

[Original Articles]

1. Melig G, Nobuhisa I, Saito K, Tsukahara R, Itabashi A, Kanai Y, Kanai-Azuma M, Osawa M, Oshima M, Iwama A, Taga T. A Sox17 downstream gene Rasip1 is involved in the hematopoietic activity of intra-aortic hematopoietic clusters in the midgestation mouse embryo. *Inflamm Regen.* 2023.08; 43(1); 41
2. Yoshitaka Murota, Mariko Nagane, Mei Wu, Mithun Santra, Seshasailam Venkateswaran, Shinji Tanaka, Mark Bradley, Tetsuya Taga, Kouichi Tabu . A niche-mimicking polymer hydrogel-based approach to identify molecular targets for tackling human pancreatic cancer stem cells *Inflammation and Regeneration.* 2023.09; 43(1); 46
3. Murota Y, Nagane M, Wu M, Santra M, Venkateswaran S, Tanaka S, Bradley M, Taga T, Tabu K. A niche-mimicking polymer hydrogel-based approach to identify molecular targets for tackling human pancreatic cancer stem cells. *Inflammation and regeneration.* 2023.09; 43(1); 46
4. Kashiwagi Taichi, Takazawa Yuuki, Kagawa Tetsushi, Taga Tetsuya. Organization of self-advantageous niche by neural stem/progenitor cells during development via autocrine VEGF-A under hypoxia *INFLAMMATION AND REGENERATION.* 2023.02; 43(1); 8

[Conference Activities & Talks]

1. Tarapongpun Tanakorn, Chuthapisith Suebwong, Onlamoon Nattawa, Kouichi Tabu, Yoshitaka Murota, Tetsuya Taga. Combinatorial Use of EGF and FGFs to Prime Human Adipose-derived Mesenchymal Stem Cells for Pre-adipocyte Commitment. 第18回生命医科学研究所ネットワーク国際シンポジウム 2023.10.06 Tokyo Medical and Dental University (TMDU), Tokyo
2. Wenyu Liu, Kouichi Tabu, Yoshitaka Murota, Tetsuya Taga. Differential susceptibility of mouse adult neural stem cells and astrocytes to oncogenic transformation. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 PACIFICO Yokohama, Yokohama, Japan
3. Yoshitaka Murota, Shinji Tanaka, Tetsuya Taga, Kouichi Tabu. Niche-mimicking polymer hydrogel-based identification of fetuin-B as a potential target for pancreatic cancer. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.22 PACIFICO Yokohama, Yokohama, Japan
4. Tarapongpun Tanakorn, Chuthapisith Suebwong, Onlamoon Nattawa, Kouichi Tabu, Tetsuya Taga. Effect of Growth Factors on Priming Human Adipose-Derived Mesenchymal Stem Cells to Committed Preadipocytes Before Lipofilling. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.22 PACIFICO Yokohama, Yokohama, Japan
5. Gerel Melig, Ikuo Nobuhisa, Kiyoka Saito, Ryota Tsukahara, Ayumi Itabashi, Yoshiakira Kanai, Masami Kanai-Azuma, Tetsuya Taga. Rasip1 helps maintenance of hematopoietic activities of mouse embryonic intra-aortic hematopoietic clusters.. The 44th Annual Meeting of the Japanese Society of Inflammation and Regeneration 2023.07.12
6. Norihisa Bizen, Kouichi Tabu, Mei Wu, Christian Mangani, Rong Zhang, Mark Bradley, Tetsuya Taga . Development of synthetic polymer scaffolds mimicking a niche that maintains neural stem cells in a growth factor- and serum-free system. The 20th Stem Cell Research Symposium 2023.05.19 Awaji Yumebutai International Conference Center, Awaji, Japan
7. Gerel Melig, Ikuo Nobuhisa, Kiyoka Saito, Ryota Tsukahara, Ayumi Itabashi, Yoshiakira Kanai, Masami Kanai-Azuma, Tetsuya Taga. Rasip1 gene functioning downstream of Sox17 maintains the hematopoietic cluster-forming cells in E10.5 mouse embryos.. The 20th Stem Cell Research Symposium 2023.05.19
8. Taichi Kashiwagi, Yuuki Takazawa, Tetsushi Kagawa, Tetsuya Taga. Self-maintenance strategies of neural stem/progenitor cells via autocrine VEGF-A under hypoxia in the developing brain.. The 20th Stem Cell Research Symposium 2023.05.19

Respiratory Medicine

Professor: Yasunari Miyazaki
 Junior Associate Professor: Furusawa Haruhiko,
 Assistant Professor: Tuyoshi Shirai, Takayuki Honda, Sho Shibata, Rie Sakakibara
 Project Assistant Professor: Shiro Sonoda, Sho Shimada, Hikaru Aoki
 Clinical Fellow: Rina Kato, Ryou Sunohara, Sho Yasui, Shunya Hanawa, Atsushi Sawada, Ayaaki Kai
 Resident: Tomoka Yasuda, Hyosuke Ishikawa
 Ph.D. student: Takahiro Ando, Shun Endo, Jun Sugihara, Akifumi Mochizuki, Takashi Shimamura,
 Masaru Ito, Shinya Fujii, Nobuyuki Kondou, Takemoto Abe, Natsumi Asao, Wataru Inoue
 Professor, Department of Respiratory and Nervous System Science: Yuki Sumi
 Professor, Health Administration Center: Ryushi Tazawa
 Assistant Professor, Health Administration Center: Seiko Takasawa
 Associate Professor, Department of Respiratory Physiology and Sleep Medicine: Tomoya Tateishi
 Associate Professor, The Center for Personalized Medicine for Healthy Aging : Tsukasa Okamoto
 Junior Assistant Professor, Department of Pulmonary Immunotherapeutics: Masahiro Ishizuka
 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 lung diseases in Japan are referred to our clinic.

(7) Publications

[Original Articles]

1. Funaita C, Furuie W, Koike F, Oyama S, Endo J, Otani Y, Ichikawa Y, Ito M, Nakamura Y, Komatuzaki K, Hirata A, Miyazaki Y, Sumi Y. Pattern recognition of forced oscillation technique measurement results using deep learning can identify asthmatic patients more accurately than setting reference ranges. *Scientific reports*. 2023.12; 13(1); 21608
2. Endo S, Okamoto T, Kawahara T, Anzai T, Takahashi K, Miyazaki Y. Effect of warm and humid days on the positivity rate of anti-Trichosporon asahii antibody test for the diagnosis of summer-type hypersensitivity pneumonitis. *Respiratory investigation*. 2023.12; 62(1); 150-156
3. Takahiro Ando, Sho Shimada, Jun Sugihara, Koji Takayama, Masayoshi Kobayashi, Yoshihiro Miyashita, Tatsuya Ito, Kaori Okayasu, Shun Tsuyuki, Takehiko Ohba, Masafumi Doi, Hiroaki Saito, Toshihide Fujie, Tomoshige Chiaki, Atsushi Nakagawa, Tatsuhiko Anzai, Kunihiko Takahashi, Sho Shibata, Tomoya Tateishi, Yasunari Miyazaki. Impairment of Social-Related Quality of Life in COVID-19 Pneumonia Survivors: A Prospective Longitudinal Study. *J Clin Med*. 2023.12; 12(24);
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7. Komatsuzaki K, Kageshima H, Sekino Y, Suzuki Y, Ugajin T, Tamaoka M, Hanazawa R, Hirakawa A, Miyazaki Y. Local nasal immunotherapy with birch pollen-galactomannan conjugate-containing ointment in mice and humans. *Allergology international : official journal of the Japanese Society of Allergology*. 2023.11;

8. Shiraishi K, Takahashi A, Momozawa Y, Daigo Y, Kaneko S, Kawaguchi T, Kunitoh H, Matsumoto S, Horinouchi H, Goto A, Honda T, Shimizu K, Torasawa M, Takayanagi D, Saito M, Saito A, Ohe Y, Watanabe SI, Goto K, Tsuboi M, Tsuchihara K, Takata S, Aoi T, Takano A, Kobayashi M, Miyagi Y, Tanaka K, Suzuki H, Maeda D, Yamaura T, Matsuda M, Shimada Y, Mizuno T, Sakamoto H, Yoshida T, Goto Y, Yoshida T, Yamaji T, Sonobe M, Toyooka S, Yoneda K, Masago K, Tanaka F, Hara M, Fuse N, Nishizuka SS, Motoi N, Sawada N, Nishida Y, Kumada K, Takeuchi K, Tanno K, Yatabe Y, Sunami K, Hishida T, Miyazaki Y, Ito H, Amemiya M, Totsuka H, Nakayama H, Yokose T, Ishigaki K, Nagashima T, Ohtaki Y, Imai K, Takasawa K, Minamiya Y, Kobayashi K, Okubo K, Wakai K, Shimizu A, Yamamoto M, Iwasaki M, Matsuda K, Inazawa J, Shiraishi Y, Nishikawa H, Murakami Y, Kubo M, Matsuda F, Kamatani Y, Hamamoto R, Matsuo K, Kohno T. Identification of telomere maintenance gene variations related to lung adenocarcinoma risk by genome-wide association and whole genome sequencing analyses. *Cancer communications* (London, England). 2023.10;
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10. Saito Sho, Kutsuna Satoshi, Imamura Akifumi, Hase Ryota, Oda Rentaro, Terada Junko, Shimizu Yosuke, Uemura Yukari, Takamatsu Yuki, Yasuhara Akemi, Shiratori Katsuyuki, Satake Masahiro, Sakamoto Naoya, Miyazaki Yasunari, Shimizu Hidefumi, Togano Tomiteru, Matsunaga Akihiro, Okuma Kazu, Hamaguchi Isao, Fujisawa Kyoko, Nagashima Maki, Ashida Shinobu, Terada Mari, Kimura Akiko, Morioka Shinichiro, Matsubayashi Keiji, Tsuno Nelson Hirokazu, Kojima Makiko, Kuramitsu Madoka, Tezuka Kenta, Ikebe Emi, Ishizaka Yukihito, Maeda Kenji, Hangaishi Akira, Mikami Ayako, Sugiura Wataru, Ohmagari Norio, Mitsuya Hiroaki. Efficacy of convalescent plasma therapy for COVID-19 in Japan: An open-label, randomized, controlled trial(タイトル和訳中) *Journal of Infection and Chemotherapy*. 2023.09; 29(9); 869-874
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14. Nishioka Y, Homma S, Ogura T, Sato S, Arai N, Tomii K, Kamio K, Sakamoto S, Miyazaki Y, Tomioka H, Hisata S, Handa T, Azuma A. Exploratory phase 2 study of the novel oral multi-kinase inhibitor TAS-115 in patients with idiopathic pulmonary fibrosis. *Respiratory investigation*. 2023.07; 61(4); 498-507
15. Mitsui Y, Suzuki T, Kuniyoshi K, Inamo J, Yamaguchi K, Komuro M, Watanabe J, Edamoto M, Li S, Kouno T, Oba S, Hosoya T, Masuhiro K, Naito Y, Koyama S, Sakaguchi N, Standley DM, Shin JW, Akira S, Yasuda S, Miyazaki Y, Kochi Y, Kumanogoh A, Okamoto T, Satoh T. Expression of the readthrough transcript CiDRE in alveolar macrophages boosts SARS-CoV-2 susceptibility and promotes COVID-19 severity. *Immunity*. 2023.07; 56(8); 1939-1954.e12
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- budgerigar/pigeon/parrot-specific IgG antibody with ImmunoCAP® in bird-related hypersensitivity pneumonitis caused by other bird species and duvet. *Respiratory investigation*. 2023.07; 61(4); 520-526
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[Conference Activities & Talks]

1. Yuko Kawamoto, Nana Oga, Haruhiko Furusawa, Satoshi Hanzawa, Yasunari Miyazaki, Makoto Tanaka. The experience of patients' families in the process of implementing antigen avoidance for patients with hypersensitivity pneumonitis: A qualitative study. 26th East Asian Forum of Nursing Scholars 2023.03.10 Tokyo
2. Yuko Kawamoto, Yuka Nakahama, Nana Oga, Haruhiko Furusawa, Satoshi Hanzawa, Yasunari Miyazaki, Makoto Tanaka. Healthcare needs in implementing antigen avoidance as perceived by patients with hypersensitivity pneumonitis: A qualitative research. 26th East Asian Forum of Nursing Scholars 2023.03.10 Tokyo
1. Hiroyuki Ishiyama, Masayuki Hidashima, Shusuke Inukai, Meiyo Tamaoka, Akira Nishiyama, Yasunari Miyazaki, Kenji Fueki. The effect of reduction rate of respiratory resistance associated with mandibular advancement on the efficacy of oral appliance for obstructive sleep apnea.. The 22nd Annual Meeting of the Japanese Academy of Dental Sleep Medicine 2023.10.08 Kyoto, Japan

Gastroenterology and Hepatology

Professor

Ryuichi OKAMOTO(Department of Gastroenterology and Hepatology)

Professor

Yasuhiro ASAHINA(Department of Liver Disease Control)

Kazuo OHTSUKA(Endoscopy)

Sei KAKINUMA(Department of Clinical and Diagnostic Laboratory Science)

Shigeru OSHIMA(Institute of Research)

Distinguished Professor

Mamoru WATANABE

Associate Professor

Yasuhiro NEMOTO(Department of Gastroenterology and Hepatology)

Takashi NAGAISHI(Department of Advanced Therapeutics for GI Diseases)

Toshimitsu FUJII(Department of Collaborative Medicine for Gastroenterology and Hepatology)

Masakazu NAGAHORI(Clinical Research Center)

Mina NAKAGAWA(Curricular Management Division)

Eriko OKADA(Department of Medical Education Research and Development)

Shiro YUI(Center for Stem Cell and Regenerative Medicine)

Yu MATSUZAWA(Department of Clinical and Diagnostic Laboratory Science)

Junior Associate Professor

Hiromichi SHIMIZU(Gastroenterology and Hepatology)

Tomohiro MIZUTANI(Department of Gastroenterology and Hepatology)

Masayohi FUKUDA(Endoscopy)

Kento TAKENAKA(Department of Collaborative Medicine for Gastroenterology and Hepatology)

Yoshihito KANO(Department of Clinical Oncology)

Assistant Professor

Eiko SAITO

Miyako MURAKAWA(Gastroenterology and Hepatology)

Masato MIYOSHI(Department of Gastroenterology and Hepatology)

Masanori KOBAYASHI(Gastroenterology and Hepatology)

Shun KANEKO(Gastroenterology and Hepatology)

Fukiko KITAHATA

Ami KAWAMOTO(Endoscopy)

Shuji HIBIYA(Endoscopy)

Project Assistant Professor

Satoru FUJII(Department of Gastroenterology and Hepatology)

Junichi TAKAHASHI (Department of Gastroenterology and Hepatology)

Specially Appointed Assistant Professor

Go ITO(Inflammatory Bowel Disease Laboratory)

Akiko TAMURA (Gastroenterology and Hepatology)

Senior Resident

Minami ENDO, Ryo MORIKAWA, Satoshi WATANABE,

Tsubasa NOBUSAWA, Kanako, OGATA, Kazuma SAITO (Gastroenterology and Hepatology)

Yuka HAYAKAWA, Shun ISHIDO(Endoscopy)

Shun FUJIWARA(Department of Clinical Oncology)

Sakurako KOBAYASHI

(1) Outline

Research project is selected from the clinical problems in the Gastroenterology and Hepatology to understand the research policy, as clinical science that the results of research project finally should be restored to clinical medicine.

The purpose of this course is the understanding the situation of inflammatory bowel disease (IBD) in Japan and the problems about the pathogenesis and intractable cause of IBD. In addition, the understanding the pathogenesis and problems about the liver diseases such as viral hepatitis, cirrhosis and hepatocellular carcinoma is the purpose of this course.

(2) Research

Basic Research Projects

Systemic Organ Regulation

- Elucidating the pathophysiology of inflammatory bowel diseases and development of treatment by diseasespecific immune regulation.
- Development of novel therapeutics for inflammatory and allergic diseases based on gut-specific mucosal immune regulation.
- Basic research and clinical application of regenerative medicine in gastrointestinal diseases.
- Comprehensive analysis of susceptibility genes for various gastrointestinal diseases.
- Crosstalk of the signaling pathways in intestinal epithelial cells.
- Functional analysis of the intestine using primary cell culture in vitro.

(3) Education

We believe that the central role of clinical departments in the graduate school is to establish basis for the innovative medicine / medical treatment in the next generation. Basic research lead by clinical concepts, and development of novel therapeutics established upon basic research are both critically required to achieve our mission. Therefore, our primary goal is set to train highly educated and experienced clinician-researchers in the field of gastroenterology and hepatology.

In the clinical area, we pursue development and application of highly advanced technologies, including novel endoscopic procedures, for sophisticated diagnosis and treatment of gastrointestinal and liver diseases. In basic research, our principle is to achieve "clinical science", a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice. Based on these principals, we are running research projects to 1) develop novel therapy for refractory inflammatory bowel diseases, 2) prevent progression of liver failure in chronic hepatitis patients and 3) improve anti-cancer therapy for the treatment of gastrointestinal malignancies, by expanding our distinct basic research findings in the area of mucosal immunology, liver immunology, regenerative medicine and virology, to various clinical settings. Moreover, we promote both intra- and inter-national exchanges of researchers, and provide good opportunities to study abroad. The final goal of our education is to promote students to become a well-developed clinician researcher, and also a leading expert in the field of gastroenterology and hepatology.

(4) Lectures & Courses

Research Conference	every Tuesday 18:00 19:30
Journal Club	every Tuesday 18:00 19:30

(5) Clinical Services & Other Works

Expert Areas in Clinical Practice

- Immune-regulation based treatment of inflammatory bowel diseases.
- Prevention of chronic hepatitis progression to hepatocellular cancer and liver failure, by virology-based treatment strategy.
- Clinical trial of innovative treatment for hepatocellular cancer.

- Diagnosis and treatment of small intestinal diseases by balloon assisted enteroscopy and capsule enteroscopy.
- Advanced diagnosis and treatment of colonic diseases by colonoscopy.
- Development of minimally-invasive diagnostic modalities for gastrointestinal diseases (i.e. MR enterography).
- Improved chemotherapy for gastric and pancreatic malignancies.

(6) Clinical Performances

Therapeutics of inflammatory bowel diseases by corrections of immunological disfunctions.

Diagnostic and interventional gastrointestinal endoscopy.

Antiviral therapies against chronic viral hepatitis and preventions of hepatic malignancy novel interventions of hepatic malignancy.

(7) Publications

[Original Articles]

1. Sylvia Leo, Yusuke Kato, Yu Meng Wu, Mutsumi Yokota, Masato Koike, Shiro Yui, Kiichiro Tsuchiya, Nobuaki Shiraki, Shoen Kume. The effect of Vitamin D3 and Valproic Acid on the maturation of human induced pluripotent stem cell-derived enterocyte-like cells. *Stem Cells*. 2023.05;
2. Kirino Sakura, Tamaki Nobuharu, Kurosaki Masayuki, Takahashi Yuka, Higuchi Mayu, Itakura Yoshie, Tanaka Yuki, Inada Kento, Ishido Shun, Yamashita Koji, Nobusawa Tsubasa, Matsumoto Hiroaki, Hayakawa Yuka, Kakegawa Tatsuya, Takaura Kenta, Tanaka Shohei, Maeyashiki Chiaki, Kaneko Shun, Yasui Yutaka, Tsuchiya Kaoru, Nakanishi Hiroyuki, Okamoto Ryuichi, Izumi Namiki. Detecting advanced liver fibrosis using ultrasound shear wave velocity measurement in the general population QUANTITATIVE IMAGING IN MEDICINE AND SURGERY. 2023.10; 13(10); 6493-6502
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5. Yuki Tahata, Hayato Hikita, Satoshi Mochida, Nobuyuki Enomoto, Akio Ido, Hidekatsu Kuroda, Daiki Miki, Masayuki Kurosaki, Yoichi Hiasa, Ryotaro Sakamori, Norifumi Kawada, Taro Yamashita, Goki Suda, Hiroshi Yatsuhashi, Hitoshi Yoshiji, Naoya Kato, Taro Takami, Kazuhiko Nakao, Kentaro Matsuura, Yasuhiro Asahina, Yoshito Itoh, Ryosuke Tateishi, Yasunari Nakamoto, Eiji Kakazu, Shuji Terai, Masahito Shimizu, Yoshiyuki Ueno, Norio Akuta, Masanori Miyazaki, Yasutoshi Nozaki, Masayuki Kabayama, Satoshi Sobue, Akihiro Moriuchi, Tomokatsu Miyaki, Takahiro Kodama, Tomohide Tatsumi, Tomomi Yamada, Tetsuo Takehara. Posttreatment liver function, but not baseline liver function stratifies patient survival after direct-acting antiviral treatment in decompensated cirrhosis with hepatitis C virus. *J Gastroenterol*. 2023.12; 58(12); 1211-1221
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12. Kentaro Miyamoto, Tomohisa Sujino, Yosuke Harada, Hiroshi Ashida, Yusuke Yoshimatsu, Yuki Yonemoto, Yasuhiro Nemoto, Michio Tomura, Hassan Melhem, Jan Hendrik Niess, Toshihiko Suzuki, Toru Suzuki, Shohei Suzuki, Yuzo Koda, Ryuichi Okamoto, Yohei Mikami, Toshiaki Teratani, Kenji F. Tanaka, Akihiko Yoshimura, Toshiro Sato, Takanori Kanai. The gut microbiota-induced kynurenic acid recruits GPR35-positive macrophages to promote experimental encephalitis. *Cell Rep.* 2023.08; 42(8); 113005
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- Akira Nishiyama, Tomohiko Tamura, Takashi Kamatani, Tatsuhiko Tsunoda, Miyako Murakawa, Yasuhiro Asahina, Yoshihiro Hayashi, Hironori Harada, Yuka Harada, Asumi Yokota, Hideyo Hirai, Takao Seki, Makoto Kuwahara, Masakatsu Yamashita, Shigeyuki Shichino, Masato Tanaka, Kenichi Asano. The early neutrophil-committed progenitors aberrantly differentiate into immunoregulatory monocytes during emergency myelopoiesis. *Cell Rep.* 2023.03; 42(3); 112165
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3. Mina Nakagawa, Yasuhiro Asahina, Sei Kakinuma, Ryuichi Okamoto. Impact of eradication of hepatitis C virus on liver-related and -unrelated diseases: morbidity and mortality of chronic hepatitis C after SVR. J Gastroenterol. 2023.04; 58(4); 299-310

[Conference Activities & Talks]

1. Ryuichi Okamoto. Clinical Application of Patient-derived Organoids. World Bio Innovation Forum Invitation 2023.12.06 WEB
2. Ryuichi Okamoto, Yasuhiro Nemoto, Tomohiro Mizutani, Hiromichi Shimizu. Recent Progress in the Treatment of Tissue Specific Immunological Diseases. The 2nd International Symposium of Clinical Immunology 2023.05.19 Kamakura_JAPAN
3. Ryuichi Okamoto. Bench-to-bedside research: Patient-derived organoid transplantation for treatment of intractable ulcerative colitis. SIDDS 2023 2023.04.08 Grand Walkerhill Seoul_Korea
4. Kento Takenaka. Deep neural network for video colonoscopy of ulcerative colitis. JDDW2023 2023.11.04 Kobe_Japan
5. Shun Kaneko, Yasuhiro Asahina, Miyako Murakawa, Ryuichi Okamoto. Liver stiffness stratify the disease progression and hepatocellular carcinoma predictive risk score on chronic hepatitis B patients. JDDW2023 2023.11.03 Kobe_Japan
6. Marla C. Dubinsky, Geert D' Haens, Olivier Dewit, Pascal Juillerat, Remo Panaccione, Toshimitsu Fujii, Ana P Lacerda, Elena Dubcenco, Samuel Anyanwu, Chirag Doshi, John Liu, Andrew Garrison, Edward V Loftus Jr. Corticosteroid-Sparing Effect of Upadacitinib in Patients With Moderately to Severely Active Crohn' s Disease. ACG 2023 - American College of Gastroenterology 2023.10.20 Vancouver_Canada
7. B.Bressler, L.Peyrin-Biroulet, J.R.Allegretti, K.G.Huang, M.Germinaro, N.Shipitofsky, Y.Miao, H.Zhang, M.Bortlik, T.Hlavaty, T.Fujii, B.G.Feagan, B.E.Sands, A.Dignass on behalf of the QUASAR Investigators. The Efficacy of Induction Treatment With Guselkumab in Patients with Moderately to Severely Active Ulcerative Colitis: Phase 3 QUASAR Induction Study Results at Week 12 by Prior Advanced Therapy History. ACG 2023 - American College of Gastroenterology 2023.10.20 Vancouver_Canada
8. T. Fujii , S. Hibiya , H. Shimizu , A. Kawamoto , K. Takenaka , E. Saito , M. Nagahori , K. Ohtsuka , R. Okamoto. DUAL THERAPY WITH CAROTEGRAST (AJM300: ORAL α 4 INTEGRIN ANTAGONIST) AND BIOLOGICS FOR REFRACTORY ULCERATIVE COLITIS. UEGW2023 2023.10.15 Copenhagen_Denmark
9. Mone Fushimi, Tadahiko Inoue, Daiki Yamada, Taro Watabe, Mamoru Watanabe, Ryuichi Okamoto, Takashi Nagaishi. APL downregulation in T cells in the setting of chronic colitis. UEGW2023 2023.10.15 Copenhagen_Denmark
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11. B.Bressler, L.Peyrin-Biroulet, J.R.Allegretti, K.G.Huang, M.Germinaro, N.Shipitofsky, Y.Miao, H.Zhang, M.Bortlik, T.Hlavaty, T.Fujii, B.G.Feagan, B.E.Sands, A.Dignass on behalf of the QUASAR Investigators. The Efficacy of Induction Treatment With Guselkumab in Patients with Moderately to Severely Active Ulcerative Colitis: Phase 3 QUASAR Induction Study Results at Week 12 by Prior Advanced Therapy History. UEGW2023 2023.10.15 Copenhagen_Denmark
12. Hiromune Katsuda, Go Ito, Yui Hiraguri, Tomohiro Muto, Shun Ishido, Masanori Kobayashi, Hironari Yamashita, Akira Ito, Hiroaki Ono, Atsushi Kudo, Mamoru Watanabe, Minoru Tanabe, Ryuichi Okamoto. Analysis of gene expression to elucidate the pathogenesis of pancreatic solid pseudopapillary neoplasm. UEGW2023 2023.10.14 Copenhagen_Denmark

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15. Shiro Yui. Fetal-like reprogramming is the key to understand the heterogeneity of colorectal cancer. SICS-OMICS2023, The 41st Sapporo International Cancer Symposium 2023.10.13 Tokyo, Japan
16. Marc Ferrante, Laurent Peyrin-Biroulet, Axel Dignass, David T. Rubin, Silvio Danese, Geert D'Haens, Kristina Kligys, Sofie Berg, Jasmina Kalabic, Javier Zambrano, Yafei Zhang, Toshimitsu Fujii, and Remo Panaccione. Clinical and Endoscopic Improvements with Risankizumab Induction and Maintenance Dosing Versus Placebo are Observed Irrespective of Number of Prior Failed Biologics. UEGW2023 2023.10.11 Copenhagen_Denmark
17. Marla C. Dubinsky, Geert D' Haens, Olivier Dewit, Pascal Juillerat, Remo Panaccione, Toshimitsu Fujii, Ana P Lacerda, Elena Dubcenco, Samuel Anyanwu, Chirag Doshi, Madhuja Mallick, Andrew Garrison, John Liu, Edward V Loftus Jr. Corticosteroid discontinuation and clinical outcomes in patients with moderately to severely active Crohn' s disease treated with upadacitinib. SGG Swiss congress 2023 2023.09.23 Interlaken_Switzerland
18. Nobuhiko Ogasawara, Shiro Yui et al. ECM-niche dependent plasticity controls the acquisition of invasive phenotype in colorectal cancer. 第 82 回日本癌学会学術総会 2023.09.21 Yokohama
19. Nobuhiko Ogasawara, Yoshihito Kano, Sakurako Kobayashi, Satoshi Watanabe, Sakura Kirino, Iichiroh Onishi, Shinichi Yamauchi, Yui Hiraguri, Go Ito, Mamoru Watanabe, Yusuke Kinugasa, Kenichi Ohashi, Ryuichi Okamoto, Shiro Yui. ECM-niche dependent plasticity controlsthe acquisition of invasive phenotype in colorectal cancer. The 82nd Annual Meeting Of The Japanese Cancer Association 2023.09.21 Yokohama_Japan
20. Mina Nakagawa, Miyako Murakawa, Masato Miyoshi, Shun Kaneko, Fukiko Kawai-Kitahata, Sayuri Nitta, Sei Kakinuma, Yasuhiro Asahina, Ryuichi Okamoto. Factors associated with HCC development and patients' survival in patients with an SVR. The 3rd JSH International Liver Conference 2023.09.07
21. Marla C. Dubinsky, Geert D' Haens, Olivier Dewit, Pascal Juillerat, Remo Panaccione, Toshimitsu Fujii, Ana P Lacerda, Elena Dubcenco, Samuel Anyanwu, Chirag Doshi, Madhuja Mallick, Andrew Garrison, John Liu, Lena Thin, Edward V Loftus Jr. Corticosteroid discontinuation and clinical outcomes in patients with moderately to severely active Crohn' s disease treated with upadacitinib. AGW2023 2023.09.02 Brisbane_Australia
22. Kaneko Shun, Asahina Yasuhiro, Murakawa Miyako, Okamoto Ryuichi. 慢性B型肝炎患者において肝スティフネスは疾患進行と肝細胞癌予測リスクスコアを層別化する (Liver stiffness stratify the disease progression and hepatocellular carcinoma predictive risk score on chronic hepatitis B patients). 肝臓 2023.09.01
23. Kazuo Ohtsuka. Endoscopic and imaging diagnosis and assessment of inflammatory bowel disease. 7th TASSID TSIBD Joint Symposium 2023.08.05 Tainan_Taiwan
24. Kazuo Ohtsuka, Kento Takenaka, Ryuichi Okamoto. Cutting-edge of clinical practice in SBE. The 105th Congress of the Japan Gastroenterological Endoscopy Society 2023.05.26 Tokyo_Japan
25. Nobuhiko Ogasawara, Yoshihito Kano, Sakurako Kobayashi, Satoshi Watanabe, Sakura Kirino, Shinichi Yamauchi, Yui Hiraguri, Go Ito, Tomohiro Mizutani, Mamoru Watanabe, Yusuke Kinugasa, Ryuichi Okamoto, Shiro Yui. Unveiling the gene network behind cell plasticity provides a novel insight into the therapeutic approach for human colorectal cancer. Keystone Symposia 2023.05.11 Vancouver_Canada
26. Marla C. Dubinsky, Geert D' Haens, Olivier Dewit, Pascal Juillerat, Remo Panaccione, Toshimitsu Fujii, Ana P. Lacerda, Elena Dubcenco, Samuel Anyanwu, Chirag Doshi, Madhuja Mallick, Andrew Garrison, John Liu, Edward V. Loftus Jr. Corticosteroid Discontinuation and Clinical Outcomes in Patients With Moderately to Severely Active Crohn' s Disease Treated With Upadacitinib. DDW2023 2023.05.09 Washington,D.C._USA

27. Marc Ferrante, Qian Cao, Toshimitsu Fujii, Astrid Rausch, Ezequiel Neimark, Alexandra Song, Kori Wallace, Kristina Kligys, Qing Zhou, Jasmina Kalabic, Brian Feagan. Patients with Moderate-to-Severe Crohn's Disease with and without Prior Biologic Failure Demonstrate Improved Endoscopic Outcomes with Risankizumab: Results from Phase 3 Induction and Maintenance Trials Marc. DDW2023 2023.05.09 Washington,D.C._USA
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29. Junichi Takahashi, Tomohiro Mizutani, Ryuichi Okamoto. A suspension method for efficient induction and maturation of human intestinal organoids using a rotational bioreactor. 2023 RIKEN BDR-CuSTOM Joint Organoid Symposium 2023.02.17 Kobe_Japan
30. Junichi Takahashi, Tomohiro Mizutani, Ryuichi Okamoto. A suspension method for efficient induction and maturation of human intestinal organoids using a rotational bioreactor. 2023 RIKEN BDR-CuSTOM Joint Organoid Symposium 2023.02.15 Kobe_Japan

Specialized Surgeries

< Division of Specialized Surgeries >

Junior Associate Professor: Kentaro OKAMOTO

Assistant Professor: Toshiyuki ISHIBA, Yuichi KUMAKI

Attending staff: Mio ADACHI, Keishi ITO, Kumiko HAYASHI, Masatake HARA, Shota OKAMOTO

< Facility of Medical Informatics >

Junior Associate Professor: Goshi ODA

< Department of International Medicine >

Assistant Professor: Hirotaka MIZUNO

(1) Outline

Division of Specialized Surgeries have been launched in April 2015, which consists of 2 clinical departments in the Medical Hospital:

- Division of Breast Surgery
- Division of Pediatric surgery

(2) Research

Research topics in the area of breast surgery include: 1) search for driver genes and new biomarkers using cancer gene panels, 2) AI-based diagnostic imaging (in collaboration with the Department of Radiology), 3) evaluation of skin blood flow after breast surgery, and 4) research on the localization of breast cancer TILs using immunomultiplex staining methods.

Research projects in the field of pediatric surgery include (1) anatomical analysis of blood vessels in the upper extremities and (2) telemedicine using smartphones. (1) is performed non-invasively using a newly developed vascular transmission device. This will be clinically applied to the safe insertion of peripherally inserted central venous catheters. (2) will be incorporated into day surgery and is being performed in cooperation with other departments and the nursing department.

(3) Education

Main objective in the graduate course is to bring up the well-rounded surgeons who has international and scientific feelings.

(4) Clinical Services & Other Works

The Breast Surgery Department performs 130-160 surgeries per year. All breast cancer cases are treated in a joint conference (every Wednesday) by the four departments of surgery, radiology, plastic surgery, and pathology

to determine the treatment plan.

Pediatric Surgery treats a wide range of pediatric surgical conditions other than heart and head, from neonates to carry-over adults. We are committed to minimally invasive treatment, including the safe insertion of central venous catheters in affected children using a novel device, the vascular permeation device.

(5) Publications

[Original Articles]

1. Kamata Y, Mizuno Y, Okamoto K, Okamoto S, Ito Y, Nishigata A. Peripherally inserted central catheters can be an alternative to tunneled central venous catheters in chemotherapy for hematological and oncological pediatric patients. *Pediatric surgery international*. 2023.09; 39(1); 264
2. Ryosuke Kikuchi, Kazuhito Sasaki, Hiroaki Nozawa, Koji Muro, Shigenobu Emoto, Shinichi Yamauchi, Kenichi Sugihara, Soichiro Ishihara. Prognosis of Inferior Mesenteric and Para-aortic Lymph Node Metastases in Rectal Cancer: A Multicenter Study Anticancer research. 2023.09; 43(9); 4213-4219
3. Sasada Shinsuke, Kondo Naoto, Hashimoto Hiroya, Takahashi Yuko, Terata Kaori, Kida Kumiko, Sagara Yasuaki, Ueno Takayuki, Anan Keisei, Suto Akihiko, Kanbayashi Chizuko, Takahashi Mina, Nakamura Rikiya, Ishiba Toshiyuki, Tsuneizumi Michiko, Nishimura Seiichiro, Naito Yoichi, Hara Fumikata, Shien Tadahiko, Iwata Hiroji. Prognostic impact of adjuvant endocrine therapy for estrogen receptor-positive and HER2-negative T1a/bN0M0 breast cancer. *Breast Cancer Res Treat*. 2023.09;
4. Tsuyoshi Nakagawa, Hiroki Mori, Noriko Uemura, Ichiro Onishi, Goshi Oda. A Case of Breast Cancer With Ulceration of a Reconstructed Nipple Due to Local Recurrence. *Cureus*. 2023.05; 15(5); e39563
5. Honda M, Shimojima N, Maeda Y, Ito Y, Miyaguni K, Tsukizaki A, Abe K, Hashimoto M, Ishikawa M, Tomita H, Shimotakahara A, Hirobe S. Factors predicting surgical difficulties in congenital biliary dilatation in pediatric patients. *Pediatric surgery international*. 2023.01; 39(1); 79
6. Ishiba Toshiyuki, Nishibuchi Ikuno, Hara Fumikata, Shikama Naoto, Shien Tadahiko, Iwata Hiroji. Metastasis-directed therapy for oligometastases in breast cancer. *Jpn J Clin Oncol*. 2023.07;
7. Mori M, Fujioka T, Hara M, Katsuta L, Yashima Y, Yamaga E, Yamagiwa K, Tsuchiya J, Hayashi K, Kumaki Y, Oda G, Nakagawa T, Onishi I, Kubota K, Tateishi U. Deep Learning-Based Image Quality Improvement in Digital Positron Emission Tomography for Breast Cancer. *Diagnostics (Basel, Switzerland)*. 2023.02; 13(4);
8. Sato A, Fujioka T, Mori M, Oda G, Nakagawa T, Kubota K, Tateishi U. A case in which ultrasonography was useful in differentiating between rib fracture due to compression after biopsy and rib metastasis of breast cancer. *Journal of medical ultrasonics (2001)*. 2023.02; 50(2); 265-266
9. Yashima Y, Fujioka T, Kubota K, Mori M, Sato A, Oda G, Nakagawa T, Onishi I, Tanaka M, Tateishi U. Comparison of the clinical and pathological characteristics of ultrasound-guided biopsy for breast masses and non-mass lesions between 16-gauge spring-loaded core needle biopsy and 12-gauge spring-loaded vacuum-assisted biopsy. *Journal of medical ultrasonics (2001)*. 2023.01; 50(2); 205-212

[Misc]

1. Kumaki Y, Oda G, Ikeda S. Targeting MET Amplification: Opportunities and Obstacles in Therapeutic Approaches. *Cancers*. 2023.09; 15(18);

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,

Tomomasa Takamiya, Takuro Nishimura, Kensuke Hirasawa, Makoto Araki,

Yuji Matsuda, Kentaro Goto, Masateru Takigawa, Mie Ochida, Junji Yamaguchi,

Yosuke Yamakami, Takashi Ikenouchi, Kensuke Ihara, Shun Nakagama,

Iwanari Kawamura

Medical Staff, Resident

Yoshinori Kanno, Mari Omori, Miho Negishi, Hiroshi Yoshikawa, Naoya Kikkoji,

Tetsuya Kishigami, Sayumi Nozaki, Eiko Sakai, Takumi Watanabe, Akira Nakashima,

Masayuki Noda, Hiroyuki Masumoto, Takuto Koyama, Nao Yanagihara,

Kosuke Nakada

Graduate student, Research student

Satoshi Iwamiya, Giichi Nitta, Nyo Zin Lei Mon, Fan Quintao, Kohei Kawajiri,

Niu Yaqianqian, Sadahiro Hijikata, Miki Amemiya, Reo Yaga, Ikhtiyorjon Khamdamov,

Wang Yongjie, Shun Nakamura, Suzuka Ishikawa, Ummatalieva Nurjahon Muhiddin Kizi

(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]

1. Katherine-Sofia Candray-Medina, Yu Nakagama, Masamichi Ito, Shun Nakagama, Evariste Tshibangu-Kabamba, Norihiko Takeda, Yuki Sugiura, Yuko Nitahara, Yu Michimuko-Nagahara, Natsuko Kaku, Yoko Onizuka, Carmen-Elena Arias, Maricela Mejia, Karla Alas, Susana Peña, Yasuhiro Maejima, Issei Komuro, Junko Nakajima-Shimada, Yasutoshi Kido. Differential cardiomyocyte transcriptomic remodeling during in vitro Trypanosoma cruzi infection using laboratory strains provides implications on pathogenic host responses. Trop Med Health. 2023.12; 51(1); 68
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[Misc]

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[Conference Activities & Talks]

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3. 大方 信一郎, 内藤 倫人, 岸上 哲也, 加地 大悟, 照井 麻央, 堀江 知樹, 長瀬 将, 埤本 優太, 三澤 透, 宮崎 亮一, 金子 雅一, 李 哲民, 永田 恭敏, 野里 寿史, 足利 貴志, 笹野 哲郎. de novo 冠動脈病変に対する DCB 治療直後の FFR 値と退院後の FFRCT との関連性. 日本心血管インターベンション治療学会抄録集 2023.08.01
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6. 菅野 義典, 米津 太志, 酒井 瑛子, 吉川 宏, 大森 麻理, 松田 祐治, 荒木 誠, 杉山 知代, 梅本 朋幸, 笹野 哲郎. INOCA における angio IMR の測定. 日本心血管インターベンション治療学会抄録集 2023.08.01
7. 坂本 達哉, 星野 昌弘, 白井 英祐, 羽田 昌浩, 長嶺 竜宏, 羽生 佳弘, 野上 開, 上野 弘貴, 松田 和樹, 米津 太志, 笹野 哲郎, 角田 恒和. Myocardial Bridge が PCI 前後で経胸壁ドップラー心エコーの指標に与える影響. 日本心血管インターベンション治療学会抄録集 2023.08.01
8. 長嶺 竜宏, 星野 昌弘, 白井 英祐, 羽田 昌浩, 羽生 佳弘, 野上 開, 上野 弘貴, 松田 和樹, 坂本 達哉, 米津 太志, 笹野 哲郎, 角田 恒和. NIRS で定義される Lipid-rich plaque の冠動脈 CT での予測因子. 日本心血管インターベンション治療学会抄録集 2023.08.01

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13. Iiya Munehiro, Kashiwa Ryonosuke, Nishio Yoshiro, Yasui Yumi, Sumino Yohei, Kobayashi Issi, Onishi Yuko, Yonetsu Taishi, Sasano Tetsuo. エキシマレーザー冠動脈アテレクトミーによる経皮的冠動脈インターベンションを施行した急性冠症候群患者の治療成績 (Outcome of patients with acute coronary syndrome who underwent percutaneous coronary intervention with excimer laser coronary atherectomy). 日本心臓血管インターベンション治療学会抄録集 2023.08.01
14. Araki Makoto, Yonetsu Taishi, Horiuchi Yuna, Miyakoshi Tsunehiro, Nakashima Akira, Noda Masayuki, Masumoto Hiroyuki, Sakai Eiko, Yoshikawa Hiroshi, Omori Mari, Kanno Yoshinori, Matsuda Yuji, Hirasawa Kensuke, Sugiyama Tomoyo, Umemoto Tomoyuki, Totsuka Minoru, Okawa Ryunosuke, Sasano Tetsuo. 光干渉断層法で評価した冠動脈プラークにおけるコレステロール排出能と脂質リッチプラークとの関連性 (Association between cholesterol efflux capacity and lipid-rich plaque in coronary plaques assessed by optical coherence tomography). 日本心臓血管インターベンション治療学会抄録集 2023.08.01
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Cardiovascular Surgery

Professor : Tomoyuki FUJITA

Associate Professor: Tomohiro MIZUNO, Eiki NAGAOKA

Junior Associate Professor: Keiji OI, Eiki NAGAOKA, Masafumi YASHIMA, Tatsuki FUJIWARA

Assistant Professor:

Masafumi YASHIMA, Tatsuki FUJIWARA, Kiyotoshi OISHI, Masashi TAKESHITA, Youhei YAMAMOTO,

Junya NABESHIMA, Hironobu SAKURAI, Tomoki TAHARA

Graduate Student:

Masashi TAKESHITA, Hironobu SAKURAI, Haruna SEKI, Kenji YOKOYAMA

, Tomoki TAHARA, Junya NABESHIMA

Hospital Staff: 5

(1) Research

- 1) Developing safe and high quality surgical strategy in coronary artery bypass grafting surgery.
- 2) Developing new surgical technique for ischemic heart disease
- 3) Developing new surgical technique for beating mitral valve surgery
- 4) Clinical research for artificial heart
- 5) Research for new regenerative therapy for failing heart to recover cardiac function

(2) Education

Cardiovascular Surgery is a branch of surgery which deals with heart and vascular (mainly aortic) disease. Main objective of our department in the graduate course is to provide medical students an opportunity to study surgical anatomy, pathophysiology, pharmacology, and advanced surgical treatment for heart and aortic disease. Students are also taught basic research for the surgical treatment for heart and aortic disease. We also provide clinical training program for young surgeon to obtain Japanese cardiovascular surgical board.

(3) Clinical Performances

Our department provides well-advanced surgical treatment of heart and aortic surgery. We perform off-pump coronary artery bypass grafting for more than 90% of patients with coronary artery disease, mitral valve repair, not valve replacement, for almost all patients with mitral valve regurgitation. New surgical reconstruction technique is provided for patients with functional mitral regurgitation due to severe heart failure. For elderly patients, we offer minimally invasive aortic surgery such as thoracic endovascular aortic repair (TEVAR) and hybrid aortic surgery without cardiopulmonary bypass for aortic arch and thoracoabdominal aortic disease.

(4) Publications

[Original Articles]

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29. [Cardiovascular Surgery : FUJITA TOMOYUKI] Anegawa Eiji, Seguchi Osamu, Mochizuki Hiroki, Kuroda Kensuke, Doi Nakajima Seiko, Watanabe Takuya, Yanase Masanobu, Tadokoro Naoki, Fukushima Satsuki, Fujita Tomoyuki, Fukushima Norihide. Pulmonary Vascular Reverse Remodeling After Left Ventricular Assist Device Implantation in Patients With Pulmonary Hypertension. *ASAIO J*. 2023.02; 69(2); 151-158
30. [Cardiovascular Surgery : FUJITA TOMOYUKI] Amemiya Kisaki, Yonemoto Yumiko, Ishibashi-Ueda Hatsue, Matsumoto Manabu, Ohta-Ogo Keiko, Ikeda Yoshihiko, Kobayashi Junjiro, Fukushima Satsuki, Fujita Tomoyuki, Hatakeyama Kinta. Morphological characteristics of cardiac myxoma causing embolism: a series of 40 years of experience at a single institute. *Virchows Arch*. 2023.02; 482(2); 377-384

[Conference Activities & Talks]

1. [Cardiovascular Surgery : FUJITA TOMOYUKI] Fujita Tomoyuki. Lessons learnt from 100 Heartmate3 implants. *International Symposium of Left Ventricular Assist Device* 2023.09.09 Web
2. [Cardiovascular Surgery : FUJITA TOMOYUKI] Fujita Tomoyuki. SURGICAL EXPERT PROGRAM. APAC HEART FAILURE NETWORK OF EXCELLENCE 2023.04.06 Web
1. [Cardiovascular Surgery : NAGAOKA Eiki] Application of Pneumatically Driven Surgical Robot with Dynamic Force Feedback in Cardiac Surgeries. 2023.10.19
2. [Cardiovascular Surgery : NAGAOKA Eiki] Eiki Nagaoka. Cannula Selection for Adult ECMO. 2023.03.20

Nephrology

Professor:

Shinichi UCHIDA

Associate Professor:

Eisei SOHARA

Shotaro NAITO (Dept. of Blood Purification)

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)

Hiroaki KIKUCHI (Endowed Chair)

Tamami FUJIKI

Project Assistant Professor

Yuu HARA, Shingo SHIOJI

Graduate Student:

Hisazumi MATSUKI, Hideki YANAGAWA, Takefumi SUZUKI

Shunsuke INABA, Kanako NAGAOKA

Hospital Staff:

Nobuhisa MORIMOTO, Tomohiro TSUBOYA, Yumi TOBARI

Yuki TANAKA, Ayaka KUMAGAI, Hitoshi NOSHIRO

Technician:

Chieko IJIMA, Motoko CHIGA

Secretary:

Asa MURANO, Yukiko ITO

(1) Outline

In the Department of Nephrology, we strive to provide "trusted medical care" and aim for the "cultivation of excellent physicians" through our activities in clinical practice, education, and research. We have extensive clinical experience in dealing with all kinds of renal diseases and have developed high-quality medical care through close collaboration with many other medical institutions, training numerous nephrology specialists in the process.

In recent years, we have been unraveling the genetic abnormalities and pathophysiology of various renal diseases, including hereditary kidney diseases, aiming to use these findings to develop innovative treatments. With the aging population and changes in lifestyle, the number of patients with chronic kidney disease is steadily increasing. To meet the expectations placed on nephrology specialists, we are dedicated to continuous learning and improvement.

(2) Research

Our research theme centers on elucidating the mechanisms by which the kidneys maintain blood pressure and bodily fluid homeostasis, understanding the pathology that arises when these mechanisms fail and affect the entire body, and developing treatment strategies to address these issues. This pursuit not only leads to the development of treatments for kidney disease itself but also facilitates research aimed at addressing multi-organ disorders originating from the kidneys in the context of chronic kidney disease (CKD). Academic and research activities, which were restricted due to the COVID-19 pandemic, have gradually been returning to normal since 2023, as the infection subsided. In the fiscal year 2023 (January to December), following the tradition of previous years, many awards were bestowed at academic conferences and workshops, and active press releases were made. Dr. Yu Hara received the 2022 Young Investigator Award (YIA) from the Japanese Society of Nephrology, awarded to outstanding young researchers under the age of 37 nationwide. Dr. Hara also won the Excellent Presentation Award at the 32nd Vasopressin and Oxytocin Research Symposium. Assistant Professor Yutaro Mori received the Tokyo Medical Association Medical Research Award Encouragement Prize and the Japan Medical Association Medical Research Encouragement Prize in fiscal year 2022. At the Young Basic Research Forum 2023, Dr. Hisazumi Matsuki was awarded the Excellent Presentation Award. In terms of paper publications, the papers by Assistant Professor Shintaro Mandai and Dr. Takahiro Koide were accepted by Circulation Research (IF: 23.1), and papers by Assistant Professor Mandai, Dr. Matsuki, and Dr. Taku Genma were accepted by Hypertension (IF: 8.3), with press releases issued for both. Assistant Professor Hiroaki Kikuchi's paper, submitted after returning from studying abroad, was accepted by Nature Communications (IF: 17.7), and a press release was issued. From January to December 2023, our department had a total of 13 academic papers accepted, including case reports, with five press releases issued during the period.

From February to March 2023, we conducted crowdfunding for our research on comprehensive genetic analysis related to hereditary kidney diseases. We received donations totaling 19.5 million yen and numerous messages of support from approximately 400 donors. We would like to take this opportunity to express our heartfelt gratitude to all those who supported us. We have continued to stably operate clinical research related to comprehensive genetic diagnosis and genome information, conducting analyses for 91 individuals over the year.

(3) Education

Pre-graduation Education

In the Department of Nephrology, we are responsible for the education of medical school students, specifically conducting systematic lectures for third-year medical students, project semesters for fourth-year students, and overseeing clinical internships for fifth and sixth-year students.

< Systematic Lectures >

Systematic lectures are conducted jointly with the Urology and Pathology departments, focusing intensively on diseases within the renal and urological field over a three-week period. In the 2023 academic year, all lectures and Problem-Based Learning (PBL) sessions in the Nephrology Department were returned to in-person instruction. PBL involves students engaging in discussions within small groups, performing differential diagnoses on scenario-based cases. This method was implemented with the participation of Nephrology Department staff and graduate students, organized into two groups with one tutor each. We received positive feedback from students who appreciated the enriching discussions facilitated by the tutors' supportive guidance.

< Project Semester >

Regarding students enrolled in the Project Semester, we plan to accept approximately two students annually.

< Clinical Internships >

Clinical internships commence in December for fourth-year students following the conclusion of the Project Semester. Initially, from late November to February, we conduct Preclinical Clerkship (PCC) sessions, providing practical and comprehensive learning in small groups. From the fifth year onwards, students transition to Clinical Clerkship (CC) with practical training on the ward. CC students are assigned to care for actual patients in a two-week internship, studying nephrology diseases. Students had the opportunity to delve deeper into the pathophysiology of various nephrology diseases. During clinical internships, Differential Diagnosis Exercises (WoSAC - Workplace-based Student Assessment with Clinical reasoning focus) were conducted, where supervising physicians played the role of patients, guiding students in presenting differential diagnoses and

outlining examination and treatment plans. This training, as before, concluded with a comprehensive review by the faculty. Additionally, for sixth-year students, a two-week internship for up to two students per term is provided as part of the Advanced Course, offering higher-level learning goals and opportunities for motivated engagement. We attribute the success of these efforts to the dedication of the faculty members and staff who guide the students.

Furthermore, lectures and examinations for dental students, health and hygiene science students, dental hygienists, and master's students were also conducted by faculty members from the Nephrology Department.

Postgraduate Education

After completing a two-year initial training period following graduation, we conduct advanced training as part of the postgraduate education in collaboration with universities and affiliated hospitals, focusing on specialized training in nephrology. During this period, our goal is to guide individuals to develop awareness of unresolved clinical issues and cultivate an academic doctor's mindset, one that consistently seeks to uncover the essence of matters. The emphasis is on fostering a commitment to addressing clinical challenges and maintaining an attitude of continually seeking the fundamental truths in medical practice.

Research activities at the graduate level are highly active, contributing to the cultivation of physicians who excel in both foundational and clinical aspects through the pursuit of cutting-edge research.

(4) Clinical Services & Other Works

In March 2023, the government introduced guidelines for the principle removal of masks, and significant measures were taken to relax COVID-19 prevention protocols within the university's healthcare system. After approximately three years of disruption caused by the COVID-19 pandemic, the situation has begun to stabilize, and we are gradually returning to normalcy. The number of referred patients, which had declined in most departments, is now slowly recovering. While the number of inpatients and outpatients in the nephrology department, as well as operational revenues, have not yet returned to pre-COVID levels, they are approaching those levels. Outpatient maintenance dialysis, which was once suspended during the pandemic, is also being gradually resumed, with an increase in the number of patients.

The "Function Enhancement Building," located at the front of the university and under construction for a long time, officially opened on October 1st. With the relocation of the Life-Saving Emergency Center, emergency (ER) outpatient services, ICU, ER wards, and the establishment of hybrid operating rooms, we are now able to accept a wide range of emergency patients and provide the highest standard of surgical care. From the end of 2023, to enable smoother appointments for specialized outpatient services, the nephrology department took the lead in implementing a web reservation system through Office Bookings. The number of appointment patients is gradually increasing, aiming for further patient acquisition. We aim to continue enhancing our medical services through stronger collaboration between hospitals and clinics, promoting visits to the dialysis complication clinic, increasing the number of peritoneal dialysis procedures, increasing the number of day surgery PTA (percutaneous transluminal angioplasty), and expanding the diagnosis and treatment options for rare kidney diseases.

(5) Publications

[Original Articles]

1. Yanagawa H, Hara Y, Ando F, Suzuki S, Fujiki T, Oikawa D, Yui N, Mandai S, Mori Y, Susa K, Mori T, Sohara E, Tokunaga F, Uchida S. LRBA signalosomes activate vasopressin-induced AQP2 trafficking at recycling endosomes. *The Journal of physiology*. 2023.12; 601(23); 5437-5451
2. Ohkubo A, Sakurasawa T, Hoshikawa Y, Usui M, Hoshi M, Shiga T, Deushi M, Komori S, Itagaki A, Yamamoto H, Seshima H, Kurashima N, Iimori S, Naito S. Evaluation of the treatment volume and removal rate of Rheocarna: A novel adsorption-type blood purification device for patients with chronic limb-threatening ischemia. *Therapeutic apheresis and dialysis : official peer-reviewed journal of the*

- International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy. 2023.12; 27(6); 1017-1022
3. Yuta Nakano, Shintaro Mandai, Shotaro Naito, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Eisei Sohara, Shinichi Uchida. Effect of osteosarcopenia on longitudinal mortality risk and chronic kidney disease progression in older adults. *Bone*. 2023.11; 116975
4. Sakurada T, Kojima S, Yamada S, Koitabashi K, Taki Y, Matsui K, Murasawa M, Kawarazaki H, Shimizu S, Kobayashi H, Asai T, Hashimoto K, Hoshino T, Sugitani S, Maoka T, Nagase A, Sato H, Fukuoka K, Sofue T, Koibuchi K, Nagayama K, Washida N, Koide S, Okamoto T, Ishii D, Furukata S, Uchiyama K, Takahashi S, Nishizawa Y, Naito S, Toda N, Naganuma T, Kikuchi H, Suzuki T, Komukai D, Kimura T, Io H, Yoshikawa K, Naganuma T, Morishita M, Oshikawa J, Tamagaki K, Fujisawa H, Ueda A, Kanaoka T, Nakamura H, Yanagi M, Udagawa T, Yoneda T, Sakai M, Gunji M, Osaki S, Saito H, Yoshioka Y, Kaneshiro N. A multi-institutional, observational study of outcomes after catheter placement for peritoneal dialysis in Japan. *Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis*. 2023.11; 43(6); 457-466
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6. Kikuchi H, Chou CL, Yang CR, Chen L, Jung HJ, Park E, Limbutara K, Carter B, Yang ZH, Kun JF, Remaley AT, Knepper MA. Signaling mechanisms in renal compensatory hypertrophy revealed by multi-omics. *Nature communications*. 2023.06; 14(1); 3481
7. Ines P D Costa, Nicolas Hautem, Guglielmo Schiano, Shinichi Uchida, Tomoya Nishino, Olivier Devuyst. Fasting influences aquaporin expression, water transport and adipocyte metabolism in the peritoneal membrane. *Nephrol Dial Transplant*. 2023.05; 38(6); 1408-1420
8. Nobuhisa Morimoto, Takayasu Mori, Shingo Shioji, Towako Taguchi, Hatsumi Watanabe, Keigo Sakai, Katsuo Mori, Ayumi Yamamura, Asami Hanioka, Yuichiro Akagi, Tamami Fujiki, Shintaro Mandai, Yutaro Mori, Fumiaki Ando, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Kenichi Ohashi, Shinichi Uchida. Rapidly progressive IgA nephropathy with membranoproliferative glomerulonephritis-like lesions in an elderly man following the third dose of an mRNA COVID-19 vaccine: a case report. *BMC Nephrol*. 2023.04; 24(1); 108
9. Madoka Kondo, Takayasu Mori, Tadashi Oshita, Atsuki Ohashi, Eisei Sohara, Shinichi Uchida, Yoshitaka Maeda. Case of hereditary kidney disease presenting thin basement membrane with a single heterozygous variant of Intersectin 2. *J Rural Med*. 2023.04; 18(2); 143-148
10. Nobuhisa Morimoto, Takayasu Mori, Shingo Shioji, Hatsumi Watanabe, Keigo Sakai, Katsuo Mori, Ayumi Yamamura, Asami Hanioka, Yuichiro Akagi, Tamami Fujiki, Shintaro Mandai, Yutaro Mori, Fumiaki Ando, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Shinichi Uchida. Thrombocytopenia during avacopan administration: A case report. *Int J Rheum Dis*. 2023.03;
11. Bingham MA, Neijman K, Yang CR, Aponte A, Mak A, Kikuchi H, Jung HJ, Poll BG, Raghuram V, Park E, Chou CL, Chen L, Leipziger J, Knepper MA, Dona M. Circadian gene expression in mouse renal proximal tubule. *American journal of physiology. Renal physiology*. 2023.03; 324(3); F301-F314
12. Junki Kurimoto, Hiroshi Takagi, Takashi Miyata, Yohei Kawaguchi, Yuichi Hodai, Tetsuro Tsumura, Daisuke Hagiwara, Tomoko Kobayashi, Yoshinori Yasuda, Mariko Sugiyama, Takeshi Onoue, Shintaro Iwama, Hidetaka Suga, Ryoichi Banno, Takeshi Katsuki, Fumiaki Ando, Shinichi Uchida, Hiroshi Arima. Mineralocorticoids induce polyuria by reducing apical aquaporin-2 expression of the kidney in partial vasopressin deficiency. *Endocr J*. 2023.03; 70(3); 295-304
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14. Park E, Yang CR, Raghuram V, Deshpande V, Datta A, Poll BG, Leo KT, Kikuchi H, Chen L, Chou CL, Knepper MA. Data resource: vasopressin-regulated protein phosphorylation sites in the collecting duct. *American journal of physiology. Renal physiology*. 2023.01; 324(1); F43-F55

15. Soichiro Suzuki, Fumiaki Ando, Sae Kitagawa, Yu Hara, Tamami Fujiki, Shintaro Mandai, Koichiro Susa, Takayasu Mori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. ZNF185 prevents stress fiber formation through the inhibition of RhoA in endothelial cells. *Commun Biol.* 2023.01; 6(1); 29
16. Ohkubo A, Sakurasawa T, Naito S. Low-Density Lipoprotein Adsorption by Centrifugal Plasma Separation Can Shorten Treatment Time. *Case reports in nephrology and dialysis.* 2023.01; 13(1); 51-56
17. Shizuka Kirino, Analia Yogi, Eriko Adachi, Hisae Nakatani, Maki Gau, Ryosei Iemura, Haruki Yamano, Toru Kanamori, Takayasu Mori, Eisei Sohara, Shinichi Uchida, Kentaro Okamoto, Tomohiro Udagawa, Kei Takasawa, Tomohiro Morio, Kenichi Kashimada. Phenotypic Variation in 46,XX Disorders of Sex Development due to the Fourth Zinc Finger Domain Variant of WT1: A Familial Case Report. *Sex Dev.* 2023; 17(1); 51-55
18. Kurimoto Junki, Takagi Hiroshi, Miyata Takashi, Kawaguchi Yohei, Hodai Yuichi, Tsumura Tetsuro, Hagiwara Daisuke, Kobayashi Tomoko, Yasuda Yoshinori, Sugiyama Mariko, Onoue Takeshi, Iwama Shintaro, Suga Hidetaka, Banno Ryoichi, Katsuki Takeshi, Ando Fumiaki, Uchida Shinichi, Arima Hiroshi. Mineralocorticoids induce polyuria by reducing apical aquaporin-2 expression of the kidney in partial vasopressin deficiency *ENDOCRINE JOURNAL.* 2023; 70(3); 295-304
19. Susa K, Kobayashi K, Galichon P, Matsumoto T, Tamura A, Hiratsuka K, Gupta NR, Yazdi IK, Bonventre JV, Morizane R. ATP/ADP biosensor organoids for drug nephrotoxicity assessment. *Frontiers in cell and developmental biology.* 2023; 11; 1138504
20. Hisazumi Matsuki, Taku Genma, Shintaro Mandai*, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Tatemitsu Rai, Kiyohide Fushimi, Shinichi Uchida. National Trends in Mortality and Urgent Dialysis after Acute Hypertension in Japan From 2010 Through 2019. *Hypertension.* 2023.10;
21. Hisazumi Matsuki, Shintaro Mandai*, Hiroki Shiwaku, Takaaki Koide, Naohiro Takahashi, Tomoki Yanagi, Shunsuke Inaba, Saaya Ida, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Eisei Sohara, Hidehiko Takahashi, Shinichi Uchida. Chronic kidney disease causes blood-brain barrier breakdown via urea-activated matrix metalloproteinase-2 and insolubility of tau protein. *Aging (Albany NY).* 2023.10; 15;
22. Hashimoto H, Mandai S*, Shikuma S, Kimura M, Toma H, Sakaguchi Y, Shiraishi S, Toshima N, Hoshino M, Kimura M, Ota J, Horiuchi S, Adachi S, Uchida S. The effect of antihypertensive therapy on skeletal muscle mass and bone mineral density in patients with end-stage kidney disease. *J Ren Nutr.* 2023.10;
23. Takaaki Koide, Shintaro Mandai*, Reo Kitaoka, Hisazumi Matsuki, Motoko Chiga, Kouhei Yamamoto, Kotaro Yoshioka, Yohsuke Yagi, Soichiro Suzuki, Tamami Fujiki, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Tatemitsu Rai, Takanori Yokota, Shinichi Uchida. Circulating Extracellular Vesicle-Propagated microRNA Signature as a Vascular Calcification Factor in Chronic Kidney Disease. *Circ Res.* 2023.01;

[Misc]

1. Fumiaki Ando, Yu Hara, Shinichi Uchida. Identification of protein kinase A signalling molecules in renal collecting ducts. *J Physiol.* 2023.04;
1. Makiko Mori, Yuki Nakao, Yutaro Mori. Renal tubular organoids as a new pathophysiological model *The CELL.* 2023.04; 55(4); 76-79
2. Cardio-Renal Sarcopenia Syndrome 2023.03; 2(1); 32-52

[Conference Activities & Talks]

1. Takayasu Mori, Takuya Fujimaru, Chunyu Liu, Karynne Patterson, Kohei Yamamoto, Takefumi Suzuki, Motoko Chiga, Shintaro Mandai, Fumiaki Ando, Yutaro Mori, Koichiro Susa, Yue-Qiu Tan, Feng Zhang, Shinichi Uchida, Eisei Sohara. Discovery of a Novel Candidate Gene Implicated in X-Linked Polycystic Kidney Disease. *Kidney Week 2023* 2023.11.04
2. Amrendra K. Ajay, Yutaro Mori, Venkata Sabbiseti, Joseph V. Bonventre. Screening for Small-Molecule Inhibitor for KIM-1 and Its Functional Validation in Kidney Fibrosis. *Kidney Week 2023* 2023.11.04

3. Yuki Nakao, Yutaro Mori, Makiko Mori, Shintaro Mandai, Tamami Fujiki, Fumiaki Ando, Koichiro Susa, Takayasu Mori, Eisei Sohara, Shinichi Uchida. Tubuloids on Primary Human Renal Tubular Epithelial Cells (hRTECs) Recapitulates Cisplatin-Induced Kidney Injury. Kidney Week 2023 2023.11.04 Philadelphia
4. Takuya Fujimaru, Takayasu Mori, Motoko Chiga, Shintaro Mandai, Yu Hara, Tamami Fujiki, Hiroaki Kikuchi, Yutaro Mori, Fumiaki Ando, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Shinichi Uchida, Eisei Sohara.. Monoallelic IFT140 Pathogenic Variants in Adult Polycystic Kidney Disease Patients Without Family History.. ASN Kidney Week 2023 2023.11.04 Philadelphia
5. Makiko Mori, Yutaro Mori, Corby Fink, Takaharu Ichimura, Keisuke Sako, Yuki Nakao, Astrid Weins, Shinichi Uchida, Joseph V. Bonventre. Kidney Injury Molecule-1 Is an Independent Receptor from ACE2 for SARS-CoV-2 in Lung and Kidney. Kidney Week 2023 2023.11.03 Philadelphia
6. Yu Hara, Fumiaki Ando, Hideki Yanagawa, Soichiro Suzuki, Tamami Fujiki, Shintaro Mandai, Yutaro Mori, Koichiro Susa, Takayasu Mori, Eisei Sohara, Shinichi Uchida.. LRBA Signalosomes Activate Vasopressin-Induced AQP2 Trafficking at Recycling Endosomes.. ASN Kidney Week 2023 2023.11.03 Philadelphia
7. Shunsuke Inaba, Shintaro Mandai, Yuta Nakano, Hisazumi Matsuki, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Shotaro Naito, Eisei Sohara, Shinichi Uchida.. The Transcriptomic Landscape of microRNAs Encapsulated in Circulating Extracellular Vesicles and CKD Progression in Japanese Adults.. ASN Kidney Week 2023 2023.11.03 Philadelphia
8. Kikuchi H, Knepper MA.. PPAR α , as the key determinant of kidney size, Revealed by Multi-Omics.. The 56th Annual Meeting of American Society of Nephrology 2023. 2023.11.02 Philadelphia, PA
9. Yuta Nakano, Shintaro Mandai, Shotaro Naito, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Eisei Sohara, Shinichi Uchida.. Association Among Bone Mass, Muscle Mass and Strength, Mortality, and CKD Progression in Older Adults.. ASN Kidney Week 2023 2023.11.02 Philadelphia
10. Takayasu Mori, Takuya Fujimaru, Chunyu Liu, Karynne Patterson, Kohei Yamamoto, Takefumi Suzuki, Motoko Chiga, Shintaro Mandai, Fumiaki Ando, Yutaro Mori, Koichiro Susa, University of Washington Center for Rare Disease Research, Yue-Qiu Tan, Feng Zhang, Shinichi Uchida, Eisei Sohara. Discovery of a Novel Candidate Gene Implicated in X-Linked Polycystic Kidney Disease. ASN Kidney Week 2023 2023.11 Philadelphia
11. Takayasu Mori, Takuya Fujimaru, Chunyu Liu, Karynne Patterson, Kohei Yamamoto, Takefumi Suzuki, Motoko Chiga, Danny E Miller, Miranda PG Zalusky, Shintaro Mandai, Fumiaki Ando, Yutaro Mori, Hiroaki Kikuchi, Koichiro Susa, University of Washington Center for Rare Disease Research, Jessica X. Chong, Michael J. Bamshad, Yue-Qiu Tan, Feng Zhang, Shinichi Uchida, Eisei Sohara. Discovery of a novel responsible gene implicated in X-linked polycystic kidney disease. 第7回文京腎研究会 2023.10.19 東京/Web
12. Hara Yu. LRBA is essential for urinary concentration and body water homeostasis. 第66回日本腎臓学会総会 2023.06.11 横浜
13. Makiko Mori, Yutaro Mori, Takaharu Ichimura, Keisuke Sako, Shinichi Uchida, Joseph V. Bonventre. Kidney Injury Molecule-1 (KIM-1) is a Receptor for SARS-CoV-2 in Lung and Kidney. 第66回日本腎臓学会学術総会 2023.06.10 横浜
14. Shintaro Mandai. Signature Analyses for Circulating Extracellular Vesicle-Propagated MicroRNAs Reveal VEGFA as a Key Molecule for Vascular Calcification in Chronic Kidney Disease. The 66th Annual Meeting of the Japanese Society of Nephrology 2023.06.09 横浜
15. Hisazumi Matsuki, Shintaro Mandai, Takaaki Koide, Naohiro Takahashi, Tomoki Yanagi, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Eisei Sohara, Shinichi Uchida. A brain proteomic signature of chronic kidney disease uncovers blood-brain barrier breakdown via urea-activated matrix metalloproteinase-2. 第66回日本腎臓学会学術総会 2023.06.09 横浜

16. Yuta Nakano, Shintaro Mandai, Shotaro Naito, Tamami Fujiki, Yutaro Mori, Fumiaki Ando, Takayasu Mori, Koichiro Susa, Soichiro Iimori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Impact of Osteosarcopenia on Mortality and CKD Progression: A Prospective Observational Cohort Study. 第66回日本腎臓学会学術総会 2023.06.09 横浜
17. Kikuchi Hiroaki, Knepper Mark A., Chou Chun-Lin, Yang Chin-Rang, Chen Lihe, Jung Hyun Jun, Limbutara Kavee, Carter Benjamin. マルチオミクスが明らかにした腎代償性肥大の初期シグナル伝達イベント (Early Signaling Events in Renal Compensatory Hypertrophy Revealed by Multi-Omics). 第66回日本腎臓学会総会 2023.05.01 神奈川

[Awards & Honors]

1. Yutaro Mori. 2022 Tokyo Medical Association Medical Research Award Encouragement Award, Tokyo Medical Association, 2023.03
2. Yuu Hara. Young Investigator Award, Japanese Society of Nephrology, 2023.06
3. Yutaro Mori. Medical Research Encouragement Prize of The Japan Medical Association, Japan Medical Association, 2023.11

[Social Contribution]

1. Yutaro Mori. Peer Review for Biomedicine & Pharmacotherapy, Elsevier, 2023.09.03
2. Yutaro Mori. Peer Review for Frontiers in Bioscience-Landmark, IMR Press, 2023.11.01 - 2024.01.25
3. Yutaro Mori. Peer Review for Physiology, American Physiological Society, 2023.12.03 - 2024.01.04

Comprehensive Reproductive Medicine

2024.1.1

Professor : Naoyuki MIYASAKA

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(1) Research

Research divisions :

- 1) Research in physiology, endocrinology and metabolism in the reproductive medicine
- 2) Research of female physical and mental change with aging
- 3) Pathophysiological examination of gynecological malignant tumor
- 4) Clinical research and basic research in perinatal medicine

Available scientific procedures :

- 1, Cell culture technique of ovarian granulosa cells, endometrial cells, malignant cells, osteoblast and so on.
- 2, Determination of intracellular calcium (by Fura 2 method and patch clamp)
- 3, Measurement of intra-cellular IP3
- 4, Hormonal assay in plasma, urine, follicular fluid (RIA & EIA)
- 5, Immunohistochemistry with ABC method
- 6, Analysis of micro-structure with electrical microscopy
- 7, Determination with molecular biological technique.
- 8, Physiological determination with isometric tension change
- 9, Determination of cerebral blood flow with MRI in cerebral infarction
- 10, Analysis of protein expression with flow cytometry

(2) Education

CRM (OB/GY) department has an obligation to offer medical services, education, research as one of the clinical departments in national graduate school, and has duty on making a mutual cooperation with local gynecological institutions.

Our main objectives are

- 1, Investigation for a new progress in treatment technique
- 2, Acquisition of medical knowledge and procedure
- 3, Providing systemic lecture about women's physiological and pathological change during adolescence through

senescence.

Aims of research works are focusing on reproductive medicine, perinatal medicine and oncology.

Educational intention in medical doctor course and nursing course includes systemic lectures, clinical conferences and special lecture by many extramural speakers. During Bed-Side Learning period, students should be treated as one of medical stuffs, attend all of deliveries and be present at gynecological procedure. Several OB/GY institutions will be provided as an extramural drills.

(3) Clinical Performances

For intractable sterilization, satisfactory results are obtained with endoscopic examinations and IVF-ET methods. Health care unit for menopausal women was established, where inspections for atherosclerosis, osteoporosis (DEXA), autonomic nervous system are performed, and postmenopausal managements are provided including HRT, mental care and counseling.

After construction of LDR(labor, delivery, recovery) unit, cure for complicated pregnancies is now carried out, and cases of deliveries are rising now.

Malignant gynecological tumor is also an important aim of this department, for which surgery, chemotherapy and radiotherapy with complete cure are applied to patients. For benign tumor and endometriosis, laparoscopic operations are aggressively performed, whose number is now increasing.

(4) Publications

[Original Articles]

1. Yamashita M, Tomoda T, Mizuo A, Isoda T, Egawa M, Yoshida M, Toki T, Kudo K, Terui K, Ito E, Morio T, Takagi M. Transient erythroblastopenia due to a GATA1 variant in an infant female. *Pediatric blood & cancer*. 2023.12; e30834
2. Aizawa R, Ibayashi M, Mitsui J, Tsukamoto S. Lipid droplet formation is spatiotemporally regulated in oocytes during follicular development in mice. *The Journal of reproduction and development*. 2023.12;
3. Ota, K; Mitsui, J; Katsumata, S; Takayanagi, Y; Nako, Y; Tajima, M; Komiya, A; Takahashi, T; Kawai, K. Seasonal Serum 25(OH) Vitamin D Level and Reproductive or Immune Markers in Reproductive-Aged Women with Infertility: A Cross-Sectional Observational Study in East Japan *NUTRIENTS*. 2023.12; 15(24);
4. Masakazu Terauchi, Tsuyoshi Higuchi. Women's Health Care Committee, Japan Society of Obstetrics and Gynecology: Annual report-2023. *J Obstet Gynaecol Res*. 2023.11; 49(11); 2602-2619
5. Yoshino Y, Yanai S, Sawada M, Sakate S, Kanno K, Hada T, Ueda T, Tabata T, Omori M, Andou M. Extraovarian Dysgerminoma Involving the Uterine Cervix: A Rare Case Report With Literature Review *Int J Gynecol Pathol*. 2023.11; 42(6); 544-549
6. Terauchi Masakazu, Higuchi Tsuyoshi. Women's Health Care Committee, Japan Society of Obstetrics and Gynecology: Annual report-2023(タイトル和訳中) *The Journal of Obstetrics and Gynaecology Research*. 2023.11; 49(11); 2602-2619
7. Takashi Takeda, Kana Yoshimi, Fumi Inoue, Tamami Odai, Nahoko Shirato, Zen Watanabe, Tempei Otsubo, Masakazu Terauchi. Gender Differences in Premenstrual Syndrome and Premenstrual Dysphoric Disorder Diagnosis and Treatment among Japanese Obstetricians and Gynecologists: A Cross-Sectional Study *Tohoku J Exp Med*. 2023.10; 261(2); 95-101
8. Takeda Takashi, Yoshimi Kana, Inoue Fumi, Odai Tamami, Shirato Nahoko, Watanabe Zen, Otsubo Tempei, Terauchi Masakazu. Gender Differences in Premenstrual Syndrome and Premenstrual Dysphoric Disorder Diagnosis and Treatment among Japanese Obstetricians and Gynecologists: A Cross-Sectional Study(タイトル和訳中) *The Tohoku Journal of Experimental Medicine*. 2023.10; 261(2); 95-101
9. Rika Murakami, Midori Natsume, Kentaro Ito, Shukuko Ebihara, Masakazu Terauchi. Effect of Flavanol-Rich Cacao Extract on the Profile of Mood State in Healthy Middle-Aged Japanese Women: A Randomized, Double-Blind, Placebo-Controlled Pilot Study *Nutrients*. 2023.09; 15; 3843

10. Kidera N, Ishikawa T, Kawamura T, Miyasaka N. Maternal body mass index is not associated with assisted reproductive technology outcomes. *Scientific reports*. 2023.09; 13(1); 14817
11. Masakazu Terauchi, Jocelyn Y Cheng, Jane Yardley, Kate Pinner, Margaret Moline, Manoj Malhotra, Kanako Inabe, Maika Nishida, Elizabeth Pappadopulos. Efficacy and safety of lemborexant in midlife women with insomnia disorder. *Menopause*. 2023.08; 30(8); 839-848
12. Higashide R, Saito K, Hashido N, Ishikawa T, Miyasaka N. Step-by-step instructions for detecting whirlpool sign in adnexal torsion. *Journal of rural medicine : JRM*. 2023.07; 18(3); 189-193
13. Ochi Y, Yanai S, Yoshino Y, Sawada M, Sakate S, Kanno K, Andou M. Clinical use of mixed reality for laparoscopic myomectomy *Int J Gynaecol Obstet*. 2023.07; 162(1); 364-365
14. Asuka Hirose, Masakazu Terauchi, Tamami Odai, Ayako Fudono, Kotoi Tsurane, Masaki Sekiguchi, Misako Iwata, Tatsuhiko Ando, Kunihiro Takahashi, Miyasaka Naoyuki.. Investigation of exacerbating factors for postpartum hair loss: a questionnaire-based cross-sectional study *International Journal of Women' s Dermatology* . 2023.06; (9(2)); e84
15. Naoyuki Yoshiki, Kaoru Kato, Junichi Sasaki. Laparoscopic Retrieval of a Retained Foreign Body Embedded in the Retroperitoneum. *The Journal of Minimally Invasive Gynecology*. 2023.06; 30(6); 431-432
16. Kana Yoshimi, Fumi Inoue, Tamami Odai, Nahoko Shirato, Zen Watanabe, Tempei Otsubo, Masakazu Terauchi, Takashi Takeda. Current status and problems in the diagnosis and treatment of premenstrual syndrome and premenstrual dysphoric disorder from the perspective of obstetricians and gynecologists in Japan *J Obstet Gynaecol Res*. 2023.05; 49(5); 1375-1382
17. Fang Yuan, Satoshi Obayashi, Ayumi Yamaguchi, Natsuki Yatabe, Chihiro Mano, Makoto Iizuka, Yoshinori Ohkura, Naoyuki Miyasaka. 17 α -ethinylestradiol modulates endothelial function in ovariectomized rat carotid arteries *European Journal of Pharmacology*. 2023.04; 944; 175525
18. Mitsui, J; Ota, K; Yamashita, H; Sujino, T; Hiraoka, K; Katsumata, S; Takayanagi, Y; Nako, Y; Tajima, M; Ohuchi, K; Hayashi, M; Ishikawa, T; Kawai, K. Predictive Factors for Empty Follicle Syndrome in Infertile Patients Undergoing Assisted Reproductive Technology Treatment: A Retrospective Cohort Study and Brief Literature Review *CLINICAL AND EXPERIMENTAL OBSTETRICS & GYNECOLOGY*. 2023.04; 50(4);
19. Ibayashi M, Aizawa R, Mitsui J, Tsukamoto S. Lipid droplet synthesis is associated with angiogenesis in mouse ovarian follicles $\uparrow$. *Biology of reproduction*. 2023.03; 108(3); 492-503
20. Mayuko Kazama, Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. Associations of fat mass index with hot flashes and lean mass index with insomnia in middle-aged women. *Climacteric*. 2023.02; 26(2); 161-166
21. Yomogita Hiroshi, Ito Hikaru, Hashimoto Kento, Kudo Akihiko, Fukushima Toshiaki, Endo Tsutomu, Hirate Yoshikazu, Akimoto Yoshihiro, Komada Masayuki, Kanai Yoshiakira, Miyasaka Naoyuki, Kanai-Azuma Masami. A possible function of Nik-related kinase in the labyrinth layer of delayed delivery mouse placentas(タイトル和訳中) *The Journal of Reproduction and Development*. 2023.02; 69(1); 32-40
22. Yomogita H, Ito H, Hashimoto K, Kudo A, Fukushima T, Endo T, Hirate Y, Akimoto Y, Komada M, Kanai Y, Miyasaka N, Kanai-Azuma M. A possible function of Nik-related kinase in the labyrinth layer of delayed delivery mouse placentas. *The Journal of reproduction and development*. 2023.02; 69(1); 32-40
23. Mitsui, J; Ota, K; Takayanagi, Y; Nako, Y; Tajima, M; Fukui, A; Kawai, K. Successful Pregnancy and Delivery at Term Following Intravenous Immunoglobulin Therapy with Heparin for Unexplained Recurrent Pregnancy Loss Suspected of Immunological Abnormalities: A Case Report and Brief Literature Review *JOURNAL OF CLINICAL MEDICINE*. 2023.02; 12(4);
24. Tamaoka S, Saito K, Yoshida T, Nakabayashi K, Tatsumi K, Kawamura T, Matsuzaki T, Matsubara K, Ogata-Kawata H, Hata K, Kato-Fukui Y, Fukami M. Exome-based genome-wide screening of rare variants associated with the risk of polycystic ovary syndrome. *Reproductive medicine and biology*. 2023.01; 22(1); e12504

25. Egawa M, Kanda E, Ohtsu H, Nakamura T, Yoshida M. Hypertensive Disorders of Pregnancy are Associated with Cardiovascular Disease in Middle- and Older-Aged Japanese Women. *Journal of atherosclerosis and thrombosis*. 2023.01; 30(10); 1420-1426
26. Ryo Higashide, Kazuki Saito, Nanako Hashido, Tomonori Ishikawa, and Naoyuki Miyasaka. Step-by-step instructions for detecting whirlpool sign in adnexal torsion *Journal of Rural Medicine*. 2023; 189-193

[Conference Activities & Talks]

1. Masakazu Terauchi. Symposium 2. Cancer and Bone "Management manual for cancer treatment-induced bone loss (CTIBL): position statement of the JSBMR". 35th Fall Scientific Congress of the Korean Society for Bone and Mineral Research 2023.11.11 Seoul
2. Masakazu Terauchi. Special lecture "Psychological Aspects of the Menopause". 28th Annual Scientific Meeting of the Korean Society of Psychosomatic Obstetrics and Gynecology 2023.10.22 Seoul, Korea
3. Masakazu Terauchi. Parallel Session 4 Lifestyle Management and Rehabilitative Aspect of Menopausal Women "Estrogen Deficiency, Oxidative Stress, and Bone Loss in Postmenopausal Women: Protection by Antioxidants". 9th Scientific Meeting of the Asia Pacific Menopause Federation 2023.10.08 Bali, Indonesia
4. Masakazu Terauchi. Parallel Session 7 MHT and Adjuvant Therapy for Menopausal Women "Isoflavones and S-Equol for Women's Midlife Health". 9th Scientific Meeting of the Asia Pacific Menopause Federation 2023.10.08 Bali, Indonesia
5. 寺内公一. 特別講演「月経困難症・子宮内膜症の薬物療法 Up to Date ～患者志向の治療戦略とは～」. 令和5年度群馬産科婦人科学会・群馬県産婦人科医会集談会 2023.07.15 前橋
6. Fang Yuan, Satoshi Obayashi, Naoyuki Miyasaka. 17 α -ethinylestradiol modulates endothelial function in ovariectomized rat carotid arteries. 第75回日本産科婦人科学会学術講演会 2023.05.12 東京国際フォーラム
7. Satoru Aoyama, Takashi Kamatani, Kousuke Tanimoto, Junko Yokobori, Eriko Takamine, Makiko Egawa, Yuki Kato, Susumu Kirimura, Ichiro Ohnishi, Kouichiro Kimura, Takahiro Asakage, Sadakatsu Ikeda. Case report: Myxofibrosarcoma in the head and neck region with rare TP53 aberration in the background of retinoblastoma.. 2023 the Japanese Society of Medical Oncology Annual Meeting 2023.03.17
8. Yuan Fang, Obayashi Satoshi, Miyasaka Naoyuki. 卵巣摘出ラット頸動脈における Ethinylestradiol(EE2)の内皮機能調節作用 (Ethinylestradiol(EE2) modulates endothelial function in ovariectomized rat carotid arteries). 日本産科婦人科学会雑誌 2023.02.01
9. Takahashi Ken, Samura Osamu, Hasegawa Akihiro, Ookubo Haruna, Morimoto Keiji, Horiya Madoka, Okamoto Aikou, Ochiai Daigo, Tanaka Mamoru, Sekiguchi Masaki, Miyasaka Naoyuki, Suzuki Yuto, Tabata Tsutomu, Hayata Eijiro, Nakata Masahiko, Suzuki Tomoo, Nishi Hirotaka, Toda Yumi, Tanigaki Shinji, Furuya Natsumi, Hasegawa Junichi, Tamaru Shunsuke, Kamei Yoshimasa, Sayama Seisuke, Nagamatsu Takeshi, Takahashi Yuka, Kitagawa Michihiro, Arakaki Tatsuya, Sekizawa Akihiko. 日本における妊婦の COVID-19 mRNA ワクチン接種状況と課題 多施設共同後ろ向き質問紙調査 (COVID-19 mRNA vaccination status and issues among pregnant women in Japan: a multicenter retrospective questionnaire survey). 日本産科婦人科学会雑誌 2023.02.01
10. Odai Tamami, Ohno Haruko, Nakamura Reiko, Tsukada Takafumi, Oshima Noriko, Wakana Kimio, Miyasaka Naoyuki. Primary pulmonary choriocarcinoma diagnosed by histopathologic and genetic examination(タイトル和訳中). *The Journal of Obstetrics and Gynaecology Research* 2023.01.01
11. Odai Tamami, Ohno Haruko, Nakamura Reiko, Tsukada Takafumi, Oshima Noriko, Wakana Kimio, Miyasaka Naoyuki. Primary pulmonary choriocarcinoma diagnosed by histopathologic and genetic examination(タイトル和訳中). *The Journal of Obstetrics and Gynaecology Research* 2023.01.01
12. Odai Tamami, Ohno Haruko, Nakamura Reiko, Tsukada Takafumi, Oshima Noriko, Wakana Kimio, Miyasaka Naoyuki. 組織病理学および遺伝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). *The Journal of Obstetrics and Gynaecology Research* 2023.01.01

Gastrointestinal Surgery

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Associate Professor

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Shigeo, HARUKI, Kenro KAWADA

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Toshiro TANIOKA, Keisuke OKUINO, Shinichi YAMAUCHI

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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,

Hirofumi 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, Sakiko ASANO,

Syota ARIGA, Hayato IKAWA, Kei ISHIHARA, Yuki TADOKORO,

Keiji TSUKAHARA, Hiroaki TSUJI, Mari NAKAGAWA, Takamasa FUJITA,

Masahiro FUSE, Kenta YAO, Yurina YASUI, Yusuke YATABE

(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]

1. S Arai, Y Yamaoka, A Shiomi, H Kagawa, H Hino, S Manabe, K Chen, K Nanishi, C Maeda, A Notsu, Y Kinugasa. Efficacy of laparoscopic surgery for loop colostomy: a propensity-score-matched analysis Techniques in coloproctology. 2023.12; 27(12); 1319-1326
2. Yuriko Matsumiya, Mitsukuni Suenaga, Toshiaki Ishikawa, Toshifumi Kudo, Tsuyoshi Nakagawa, Kentaro Okamoto, Masanori Tokunaga, Claudia Hurtado, Yuki Yamada, Kentaro Oka, Motomichi Takahashi, Luis Francisco Lopez Kostner, Miguel Luis O'Ryan Gallardo, Hiroyuki Uetake, Yusuke Kinugasa. Clinical significance of *Bacteroides fragilis* as a potential prognostic factor in colorectal cancer Anaerobe. 2023.12; 84:102784;
3. Marie Hanaoka, Yusuke Kinugasa, Yoshihiro Sakai, Masanori Tokunaga. World's first report of sigmoidectomy for sigmoid cancer using the Soroa surgical system with tactile feedback Updates in surgery. 2023.12; 75(8); 2395-2401
4. Takashi Shigeno, Daisuke Kajiyama, Kazuma Sato, Naoto Fujiwara, Yusuke Kinugasa, Tomonori Yano, Hiroyuki Daiko, Takeo Fujita. The feasibility of post-photodynamic therapy salvage esophagectomy in patients with esophageal squamous cell carcinoma treated with definitive chemoradiotherapy Esophagus. 2023.10; 20(4); 643-650
5. Shunsuke Kasai, Hiroyasu Kagawa, Akio Shiomi, Hitoshi Hino, Shoichi Manabe, Yusuke Yamaoka, Kai Chen, Kenji Nanishi, Chikara Maeda, Yusuke Kinugasa. Long-term outcomes of upfront robotic rectal cancer surgery: a single-center, retrospective cohort study in Japan Surgery today. 2023.09; 53(9); 1028-1037
6. Ryosuke Kikuchi, Kazuhito Sasaki, Hiroaki Nozawa, Koji Muro, Shigenobu Emoto, Shinichi Yamauchi, Kenichi Sugihara, Soichiro Ishihara. Prognosis of Inferior Mesenteric and Para-aortic Lymph Node Metastases in Rectal Cancer: A Multicenter Study Anticancer research. 2023.09; 43(9); 4213-4219

7. Hiroyasu Kagawa, Yusuke Kinugasa, Tomohiro Yamaguchi, Masayuki Ohue, Kazushige Kawai, Junichiro Hiro, Seiichi Shinji, Hiroaki Nozawa, Yasumitsu Hirano, Koji Komori, Yasumasa Takii, Takeshi Suto, Shunsuke Tsukamoto, Yoshito Akagi, Heita Ozawa, Yuji Toiyama, Kazuhito Minami, Tomoharu Shimizu, Kay Uehara, Kazuhiro Sakamoto, Keita Mori, Kenichi Sugihara, Yoichi Ajioka. Impact of resection for ovarian metastases from colorectal cancer and clinicopathologic analysis: A multicenter retrospective study in Japan *Annals of Gastroenterological Surgery*. 2023.09; 14;8(2); 273-283
8. Keisuke Okuno, Muhammad Yogi Pratama, Jiang Li, Masanori Tokunaga, Xin Wang, Yusuke Kinugasa, Ajay Goel. Ginseng mediates its anti-cancer activity by inhibiting the expression of DNMTs and reactivating methylation-silenced genes in colorectal cancer *Carcinogenesis*. 2023.08; 10;44(5); 394-403
9. Guglielmo Niccolò Piozzi, Krunal Khobragade, Vusal Aliyev, Oktar Asoglu, Paolo Pietro Bianchi, Vlad-Olimpiu Butiurca, William Tzu-Liang Chen, Ju Yong Cheong, Gyu-Seog Choi, Andrea Coratti, Quentin Denost, Yosuke Fukunaga, Emre Gorgun, Francesco Guerra, Masaaki Ito, Jim S Khan, Hye Jin Kim, Jin Cheon Kim, Yusuke Kinugasa, Tsuyoshi Konishi, Li-Jen Kuo, Mehmet Ayhan Kuzu, Jeremie H Lefevre, Jin-Tung Liang, John Marks, Călin Molnar, Yves Panis, Philippe Rouanet, Eric Rullier, Avanish Saklani, Antonino Spinelli, Petr Tsarkov, Shunsuke Tsukamoto, Martin Weiser, Seon Hahn Kim. International standardization and optimization group for intersphincteric resection (ISOG-ISR): modified Delphi consensus on anatomy, definition, indication, surgical technique, specimen description and functional outcome *Colorectal disease*. 2023.08; 25(9); 1896-1909
10. Takahiro Igaki, Daichi Kitaguchi, Hiroki Matsuzaki, Kei Nakajima, Shigehiro Kojima, Hiro Hasegawa, Nobuyoshi Takeshita, Yusuke Kinugasa, Masaaki Ito. Automatic Surgical Skill Assessment System Based on Concordance of Standardized Surgical Field Development Using Artificial Intelligence *JAMA surgery* (Journal of the American Medical Association surgery) . 2023.08; 1;158(8); e231131
11. Toshiro Tanioka, Yusuke Yatabe, Toshifumi Saito, Kazuya Yamaguchi, Hisashi Fujiwara, Yuya Sato, Kenro Kawada, Shigeo Haruki, Masanori Tokunaga, Yusuke Kinugasa. Optimal placement of self-fixating mesh in the rectus abdominis muscle for ventral hernia repair when using the enhanced-view totally extraperitoneal Rives-Stoppa technique *Asian journal of endoscopic surgery*. 2023.07; 16(3); 653-657
12. Yutaka Tokairin, Yudai Kawamura, Satoru Muro, Kagami Nagai, Kenro Kawada, Takuya Okada, Suthasinee Tharnmanularp, Areeya Jiamjunyasiri, Keiichi Akita, Yusuke Kinugasa. Histological study of the thin membranous dense connective tissues around the curving portion of the bilateral recurrent laryngeal nerves *Esophagus*. 2023.07; 20(3); 410-419
13. Ryo Seishima, Koji Okabayashi, Hiroki Ikeuchi, Motoi Uchino, Kitaro Futami, Tatsuki Noguchi, Hiroki Ohge, Yasuhito Iseki, Kazuhiro Watanabe, Michio Itabashi, Kinya Okamoto, Yuji Toiyama, Takayuki Ogino, Masafumi Nakamura, Kazutaka Yamada, Toshifumi Wakai, Yu Sato, Hideaki Kimura, Kenichi Takahashi, Koya Hida, Yusuke Kinugasa, Fumio Ishida, Junji Okuda, Koji Daito, Fumikazu Koyama, Hideki Ueno, Takayuki Yamamoto, Seiichiro Yamamoto, Tsunekazu Hanai, Atsuo Maemoto, Junya Arakaki, Koji Komori, Yoshito Akagi, Dai Shida, Shigeki Yamaguchi, Keiji Matsuda, Kiyoshi Maeda, Toshihiro Noake, Riichiro Nezu, Shin Sasaki, Junichi Hasegawa, Eiji Sunami, Yukihide Kanemitsu, Kenji Katsumata, Kei Uehara, Tomomichi Kiyomatsu, Takeshi Suto, Shinsuke Kazama, Takeshi Yamada, Takenori Goi, Soichiro Ishihara, Yoichi Ajioka, Kenichi Sugihara. Effect of Biologics on the Risk of Advanced-Stage Inflammatory Bowel Disease-Associated Intestinal Cancer: A Nationwide Study *The American journal of gastroenterology*. 2023.07; 1;118(7); 1248-1255
14. Toshifumi Saito, Satoru Muro, Hisashi Fujiwara, Yuya Umebayashi, Yuya Sato, Masanori Tokunaga, Keiichi Akita, Yusuke Kinugasa. Histological study of the structural layers around the esophagus in the lower mediastinum *World Journal of Gastrointestinal Surgery*. 2023.07; 15(7); 1331-1339
15. Yudai Yamamoto, Shu Shimada, Yoshimitsu Akiyama, Shu Tsukihara, Raizo Sugimoto, Ayano Kabashima, Masanori Tokunaga, Yusuke Kinugasa, Yutaka Kawakami, Shinji Tanaka. RTP4 silencing provokes tumor-intrinsic resistance to immune checkpoint blockade in colorectal cancer *Journal of gastroenterology*. 2023.06; 58(6); 540-553
16. Tetsuo Sugishita, Masanori Tokunaga, Kenjiro Kami, Kozue Terai, Hiroyuki Yamamoto, Hajime Shinohara, Yusuke Kinugasa. Determination of the Minimum Sample Amount for Capillary Electrophoresis-Fourier Transform Mass Spectrometry (CE-FTMS)-Based Metabolomics of Colorectal Cancer Biopsies *Biomedicines*. 2023.06; 13;11(6); 1706

17. Megumi Sasaki, Yasumitsu Hirano, Kojun Okamoto, Isamu Koyama & Yusuke Kinugasa. Outcomes of Colorectal Cancer Surgery in Nonagenarian Patients Indian Journal of Surgery. 2023.06; published online:22 June 2023;
18. Takashi Shigeno, Masashi Kizuki, Masanori Tokunaga, Kiyohide Fushimi, Yusuke Kinugasa, Takeo Fujiwara. A comparison of the short-term outcomes between laparoscopic and robotic distal gastrectomy: A retrospective study using a nationwide inpatient database. Surgery. 2023.05; 173(5); 1169-1175
19. Marie Hanaoka, Hiroyasu Kagawa, Akio Shiomi, Hitoshi Hino, Shoichi Manabe, Yusuke Yamaoka, Yusuke Kinugasa. Risk factors for and longitudinal course of male sexual dysfunction after robotic rectal cancer surgery Colorectal disease. 2023.05; 25(5); 932-942
20. Shinichi Yamauchi, Akio Shiomi, Chu Matsuda, Ichiro Takemasa, Tsunekazu Hanai, Mamoru Uemura, Yusuke Kinugasa. Robotic-assisted colectomy for right-sided colon cancer: Short-term surgical outcomes of a multi-institutional prospective cohort study in Japan Annals of Gastroenterological Surgery. 2023.05; 2023(00); 1-8
21. Yuya Umebayashi, Satoru Muro, Masanori Tokunaga, Toshifumi Saito, Yuuya Sato, Toshiro Tanioka, Yusuke Kinugasa, Keiichi Akita. Distribution of splenic artery lymph nodes and splenic hilar lymph nodes World Journal of Gastrointestinal Surgery. 2023.05; 15(5); 812-824
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28. Keisuke Okuno, Caiming Xu, Silvia Pascual-Sabater, Masanori Tokunaga, Tetsuji Takayama, Haiyong Han, Cristina Fillat, Yusuke Kinugasa, Ajay Goel. Andrographis Reverses Gemcitabine Resistance through Regulation of ERBB3 and Calcium Signaling Pathway in Pancreatic Ductal Adenocarcinoma. Biomedicine. 2023.01; 11(1);
29. Keisuke Okuno, Raju Kandimalla, Marta Mendiola, Francesc Balaguer, Luis Bujanda, Carlos Fernandez-Martos, Jorge Aparicio, Jaime Feliu, Masanori Tokunaga, Yusuke Kinugasa, Joan Maurel, Ajay Goel. A microRNA signature for risk-stratification and response prediction to FOLFOX-based adjuvant therapy in stage II and III colorectal cancer. Mol Cancer. 2023.01; 22(1); 13

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[Misc]

1. Keisuke Okuno, Masanori Tokunaga, Daniel Von Hoff, Yusuke Kinugasa, Ajay Goel; The PDAC Biomarker Working Group. Intratumoral Malassezia globosa Levels Predict Survival and Therapeutic Response to Adjuvant Chemotherapy in Patients With Pancreatic Ductal Adenocarcinoma Gastroenterology. 2023.04; Online ahead of print;

[Conference Activities & Talks]

1. Yusuke Kinugasa. Lateral lymph node dissection, YES(JAPAN). 18th Scientific Conference (European Society of Coloproctology Vilnius 2023) 2023.09.29 Vilnius
2. Shinichi Yamauchi, Ayumi Takaoka, Megumi Sasaki, Marie Hanaoka, Kenichi Sugihara, Yusuke Kinugasa. Clinical significance of extended lateral lymph node dissection for lower rectal cancer: A propensity score analysis in a multicenter retrospective study. 18th Scientific Conference (European Society of Coloproctology Vilnius 2023) 2023.09.29 Vilnius
3. Marie Hanaoka, Ayumi Takaoka, Megumi Sasaki, Shinichi Yamauchi, Yusuke Kinugasa. Methods and short-term outcomes of total colectomy: Short-term outcomes and evaluation of defecatory function. 18th Scientific Conference (European Society of Coloproctology Vilnius 2023) 2023.09.29 Vilnius
4. Toshiro Tanioka, Ayumi Takaoka, Keisuke Okuno, Megumi Sasaki, Taichi Ogo, Marie Hanaoka, Hisashi Fujiwara, Kenro Kawada, Shigeo Haruki, Masanori Tokunaga, Yusuke Kinugasa. Enhanced view totally extraperitoneal approach (eTEP) for ventral and incisional hernia repair. 18th Annual International Congress of the Asia Pacific Hernia Society 2023 (APHS2023) 2023.09.22 Pennang
5. Yusuke Kinugasa. Current status of robotic colorectal cancer surgery in Japan. Minimally Invasive Surgery and Multidisciplinary Treatment for Colorectal Cancer 2023.08.26 Taipei
6. 渡辺秀一、奥野圭祐、石川喜也、上田浩樹、赤星径一、小野宏晃、工藤篤、田中真二、絹笠祐介、田邊稔. マイクロ RNA と MSI で胃がん早期再発例を予測する. 第 78 回日本消化器外科学会総会 2023.07.12 函館
7. Toshiro Tanioka, Kazuya Yamaguchi, Hisashi Fujiwara, Yuya Sato, Kenro Kawada, Shigeo Haruki, Masanori Tokunaga, Yusuke Kinugasa. Robotic-assisted gastrectomy for type 4 gastric cancer. International Gastric Cancer Congress 2023 (IGCC2023) 2023.06.17 Yokohama
8. Masanori Tokunaga, Yuya Sato, Toshiro Tanioka, Kazuya Yamaguchi, Hisashi Fujiwara, Kenro Kawada, Shigeo Haruki, Yusuke Kinugasa. Optimal treatment for patients with resectable gastric cancer. International Gastric Cancer Congress 2023 (IGCC2023) 2023.06.16 Yokohama
9. Yuya Sato, Masanori Tokunaga, Kazuya Yamaguchi, Hisashi Fujiwara, Toshiro Tanioka, Kenro Kawada, Shigeo Haruki, Yusuke Kinugasa. Development of prediction model of intra-abdominal infectious complication after gastrectomy with machine learning. International Gastric Cancer Congress 2023 (IGCC2023) 2023.06.15 Yokohama
10. Marie Hanaoka, Yusuke kinugasa. Robotic assisted lateral lymph node dissection: A gastrointestinal surgical perspective. The 110th Annual Meeting of the Japanese Urological Association 2023.04.21 Kobe
11. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairou Ryoutokuji, Takuya Okada, Yutaka Miyawaki, Youichi Kumagai, Kagami Nagai, Tatsuyuki Kawano. . Efficacy of endoscopy for evaluating esophago-gastric anastomosis on post-esophagectomy day 1. . 14th World Congress of the International Society for Diseases of the Esophagus

Thoracic Surgery

Professor	Kenichi Okubo
Associate professor	Hironori Ishibashi
Assistant professor	Ryo Wakejima
Assistant professor	Syunichi Baba
Assistant professor	Ayaka Asakawa
Graduate Student	Yuya Ishikawa
Graduate Student	Yasuyuki Kurihara
Graduate Student	Yusuke Sugita
Graduate Student	Hiroto Tomo Takahara
Graduate Student	Kuniyo Sueyoshi
Graduate Student	Ryota Ishizawa

(1) Outline

Department of Thoracic Surgery deal with clinical management, basic and clinical research, and education of thoracic surgery, which includes surgical diagnosis and treatment of respiratory diseases.

(2) Research

- Minimally invasive surgery for lung cancer
- Multimodal treatments for thoracic malignancies
- Surgery for metastatic lung tumors
- Clinico-pathological studies on lung cancer

(3) Education

Department of Thoracic Surgery has a mission to educate medical post-graduates for expert thoracic surgeons. Thoracic surgeon requires the Board of Surgery and the Board of Thoracic Surgery to perform clinical cares as a specialist. We provide clinical specialty course for thoracic surgery and graduate course for thoracic surgery, and support to obtain the boards.

(4) Clinical Services & Other Works

Out-patient Clinic: Tuesday, Thursday, Friday
 Operative Day: Monday, Wednesday, Friday
 Clinical Conference: Monday
 Chest Conference : Monday
 Clinico-pathological Conference: Wednesday
 Medical Round: every morning
 Professor's Round: Tuesday
 Journal Club: Tuesday (every other week)
 Mortality & Morbidity Conference: Tuesday (every other week)
 Lab Meeting: Tuesday (monthly)

Scientific Meeting: Japan Surgical Society, Japanese Association for Chest Surgery, Japanese Association for Thoracic Surgery, Japan Lung Cancer Society, Japan Society for Respiratory Endoscopy

(5) Clinical Performances

Thoracic Surgery deal with surgical treatment for lung, mediastinum, pleura and chest wall. We provide high-grade medical care as a university hospital. We offer less invasive surgery for early-stage lung cancers or benign diseases, and multimodality treatment for locally advanced thoracic malignancies.

(6) Publications

[Original Articles]

1. Shiraishi K, Takahashi A, Momozawa Y, Daigo Y, Kaneko S, Kawaguchi T, Kunitoh H, Matsumoto S, Horinouchi H, Goto A, Honda T, Shimizu K, Torasawa M, Takayanagi D, Saito M, Saito A, Ohe Y, Watanabe SI, Goto K, Tsuboi M, Tsuchihara K, Takata S, Aoi T, Takano A, Kobayashi M, Miyagi Y, Tanaka K, Suzuki H, Maeda D, Yamaura T, Matsuda M, Shimada Y, Mizuno T, Sakamoto H, Yoshida T, Goto Y, Yoshida T, Yamaji T, Sonobe M, Toyooka S, Yoneda K, Masago K, Tanaka F, Hara M, Fuse N, Nishizuka SS, Motoi N, Sawada N, Nishida Y, Kumada K, Takeuchi K, Tanno K, Yatabe Y, Sunami K, Hishida T, Miyazaki Y, Ito H, Amemiya M, Totsuka H, Nakayama H, Yokose T, Ishigaki K, Nagashima T, Ohtaki Y, Imai K, Takasawa K, Minamiya Y, Kobayashi K, Okubo K, Wakai K, Shimizu A, Yamamoto M, Iwasaki M, Matsuda K, Inazawa J, Shiraishi Y, Nishikawa H, Murakami Y, Kubo M, Matsuda F, Kamatani Y, Hamamoto R, Matsuo K, Kohno T. Identification of telomere maintenance gene variations related to lung adenocarcinoma risk by genome-wide association and whole genome sequencing analyses. *Cancer communications* (London, England). 2023.10;
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3. Kanda K, Nishimura H, Koiso T, Takemoto K, Nakagoe K, Yamada T, Takahashi M, Hanafusa M, Kawahara T, Yanagida Y, Kuramochi J, Fujiwara T. Applying negative ions and an electric field to countermeasure droplets/aerosol transmission without hindering communication. *Scientific reports*. 2023.08; 13(1); 13965
4. Shi J, Shiraishi K, Choi J, Matsuo K, Chen TY, Dai J, Hung RJ, Chen K, Shu XO, Kim YT, Landi MT, Lin D, Zheng W, Yin Z, Zhou B, Song B, Wang J, Seow WJ, Song L, Chang IS, Hu W, Chien LH, Cai Q, Hong YC, Kim HN, Wu YL, Wong MP, Richardson BD, Funderburk KM, Li S, Zhang T, Breeze C, Wang Z, Blechter B, Bassig BA, Kim JH, Albanes D, Wong JYY, Shin MH, Chung LP, Yang Y, An SJ, Zheng H, Yatabe Y, Zhang XC, Kim YC, Caporaso NE, Chang J, Ho JCM, Kubo M, Daigo Y, Song M, Momozawa Y, Kamatani Y, Kobayashi M, Okubo K, Honda T, Hosgood DH, Kunitoh H, Patel H, Watanabe SI, Miyagi Y, Nakayama H, Matsumoto S, Horinouchi H, Tsuboi M, Hamamoto R, Goto K, Ohe Y, Takahashi A, Goto A, Minamiya Y, Hara M, Nishida Y, Takeuchi K, Wakai K, Matsuda K, Murakami Y, Shimizu K, Suzuki H, Saito M, Ohtaki Y, Tanaka K, Wu T, Wei F, Dai H, Machiela MJ, Su J, Kim YH, Oh IJ, Lee VHF, Chang GC, Tsai YH, Chen KY, Huang MS, Su WC, Chen YM, Seow A, Park JY, Kweon SS, Chen KC, Gao YT, Qian B, Wu C, Lu D, Liu J, Schwartz AG, Houlston R, Spitz MR, Gorlov IP, Wu X, Yang P, Lam S, Tardon A, Chen C, Bojesen SE, Johansson M, Risch A, Bickeböller H, Ji BT, Wichmann HE, Christiani DC, Rennert G, Arnold S, Brennan P, McKay J, Field JK, Shete SS, Le Marchand L, Liu G, Andrew A, Kiemeny LA, Zienolddiny-Narui S, Grankvist K, Johansson M, Cox A, Taylor F, Yuan JM, Lazarus P, Schabath MB, Aldrich MC, Jeon HS, Jiang SS, Sung JS, Chen CH, Hsiao CF, Jung YJ, Guo H, Hu Z, Burdett L, Yeager M, Hutchinson A, Hicks B, Liu J, Zhu B, Berndt SI, Wu W, Wang J, Li Y, Choi JE, Park KH, Sung SW, Liu L, Kang CH, Wang WC, Xu J, Guan P, Tan W, Yu CJ, Yang G, Siho ADL, Chen Y, Choi YY, Kim JS, Yoon HI, Park IK, Xu P, He Q, Wang CL, Hung HH, Vermeulen RCH, Cheng I, Wu J, Lim WY, Tsai FY, Chan JKC, Li J, Chen H, Lin HC, Jin L, Liu J, Sawada N, Yamaji T, Wyatt K, Li SA, Ma H, Zhu M, Wang Z, Cheng S, Li X, Ren Y, Chao A, Iwasaki M, Zhu J, Jiang G, Fei K, Wu G, Chen CY, Chen CJ, Yang PC, Yu J, Stevens VL, Fraumeni JF Jr, Chatterjee N, Gorlova OY, Hsiung CA, Amos CI, Shen H, Chanock SJ, Rothman N, Kohno T, Lan

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 6. Ayaka Asakawa, Hironori Ishibashi, Shunichi Baba, Katsutoshi Seto, Ryo Wakejima, Kenichi Okubo. Usefulness of the Global Leadership Initiative on malnutrition (GLIM) criteria in preoperative nutritional assessment of patients with primary lung cancer *Clinical Nutrition ESPEN*. 2023.12; Online first (Epub);
 7. Yuya Ishikawa, Takaaki Sugino, Kenichi Okubo, Yoshikazu Nakajima. Detecting the location of lung cancer on thoracoscopic images using deep convolutional neural networks *Surgery Today*. 2023.12; 53(12); 1380-1387
 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*. 2023.04; 53(4); 287-296
 9. Hironori Ishibashi, Ryo Wakejima, Yasuyuki Kurihara, Katsutoshi Seto, Shunichi Baba, Ayaka Asakawa, Satoshi Toyama, Tokujiro Uchida, Kenichi Okubo. Extubation by supraglottic airway after lobectomy prevents cough-associated air leaks and prolonged coughing or sore throat *European Journal of Cardio-Thoracic Surgery*. 2023.05; 63(5); ezad158
 10. Yuting Yin, Rie Sakakibara, Takayuki Honda, Susumu Kirimura, Pissacha Daroonpan, Masashi Kobayashi, Kohei Ando, Hideki Ujiie, Tatsuya Kato, Kichizo Kaga, Takahiro Mitsumura, Ryoji Nakano, Hiroyuki Sakashita, Shinichi Matsuge, Hironori Ishibashi, Takumi Akashi, Yasuhiro Hida, Takao Morohoshi, Miyuki Azuma, Kenichi Okubo, Yasunari Miyazaki. High density and proximity of CD8+ T cells to tumor cells are correlated with better response to nivolumab treatment in metastatic pleural mesothelioma *Thorac Cancer*. 2023.07; 14(20); 1991-2000
 11. Kenichi Okubo, Hironori Ishibashi, Ryo Wakejima, Shunichi Baba, Ayaka Asakawa, Hiroshi Seshima. Extended pleurectomy/decortication and hyperthermic intraoperative intrapleural cisplatin perfusion for malignant pleural mesothelioma *JTCVS Open*. 2023.12; 16; 977-986

[Others]

1. A case of repeat oligoprogressive castration-resistant prostate cancer treated with pulmonary metastasectomy, 2023.07
IJU Case Report. 2023 Jul; 6(4): 216-218. Takahiko Soma, Soichiro Yoshida, Ryo Wakejima, Towako Taguchi, Shohei Fukuda, Hajime Tanaka, Minato Yokoyama, Kenichi Ohashi, Kenichi Okubo, and Yasuhisa Fujii
2. Pulmonary Artery Aneurysm in a Patient with Nontuberculous Mycobacteria Infection, 2023.08
Internal Medicine. 2023 Aug 9. doi: 10.2169/internalmedicine.2199-23. Online ahead of print. Soichi Maruyama, Haruhiko Furusawa, Satoshi Endo, Takashi Kumagai, Takahiro Mitsumura, Sho Shimada, Takashi Yamana, Rie Sakakibara, Yuki Iijima, Sho Shibata, Takayuki Honda, Tsuyoshi Shirai, Tsukasa Okamoto, Tomoya Tateishi, Meiyo Tamaoka, Yuko Kinowaki, Hironori Ishibashi, Kenichi Okubo, Yasunari Miyazaki
3. Pulmonary Mucormycosis Involving the Left Main Bronchus and the Pulmonary Artery, 2023.12
Annals of Thoracic and Cardiovascular Surgery. December 2023, Vol.29(6):315-318. Katsutoshi Seto, Rika Nohara, Yusuke Sugita, Hironori Ishibashi, Kenichi Okubo

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara

Visiting Professor Makoto Arai

Visiting Professor Masato Hasegawa

Associate Visiting Professor Yuichiro Mitaoka

Associate Visiting Professor Hidetaka Tannno

Graduate Student Mai Asakura, Akari

Nakamura, Kyoka Iino, Ittetsu Nakajima,

Fumiya Seki, Hikaru Ando, Riku Takahashi,

Minato Maeda, Anri Saito, Lanyu Huang,

Kayoko Shinozaki (April~), Yuga Yasuda

(April~), Kanata Imamura (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.

[Yuichiro Mitaoka] 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.

[Hidetaka Tanno] By applying high-throughput single-cell technology to cancer patient-derived samples, we analyze the immune responses in cancer patients at the single-cell level. We develop novel cancer therapeutics and diagnostic methods by utilizing the obtained results. We also create new technologies that are useful in immunology.

(2) Education

We will educate students for the purpose that they could investigate molecular mechanisms of life-threatening diseases such as cancer, diabetes, schizophrenia, amyotrophic lateral sclerosis, and 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

[Original Articles]

1. K. Miyashita, T. Yagi, N. Kagaya, A. Takechi, C. Nakata, R. Kanda, H. Nuriya, K. Tanegashima, S. Hoyano, F. Seki, C. Yoshida, Y. Hachiro, T. Higashi, N. Kitada, T. Toya, T. Kobayashi, Y. Najima, S. Goyama, S. A. Maki, T. Kitamura, N. Doki, K. Shin-ya, and T. Hara. Identification of compounds that preferentially suppress the growth of T cell acute lymphoblastic leukemia-derived cells. *Cancer Sci.*, 114: 4032-4040, 2023.
2. T. Higashi, C. Yoshida, Y. Hachiro, C. Nakata, A. Takechi, T. Yagi, K. Miyashita, N. Kitada, R. Obata, T. Hirano, T. Hara, and S. A Maki. Synthesis and anti-tumor activities in human leukemia-derived cells of polyenylpyrroles with a methyl group at the conjugated polyene terminus. *Bioorg. Med. Chem. Lett.*, 95: 129471, 2023.
3. K. Toriumi, K. Iino, A. Ozawa, M. Miyashita, S. Yamasaki, K. Suzuki, H. Sugawa, K. Tabata, S. Yamaguchi, S. Usami, M. Itokawa, A. Nishida, R. Nagai, H. Kamiguchi,

- and M. **Arai**. Glucuronic acid is a novel source of pentosidine, associated with schizophrenia. *Redox Biol.*, 67: 102876, 2023.
4. S. Son, M. **Arai**, K. Toriumi, C. Andica, D. Matsuyoshi, K. Kamagata, S. Aoki, T. Kawashima, T. Kochiyama, T. Okada, Y. Fushimi, Y. Nakamoto, Y. Kobayashi, T. Mura, M. Itokawa, and J. Miyata. Association between enhanced carbonyl stress and decreased apparent axonal density in schizophrenia by multimodal white matter imaging. *Sci. Rep.*, 13: 12220, 2023.
 5. R. Mizutani, R. Saiga, Y. Yamamoto, M. Uesugi, A. Takeuchi, K. Uesugi, Y. Terada, Y. Suzuki, V. De Andrade, F. De Carlo, S. Takekoshi, C. Inomoto, N. Nakamura, Y. Torii, I. Kushima, S. Iritani, N. Ozaki, K. Oshima, M. Itokawa, and M. **Arai**. Structural aging of human neurons is opposite of the changes in schizophrenia. *PLoS One*, 18 :e0287646, 2023.
 6. Y. H. Hsu, G. Pintacuda, R. Liu, E. Nacu, A. Kim, K. Tsafou, N. Petrossian, W. Crotty, J. M. Suh, J. Riseman, J. M. Martin, J. C. Biagini, D. Mena, J. K. T. Ching, E. Malolepsza, T. Li, T. Singh, T. Ge, S. B. Egri, B. Tanenbaum, C. R. Stanclift, A. M. Appfel. Schizophrenia Working Group of the Psychiatric Genomics Consortium; Stanley Global Asia Initiatives; S. A. Carr, M. Schenone, J. Jaffe, N. Fornelos, H. Huang, K. C. Eggan, and K. Lage. Using brain cell-type-specific protein interactomes to interpret neurodevelopmental genetic signals in schizophrenia. *iScience*, 26: 106701, 2023.
 7. Y. Tomita, K. Suzuki, S. Yamasaki, K. Toriumi, M. Miyashita, S. Ando, K. Endo, A. Yoshikawa, K. Tabata, S. Usami, M. Hiraiwa-Hasegawa, M. Itokawa, H. Kawaji, K. Kasai, A. Nishida, and M. **Arai**. Urinary exosomal microRNAs as predictive biomarkers for persistent psychotic-like experiences. *Schizophrenia (Heidelb)*, 9: 14, 2023.
 8. D. Arseni, R. Chen, A. G. Murzin, S. Y. Peak-Chew, H. J. Garringer, K. L. Newell, F. Kametani, A. C. Robinson, R. Vidal, B. Ghetti, M. Hasegawa, and B. Ryskeldi-Falcon. TDP-43 forms amyloid filaments with a distinct fold in type A FTLD-TDP. *Nature*, 620: 898-903, 2023.
 9. A. Tarutani, F. Kametani, M. Tahira, Y. Saito, M. Yoshida, A. C. Robinson, D. M. A. Mann, S. Murayama, T. Tomita, and M. Hasegawa. Distinct tau folds initiate templated seeding and alter the post-translational modification profile. *Brain*, 146: 4988-4999, 2023.
 10. C. Qi, M. Hasegawa, M. Takao, M. Sakai, M. Sasaki, M. Mizutani, A. Akagi, Y. Iwasaki, H. Miyahara, M. Yoshida, S. H. W. Scheres, and M. Goedert. Identical tau

- filaments in subacute sclerosing panencephalitis and chronic traumatic encephalopathy. *Acta. Neuropathol. Commun.*, 11: 74, 2023.
11. C. Qi, B. M. Verheijen, Y. Kokubo, Y. Shi, S. Tetter, A. G. Murzin, A. Nakahara, S. Morimoto, M. Vermulst, R. Sasaki, E. Aronica, Y. Hirokawa, K. Oyanagi, A. Kakita, B. Ryskeldi-Falcon, M. Yoshida, M. Hasegawa, S. H. W. Scheres, and M. Goedert. Tau Filaments from Amyotrophic Lateral Sclerosis/Parkinsonism-Dementia Complex (ALS/PDC) adopt the CTE Fold. *Proc. Natl. Acad. Sci. U.S.A.*, 120: e2306767120, 2023.
 12. I. Nakajima, T. Tsukimura, T. Ono, T. Shiga, H. Shitara, T. Togawa, H. Sakuraba, and Y. Miyaoka. In vivo delivery of therapeutic molecules by transplantation of genome-edited induced pluripotent stem cells. *Cell Transplant.*, 32: 9636897231173734, 2023.
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[Review Articles]

1. K. Iino, K. Toriumi, and M. Arai. Genetic Analysis of AKR1A1 in Patients with Schizophrenia with Pentosidine Accumulation. *IMARS Highlights*, 18: 5-9, 2023.
2. T. Wang, K. Toriumi, K. Suzuki, M. Itokawa, and M. Arai. Long-lasting effects of prenatal methylglyoxal exposure on behavior and the neurotransmitter system in adult mice. *IMARS Highlights*, 18: 12-13, 2023.
3. G. Takahashi, and Y. Miyaoka. Large-scale single-cell cloning of genome-edited cultured human cells by On-chip SPiS. *STAR Protoc.*, 4: 102364. 2023.

[Books]

[Conference Activities & Talks]

- 1 T. Wang, K. Toriumi, K. Suzuki, M. Miyashita, A. Ozawa, M. Masada, M. Itokawa, and M. Arai. Amyloban, extracted from *Herichium erinaceus*, recovers social defeat

- stress-mediated social deficits by suppressing the dopaminergic system. Society for Neuroscience. 2023.11.14, Washington.
- 2 Y. Tomita, K. Suzuki, S. Yamasaki, M. Miyashita, K. Toriumi, M. Itokawa, A. Nishida, and M. Arai. Urinary exosomal microRNAs as predictive biomarkers for persistent psychotic-like experiences. Society for Neuroscience. 2023.11.13, Washington.
 - 3 K. Tabata, H. Shiwaku, H. Takahashi, and M. Arai. Hypozincemia is associated with clinical severities of schizophrenia. The 5th UK-Japan Neuroscience Symposium. 2023.9.1, Wales.
 - 4 M. Hasegawa. Molecular dissection of TDP-43 proteinopathies. 2nd Perry disease international conference in Fukuoka. 2023.10.21, Fukuoka.

Clinical Anatomy

Professor : Keiichi AKITA
 Professor : Akimoto NIMURA (Department of Functional Joint Anatomy)
 Associate Professor : Kumiko YAMAGUCHI (Institute of Education Curricular Management Division)
 Junior Associate Professor : Kouji FUJITA (Department of Functional Joint Anatomy)
 (September~December: Professor [Institute of Innovation Medical Design Division])
 Junior Associate Professor (Career Track) : Masayo HARADA
 Junior Associate Professor : Satoru MURO (January~September: Assistant Professor)
 Assistant Professor : Takuya IBARA (Department of Functional Joint Anatomy), Shigeru OKUHARA (January)
 Research Technician : Rintaro YAMAMOTO
 Staff Assistant : Mayuri IKEDA
 Parttime Lecturer : Kenji IBUKURO (~March), Itsuko OKUDA, Shirou SUZUKI (~March),
 Kenro CHIKAZAWA, Sachiyuki TSUKADA, Masahiro TSUTSUMI,
 Masataka NAKAZAWA, Tomoyuki YANO, Shota Hoshika (April~),
 Motoki Tanaka (April~)
 Graduate Student : Syuusaku HOSONO, Shouko MOUE, Areeya JIAMJUNYASIRI (~September),
 Atsuhiko FUKAI (~March), Suthasinee THARNMANULARP (~September),
 Ryo KARAKAWA, Hidehiko YOSHIMATSU, Isabella Georgina DJAMEH,
 Yuzuki SUGIYAMA, Tong LIU,
 Jennifer Edinam DANYO (April~), Nina Hirano (April~)
 Research student : Weiyi WANG (April~), Takahiro KASHIYAMA (October~)

(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 techniques and surgical procedures. Our researches are aimed to share languages among all clinicians based on clinical anatomy by describing the results of observations in an accessible way for clinicians. In addition, we perform analyses using experimental embryological approaches and developmental biological approaches, because we think it is important to consider how human structures are constructed.

(2) Research

- 1) Clinical anatomic study of the shoulder joint and rotator cuff.
- 2) Clinical anatomic study of the anal region for the rectoanal surgery.
- 3) Cadaveric study of the female pelvis for the gynecologic oncology and colposcopy.
- 4) Analyses of the lamination in the masticatory muscles with special reference of nerve supply.
- 5) Embryological study of the differentiation of cloaca and surrounding muscles.

(3) Education

Clinical anatomy is generally considered as the practical application of anatomical knowledge to diagnosis and treatment, however we think that this course is a part of pure anatomical science based on the findings of the morphological observations of the human bodies. Main objective of Clinical anatomy in the graduate course is to make detailed anatomical data to answer the questions developed from clinical fields especially by surgeons and radiologists. We collaborate with many clinicians: ENT, orthopedics, gynecology, thoracic surgery, radiology and so on, and our projects have been broad areas. Students are expected to get fine dissection techniques of human bodies and also learn techniques of histology and embryological experiments. By using these techniques, we study the spatial relationships of organs, vessels nerves, and also try to examine their developmental processes in various projects.

(4) Lectures & Courses

Theories and hypotheses of morphogenesis derived from descriptive anatomy and descriptive biology have been confirmed and modified by experimental biology. Furthermore, progresses of developmental biology identified molecules and signaling pathways involved in the morphogenesis. Progresses in the developmental biology also verified morphological hypotheses, and added revisions to the morphological models. The postulates of the morphological models which are currently investigated were built and completed by Anatomy. However, we find Anatomy is still not completed and has many obscure issues through careful dissection of human body. It might be thought that everything was done and there could be no new finding in the human anatomical field anymore because the anatomy employs the classic procedures such as the gross anatomy. However, there are still a lot of unclear anatomical topics, because they had not been focused and not investigated with their clinical significances.

(5) Publications

[Original Articles]

1. Shintarou Kudo, Mizuki Hatanaka, Seiya Kanazawa, Keisuke Hirakawa, Shigeyuki Hara, Masahiro Tsutsumi. Effects of short foot exercises with ultrasound bio-feedback on motor learning and foot alignment: A double blinded randomized control trial. *J Back Musculoskelet Rehabil.* 2023.12;
2. Tharnmanularp S, Muro S, Nimura A, Ibara T, Akita K. Significant relationship between musculoaponeurotic attachment of the abdominal and thigh adductor muscles to the pubis: implications for the diagnosis of groin pain. *Anatomical science international.* 2023.11; 99(2); 190-201
3. Muro S, Moue S, Akita K. Twisted orientation of the muscle bundles in the levator ani functional parts in women: Implications for pelvic floor support mechanism. *Journal of anatomy.* 2023.10; 244(3); 486-496
4. Jiamjunyasiri A, Tsutsumi M, Muro S, Akita K. Origin, course, and distribution of the posterior femoral cutaneous nerve and the spatial relationship among its branches. *Anatomical science international.* 2023.09; 98(4); 540-547
5. Yamamoto A, Fujita K, Yamada E, Ibara T, Nihey F, Inai T, Tsukamoto K, Kobayashi Y, Nakahara K, Okawa A. Foot characteristics of the daily-life gait in postmenopausal females with distal radius fractures: a cross-sectional study. *BMC musculoskeletal disorders.* 2023.09; 24(1); 706
6. Masahiro Yamane, Yoshiya Ishikawa, Daisuke Asano, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Yuzuki Sugiyama, Satoru Muro, Keiichi Akita, Minoru Tanabe. Surgical anatomy of the dorsal pancreatic artery: Considering embryonic development. *Pancreatology.* 2023.09; 23(6); 697-703
7. Kuroiwa T, Sarcon A, Ibara T, Yamada E, Yamamoto A, Tsukamoto K, Fujita K. The Potential of ChatGPT as a Self-Diagnostic Tool in Common Orthopedic Diseases: Exploratory Study. *Journal of medical Internet research.* 2023.09; 25; e47621
8. Kyosuke Kamijo, Kentaro Ishida, Shiho Oide, Keisuke Anan, Shunsuke Taito, Yuki Kataoka, Kenro Chikazawa. Efficacy and Safety of the Surgery-First Approach Compared to the Chemotherapy-First Approach for Treating Low-Risk Gestational Trophoblastic Neoplasia: A Systematic Review and Meta-Analysis. *Cureus.* 2023.09; 15(9); e45726

9. 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.* 2023.09; 28(5); 1018-1022
10. Ibara T, Fujita K, Watanabe N, Takada R, Miyatake K, Nimura A, Akita K. Stabilization and compensation strategy of the hip angle during gait in hip-osteoarthritis patients from the perspective of whole-body movement synergy. *Gait & posture.* 2023.08; 106; 65-71
11. Ryo Karakawa, Hidehiko Yoshimatsu, Yuma Fuse, Tomoyuki Yano. Comparison of outcomes following pedicled and free flap transfers for the defect after shoulder sarcoma resection. *J Plast Reconstr Aesthet Surg.* 2023.08; 83; 373-379
12. Fujishiro H, Nimura A, Azumaya M, Hattori S, Hoshi O, Akita K. Anatomical study of the bone morphology of the anterior talofibular ligament attachment. *Anatomy & cell biology.* 2023.07;
13. Nawa N, Numasawa M, Yamaguchi K, Morita A, Fujiwara T, Akita K. Association between the social network of medical students and their academic performance on the anatomy written examination. *Anatomical sciences education.* 2023.07; 16(4); 654-665
14. Fukino K, Iida K, Tsutsumi M, Iwanaga J, Akita K. Evaluation of morphological features of palatopharyngeus insertion into the thyroid cartilage. *Anatomical science international.* 2023.07; 98(3); 448-453
15. Tokairin Y, Kawamura Y, Muro S, Nagai K, Kawada K, Okada T, Tharnmanularp S, Jiamjunyasiri A, Akita K, Kinugasa Y. Histological study of the thin membranous dense connective tissues around the curving portion of the bilateral recurrent laryngeal nerves. *Esophagus : official journal of the Japan Esophageal Society.* 2023.07; 20(3); 410-419
16. Tsutsumi M, Nimura A, Tharnmanularp S, Kudo S, Akita K. Posteromedial capsular anatomy of the tibia for consideration of the medial meniscal support structure using a multidimensional analysis. *Scientific reports.* 2023.07; 13(1); 12030
17. Saito T, Muro S, Fujiwara H, Umebayashi Y, Sato Y, Tokunaga M, Akita K, Kinugasa Y. Histological study of the structural layers around the esophagus in the lower mediastinum. *World journal of gastrointestinal surgery.* 2023.07; 15(7); 1331-1339
18. Hidehiko Yoshimatsu, Ryo Karakawa, Mario F Scaglioni, Yuma Fuse, Tomoyuki Yano. Use of intraoperative indocyanine green angiography for detection and prediction of congestion in pedicled island flaps. *Microsurgery.* 2023.07; 43(5); 452-459
19. Kenro Chikazawa, Ken Imai, Tomoyuki Kuwata, Ryo Konno. infection on gastric cancer development. *Int J Gynecol Cancer.* 2023.07; 33(7); 1164
20. Yoshimatsu H, Karakawa R, Fuse Y, Yano T, Muro S, Akita K. The Use of the Deep Brachial Artery as the Recipient Artery for Free Perforator Flap Transfer: An Anatomic Study and Clinical Applications. *Medicina (Kaunas, Lithuania).* 2023.06; 59(6);
21. Yamada E, Fujita K, Watanabe T, Koyama T, Ibara T, Yamamoto A, Tsukamoto K, Kaburagi H, Nimura A, Yoshii T, Sugiura Y, Okawa A. A screening method for cervical myelopathy using machine learning to analyze a drawing behavior. *Scientific reports.* 2023.06; 13(1); 10015
22. Ibara Takuya, Matsui Ryota, Koyama Takafumi, Yamada Eriku, Yamamoto Akiko, Tsukamoto Kazuya, Kaburagi Hidetoshi, Nimura Akimoto, Yoshii Toshitaka, Okawa Atsushi, Saito Hideo, Sugiura Yuta, Fujita Koji. Screening for degenerative cervical myelopathy with the 10-second grip-and-release test using a smartphone and machine learning: A pilot study *DIGITAL HEALTH.* 2023.06; 9; 20552076231179030
23. Keisuke Anegawa, Kengo Kawanishi, Misaki Nakamura, Meika Izumi, Masahiro Tsutsumi, Shintarou Kudo. Tibial nerve dynamics during ankle dorsiflexion: The relationship between stiffness and excursion of the tibial nerve. *J Biomech.* 2023.06; 155; 111646
24. Umebayashi Y, Muro S, Tokunaga M, Saito T, Sato Y, Tanioka T, Kinugasa Y, Akita K. Distribution of splenic artery lymph nodes and splenic hilar lymph nodes. *World journal of gastrointestinal surgery.* 2023.05; 15(5); 812-824

25. Ryo Karakawa, Hidehiko Yoshimatsu, Kengo Nakatsuka, Yuma Fuse, Shohei Nishiyama, Tomohiro Kawahara, Tomoyuki Yano. "Super-Microsurgical Anastomosis training using the chick embryos within the "Egg-in-Cube" system.". *Plast Reconstr Surg.* 2023.05;
26. Kengo Kawanishi, Akihiro Kakimoto, Keisuke Anegawa, Masahiro Tsutsumi, Isao Yamaguchi, Shintarou Kudo. Automatic Identification of Ultrasound Images of the Tibial Nerve in Different Ankle Positions Using Deep Learning. *Sensors (Basel).* 2023.05; 23(10);
27. Muro S, Nimura A, Ibara T, Chikazawa K, Nakazawa M, Akita K. Anatomical basis for contribution of hip joint motion by the obturator internus to defaecation/urinary functions by the levator ani via the obturator fascia. *Journal of anatomy.* 2023.04; 242(4); 657-665
28. Masayo Harada, Keiichi Akita. Mouse vaginal development with lateral enlargement at late embryonic stages and caudal elongation after birth. *Congenit Anom (Kyoto).* 2023.03; 63(2); 30-39
29. Okuda Itsuko, Akita Keiichi, Komemushi Takayoshi, Imaizumi Kazuhiko, Jinzaki Masahiro, Ohjimi Hiroyuki. Basic Consideration for Facial Aging: Age-Related Changes of the Bony Orbit and Orbicularis Oculi Muscle in East Asians *AESTHETIC SURGERY JOURNAL.* 2023.03; 43(4); 408-419
30. Haruhiko Shimura, Tatsunobu Ikeda, Koji Fujita, Hidetoshi Kaburagi, Akimoto Nimura. Radiation educational program significantly reduces intraoperative fluoroscopy time during locking plate fixation for distal radius fractures. *J Orthop Sci.* 2023.01; 28(1); 251-254
31. Hasegawa S, Yoshimura H, Mochizuki T, Arai R, Akita K, Nimura A. High diagnostic accuracy of magnetic resonance imaging in detecting subscapularis tendon tears by focusing on the most superior portion of the subscapularis tendon. *Surgical and radiologic anatomy : SRA.* 2023.01; 45(1); 17-24
32. Kenro Chikazawa. Four-step Technique on Ureteral Safety in Total Laparoscopic Hysterectomy. *Gynecol Minim Invasive Ther.* 2023; 12(4); 251-252
33. Kenro Chikazawa, Ken Imai, Naoki Ichi, Tomoyuki Kuwata. Easy and Standardized Technique for the Dissection of Severe Pouch of Douglas Obliteration Mainly by Blunt Dissection in Total Laparoscopic Hysterectomy for Deep Infiltrating Endometriosis. *Gynecol Minim Invasive Ther.* 2023; 12(3); 179-180
34. Kouki Samejima, Sachiho Netsu, Junji Mitsushita, Kenro Chikazawa, Tomoyuki Kuwata. Modified Laparoscopic Cornual Resection for Cornual Pregnancy. *Gynecol Minim Invasive Ther.* 2023; 12(2); 101-102
35. Ken Imai, Kenro Chikazawa, Tomoyuki Kuwata, Ryo Konno. Volume Index Measured Using Magnetic Resonance Imaging for Diagnosing Cervical Cancer Tumors < 2 cm. In Vivo. 2023; 37(4); 1786-1789
36. Kenro Chikazawa, Ken Imai, Masahiro Misawa, Tomoyuki Kuwata. A Safe and Standardized Strategy for Laparoscopic Hysterectomy in Patients with a History of Cesarean Section. *Gynecol Minim Invasive Ther.* 2023; 12(1); 46-47
37. Kengo Kawanishi, Daisuke Fukuda, Toshinori Miyashita, Takashi Kitagawa, Hiroyuki Niwa, Taisuke Okuno, Takashi Kinoshita, Masahiro Tsutsumi, Shintarou Kudo. Effects of Compression Intervention on the Thigh Using Elastic Bandage on Lateral Femoral Pain After Trochanteric Fractures: A Multicenter Randomized Controlled Trial. *Gerontol Geriatr Med.* 2023; 9; 23337214231214405

[Misc]

1. Muro S, Akita K. Novel combination method of wide-range serial sectioning and 3D reconstruction visualizing both macro-level dynamics and micro-level interactions in an attempt to analyze the female pelvic floor. *Anatomical science international.* 2023.07; 98(3); 343-352
2. Muro S, Akita K. Pelvic floor and perineal muscles: a dynamic coordination between skeletal and smooth muscles on pelvic floor stabilization. *Anatomical science international.* 2023.07; 98(3); 407-425

[Conference Activities & Talks]

1. Georgina Djameh, Masayo Harada, Keiichi Akita. Cervical vertebrae fusion in elbow knee synostosis (Eks) mutant mice with fibroblast growth factor 9 N143T mutation. The 46th Annual Meeting of the Molecular Biology Society of Japan 2023.12.07 Kobe, Hyogo
2. Masayo Harada, Keiichi Akita. The mouse vagina develops laterally at the late embryonic stages and elongates caudally after birth. 第46回日本分子生物学会年会 2023.12.06 神戸市, 兵庫県
3. Satoru Muro, Shoko Moue, Keiichi Akita. Stratified relationship of the muscle bundles in the levator ani functional parts: Implications for pelvic floor support mechanism. the combined 10th congress of the Asia Pacific International Congress of Anatomists (APICA) and 20th Annual Meeting of the Australian and New Zealand Association of Clinical Anatomists (ANZACA) 2023.12.03 Dunedin, New Zealand
4. Keiichi AKITA, Satoru MURO. Dynamic coordination of the smooth and skeletal muscles in the pelvic floor. the combined 10th congress of the Asia Pacific International Congress of Anatomists (APICA) and 20th Annual Meeting of the Australian and New Zealand Association of Clinical Anatomists (ANZACA) 2023.12.03 Dunedin, New Zealand
5. 辛川 頌. Sarcoma reconstruction using a Minimally-invasive flap. PRS Korea 2023 2023.11.10 Seoul, Korea
6. Satoru Muro, Suthasinee Tharnmanularp, Yuichiro Tsukada, Masaaki Ito, Keiichi Akita. Analysis of smooth muscle fiber density in anterior to male rectum. The 17th Annual Congress of the European Association of Clinical Anatomy (EACA) and the 14th Annual Congress of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2023.09.15 Prague, Czech
7. Yuzuki Sugiyama, Satoru Muro, Daisuke Ban, Keiichi Akita. The fusion fascia affects the course of the nerves to the pancreas. The 17th Annual Congress of the European Association of Clinical Anatomy (EACA) and the 14th Annual Congress of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2023.09.15 Prague, Czech
8. Suthasinee Tharnmanularp, Satoru Muro, Akimoto Nimura, and Keiichi Akita. Insights into the aponeurotic attachment of abdomen-thigh adductor muscles to pubis and MRI diagnosis for groin pain. The 17th Annual Congress of the European Association of Clinical Anatomy (EACA) and the 14th Annual Congress of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2023.09.14 Prague, Czech
9. Nimura A, Fukai A. What is the lateral ulnar collateral ligament?; an anatomical study. 15th International congress on shoulder and elbow surgery 2023.09.06 Roma, Italy
10. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Eriko Okada, Eiji Kaneko, Janelle Moross, Jun Tsuruta, Keiichi Akita, Masanaga Yamawaki. Patients as teachers: a novel IPE curriculum . AMEE2023 2023.08.28
11. 辛川 頌. Imaging Application for Sarcoma Reconstruction. 5th Congress of Imaging in Reconstructive Microsurgery 2023.08.20 Singapore
12. 辛川 頌. High-Precision Reconstructive Surgery with Advanced Visualization Technology. 12th Congress of World Society for Reconstructive Microsurgery 2023.08.18 Singapore
13. 辛川 頌. Advances in Sarcoma Reconstruction New Technology and Minimally invasive surgery. 12th Congress of World Society for Reconstructive Microsurgery 2023.08.18 Singapore
14. Takuya Ibara, Koji Fujita, Naoto Watanabe, Ryohei Takada, Kazumasa Miyatake, Akimoto Nimura, Keiichi Akita. Time series for the whole-body synergy of the hip angle during gait in patients with hip osteoarthritis. ISB 2023 Congress XXIX 2023.07.30 FUKUOKA CONVENTION CENTER
15. Masayo Harada, Keiichi Akita. The mouse vagina develops laterally at the late embryonic stages and caudally after birth. The 56th Annual Meeting of the Japanese Society of Developmental Biologists 2023.07.23 Sendai, Miyagi
16. 馬上 頌子. Endoscopic Phenotype Analysis of Postoperative Acute and Chronic Pouchitis in Ulcerative Colitis. 第78回 日本消化器外科学会 2023.07.14 函館市, 北海道

17. Takuya Ibara, Koji Fujita, Naoto Watanabe, Ryohei Takada, Kazumasa Miyatake, Akimoto Nimura, Keiichi Akita. Synergy for center of mass trajectory in the medial-lateral direction of patients with hip osteoarthritis. ISPGR World Congress 2023.07.09 Brisbane Convention Centre
 18. 石川 喜也, 杉山 夕月, 室生 暁, 山根 聖弘, 竹内 将, 浅野 大輔, 渡辺 秀一, 上田 浩樹, 赤星 径一, 小野 宏晃, 工藤 篤, 田中 真二, 秋田 恵一, 田邊 稔. Novel landmarks for SMA left approach based on the anatomical study. 第 35 回日本肝胆膵外科学会学術集会 2023.07.01 東京
 19. 杉山 夕月, 室生 暁, 伴 大輔, 秋田 恵一. Morphology of the fusion fascia, nerves, and arteries around the pancreatic head. 第 35 回日本肝胆膵外科学会学術集会 2023.07.01 東京
 20. Itsuko Okuda. Objective analysis of age-related changes in the superficial musculoaponeurotic system using computed tomography. Aesthetic Surgery Journal Open Forum, YouTube 2023.07.01 Web
 21. Kenro Chikazawa, Ken Imai, Tomoyuki Kuwata, Ryo Konno. . The ideal format to exchange patient information for the next on service team. The 31th international Congress of the European Association for Endoscopic Surgery 2023.06.20 Rome, Italy
 22. Keiichi Akita. Dynamic coordination of the smooth and skeletal muscles in the pelvic floor. Songdo International Proctology Symposium 2023 2023.06.17 Seoul, Korea
 23. Sultana Farzana, Zhang Chenyang, Okuhara Shigeru, Nagai Shigenori, Azuma Miyuki. 新規の炎症チェックポイント分子である ILDR2 は脳炎において発現量が増加している (A novel immune checkpoint molecule, ILDR2 is upregulated in the inflammatory brain). 口腔病学会雑誌 2023.03.01
 24. Akimoto Nimura. Reconsideration of anatomy in the lateral part of elbow joint; what are LCL and LUCL?. 7th FIPAR webinar 2023.02.01 Web
1. Anatomy of rotator interval in terms of layered and histological concepts. 2023.07.08
 2. Atsuhiro Fukai, Akimoto Nimura, MasahiroTsutsumi, 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 Structure. The 35th Annual Meeting of the Japan Elbow Society 2023.02.03 Yamagata City, Yamagata Prefecture

Systems BioMedicine

Professor Hiroshi ASAHARA

Project Associate Professor Yuki NAITO

Junior Associate Professor Ryouta KURIMOTO

Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA, Yuta Fujii

Postdoctoral fellow Yutaro UCHIDA, Lin LIU, Maiko INOTSUME, Shosei YOSHINOCHI

Graduate Students Lisa YAGASAKI, Suzu CHIDA, Masayasu SEGA, Kohei NAKAMURA, Takahiro MORITA, Nao WATANABE

Hiroki ONO, Mikoto KATAGIRI, Hifumi TAGUCHI, Waka MIYAMOTO

Kana KOTUDUMI, Maho HASHIMOTO, Reiji HIRAI, Kasumi YUMOTO, Rina WATASE

(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]

1. Jaehoon Shin, Shigeru Miyaki, Hiroshi Asahara, Takayuki Akimoto. MicroRNA-140 is not involved in sepsis-induced muscle atrophy. *Am J Physiol Cell Physiol.* 2023.08; 325(2); C509-C518
2. Yudai Ono, Sandra Schlesinger, Kanako Fukunaga, Shinsei Yambe, Tempei Sato, Takako Sasaki, Chisa Shukunami, Hiroshi Asahara, Masafumi Inui. Scleraxis-lineage cells are required for correct muscle patterning. *Development.* 2023.05; 150(10);
3. Maiko Inotsume, Tomoki Chiba, Takahide Matsushima, Ryota Kurimoto, Mitsuyo Nakajima, Tomomi Kato, Kana Shishido, Lin Liu, Koichi Kawakami, Hiroshi Asahara. One-step generation of mice with gene editing by Tol2 transposon-dependent gRNA delivery. *FEBS Lett.* 2023.03;
4. Hiroto Yamamoto, Yutaro Uchida, Ryota Kurimoto, Tomoki Chiba, Takahide Matsushima, Yoshiaki Ito, Maiko Inotsume, Kohei Miyata, Kenta Watanabe, Masaki Inada, Naoki Goshima, Tokujiro Uchida, Hiroshi Asahara. RNA-binding protein LIN28A upregulates transcription factor HIF1 α by posttranscriptional regulation via direct binding to UGAU motifs. *J Biol Chem.* 2023.01; 299(1); 102791

[Conference Activities & Talks]

1. Hiroshi Asahara. Athletic performance and Genes. Japan Bone Academy 2023 2023.12.16
2. Lin Liu, Kohei Miyata, Ryo Nakamichi, Tomoki Chiba, Hiroshi Asahara. The regulation of satellite cells by RP58. 第10回JCR ベーシックリサーチカンファレンス 2023.11.24
3. 栗本遼太、宮本和佳、平井玲士、千葉朋希、松島隆英、内田雄太郎、手塚叶子、七野悠一、水戸麻里、岩崎信太郎、浅原弘嗣. Regulation of lung cancer metastasis by the RNA-modifying enzyme. 第96回日本生化学会大会 2023.11.01
4. 栗本遼太、宮本和佳、平井玲士、千葉朋希、松島隆英、内田雄太郎、手塚叶子、七野悠一、水戸麻里、岩崎信太郎、浅原弘嗣. Regulation of lung cancer metastasis by the RNA-modifying enzyme. 第96回日本生化学会大会 2023.10.31
5. Hiroshi Asahara. Athlete Giftedness and Genetics. Wu Tsai Human Performance Seminar Series 2023.10.13
6. 浅原弘嗣. Athlete Giftedness and Genetics. 大阪大学 WPI のセミナー 2023.09.21
7. 浅原弘嗣. Regulation of tendon-based-motor functions. 第19回 Bone Biology Forum 2023.08.18
8. 劉琳、宮田康平、中道亮、千葉朋希、浅原弘嗣. Rp58 による筋サテライト細胞の制御. 第9回日本筋学会学術集会 2023.08.18
9. 矢ヶ崎理紗、千葉朋希、栗本遼太、浅原弘嗣. Mxk ノックアウトラットを用いた Mxk の歯周病における役割の解明. 第9回日本筋学会学術集会 2023.08.18
10. 矢ヶ崎理紗、千葉朋希、栗本遼太、浅原弘嗣. Mxk ノックアウトラットを用いた Mxk の歯周病における役割の解明. 第41回日本骨代謝学会学術集会 2023.07.29
11. 劉琳、千葉朋希、浅原弘嗣. 新規コンディショナル Mxk ノックアウトマウスの作製と特性評価. 第41回日本骨代謝学会学術集会 2023.07.28
12. Hiroshi Asahara. Well-Being Research in Tendon Function and Homeostasis. The 8th Diabetes Research Innovation Symposium 2023 2023.07.09
13. Yutaro Uchida, Ryota Kurimoto, Tomoki Chiba, Yasuto Takeuchi, Noriko Gotoh, Hiroshi Asahara. Targeting novel RNA binding protein for overcoming treatment resistance of triple negative breast cancer. 第24回日本 RNA 学会年会 2023.07.05

14. Ryota Kurimoto, Waka Miyamoto, Maiko Inotsume, Reiji Hirai, Tomoki Chiba, Takahide Matsushima, Yutaro Uchida, Yuta Fujii, Yuki Naito, Yuichi Shichino, Mari Mito, Shintaro Iwasaki, Hiroshi Asahara. Regulation of lung cancer metastasis by the RNA-modifying enzyme. 第 24 回日本 RNA 学会年会 2023.07.05
15. 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. RNA2023 2023.05.31
16. Hiroshi Asahara. Tendon regeneration and functional enhancement for physical performance via Piezo1-Mkx axis. International Symposium on Mechanobiology for Human Health : 8 years 2023.03.22

Comprehensive Pathology

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(1) Outline

A major goal in the field of comprehensive pathology is to understand and overcome many intractable diseases such as leukaemia, lymphomas and tumours. In research, the patient is the starting point for research and the goal of research is also to help the patient. We share the motivation to help and support patients across disciplines, from sequencing, computation and drug discovery, while valuing the classical approach of pathology = sectioning, utilising the foundation of pathological diagnosis to determine the disease and its severity, and we all work together to help and support patients. We are conducting research by incorporating a wide variety of science and technology. We share the 'desire to overcome disease = pathology that helps' across all generations, from staff to students. The real world at the bedside is one in which the same diagnosis can lead to different disease states and different responses to treatment. The importance of this system is to perform comprehensive measurements from the individual, connecting multiple layers of tissues/organs, cells, proteins, genes, metabolites, etc., and to find the essence of the disease and weaknesses in the disease from the data. Every staff member brings his or her own area of specialisation to the table, with each disease they wish to understand and each patient they wish to help in mind. We don't just work in the world of pathology, we work with many collaborators and encourage you to learn from them. Whether you are an undergraduate, postgraduate or doctor, you will also be a link between knowing and seeing the world and meeting amazing people. We also collaborate with the business development world to develop new treatments and bring them to patients, both nationally and internationally. We will also introduce you to our collaborators, so doing research while moving between medicine, dentistry and various other areas may be a good way to broaden your horizons, deepen your research and realise your dreams.

(2) Research

1. reproduction of human blood, immunity and disease As mentioned above, each patient has a different disease and a different immune system that tries to suppress it. Immunity is created from haematopoietic stem cells, and while reproducing this process in mice, we are researching what genes are needed to create a strong immunity, how leukaemia develops in the bones and spreads throughout the body, and what treatments can stop it. Diverse ideas and research tools are needed for research that can help. 2. understanding leukaemia relapse and developing treatments Our major goal is to eradicate 'relapse', where leukaemia cells, once reduced by chemotherapy and other treatments, reappear. To achieve this, we find the cells that cause the relapse, identify therapeutic targets in them and create a treatment. We have been working on these

efforts together with the wishes of a large number of patients. We have a continuum of research to track down leukaemia, and as we proceed, we also have the desire to learn about changing technologies and build even better teamwork. 3. visualisation of the bone marrow microenvironment Pathological assessment of the bone marrow microenvironment in human bone marrow What is needed to capture the bone marrow microenvironment as it is known in haematology with optical microscopy? We will also approach this from a molecular biological aspect. Construction of the bone marrow microenvironment using random mutations - Understanding cell-cell interactions in the cancer microenvironment - While many previous reports on the 'cancer microenvironment' have mainly focused on poor prognosis cancers themselves, this research team has comprehensively investigated the mechanism of induction of drug resistance by tumour peritumour support cells. In contrast, the research team established a new CRISPR screening method*3 to comprehensively elucidate the mechanism of drug resistance induction by per tumour support cells. Understanding treatment resistance in disease using CRISPR-Cas Associate Professor Kurata was one of the first to learn about CRISPR and has taken an international leadership role. He is taking on challenges that he has wanted to solve for many years but has not been able to do so, such as tumour resistance to treatment. Postgraduate students and young pathologists are also successfully including CRISPR in their respective research topics to improve their research. 4. deepening pathology and medicine for a wide range of diseases, including breast cancer, pancreatic endocrine tumours, endometriosis, liposarcoma and malignant mesothelioma. 5. visualisation of disease cell/stromal relationships.

(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

[Original Articles]

1. Sugita K, Onishi I, Nakayama R, Ishibashi S, Ikeda M, Inoue M, Narita R, Oshima S, Shimizu K, Saito S, Sato S, Moriarity BS, Yamamoto K, Largaespada DA, Kitagawa M, Kurata M. Indirect CRISPR screening with photoconversion revealed key factors of drug resistance with cell-cell interactions. Communications biology. 2023.06; 6(1); 582

2. Maruyama S, Furusawa H, Endo S, Kumagai T, Mitsumura T, Shimada S, Yamana T, Sakakibara R, Iijima Y, Shibata S, Honda T, Shirai T, Okamoto T, Tateishi T, Tamaoka M, Kinowaki Y, Ishibashi H, Okubo K, Miyazaki Y. Pulmonary Artery Aneurysm in a Patient with Nontuberculous Mycobacteria Infection. *Internal medicine* (Tokyo, Japan). 2023.08; 63(7); 989-992
3. Watabe S, Aruga Y, Kato R, Kawade G, Kubo Y, Tatsuzawa A, Onishi I, Kinowaki Y, Ishibashi S, Ikeda M, Fukawa Y, Akahoshi K, Tanabe M, Kurata M, Ohashi K, Kitagawa M, Yamamoto K. Regulation of 4-HNE via SMARCA4 Is Associated with Worse Clinical Outcomes in Hepatocellular Carcinoma. *Biomedicines*. 2023.08; 11(8);
4. Yagi K, Ono H, Kudo A, Kinowaki Y, Asano D, Watanabe S, Ishikawa Y, Ueda H, Akahoshi K, Tanaka S, Tanabe M. MGMT is frequently inactivated in pancreatic NET-G2 and is associated with the therapeutic activity of STZ-based regimens. *Sci Rep*. 2023.05; 13(1); 7535
5. Hata C, Fukawa Y, Motoi T, Kinowaki Y, Akashi T, Ohashi K, Ishikawa Y, Waseda Y, Fujii Y, Kakuta R, Ikeda S, Onishi I. A Primary Kidney Giant Cell Tumor of Soft Tissue Caused Peritoneal Dissemination, Considered to Be Malignant Transformation: A Case Report. *Diagnostics* (Basel, Switzerland). 2023.02; 13(4);
6. Nonaka Keisuke, Kurata Morito, Tachibana Moriaki, Komatsu Akiko, Shichi Yuuki, Gomi Fujiya, Ishiwata Toshiyuki, Miyamoto Kou, Arai Tomio. 異なる解剖学的部位で免疫グロブリン軽鎖制限の不一致が認められたクローン性B細胞リンパ腫の染色体分析 (Chromosomal analysis of clonally related B-cell lymphomas with discordant immunoglobulin light-chain restrictions at different anatomical sites) *Pathology International*. 2023.02; 73(2); 100-102
7. Mori S, Ai T, Taguchi T, Negi M, Otomo Y. Aggressive diffuse large B-cell lymphoma manifested by splenic rupture progressed 2 months after transverse myelitis: an autopsy case report. *Acute medicine & surgery*. 2023.01; 10(1); e822

[Conference Activities & Talks]

1. Saumya Agrawal, Fumihiko Ishikawa 他. Comparative analysis of cellular response to onset of infection due to SARS-CoV-2 strains . The 46th Annual Meeting of the Molecular Biology Society of Japan 2023.12.06 兵庫・神戸ポートアイランド
2. 中川諒, 石川文彦. Targeting patient-specific anti-apoptotic molecules and cell surface proteins in high-risk leukemia. 第 85 回日本血液学会学術集会 2023.10.13 東京・東京国際フォーラム
3. Saumya Agrawal, Fumihiko Ishikawa 他. Comparative analysis of transcriptome landscape and chromatin conformation in response to onset of infection due to different SARS-CoV-2 strains . The 14th International Workshop on Advanced Genomics (14AGW) 2023.10.04 東京・一橋講堂
4. 野上 彩子, 倉田 盛人, 田口 登和子, 小山 祥美, 永野 勝稔, 田中 圭祐, 吉藤 康太, 梅澤 佳央, 市村 直也, 東田 修二, 森 毅彦. 尿セルブロックを用いた出血性膀胱炎起因ウイルスの病理学的同定法の有用性. 日本血液学会学術集会 2023.10.01
5. 大西 威一郎, 倉田 盛人, 大橋 健一. CRISPR screening データベースを用いた、遺伝性乳癌の新たな合成致死因子の探索 (Identification of synthetic lethal genes of hereditary breast cancer using CRISPR screening database). 日本癌学会総会記事 2023.09.01
6. 田村 一洋, 山本 浩平, 渡部 紫織, 川出 玄二, 大西 威一郎, 木脇 祐子, 石橋 佐知子, 池田 真住, 倉田 盛人, 大橋 健一. 肝細胞癌 (HCC) における 4-hydroxynonenal(4-HNE) の臨床病理学および分子生物学的検討 (Clinicopathological and molecular analysis of 4-hydroxynonenal(4-HNE) in Hepatocellular carcinoma). 日本病理学会会誌 2023.03.01
7. 田村 一洋, 山本 浩平, 渡部 紫織, 川出 玄二, 大西 威一郎, 木脇 祐子, 石橋 佐知子, 池田 真住, 倉田 盛人, 大橋 健一. 肝細胞癌 (HCC) における 4-hydroxynonenal(4-HNE) の臨床病理学および分子生物学的検討 (Clinicopathological and molecular analysis of 4-hydroxynonenal(4-HNE) in Hepatocellular carcinoma). 日本病理学会会誌 2023.03.01
1. Ayako Nogami, Morito Kurata, Towako Taguchi, Shomi Koyama, Katsutoshi Nagano, Keisuke Tanaka, Kota Yoshifuji, Yoshihiro Umezawa, Naoya Ichimura, Shuji Tohda, and Takehiko Mori. Efficacy of pathological method of identifying causative virus of hemorrhagic cystitis by cell block. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo

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
Graduate Student: Yu MIYATA

(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]

1. Hatano M, Akiyama Y, Shimada S, Yagi K, Akahoshi K, Itoh M, Tanabe M, Ogawa Y, Tanaka S. Loss of KDM6B epigenetically confers resistance to lipotoxicity in nonalcoholic fatty liver disease-related hepatocellular carcinoma. *Hepatology Communications*. 2023.10; 7(10); e0277
2. Yamane M, Ishikawa Y, Asano D, Watanabe S, Ueda H, Akahoshi K, Ono H, Kudo A, Tanaka S, Sugiyama Y, Muro S, Akita K, Tanabe M. Surgical anatomy of the dorsal pancreatic artery: Considering embryonic development. *Pancreatology*. 2023.09; 23(6); 697-703
3. Murota Y, Nagane M, Wu M, Santra M, Venkateswaran S, Tanaka S, Bradley N, Taga T, Tabu K. A niche-mimicking polymer hydrogel-based approach to identify molecular targets for tackling human pancreatic cancer stem cells. *Inflammation and Regeneration*. 2023.09; 43(1); 46
4. Morimoto K, Ueda H, Asano D, Ishikawa Y, Watanabe S, Akahoshi K, Ono H, Kobayashi M, Okamoto R, Tanaka S, Tanabe M. Incidence and Mechanism of Refractory Postoperative Cholangitis After Hepatectomy with Hepaticojejunostomy. *Journal of Gastrointestinal Surgery*. 2023.06; 27(8); 1668-1676
5. Yagi K, Shimada S, Akiyama Y, Hatano M, Asano D, Ishikawa Y, Ueda H, Watanabe S, Akahoshi K, Ono H, Tanabe M, Tanaka S. Loss of SFXN1 mitigates lipotoxicity and predicts poor outcome in non-viral hepatocellular carcinoma. *Sci Rep*. 2023.06; 13(1); 9449
6. 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*. 2023.06; 58(6); 540-553
7. Yagi K, Ono H, Kudo A, Kinowaki Y, Asano D, Watanabe S, Ishikawa Y, Ueda H, Akahoshi K, Tanaka S, Tanabe M. MGMT is frequently inactivated in pancreatic NET-G2 and is associated with the therapeutic activity of STZ-based regimens. *Sci Rep*. 2023.05; 13(1); 7535
8. Ono H, Murase Y, Yamashita H, Kato T, Asano D, Ishikawa Y, Watanabe S, Ueda H, Akahoshi K, Ogawa K, Kudo A, Akiyama Y, Tanaka S, Tanabe M. RRM1 is mediated by histone acetylation through gemcitabine resistance and contributes to invasiveness and ECM remodeling in pancreatic cancer. *International Journal of Oncology*. 2023.04; 62(4); 51
9. 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*. 2023.02; 114(2); 463-476
10. Shimada S, Tanaka S. The chronicles of hepatocellular carcinoma classification: subtyping, modeling and treatment. *Hepatology*. 2023; in press

[Conference Activities & Talks]

1. Atsushi Nara, Hiroki Ueda, Keiichi Akahoshi, Akira Ito, Shotaro Gan, Hironari Yamashita, Koichiro Morimoto, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Preoperative sarcopenia assessment predicts loss of independence after Pancreaticoduodenectomy (PD) in pancreatic cancer patients. The 3rd International Congress of the Asian Oncology Society 2023.10.20 Yokohama
2. Akira Ito, Keiichi Akahoshi, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Prognostic Impact of Reticular Pattern around Superior Mesenteric Artery in CT Images of Pancreatic Cancer. The 3rd International Congress of the Asian Oncology Society 2023.10.20 Yokohama
3. Shotaro Gan, Daisuke Asano, Akira Ito, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Determining the Indication of Surgery for High grade pNENs. The 3rd International Congress of the Asian Oncology Society 2023.10.20 Yokohama

4. Hiroaki Ono, Keiichi Akahoshi, Shinji Tanaka, Minoru Tanabe. RRM1 is mediated by H3 acetylation through GEM resistance and contributes to invasiveness and ECM remodeling in PDAC. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
5. Hironari Yamashita, Hiroaki Ono, Kotaro Takizawa, Shuichi Watanabe, Kosuke Ogawa, Daisuke Asano, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Yoshimitsu Akiyama, Shinji Tanaka, Minoru Tanabe. PCNA-I1 is identified as a novel therapeutic agent in pancreatic cancer. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
6. Koya Yasukawa, Shu Shimada, Yoshimitsu Akiyama, Shinji Tanaka. Elucidation of immunotherapy resistance in hepatocellular carcinoma: Novel treatment based on lactate metabolism. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.22 Yokohama
7. Yoshimitsu Akiyama, Shu Shimada, Shinji Tanaka. Overexpression of PADI2 and histone citrullination change in gastric cancer. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.21 Yokohama
8. Masahiro Yamane, Yoshiya Ishikawa, Masaru Takeuchi, Shotaro Gan, Kohei Yagi, Daisuke Asano, Shuichi Watanabe, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Middle-segment Preserving Pancreatectomy versus Total pancreatectomy: a comparative study of surgical and functional outcomes. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
9. Shotaro Gan, Daisuke Asano, Masaru Takeuchi, Masahiro Yamane, Akira Ito, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Kohei Yagi, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. A case of unresectable pancreatic ductal adenocarcinoma (UR-PDAC) in an elderly patient who underwent radical resection after preoperative chemotherapy and survived without recurrence for 1 year. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
10. Atsushi Nara, Keiichi Akahoshi, Akira Ito, Shotaro Gan, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Pancreatic duct stent AMY after pancreaticoduodenectomy is a predictor of pancreatic fistula. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
11. Akira Ito, Keiichi Akahoshi, Masaru Takeuchi, Masahiro Yamane, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Hepatectomy After Pancreatoduodenectomy Has a High Risk of Postoperative Complications. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
12. Shinji Tanaka. Educational Session : New currents in the field of HBP surgery. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
13. Shu Tsukihara, Yoshimitsu Akiyama, Shu Shimada, Megumi Hatano, Yusuke Kinugasa, Ken Eto, Shinji Tanaka. Histone H3 lysin 9 methyltransferase SETDB1 promotes gastric carcinogenesis by multiple signaling pathways. Digestive Disease Week 2023 2023.05.10 Chicago
14. A.Nara, K.Akahoshi, H.Ueda, D.Asano, S.Watanabe, Y.Ishikawa, H.Ono, A.Kudo, S.Tanaka, M.Tanabe. Usefulness of the NRSS in Determining the Timing of TAE for Ruptured Hepatocellular Carcinoma. 18th Annual Academic Surgical Congress 2023.02.08 Houston
1. Hironari Yamashita, Hiroaki Ono, Kotaro Takizawa, Shuichi Watanabe, Kosuke Ogawa, Daisuke Asano, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Yoshimitsu Akiyama, Shinji Tanaka, Minoru Tanabe. PCNA-I1 is identified as a novel therapeutic agent in pancreatic cancer. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
2. Shu Shimada, Yoshimitsu Akiyama, Shinji Tanaka. RTP4 silencing provokes tumor-intrinsic resistance to immunecheckpoint blockade in colorectal cancer. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.22 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

[Others]

1. Shinji Tanaka, Tatsuya Oda, Chair, Workshop 9: The latest translational research for HBP surgery, 2023.07
The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery, Tokyo
2. Yoshimitsu Akiyama, Chair, poster, Gastric cancer, esophageal cancer (1), P-1171~P-1178, 2023.09
The 82nd Annual Meeting of the Japanese Cancer Association
3. Shinji Tanaka, Luncheon Seminar 4 (AstraZeneca), Consideration of Combined Immunotherapy from Basic and Clinical Research, 2023.09
The 3rd JSH International Liver Conference, Tokyo
4. Shinji Tanaka, Chair, Workshop 12; Surgery & Transplantation, TACE, HAIC & Vascular Interventions, 2023.10
APASL Oncology 2023, Sendai
5. Shinji Tanaka, Chair, Dan Gabriel Duda; Restore function in a gene that can suppress liver cancer and enhance immunotherapy, 2023.11
JDDW 2023, Kobe

Surgical Pathology

Associate Professor: Takumi AKASHI

Assistant Professor: Ichiro Onishi ,Susumu KIRIMURA, Junko KUNIEDA
,Hiroshi Shintaku

Project Assistant Professor: Keiko MIURA

Secretary: Ayako UENO

(1) Outline

Missions of diagnostic pathology are summarized to following 4 items. 1) participation to the medical treatment of the patients through anatomical diagnosis 2) assessment of medical treatment through autopsy examination 3) training of diagnostic pathologists 4) development of diagnostic methods by anatomical, immunohistochemical, microbiological and molecular technologies.

In cooperation with departments of human pathology and comprehensive pathology, pathology and anatomical sciences and oral 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,comprehensive pathology,pathology and anatomical sciences,oral pathology, oral pathology 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.

(6) Clinical Performances

Department of diagnostic pathology participates in the medical treatment of the patients through anatomical diagnosis. In the era of molecule-targeted therapy, specialized information has been requested in the field of pathological diagnosis. In order to appropriately respond to a latest request of clinicians, we practice pathological diagnosis in cooperation with departments of human pathology and comprehensive pathology with latest techniques, such as immunohistochemistry, electron microscopy, and FISH.

(7) Publications

[Original Articles]

1. Kinowaki Y, Fukumura Y, Kawade G, Sugita K, Kinowaki K, Akahoshi K, Kobayashi M, Ono H, Kudo A, Tanabe M, Akashi T, Ohashi K, Kurata M. Gene expression profiling of pancreatic neuroendocrine carcinoma and mixed neuroendocrine-non-neuroendocrine neoplasm. *Gene*. 2023.10;
2. Shintaku H, Gokita K, Oshima T, Suzuki K, Fujii K, Sugaya N, Tomii S, Onishi I, Shimada K, Ohashi K. Pancreatic hamartoma: Possibility of a preoperative diagnosis via endoscopic ultrasound-guided fine-needle aspiration biopsy. *Diagnostic cytopathology*. 2023.09; 51(9); E267-E272
3. Yuka Saeki, Hideaki Miyachi, Keiko Miura, Daijiro Okazaki, Makoto Yamamoto, Yumika Yuki, Michiyo Nakano. Mycosis fungoides with pseudocarcinomatous hyperplasia masquerading as verrucous carcinoma. *JAAD Case Rep*. 2023.09; 39; 130-134
4. Watabe S, Aruga Y, Kato R, Kawade G, Kubo Y, Tatsuzawa A, Onishi I, Kinowaki Y, Ishibashi S, Ikeda M, Fukawa Y, Akahoshi K, Tanabe M, Kurata M, Ohashi K, Kitagawa M, Yamamoto K. Regulation of 4-HNE via SMARCA4 Is Associated with Worse Clinical Outcomes in Hepatocellular Carcinoma. *Biomedicines*. 2023.08; 11(8);
5. Yin Y, Sakakibara R, Honda T, Kirimura S, Daroonpan P, Kobayashi M, Ando K, Ujiie H, Kato T, Kichizo Kaga, Mitsumura T, Nakano R, Sakashita H, Matsuge S, Ishibashi H, Akashi T, Hida Y, Morohoshi T, Azuma M, Okubo K, Miyazaki Y. High density and proximity of CD8⁺ T cells to tumor cells are correlated with better response to nivolumab treatment in metastatic pleural mesothelioma. *Thorac Cancer*. 2023.07; 14; 1991-2000
6. Yin Y, Sakakibara R, Honda T, Kirimura S, Daroonpan P, Kobayashi M, Ando K, Ujiie H, Kato T, Kaga K, Mitsumura T, Nakano R, Sakashita H, Matsuge S, Ishibashi H, Akashi T, Hida Y, Morohoshi T, Azuma M, Okubo K, Miyazaki Y. High density and proximity of CD8(+) T cells to tumor cells are correlated with better response to nivolumab treatment in metastatic pleural mesothelioma. *Thoracic cancer*. 2023.07; 14(20); 1991-2000
7. Sugita K, Onishi I, Nakayama R, Ishibashi S, Ikeda M, Inoue M, Narita R, Oshima S, Shimizu K, Saito S, Sato S, Moriarity BS, Yamamoto K, Largaespada DA, Kitagawa M, Kurata M. Indirect CRISPR screening with photoconversion revealed key factors of drug resistance with cell-cell interactions. *Communications biology*. 2023.06; 6(1); 582

8. Fujiwara S, Kano Y, Maejima Y, Fujioka T, Tamura K, Kirimura S, Miyake S, Okamoto R. Clinical Response of Primary Malignant Pericardial Mesothelioma with Peritoneal Dissemination to Nivolumab. *Internal medicine* (Tokyo, Japan). 2023.06;
9. Nakagawa T, Mori H, Uemura N, Onishi I, Oda G. A Case of Breast Cancer With Ulceration of a Reconstructed Nipple Due to Local Recurrence. *Cureus*. 2023.05; 15(5); e39563
10. Yashima Yuka, Fujioka Tomoyuki, Kubota Kazunori, Mori Mio, Sato Arisa, Oda Goshi, Nakagawa Tsuyoshi, Onishi Iichiroh, Tanaka Mayuko, Tateishi Ukihide. Comparison of the clinical and pathological characteristics of ultrasound-guided biopsy for breast masses and non-mass lesions between 16-gauge spring-loaded core needle biopsy and 12-gauge spring-loaded vacuum-assisted biopsy *Journal of Medical Ultrasonics*. 2023.04; 50(2); 205-212
11. Hata C, Fukawa Y, Motoi T, Kinowaki Y, Akashi T, Ohashi K, Ishikawa Y, Waseda Y, Fujii Y, Kakuta R, Ikeda S, Onishi I. A Primary Kidney Giant Cell Tumor of Soft Tissue Caused Peritoneal Dissemination, Considered to Be Malignant Transformation: A Case Report. *Diagnostics* (Basel, Switzerland). 2023.02; 13(4);
12. Takeshi Namiki, Moe Makiguchi, Shogo Wada, Hind Al-Busani, Makiko Nishida, Tsukasa Ugajin, Keiko Miura, Kota Yokoyama, Naoko Okiyama. The potential value of thallium-201 scintigraphy in the diagnosis of squamous cell carcinoma arising from extensive pyoderma. *J Dermatol*. 2023.02;
13. Hata C, Fukawa Y, Motoi T, Kinowaki Y, Akashi T, Ohashi K, Ishikawa Y, Waseda Y, Fujii Y, Kakuta R, Ikeda S, Onishi I. A Primary Kidney Giant Cell Tumor of Soft Tissue Caused Peritoneal Dissemination, Considered to Be Malignant Transformation: A Case Report. *Diagnostics* (Basel, Switzerland). 2023.02; 13(4);
14. Toshiyuki Yamamoto, Keiko Miura, Yoshinobu Eishi. Detection of *Propionibacterium acnes* in cutaneous lichenoid sarcoidosis in a patient with Blau syndrome. *Int J Dermatol*. 2023.01;
15. Mori M, Fujioka T, Hara M, Katsuta L, Yashima Y, Yamaga E, Yamagiwa K, Tsuchiya J, Hayashi K, Kumaki Y, Oda G, Nakagawa T, Onishi I, Kubota K, Tateishi U. Deep Learning-Based Image Quality Improvement in Digital Positron Emission Tomography for Breast Cancer. *Diagnostics* (Basel, Switzerland). 2023.02; 13(4);
16. Yashima Y, Fujioka T, Kubota K, Mori M, Sato A, Oda G, Nakagawa T, Onishi I, Tanaka M, Tateishi U. Comparison of the clinical and pathological characteristics of ultrasound-guided biopsy for breast masses and non-mass lesions between 16-gauge spring-loaded core needle biopsy and 12-gauge spring-loaded vacuum-assisted biopsy. *Journal of medical ultrasonics* (2001). 2023.01; 50(2); 205-212

[Social Contribution]

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

Signal Gene Regulation

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

[Conference Activities & Talks]

1. 船戸 紀子. DiGeorge 症候群疾患遺伝子 TBX1 は口蓋形成において miR-200-ZEB2 軸を標的にする. 第 65 回歯科基礎医学会学術大会 2023.09.17 東京
2. Noriko Funato, Hiromi Yanagisawa. TBX1 associated with DiGeorge syndrome targets the miR-200-ZEB2 axis. Gordon Research Conference (Human Genetics and Genomics) 2023.07.11 Waterville Valley, NH, United States

[Others]

1. Novel tripeptide, differentiation inducer for osteoblasts, and bone formation accelerator., 2023
Rights Maintenance (Patent Number: 6989842)
Nippi Corporation & Tokyo Medical and Dental University
2. Osteoblast differentiation inducer and bone formation accelerator, 2023
Rights Maintenance (Patent Number: 6860877)
Nippi Corporation & Tokyo Medical and Dental University
3. Grants-in-Aid for Scientific Research (C), 2023.04
"Integrated analysis of single nucleotide polymorphisms associated with "nonsyndromic" cleft lip and palate" Noriko Funato

[Social Contribution]

1. Japanese Association of Oral Biology, Delegate, Japanese Association of Oral Biology, 2016.04.01 - Now
2. QS Global Academic Survey (QS World University Rankings), 2020 - 2023
3. Times Higher Education (THE)'s Global Academic Reputation Survey, 2021 - 2023
4. The National Institute of Science and Technology Policy (NISTEP): Survey to assess the current state of science, technology, and innovation creation., 2021 - Now

Hematology

Professor: Takehiko Mori

Junior Associate Professor: Masahide Yamamoto, Toshikage Nagao

Assistant Professor: Yoshihiro Umezawa, Kota Yoshifuji, Keisuke Tanaka

Project Assistant Professor: Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory): Ayako Nogami

Senior Resident : Hisako Nakamaki, Aina Tomori, Yuya Sasaki,
Yasumasa Nakata, Maho Kawakami, Makiko Ogawa, Megumi Akiyama

Graduate Student: Yotaro Motomura, Makiko Saito, Junichi Mukae,
Yuma Noguchi, Mai Soejima, Yuuki Osada

(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

[Original Articles]

1. Motomura, Y; Yoshifuji, K; Tachibana, T; Takase, H; Arai, A; Tanaka, K; Okada, K; Nogami, A; Umezawa, Y; Sakashita, C; Yamamoto, M; Mori, T; Nagao, T. Clinical factors for central nervous system progression and survival in primary vitreoretinal lymphoma BRITISH JOURNAL OF HAEMATOLOGY. 2023.12;
2. Takashi Toya, Kota Mizuno, Masatoshi Sakurai, Jun Kato, Takehiko Mori, Noriko Doki, Shinichi Masuda, Nobuyuki Aotsuka, Shokichi Tsukamoto, Emiko Sakaida, Yuki Nakajima, Shin Fujisawa, Shinichiro Machida, Yasuyuki Aoyama, Hiroki Yokoyama, Katsuhiro Shono, Yoshihiro Hatta, Kensuke Usuki, Keisuke Kataoka, Yoshinobu Kanda. Differential Clinical Impact of Letermovir Prophylaxis According to Graft Sources: a KSGCT Multicenter Retrospective Analysis Blood Adv. 2023.12;
3. Asuka Kono, Manabu Wakamatsu, Yoshihiro Umezawa, Hideki Muramatsu, Hiroki Fujiwara, Dan Tomomasa, Kento Inoue, Keiichiro Hattori, Tetsuo Mitsui, Hidetoshi Takada, Yoshiyuki Minegishi, Yoshiyuki Takahashi, Masahide Yamamoto, Takehiko Mori, Hirokazu Kanegane. Successful treatment of DOCK8 deficiency by allogeneic hematopoietic cell transplantation from alternative donors. Int J Hematol. 2023.10; 118(4); 519-525

4. Fujita S, Kasahara H, Kato J, Koda Y, Shiroshta K, Yamaguchi K, Okayama M, Abe R, Kikuchi T, Shimizu T, Mori T, Kataoka K, Okamoto S. The Impact of Pretransplant Use of Tyrosine Kinase Inhibitors on Allogeneic Stem Cell Transplantation in Patients with Chronic Myeloid Leukemia-A Single-institution Retrospective Study. *Internal medicine* (Tokyo, Japan). 2023.10;
5. Onishi Y, Mori T, Yamazaki H, Hiramoto N, Zaimoku Y, Kanaya M, Matsue K, Onizuka M, Aotsuka N, Uchida N, Onodera K, Kanda J, Nakamae H, Yamamoto R, Kuriyama T, Kimura T, Ichinohe T, Atsuta Y, Adult Aplastic Anemia Working Group of the Japanese Society for Transplantation and Cellular Therapy. Comparison of haploidentical stem cell transplantation with post-transplant cyclophosphamide versus umbilical cord blood transplantation in adult patients with aplastic anemia. *Transplantation and cellular therapy*. 2023.09; 29(12); 766.e1-766.e8
6. Keisuke Tanaka, Ayako Ichikawa, Natsuka Umezawa, Kouhei Yamamoto, Kota Yoshifuji, Keigo Okada, Ayako Nogami, Yoshihiro Umezawa, Toshikage Nagao, Chizuko Sakashita, Takehiko Mori, Shuji Tohda, Ryuji Koike, Shinsuke Yasuda, Masahide Yamamoto. Lymphoproliferative disorder risk after methotrexate treatment for rheumatoid arthritis. *Cancer Sci*. 2023.09; 114(9); 3719-3727
7. Shimizu H, Najima Y, Kako S, Tanaka M, Fujiwara SI, Mori T, Usuki K, Gotoh M, Hagihara M, Tsukada N, Oniduka M, Takada S, Sakaida E, Fujisawa S, Onoda M, Aotsuka N, Yano S, Ohashi K, Takahashi S, Okamoto S, Kanda Y, Kanto Study Group for Cell Therapy (KSGCT). Clinical significance of late CMV disease in adult patients who underwent allogeneic stem cell transplant. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2023.08; 29(12); 1103-1108
8. Kako S, Kimura SI, Wada H, Komiya Y, Nakasone H, Sakurai M, Kato J, Tanaka M, Fujii E, Tachibana T, Yamamoto W, Hagihara M, Watanabe R, Yokota A, Nakano H, Mori T, Nakaseko C, Kanamori H, Okamoto S, Kanda Y. Treatment strategy at the decision for allogeneic transplantation in patients with myelodysplastic syndrome in the era of azacitidine: A KSGCT prospective study. *Leukemia research*. 2023.08; 133; 107371
9. Okinaka K, Inoue Y, Uchida N, Toya T, Ogawa H, Ozawa Y, Eto T, Mori T, Sugita J, Kondo T, Kato K, Suzuki R, Fukuda T. Clinical characteristics and risk factors of pneumococcal diseases in recipients of allogeneic hematopoietic stem cell transplants in the late phase: A retrospective registry study. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2023.07; 29(7); 726-730
10. Tomoyasu Jo, Satoshi Yoshihara, Yoshiki Okuyama, Keiko Fujii, Tomoko Henzan, Kaoru Kahata, Rie Yamazaki, Wataru Takeda, Yoshihiro Umezawa, Kentaro Fukushima, Takashi Ashida, Minami Yamada-Fujiwara, Ryo Hanajiri, Noboru Yonetani, Yuma Tada, Yuji Shimura, Hidekazu Nishikii, Norio Shiba, Naoya Mimura, Jun Ando, Takayuki Sato, Yasuhiro Nakashima, Junko Ikemoto, Keita Iwaki, Shin-Ichiro Fujiwara, Masaki Ri, Tokiko Nagamura-Inoue, Ryuji Tanosaki, Yasuyuki Arai. Risk factors for CAR-T cell manufacturing failure among DLBCL patients: A nationwide survey in Japan. *Br J Haematol*. 2023.07; 202(2); 256-266
11. Harada K, Onizuka M, Mori T, Shimizu H, Seo S, Aotsuka N, Takeda Y, Sekiya N, Kusuda M, Fujihara S, Shiraiwa S, Shono K, Shingai N, Kanamori H, Momoki M, Takada S, Mukae J, Masuda S, Mitani K, Sakaida E, Tomikawa T, Takahashi S, Usuki K, Kanda Y. Prognostic factors for the development of lower respiratory tract infection after influenza virus infection in allogeneic hematopoietic stem cell transplantation recipients: A KSGCT Multicenter Analysis. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*. 2023.03; 131; 79-86
12. Kanda Y, Mori T, Narita A, Wolter KD, Yoshimatsu H, Nishimura K. Efficacy and safety of equine anti-thymocyte immunoglobulin (eATG) in three Japanese patients with moderate to very severe aplastic anemia: a case series. *International journal of hematology*. 2023.01; 117(3); 469
13. Yoshihiro Umezawa, Koji Sasaki. Dose optimization of tyrosine kinase inhibitor therapy in chronic myeloid leukemia. *Int J Hematol*. 2023.01; 117(1); 24-29
1. Hirate T, Kitazawa H, Sakaguchi H, Akita N, Hasegawa C, Yamamoto K, Kutsuna S, Mikita K, Mori T, Hama A, Yoshida N. Cerebral toxoplasmosis developed after unrelated bone marrow transplantation for acute myeloid leukemia. *Rinsho ketsueki*. 2023; 64(10); 1275-1279

2. Koi S, Nogami A, Fujiwara H, Bando K, Saito M, Osada Y, Tanaka K, Sakashita C, Yoshifuji K, Okada K, Umezawa Y, Nagao T, Yamamoto M, Mori T. Acute promyelocytic leukemia with asymptomatic cerebral hemorrhage. *Rinsho ketsueki*. 2023; 64(11); 1426-1430
3. Tomoyasu Jo, Tomoko Henzan, Daisuke Tomizawa, Satoru Yoshihara, Kaoru Kahata, Minami Yamada-Fujiwara, Yoshiki Okuyama, Norio Shiba, Keiko Fujii, Yoshihiro Umezawa, Rie Yamazaki, Wataru Takeda, Ryo Hanajiri, Kentaro Fukushima, Naoya Mimura, Junko Ikemoto, Keita Iwaki, Noboru Yonetani, Shin-Ichiro Fujiwara, Masaki Ri, Tokiko Nagamura-Inoue, Ryuji Tanosaki, Yasuyuki Arai. Manufacturing results of tisagenlecleucel for acute lymphoblastic leukemia: a survey by the CAR-T cell therapy taskforce of the Japan Society of Transfusion Medicine and Cell Therapy. *Rinsho Ketsueki*. 2023; 64(5); 331-337

[Conference Activities & Talks]

1. Yuka Sugimoto, Keiki Nagaharu, Eiko Oya, Takehiko Mori, et al.. Thrombotic and Bleeding Events in Japanese Adolescent and Young Adult PV and ET: Results from Japanese Multicenter Retrospective Study. 2023.12 San Diego
2. Sanjay Mohan, Stephen T. Oh, Jean-Jacques Kiladjian, Masahiro Takeuchi, Jason Gotlib, Ellen Ritchie, Taizo Shimomura, Paola Guglielmelli, Anthony M. Hunter, Francesca Palandri, Francoise Boyer, Alessandro Rambaldi, Takehiko Mori, Tomoki Ito, Betty Lamothe, Yan-ou Yang, Yi Cui, Francis Seguy, Amanda McBride, Prithviraj Bose. Phase 1/2 Study of the Activin Receptor-like Kinase-2 Inhibitor Zilurgisertib (INCB000928, LIMBER-104) as Monotherapy or With Ruxolitinib in Patients With Anemia due to Myelofibrosis. 65th Annual Meeting of American Society of Hematology, 2023.12 San Diego
3. Satoru Aoyama, Ayako Nogami, Sadakatsu Ikeda, Takehiko Mori. Novel protease-mediated double antigen recognizing Chimeric Antigen Receptor (CAR) enhances the directionality of CAR-T cell activity and improves target cell specificity.. Keystone symposia A4: Emerging Cellular Therapies at the Forefront of Cancer Immunotherapy 2023.01.31
1. Kota Yoshifuji, Daichi Sadato, Takashi Toya, Yotaro Motomura, Hiroshi Takase, Yuka Harada, Takehiko Mori, Toshikage Nagao. Genetic alterations of primary vitreoretinal lymphoma are associated with CNS progression. 85th Congress of the Japanese Society of Hematology 2023.10.14 Tokyo
2. Ayako Nogami, Morito Kurata, Towako Taguchi, Shomi Koyama, Katsutoshi Nagano, Keisuke Tanaka, Kota Yoshifuji, Yoshihiro Umezawa, Naoya Ichimura, Shuji Tohda, and Takehiko Mori. Efficacy of pathological method of identifying causative virus of hemorrhagic cystitis by cell block. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo
3. Keigo Okada, Makiko Saito, Yotaro Motomura, Kota Yoshifuji, Satoru Aoyama, Toshikage Nagao, and Ayako Nogami. FLT3-ITD activates PDK1 which phosphorylates N-Rsk and inhibits Bim to enhance survival in AML cells. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo
4. Eiko Ohya, Keiki Nagaharu, Yuka Sugimoto, Kohshi Ohishi, Isao Tawara, Tomoki Ito, Akihiko Gotoh, Mika Nakamae, Fumihiko Kimura, Michiaki Koike, Keita Kirito, Hideho Wada, Kensuke Usuki, Takayuki Tanaka, Takehiko Mori, Satoshi Wakita, Toshiki Saito, Akiko Kada, Akiko Saito M., Kazuya Shimoda, Toshiro Kurokawa, Akihiro Tomita, Yoko Edahiro, Yoshinori Hashimoto, Hitoshi Kiyoi, Itaru Matsumura, Katsuto Takenaka, Norio Komatsu. Relevance of the treatment and thrombotic/bleeding events in PV and ET; subanalysis of JSH-MPN-R18. 85th annual meeting of Japanese Society of Hematology 2023.10.13 Tokyo
5. Keiki Nagaharu, Eiko Ohya, Yuka Sugimoto, Kohshi Ohishi, Isao Tawara, Tomoki Ito, Akihiko Gotoh, Mika Nakamae, Fumihiko Kimura, Michiaki Koike, Keita Kirito, Hideho Wada, Kensuke Usuki, Takayuki Tanaka, Takehiko Mori, Satoshi Wakita, Toshiki Saito, Akiko Kada, Akiko Saito M., Kazuya Shimoda, Toshiro Kurokawa, Akihiro Tomita, Yoko Edahiro, Yoshinori Hashimoto, Hitoshi Kiyoi, Itaru Matsumura, Katsuto Takenaka, Norio Komatsu. The identification of predictive parameters for thrombotic events in MPN; sub-analysis of MPN-R18. 85th annual meeting of Japanese Society of Hematology 2023.10.13 Tokyo

6. Yuya Sugimoto, Keiki Nagaharu ,Eiko Ohya,Kohshi Ohishi ,Isao Tawara ,Tomoki Ito ,Akihiko Gotoh, Mika Nakamae ,Fumihiko Kimura,Michiaki Koike ,Keita Kirito ,Hideho Wada ,Kensuke Usuki ,Takayuki Tanaka ,Takehiko Mori ,Satoshi Wakita ,Toshiki Saito ,Akiko Kada ,Akiko Saito M. ,Kazuya Shimoda ,Toshiro Kurokawa ,Akihiro Tomita ,Yoko Edahiro ,Yoshinori Hashimoto ,Hitoshi Kiyoi ,Itaru Matsumura ,Katsuto Takenaka ,Norio Komatsu . Clinical features in AYA PV and ET in Japan; secondary data analysis of JSH-MPN-R18. 85th annual meeting of Japanese society of Hematology 2023.10.13 Tokyo
7. Keisuke Tanaka, Hikari Kanai, Hiroya Kuwahara, Kota Yoshifuji, keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Toshikage Nagao, Chizuko Sakashita, Takehiko Mori, Masahide Yamamoto. Diffuse large B-cell lymphoma developed under the treatment of fingolimod. The Japanese Society for Lymphoreticular Tissue Reserch 2023.06.24
8. Yotaro Motomura, Kota Yoshifuji, Daichi Sadato , Ayako Nogami, Makiko Saito, Keigo Okada, Satoru Aoyama, Takehiko Mori, and Toshikage Nagao. Establishment and characterization of TMD13. a novel GCB-type DLBCL cell line. The 63th Annual Meeting of the Japanese Society for Lymphoreticular Tissue Research 2023.06.22 Saitama
9. Yasushi Onishi, Takehiko Mori, Hirohito Yamazaki, Nobuhiro Hiramoto, Yoshitaka Zaimoku, Minoru Kanaya, Takao Suenaga, Makoto Onizuka, Nobuyuki Aotsuka, Naoyuki Uchida, Koichi Onodera, Junya Kanda, Hirohisa Nakamae, Ryusuke Yamamoto, Tetsuya Eto, Takafumi Kimura, Tatsuo Ichinohe, Yoshiko Atsuta . Haploidentical transplantation with PTCY and cord blood transplantation for aplastic anemia. 45th annual meeting Japanese Society for Transplantation and Cellular therapy 2023.02.12 Nagoya
10. Ryusuke Yamamoto, Nobuhiro Hiramoto, Ayumi Fujimoto, Hirohito Yamazaki, Takehiko Mori, Naoyuki Uchida, Noriko Doki, Jun Kato, Yukiyasu Ozawa, Shuichi Ota, Makoto Onizuka, Tetsuya Eto, Yoshinobu Kanda, Takahiro Fukuda, Yoshiko Atsuta, Yasushi Onishi . Risk Factors for the Development of Posttransplant Lymphoproliferative Disease in Aplastic Anemia. 45th annual meeting Japanese Society for Transplantation and Cellular therapy 2023.02.12 Nagoya
11. Momoko Chiba, Keisuke Tanaka, Fumihiko Ouchi, Marie Yagi, Hikari Kanai, Takuma Harada, Hiroki Hatsuzawa, Kota Yoshifuji, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Chizuko Sakashita, Toshikage Nagao, Takehiko Mori, Masahide Yamamoto. Evaluation of autologous stem cell transplantation using busulfan-containing conditioning for central nervous system lymphoma. 5th JSTCT Annual Meeting Japanese Society for Transplantation and Cellular Therapy 2023.02.11 Nagoya
12. Hiroki Hatsusawa, Keisuke Tanaka, Marie Yagi, Fumihiko Ouchi, Hikari Kanai, Momoko Chiba, Takuma Harada, Kota Yoshifuji, Keigo Okada, Yoshihiro Umezawa, Chizuko Sakashita, Toshikage Nagao, Masahide Yamamoto, Takehiko Mori. Viral infection monitoring early after tisagenlecleucel therapy. 45th Japanese society for transplantation and cellular therapy annual meeting 2023.02.11 Nagoya

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: Ryoko Ishii, Kuniyuki Taguchi, Oriie Shiraishi, Noriko Takagi, Junnosuke Nakagawa

Resident: Yuko Ofuchi, Hiroko Sasaoka

Project Associate professor/lecturer: Mitsuyuki Numasawa

Graduate Students (Doctor's course): Akira Takeuchi, Kazunari Hara, Masato Horino, Jun Aoki, Rei Okazaki, Ryo Kaneda

(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]

1. Kawana Y, Imai J, Morizawa YM, Ikoma Y, Kohata M, Komamura H, Sato T, Izumi T, Yamamoto J, Endo A, Sugawara H, Kubo H, Hosaka S, Munakata Y, Asai Y, Kodama S, Takahashi K, Kaneko K, Sawada S, Yamada T, Ito A, Niizuma K, Tominaga T, Yamanaka A, Matsui K, Katagiri H. Optogenetic stimulation of vagal nerves for enhanced glucose-stimulated insulin secretion and β cell proliferation. *Nature biomedical engineering*. 2023.11;

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[Conference Activities & Talks]

1. Masanori Murakami. Single-Nuclei Analysis of Aldosterone-Producing Adenoma. The joint 22nd ENS@T and 2nd COST Harmonis@tion meeting 2023.10.13 Dubrovnik, Croatia
2. Mina Nakagawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Kanako Noritake, Eriko Okada, Eiji Kaneko, Janelle Moross, Jun Tsuruta, Keiichi Akita, Masanaga Yamawaki. Patients as teachers: a novel IPE curriculum . AMEE2023 2023.08.28
3. Kumiko Yamaguchi, Nobutoshi Nawa, Mitsuyuki Numasawa, Keiichi Akita. Development of an anatomy education program to consolidate learning content. AMEE 2023 2023.08.28 Glasgow, UK
4. 宮 真里, 赤石 雄, 沼沢 益行, 鹿島田 彩子, 岡田 英理子, 鈴木 健嗣, 山脇 正永. AI を活用した表情分析における瞬目頻度と講義満足度との関連. 第 55 回日本医学教育学会大会 2023.07.28 長崎
5. Otsubo Naoya, Fukuda Tatsuya, Maki Chisato, Beppu Hiroko, Hanawa Tomohide, Sugita Chise, Yamada Tetsuya, Wakai SachikoNaoya Otsubo, Tatsuya Fukuda, Chisato Maki, Hiroko Beppu, Tomoko Kawanishi, Toshie Ogawa, Yasutomo Abe, Mariko Endo, Tomohide Hanawa, Chise Sugita, Tetsuya Yamada, and Sachiko Wakai.. Serum chemokine CC-motif ligand 17 is a predictive marker of severe COVID-19 in patients with diabetes.. IDF-WPR Congress 2023/15th Scientific Meeting of AASD 2023 2023.07.21

[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

Toshitaka Sugawara MD, PhD(from October)

Graduate School Students

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

Masahiro Yamane MD

Teruchika Koyama MD(from April)

Suguru Miyazawa MD(from April)

Shohei Motohashi 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:

- Biomolecular mechanisms of carcinogenesis, cancer growth, invasion and metastasis
- Molecular target therapy for malignant diseases

- Cancer stem cell
- Extended indication for hepatectomy
- The system of liver microcirculation
- Laparoscopic surgery for hepatobiliary and pancreatic cancers
- Liver transplantation and organ preservation
- Treatments for neuroendocrine tumor
- Innovation of imaging modality for hepatobiliary and pancreatic cancers
- 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 2023, the influence of surgery restrictions by COVID-19 was strong, and the total number of surgeries was 184 (255 in 2019), 45 hepatectomy and 67 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: 17 robotic pancreaticoduodenectomies and 10 distal pancreatectomy were successfully performed. Robotic liver resection also began in 2023. This is also being introduced safely.

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]

1. Wang JJ, Feng J, Gomes C, Calthorpe L, Ashraf Ganjouei A, Romero-Hernandez F, Benedetti Cacciaguerra A, Hibi T, Abdelgadir Adam M, Alseidi A, Abu Hilal M, Rashidian N; International Post-Hepatectomy Liver Failure Study Group. Development and Validation of Prediction Models and Risk Calculators for Post-Hepatectomy Liver Failure and Postoperative Complications using a Diverse International Cohort of Major Hepatectomies. *Ann Surg.* 2023.12;
2. Endo Y, Shinoda M, Maehara J, Hibi T, Hasegawa Y, Obara H, Kitago M, Ojima H, Tanabe M, Kitagawa Y. Early-onset hepatic veno-occlusive disease after liver transplantation: an institutional experience and analysis of a literature-based cohort. *Surg Today.* 2023.12;
3. Shun Kaneko, Yasuhiro Asahina, Miyako Murakawa, Shunsuke Ueyama, Chiaki Maeyashiki, Hideki Watanabe, Akiko Kusano-Kitazume, Ayako Sato, Kozue Uchidate, Takehito Asakawa, Sho Watanabe, Yasuhiro Iizuka, Isamu Shibata, Shinya Oooka, Yuko Karakama, Takashi Fujii, Taro Watabe, Keiichi Akahoshi, Minoru Tanabe, Kento Inada, Tomohiro Mochida, Keiya Watakabe, Taro Shimizu, Jun Tsuchiya, Masato Miyoshi, Fukiko Kitahata-Kawai, Sayuri Nitta, Mina Nakagawa, Sei Kakinuma, Ryuichi Okamoto, . Prognostic Significance of C-Reactive Protein in Unresectable Hepatocellular Carcinoma treated with Atezolizumab and Bevacizumab. *Hepatol Res.* 2023.12; Online ahead of print.;
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6. PancreasGroup.org Collaborative. Pancreatic surgery outcomes: multicentre prospective snapshot study in 67 countries. *British Journal of Surgery.* 2023.11;
7. Kentaro Yamada, Toshitaka Yoshii, Mikayo Toba, Atsushi Kudo, Satoru Egawa, Yu Matsukura, Takashi Hirai, Hiroyuki Inose, Kiyohide Fushimi, Atsushi Okawa. Risk Factors for Postoperative Unfavorable Ambulatory Status After Spinal Surgery for Metastatic Spinal Tumor. *Spine (Phila Pa 1976).* 2023.10; 48(20); 1419-1426
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10. Stuart CM, Kirsch MJ, Zhuang Y, Meguid CL, Sugawara T, Colborn KL, Messersmith W, Lieu C, Gleisner AL, Del Chiaro M, Schulick RD, Meguid RA. Pulmonary metastasectomy is associated with survival after lung-only recurrence in pancreatic cancer. *Surgery.* 2023.09; 174(3); 654-659

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13. Ichida A, Kokudo T, Shimada S, Hatano E, Kubo S, Kato Y, Ishikawa Y, Mori A, Baba H, Matsuyama Y, Endo I, Yamaue H, Yamamoto M, Kokudo N, Hasegawa K. Liver Resection for Hepatocellular Carcinoma With Tumor Thrombus in the Inferior Vena Cava or Right Atrium: A Large-scale Multicenter Survey Conducted in Japan. *Ann Surg*. 2023.09; 278(3); e549-e555
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19. Sugawara T, Rodriguez Franco S, Franklin O, Kirsch MJ, Colborn K, Del Chiaro M, Schulick RD. Management of Localized Small and Large Cell Pancreatic Neuroendocrine Carcinoma in the National Cancer Database. *J Am Coll Surg*. 2023.05;
20. Sugawara T, Rodriguez Franco S, Sherman S, Torphy RJ, Colborn K, Franklin O, Ishida J, Grandi S, Al-Musawi MH, Gleisner A, Schulick RD, Del Chiaro M. Neoadjuvant Chemotherapy versus Upfront Surgery for Resectable Pancreatic Adenocarcinoma: An Updated Nationwide Study. *Ann Surg*. 2023.05; 279(2); 331-339
21. Ishida H, Ogura T, Takahashi A, Kitamura K, Miyamoto R, Matsudaira S, Tanabe M, Kanda H, Kawashima Y. Prognostic Value of Peritoneal Lavage Cytology in Potentially Resectable Pancreatic Cancer Stratified by Cytologic Status. *Cancer Diagn Progn*. 2023.05; 3(3); 338-346
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27. Sugawara T, Rodriguez Franco S, Kirsch MJ, Colborn KL, Ishida J, Grandi S, Al-Musawi MH, Gleisner A, Del Chiaro M, Schulick RD. Evaluation of Survival Following Surgical Resection for Small Nonfunctional Pancreatic Neuroendocrine Tumors. *JAMA Netw Open*. 2023.03; 6(3); e234096
28. Sugawara T, Rodriguez Franco S, Sherman S, Kirsch MJ, Colborn K, Ishida J, Grandi S, Al-Musawi MH, Gleisner A, Schulick RD, Del Chiaro M. Association of Adjuvant Chemotherapy in Patients With Resected Pancreatic Adenocarcinoma After Multiagent Neoadjuvant Chemotherapy. *JAMA Oncol*. 2023.03; 9(3); 316-323
29. Woohyung Lee, Dae Wook Hwang, Ho-Seong Han, In Woong Han, Jin Seok Heo, Michiaki Unno, Masaharu Ishida, Hiroshi Tajima, Nobuyuki Nishizawa, Kohei Nakata, Yasuji Seyama, Yoshiya Ishikawa, Ho Kyoung Hwang, Jin-Young Jang, Taeho Hong, Joon Seong Park, Hee Joon Kim, Chi-Young Jeong, Ippei Matsumoto, Hiroki Yamaue, Manabu Kawai, Masayuki Ohtsuka, Shugo Mizuno, Mitsuhiro Asakuma, Yuji Soejima, Teijiro Hirashita, Masayuki Sho, Yutaka Takeda, Jeong-Ik Park, Yong Hoon Kim, Hwa Jung Kim, Hiroki Yamaue, Masakazu Yamamoto, Itaru Endo, Masafumi Nakamura, Yoo-Seok Yoon. Comparison of infectious complications after spleen preservation versus splenectomy during laparoscopic distal pancreatectomy for benign or low-grade malignant pancreatic tumors: A multicenter, propensity score-matched analysis. *J Hepatobiliary Pancreat Sci*. 2023.02; 30(2); 252-262
30. Otsubo T, Kobayashi S, Sano K, Misawa T, Katagiri S, Nakayama H, Suzuki S, Watanabe M, Ariizumi S, Unno M, Tanabe M, Nagano H, Kokudo N, Hirano S, Nakamura M, Shirabe K, Suzuki Y, Yoshida M, Takada Y, Nakagohri T, Horiguchi A, Ohdan H, Eguchi S, Ohtsuka M, Sho M, Rikiyama T, Hatano E, Taketomi A, Fujii T, Yamaue H, Miyazaki M, Yamamoto M, Takada T, Endo I. A nationwide certification system to increase the safety of highly advanced hepatobiliary-pancreatic surgery. *J Hepatobiliary Pancreat Sci*. 2023.01; 30(1); 60-71

[Conference Activities & Talks]

1. Minoru Tanabe. Knack for Whipple operation: Anatomy around SMA & SMV. IRCAD 2023.12.07 Taiwan
2. Minoru Tanabe. Basic principles of laparoscopic liver resection: patient selection, OR set up and instruments. IRCAD 2023.11.30 Taiwan
3. Atsushi Nara, Hiroki Ueda, Keiichi Akahoshi, Akira Ito, Shotaro Gan, Hironari Yamashita, Koichiro Morimoto, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Preoperative sarcopenia assessment predicts loss of independence after Pancreaticoduodenectomy (PD) in pancreatic cancer patients. The 3rd International Congress of the Asian Oncology Society 2023.10.20 Yokohama
4. Akira Ito, Keiichi Akahoshi, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Prognostic Impact of Reticular Pattern around Superior Mesenteric Artery in CT Images of Pancreatic Cancer. The 3rd International Congress of the Asian Oncology Society 2023.10.20 Yokohama
5. Shotaro Gan, Daisuke Asano, Akira Ito, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Determining the Indication of Surgery for High grade pNENs. The 3rd International Congress of the Asian Oncology Society 2023.10.20 Yokohama
6. Minoru Tanabe. Operative difficulty on laparoscopic liver resection: What has changed in the last decade?. 9th Biennial Congress of the Asian-Pacific Hepato Pancreato Biliary Association 2023.09.29 Bangalore, India

7. Hiroaki Ono, Keiichi Akahoshi, Shinji Tanaka, Minoru Tanabe. RRM1 is mediated by H3 acetylation through GEM resistance and contributes to invasiveness and ECM remodeling in PDAC. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
8. Hironari Yamashita, Hiroaki Ono, Kotaro Takizawa, Shuichi Watanabe, Kosuke Ogawa, Daisuke Asano, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Yoshimitsu Akiyama, Shinji Tanaka, Minoru Tanabe. PCNA-I1 is identified as a novel therapeutic agent in pancreatic cancer. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
9. Yuzuki Sugiyama, Satoru Muro, Daisuke Ban, Keiichi Akita. The fusion fascia affects the course of the nerves to the pancreas. The 17th Annual Congress of the European Association of Clinical Anatomy (EACA) and the 14th Annual Congress of the International Symposium of Clinical and Applied Anatomy (ISCAA) 2023.09.15 Prague, Czech
10. Minoru Tanabe. Robotic liver surgery: current status and beyond. ILLS 4th WORLD CONGRESS 2023.09.14 Rome, Italy
11. Minoru Tanabe. Curative surgery and survival. 34th IASGO World Congress 2023.09.11 Verona, Italy
12. Atsushi Kudo, Minoru Tanabe. SP1-3 PRRT will expand surgical indication for pancreatic neuroendocrine neoplasms. The 54th Annual Meeting of the Japanese Pancreas Society 2023.07.21 Fukuoka
13. 杉山 夕月, 室生 暁, 伴 大輔, 秋田 恵一. Morphology of the fusion fascia, nerves, and arteries around the pancreatic head. 第 35 回日本肝胆膵外科学会学術集会 2023.07.01 東京
14. Hiroki Ueda, Atsushi Nara, Masaru Takeuchi, Masahiro Yamane, Akira Ito, Koichiro Morimoto, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Age and Sarcopenia Are Risk Factors for ADL Decline After Pancreaticoduodenectomy; Our approach to maintain ADLs before and after surgery. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
15. Hiroaki Ono, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Emerging Multidisciplinary Therapies Including PRRT Therapy in Pancreatic Neuroendocrine Neoplasms. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
16. Koichiro Morimoto, Hiroki Ueda, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Shinji Tanaka, Minoru Tanabe. Characteristics of refractory postoperative cholangitis after hepatectomy with hepaticojejunostomy: Anastomotic stenosis is not the only cause. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
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18. Shotaro Gan, Daisuke Asano, Masaru Takeuchi, Masahiro Yamane, Akira Ito, Atsushi Nara, Koichiro Morimoto, Hironari Yamashita, Kohei Yagi, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Keiichi Akahoshi, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. A case of unresectable pancreatic ductal adenocarcinoma (UR-PDAC) in an elderly patient who underwent radical resection after preoperative chemotherapy and survived without recurrence for 1 year. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
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22. Daisuke Asano, Keiichi Akahoshi, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. How to achieve the negative surgical margin for ICC suspicious of invasion to hilum: with the video of laparoscopic left hepatectomy by hilar dissection approach. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
23. Shuichi Watanabe, Daisuke Asano, Yoshiya Ishikawa, Hiroki Ueda, Keiichi Akahoshi, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Investigation of recurrence format of single recurrent lesions using genomic analysis. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
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25. Arimasa Miyama, Zenichi Morise, Minoru Tanabe, Go Wakabayashi, ILLS-Tokyo collaborator group. International multicenter retrospective Study of liver functional deterioration after liver resection for HCC/CLD patients. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.07.01 Tokyo
26. Keiichi Akahoshi, Junichi Shindo, Susumu Eguchi, Itaru Endo, Shoji Kubo, Mitsuo Shimada, Akinobu Taketomi, Hiroaki Nagano, Masafumi Nakamura, Kiyoshi Hasegawa, Etsuro Hatano, Tomoharu Yoshizumi, Minoru Tanabe, Norihiro Kokudo. Questionnaire survey on surgical indications of hepatocellular carcinoma for the board-certified expert surgeons and instructors (hepato-biliary-pancreatic field). The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
27. Atsushi Nara, Keiichi Akahoshi, Akira Ito, Shotaro Gan, Daisuke Asano, Shuichi Watanabe, Yoshiya Ishikawa, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Pancreatic duct stent AMY after pancreaticoduodenectomy is a predictor of pancreatic fistula. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
28. Akira Ito, Keiichi Akahoshi, Masaru Takeuchi, Masahiro Yamane, Shotaro Gan, Atsushi Nara, Koichiro Morimoto, Munetaka Kimura, Hironari Yamashita, Kohei Yagi, Daisuke Asano, Yoshiya Ishikawa, Shuichi Watanabe, Hiroki Ueda, Hiroaki Ono, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Hepatectomy After Pancreatoduodenectomy Has a High Risk of Postoperative Complications. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
29. Oskar Franklin, Toshitaka Sugawara, Salvador Rodriguez Franco, Kathryn Colborn, Richard D Schulick, Marco Del Chiaro. Addition and timing of surgery in multiagent chemotherapy treatment of metastatic pancreatic cancer. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
30. Salvador Rodriguez Franco, Andrii Khomiak, Toshitaka Sugawara, Oskar Franklin, Michael Kirsch, Chiara Croce, Richard D Schulick, Marco Del Chiaro. Optimal perioperative multiagent chemotherapy in resected pancreatic cancer: A high-volume center report. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
31. Toshitaka Sugawara, Salvador Rodriguez Franco, Oskar Franklin, Chiara Croce, Jun Ishida, Samuele Grandi, Richard D. Schulick, Marco Del Chiaro. Management for resectable and borderline resectable pancreatic adenocarcinoma in University of Colorado Hospital. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
32. Shigenori Ei, Minoru Kitago, Masahiro Shinoda, Osamu Itano, Minoru Tanabe, Yuko Kitagawa. Report on experiences of conducting clinical and basic research at the University of Heidelberg, Germany -Study abroad life in Europe in the COVID-19 pandemic-. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo

33. Minoru Kitago, Gaku Shimane, Hiroshi Yagi, Yuta Abe, Yasuhi Hasegawa, Shutaro Hori, Masayuki Tanaka, Yutaka Nakano, Minoru Tanabe, Yuko Kitagawa. Two cases of hepatic cystic tumor that was difficult to differentiate from the mucinous cystic tumor of the liver. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
34. Minoru Tanabe. The Spirit of HBP Surgeons. The 35th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2023.06.30 Tokyo
35. Atsushi Kudo. Advance in treatment strategy for neuroendocrine tumors. The 18th Congress of the Asian Association of Endocrine Surgeons 2023.03.17 Tokyo
36. Minoru Tanabe. Update in Management on Pancreatic Cancer from a Surgeon's Perspective. 11th Annual Scientific Meeting 2023.03.04 Hong Kong
37. K.Akahoshi, A.Nara, A.kudo, H.Ono, S.Watanabe, D.Asano, H.Ueda, Y.Ishikawa, M.Tanabe. Impact of Sunitinib Followed by Liver Resection for Metastatic Pancreatic Neuroendocrine Neoplasms. 18th Annual Academic Surgical Congress 2023.02.08 Houston
38. A.Nara, K.Akahoshi, H.Ueda, D.Asano, S.Watanabe, Y.Ishikawa, H.Ono, A.Kudo, S.Tanaka, M.Tanabe. Usefulness of the NRSS in Determining the Timing of TAE for Ruptured Hepatocellular Carcinoma. 18th Annual Academic Surgical Congress 2023.02.08 Houston

[Others]

1. Current status of minimally invasive surgery (non-robot) in Asian countries, 2023.10
Minoru Tanabe, Chair, Symposium, The 3rd International Congress of the Asian Oncology Society, 20231020, Yokohama
2. THEORETICAL SESSION, 2023.11
Minoru Tanabe, Chairman, IRCAD, 20231130, Taiwan
3. THEORETICAL SESSION, 2023.12
Minoru Tanabe, Chairman, IRCAD, 20231202, Taiwan

Orthopaedic and Spinal Surgery

Professor: Toshitaka Yoshii

Junior Associate Professor: Yuko Segawa, Takashi Hirai

Assistant Professor: Yu Matsukura, Yuki Funauchi, Shingo Morishita, Satoru Egawa, Toru Sasaki

Specially Appointed Assistant Professor: Takumi Kaku, Aritoshi Yoshihara, Takuya Takahashi, Yusuke Amano

「Department of Orthopaedic and Trauma Research」

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

Assistant Professor: Jun Hashimoto

Adjunct Lecturer : Kensuke Sekihara, Isamu Ozaki, Nobuhiro Genma

(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, motion analysis, pain control and application of AI. 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 and regeneration
2. Research for clinical application of artificial materials (bone, nerve)
3. Elucidation of the mechanism of spinal ligament ossification
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
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)
11. Radiological analysis using AI
12. Motion analysis in kyphotic patients
13. Development of antibiotic implant

(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, hip surgery, orthopedic trauma surgery, and pediatric orthopedics. 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]**

1. Tomoyuki Tanaka, Yuri Miyakoshi, Yutaka Kobayashi, Sun Xiaolong, Yu Daiyang, Hiroki Ochi, Shingo Sato, Tsuyoshi Kato, Toshitaka Yoshii, Atsushi Okawa, Philipp Kaldis, Hiroyuki Inose. Regulation of Osteoblast to Osteocyte Differentiation by Cyclin-Dependent Kinase-1. *Adv Biol (Weinh)*. 2023.12; 7(12); e2300136
2. Naoto Watanabe, Takahisa Ogawa, Ryohei Takada, Yusuke Amano, Tetsuya Jinno, Hideyuki Koga, Toshitaka Yoshii, Atsushi Okawa, Kazumasa Miyatake. Association of osteoporosis and high serum homocysteine levels with intraoperative periprosthetic fracture during total hip arthroplasty: a propensity-score matching analysis. *Arch Orthop Trauma Surg*. 2023.12; 143(12); 7219-7227
3. Motohashi M, Funauchi Y, Adachi T, Fujioka T, Otaka N, Kamiko Y, Okada T, Tateishi U, Okawa A, Yoshii T, Sato S. A New Deep Learning Algorithm for Detecting Spinal Metastases On CT Images. *Spine*. 2023.12; 49(6); 390-397
4. Hao Ding, Hideyuki Koga, Hiroki Katagiri, Shoichi Hasegawa, Tatushiko Anzai, Mai Katakura, Aritoshi Yoshihara, Masaki Amemiya, Takashi Hoshino, Nobutake Ozeki, Tomomasa Nakamura, Yusuke Nakagawa. Low central sensitisation inventory score is associated with better post-operative outcomes of osteotomy around the knee. *Knee Surg Sports Traumatol Arthrosc*. 2023.12; 31(12); 5896-5904
5. Takuya Takahashi, Hiroyuki Inose, Takashi Hirai, Yu Matsukura, Shingo Morishita, Satoru Egawa, Jun Hashimoto, Kunihiro Takahashi, Toshitaka Yoshii. Factors associated with the time required for CRP normalization in pyogenic spondylitis: A retrospective observational study. *N Am Spine Soc J*. 2023.12; 17; 100301
6. Norimitsu Wakao, Takeo Furuya, Toshitaka Yoshii, Hideyuki Arima, Yu Yamato, Hiroaki Nakashima, Shiro Imagama, Yasuaki Imajo, Hiroshi Miyamoto, Gen Inoue, Masayuki Miyagi, Shunsuke Kanbara, Yoichi Iizuka, Hirotaka Chikuda, Kei Watanabe, Kazuyoshi Kobayashi, Mikito Tsushima, Masashi Miyazaki, Mitsuru Yagi, Satoshi Suzuki, Masahiko Takahata, Michio Hongo, Masao Koda, Keiji Nagata, Kanji Mori, Akinobu Suzuki, Takashi Kaito, Kenta Murotani, Naohisa Miyakoshi, Hiroshi Hashizume, Yukihiro Matsuyama, Mamoru Kawakami, Hirotaka Haro, . A nationwide multicenter study of the cost effectiveness of five leading drugs for pharmacological management of cervicobrachial symptoms. *J Orthop Sci*. 2023.12; S0949-2658(23); 00334-2
7. Hiroyuki Inose, Takuya Takahashi, Yu Matsukura, Jun Hashimoto, Kurando Utagawa, Satoru Egawa, Kentaro Yamada, Takashi Hirai, Toshitaka Yoshii. Factors Associated With Nonunion After Cervical Fusion Surgery. *Cureus*. 2023.12; 15(12); e50866
8. Yamamoto Kie, Shimura Haruhiko, Suzuki Hidetsugu, Yamada Eriku, Fujita Koji, Nimura Akimoto. Acute osteomyelitis after the physeal injury of the distal phalanx of the hand(Seymour fracture): A report of two cases *JOS Case Reports*. 2023.12; 2(4); 165-168
9. Shimura Haruhiko, Fujita Koji, Sasaki Toru, Nimura Akimoto. Pediatric olecranon osteochondral fracture with delayed diagnosis: A case report *JOS Case Reports*. 2023.12; 2(4); 192-194
10. 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*. 2023.11; 28(6); 1298-1302
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20. Takashi Hirai, Satoru Egawa, Kenichiro Sakai, Hiroaki Onuma, Jun Hashimoto, Kurando Utagawa, Shingo Morishita, Kentaro Yamada, Yu Matsukura, Yoshiyasu Arai, Toshitaka Yoshii. Novel Technique of Anterior Foraminotomy Based on Augmented Reality with Computed Tomography Navigation System: A Case Report. *Spine Surg Relat Res*. 2023.10; 8(1); 114-117
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 24. Yohei Tomaru, Makoto Kamegaya, Takashi Saisu, Yasuhiro Oikawa, Jun Kakizaki, Yuko Segawa, Yuta Tsukagoshi, Hiroshi Kamada, Masashi Yamazaki. Radiologic Changes After 10 Years Postreduction in Developmental Dysplasia of the Hip Treated With Different Reduction Methods and Risk Factors for Osteoarthritis. *J Pediatr Orthop*. 2023.09; 43(8); e633-e638
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[Misc]

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[Conference Activities & Talks]

1. Yoto Oh. Hybrid knee arthrodesis using a Masquelet induced membrane technique for severe periprosthetic joint infection after TKA: a case report. 2nd Japan-Taiwan Exchange Trauma Conference (JT-ETC) 2023.12.02 Taiwan
2. Jun Hashimoto, Shigenori Kawabata, Takashi Hirai, Yu Matsukura, Satrou Egawa, Toshitaka Yoshii. The Incidence and Alert Timing of Spontaneous Electromyogram in Surgery for Ossification of the Posterior Longitudinal Ligament. 51st Annual Meeting of the Cervical Spine Research Society (CSRS) 2023.12.01 Las Vegas
3. Go Uesugi, Takashi Hirai, Toshitaka Yoshii, Jun Hashimoto, Masashi Yamazaki, Yoshiharu Kawaguchi. The Comparison between Cervical Ossification of the Posterior Longitudinal Ligament and Cervical Spondylotic Myelopathy Patients in Health-Related Quality of Life: a Multicenter Cross-Sectional Study. 51st Annual Meeting of the Cervical Spine Research Society (CSRS) 2023.12.01 Las Vegas
4. Yu Matsukura, Toshitaka Yoshii, Hiroyuki Inose, Takashi Hirai, Satoru Egawa, Kentaro Yamada, Jun Hashimoto, Kurando Utagawa, Yuri Tamura, Go Uesugi, Atsushi Okawa. Investigation of Risk Factors of C5 Palsy After Anterior Cervical Spine Surgery. 51st Annual Meeting of the Cervical Spine Research Society (CSRS) 2023.11.30 Las Vegas
5. Motonori Hashimoto, Toshitaka Yoshii, Satoru egawa, Takashi Hirai, Kenichiro Sakai. Comparison of complication frequency after anterior cervical spine surgery - CSM vs OPLL. 51st Annual Meeting of the Cervical Spine Research Society (CSRS) 2023.11.29 Las Vegas
6. Toshitaka Yoshii, Yu Matsukura, Satoru Egawa, Kenichiro Sakai, Takashi Hirai, Masao Koda, Masashi Yamazaki. Preoperative Symptom Duration Influences Neurological Recovery and Achievement of the Minimal Clinically Important Difference After Surgical Treatment of Cervical Ossification of the Posterior Longitudinal Ligament. 51st Annual Meeting of the Cervical Spine Research Society (CSRS) 2023.11.29 Las Vegas
7. Motonori Hashimoto, Toshitaka Yoshii, Satoshi Egawa, Takashi Hirai. Imaging Features and Treatment of ossification of the posterior longitudinal ligament in the upper cervical spine. 51st Annual Meeting of the Cervical Spine Research Society (CSRS) 2023.11.29 Las Vegas
8. Kiminori Hori, Makoto Konishi, Makiko Yamashita, Takashi Kamatani, Kyoko Yamashita, Yuki Funauchi, Keisuke Ae, Shigehisa Kitano, Koichi Matsuda, Tatsuhiko Tsunoda, Koji Ueda. Proteogenomic approach to explore prognostic biomarkers for myxoid liposarcoma. The 82nd Annual Meeting of the Japanese Cancer Association 2023.09.23 Yokohama
9. Toshitaka Yoshii. Complications of OPLL surgery: incidence and prevention. Neuro Spine Congress 2023 2023.09.22 Korea
10. Koji Fujita. Motion analysis of the hand and Screening diseases. Department of Orthopaedics, National Cheng Kung University 2023.09.14 Tainan City, Taiwan
11. Koji Fujita. Creation of new technologies through medical-engineering collaboration. Department of Biomedical Engineering, National Cheng Kung University 2023.09.14 Tainan City, Taiwan
12. Nimura A, Fukai A. What is the lateral ulnar collateral ligament?; an anatomical study. 15th International congress on shoulder and elbow surgery 2023.09.06 Roma, Italy
13. Yoto Oh. The 2018 AO/OTA Fracture and Dislocation Classification Compendium. AO Trauma Course - Basic Principles of Fracture Management 2023.08 Yokohama
14. Yoto Oh. Ankle fractures—a systematic approach to their fixation. AO Trauma Course - Basic Principles of Fracture Management 2023.08 Yokohama

15. Yoto Oh. Treatment algorithms for the polytrauma patient. AO Trauma Course - Basic Principles of Fracture Management 2023.08 Yokohama
16. Yoto Oh. Implant removal—Why, when, and how?. AO Trauma Course - Basic Principles of Fracture Management 2023.08 Yokohama
17. Takumi Kaku, Yoto Oh. Urethral injury secondary to advanced fragility fracture of the pelvis: a case report. 23rd Pelvic Acetabular Fracture Conference 2023.07.01 Shizuoka
18. Toshitaka Yoshii. Short-term clinical results of total disc replacement and future perspective. The 38th Annual Meeting of the Neurospinal Society of Japan· The 14th Annual Meeting of Asia Spine 2023.06.17 Aichi
19. Ryohei Takada, Naoto Watanabe, Kazumasa Miyatake, Naohiko Sugita, Tetsuya Jinno, Toshitaka Yoshii, Hideyuki Koga. Development of non-invasive augmented reality-based navigation system for total hip arthroplasty. 22nd Annual Meeting of CAOS 2023.06.07 Pattaya, Thailand
20. Yuta Tanaka, Shigenori Kawabata, Toru Sasaki, Jun Hashimoto, Hisato Higashikawa, Yoshiaki Adachi, Taishi Watanabe, Yuki Miyano, Saeri Kaminaka, Yusuke Yamamoto, Hidetoshi Kaburagi, Koji Fujita, Akimoto Nimura, Toshitaka Yoshii, Atsushi Okawa. Evaluation of nerve conduction in patients with ulnar neuropathy at the elbow using magnetoneurography. ISACM and JBBS 2023 2023.05.25 Osaka
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23. Yoshiaki Adachi, Shigenori Kawabata. Simultaneous recording of biomagnetic signals using SQUIDS and relocatable room-temperature flux sensors. ISACM and JBBS 2023 2023.05.25 Osaka
24. Isamu Ozakia, Miho Akaza, Taishi Watanabe, Yuki Miyano, Yoshiaki Adachi, Shigenori Kawabata. Peripheral Magnetoneurography with a SQUID Biomagnetometer System: Comparison with Surface Electric Potential Recordings. ISACM and JBBS 2023 2023.05.25 Osaka
25. Eriku Yamada, Takuya Ibara, Akiko Yamamoto, Kazuya Tsukamoto, Koji Fujita . Development of a Screening Method for Cervical Myelopathy by Hand Movements Using Machine Learning. XXVIII FESSH-EFSHT CONGRESS 2023.05.12 Italy
26. Koji Fujita, Takuya Ibara, Ryota Matsui, Hideo Saito, Yuta Sugiura. Smartphone-based machine learning algorithm for disease screening with the 10-s grip-and-release test. XXVIII FESSH-EFSHT CONGRESS 2023.05.11 Italy
27. Yoto Oh, Toshitaka Yoshii, Atsushi Okawa. Development of a CT-based finite element analysis model for verifying the effect of shock-absorbing floors on hip fracture prevention. 22nd European Congress of Trauma & Emergency Surgery 2023.05.07 Slovenia
28. Takumi Kaku, Yoto Oh, Toshitaka Yoshii, Atsushi Okawa. Urethral injury secondary to advanced fragility fracture of the pelvis: a case report. 22nd European Congress of Trauma & Emergency Surgery 2023.05.07 Slovenia
29. Yamada K, Yoshii T, Toba M, Egawa S, Matsukura Y, Hirai T, Inose H, Fushimi K, Okawa A. Risk factors for postoperative unexpected ambulatory status after spinal surgery for metastatic spinal tumor.. ISSLS 2023 SPINE WEEK 2023.05.04 Melbourne
30. Yamada K.. Life Expectancy is Poor in Patients with Diffuse Idiopathic Skeletal Hyperostosis-Related Pyogenic Vertebral Osteomyelitis. ISSLS 2023 SPINE WEEK 2023.05.04 Melbourne
31. Takashi Hirai, Toshitaka Yoshi, Kenichiro Sakai, Yoshiharu Kawaguchi. CSM case treated with salvage LAM after ACDF. ISSLS 2023 SPINE WEEK 2023.05.01 Melbourne, Australia

32. Takashi Hirai, Toshitaka Yoshi, Kenichiro Sakai, Yoshiharu Kawaguchi. Association between clinical symptoms and distribution of OPLL based on prospective nationwide study. ISSLS 2023 SPINE WEEK 2023.05.01 Melbourne, Australia
33. Shigenori Kawabata. Magnetoneurography(MNG) of Peripheral Nerves, brachial plexus and Magnetospinography (MSG). American Clinical Neurophysiology Society 2023 ANNUAL MEETING & COURSES 2023.03.25 Austin,USA
34. Takashi Hirai. Clinical and radiologic evidences in cervical compressive diseases. 13th Annual Meeting of CSRS-AP 2023.03.11 Yokohama
35. Yu Matsukura, Toshitaka Yoshii, Hiroyuki Inose, Takashi Hirai, Satoru Egawa, Kentaro Yamada, Jun Hashimoto, Kurando Utagawa, Yuri Tamura, Go Uesugi , Atsushi Okawa. Investigation of risk factors of C5 palsy after anterior cervical spine surgery. 13th Annual Meeting of CSRS-AP 2023.03.11 Yokohama
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37. Kanji Mori, Toshitaka Yoshii, Satoru Egawa, Masao Koda, Takeo Furuya, Katsushi Takeshita, Morio Matsumoto, Shiro Imagama , Atsushi Okawa, Masashi Yamazaki. Impact of obesity on cervical ossification of the posterior longitudinal ligament: a nationwide prospective study. 13th Annual Meeting of CSRS-AP 2023.03.10 Yokohama
38. Toshitaka Yoshii. Early experiences and Short-term clinical results of Prestige LP in Japan. 13th Annual Meeting of CSRS-AP 2023.03.10 Yokohama
39. Akimoto Nimura. Reconsideration of anatomy in the lateral part of elbow joint; what are LCL and LUCL?. 7th FIPAR webinar 2023.02.01 Web
40. Yoto Oh. Interactive case presentation: Forearm. AO Trauma Masters Seminar 2023.02 Yokohama
41. Yoto Oh. Bone healing and the effect of patient factors and injury mechanism on fracture management. AO Trauma Course - Basic Principles of Fracture Management 2023.02 Yokohama
42. Yoto Oh. Fixation principles in osteoporotic bone—the geriatric patient. AO Trauma Course - Basic Principles of Fracture Management 2023.02 Yokohama
43. Yoto Oh. Fractures in the growing skeleton—how are they different?. AO Trauma Course - Basic Principles of Fracture Management 2023.02 Yokohama
44. Toshitaka Yoshii. Avoiding the Complications of Instrumented Fixation in Osteoporosis, and their management when they occur. DePuy Synthes Spine Inaugural Asia Pacific Osteoporosis Forum 2023.01.20

[Patents]

1. BIOMAGNETISM MEASURING DEVICE, Patent Number : ZL201780047125.1
2. BIOMETRIC INFORMATION MEASURING DEVICE, Patent Number : 11612368
3. BIOMAGNETISM MEASUREMENT DEVICE, Patent Number : 11666261
4. NERVE STIMULATING APPARATUS, BIOMETRIC INFORMATION MEASURING SYSTEM, AND METHOD OF SETTING STIMULUS GENERATING TIMINGS OF BIOMETRIC INFORMATION MEASURING SYSTEM, Patent Number : 11666759
5. BIOMETRIC INFORMATION DISPLAY DEVICE, BIOMETRIC INFORMATION DISPLAY METHOD, AND COMPUTER-READABLE RECORDING MEDIUM, Patent Number : 3824812
6. THROMBIN-LOADED HEMOSTATIC SHEET, Patent Number : ZL202080022290.3

Diagnostic Radiology and Nuclear Medicine

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(1) Outline

While diagnostic radiology and nuclear medicine demand high-level capabilities and therefore extensive training to acquire those capabilities, keeping a watch on developments in medical knowledge and maintaining those skills is also an issue for these disciplines. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Contributing to the community is a basic responsibility of diagnostic radiology so it remains the university's mission to unflinchingly fulfill its responsibility to provide high-level, advanced medical care, working toward resolution of community problems through education, research and medical activities, as well as to develop the diagnostic radiology professionals who will bear the responsibility for providing community medical care, and to develop professionals who have a global outlook and can flourish in this age of globalization. More than ever, advancing the fundamental medical concepts of "patient-oriented medical care" and "thorough medical safety management" are core principles in the field of diagnostic radiology and nuclear medicine, so continuing to maintain capabilities from this perspective is essential in daily practice. Under the new radiologist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiologist examination (sixth year after graduation). After passing that examination, it is then possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

Diagnostic radiology and nuclear medicine was divided off the specialist field responsible for diagnostic radiology in July 2013. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide it without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 15 external affiliated hospitals approved by JRS as training hospitals. When commencing specialist training, students are allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. In addition, many also obtain certification as a senior (first class) radiation protection supervisor.

In recent times, diagnostic radiology has been experiencing an increasing load in terms of image processing, the number of image readings, and server storage, owing to improvements in instrument performance. As hybrid imaging such as PET/CT, SPECT/CT, PET/MRI become more prevalent, the diversification of diagnostic methods is accelerating. This trend is expected to continue, so there is a need for work on adequate personnel responses, including infrastructure improvement. And because the combined use of functional images to monitor metabolism and blood flow from morphologic images alone will be fundamental, it is essential that the university goes on enhancing education for radiologists so that they acquire the capabilities to extract and analyze clinically useful information from the complex data gathered.

Remote diagnostic imaging is a good example of this. In regard to its responsibility to contribute to the community, there have been changes in the way diagnostic radiology today has been active in society. The community gives special privileges to the diagnosing doctor, including the exclusive or primary responsibility to provide specified medical services. The university must unwaveringly fulfill its mission as such by providing advanced medical care through medical practice, as well as developing the doctors who will provide healthcare to communities. Although it could not be claimed that the environment surrounding diagnostic radiology in community healthcare has fully matured, as specialists, it is necessary to contribute to the development of local communities and to exercise the privileges granted as specialists: we should carry out our responsibilities while firmly holding to this approach.

(2) Research

Diagnostic specialists must keep up with the latest research in their fields, applying medical research findings to clinical practice, and making use of continuing education, continuing professional development programs, medical journals, society activities and the internet to maintain their skills. Along with the importance of maintaining awareness of how to interpret and apply research findings to the patient, it is also necessary to go on formulating broad education programs from a specialist perspective, in order to stay well informed about the fundamentals of research methods and to practice appropriate medicine. By managing the faculty effectively, it will go on clarifying radiological perspectives designed to effect inter-disciplinary research activities, taking a whole-university outlook that crosses over the limits of individual departments or graduate schools. The faculty ensures the education and research activities at graduate schools are reflected in the departments while also energetically tackling strategies to secure external funding and strengthen industry collaborations, with the aim of further improving research results. The faculty continues to actively advance international cooperative networks with the Radiological Society of North America (RSNA), the European Congress of Radiology (ECR), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), etc. from the standpoint of diagnostic radiology and nuclear medicine, and continues to advance research based on a thorough awareness of the impacts emerging in the field and the potentialities developing in related practical application fields.

Diagnostic radiology provides diagnoses by extracting information about the morphology of organs and tissues, three-dimensional structures. It is important in terms of learning to systematically organize that information for comparison of imaging study analyses with the reference pathological tissue. Within that, using CT or MRI for tissue characterization that reflects the macro-pathology is important for identifying diseases.

Diagnostic radiology is a discipline in which it is possible to zero in on understanding of a pathological condition by collecting and analyzing blood flow and metabolic data over time. The faculty is continuing research into a minimally invasive method of extracting in vivo blood flow data to enable the use of in vivo dynamic analysis as a biomarker with formulation of dynamic scan protocols that obtain images over time with bolus contrast injection before high-resolution, multi-slice CT or high magnetic field MRI. Texture analysis and AI imaging are applied to both of anatomic and functional imaging modalities. We investigate from first order (kurtosis) to high order (NGLCM, NGTDM, GLSZM). The faculty is also formulating scan protocols that obtain images over time with 3D PET/CT, as a minimally invasive technique of extracting in vivo metabolic data. Known tracers include 18F-FDG (glucose metabolism), 11C-choline (lipid metabolism), 11C-acetate (lipid metabolism), 18F-FAZA (hypoxia), 18F-FACBC (amino acid metabolism), 62/64Cu-ATSM (redox), 18F-FLT (DNA synthesis), 18F-NaF (bone metabolism), 68Ga-DOTATATE (somatostatin receptor), and 18F-Fluorobeta-ir (Amyloid), 18F-Flutemetamol (Amyloid). The usefulness of multiple tracers in the discipline of oncology has been observed in numerous carcinomas. 177Lu-DOTATATE PRRT started as the first domestic Phase I study. Given the need for examination with standardized imaging and assessment techniques, by conducting a multi-center joint study using PET/CT, the faculty is working to realize and to formulate methodologies for standardization to facilitate participation in global clinical trials in Japan.

(3) Education

In order to meet the expectations of both the patient and diagnostic radiologist, it is important to know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care, and to continue to independently demonstrate them. Diagnostic radiology demands high-level capabilities, so extensive training is required to acquire those capabilities, while keeping a watch on developments in medical knowledge and maintaining those capabilities is also an issue for the discipline. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global viewpoint, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective. An essential aspect of postgraduate school education is the ongoing maintenance of capabilities from that perspective.

Under the new radiology specialist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiology specialist examination (sixth year after graduation). After passing that examination, it is possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

In July 2013, radiation oncology was divided into diagnostic radiology and nuclear medicine responsible for diagnostic radiology and radiotherapeutic oncology, in turn responsible for radiotherapy. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide the training without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 11 external affiliated hospitals (five in Tokyo and six in the Kanto region) approved by the Society as training hospitals. When students commence specialist training, they will be allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all students then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. From the standpoint of managing sealed and unsealed sources in nuclear medicine, many students also obtain certification as a senior (first class) radiation protection supervisor before engaging in clinical and research work.

(4) Lectures & Courses

The department delivers education based on the university's fundamental policy aimed at realization of its mission: to contribute to the development of society, with a specific mission to bear the responsibility for the basic functions of education, research and medical care. As a department at the core of medical care, it develops professionals who can engage in practice across different fields, taking the approach that the standards of behavior demonstrated by diagnostic radiologists in clinical practice have far more impact than the formal curriculum in ethics.

The department develops professionals who can continue to work to resolve the issues faced by the university hospital, professionals who know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care to meet the expectations of both the patient and student, can independently demonstrate them, and can flourish while maintaining a global outlook. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global perspective, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research

capabilities, from the radiological perspective.

(5) Clinical Services & Other Works

Diagnostic Radiology

- CT: A total of three CT scanners are involved in diagnostic radiology: five in the radiology department and one in the ER center.
- 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.
- Ultrasound: The main examinations carried out by diagnostic radiologists are breast and abdominal examinations.
- Angiography and Interventional Radiology (IVR): In the vascular area: TACE for hepatic carcinoma, PTA and stent placement for occlusive arterial disease, intraarterial injection for pelvic tumor, and emergency hemostasis for ER center patients. In the non-vascular area: mainly CT-guided chest biopsy, breast mass biopsy and lymph node biopsy.
- Breast: The department is responsible for breast diagnostic radiology and collaborates with the breast surgery department in team medical care. The department endeavors to diagnose breast cancer at an early stage, provide accurate pre-surgery diagnoses, and formulate treatment plans by providing high-quality diagnostic radiology services combining mammography reading, ultrasound examination, as well as MRI and FDG-PET/CT, in addition to providing image-guided biopsy and surgical marking.
- Conferences: The department holds inter-disciplinary conferences with all departments on a daily basis. The department holds its internal conference every Friday and participates in externally conducted conferences, as appropriate.

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. Motohashi M, Funauchi Y, Adachi T, Fujioka T, Otaka N, Kamiko Y, Okada T, Tateishi U, Okawa A, Yoshii T, Sato S. A New Deep Learning Algorithm for Detecting Spinal Metastases On CT Images. *Spine*. 2023.12; 49(6); 390-397
2. Tateishi U, Kimura K, Tsuchiya J, Kano D, Watabe T, Nonomura N, Saito K, Yokoyama K, Yamagiwa K, Adachi T, Kojima Y, Yoshida S, Fujii Y. Phase I/IIa trial of 18F-prostate specific membrane antigen (PSMA) 1007 PET/CT in healthy volunteers and prostate cancer patients. *Japanese journal of clinical oncology*. 2023.12;
3. Kawamura M, Kamomae T, Yanagawa M, Kamagata K, Fujita S, Ueda D, Matsui Y, Fushimi Y, Fujioka T, Nozaki T, Yamada A, Hirata K, Ito R, Fujima N, Tatsugami F, Nakaura T, Tsuboyama T, Naganawa S. Revolutionizing radiation therapy: the role of AI in clinical practice. *Journal of radiation research*. 2023.11; 65(1); 1-9

4. Ozawa A, Iwasaki M, Yokoyama K, Tsuchiya J, Kawano R, Nishihara H, Tateishi U. Correlation between choline kinase alpha expression and (11)C-choline accumulation in breast cancer using positron emission tomography/computed tomography: a retrospective study. *Scientific reports*. 2023.10; 13(1); 17620
5. Fujioka Tomoyuki, Kubota Kazunori, Hsu Jen Feng, Chang Ruey Feng, Sawada Terumasa, Ide Yoshimi, Taruno Kanae, Hankyo Meishi, Kurita Tomoko, Nakamura Seigo, Tateishi Ukihide, Takei Hiroyuki. Examining the effectiveness of a deep learning-based computer-aided breast cancer detection system for breast ultrasound *Journal of Medical Ultrasonics*. 2023.10; 50(4); 511-520
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7. Fujioka T, Kubota K, Hsu JF, Chang RF, Sawada T, Ide Y, Taruno K, Hankyo M, Kurita T, Nakamura S, Tateishi U, Takei H. Examining the effectiveness of a deep learning-based computer-aided breast cancer detection system for breast ultrasound. *Journal of medical ultrasonics (2001)*. 2023.07; 50(4); 511-520
8. Kitazume Yoshio, Takenaka Kento, Ohtsuka Kazuo, Ozawa Yasuo, Kimura Koichiro, Watanabe Ryosuke, Tsuchiya Junichi, Fujii Toshimitsu, Nagahori Masakazu, Watanabe Mamoru, Tateishi Ukihide. Motility Mapping Quantification Using the Classical Optical Flow Algorithm for Small Bowel Crohn's Disease: Comparison with Balloon-assisted Enteroscopy Findings *Magnetic Resonance in Medical Sciences*. 2023.07; 22(3); 325-334
9. Kubota Kazunori, Mori Mio, Fujioka Tomoyuki, Watanabe Kaoru, Ito Yuko. 【Ultrasound diagnosis of breast non-mass abnormalities Including diagnosis with other modalities】 *Magnetic resonance imaging diagnosis of non-mass enhancement of the breast* *Journal of Medical Ultrasonics*. 2023.07; 50(3); 361-366
10. Shun Fujiwara, Yoshihito Kano, Yasuhiro Maejima, Tomoyuki Fujioka, Kazuhiro Tamura, Susumu Kirimura, Satoshi Miyake, Ryuichi Okamoto. Clinical Response of Primary Malignant Pericardial Mesothelioma with Peritoneal Dissemination to Nivolumab. *Intern Med*. 2023.06;
11. Yamaguchi Y, Tanaka H, Kimura K, Fukuda S, Fukushima H, Waseda Y, Yoshida S, Yokoyama M, Hirakawa A, Tateishi U, Campbell SC, Fujii Y. Prognostic impact of the radiological infiltrative feature of primary renal tumor in metastatic renal cell carcinoma. *International journal of urology : official journal of the Japanese Urological Association*. 2023.06;
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13. Yamada A, Kamagata K, Hirata K, Ito R, Nakaura T, Ueda D, Fujita S, Fushimi Y, Fujima N, Matsui Y, Tatsugami F, Nozaki T, Fujioka T, Yanagawa M, Tsuboyama T, Kawamura M, Naganawa S. Clinical applications of artificial intelligence in liver imaging. *La Radiologia medica*. 2023.05; 128(6); 655-667
14. Ichikawa R, Yokoyama K, Tsuchiya J, Namiki T, Tateishi U. [(18)F] -FDG PET/CT is useful for early detection of Stewart-Treves syndrome, in patients with chronic lymphedema. *European journal of nuclear medicine and molecular imaging*. 2023.04; 50(9); 2916-2917
15. Kimura K, Yoshida S, Tsuchiya J, Kitazume Y, Waseda Y, Tanaka H, Yokoyama M, Toda K, Yoshimura R, Masaya I, Koga F, Tateishi U, Fujii Y. Novel utility of Vesical Imaging-Reporting and Data System in multimodal treatment for muscle-invasive bladder cancer. *European radiology*. 2023.04;
16. Yashima Yuka, Fujioka Tomoyuki, Kubota Kazunori, Mori Mio, Sato Arisa, Oda Goshi, Nakagawa Tsuyoshi, Onishi Ichiroh, Tanaka Mayuko, Tateishi Ukihide. Comparison of the clinical and pathological characteristics of ultrasound-guided biopsy for breast masses and non-mass lesions between 16-gauge spring-loaded core needle biopsy and 12-gauge spring-loaded vacuum-assisted biopsy *Journal of Medical Ultrasonics*. 2023.04; 50(2); 205-212
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18. Oishi K, Arai H, Kuroki H, Fujioka T, Tomita M, Tasaki D, Oi K, Nagaoka E, Fujiwara T, Takeshita M, Yoshizaki T, Someya T, Mizuno T. A prospective randomized controlled study to assess the effectiveness of super FIXSORB WAVE(®) for sternal stabilization after sternotomy. General thoracic and cardiovascular surgery. 2023.03;
19. Yoshida Soichiro, Takahara Taro, Arita Yuki, Toda Kazuma, Kimura Koichiro, Fujiwara Motohiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Patterns of recurrence in genuine and induced oligometastatic castration-resistant prostate cancer treated with progressive sitedirected therapy International Journal of Urology. 2023.02; 30(2); 204-210
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21. Nara Miyako, Fujioka Tomoyuki, Mori Mio, Aruga Tomoyuki, Tateishi Ukihide. Prediction of breast cancer risk by automated volumetric breast density measurement Japanese Journal of Radiology. 2023.01; 41(1); 54-62
22. Inaba, Y; Hashiuchi, E; Watanabe, H; Kimura, K; Oshima, Y; Tsuchiya, K; Murai, S; Takahashi, C; Matsumoto, M; Kitajima, S; Yamamoto, Y; Honda, M; Asahara, SI; Ravnskjaer, K; Horike, SI; Kaneko, S; Kasuga, M; Nakano, H; Harada, K; Inoue, H. The transcription factor ATF3 switches cell death from apoptosis to necroptosis in hepatic steatosis in male mice NATURE COMMUNICATIONS. 2023.01; 14(1);
23. Zama S, Fujioka T, Yamaga E, Kubota K, Mori M, Katsuta L, Yashima Y, Sato A, Kawauchi M, Higuchi S, Kawanishi M, Ishiba T, Oda G, Nakagawa T, Tateishi U. Clinical Utility of Breast Ultrasound Images Synthesized by a Generative Adversarial Network. Medicina (Kaunas, Lithuania). 2023.12; 60(1);
24. Mori M, Fujioka T, Hara M, Katsuta L, Yashima Y, Yamaga E, Yamagiwa K, Tsuchiya J, Hayashi K, Kumaki Y, Oda G, Nakagawa T, Onishi I, Kubota K, Tateishi U. Deep Learning-Based Image Quality Improvement in Digital Positron Emission Tomography for Breast Cancer. Diagnostics (Basel, Switzerland). 2023.02; 13(4);
25. Yashima Y, Fujioka T, Kubota K, Mori M, Sato A, Oda G, Nakagawa T, Onishi I, Tanaka M, Tateishi U. Comparison of the clinical and pathological characteristics of ultrasound-guided biopsy for breast masses and non-mass lesions between 16-gauge spring-loaded core needle biopsy and 12-gauge spring-loaded vacuum-assisted biopsy. Journal of medical ultrasonics (2001). 2023.01; 50(2); 205-212

[Books etc]

1. Yukihisa Saida, Tomoyuki Fujioka, Ryosuke Watanabe, Jun Ooyama, Junichi Tsuchiya et al.. The Art of Learning Radiology Reports through 300 Examples. Gakken Corporation, 2023.01 (ISBN : 978-4-7809-0443-7)

[Misc]

1. Fujima N, Kamagata K, Ueda D, Fujita S, Fushimi Y, Yanagawa M, Ito R, Tsuboyama T, Kawamura M, Nakaura T, Yamada A, Nozaki T, Fujioka T, Matsui Y, Hirata K, Tatsugami F, Naganawa S. Current State of Artificial Intelligence in Clinical Applications for Head and Neck MR Imaging. Magnetic resonance in medical sciences : MRMS : an official journal of Japan Society of Magnetic Resonance in Medicine. 2023.10; 22(4); 401-414
2. Hirata K, Kamagata K, Ueda D, Yanagawa M, Kawamura M, Nakaura T, Ito R, Tatsugami F, Matsui Y, Yamada A, Fushimi Y, Nozaki T, Fujita S, Fujioka T, Tsuboyama T, Fujima N, Naganawa S. From FDG and beyond: the evolving potential of nuclear medicine. Annals of nuclear medicine. 2023.09; 37(11); 583-595
3. Ueda D, Kakinuma T, Fujita S, Kamagata K, Fushimi Y, Ito R, Matsui Y, Nozaki T, Nakaura T, Fujima N, Tatsugami F, Yanagawa M, Hirata K, Yamada A, Tsuboyama T, Kawamura M, Fujioka T, Naganawa S. Fairness of artificial intelligence in healthcare: review and recommendations. Japanese journal of radiology. 2023.08; 42(1); 3-15

4. Tatsugami F, Nakaura T, Yanagawa M, Fujita S, Kamagata K, Ito R, Kawamura M, Fushimi Y, Ueda D, Matsui Y, Yamada A, Fujima N, Fujioka T, Nozaki T, Tsuboyama T, Hirata K, Naganawa S. Recent advances in artificial intelligence for cardiac CT: Enhancing diagnosis and prognosis prediction. *Diagnostic and interventional imaging*. 2023.07;
5. Kubota K, Mori M, Fujioka T, Watanabe K, Ito Y. Magnetic resonance imaging diagnosis of non-mass enhancement of the breast. *Journal of medical ultrasonics* (2001). 2023.02; 50(3); 361-366

[Conference Activities & Talks]

1. Yoshida Souichirou, Takahara Taro, Arita Yuki, Toda Kazuma, Kimura Koichiro, Fujiwara Motohiro, Tanaka Hajime, Yokoyama Minato, Matsuoka Yoh, Yoshimura Ryoichi, Fujii Yasuhisa. Patterns of recurrence in genuine and induced oligometastatic castration-resistant prostate cancer treated with progressive site-directed therapy. *Annual Meeting of the Japanese Urological Association* 2023.04.01
2. Kobayashi M., Matsuoka Y., Fukuda S., Kimura K., Fujiwara M., Nakamura Y., Ishikawa Y., Waseda Y., Tanaka H., Yoshida S., Yokoyama M., Fujii Y.. Significance of MRI-ultrasound fusion targeted prostate biopsy for non-index PI-RADS ≥ 3 lesions in combination with index lesion-targeted biopsy and systematic biopsy. *EUROPEAN UROLOGY* 2023.02.01

[Awards & Honors]

1. Cum Laude Award, 109th Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA), 2023.11

Department of Genomic Function and Diversity

Professor Yuta Kochi
Associate Professor Nao Nishida
Assistant Professor Mahoko Ueda
Specially appointed assistant professor Kensuke Yamaguchi

Part-time Lecturer Jun Inamo
Part-time Lecturer Satomi Mitsunashi

Collaborative Researcher Suguru Honda

Assistant Technical Staff Rie Ito

Assistant Administrative Staff Naomi Iwasa

(1) Outline

Complex diseases such as immunological diseases, metabolic diseases and cancer diseases are caused by both genetic and environmental factors, with varying combinations in different individuals. Genome-wide association studies (GWAS) have led to the discovery of thousands of risk variants involved in these diseases, but the precise mechanisms of the diseases are not fully understood. Our laboratory aims to elucidate the disease etiology by dissecting the diversity of genomic function among individuals. To this end, we integrate bioinformatic approaches with molecular biology techniques in the analysis of genetic variants such as expression QTL and splicing QTL mapping. We will also establish to predict each individual' s pathophysiology (disease severity, drug response, etc.) based on the individual' s genome information to bring precision medicine into clinical practice.

(2) Research

1. To dissect pathological mechanism of complex traits, we integrated the disease GWAS data with expression QTL and splicing QTL data, and we comprehensively identified disease-associated alternative isoforms.
2. To further seek disease susceptible loci for rheumatoid arthritis and systemic lupus erythematosus, we are performing GWAS meta-analysis in world-wide collaboration.
3. Using polygenic risk score (PRS), we established a statistical model to predict radiographic progression in rheumatoid arthritis.
4. Using long-read sequencing technology, we unraveled disease-associated structural and repetitive variants.

(3) Education

We lectured how to understand the etiology of complex traits through big data such as GWAS and eQTL/sQTL for undergraduate students and postgraduate students.

(4) Lectures & Courses

With the advent of research methods and technologies such as GWAS and next-generation sequencers, we can easily access to disease big-data in public databases. We will bring up young researchers to have skills to understand the fundamental of disease etiology by data-driven approaches.

(5) Publications

[Original Articles]

1. Shichen Chang, Satoru Torii, Jun Inamo, Kinya Ishikawa, Yuta Kochi, Shigeomi Shimizu. Uncovering the Localization and Function of a Novel Read-Through Transcript ' TOMM40-APOE' Cells. 2023.12; 13(1);
2. Ueda, MT. Retrotransposon-derived transcripts and their functions in immunity and disease GENES & GENETIC SYSTEMS. 2023.12; 98(6); 305-319
3. Chisato Ono, Shinya Tanaka, Keiko Myouzen, Takeshi Iwasaki, Mahoko Ueda, Yoshinao Oda, Kazuhiko Yamamoto, Yuta Kochi, Yoshihiro Baba. Upregulated Fcrl5 disrupts B cell anergy causes autoimmune disease Frontiers in Immunology. 2023.09; 14; 276014
4. Mitsui Y, Suzuki T, Kuniyoshi K, Inamo J, Yamaguchi K, Komuro M, Watanabe J, Edamoto M, Li S, Kouno T, Oba S, Hosoya T, Masuhiro K, Naito Y, Koyama S, Sakaguchi N, Standley DM, Shin JW, Akira S, Yasuda S, Miyazaki Y, Kochi Y, Kumanogoh A, Okamoto T, Satoh T. Expression of the readthrough transcript CiDRE in alveolar macrophages boosts SARS-CoV-2 susceptibility and promotes COVID-19 severity. Immunity. 2023.07; 56(8); 1939-1954.e12
5. Nao Otomo, Anas M Khanshour, Masaru Koido, Kazuki Takeda, Yukihide Momozawa, Michiaki Kubo, Yoichiro Kamatani, John A Herring, Yoji Ogura, Yohei Takahashi, Shohei Minami, Koki Uno, Noriaki Kawakami, Manabu Ito, Tatsuya Sato, Kei Watanabe, Takashi Kaito, Haruhisa Yanagida, Hiroshi Taneichi, Katsumi Harimaya, Yuki Taniguchi, Hideki Shigematsu, Takahiro Iida, Satoru Demura, Ryo Sugawara, Nobuyuki Fujita, Mitsuru Yagi, Eijiro Okada, Naobumi Hosogane, Katsuki Kono, Masaya Nakamura, Kazuhiro Chiba, Toshiaki Kotani, Tsuyoshi Sakuma, Tsutomu Akazawa, Teppei Suzuki, Kotaro Nishida, Kenichiro Kakutani, Taichi Tsuji, Hideki Sudo, Akira Iwata, Satoshi Inami, Carol A Wise, Yuta Kochi, Morio Matsumoto, Shiro Ikegawa, Kota Watanabe, Chikashi Terao. Evidence of causality of low body mass index on risk of adolescent idiopathic scoliosis: a Mendelian randomization study. Front Endocrinol (Lausanne). 2023.06; 14; 1089414
6. Fujitani H, Eguchi H, Kochi Y, Arai T, Muramatsu M, Okazaki Y. Rare germline variants in pancreatic cancer and multiple primary cancers: an autopsy study. European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP). 2023.05; 32(3); 286-297

[Misc]

1. Mahoko Takahashi Ueda. Retrotransposon-derived transcripts and their functions associated with immunity and disease Genes & Genetic Systems. 2023.09; in press;

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka
 Assistant professor, Yuki Nagata
 Assistant professor, Kentaro Takahashi

(1) Research

- 1) Elucidation of genetic architecture of human metabolic diseases using genome and meta-genome information
- 2) Identification of biomarkers for personalized medicine
- 3) Pharmacogenomics
- 4) Functional genomics
- 5) Statistical genetics and genome drug discovery

(2) Lectures & Courses

As we say “Every human is different” , human genetic diversity has essential impacts on clinical fields, e.g. disease risk, clinical efficacy, and drug responses. Our laboratory aims to elucidate the diversity of human being through comprehensive research activities including genome and epi-genome analyses of human diseases, methodological development of statistical genetics, and human resources cultivation to achieve personalized medicine.

(3) Publications

[Original Articles]

1. Mayumi Hangai, Takahisa Kawaguchi, Masatoshi Takagi, Keitaro Matsuo, Soyoung Jeon, Charleston W K Chiang, Andrew T Dewan, Adam J De Smith, Toshihiko Imamura, Yasuhiro Okamoto, Akiko M Saito, Takao Deguchi, Michiaki Kubo, Yoichi Tanaka, Yoko Ayukawa, Toshinari Hori, Kentaro Ohki, Nobutaka Kiyokawa, Takeshi Inukai, Yuki Arakawa, Makiko Mori, Daisuke Hasegawa, Daisuke Tomizawa, Hiroko Fukushima, Yuki Yuza, Yasushi Noguchi, Yuichi Taneyama, Setsuo Ota, Hiroaki Goto, Masakatsu Yanagimachi, Dai Keino, Kazutoshi Koike, Daisuke Toyama, Yozo Nakazawa, Kozue Nakamura, Koichi Moriwaki, Yujin Sekinaka, Daisuke Morita, Shinsuke Hirabayashi, Yosuke Hosoya, Yuri Yoshimoto, Hiroki Yoshihara, Miwa Ozawa, Shinobu Kobayashi, Naho Morisaki, Tshewang Gyeltshen, Osamu Takahashi, Yukinori Okada, Makiko Matsuda, Toshihiro Tanaka, Johji Inazawa, Junko Takita, Yasushi Ishida, Akira Ohara, Catherine Metayer, Joseph L Wiemels, Xiaomei Ma, Shuki Mizutani, Katsuyoshi Koh, Yukihide Momozawa, Keizo Horibe, Fumihiko Matsuda, Motohiro Kato, Atsushi Manabe, Kevin Y Urayama. Genome-wide assessment of genetic risk loci for childhood acute lymphoblastic leukemia in Japanese patients. *Haematologica*. 2023.10;
2. Sasano T, Ihara K, Tanaka T, Furukawa T. Risk stratification of atrial fibrillation and stroke using single nucleotide polymorphism and circulating biomarkers. *PloS one*. 2023.10; 18(10); e0292118
3. Takayuki Honda, Katsutoshi Seto, Satoshi Endo, Akira Takemoto, Kousuke Tanimoto, Masashi Kobayashi, Masatake Kitano, Rie Sakakibara, Takahiro Mitsumura, Hironori Ishibashi, Johji Inazawa, Toshihiro Tanaka, Yasunari Miyazaki, Kenichi Okubo. The possibility of mutations of RAS signaling

genes and/or TP53 in combination as a negative prognostic impact on pathological stage I non-small cell lung cancer. *Cancer Med.* 2023.10; 12(19); 19406-19413

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Applied Regenerative Medicine

Professor: Ichiro SEKIYA

Associate Professor : Hisako KATANO

Junior Associate Professor: Nobutake OZEKI

Assistant Professor: Mitsuru MIZUNO

Project Assistant Professor: Kentaro ENDO

Project Researcher: Kimiko TAKANASHI

Graduate Student: Yugo MIURA, Hideto FURUOKA, Takahiro TANIMOTO

Seiya MATSUTA, Yusuke AIMONO, Hayato KODAMA,

Tomoko MEGURO, Yusuke FUCHIOKA, Yuki HIDAKA

Assistant Researcher : Asuka ASAMI, Sayaka KOMURA

Technical Assistant: Junko MIURA, Haya ADACHI, Megumi KOBAYASHI

Staff Assistant: Chiaki OKUMURA

(1) Outline

The development of stem cell and regenerative medicine has been remarkable in recent years, and there is competition to develop regenerative medicine products for the global market. In this field, the aim is to conduct basic research in stem cell and regenerative medicine from the perspective of commercializing regenerative treatments that demonstrate high efficacy compared to existing treatments. This involves enhancing translational research to apply the outcomes to clinical practice, with the ultimate goal of 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 have been conducting basic research, translational research, and practical application research to establish a new treatment method for osteoarthritis of the knee. From 2000 to 2010, we clarified that mesenchymal stem cells derived from the synovium (synovial stem cells) have a high capacity for differentiation into cartilage and meniscus, and that their transplantation can promote the natural healing process. We also developed a method for cell transplantation using minimally invasive arthroscopic surgery. These basic research efforts were highly regarded, and in 2013, they were selected as one of the national projects, "Highway for the Realization of Regenerative Medicine" (Project Leader: Ichiro Sekiya), receiving long-term support for the research project aimed at "Regeneration of the Meniscus with Synovial Stem Cells" to establish a new meniscus treatment with less patient burden. After conducting translational research with medium-sized animals, supported by the Ministry of Education, Culture, Sports, Science, and Technology, a physician-led clinical trial targeting meniscus damage using autologous synovial stem cells began in August 2017, with support from the Ministry of

Health, Labour, and Welfare. In March 2019, a patent license agreement was signed with a company regarding the technology for transplanting synovial stem cells to the site of meniscus tears. Then, in January 2023, a phase III clinical trial (corporate trial) began to verify the efficacy and safety of regenerative medicine products utilizing this cell transplantation technology.

As a second project, to develop a treatment method through a new administration route of synovial stem cells, a clinical study "Intra-articular Injection of Synovial Stem Cells for Osteoarthritis of the Knee" was conducted from December 2017 to March 2020, supported by the Japan Agency for Medical Research and Development (AMED) regenerative medicine practical application research project. Following the results, a comparative trial against existing treatments as a physician-led clinical trial began in April 2023.

The third project "MRI 3D Analysis" has been supported since 2015 by the AMED's project for developing evaluation technology for industrialization of regenerative medicine. In collaboration with companies, we developed MRI 3D analysis software capable of automatically extracting bones, cartilage, and meniscus from knee MRI proton density-weighted images and T2* weighted images and measuring the thickness of the cartilage. In 2018, the "Kanagawa Knee Study," a survey on the actual condition of MRI for Japanese osteoarthritis of the knee, began, assuming analysis using this software, and MRI data was acquired through a regional resident cohort. Subsequently, in 2019, it was launched as a knee joint analysis application for a 3D image analysis system. Aiming for widespread use in orthopedic research and clinical practice both domestically and internationally, since 2022, a multicenter study to measure the inter-device error using this software has been conducted with five major universities in Japan.

(4) Publications

[Original Articles]

1. Mitsuru Mizuno, Koki Abe, Takashi Kakimoto, Keiichi Yano, Yukiko Ota, Kengo Tomita, Naoki Kagi, Ichiro Sekiya. Volatile organic compounds and ionic substances contamination in cell processing facilities during rest period; a preliminary assessment of exposure to cell processing operators. *Regen Ther.* 2023.12; 24; 211-218
2. Hisako Katano, Nobutake Ozeki, Mitsuru Mizuno, Kentaro Endo, Noriya Okanouchi 1,2, Jo Fujita, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Morphological analysis of three-dimensional MR images of patellofemoral joints in asymptomatic subjects *Sci Rep.* 2023.12; 13(1); 16570
3. Hao Ding, Hideyuki Koga, Hiroki Katagiri, Shoichi Hasegawa, Tatushiko Anzai, Mai Katakura, Aritoshi Yoshihara, Masaki Amemiya, Takashi Hoshino, Nobutake Ozeki, Tomomasa Nakamura, Yusuke Nakagawa. Low central sensitisation inventory score is associated with better post-operative outcomes of osteotomy around the knee. *Knee Surg Sports Traumatol Arthrosc.* 2023.12; 31(12); 5896-5904
4. Zhen Qu, Hideyuki Koga, Kunikazu Tsuji, Guo Tang, Yang Yang, Aritoshi Yoshihara, Mai Katakura, Hiroki Katagiri, Kazumasa Miyatake, Tomomasa Nakamura, Ichiro Sekiya, Yusuke Nakagawa. Hyaluronic acid sheet transplantation attenuates infrapatellar fat pad fibrosis and pain in a rat arthritis model. *J Orthop Res.* 2023.11; 41(11); 2442-2454
5. Ichiro Sekiya, Hisako Katano, Ali Guerhazi, Yugo Miura, Noriya Okanouchi, Makoto Tomita, Jun Masumoto, Yoshio Kitazume, Hideyuki Koga, Nobutake Ozeki. Association of AI-determined Kellgren-Lawrence grade with medial meniscus extrusion and cartilage thickness by AI-based 3D MRI analysis in early knee osteoarthritis. *Sci Rep.* 2023.11; 13(1); 20093
6. Zhu Ling, Hailati Aini, Shuhei Kajikawa, Jumpei Shirakawa, Kunikazu Tsuji, Yoshinori Asou, Hideyuki Koga, Ichiro Sekiya, Akira Nifuji, Masaki Noda, Yoichi Ezura. Mutation Are Treatable by Alendronate. *Pharmaceuticals (Basel).* 2023.10; 16(10);
7. Aritoshi Yoshihara, Renaud Siboni, Yusuke Nakagawa, Caroline Mouton, Christophe Jacquet, Tomomasa Nakamura, Ichiro Sekiya, Romain Seil, Hideyuki Koga. Lateral-medial asymmetry of posterior tibial slope and small lateral tibial plateau articular surface depth are morphological factors of lateral meniscus posterior root tears in ACL-injured patients. *Knee Surg Sports Traumatol Arthrosc.* 2023.09; 31(9); 3594-3603
8. Hideto Furuoka, Kentaro Endo, Ichiro Sekiya. Mesenchymal stem cells in synovial fluid increase in number in response to synovitis and display more tissue-reparative phenotypes in osteoarthritis. *Stem Cell Res Ther.* 2023.09; 14(1); 244

9. Shoichi Hasegawa, Yusuke Nakagawa, Aritoshi Yoshihara, Tomomasa Nakamura, Hiroki Katagiri, Masaya Hayashi, Hideya Yoshimura, Tsuyoshi Nagase, Ichiro Sekiya, Hideyuki Koga. Older Age, Poor Preoperative Quadriceps Muscle Strength, and Residual Pain as Risk Factors for Poor Quadriceps Muscle Strength Recovery at 1 Year After ACL Reconstruction: A TMDU MAKs Study of 402 Patients. *Orthop J Sports Med.* 2023.09; 11(9); 23259671231194593
10. Hiroki Katagiri, Yusuke Nakagawa, Yusuke Amano, Yoshiko Shirakawa, Nobutake Ozeki, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga. Decision regret following opening wedge high tibial osteotomy: Older age as a risk factor. *Knee.* 2023.06; 43; 62-69
11. Nobutake Ozeki, Hideyuki Koga, Yusuke Nakagawa, Hiroki Katagiri, Hisako Katano, Makoto Tomita, Jun Masumoto, Ichiro Sekiya. Association between knee cartilage thickness determined by magnetic resonance imaging three-dimensional analysis and the International Cartilage Repair Society (ICRS) arthroscopic grade. *Knee.* 2023.06; 42; 90-98
12. Shoichi Hasegawa, Jae-Sung An, Jun Hino, Yusuke Amano, Yusuke Nakagawa, Kazumasa Miyatake, Hiroki Katagiri, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga, Kunikazu Tsuji. Therapeutic effect of C-type natriuretic peptide on persistent pain in a rat knee arthritis model. *J Orthop Surg (Hong Kong).* 2023.06; 31(2); 10225536231181708
13. Amano Y, Ozeki N, Matsuda J, Nakamura T, Nakagawa Y, Sekiya I, Koga H. Augmentation of a Nonanatomical Repair of a Medial Meniscus Posterior Root Tear With Centralization Using Three Knotless Anchors May Be Associated With Less Meniscal Extrusion and Better Compressive Load Distribution in Mid-Flexion Compared With Non-Anatomical Root Repair Alone in a Porcine Knee Model. *Arthroscopy : the journal of arthroscopic & related surgery : official publication of the Arthroscopy Association of North America and the International Arthroscopy Association.* 2023.05; 39(12); 2487-2498
14. Misaki Yagi, Kentaro Endo, Keiichiro Komori, Ichiro Sekiya. Comparison of the effects of oxidative and inflammatory stresses on rat chondrocyte senescence. *Sci Rep.* 2023.05; 13(1); 7697
15. Yusuke Nakagawa, Kunikazu Tsuji, Tomomasa Nakamura, Hiroki Katagiri, Nobutake Ozeki, Mikio Shioda, Jae-Sung An, Ryu Yoshida, Ichiro Sekiya, Hideyuki Koga. Association of Infrapatellar Fat Pad Fibrosis at 3 Months After ACL Reconstruction With Short-term Clinical Outcomes and Inflammatory Cytokine Levels in the Synovial Fluid. *Orthop J Sports Med.* 2023.04; 11(4); 23259671231164122
16. Ozeki N, Mizuno M, Yanada S, Okada T, Kubota R, Kushida Y, Furuoka H, Endo K, Katano H, Nakamura K, Ohya S, Koga H, Sekiya I. Autologous Synovial Mesenchymal Stem Cell Transplantation Suppresses Inflammation Caused by Synovial Harvesting and Promotes Healing in a Micro Minipig Repaired Meniscus Model. *Transplantation proceedings.* 2023.03; 55(2); 470-480
17. Mizuno M, Matsuda J, Watanabe K, Shimizu N, Sekiya I. Effect of disinfectants and manual wiping for processing the cell product changeover in a biosafety cabinet. *Regenerative therapy.* 2023.03; 22; 169-175
18. M Isono, H Koga, Y Nakagawa, T Nakamura, I Sekiya, H Katagiri. Inferior Healing Rate in Isolated Meniscal Repair than that in Meniscal Repair with Concomitant ACL Reconstruction Evaluated with MRI. *Malays Orthop J.* 2023.03; 17(1); 61-69
19. Mizuno Mitsuru, Matsuda Junpei, Watanabe Ken, Shimizu Norio, Sekiya Ichiro. Effect of disinfectants and manual wiping for processing the cell product changeover in a biosafety cabinet. *Regenerative Therapy.* 2023.03; 22; 169-175
20. Mizuno Mitsuru, Yori Kouichirou, Takeuchi Toshikazu, Yamaguchi Tetsuya, Watanabe Ken, Tomaru Yasuhiro, Shimizu Norio, Sekiya Ichiro. Cross-contamination risk and decontamination during changeover after cell-product processing. *Regenerative Therapy.* 2023.03; 22; 30-38
21. Nobutake Ozeki, Mitsuru Mizuno, Shinobu Yanada, Takuya Okada, Rei Kubota, Yoshihisa Kushida, Hideto Furuoka, Kentaro Endo, Hisako Katano, Kentaro Nakamura, Shoji Ohya, Hideyuki Koga, Ichiro Sekiya. Autologous Synovial Mesenchymal Stem Cell Transplantation Suppresses Inflammation Caused by Synovial Harvesting and Promotes Healing in a Micro Minipig Repaired Meniscus Model. *Transplant Proc.* 2023.03; 55(2); 470-480

22. Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. Short-Term Outcomes after High Tibial Osteotomy Aimed at Neutral Alignment Combined with Arthroscopic Centralization of Medial Meniscus in Osteoarthritis Patients. *J Knee Surg.* 2023.02; 36(3); 261-268
23. Akane Ariga, Yuji Kohno, Yusuke Nakagawa, Toshifumi Watanabe, Hiroki Katagiri, Toshiyuki Ohara, Mikio Shioda, Nobutake Ozeki, Masaki Amemiya, Atsushi Okawa, Ichiro Sekiya, Hideyuki Koga. Simultaneous bilateral total knee arthroplasty is safe and effective for patients in different ages. *J Orthop Sci.* 2023.01; 28(1); 173-179

[Conference Activities & Talks]

1. Nobutake Ozeki. Current treatment using stem cell-based meniscus treatment. 1stThe Asian Meniscus Summit 2023.10.05

JFCR Cancer Biology

Professor Toru HIROTA

Professor Noriko SAITOH

Professor Akiko TAKAHASHI

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]

1. Hara, M., Ariyoshi, M., Sano, T., Nozawa, R.S., Shinkai, S., Onami, S., Jansen, I., Hirota, T. and Fukagawa, T. (2023) Centromere/kinetochore is assembled through CENP-C oligomerization. *Mol Cell*. 83: 2188-2205. doi: 10.1016/j.molcel.2023.05.023.
2. Mahana, Y., Ariyoshi, M., Nozawa, R-S., Shibata, S., Nagao, K., Obuse, C., and Shirakawa, M. (2023) Structural evidence for protein–protein interaction between the non-canonical methyl-CpG-binding domain of SETDB proteins and C11orf46 Structure. S0969-2126(23)00443-4. doi: 10.1016/j.str.2023.12.001.
3. Kamakura, N., Takahashi, M. and Jo, M. (2023) The toxicity of dysregulated Plk1 activity revealed by its suppressor mutations *Genes Cells*. doi: 10.1111/gtc.13032
4. Wakao, S., Saitoh, N., Awazu, A. (2023) Mathematical model of structural changes in nuclear speckle. *Biophysics and Physicobiology*, 20, e200020. doi: 10.2142/biophysico.bppb-v20.0020
5. Sundararajan, S., Park, H., Kawano, S., Johansson, M., Lama, B., Saito-Fujita, T., Saitoh, N., Arnaoutov, A., Dasso, M., Wang, Z., Keifenheim, D., Clarke D.J., Azuma, Y. Methylated. (2023) histones on mitotic chromosomes promote Topoisomerase II α function for high-fidelity chromosome segregation. *iScience*, 26(5):106743. doi: 10.1016/j.isci.2023.106743.
6. Smallwood, K., Watt, K.E.N., Ide, S., Baltrunaite, K., Inskeep, K., Adam, M., Begtrup, A., Bertola, D.R., Cho, M., Demmer, L., Demo, E., Devinsky, O., Gallagher, E., Guillen, M.J. S., Keller-Ramey, J., Keren, B., Ladda, R., Mardy, A., McLaughlin, H., McWalters, K., Person, R., Schnur, R., Skorvanek, M., Slavotinek, A., Sullivan, B.R., Stark, Z., Symonds, J., Wenger, T., Saitoh, N., Whalen, S., Willaert, R., Zech, M., Zeidler, S., Stottmann, R.W., Trainor, P.A., Weaver, K. N. (2023) POLR1A variants underlie phenotypic heterogeneity in neural, craniofacial, and cardiac anomalies. *The American Journal of Human Genetics*, 110, 1–17. doi: <https://doi.org/10.1016/j.ajhg.2023.03.014>
7. Chiba, M., Miyata, K., Okawa, H., Tanaka, Y., Ueda, T., Seimiya, H. and *Takahashi, A. YBX1 regulates satellite II RNA loading into small extracellular vesicles and promotes the senescent phenotype. *International Journal of Molecular Sciences*, 24(22), 16399, 2023

8. Miyata, K., Zhou, X., Nishio, M., Hanyu, A., Chiba, M., Kawasaki, H., Osako, T., Ohno, S., Ueno, T., Maruyama, R, and *Takahashi, A. Chromatin conformational changes at human satellite II contribute to the senescence phenotype in the tumor microenvironment. *Proc. Natl. Acad. Sci. U.S.A.*, 120 (32) e2305046120, 2023
9. Misawa, T., Hitomi, K., Miyata, K., Tanaka, Y., Fujii, R., Chiba, M., Loo, T.M., Hanyu, A., Kawasaki, H., Kato, H., Maezawa, Y., Yokote, K., Nakamura, A.J., Ueda, K., Yaegashi, N. and *Takahashi, A. Identification of novel senescent markers in small extracellular vesicles. *International Journal of Molecular Sciences*, 24 (3), 2421, 2023
10. Takahashi M, Okamoto Y, Kato Y, Shirahama H, Tsukahara S, Sugimoto Y, Tomida A. (2023) Activating mutations in EGFR and PI3K promote ATF4 induction for NSCLC cell survival during amino acid deprivation. *Heliyon*. 9: e14799.
11. Mezawa, Y., Wang, T., Daigo, Y., Atsushi, T., Miyagi, Y., Yokose, T., Yamashita, T., Yang, L., Maruyama, R., Seimiya, H., Orimo, A. Glutamine deficiency induces class I histone deacetylase activity that mediates TGF- β signaling activation and the myofibroblastic state in carcinoma-associated fibroblasts. *Cancer Science*. 114:4376-4387. (2023)
12. Koyama, Y., Okazaki, H., Yang, S., Mezawa, Y., Wang, Z., Sakimoto, M., Ishizuka, A., Ito, Y., Koyama, T., Daigo, Y., Takano, A., Miyagi, Y., Yokose, Tomoyuki., Yamashita, T., Sugahara, K., Hino, O., Yang, L., Maruyama, R., Katakura, Akira., Yasukawa, T., Orimo, A. Increased RUNX3 expression mediates tumor-promoting ability of human breast cancer-associated fibroblasts. *Cancer Medicine*. 12:18062-18077 (2023)
13. *Kitajima, H., *Maruyama, R., Niinuma, T., Yamamoto, E., Takasawa, A., Takasawa, K., Ishiguro, K., Suzuki, R., Tsuyada, A., Idogawa, M., Tange, S., Toyota, M., Yoshido, A., Kumegawa, K., Kai, M., Tokino, T., Osanai, M., Nakase, H., Suzuki, H. TM4SF1-AS1 inhibits apoptosis through stress granule formation in cancer cells. *Cell Death Dis*. 14, 424 (2023) *contributed equally
14. Miyata, K., Zhou, X., Nishio, M., Hanyu, A., Chiba, M., Kawasaki, H., Osako, T., Takeuchi, K., Ohno, S., Ueno, T., Maruyama, R., Takahashi, A. Chromatin conformational changes at the human satellite II contribute to the senescence phenotype in the tumor microenvironment. *Proc Natl Acad Sci USA*. 120, e2305046120 (2023)
15. Kumegawa, K., Yang, L., Miyata, K., Maruyama, R. FOXD1 is associated with poor outcome and maintains tumor-promoting enhancer-gene programs in basal-like breast cancer. *Front Oncol*. 13, 1156111 (2023)
16. Tanaka, M., Homme, M., Teramura, Y., Kumegawa, K., Yamazaki, Y., Yamashita, K., Osato, M., Maruyama, R., Nakamura, T. HEY1-NCOA2 expression modulates chondrogenic differentiation and induces mesenchymal chondrosarcoma in mouse. *JCI insight*. 8, e160279 (2023)

17. Nakadai, T., Shimada, M., Ito, K., Cevher, MA., Chu, CS., Kumegawa, K., Maruyama, R., Malik S., Roeder, R. Two target gene activation pathways for orphan ERR nuclear receptors. *Cell Res.* 33, 165 (2023)
18. Tanaka, M., Chuaychob, S., Homme, M., Yamazaki, Y., Lyu, R., Yamashita, K., Ae, K., Matsumoto, S., Kumegawa, K., Maruyama, R., Qu, W., Miyagi, Y., Yokokawa, R., Nakamura, T. ASPSCR1::TFE3 orchestrates the angiogenic program of alveolar soft part sarcoma. *Nat Commun.* 14, 1957 (2023)
19. Saeki, S., Kumegawa, K., Takahashi, Y., Yang, L., Osako, T., Yasen M., Otsuji, K., Miyata, K., Yamakawa, K., Suzuka, J., Sakimoto, Y., Ozaki, Y., Takano, T., Sano, T., Noda, T., Ohno, S., Yao, R., Ueno, T., Maruyama, R. Transcriptomic intratumor heterogeneity of breast cancer patient-derived organoids may reflect the unique biological features of the tumor of origin. *Breast Cancer Res.* 25, 21 (2023)
20. Kumegawa, K., Saeki, S., Takahashi, Y., Yang, L., Osako, T., Nakadai, T., Mori, S., Noda, T., Ohno, S., Ueno, T., Maruyama, R. Chromatin profiles identify a novel subgroup of ER-positive breast cancer with reduced accessibility of estrogen receptor responsive elements. *Br J Cancer.* 128, 1400 (2023)
21. Nakadai, T., Yang, L., Kumegawa, K., Maruyama, R. ER α K303R mutation reorganizes its binding to FoxA1 regions and induces chromatin opening. *Mol Biol Rep.* 50, 1209 (2023)

[Review Articles]

1. Shimozaki, K., Nakayama, I., Hirota, T., Yamaguchi, K. (2023) Current strategy to treat immunogenic gastrointestinal cancers: perspectives for a new era. *Cells.* 12, 1049. doi.org/10.3390/cells12071049
2. Qian, J., Zhou, X., Tanaka, K. and *Takahashi, A. Alteration in the chromatin landscape during the DNA damage response: Continuous rotation of the gear driving cellular senescence and aging. *DNA Repair*, 131, 103572, 2023

[Conference Activities & Talks]

1. Hirota, T. “How cells enrich Aurora B activity at centromeres in mitosis” 12th Salk Cell Cycle Meeting 2023. 7, La Jolla
2. Matsui, S., Nozawa, R., Hirota, T. “How HP1-Aurora B complex concentrates to centromeres and ensures mitotic fidelity” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
3. Sako, K., Furukawa, A., Nishimura, Y., Hirota, T. “How HP1 secures binding to the Aurora B complex: a key interaction preventing chromosome segregation errors” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.

4. Nozawa, R., Matsui, S., Hirota, T. “Driving force to concentrate Aurora B activity at inner centromeres: A key cellular function ensuring mitotic fidelity” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
5. Kamakura, N., Jo, M., Hirota, T. “How Polo-like kinase 1 regulates kinetochore-microtubule attachments in cancers” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
6. Seshimo, N., Nozawa, R., Furuta, R., Kitagawa, T., Hirota, T. “Oncoprotein E6 derived from specific HPV leads to mitotic defect ECAC in cervical preneoplastic lesion.” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
7. Jo, M., Sampetean, O., Negoto, T., Kato, U., Saya, H., Hirota, T. “How chromosomal instability involves in glioma: perspectives from a syngenic model” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
8. Kusano, Y., Nozawa, R., Hirota, T. “Chromosomal instability induced by supercoiled DNAs arise during replication” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
9. Suzuki, A., Matsu, S., Hirota, T. “Intervention to mitotic chromosome segregation machinery to conditionally induce aneuploidy” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
10. Negoto, T., Jo, M., Nakamura, H., Morioka, M., Hirota, T. “Chromosome-level abnormalities shape the malignant properties in glioma” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
11. Takahashi, M., Jo, M., Kamakura, N., Kawakita, N., Kato, U., Hirota, T. “A strategy to intervene mitotic kinases to induce mitotic catastrophe in cancer cells” 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
12. Kawakita, N., Kamakura, N., Jo, M., Takahashi, M., Hirota, T. “How Plk1 activity is regulated by open/close conformational transition. 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
13. Matsui, S., Nozawa, R., Hirota, T. “How HP1-Aurora B complex concentrates to centromeres and ensures mitotic fidelity” Cell Dynamics and Chromosomal Stability Workshop, 2023. 8, Atsugi Kanagawa
14. Kamakura, N., Jo, M., Hirota, T. “How Polo-like kinase 1 regulates kinetochore-microtubule attachments in cancers” Cell Dynamics and Chromosomal Stability Workshop, 2023. 8, Atsugi Kanagawa
15. Palihati, M., Tachiwana, H., Ichikawa, Y., Fukuoka, M., Saitoh, N. “Nuclear long non-coding RNAs contribute to 3D genome structure and tumor dormancy in breast cancer” 8th Meeting of the Asian Forum For Chromosome and Chromatin Biology, 2023.11, Bangalore
16. Saitoh, N. “ELEANOR2 facilitates BRD4-chromatin interaction at the ESR1 locus in ER-positive breast cancer cells” FANTOM6 AUTUMN MEETING, 2023. 10. Online

17. Saitoh, N. “Chromatin Associating ELEANOR Long Non-coding RNAs in Breast Cancer Late Recurrence” FANTOM6 SPRING MEETING, 2023. 2, Milan.
18. Saitoh, N., Tachiwana, H. “Chromatin Associating Long Non-coding RNAs in Late Recurrence of Breast Cancer” International Symposium On Chromatin Architecture: Structure And Function (ERATO), 2023, 1. Online
19. Tachiwana, H., Saitoh, N. “A novel mechanism for transcription activation of breast cancer associated genes by an Histone deacetylase inhibitor” The 46th Annual meeting of the Molecular Biology Society of Japan. 2023, 12. Kobe
20. Ichikawa, Y., Fukuoka, M., Palihati, M., Saitoh, N. “Chromatin associating non-coding RNAs contribute to tumor dormancy in breast cancer late recurrence” The 46th Annual meeting of the Molecular Biology Society of Japan. 2023, 12. Kobe
21. Saitoh, N. “A novel mechanism for transcription activation in ER-positive breast cancer” Research Conference in National Institute of Genetics. 2023. 10, Mishima.
22. Saitoh, N. “Epigenomic regulation in Estrogen receptor” The 96th Annual Congress of the Japan Endocrine Society. 23023., 7, Nagoya
23. Takahashi A. “DNA Fragmentation and Epigenetic Alteration in Senescent Cells” The 46th Annual Meeting of the Molecular Biology Society of Japan 2022.12, Kobe
24. Takahashi A. “New Insights into Epigenetic Alteration and SASP in the Cancer Microenvironment” The 15th In vivo experimental medicine symposium 2022.11, Tokyo
25. Takahashi A. “Analysis of Senescent Cells in the Cancer Microenvironment” The 96th Annual Meeting of the Japanese Biochemical Society 2022.10, Fukuoka
26. Takahashi A. SICEM2023 Special Interest “Tumorigenic Roles of Senescent Cells in the Cancer Microenvironment” 2023.10, Seoul.
27. Takahashi A. SICS-OMICS “Epigenetic Alteration of Senescent Stromal Cells in the Cancer Microenvironment” 2023.10, Tokyo
28. Takahashi A. New function of senescent cells in the Cancer Microenvironment” The 65th Annual meeting of the Japanese Association for Dental Research. 2023.09, Tokyo.
29. Takahashi A. International Session1 “New Insights into Epigenetic Alteration and SASP in the Cancer Microenvironment” The 82nd Annual meeting of the Japanese Cancer Association. 2023.09, Yokohama.
30. Takahashi A. “Analysis of senescent stromal cells in the cancer microenvironment” The 31st Annual Meeting of the Japanese Breast Cancer Society 2023.06, Yokohama.
31. Takahashi A. Year in Review “Small Extracellular Vesicles and Cancer” The 27th Annual Meeting of The Japanese Association for Molecular Target Therapy of Cancer. 2023.06, Saga.
32. Takahashi A. “New function of senescent cells in the Cancer Microenvironment” The 50th Annual Meeting of the Japanese Society of Toxicology. 2023.06, Yokohama.

33. Tanaka, M., Teramura, Y., Honme, M., Takahara, T., Kumegawa, K., Yamashita, K., Yamazaki, Y., Nakamura, T., Maruyama, R. "HEY1::NCOA2 contributes to cartilage morphogenesis through modulation of transcriptional network" 112th Annual Meeting of the Japanese Pathological Society, April 2023, Shimonoseki.
34. Tanaka, M., Nakamura, T., Maruyama, R. "Identification of super-enhancers defining characteristics of sarcoma by CRISPR/dCas9 screening" 8th Meeting of the Japanese Genome Editing Society, June 2023, Edogawa.
35. Tanaka, M., Kumegawa, K., Nakamura, T., Maruyama, R. "Transcriptional network centered on HEY1::NCOA2 disrupts chondrogenesis" 16th Annual Meeting of the Japanese Epigenetics Society, June 2023, Chiyoda.
36. Kumegawa, K., Saeki, S., Takahashi, Y., Yang, Y., Osako, S., Ohno, S., Ueno, T., Maruyama, R. "Identification of Distinct ER-Positive Breast Cancers with Reduced Chromatin Accessibility in the ER Binding Domain" 16th Annual Meeting of the Japanese Epigenetics Society, June 2023, Chiyoda.
37. Otsuji, K., Takahashi, Y., Kobayashi, T., Saeki, S., Noda, T., Ohno, S., Takano, T., Ueno, T., Maruyama, R. "Perspectives on Breast Cancer Treatment through Elucidation of Tumor Heterogeneity" 31st Annual Meeting of the Japanese Breast Cancer Society, June 2023, Yokohama.
38. Otsuji, K., Takahashi, Y., Kobayashi, T., Saeki, S., Noda, T., Ohno, S., Takano, T., Ueno, T., Maruyama, R. "Single Cell Transcriptome Analysis of a Rapidly Enlarging Primary Lesion in Stage IV Lactational Breast Cancer" 31st Annual Meeting of the Japanese Breast Cancer Society, June 2023, Yokohama.
39. Miyata, K. "Analysis of Tumor Progression Mechanisms Due to Epigenomic Dysregulation" Workshop on Cancer Research for Well-being @ Atami, July 2023, Atami.
40. Tanaka, M. "Interactions between Fusion Genes and Enhancers in Sarcoma Development" Workshop on Cancer Research for Well-being @ Atami, July 2023, Atami.
41. Maruyama, R. "Dissecting Intra-tumor Heterogeneity in Breast Cancer" Kanazawa International Symposium on Cancer Biology 2023, July 2023, Kanazawa.
42. Kumegawa, K. "Attempts to Identify Functional Genomic Regions in Breast Cancer Clinical Specimens Using Single Cell ATAC-seq" MEXT Young Researcher Training Workshop on Advanced Model Animal Support Platform, September 2023, Nagoya.
43. Tanaka, M. "Lessons from sarcoma mouse models" MEXT Young Researcher Training Workshop on Advanced Model Animal Support Platform, September 2023, Nagoya.
44. Shibata, T., Maruyama, R. "Elucidating the Pathophysiology of Cancer Cachexia in Pancreatic Cancer Patients through Specific Analysis of Cancer Cell-Derived Extracellular

- Vesicles" MEXT Young Researcher Training Workshop on Advanced Model Animal Support Platform, September 2023, Nagoya.
45. Otsuji, K., Takahashi, Y., Kobayashi, T., Saeki, S., Noda, T., Ohno, S., Takano, T., Suzuki, H., Ueno, T., Maruyama, R. "A Case of Stage 4 Breast Cancer Analyzed for Temporal and Spatial Heterogeneity Using Single Cell Analysis" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 46. Suzuka, J., Saeki, S., Kumegawa, K., Ueno, T., Tsuda, M., Tanaka, S., Maruyama, R. "Analysis of Plasticity of Breast Cancer Cells Focusing on Dedifferentiation by Hydrogel" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 47. Kumegawa, K., Saeki, S., Takahashi, Y., Yang, Y., Osako, S., Noda, T., Ohno, S., Ueno, T., Maruyama, R. "Identification of Distinct ER-Positive Breast Cancers with Reduced Chromatin Accessibility in the ER Binding Domain" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 48. Tsuchiya, A., Kumegawa, K., Saeki, S., Otsuji, K., Yang, Y., Suzuka, J., Miyata, K., Takahashi, Y., Noda, T., Ohno, S., Imoto, S., Ueno, T., Maruyama, R. "Evaluation of Tumor Heterogeneity in Orthotopic Transplantation of Breast Cancer-Derived Organoids with Metastatic Potential" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 49. Saeki, S., Kumegawa, K., Takahashi, Y., Osako, S., Baba, M., Otsuji, K., Miyata, K., Suzuka, J., Ozaki, Y., Takano, R., Noda, T., Ohno, S., Yabu, R., Ueno, T., Maruyama, R. "Tumor Heterogeneity in Breast Cancer Patient-Derived Organoids - Identification of Shared and Unique Cell States" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 50. Miyata, K., Maruyama, R. "Analysis of the Impact of Epigenomic Abnormalities on Cancer Cell Diversity in Non-Coding DNA Regions" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 51. Maruyama, R., Yang, Y., Kumegawa, K. "High Expression of FOXD1 Correlates with Poor Prognosis in Triple-Negative Breast Cancer" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 52. Furukawa, T., Miyata, K., Shibata, T., Yang, L., Kumegawa, K., Saeki, S., Mie, T., Okamoto, T., Takeda, T., Kasuga, A., Sasaki, T., Ozaka, M., Sasahira, N., Noda, T., Maruyama, R. "Multi-omics analysis of organoids for exploring mechanisms of plasticity associated with metastases in pancreatic cancer" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
 53. Tanaka, M., Baba, M., Yokokawa, R., Nakamura, T., Maruyama, R. "Abnormal Enhancement of the Intracellular Trafficking Pathway Facilitates Vascular Network in

- Cancer" 82nd Annual Meeting of the Japanese Cancer Association, September 2023, Yokohama.
54. Tanaka, M. "Lessons from Sarcoma Mouse Models" IRCMS Symposium Rise of Diversity in Science, September 2023, Kumamoto.
 55. Maruyama, R. "Unveiling Cancer Cell Intra-tumor Heterogeneity Through Single Cell Omics Analysis" 61st Annual Meeting of the Japanese Society of Cancer Therapy, October 2023, Yokohama.
 56. Suzuka, J., Ueno, T., Tsuda, M., Gong, J.P., Tanaka, S., Maruyama, R. "Evaluation of Dedifferentiation and Phenotypic Changes in Breast Cancer Cells Induced by Hydrogel" 45th Annual Meeting of the Japanese Society of Biomaterials, November 2023, Kobe.
 57. Suzuka, J., Saeki, S., Kumegawa, K., Tsuchiya, A., Ueno, T., Tsuda, M., Gong, J.P., Tanaka, S., Maruyama, R. "Analysis of the Mechanisms of Dedifferentiation and Malignant Phenotype in Breast Cancer Cells Induced by Hydrogel" 46th Annual Meeting of the Japanese Society for Molecular Biology, December 2023, Kobe.
 58. Kumegawa, K. "Identification of Driver Cistromes in Breast Cancer Clinical Specimens Using Single Cell ATAC-seq and Clarification of Their Pathological Significance" 46th Annual Meeting of the Japanese Society for Molecular Biology, December 2023, Kobe.
 59. Miyata, K., Takahashi, A., Maruyama, R. "Analysis of SASP Induction Mechanisms in Non-coding DNA Regions with Epigenomic Abnormalities" 46th Annual Meeting of the Japanese Society for Molecular Biology, December 2023, Kobe.
 60. Tanaka, M. "Interactive effects of fusion gene and enhancers in sarcomagenesis" 46th Annual Meeting of the Japanese Society for Molecular Biology, December 2023, Kobe.
 61. Yang, Y., Furukawa, T., Maruyama, R., Miyata, K. "Analysis of the Effects of Pleural Effusion-Derived Cancer-Associated Fibroblasts on Chemotherapy for Pancreatic Cancer Cells" 46th Annual Meeting of the Japanese Society for Molecular Biology, December 2023, Kobe.
 62. Iesato, A. "The Tyrosine Kinase Inhibitor Lenvatinib Inhibits Anaplastic Thyroid Carcinoma Growth by Targeting Pericytes in the Tumor Microenvironment" 66th Annual Meeting of the Japanese Thyroid Association, December 2023, Kanazawa.
 63. Tanaka, M. "Application of epigenome editing to advance the targeted therapy for sarcoma." Study Group on Cancer Genome, Epigenome, and Mathematical Statistics, December 2023, Beppu.

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
Hirofumi Nagai, Part-time Lecturer
Yukinori Kanekawa, PYukinori Kanekawa,
Mari Maezawa, Research Assistant
Kanae Ohtsu, Research Assistant
Akiko Kinebuchi, Research Assistant
Mayuko Matsushima, Technical Assistant
Michiko Mori, Administrative Assistant
Mariko Tsuruoka, 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
Kentaro Ichimura, Graduate Student
Masaru Takeuchi, Masaru Takeuchi,

(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]

1. Múnera JO, Kechele DO, Bouffi C, Qu N, Jing R, Maity P, Enriquez JR, Han, Campbell I, Mahe MM, McCauley HA, Zhang X, Sundaram N, Hudson JR, Zarsozo-Lacoste A, Pradhan S, Tominaga K, Sanchez JG, Weiss AAC, Chatuvedi P, Spence JR, Hachimi M, North T, Daley GQ, Mayhew CN, Hu Y, Takebe T, Helmrich MA, Wells JM. Development of functional resident macrophages in human pluripotent stem cell-derived colonic organoids and human fetal colon Cell Stem Cell. 2023.11; 30(11); 1434-1451
2. Reza H, Farooqui Z, Reza A, Conroy C, Iwasawa K, Ogura Y, Okita K, Osafune K, Takebe T. Synthetic augmentation of bilirubin metabolism in human pluripotent stem cell-derived liver organoids Stem Cell Reports. 2023.11; 8(11);
3. Kawakami E, Saiki N, Yoneyama Y, Moriya C, Maezawa M, Kawamura S, Kinebuchi A, Kono T, Funata M, Sakoda A, Kondo S, Ebihara T, Matsumoto H, Togami Y, Ogura H, Sugihara F, Okuzaki D, Kojima T, Deguchi S, Vallee S, McQuade S, Islam R, Natarajan M, Ishigaki H, Nakayama M, Nguyen CT, Kitagawa Y, Wu Y, Mori K, Hishiki T, Takasaki T, Itoh Y, Takayama K, Nio Y, Takebe T. Complement factor D targeting protects endotheliopathy in organoid and monkey models of COVID-19. Cell stem cell. 2023.10; 30(10); 1315-1330.e10
4. Kawakami E, Saiki N, Yoneyama Y, Takayama K, Nio Y, Takebe T. Complement factor D targeting protects endotheliopathy in organoid and monkey models of COVID-19 Cell Stem Cell. 2023.10; 30 (10); 1315-1330
5. Matsuzaki T, Kawano Y, Horikiri M, Shimokawa Y, Yamazaki T, Okuma N, Koike H, Kimura M, Kawamura R, Yoneyama Y, Furuichi Y, Hakuno F, Takahashi SI, Nakabayashi S, Okamoto S, Nakauchi H, . Preparation of mechanically patterned hydrogels for controlling the self-condensation of cells STAR protocols. 2023.07; 4(3); 102471

6. Takahisa Matsuzaki, Yuma Kawano, Momoka Horikiri, Yuko Shimokawa, Takashi Yamazaki, Nao Okuma, Hiroyuki Koike, Masaki Kimura, Ryuzo Kawamura, Yosuke Yoneyama, Yasuro Furuichi, Fumihiko Hakuno, Shin-Ichiro Takahashi, Seiichiro Nakabayashi, Satoshi Okamoto, Hiromitsu Nakauchi, Hideki Taniguchi, Takanori Takebe, Hiroshi Y Yoshikawa. Preparation of mechanically patterned hydrogels for controlling the self-condensation of cells. STAR Protocols. 2023.07; 4(3); 102471
7. Yunheng Wu, Masahiro Oda, Yuichiro Hayashi, Shuntaro Kawamura, Takanori Takebe, Kensaku Mori. Thrombosis region extraction and quantitative analysis in confocal laser scanning microscopic image sequence in in-vivo imaging Medical Imaging 2023: Biomedical Applications in Molecular, Structural, and Functional Imaging. 2023.05; 12468; 71-77
8. Tamaoki N, Siebert S, Maeda T, Ha NH, Good ML, Huang Y, Vodnala SK, Haro-Mora JJ, Uchida N, Tisdale JF, Sweeney CL, Choi U, Brault J, Koontz S, Malech HL, Yamazaki Y, Isonaka R, Goldstein DS, Kimura M, Takebe T, Zou J, Stroncek DF, Robey PG, Kruhlak MJ, Restifo NP, Vizcardo R.. Self-organized yolk sac-like organoids allow for scalable generation of multipotent hematopoietic progenitor cells from induced pluripotent stem cells Cell Reports Methods. 2023.04; 3(4); 100460
9. Fujii T, Yoneyama Y, Kinebuchi A, Ozeki N, Maeda S, Saiki N, Chen-Yoshikawa TF, Date H, Nishiwaki K, Takebe T. Enteral liquid ventilation oxygenates a hypoxic pig model. iScience. 2023.03; 26(3); 106142
10. Fujii T, Yoneyama Y, Kinebuchi A, Ozeki N, Maeda S, Saiki N, Fengshi Chen-Yoshikawa T.F., Date H, Nishiwaki K, Takebe T. Enteral liquid ventilation oxygenates a hypoxic pig model iScience. 2023.03; 26(3);
11. Kang S, Kimura M, Shrestha S, Lewis P, Lee S, Cai Y, Joshi P, Acharya P, Liu J, Yang Y, Sanchez J, Ayyagari S, Alsberg E, Wells J, Takebe T, Lee M. A Pillar and Perfusion Plate Platform for Robust Human Organoid Culture and Analysis bioRxiv. 2023.03;

[Conference Activities & Talks]

1. Takanori Takebe. Organoids for Liver Replacement Therapy. Asian Transplantation Week 2023 2023.11.17
2. Takanori Takebe. Understanding interconnectedness in liver development and disease. Germany EMBO Organoids 2023.10.20
3. Takanori Takebe. Stem cell technology for studying hepatology and hepatitis viruses. 2023 International Hepatitis B Virus Meeting 2023.09.19
4. Yosuke Yoneyama. Modeling human fatty liver diseases with iPSC-derived organoid. Global Regenerative Medicine Trainee Speaker Series 2023.07.27
5. Takanori Takebe. Developmental Origin of the Liver. Society for Developmental Biology (SDB) 2023 annual meeting 2023.07.21 Chicago
6. Takanori Takebe. Promise and Impact of Organoid Medicine. AMED-SCN Showcase Event 2023 2023.07.19
7. Takanori Takebe. Modeling Hepato-biliary-pancreatic Organogenesis in a Dish. The 87th Cold Spring Harbor Laboratory Symposium on Quantitative Biology - Stem Cells 2023.05.31
8. Yosuke Yoneyama. IGFALS regulates non-alcoholic steatohepatitis progression in mouse, organoid, and human. Gordon Research Conference "IGF and Insulin System in Physiology and Disease" 2023.03.16
9. Yunheng Wu, Masahiro Oda, Yuichiro Hayashi, Shuntaro Kawamura, Takanori Takebe, and Kensaku Mori. Thrombosis region extraction and quantitative analysis in confocal laser scanning microscopic image sequence in in-vivo imaging. SPIE Medical Imaging 2023 2023.02.20
10. Takanori Takebe. Modeling Hepato-Biliary-Pancreatic Organogenesis. Keystone Symposia 2023.02.08
11. Yosuke Yoneyama. Genotype-Phenotype Association Strategy for Fatty Liver Diseases Using Human iPSC-Derived Organoids. EVIDENT ORGANOID CONFERENCE 2023 2023.02.08
12. Takanori Takebe. Human Organoids Towards Precision Hepatology. The Department of Pediatrics of UTSW and Children's Medical Center, Scientific conference 2023.01.17

13. Yunheng Wu. Quality Improvement for Low-magnification Optical Microscopic Image in Mouse Cerebral Cortex Imaging. IFMIA2023 2023.01.11
1. Shuntaro Kawamura. Revealing the mechanism of drug-induced TMA using human vascularized liver organoids. The 22nd congress of the Japanese society for regenerative medicine 2023.03.24
2. Takanori Takebe. Diversity as a mean to be creative!. The 22d Congress of the Japanese Society for Regenerative Medicine 2023.03.24
3. Takanori Takebe. Promise and Impact of My Medicine. The 22nd Congress of the Japanese Society for Regenerative Medicine 2023.03.24
4. Takanori Takebe. Organoid Medicine for Human Toxicology. The 39th Annual Meeting of the Japanese Society of Toxicologic Pathology 2023.01.25

[Awards & Honors]

1. ISSCR Outstanding Young Investigator Award, International Society for Stem Cell Research (ISSCR) , 2023.02

Department of Biostatistics

Professor TAKAHASHI Kunihiro
Junior Associate Professor ANZAI Tatsuhiko
Assistant Professor NISHIDA Yuki

(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】 Biostatistics:Basic, Biostatistics:Advance I, Biostatistics:Advance II, Introduction to AI and Big Data in Health Sciences,Public Health.

【Graduate】 Medical Data Science, Data Science I, Biostatistics I, Clinical Biostatistics and Statistical Genetics, Biostatistics: Basic, Biostatistics: Advance I, Biostatistics: Advance II, Big Data Analytics, Preemptive Medicine Basic Course, 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]

1. Miya Aishima, Takako Ishikawa, Kasumi Ikuta, Maiko Noguchi-Watanabe, Sayuri Nonaka, Kunihiro Takahashi, Tatsuhiko Anzai, Sakiko Fukui. Unplanned Hospital Visits and Poor Oral Health With Undernutrition in Nursing Home Residents. J Am Med Dir Assoc. 2023.12; 24(12): 1855-1860.e1

2. Endo S, Okamoto T, Kawahara T, Anzai T, Takahashi K, Miyazaki Y. Effect of warm and humid days on the positivity rate of anti-Trichosporon asahii antibody test for the diagnosis of summer-type hypersensitivity pneumonitis. *Respiratory investigation*. 2023.12; 62(1); 150-156
3. Hao Ding, Hideyuki Koga, Hiroki Katagiri, Shoichi Hasegawa, Tatushiko Anzai, Mai Katakura, Aritoshi Yoshihara, Masaki Amemiya, Takashi Hoshino, Nobutake Ozeki, Tomomasa Nakamura, Yusuke Nakagawa. Low central sensitisation inventory score is associated with better post-operative outcomes of osteotomy around the knee. *Knee Surg Sports Traumatol Arthrosc*. 2023.12; 31(12); 5896-5904
4. Takahiro Ando, Sho Shimada, Jun Sugihara, Koji Takayama, Masayoshi Kobayashi, Yoshihiro Miyashita, Tatsuya Ito, Kaori Okayasu, Shun Tsuyuki, Takehiko Ohba, Masafumi Doi, Hiroaki Saito, Toshihide Fujie, Tomoshige Chiaki, Atsushi Nakagawa, Tatsuhiko Anzai, Kunihiro Takahashi, Sho Shibata, Tomoya Tateishi, Yasunari Miyazaki. Impairment of Social-Related Quality of Life in COVID-19 Pneumonia Survivors: A Prospective Longitudinal Study. *J Clin Med*. 2023.12; 12(24); 7064
5. Yukako Tani, Takeo Fujiwara, Tatsuhiko Anzai, Katsunori Kondo. Cooking skills, living alone, and mortality: JAGES cohort study. *Int J Behav Nutr Phys Act*. 2023.11; 20(1); 131
6. Murakami K, Shinozaki N, Kimoto N, Onodera H, Oono F, McCaffrey TA, Livingstone MBE, Okuhara T, Matsumoto M, Katagiri R, Ota E, Chiba T, Nishida Y, Sasaki S. Web-Based Content on Diet and Nutrition Written in Japanese: Infodemiology Study Based on Google Trends and Google Search. *JMIR formative research*. 2023.11; 7; e47101
7. Yosuke Nakatani, Masateru Takigawa, F Daniel Ramirez, Takashi Nakashima, Clémentine André, Cyril Goujeau, Aline Carapezzi, Tatsuhiko Anzai, Philipp Krisai, Takamitsu Takagi, Tsukasa Kamakura, Vlachos Konstantinos, Ghassen Cheniti, Romain Tixier, Nicolas Welte, Remi Chauvel, Josselin Duchateau, Thomas Pambrun, Nicolas Derval, Frédéric Sacher, Meleze Hocini, Michel Haïssaguerre, Pierre Jaïs. Electrophysiologic Determinants of Isoelectric Intervals on Surface Electrocardiograms During Atrial Tachycardia: Insights From High-Density Mapping. *JACC Clin Electrophysiol*. 2023.10; 9(10); 2054-2066
8. Mitsuaki Nishikimi, Shinichiro Ohshimo, Jun Hamaguchi, Kenji Fujizuka, Yoshihiro Hagiwara, Tatsuhiko Anzai, Junki Ishii, Yoshitaka Ogata, Toshiyuki Aokage, Tokuji Ikeda, Tsukasa Yagi, Ginga Suzuki, Ken Ishikura, Ken Katsuta, Daisuke Konno, Noriyuki Hattori, Tomoyuki Nakamura, Yosuke Matsumura, Daisuke Kasugai, Hitoshi Kikuchi, Tatsuhiko Iino, Shinichi Kai, Haruka Hashimoto, Takeshi Yoshida, Yumi Igarashi, Takayuki Ogura, Kazuki Matsumura, Keiki Shimizu, Mitsunobu Nakamura, Shingo Ichiba, Kunihiro Takahashi, Nobuaki Shime. High versus low positive end-expiratory pressure setting in patients receiving veno-venous extracorporeal membrane oxygenation support for severe acute respiratory distress syndrome: study protocol for the multicentre, randomised ExPress SAVER Trial. *BMJ Open*. 2023.10; 13(10); e072680
9. Hiroyuki Inose, Takuya Takahashi, Yu Matsukura, Jun Hashimoto, Kurando Utagawa, Satoru Egawa, Kentaro Yamada, Takashi Hirai, Kunihiro Takahashi, Toshitaka Yoshii. Effect of vitamin D deficiency on surgical outcomes of degenerative cervical myelopathy. *N Am Spine Soc J*. 2023.09; 15; 100239
10. COVID-19 Host Genetics Initiative. A second update on mapping the human genetic architecture of COVID-19. *Nature*. 2023.09; 621(7977); E7-E26
11. Yuki Nishida, Tatsuhiko Anzai, Kunihiro Takahashi, Takahide Kozuma, Eiichiro Kanda, Keita Yamauchi, Fuminori Katsukawa. Multimorbidity patterns in the working age population with the top 10% medical cost from exhaustive insurance claims data of Japan Health Insurance Association. *PLoS One*. 2023.09; 18(9); e0291554
12. Tsubasa Ito, Takahiro Otani, Tatsuhiko Anzai, Takashi Okumura, Kunihiro Takahashi. Potential Biases of the Transmission Risks of COVID-19 estimated by Contact Tracing Surveys in Japan. *Epidemiology, Biostatistics, and Public Health*. 2023.08;
13. Hiroyuki Inose, Tsuyoshi Kato, Yu Matsukura, Takashi Hirai, Toshitaka Yoshii, Shigenori Kawabata, Kunihiro Takahashi, Atsushi Okawa. Factors influencing the long-term outcomes of instrumentation surgery for degenerative lumbar spondylolisthesis: a post-hoc analysis of a prospective randomized study. *Spine J*. 2023.06; 23(6); 799-804

14. Saeka Takabayashi, Emiko Okada, Takumi Hirata, Hidemi Takimoto, Mieko Nakamura, Satoshi Sasaki, Kunihiro Takahashi, Koshi Nakamura, Shigekazu Ukawa, Akiko Tamakoshi. Nutritional Adequacy Assessment of the Japanese Diet Using the Number of Dishes Compared to Existing Dietary Diversity Indices: A Cross-Sectional Analysis from the 2012 National Health and Nutrition Survey, Japan. *J Nutr Sci Vitaminol (Tokyo)*. 2023.06; 69(3); 197-205
15. Asuka Hirose, Masakazu Terauchi, Tamami Odai, Ayako Fudono, Kotoi Tsurane, Masaki Sekiguchi, Misako Iwata, Tatsuhiko Anzai, Kunihiro Takahashi, Naoyuki Miyasaka. Investigation of exacerbating factors for postpartum hair loss: a questionnaire-based cross-sectional study. *Int J Womens Dermatol*. 2023.06; 9(2); e084
16. Mitsuaki Nishikimi, Shinichiro Ohshimo, Wataru Fukumoto, Tatsuhiko Anzai, Kazuo Awai, Takayuki Ogura, Toshikazu Abe, Mamoru Masuda, Kenji Fujizuka, Mitsunobu Nakamura, Michihito Kyo, Kunihiro Takahashi, Nobuaki Shime. Characteristics of the pulmonary opacities on chest CT associated with difficulty in short-term liberation from veno-venous ECMO in patients with severe ARDS. *Respir Res*. 2023.05; 24(1); 128
17. Ryuya Edahiro, Yuya Shirai, Yusuke Takeshima, Shuhei Sakakibara, Yuta Yamaguchi, Teruaki Murakami, Takayoshi Morita, Yasuhiro Kato, Yu-Chen Liu, Daisuke Motooka, Yoko Naito, Ayako Takuwa, Fuminori Sugihara, Kentaro Tanaka, James B Wing, Kyuto Sonehara, Yoshihiko Tomofuji; Japan COVID-19 Task Force; Ho Namkoong, Hiromu Tanaka, Ho Lee, Koichi Fukunaga, Haruhiko Hirata, Yoshito Takeda, Daisuke Okuzaki, Atsushi Kumanogoh, Yukinori Okada. Single-cell analyses and host genetics highlight the role of innate immune cells in COVID-19 severity. *Nat Genet*. 2023.05; 55(5); 753-767
18. Shintaro Shimizu, Gen Tanabe, Kairi Hayashi, Hiroshi Churei, Tatsuhiko Anzai, Kunihiro Takahashi, Toshiaki Ueno, Kenji Fueki. Quantitative text analysis of the mechanisms of tooth injury: Analysis of accidents in five sports that occurred in 15years under school control. *Dent Traumatol*. 2023.04; 39(2); 132-139
19. Hiroyuki Inose, Tsuyoshi Kato, Shoichi Ichimura, Hiroaki Nakamura, Masatoshi Hoshino, Shinji Takahashi, Daisuke Togawa, Toru Hirano, Yasuaki Tokuhashi, Tetsuro Ohba, Hirotaka Haro, Takashi Tsuji, Kimiaki Sato, Yutaka Sasao, Masahiko Takahata, Koji Otani, Suketaka Momoshima, Takashi Hirai, Toshitaka Yoshii, Kunihiro Takahashi, Atsushi Okawa. Factors affecting the quality of life in the chronic phase of thoracolumbar osteoporotic vertebral fracture managed conservatively with a brace. *Spine J*. 2023.03; 23(3); 425-432
20. Nobuyuki Nosaka, Tatsuhiko Anzai, Ryo Uchimido, Yuka Mishima, Kunihiro Takahashi, Kenji Wakabayashi. An anthropometric evidence against the use of age-based estimation of bodyweight in pediatric patients admitted to intensive care units. *Sci Rep*. 2023.03; 13(1); 3574
21. Masaki Ozawa, Tatsuhiko Anzai, Takashi Yamauchi, Kunihiro Takahashi. Do changes in working hours increase stress in Japanese white-collar workers? *Front Public Health*. 2023.02; 11; 1076024
22. Kohtaro Kikuchi, Tatsuhiko Anzai, Kunihiro Takahashi. The Unusual Increase in Suicides Among Women in Japan During the COVID-19 Pandemic: A Time-series Analysis Until October 2021. *J Epidemiol*. 2023.01; 33(1); 45-51
23. Yamashita S, Okamoto T, Kawahara T, Tateishi T, Anzai T, Takahashi K, Fushimi K, Miyazaki Y. Database analysis of hypersensitivity pneumonitis in Japan. *Respiratory investigation*. 2023.01; 61(2); 172-180

[Books etc]

1. Yuki Nishida. Obesity and diabetes are associated with frailty. Shibusawa Eiichi Memorial Foundation, 2023.03

[Misc]

1. Kunihiro Takahashi, Takahiro Otani. Development of an integrated platform for rapid response in disasters and accidents. *Chikyu Kankyo*. 2023; 28(2); 187-194

[Conference Activities & Talks]

1. Yuki Nishida, Takahiro Arai. Relationship between online review comments patterns and satisfaction among consumers of diet food based on latent class analysis. IDR User Forum 2023 2023.12.11 Tokyo
2. Yuki Nishida, Naoki Uemura, Tatsuhiko Anzai, Kunihiro Takahashi, Keita Yamauchi, Fuminori Katsukawa. Effect of weight change on frailty in middle-aged and older obese adults. The 44th Annual Meeting of Japan Society for the Study of Obesity (JASSO 44) / The 41st Annual Meeting of the Japanese Society for Treatment of Obesity (JSTO 41) 2023.11.26 Sendai
3. Naoki Uemura, Yuki Nishida, Fuminori Katsukawa. BMI changes with aging using large-scale health checkup data. The 44th Annual Meeting of Japan Society for the Study of Obesity (JASSO 44) / The 41st Annual Meeting of the Japanese Society for Treatment of Obesity (JSTO 41) 2023.11.25 Sendai
4. Yuki Nishida, Tatsuhiko Anzai, Kunihiro Takahashi, Keita Yamauchi, Fuminori Katsukawa. Expected improvement in HbA1c with weight loss before and after specific health guidance. The 82nd Annual Meeting of Japanese Society of Public Health 2023.11.01 Tsukuba
5. Shintaro Shimizu, Gen Tanabe, Tatsuhiko Anzai, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Kunihiro Takahashi, Toshiaki Ueno . Corresponding analysis of sports injury of school life using text mining method. 24th congress of The Japanese Association of Safety Education 2023.09.09
6. Yuki Nishida, Fuminori Katsukawa. Secondary Analysis Using Real World Data.. The 24th Annual Meeting of Japan Society of Health Promotion 2023.03.04 Fukuoka

Department of AI Systems Medicine

Professor: Hideyuki Shimizu, MD, PhD

Junior Associate Professor: Satoshi Ohno, PhD

Specially Appointed Assistant Professor: Aso Hirofumi, PhD

Project Researcher: Daisuke Koga, MD

(1) Outline

We are a young team to solve life's mysteries and create the future of medicine through data-driven approaches such as bioinformatics, mathematical modeling, and artificial intelligence.

(2) Research

Under the slogan of "Creating the future of medicine with data science," we focus on computational analyses coupled with biological experiments to reveal what is currently unknown in medicine and to create methods for the prevention, diagnosis, and treatment of diseases.

(3) Publications

[Original Articles]

1. Kodama M, Toyokawa G, (20 名省略), Bamba T, Shimizu H, Yoshizumi T, Nakayama KI. Modulation of host glutamine anabolism enhances the sensitivity of small cell lung cancer to chemotherapy Cell Reports. 2023.08; 42(8); 112899
2. Fujinuma S, Nakatsumi H, Shimizu H, Sugiyama S, Harada A, Goya T, Tanaka M, Kohjima M, Takahashi M, Izumi Y, Yagi M, Kang D, Kaneko M, Shigeta M, Bamba T, Ohkawa Y, Nakayama KI. FOXK1 promotes nonalcoholic fatty liver disease by mediating mTORC1-dependent inhibition of hepatic fatty acid oxidation Cell Reports. 2023.05; 42(5); 112530
3. Hozumi H, Shimizu H. Bayesian network enables interpretable and state-of-the-art prediction of immunotherapy responses in cancer patients PNAS Nexus. 2023.04; 2(5); pgad133
4. Hirofumi Aso, Jumpei Ito, Haruka Ozaki, Yukie Kashima, Yutaka Suzuki, Yoshio Koyanagi, Kei Sato. Single-cell transcriptome analysis illuminating the characteristics of species-specific innate immune responses against viral infections. GigaScience. 2023.10; 12; giad086

[Conference Activities & Talks]

1. Hideyuki SHIMIZU. Toward personalized cancer treatment through AI drug discovery. 2023.09
2. Hideyuki Shimizu. Toward ultra-fast drug discovery for hundreds of pathogens. Japan America Frontiers of Engineering 2023.07
3. Hideyuki SHIMIZU. Future challenges of AI in oncology. Chugai Cancer Summit 2023.06
4. 清水秀幸. 臨床応用を目指したデータ科学・AI創薬研究. 東北大学主催第1回医学AIセミナー 2023.04

5. 清水秀幸. データサイエンスによる小細胞肺癌治療法の確立を目指して. 15th NUJRA special seminar 2023.03
1. Satoshi Ohno, Saori Uematsu, Shinya Kuroda. OMELET: Multi-omics-based metabolic flux inference for understanding obesity-associated dysregulatory mechanisms in liver glucose metabolism.. Metabolic Engineering 15 2023.06.12

Department of Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi
Assistant Professor: Kenta Iitani
Assistant Professor: Kenta Ichikawa
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): Wataru Hijikata
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-continuous (rapid and repeated) measurement of antigens in body and airborne allergens in living environment.
4. “Organic engine” and “Air bio-battery” based on chemo-mechanical energy conversion
Novel chemo-mechanical energy conversion systems (Organic engine and Air bio-battery) that utilize enzyme reactions and active transport of chemicals has been constructed. Biomedical applications (chemical pumps, drug release systems, etc.) are also investigated.

(3) Education

In advanced medicine, technologies enabling to accurately measure biological information are highly demanded. The development of “human-friendly” non-invasive measurement methods could release patients from the pain and the risks of sampling. The students will learn the basic knowledge and skills of biological information measurement through the lectures (e.g., “Biomedical Engineering”, “Biomedical Device Science and Engineering”, “Wearable & IoT Devices and Applications”, “Advanced Biomedical Devices”, and “Integrative Biomedical Sciences for Preemptive Medicine”), 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. Geng Zhang, Yuki Maeno, Kenta Iitani, Takahiro Arakawa, Yasuhiko Iwasaki, Koji Toma, and Kohji Mitsubayashi. Enhanced sensitivity of a fluorometric biosensor for alcohol metabolites with an enzymatic cycling reaction Sensors and Actuators: B. Chemical. 2023.11; 401; 135031
2. Mizuki Sato, Tatsuya Kamiyama, Kenta Iitani, Kazuyoshi Yano, Kohji Mitsubayashi, and Takahiro Arakawa. Wearable Biosensor Utilizing Chitosan Biopolymer for Uric Acid Monitoring Journal of Robotics and Mechatronics. 2023.10; 35(5); 1131-1134
3. Kenta Iitani, Hidehisa Mori, Kenta Ichikawa, Koji Toma, Takahiro Arakawa, Yasuhiko Iwasaki, Kohji Mitsubayashi. Gas-Phase Biosensors (Bio-Sniffers) for Measurement of 2-Nonenal, the Causative Volatile Molecule of Human Aging-Related Body Odor Sensors. 2023.06; 23(13); 5857
4. Hidekazu Matsumoto, Keisuke Tomoto, Gentaro Kawase, Kenta Iitani, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi, Keiji Moriyama. Real-time Continuous Monitoring of Oral Soft Tissue Pressure with a Wireless Mouthguard Device for Assessing Tongue Thrusting Habits Sensors. 2023.05; 23(11); 5027
5. Kenta Iitani, Kanako Kishima, Yuka Kasuga, Kumi Yokota, Hiroki Nitta, Kohki Onchi, Gentaro Kawase, Kouta Umezawa, Koji Toma, Takahiro Arakawa, Dzong Viet Dao, Kohji Mitsubayashi. Wireless Unconstrained Monitoring of Intra-oral Temperature Using Thermistor and Telemeter Sealed in Mouthguard Sensors and Materials. 2023.04; 35(4); 1315-1325
6. Koji Toma, Yui Satomura, Kenta Iitani, Takahiro Arakawa, Kohji Mitsubayashi. Long-range surface plasmon aptasensor for label-free monitoring of vancomycin Biosensors and Bioelectronics. 2023.02; 22; 114959

[Conference Activities & Talks]

1. Geng Zhang, Shota Suzuki, Kenta Iitani, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Biofluorometric gas sensor for continuous monitoring of EtOH vapor from the ear canal. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
2. Shotaro Hiramatsu, Keisuke Tomoto, Kenta Ichikawa, Kenta Iitani, Koji Toma, Takahiro Arakawa, Dzong Viet Dao, Kohji Mitsubayashi. Wireless mouthguard biosensor with cellulose acetate membrane for measurement of salivary glucose concentration. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
3. Ryotaro Ishida, Kenta Ichikawa, Kenta Iitani, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Spatiotemporal gas-mapping of acetaldehyde concentration by biofluorometric imaging system (Sniff-cam). Bio4Apps 2023 2023.12.13 Gold Coast, Australia

4. Mako Tatemori, Kanako Iwasaki, Kenta Ichiakawa, Kenta Iitani, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Biofluorometric biosensing of methanol by using AOD-FALDH enzyme cascade reactions. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
5. Seiya Fujino, Kumi Yokota, Kenta Ichikawa, Kenta Iitani, Koji Toma, Takahiro Arakawa, Dzung Viet Dao, Kohji Mitsubayashi. Wireless mouthguard thermistor for unconstrained monitoring of intra-oral temperature. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
6. Kenta Iitani, Naoki Mizukoshi, Ye Ming, Kenta Ichikawa, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. SENSING AND IMAGING OF ACETONE VAPOR BASED ON ENZYMATIC BIOFLUOROMETRY. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
7. Takahiro Arakawa, Riki Ishikawa, Kenta Iitani, Koji Toma, Kohji Mitsubayashi. HEADSET BIO-SNIFFER WITH WIRELESS CMOS CAMERA FOR MONITORING OF ETHANOL VAPOR FROM THE EAR CANAL. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
8. Naoya Takeda, Tsubomi Tomono, Misa Nakaya, Miwa Takano, Kenta Iitani, Kenta Ichikawa, Koji Toma, Takahiro Arakawa, Yuji Tsuchido, Kohji Mitsubayashi. ENZYME-EMBEDDED ELECTROSPUN POLYMERIC MICROFIBER SENSOR FOR FLUOROMETRIC ETHANOL GAS DETECTION. Bio4Apps 2023 2023.12.13 Gold Coast, Australia
9. Kohji Mitsubayashi, Riki Ishikawa, Shota Suzuki, Kenta Ichikawa, Kenta Iitani. Bio-fluorometric Ear-gas Sensor for Non-invasive Blood Volatile Monitoring. 2023 7th International Conference on Sensors, Materials and Manufacturing 2023.11.22 Chiang Mai, Thai
10. Kenta Iitani, Misa Nakawa, Tsubomi Tomono, Kenta Ichikawa, Yuji Tsuchido, Naoya Takeda, Kohji Mitsubayashi. Biofluorometric ethanol vapor imaging using enzyme-encapsulated electrospun fiber mesh. The 8th International Symposium on Biomedical Engineering & International Workshop on Nanodevice Technologies 2023 2023.11.21 Hiroshima, Japan
11. Kohji Mitsubayashi. Cavitas Biosensors for Non-Invasive Monitoring of Blood Chemicals. 244th ECS meeting 2023.10.08 Gothenburg, Sweden
12. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Enzyme-based fluorometric image-sensing of transdermal gases for monitoring metabolisms. IEEE BioSensors 2023 2023.07.30 London, England
13. Mitsubayashi K. Noninvasive medical sensing in human cavities such as the lacrimal sac. Proteins & Peptides 2023 2023.07.24 Geneva, Switzerland
14. Iitani K, Di H, Zhang G, Toma K, Arakawa T, Mitsubayashi K. A wireless headset biosensor measuring volatile chemicals emitted from the auris externa for monitoring metabolisms. The 22nd International Conference on Solid-state Sensors, Actuators and Microsystems (Transducers 2023) 2023.06.25 Kyoto, Japan
15. Mitsubayashi K, Suzuki S, Ichikawa K, Iitani K, Toma K, Arakawa T. Headset gas sensor for monitoring of blood EtOH. 32nd International Symposium on Industrial Electronics (ISIE) 2023.06.19 Helsinki-Espoo, Finland
16. Toma K, Satomura Y, Iitani K, Arakawa T, Mitsubayashi K. Long-range surface plasmon aptasensor for label-free vancomycin monitoring. 33rd Anniversary World Congress of Biosensors 2023.06.05 Busan, South Korea
17. Iitani K, Suzuki M, Toma K, Arakawa T, Mitsubayashi K. Gas-phase biosensor based on fluorometric imaging by S-ADH (secondary-alcohol dehydrogenase) for breath acetone. 33rd Anniversary World Congress of Biosensors 2023.06.05 Busan, South Korea
18. Zhang G, Suzuki S, Iitani K, Toma K, Arakawa T, Mitsubayashi K. Biofluorometric sensors for monitoring of transcutaneous VOCs from the ear canal. 33rd Anniversary World Congress of Biosensors 2023.06.05 Busan, South Korea
19. Arakawa T, Tomoto K, Iitani K, Toma K, Mitsubayashi K. Mouthguard biosensor covered with cellulose acetate integrated with telemetry system for in-vivo measurement of salivary glucose. 33rd Anniversary World Congress of Biosensors 2023.06.05 Busan, South Korea

20. Iitani K, Tomono T, Nakaya M, Takeda N, Mitsubayashi K. Enzyme and coenzyme-integrated electrospun fiber mesh for biosensing of breath volatiles. 33rd Anniversary World Congress of Biosensors 2023.06.05 Busan, South Korea
21. Mitsubayashi K, Kawase G, Iitani K, Arakawa T, Dao D. Bluetooth wireless mouthguard sensor for real-time measurement of saliva glucose as oral information. 2023 International Conference on Electronics Packaging (ICEP2023) 2023.04.19 Kumamoto, Japan
22. Mitsubayashi K, Zhang G, Iitani K. Biofluorometric gas sensing and imaging for volatile markers. SPIE Future Sensing Technologies 2023 2023.04.18 Yokohama, Japan
23. Iitani K, Mizukoshi N, Zhang G, Mitsubayashi K. Acetone vapor imaging using secondary alcohol dehydrogenase immobilized on a laser-patterned hydrophilic PTFE mesh. SPIE Future Sensing Technologies 2023 2023.04.18 Yokohama, Japan
24. Zhang G, Suzuki S, Iitani K, Mitsubayashi K. Biofluorometric gas-sensing of ear ethanol as transcutaneous monitoring of blood VOCs. SPIE Future Sensing Technologies 2023 2023.04.18 Yokohama, Japan
25. Kohji Mitsubayashi, Kumi Yokota, Kenta Iitani, Dzung Dao, Takahiro Arakawa. Biomedical wireless mouthguard sensor with Dental-MEMS in oral cavity. International Conference on Biomedical Robotics and Biomechatronics - (ICBRB-23) 2023.03.23 Sydney, Australia
26. Kohji Mitsubayashi, K. Yokota, K. Iitani, D.V. Dao, T Arakawa. Wireless mouthguard sensor for saliva glucose in oral cavity. 5th International Conference on BioMedical Technology (ICBMT 2023) 2023.02.25 Da Nang, Vietnam
27. Kenta Iitani, Kohji Mitsubayashi. Real-time biosensors for assessing biochemical conditions of humans. The 9th Joint Symposium between IBB/TMDU and Chulalongkorn University on "Biomedical Materials and Engineering" 2023.01.23 Bangkok
28. Kenta Iitani, Zhang Geng, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Bio-fluorometric imaging system for volatile organic compounds in breath and transdermal gas. Advances in Functional Materials (AFM-2023) 2023.01.09 Fukuoka, Japan
29. Zhang Geng, Shota Suzuki, Kenta Iitani, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Biochemical monitoring of external ear-derived ethanol vapor after drinking. Advances in Functional Materials (AFM-2023) 2023.01.09 Fukuoka, Japan

[Awards & Honors]

1. Young Researchers Poster Award, The 8th International Symposium on Biomedical Engineering & International Workshop on Nanodevice Technologies 2023, 2023.11

[Others]

1. TMDU Research Activities 2022-2023 Building Better Gas-phase Biosensors for Fight Against Diseases by Kenta Iitani, 2023.03
https://www.tmd.ac.jp/english/research_activities/Vol-8/iitani/

Department of Biomedical Informatics

Professor NAKAJIMA Yoshikazu
Associate Professor
ONOGI Shinnya
Assistant Professor
SHU TOHAKU
Assistant Professor
SUGINO Takaaki

(1) Publications

[Original Articles]

1. Ishikawa Yuya, Sugino Takaaki, Okubo Kenichi, Nakajima Yoshikazu. Detecting the location of lung cancer on thoracoscopic images using deep convolutional neural networks SURGERY TODAY. 2023.06; 53(12); 1380-1387
2. Onogi Shinya, Nakajima Yoshikazu. Assessment of All-in-focus Image Quality in Shape-from-focus Technique SENSORS AND MATERIALS. 2023.04; 35(4); 1327-1337
3. Zhou Dongbo, Hayakawa Wataru, Nakajima Yoshikazu, Tadano Kotaro. Development of a Wearable Haptic Glove Presenting Haptic Sensation by Electrical Stimulation SENSORS. 2023.01; 23(1);

[Conference Activities & Talks]

1. Dongbo Z, Hengbing Ge, Nakajima Y. Noninvasive and stable organ manipulation forceps with stiffness tunable gripper. The 8th International Symposium on Biomedical Engineering (ISBE 2023) 2023.11.22
2. Jiang P, Onogi S, Yamada K, Nakajima Y. GPT-based operation capturing interface for emergency medicine. The 8th International Symposium on Biomedical Engineering (ISBE 2023) 2023.11.22
3. Sugino T, Kin T, Saito N, Nakajima Y. Automatic nerve detection for ultrasound -guided peripheral nerve blocks using deep convolutional neural networks. The 8th International Symposium on Biomedical Engineering (ISBE 2023) 2023.11.22
4. Takahashi T, Nakashima Y, Kobayashi M, Sugino T, Onogi S, Wada Y, Okumiya Y, OkuboK, Nakajima Y. Pulmonary respiratory classification with intercostal movement by using variance analysis in complex wavelet domain. The 8th International Symposium on Biomedical Engineering (ISBE 2023) 2023.11.22
5. Rathnayake Mudiyanse Migara Harshaka Bandara Rathnayake, Xu Y, Yonemitsu Y, Shimizu M, Sugino T, Onogi S, Moriyama K, Nakajima Y. Two-level feature points detection of mandibular using 3D U-Net and curvature analysis. The 8th International Symposium on Biomedical Engineering (ISBE 2023) 2023.11.22
6. Nakajima Y, Yashima Y, Onogi S. Navigation error estimation with considering human's discriminative sensitivity in AR surgical navigation. 2023 Computer Assisted Radiology and Surgery International Congress (CARS 2023) 2023.06.22 Munich, Germany

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7. Sugino T, Kin T, Saito N, Nakajima Y. Improved segmentation of basal ganglia from MR images using convolutional neural network with crossover-typed skip connection. 2023 Computer Assisted Radiology and Surgery International Congress (CARS 2023) 2023.06.21 Munich, Germany / Online

Biodesign

Professor Masashi IKEUCHI
 Assistant Professor Daisuke ISHIKAWA
 Researcher Chihiro AOYAMA, Ph.D., Yuuki SHICHI, DVM
 Secretary Naoko NAKAMURA

(1) Outline

Our laboratory aims to innovate research and medicine in the fields of medical and biological sciences. We are conducting research on unique devices and systems by integrating microdevices based on top-down microfabrication techniques and bottom-up techniques that utilize molecular self-assembly.

(2) Research

(1) Mechano-biological ovarian follicle activation device

We devised a new method of ovarian stimulation using a microneedle array for premature ovarian failure (POF). We evaluated the invasiveness of microneedle arrays and demonstrated that the mechanical stimulation of mouse ovaries promotes follicle development in vivo. We also evaluated mechano-transduction of microneedle array stimulation by using in vitro systems to identify the mechanism of the promotion of follicle development.

(2) AR microscope system for sperm retrieval

To reduce the time required for embryologists to search for sperm, we have developed an AR microscope system. This system can detect, track, and analyze the velocity of sperm from microscope images acquired by a high-speed camera, and show the information on a microdisplay in the microscope field of view without perceptible delay. The AR microscopy system improves the speed and rate of sperm detection compared to conventional microscopy using the naked eye.

(3) Optically-controlled massively parallel cell sorter

Cell sorters are widely used in biological research to sort specific cells from cell population. However, conventional cell sorters are concerned about the effects of high-speed flow and staining on cells. Furthermore, cell sorting based on temporal observation is not possible. We have developed a novel cell sorter using photo-responsive shape memory polymer that enables parallel sorting by addressing with light irradiation.

(4) Development of a portable device for early detection of the viral infection using nucleic acid analysis

To develop a portable device that can test for viral infections at various sites, we have developed a new method for performing viral infection by using saliva by nucleic acid analysis, which requires only the addition of water to the device. We are developing a microdevice that enable minimum invasive and low-cost testing for viral infections by using this method.

(3) Education

Basic-Clinical Borderless Education

Department of Material-based Medical Engineering

Prof. Akio Kishida
Assoc. Prof. Tsuyoshi Kimura
Assist. Prof. Yoshihide Hashimoto
Research Assistant Moeko Hagiwara
Secretary Naomi Hiwatari
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
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 key words of our policy are "contribution to medical care" and "exploration of basic scientific principles".

(2) Research

In order to develop technologies that contribute to the medical and dental care, there is a need for a system to build up the design concepts at the molecular level and to realize it. Based on polymer chemistry, organic chemistry, and physical chemistry, we proceed a research aimed at specific clinical applications using cell engineering, genetic engineering techniques. Target area are new medical material development, regenerative medicine, gene therapy, and the treatment engineering.

(1) Regenerative medicine using decellularized biological tissues

In order to remove the xenogeneic cells, the living tissue is decellularized using a new processing method, high-hydrostatic pressure (HHP) method has been developed. Using this process, complete removal of infectious bacteria, viruses, and cells was accomplished.

(2) 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 macrophages polarization in vitro.

(4) Immune control system: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulates immune reactions, to be able to enhance the anti-tumor immune responses have been revealed. We are developing technologies to capture and recover Treg using interfacial science.

(3) Education

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

[Original Articles]

1. Naoto Washihira, Mika Murakami, Miho Nakamura, Sho Fujii, Takahide Matsushima, Hiroshi Asahara, Akio Kishida, Tadao Tanabe, Tsuyoshi Kimura, Mako Kobayashi, Masaya Yamamoto. Application of a genetically engineered macrophage cell line for evaluating cellular effects of UV/US-treated poly(ethylene terephthalate) microplastics. *Colloids and Surface B: Biointerfaces*. 2023.12; 234; 113735
2. Yoshihide Hashimoto, Akitatsu Yamashita, Masaki Tabuchi, Yongwei Zhang, Seiichi Funamoto, Akio Kishida. Fibrin hydrogel layer-anchored pericardial matrix prevents epicardial adhesion in the severe heart adhesion-induced miniature pig model *Annals of Biomedical Engineering*. 2023.12; 52; 282-291
3. Say sreyphich, Mika Suzuki, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Effect of multi arm-PEG-NHS (polyethylene glycol n-hydroxysuccinimide) branching on cell adhesion to modified decellularized bovine and porcine pericardium *Journal of Materials chemistry B*. 2023.12; (5); 1244-1256
4. Suphatra Hiranphinyophat, Tomoki Hiraoka, Mako Kobayashi, Sho Fujii, Akio Kishida, Tadao Tanabe, Tsuyoshi Kimura, Masaya Yamamoto. Fabrication of polypropylene nanoplastics via thermal oxidation reaction for human cells responsiveness studies *Langmuir*. 2023.11; 39(44); 15563-15571
5. Kohei Yabuuchi, Mika Suzuki, Chen Liang, Yoshihide Hashimoto, Tsuyoshi Kimura, Kazunari Akiyoshi, Akio Kishida.. Preparation of cholesterol-modified hyaluronic acid nanogel-based hydrogel and the inflammatory evaluation using macrophage-like cells *Gels*. 2023.10; 9(11); 866
6. Dongzhe Wang, Narintadeach Charoensombut, Kinyoshi Kawabata, Tsuyoshi Kimura, Akio Kishida, Takashi Ushida, Katsuko S. Furukawa. Effect of pressure conditions in uterine decellularization using hydrostatic pressure on structural protein preservation *Bioengineering*. 2023.07; 10(7); 814
7. Ikuna Kanehara, Hiromasa Yamashita, Sho Fujii, Tsuyoshi Kimura, Masaya Yamamoto and Tadao Tanabe. Nano-sized polyethylene particles produced by nano-second UV laser ablation *Lasers in Manufacturing and Materials Processing*. 2023.06; 10; 389-399
8. Kosuke Sugawa, Arisa Suzuki, Jotaro Honda, Taiku Yabuki, Hironobu Tahara, Yutaro Hayakawa, Masato Furuya, Hiroki Ikake, Tsuyoshi Kimura, Yasuhiro Kosuge, Satoshi Kurumi, Kouichi Takase, Joe Otsuki. Photothermal therapeutic ability of copper open-shell nanostructures that are effective in second biological transparency window based on symmetry breaking-induced plasmonic properties *Journal of Materials Chemistry B*. 2023.06; 11; 6837-6852
9. Watcharaphol Tiskratok, Masahiro Yamada, Jun Watanabe, Qu Pengyu, Tsuyoshi Kimura, Hiroshi Egusa. Mechanoregulation of osteoclastogenesis-inducing potentials of fibrosarcoma cell line by substrate stiffness *International Journal of Molecular Sciences*. 2023.05; 24(10); 8959

10. Watcharaphol Tiskratok, Masahiro Yamada, Jun Watanabe, Nadia Kartikasari, Tsuyoshi Kimura, Hiroshi Egusa. Substrate stiffness controls proinflammatory responses in human gingival fibroblasts. *Scientific Reports*. 2023.01; 13(1); 1358

[Books etc]

1. Yoshihide Hashimoto. Research and development on therapeutic materials for corneal stromal disease consisting of transparent decellularised porcine corneas. 2023.09

[Conference Activities & Talks]

1. Mika Suzuki, Tsuyoshi Kimura, Varja cuculovic, Ruri Ishigaki, Yoshihide Hashimoto, Takahide Matsushima, Hiroshi Asahara, Wataru Nomura, Kishida Akio. Evaluation of immunogenicity of various treated decellularized tissue using gene-modified THP-1. *Materials Research Meeting (MRM) 2023* 2023.12.16 Kyoto
2. Chen Liang, Tsuyoshi Kimura, Mika Suzuki, Yoshihide Hashimoto, Takahide Matsushima, Hiroshi Asahara, Wataru Nomura, Tadao Tanabe, Masaya Yamamoto, Naoko Nakamura, Akio Kishida. Evaluation of microplastics using Caco-2/THP-1 co-culture. *The 3rd Materials Research Meeting (MRM2023)* 2023.12.15 Kyoto
3. Ikuna Kanehara, Hiromasa Yamashita, Sho Fujii, Tsuyoshi Kimura, Masaya Yamamoto, Tadao Tanabe. Model samples of nano-sized plastics. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.21 Korea
4. Mana Kusama, Kazuma Iwasaki, Sho Fujii, Tsuyoshi Kimura, Masaya Yamamoto, Tadao Tanabe. Polymorphism control of glycine crystals by terahertz wave irradiation. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.21 Korea
5. Kazuma Iwasaki, Mana Kusama, Sho Fujii, Tsuyoshi Kimura, Masaya Yamamoto, Tadao Tanabe. Pyroelectric effect of grown triglycine sulfate crystals. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.21 Korea
6. Tsuyoshi Kimura, Chen Liang, Mika Suzuki, Yoshihide Hashimoto, Tadao Tanabe, Masaya Yamamoto, Akio Kishida. Evaluation of biological response to materials using intestinal epithelial cells and macrophages. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.19 Korea
7. Mako Kobayashi, Jun Negishi, Yoshihide Hashimoto, Masaya Yamamoto, Yoshihiro Sasaki, Kazunari Akiyoshi, Tsuyoshi Kimura, Akio Kishida. Matrix-bound nanovesicles (MBVs) extracted from various decellularized tissues for neuroregenerative effects. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.19 Korea
8. Masaya Yamamoto, Suphatra Hiranphinyophat, Tomoki Hiraoka, Naoto Washihira, Akio Kishida, Sho Fujii, Mako Kobayashi, Tadao Tanabe, Tsuyoshi Kimura. Fabrication of polypropylene nanoplastics via thermal oxidation reaction for human cells responsiveness studies. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.19 Korea
9. Akio Kishida. Decellularized biological tissues as new biomaterials. *The 11th Pacific Rim International Conference on Advanced Materials and Processing* 2023.11.19 Korea
10. Akio Kishida. Development of artificial organs using decellularized tissue. *7th APSAO 2023 Congress* 2023.09.25 Malaysia
11. Akio Kishida, Hanako Maeda, Moeko Hagiwara, Yoshihide Hashimoto, Mako Kobayashi, Tsuyoshi Kimura. Pro-inflammatory characterization of biomaterials using genetically modified THP-1 cells. *33rd Annual Conference of European Society for Biomaterials* 2023.09.04 Davos, Switzerland.
12. Akio Kishida. Is decellularized tissue the same or different from traditional biomaterial?. *Biomaterials International* 2023 2023.07.30 Hokkaido, Japan

13. Masaya Yamamoto, Mika Murakami, Naoto Washihira, Miho Nakamura, Takahide Matsushima, Hiroshi Asahara, Akio Kishida, Mako Kobayashi, Sho Fujii, Tadao Tanabe, Tsuyoshi Kimura. Evaluation of cellular responses to oxidized poly(ethylene terephthalate) microplastics using a genetically engineered macrophage. Biomaterials International 2023 2023.07.30 Hokkaido, Japan
14. Tsuyoshi Kimura, Mika Suzuki, Yoshihide Hashimoto, Masahiro Okada, Takuya Matsumoto, Naoko Nakamura, Akio Kishida. Development of soft-hard interregional tissue by mineralization of decellularized membrane. Biomaterials International 2023 2023.07.30 Hokkaido, Japan
15. Masaya Yamamoto, Tomoki Hiraoka, Suphatra Hiranphinyophat, Naoto, Washihira, Mako Kobayashi, Akio Kishida, Sho Fujii, Tadao Tanabe, Tsuyoshi Kimura. Fabrication of PP nanoparticles as nano- and microplastic models for cytotoxicity testing. The 13th SPSJ International Polymer Conference 2023.07.18 Hokkaido, Japan
16. Sreypich Say, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Fabrication and characterization of linear and branch PEGNHS to modify the porcine and bovine pericardium. 第 72 回高分子学会年次大会 2023.05.24 群馬県
17. Akio Kishida. Decellularized biological tissue as a novel biomaterial. 熊本大学 博士課程教育リーディングプログラム 最先端研究セミナー 2023.05.17 熊本県
18. Tsuyoshi Kimura, Mika Suzuki, Yoshihide Hashimoto, Masahiro Okada, Takuya Matsumoto, Naoko Nakamura, Akio Kishida. Development of soft-hard interregional tissue using a mineralized dECM membrane. Society For Biomaterials 2023 2023.04.18 USA
19. Yoshihide Hashimoto, Takuya Akizawa, Moeko Hagiwara, Tsuyoshi Kimura, Akio Kishida. Cellular behaviors of human skeletal muscle satellite cells on tissue specific extracellular matrix coating and hydrogels. TERMIS EU 2023 2023.03.28 Manchester, UK

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Yuto SUMIDA (Apr–)
Associate Professor	Takashi NIWA (–Mar)
Assistant Professor	Jumpei TAGUCHI
Assistant Professor	Yuki SAKATA (–Mar)
Technical Assistant	Yuki HAZAMA, Miho HANYA, Satomi TOMITA (–Mar), Hitomi TABUCHI (Apr–)
Graduate Students	Akihiro KOBAYASHI, Takumi OKUYAMA, Kyoko TAKAHASHI, Miho NAKAJIMA, Ryuji ISODA, Yamato EZO, Kayato NISHIDA, Daisuke YAMANAKA, Yuting ZHANG, Wenkang ZHAO
Collaborators	Honoka Akimoto, Konami UTO
IHRP student	Rui AKIBA (Dec–)

(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

[Original Articles]

1. Niwa T, Takimoto T, Sakata Y, Hosoya T. Palladium-Catalyzed *ipso*-Borylation of Aryl Halides Promoted by Lewis Acid-Mediated Electrophilic Activation of Aryl(halo)palladium(II) Complex. *Org Lett.* 2023.11; 25(45); 8173-8177
2. Taguchi J, Okuyama T, Tomita S, Niwa T, Hosoya T. Synthesis of Multisubstituted Aromatics via 3-Triazenylarynes. *Org Lett.* 2023.09; 25(38); 7030-7034
3. Zhang Z, Niwa T, Watanabe K, Hosoya T. ¹¹C-Cyanation of Aryl Fluorides via Nickel and Lithium Chloride-Mediated C-F Bond Activation. *Angew Chem Int Ed Engl.* 2023.05; 62(22); e202302956

4. Niwa T, Tahara T, Chase CE, Fang FG, Nakaoka T, Irie S, Hayashinaka E, Wada Y, Mukai H, Masutomi K, Watanabe Y, Cui Y, Hosoya T. Synthesis of ^{11}C -Radiolabeled Eribulin as a Companion Diagnostics PET Tracer for Brain Glioblastoma. *Bull Chem Soc Jpn.* 2023.03; 96(3); 283-290
5. Dubol M, Immenschuh J, Jonasson M, Takahashi K, Niwa T, Hosoya T, Roslin S, Wikström J, Antoni G, Watanabe Y, Lubberink M, Biegon A, Sundström-Poromaa I, Comasco E. Acute nicotine exposure blocks aromatase in the limbic brain of healthy women: A [^{11}C] cetrozole PET study. *Compr Psychiatry.* 2023.03; 123; 152381
6. Sakata Y, Nabekura R, Hazama Y, Hanya M, Nishiyama T, Kii I, Hosoya T. Synthesis of Functionalized Dibenzoazacyclooctynes by a Decomplexation Method for Dibenzo-Fused Cyclooctyne-Cobalt Complexes. *Org Lett.* 2023.02; 25(7); 1051-1055
7. Tabata S, Minoshima M, Kobayashi A, Matsuzawa T, Hosoya T, Yoshida S. Migrative Thioamination of Aryne Intermediates Generated from *o*-Iodoaryl Triflates. *Synlett.* 2023.02;
8. Kobayashi A, Matsuzawa T, Hosoya T, Yoshida S. Synthesis of benzo[*b*] furans from alkynyl sulfoxides and phenols by the interrupted Pummerer reaction. *RSC Adv.* 2023.01; 13(2); 839-843

[Conference Activities & Talks]

1. Sumida Y. Carbon–Carbon Bond Cleavage of Benzyl Alcohol via Benzophenone-type Organic Photocatalysis. International Joint Symposium 2023 on Synthetic Organic Chemistry The 2nd International Symposium on Digitalization-driven Transformative Organic Synthesis (ISDigiTOS-2) 2023.12.06 Awaji
2. Taguchi J, Kimura K, Okuyama T, Igawa K, Tomooka K, Hosoya T.. Synthesis of Multisubstituted Aromatics via 3-Azidoaryne and 3-Triazenylaryne Species. The 15th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-15) 2023.11.22 Kyoto
3. Ezo Y, Niwa T, Hosoya T. Photoinduced *ipso*-Azidation of 1-Aryltriazenes. The 15th International Kyoto Conference on New Aspects of Organic Chemistry (IKCOC-15) 2023.11.21 Kyoto
4. Inoue S, Muraoka K, Taguchi J, Tomita S, Takeda H, Doi T, Tachibana K, Kondoh M, Hosoya T, Fujio Y, Okada Y. Development of small molecules that bind to Claudin-5 and control blood-brain barrier. ICoLA 2023 in conjunction with AAVBM 2023.09.15 Korea
5. Takahashi K, Niwa T, Owada-Hirahara S, Tsuda J, Wada Y, Hosoya T, Watanabe Y. Aromatase imaging in the brain with [^{18}F] cetrozole and [^{18}F] iso-cetrozole. World Molecular Imaging Congress 2023 2023.09.08 Prague, Czech Republic

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D.
Associate Professor Kohei TSUJI, Ph.D.
Assistant Professor Takuya KOBAYAKAWA, Ph.D.
Technical Assistant Hiroko TAKAGI
Technical Assistant Maiko HIRAYAMA
Technical Assistant Tomoe KAMEI

Graduate students

D3 WANG RONGYI, Takahiro ISHII
D2 Peter Bolah
D1 Yutaro MIURA, Soshi NISHIMURA, Eric Coffie
M2 Shun KAWAKATSU, Yuki KISHIHARA, Koki SHINOHARA, Akito MOCHIZUKI, Kenichi YAMAMOTO
M1 HUANG XUEYUAN, Yuki KURODA, Kaito HAYAKAWA, Saho MACHIDA

Internal Collaborators
ZHANG YUMENG, BAI KENAN

External Collaborators
Marisa ARIOKA, Yuto ISHIZEKI, Atsushi HAYASHI

(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. Kohei Tsuji, Takuya Kobayakawa, Takahiro Ishii, Nobuyo Higashi-Kuwata, Chika Azuma, Kouki Shinohara, Yutaro Miura, Kenichi Yamamoto, Soshi Nishimura, Shin-ichiro Hattori, Haydar Bulut, Hiroaki Mitsuya, Hirokazu Tamamura. Exploratory Studies of Effective Inhibitors against the SARS-CoV-2 Main Protease by Halogen Incorporation and Amide Bond Replacement. *Chemical and Pharmaceutical Bulletin*. 2023.12; 71(12); 879-886
2. Takuya Kobayakawa, Masayuki Amano, Miyuki Nakayama, Kohei Tsuji, Takahiro Ishii, Yutaro Miura, Kouki Shinohara, Kenichi Yamamoto, Masao Matsuoka, Hirokazu Tamamura. Development of anti-HBV agents targeting HBV capsid proteins. *RSC Medicinal Chemistry*. 2023.10; 14(10); 1973-1980

3. Kohei Tsuji, Takahiro Ishii, Takuya Kobayakawa, Nobuyo Higashi-Kuwata, Kouki Shinohara, Chika Azuma, Yutaro Miura, Hiroki Nakano, Naoya Wada, Shin-ichiro Hattori, Haydar Bulut, Hiroaki Mitsuya, Hirokazu Tamamura. Structure-Activity Relationship Studies of SARS-CoV-2 Main Protease Inhibitors Containing 4-Fluorobenzothiazole-2-carbonyl Moieties. *Journal of Medicinal Chemistry*. 2023.10; 66(19); 13516-13529
4. Takahiro Ishii, Takuya Kobayakawa, Kouki Matsuda, Kohei Tsuji, Nami Ohashi, Shingo Nakahata, Airi Noborio, Kazuhisa Yoshimura, Hiroaki Mitsuya, Kenji Maeda, Hirokazu Tamamura. Synthesis and evaluation of DAG-lactone derivatives with HIV-1 latency reversing activity. *European Journal of Medicinal Chemistry*. 2023.08; 256; 115449
5. Kohei Tsuji, Kofi Baffour-Awuah Owusu, Yutaro Miura, Takahiro Ishii, Kouki Shinohara, Takuya Kobayakawa, Akino Emi, Takashi Nakano, Youichi Suzuki, Hirokazu Tamamura. Dimerized fusion inhibitor peptides targeting the HR1–HR2 interaction of SARS-CoV-2 RSC *Advances*. 2023.03; 13; 8779-8793
6. Nobuyo Higashi-Kuwata, Kohei Tsuji, Hironori Hayashi, Haydar Bulut, Maki Kiso, Masaki Imai, Hiromi Ogata-Aoki, Takahiro Ishii, Takuya Kobayakawa, Kenta Nakano, Nobutoki Takamune, Naoki Kishimoto, Shin-ichiro Hattori, Debananda Das, Yukari Uemura, Yosuke Shimizu, Manabu Aoki, Kazuya Hasegawa, Satoshi Suzuki, Akie Nishiyama, Junji Saruwatari, Yukiko Shimizu, Yoshikazu Sukenaga, Yuki Takamatsu, Kiyoto Tsuchiya, Kenji Maeda, Kazuhisa Yoshimura, Shun Iida, Seiya Ozono, Tadaki Suzuki, Tadashi Okamura, Shogo Misumi, Yoshihiro Kawaoka, Hirokazu Tamamura, Hiroaki Mitsuya. Identification of SARS-CoV-2 Mpro inhibitors containing P1' 4-fluorobenzothiazole moiety highly active against SARS-CoV-2. *Nature Communications*. 2023.02; 14(1); 1076
7. Kanako Matsuura, Mizuki Yamaura, Hiromi Sakawaki, Ai Himeno, Yalcin Pisil, Takuya Kobayakawa, Kohei Tsuji, Hirokazu Tamamura, Shuzo Matsushita, Tomoyuki Miura. Sensitivity to a CD4 mimic of a consensus clone of monkey-adapted CCR5-tropic SHIV-MK38C. *Virology*. 2023.01; 578; 171-179
8. Takuya Kobayakawa, Masaru Yokoyama, Kohei Tsuji, Masayuki Fujino, Masaki Kurakami, Takato Onishi, Sayaka Boku, Takahiro Ishii, Yutaro Miura, Kouki Shinohara, Yuki Kishihara, Nami Ohashi, Osamu Kotani, Tsutomu Murakami, Hironori Sato, Hirokazu Tamamura. Low-molecular-weight anti-HIV-1 agents targeting HIV-1 capsid proteins. *RSC Advances*. 2023.01; 13(3); 2156-2167

[Conference Activities & Talks]

1. Takuya Kobayakawa, Chika Azuma, Kenichi Yamamoto, Kohei Tsuji, Hirokazu Tamamura. Development of synthetic strategies for peptidomimetic based on a chloroalkene dipeptide isostere and its application to a cyclic peptide. The 15th International Kyoto Conference on New Aspects of Organic Chemistry 2023.11.21 Kyoto
2. Kohei Tsuji, Hirokazu Tamamura, Terrence R. Burke, Jr.. Utilization of a non-specific kinase inhibitor for the development of high-affinity bivalent polo-like kinase 1 polo-box domain inhibitors. The 60th Japanese Peptide Symposium 2023.11.10 Otsu
3. Takuya Kobayakawa, Chika Azuma, Kenichi Yamamoto, Kohei Tsuji, Hirokazu Tamamura. Development of convergent synthesis for peptidomimetic based on a chloroalkene dipeptide isostere and its application to a cyclic peptide. The 60th Japanese Peptide Symposium 2023.11.08 Otsu
4. Kouki Shinohara, Kohei Tsuji, Takahiro Ishii, Takuya Kobayakawa, Nobuyo Higashi-Kuwata, Yutaro Miura, Chika Azuma, Hironori Hayashi, Shin-ichiro Hattori, Haydar Bulut, Shogo Misumi, Hiroaki Mitsuya, Hirokazu Tamamura. Structure-activity relationship studies of novel SARS-CoV-2 main protease inhibitors with potent antiviral activity. The 60th Japanese Peptide Symposium 2023.11.08 Otsu
5. Yutaro Miura, Rongyi Wang, Kohei Tsuji, Yishan Liu, Takuya Kobayakawa, Kazuhisa Yoshimura, Shuzo Matsushita, Shigeyoshi Harada, Hirokazu Tamamura. Combinational use of CD4 mimic with other anti-HIV agents and development of these hybrid molecules. 14th International Peptide Symposium 2023.10.17 Brisbane
6. Hirokazu Tamamura. Anti-SARS-CoV-2 Agents Inspired from HIV Researches. The 13th International Peptide Symposium/The 15th Australian Peptide Conference 2023.10.17 Brisbane

7. Yutaro Miura, Rongyi Wang, Kohei Tsuji, Yishan Liu, Takuya Kobayakawa, Kazuhisa Yoshimura, Shuzo Matsushita, Shigeyoshi Harada, Hirokazu Tamamura. Double target inhibitors of HIV-1 entry based on hybrid molecules of CD4 mimics and HIV-1 gp41-related peptides. 26th Korean Peptide Protein Symposium 2023.07.04 Jeju
8. Takahiro Ishii, Kohei Tsuji, Takuya Kobayakawa, Nobuyo Higashi-Kuwata, Chika Azuma, Kouki Shinohara, Yutaro Miura, Hironori Hayashi, Haydar Bulut, Shogo Misumi, Hiroaki Mitsuya, Hirokazu Tamamura. Design and Synthesis of SARS-CoV-2 Mpro Inhibitors Containing Fluorine Atoms and Amide Surrogates. 26th KPPS Annual Symposium 2023.07.03 Jeju
9. Hirokazu Tamamura. Anti-SARS-CoV-2 Agents Based on HIV Researches. The Seoul National University (SNU) seminar 2023.06.30 Korea
10. Takahiro Ishii, Takuya Kobayakawa, Kouki Matsuda, Kohei Tsuji, Nami Ohashi, Kazuhisa Yoshimura, Hiroaki Mitsuya, Kenji Maeda, Hirokazu Tamamura. Structure-Activity Relationship Studies of DAG-lactone Derivatives with HIV-1 Latency Reversing Activity. 14th AFMC International Medicinal Chemistry Symposium 2023.06.27 Seoul
11. Hirokazu Tamamura. Development of potent and biostable inhibitors of the main protease of SARS-CoV-2 learned from HIV researches. The 14th AFMC International Medicinal Chemistry Symposium (AIMECS 2023) 2023.06.27 Korea
12. Yutaro Miura, Rongyi Wang, Kohei Tsuji, Yishan Liu, Takuya Kobayakawa, Kazuhisa Yoshimura, Shuzo Matsushita, Shigeyoshi Harada, Hirokazu Tamamura. Hybrid molecules of CD4 mimic and HIV-1 fusion inhibitors. 14th AFMC International Medicinal Chemistry Symposium 2023.06.26 Seoul
13. Hirokazu Tamamura. Peptidomimetic-based Anti-SARS-CoV-2 Agents Learned from Anti-HIV Agents. The 17th Chinese International Peptide Symposium 2023.06.14 China
14. Hirokazu Tamamura. Development of Anti-SARS-CoV-2 Agents Learned from Anti-HIV Agents. The 19th Akabori Conference 2023: German-Japanese Symposium on Peptide Science 2023.05.19 Otsu
15. Hirokazu Tamamura. Use of synthetic peptides in infectious diseases research; vaccines, therapeutics and diagnostics. Discovery Research Platforms 2023.03.23 Online
16. Hirokazu Tamamura. Peptide-lead medicinal chemistry: from AIDS to COVID-19. The 9th Joint Symposium between IBB/TMDU and Chulalongkorn University on Biomedical Materials and Engineering 2023.01.23 Thailand
1. Takahiro Ishii, Takuya Kobayakawa, Kouki Matsuda, Kohei Tsuji, Kazuhisa Yoshimura, Hiroaki Mitsuya, Kenji Maeda, Hirokazu Tamamura. Development of PKC activators for HIV cure. The 143rd annual meeting of the pharmaceutical society of Japan 2023.03.26 Sapporo
2. Takahiro Ishii. Synthesis of DAG-lactone derivatives for HIV cure. 2023.01.27 Tokyo

[Patents]

1. CD4 MIMIC COMPOUND WITH ANTI-HIV ACTIVITY, Patent Number : 特許第 7297220 号

[Awards & Honors]

1. The 14th AFMC International Medicinal Chemistry Symposium (AIMECS 2023) Best Oral Presentation Award (Yutaro Miura), Asian Federation for Medicinal Chemistry, 2023.06
2. 2023 Young Scientist Oral Presentation Certificate (Takahiro Ishii), 26th Korean Peptide Protein Symposium, 2023.07

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 medical devices and systems for diagnostic and therapeutic purposes 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

[Original Articles]

1. Ramalingam M, Jaisankar A, Cheng L, Krishnan S, Lan L, Hassan A, Sasmazel HT, Kaji H, Deigner HP, Pedraz JL, Kim HW, Shi Z, Marrazza G. Impact of nanotechnology on conventional and artificial intelligence-based biosensing strategies for the detection of viruses. *Discover nano*. 2023.12; 18(1); 58
2. Nashimoto, Y; Konno, A; Imaizumi, T; Nishikawa, K; Ino, K; Hori, T; Kaji, H; Shintaku, H; Goto, M; Shiku, H. Microfluidic vascular formation model for assessing angiogenic capacities of single islets BIOTECHNOLOGY AND BIOENGINEERING. 2023.12;
3. Nashimoto Y, Konno A, Imaizumi T, Nishikawa K, Ino K, Hori T, Kaji H, Shintaku H, Goto M, Shiku H. Microfluidic vascular formation model for assessing angiogenic capacities of single islets. *Biotechnology and bioengineering*. 2023.12;
4. Utagawa, Y; Ino, K; Hiramoto, K; Iwase, K; Nashimoto, Y; Honma, I; Shiku, H. Vasculature-on-a-Chip with a Porous Membrane Electrode for In Situ Electrochemical Detection of Nitric Oxide Released from Endothelial Cells *ANALYTICAL CHEMISTRY*. 2023.11; 95(49); 18158-18165

5. Hashikawa Y, Kato Y, Kaji H, Abe T, Nagai N. A comparative study between a transscleral sustained-release device and eyedrops on intraocular distribution of carteolol hydrochloride. *Heliyon*. 2023.03; 9(3); e14392
6. Ostrovidov S, Ramalingam M, Bae H, Orive G, Fujie T, Shi X, Kaji H. Latest developments in engineered skeletal muscle tissues for drug discovery and development. *Expert opinion on drug discovery*. 2023.01; 18(1); 47-63
7. Liu S, Cheng L, Liu Y, Zhang H, Song Y, Park JH, Dashnyam K, Lee JH, Khalak FA, Riester O, Shi Z, Ostrovidov S, Kaji H, Deigner HP, Pedraz JL, Knowles JC, Hu Q, Kim HW, Ramalingam M. 3D Bioprinting tissue analogs: Current development and translational implications. *Journal of tissue engineering*. 2023.01; 14; 20417314231187113
8. Ostrovidov S, Ramalingam M, Bae H, Orive G, Fujie T, Shi X, Kaji H. Bioprinting and biomaterials for dental alveolar tissue regeneration. *Frontiers in bioengineering and biotechnology*. 2023; 11; 991821
9. Yamashita K, Ostrovidov S, Raut B, Hori T, Nashimoto Y, Nagai N, Abe T, Kaji H. Minimally Invasive Sub-Retinal Transplantation of RPE-J Cells on a Biodegradable Composite PCL/Collagen Nanosheet. *Cell transplantation*. 2023; 32; 9636897231165117
10. Yamashita Kazuya, Ostrovidov Serge, Raut Bibek, Hori Takeshi, Nashimoto Yuji, Nagai Nobuhiro, Abe Toshiaki, Kaji Hirokazu. Minimally Invasive Sub-Retinal Transplantation of RPE-J Cells on a Biodegradable Composite PCL/Collagen Nanosheet CELL TRANSPLANTATION. 2023; 32; 9636897231165117
1. Serge Ostrovidov, Murugan Ramalingam, Hojae Bae, Gorka Orive, Toshinori Fujie, Takeshi Hori, Yuji Nashimoto, Xuetao Shi, Hirokazu Kaji. Molecularly Imprinted Polymer-Based Sensors for the Detection of Skeletal- and Cardiac-Muscle-Related Analytes Sensors. 2023.06; 23(12); 5625
2. Yuji Nashimoto, Rei Mukomoto, Takuto Imaizumi, Takato Terai, Shotaro Shishido, Kosuke Ino, Ryuji Yokokawa, Takashi Miura, Kunishige Onuma, Masahiro Inoue, Hitoshi Shiku. Electrochemical sensing of oxygen metabolism for a three-dimensional cultured model with biomimetic vascular flow. *Biosensors & bioelectronics*. 2023.01; 219; 114808
3. Kazuya Fujimoto, Scott Erickson, Masamune Nakayama, Hroki Ihara, Kei Sugihara, Yuji Nashimoto, Koichi Nishiyama, Takashi Miura, Ryuji Yokokawa. Pericytes and shear stress each alter the shape of a self-assembled vascular network Lab on a chip. 2023.01; 23(2); 306-317
1. Hiroya Abe, Tomoya Ina, Hirokazu Kaji, Matsuhiko Nishizawa. Mussel-inspired interfacial ultrathin films for cellular adhesion on the wrinkled surfaces of hydrophobic fluids *Polymer Journal*. 2023.06;
2. Serge Ostrovidov, Murugan Ramalingam, Hojae Bae, Gorka Orive, Toshinori Fujie, Takeshi Hori, Yuji Nashimoto, Xuetao Shi, Hirokazu Kaji. Molecularly Imprinted Polymer-Based Sensors for the Detection of Skeletal- and Cardiac-Muscle-Related Analytes Sensors. 2023.06; 23(12); 5625
3. Yuji Nashimoto, Takeshi Hori, Serge Ostrovidov, Sayaka Katagiri, Hirokazu Kaji. Engineering Oral Microenvironments Using Microphysiological Systems Sensors and Materials. 2023.04; 35(4); 1293
4. Takeshi Hori, Yuya Ito, Bibek Raut, Serge Ostrovidov, Yuji Nashimoto, Nobuhiro Nagai, Toshiaki Abe, Hirokazu Kaji. Three-dimensional-printed Refillable Drug Delivery Device for Long-term Sustained Drug Delivery to Retina Sensors and Materials. 2023.04; 35(4); 1301
5. Yuji Nashimoto, Takeshi Hori, Serge Ostrovidov, Sayaka Katagiri, Hirokazu Kaji. Engineering Oral Microenvironments Using Microphysiological Systems Sensors and Materials. 2023.04; 35(4); 1293
6. Takeshi Hori, Yuya Ito, Bibek Raut, Serge Ostrovidov, Yuji Nashimoto, Nobuhiro Nagai, Toshiaki Abe, Hirokazu Kaji. Three-dimensional-printed Refillable Drug Delivery Device for Long-term Sustained Drug Delivery to Retina Sensors and Materials. 2023.04; 35(4); 1301

[Conference Activities & Talks]

1. Takeshi Hori, Hiroaki Okae, Shun Shibata, Yuji Nashimoto, Takahiro Arima, Hirokazu Kaji. In vitro models for the human placental barrier. MPS World Summit 2023 2023.06.27 JW Marriott Hotel Berlin, Berlin, Germany
2. Advanced cell culture technologies for drug development. 2023.01.23

Molecular Cell Biology

Professor Hiroshi Shibuya
Associate Professor Toshiyasu Goto
Assistant Professor Masahiro Shimizu

(1) Research

Overview

With no lysine kinase 1 (WNK1) phosphorylates and activates STE20/SPS1-related proline-alanine-rich protein kinase (SPAK) and oxidative stress responsive kinase 1 (OSR1) to regulate ion homeostasis in the kidney. Mutations in WNK1 result in dysregulation of the WNK1-SPAK/OSR1 pathway and cause pseudohypoaldosteronism type II (PHAII), a form of hypertension. WNK1 is also involved in the autosomal recessive neuropathy, hereditary sensory and autonomic neuropathy type II (HSANII). Mutations in a neural-specific splice variant of WNK1 (HSN2) cause HSANII. However, the mechanisms underlying HSN2 regulation in neurons and effects of HSN2 mutants remain unclear.

Introduction

A neuron-specific WNK1 splice variant, called HSN2, is expressed in the brain, dorsal root ganglia and sciatic nerve. Mutations in a neural specific exon of HSN2 cause the hereditary neuropathy called HSANII. HSANII is an autosomal recessive neuropathy characterized by sensory dysfunction, such as loss of pain, touch and temperature sensation, and limb abnormalities such as finger deformity and Charcot's joint. Although HSN2 is predicted to have an essential function in neurons, the precise mechanism by which HSN2 mutants cause HSANII is still unclear. To solve the problem, we focus on the function of HSN2 mutants in neural development.

1. HSN2 mutants suppress WNK signaling pathway by inhibiting the binding to wild-type WNK1, HSN2 and SPAK/OSR1.

It has been reported that there are approximately 20 different mutations in HSN2 gene of all HSANII patients. Most mutations in HSN2 occur in the neural-specific HSN2 exon and cause deletion of subsequent domains. Previous report has shown that the C-terminal domain of WNK isoforms is important for interaction and auto-phosphorylation of WNK kinases. These data suggest that HSN2 mutants might not interact with and activate WNK kinases including WNK1 and WNK4 and downstream effectors SPAK and OSR1. To verify the hypothesis, we examined the binding of HSN2 mutants to WNK1, WNK4, HSN2, SPAK and OSR1. As a result, we found that HSN2 mutants could not interact with these proteins, suggesting that HSN2 mutants are unable to promote activation of downstream signalling.

To analyse whether HSN2 regulates activation of SPAK and OSR1, we checked phosphorylation of SPAK and OSR1 in mouse neuroblastoma Neuro2A cells treated with nerve growth factor (NGF)-containing serum-free medium. The phosphorylation of SPAK and OSR1 was observed at 10 to 15 minutes after treatment with NGF-containing medium. We next analysed the effect of HSN2 constructs on the phosphorylation of SPAK and OSR1 mediated by NGF, and found that HSN2 expression increased the level of SPAK and OSR1 phosphorylation identically to that following WNK1 expression. By contrast, the expression of HSN2 mutants suppressed the NGF-induced phosphorylation of SPAK and OSR1. These results indicate that HSN2 mutants cannot activate SPAK and OSR1 by inhibiting the binding to the effectors of WNK signalling pathway.

2. HSN2 mutants suppress neurite outgrowth and neural development.

We have previously reported that WNK1 is involved in induction of neural marker genes and neurite outgrowth in Neuro2A cells (Sato A et al. PLoS One, 2013). HSN2 may, therefore, have similar functions in neurite

outgrowth and HSN2 mutants may exhibit loss of function. To examine whether HSN2 is involved in neurite outgrowth, we transiently expressed HSN2 in Neuro2A cells and observed that HSN2 induced neurite outgrowth identically to WNK1. We then examined the effect of HSN2 mutants on neurite outgrowth and found that HSN2 mutants could not induce neurite outgrowth. Next, we checked the effects of wild-type and mutant HSN2 on neurite outgrowth induced by NGF. NGF treatment induced neurite outgrowth, and the expression of WNK1 or HSN2 enhanced this induction. In contrast, the expression of HSN2 mutants suppressed neurite outgrowth in response to NGF-containing medium. We also examined the effect of WNK1, HSN2 and HSN2 mutants on neurite outgrowth of mouse primary cortical neuron. Consistent with the results from Neuro2A, neurite outgrowth of primary neuron was enhanced by WNK1 and HSN2 expression, but suppressed by HSN2 mutants. We next analysed the expression of neural marker genes, *Lhx8* and Choline acetyltransferase (ChAT) for cholinergic neurons and Glutamine acid decarboxylase 1 (*Gad1*) for GABAergic neurons. qPCR analysis indicated that NGF treatment greatly induced the expression of *Lhx8*, ChAT and *Gad1*, and that exogenous expression of WNK1 or HSN2 induced *Lhx8* and ChAT expression. WNK1 and HSN2 enhanced NGF-mediated expression of *Lhx8* and ChAT, but reduced that of *Gad1*. In contrast, expression of HSN2 mutants decreased *Lhx8* and ChAT expression and increased *Gad1* expression. These results indicate that WNK1 and HSN2 are involved in neurite outgrowth, but that HSN2 mutants fail in this activity.

3. HSN2 mutants have dominant negative functions for GSK3 β .

Previously, we have also reported GSK3 β to be a positive downstream regulator in the WNK-SPAK/OSR1 pathway, which regulates neurite outgrowth (Sato A et al. PLoS One, 2018). To identify the function of HSN2 mutants on GSK3 β , we analyzed the interaction between GSK3 β and HSN2 mutants. Immunoprecipitation analysis showed that HSN2 interacted more strongly with GSK3 β than with WNK1. Interestingly, HSN2 mutants associated more robustly with GSK3 β than with wild-type HSN2. From these results, we predicted that HSN2 mutants might suppress the binding of WNK1 and HSN2 to GSK3 β by covering the binding sites of GSK3 β . To confirm this hypothesis, we checked interaction of WNK1, HSN2 and GSK3 β with HSN2 mutant expression. As a result, the binding of WNK1 and HSN2 to GSK3 β was inhibited by expression of HSN2 mutants. Moreover, these mutants also prevented the homo-dimerization of WNK1 and HSN2 respectively, indicating that HSN2 mutants suppress the function of GSK3 β in the WNK1/HSN2 pathway by preventing the interaction. We then examined the effect of HSN2 mutants on GSK3 β function in neurite outgrowth. While transient GSK3 β expression in Neuro2A cells enhanced neurite outgrowth and expression of cholinergic neural marker genes *Lhx8* and ChAT, the expression of HSN2 mutants suppressed these effects of GSK3 β . Moreover, similar results were observed in mouse primary cortical neuron. These results suggest that HSN2 mutants preferentially bind to GSK3 β and function as dominant negative mutants which suppress the function of GSK3 β in neurite outgrowth.

In conclusion, we showed the biochemical function of HSN2 mutants in neural development, providing insight into the pathological mechanism of HSANII.

(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

[Original Articles]

1. Nishita M, Kamizaki K, Hoshi K, Aruga K, Nishikaku I, Shibuya H, Matsumoto K, Minami Y. Rho family small GTPase Rif regulates Wnt5a-Ror1-Dvl2 signaling and promotes lung adenocarcinoma progression. *The Journal of biological chemistry*. 2023.09; 299(10); 105248
2. Goto Toshiyasu, Michiue Tatsuo, Shibuya Hiroshi. ccl19 and ccl21 affect cell movements and differentiation in early *Xenopus* development DEVELOPMENT GROWTH & DIFFERENTIATION. 2023.04; 65(3); 175-189

Department of Advanced Nanomedical Engineering

Professor Satoshi Uchida

Junior Associate Professor Yuki Mochida

(1) Outline

The applications of mRNA therapeutics extend far beyond COVID-19 vaccines. They include preventive vaccines for other infectious diseases, cancer immunotherapy, protein replacement therapy for single-gene disorders, regenerative medicines, and genome editing. Nano-sized drug delivery systems (nano DDS) are crucial in these applications, as they enable safe, efficient, and selective delivery to target cells and tissues. Our laboratory focuses on developing nano DDS, exploring its therapeutic applications, and conducting clinical translational research.

(2) Research

1. Development of nano DDS

Our polymeric nano DDS is designed to be low immunostimulatory, allowing for mRNA delivery without causing unwanted inflammation. This is a significant advantage over commonly used lipid nanoparticles, which are highly inflammatory. For effective in vivo delivery, nano DDS must possess various functionalities, such as sufficient nuclease stability and the ability to selectively target specific organs. To achieve these functionalities, we are developing novel nano DDS through advanced polymer design and proprietary mRNA engineering techniques.

2. Applications of mRNA vaccines and therapeutics

Our research targets a wide range of applications, including vaccines for infectious diseases and cancers, as well as other therapeutic use beyond vaccines. Current mRNA vaccines for infectious diseases face safety concerns due to the use of lipid nanoparticles. To address this, we are developing “naked” mRNA vaccines that do not rely on lipid nanoparticles. In the field of cancer vaccines, we are working to enhance their efficacy through mRNA engineering, which can improve the adjuvanticity of the vaccines and enable selective mRNA delivery to lymphoid organs. Beyond vaccines, we are also exploring mRNA applications for single-gene disorders, genome editing, and antibody therapy.

(3) Lectures & Courses

The success of mRNA vaccines against COVID-19 was a result of the fusion of medical and engineering sciences. Our laboratory aims to learn and practice such interdisciplinary research. In this context, we place a strong emphasis on actively engaging in research.

(4) Publications

[Original Articles]

1. Theofilus A Tockary, Saed Abbasi, Miki Matsui-Masai, Akimasa Hayashi, Naoto Yoshinaga, Eger Boonstra, Zheng Wang, Shigeto Fukushima, Kazunori Kataoka, Satoshi Uchida. Comb-structured mRNA vaccine tethered with short double-stranded RNA adjuvants maximizes cellular immunity for cancer treatment. *Proc Natl Acad Sci U S A*. 2023.07; 120(29); e2214320120

2. Masahito Inagaki, Naoko Abe, Zhenmin Li, Yuko Nakashima, Susit Acharyya, Kazuya Ogawa, Daisuke Kawaguchi, Haruka Hiraoka, Ayaka Banno, Zheyu Meng, Mizuki Tada, Tatsuma Ishida, Pingxue Lyu, Kengo Kokubo, Hirotaka Murase, Fumitaka Hashiya, Yasuaki Kimura, Satoshi Uchida, Hiroshi Abe. Cap analogs with a hydrophobic photocleavable tag enable facile purification of fully capped mRNA with various cap structures. *Nature Communications*. 2023.05; 14(1); 2657
3. Makoto Oba, Mika Shibuya, Yuto Yamaberi, Hidetomo Yokoo, Satoshi Uchida, Atsushi Ueda, Masakazu Tanaka. An Amphipathic Structure of a Dipropylglycine-Containing Helical Peptide with Sufficient Length Enables Safe and Effective Intracellular siRNA Delivery. *Chemical and Pharmaceutical Bulletin*. 2023.03; 71(3); 250-256

[Misc]

1. Satoshi Uchida, Chun Yin Jerry Lau, Makoto Oba, Kanjiro Miyata. Polyplex designs for improving the stability and safety of RNA therapeutics. *Advanced Drug Delivery Reviews* . 2023.08; 199; 114972

[Conference Activities & Talks]

1. Satoshi Uchida. Next-generation mRNA vaccines against infectious diseases and cancer. "Integrated Science for a Sustainable Society" 14th Indian Scientists Association in Japan (ISAJ) Annual Symposium 2023.11.10
2. Satoshi Uchida, Saed Abbasi, Miki Matsui-Masai, Fumihiko Yasui, Akimasa Hayashi, Theofilus A. Tockary, Shiro Akinaga, Michinori Kohara, Kazunori Kataoka. Naked mRNA Jet Injection into the Skin Enables the Robust Vaccination against SARS-CoV-2 in Mice and Cynomolgus Monkeys. 11th International mRNA Health Conference 2023.10.31
3. Satoshi Uchida. mRNA vaccine development for infectious disease prevention and cancer treatment. The 18th international Symposium of the institute Network for Biomedical Science 2023.10.05
4. Satoshi Uchida, Saed Abbasi, Miki Masai, Akimasa Hayashi, Theofilus Tockary, Shiro Akinaga, Kazunori Kataoka. Small and large animal studies of COVID-19 vaccines based on naked mRNA jet-injection. 日本核酸医薬学会第8回年会 2023.07.14

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. Bekker GJ, Numoto N, Kawasaki M, Hayashi T, Yabuno S, Kozono Y, Shimizu T, Kozono H, Ito N, Oda M, Kamiya N. Elucidation of binding mechanism, affinity and complex structure between mWT1 tumor-associated antigen peptide and HLA-A*24:02. *Protein Science*. 2023.09; 32(10); e4775
2. Akiko Kamegawa, Shota Suzuki, Hiroshi Suzuki, Kouki Nishikawa, Nobutaka Numoto, Yoshinori Fujiyoshi. Structural analysis of the water channel AQP2 by single-particle cryo-EM. *J Struct Biol*. 2023.06; 215; 107984
3. Daisuke Kozai, Nobutaka Numoto, Kouki Nishikawa, Akiko Kamegawa, Shohei Kawasaki, Yoko Hiroaki, Katsumasa Irie, Atsunori Oshima, Hiroyuki Hanzawa, Kousei Shimada, Yutaka Kitano, Yoshinori Fujiyoshi. Recognition Mechanism of a Novel Gabapentinoid Drug, Mirogabalin, for Recombinant Human $\alpha 2 \delta 1$, a Voltage-Gated Calcium Channel Subunit *J Mol Biol*. 2023.03; 168049

[Misc]

1. Yuya Hanazono, Yu Hirano, Taro Tamada, Kunio Miki. Description of peptide bond planarity from high-resolution neutron crystallography *Biophysics and Physicobiology*. 2023.09; 20(3); e200035
1. Yuya Hanazono. Revisiting the Peptide Bond Planarity by High-resolution Neutron Crystallography *SEIBUTSU BUTSURI*. 2023.08; 63(4); 205-206

[Conference Activities & Talks]

1. Yuya Hanazono, Yu Hirano, Nobutoshi Ito, Taro Tamada, Kunio Miki. Fine structure analysis of protein: Unraveling molecular details through ultra-high-resolution X-ray and neutron crystallography. The 18th International Symposium of the Institute Network for Biomedical Sciences 2023.10.06
2. Xibin Quan, Nobutaka Numoto, Takeshi Tsubata, Nobutoshi Ito. Structure and function analysis of human B cell inhibitory co-receptor CD72. The 23rd Annual Meeting of the Protein Science Society of Japan 2023.07.06
1. Yabuno S, Numoto N, Ito N, Azuma T, Oda Y. Trade-off between Affinity Maturation and Destabilization in anti-NP Antibodies. 2nd Meeting of the Antibody Society of Japan 2023.12.02
2. Role of a disulfide bond in H-CDR3 loop of antibody for antigen binding and stability. The 61st Annual Meeting of the Biophysical Society of Japan 2023.11.14 Nagoya, Japan
3. Nobutaka Numoto, Gert-Jan Bekker, Narutoshi Kamiya, Masayuki Oda, Nobutoshi Ito. Rational design of function-enhancing mutants of the PET-degrading enzyme Cut190 based on the allosteric reaction mechanism. The 23rd Annual Meeting of the Protein Science Society of Japan 2023.07.07
4. Nobutaka Numoto. Where to look after getting the results of automated measurement data. 16th Workshop of Synchrotron Structural Biology Research Group, SPring-8 User Community (SPRUC) 2023.07.06
5. Development of novel non-secosteroidal VDR ligands based on diphenylsilane scaffold: Structure-activity relationship of hydrophobic core structure. Reports of Research Center for Biomedical Engineering 2023.04.01

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

[Original Articles]

1. Yamano K, Kinefuchi H, Kojima W. Mitochondrial quality control via organelle and protein degradation. *Journal of biochemistry*. 2023.12;
2. Kurusu R, Fujimoto Y, Morishita H, Noshiro D, Takada S, Yamano K, Tanaka H, Arai R, Kageyama S, Funakoshi T, Komatsu-Hirota S, Taka H, Kazuno S, Miura Y, Koike M, Wakai T, Waguri S, Noda NN, Komatsu M. Integrated proteomics identifies p62-dependent selective autophagy of the supramolecular vault complex. *Developmental cell*. 2023.07; 58(13); 1189-1205.e11
3. Akabane S, Watanabe K, Kosako H, Yamashita SI, Nishino K, Kato M, Sekine S, Kanki T, Matsuda N, Endo T, Oka T. TIM23 facilitates PINK1 activation by safeguarding against OMA1-mediated degradation in damaged mitochondria. *Cell reports*. 2023.05; 42(5); 112454
4. Hayashida R, Kikuchi R, Imai K, Kojima W, Yamada T, Iijima M, Sesaki H, Tanaka K, Matsuda N, Yamano K. Elucidation of ubiquitin-conjugating enzymes that interact with RBR-type ubiquitin ligases using a liquid-liquid phase separation-based method. *The Journal of biological chemistry*. 2023.02; 299(2); 102822
5. Yamano K, Sawada M, Kikuchi R, Nagataki K, Kojima W, Sugihara A, Fujino T, Tanaka K, Hayashi G, Murakami H, Matsuda N. . Optineurin provides a mitophagy contact site for TBK1 activation *bioRxiv*. 2023.02;
1. Noriyuki Matsuda. Current methods and problems to monitor mitophagy correctly - considered from Parkin study. *Experimental Medicine*. 2023.03; 41(5); 682-687

[Conference Activities & Talks]

1. Koji Yamano. Identification and functional analysis of a folding chaperone for RAB7A GTPase. 第46回日本分子生物学会年会 2023.12.06
1. Ryu Endo, Noriyuki Matsuda, Koji Yamano. Quality control of RAB proteins by stabilization and degradation. The 46th Annual Meeting of the Molecular Biology Society of Japan 2023.12.07 Kobe Port Island
2. Kei Okatsu, Koji Yamano, Noriyuki Matsuda, Shuya Fukai. The structural basis of RAB7A recognition by the RAB7A chaperone. The 46th Annual Meeting of the Molecular Biology Society of Japan 2023.12.07 Kobe Port Island
3. Noriyuki Matsuda, Waka Kojima, Koji Yamano. Molecular mechanisms underlying TBK1 activation during ubiquitin-dependent mitophagy. The 15th Autophagy Meeting 2023.11.28 Nاسpa New Otani, Niigata
4. Noriyuki Matsuda. Causal factors for hereditary Parkinson's disease and their proteostatic regulation. The 17th Meeting for Biomedical Society for Stress Response 2023.11.18 Fujii Memorial Institute of Medical Sciences in Tokushima University
5. Noriyuki Matsuda, Waka Kojima, Fumika Koyano, Koji Yamano. Regulatory mechanisms for mitochondria and peroxisomes via selective autophagy coupled with post-translational modifications. The 96th Annual Meeting of the Japanese Biochemical Society 2023.11.01 Fukuoka International Congress Center, Marine Messe Fukuoka Hall
6. Fumika Koyano, Koji Yamano, Hidetaka Kosako, Yukio Fujiki, Keiji Tanaka, Noriyuki Matsuda. p97/VCP-FAF2 complex suppresses basal pexophagy. The 96th Annual Meeting of the Japanese Biochemical Society 2023.10.31 Fukuoka International Congress Center, Marine Messe Fukuoka Hall
7. Aiko Watanabe, Yohei Hizukuri, Yoshinori Akiyama, Noriyuki Matsuda. Molecular function of the Parkinson's disease causative factor DJ-1 inferred from oxoaldehyde metabolism of YhbO. The 96th Annual Meeting of the Japanese Biochemical Society 2023.10.31 Fukuoka International Congress Center, Marine Messe Fukuoka Hall
8. Shizuka Ogiwara, Ozawa Azuna, Toriumi Kazuya, Wang Tianran, Matsuda Noriyuki, Arai Makoto. Characteristics of pentosidine implicated in Schizophrenia. The 96th Annual Meeting of the Japanese Biochemical Society 2023.10.31 Fukuoka International Congress Center, Marine Messe Fukuoka Hall
9. Noriyuki Matsuda. Intracellular degradation mediated by causative factors of hereditary Parkinson's Disease. Mizushima ERATO intracellular degradation dynamics project symposium 2023.07.31 Ito International Hall, The University of Tokyo
10. Noriyuki Matsuda. Mitochondrial quality control and cell death relevant to the onset of hereditary Parkinson's disease.. the 31st Cell Death Meeting in Japan 2023.07.15 Ogawa Hall, Juntendo University
11. Noriyuki Matsuda. PINK1-PARKIN mediated mitophagy. The 9th meeting for cancer and metabolism 2023.06.01 Ehime Citizens' Culture Hall

Department of Functional Genome Informatics

Professor NIKAIDO Itoshi
Graduate Student
TANAKA Yuuki
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

[Original Articles]

1. Tsuyuzaki K, Ishii M, Nikaido I. Sctensor detects many-to-many cell-cell interactions from single cell RNA-sequencing data. BMC bioinformatics. 2023.11; 24(1); 420
2. Shima, Y; Skibbe, H; Sasagawa, Y; Fujimori, N; Iwayama, Y; Isomura-Matoba, A; Yano, M; Ichikawa, T; Nikaido, I; Hattori, N; Kato, T. Distinctiveness and continuity in transcriptome and connectivity in the anterior-posterior axis of the paraventricular nucleus of the thalamus CELL REPORTS. 2023.10; 42(10); 113309
3. Ogura Nao, Sasagawa Yohei, Ito Tasuku, Tameshige Toshiaki, Kawai Satomi, Sano Masaki, Doll Yuki, Iwase Akira, Kawamura Ayako, Suzuki Takamasa, Nikaido Itoshi, Sugimoto Keiko, Ikeuchi Momoko. WUSCHEL-RELATED HOMEODOMAIN 13 suppresses de novo shoot regeneration via cell fate control of pluripotent callus SCIENCE ADVANCES. 2023.07; 9(27); eadg6983
4. Tsuyuzaki Koki, Yamamoto Kentaro, Toyoshima Yu, Sato Hirofumi, Kanamori Manami, Teramoto Takayuki, Ishihara Takeshi, Iino Yuichi, Nikaido Itoshi. WormTensor: a clustering method for time-series whole-brain activity data from C. elegans BMC BIOINFORMATICS. 2023.06; 24(1); 254
5. Takada Hitomi, Sasagawa Yohei, Yoshimura Mika, Tanaka Kaori, Iwayama Yoshimi, Hayashi Tetsutaro, Isomura-Matoba Ayako, Nikaido Itoshi, Kurisaki Akira. Single-cell transcriptomics uncovers EGFR signaling-mediated gastric progenitor cell differentiation in stomach homeostasis NATURE COMMUNICATIONS. 2023.06; 14(1); 3750
6. nnTensor: An R package for non-negative matrix/tensor decomposition. 2023.04;

[Conference Activities & Talks]

1. Identification of gene fusion at the single-cell level from transcriptome data. 2023.01.16

Department of Medical Chemistry

Professor: Katsumori Segawa, Ph.D.

Assistant Professor: Yugo Miyata, Ph.D.

JSPS Research Fellow: Sultan Cheryl Sophia, Ph.D.

Technical Assistant: Risa Kuribayashi, Moe Nishimoto

Secretary: Chikako Sawada

(1) Outline

Although the discovery of DNA has significantly advanced our understanding of life, we still do not fully understand even a single "cell," the basic unit of multicellular organisms. How do cells react with myriad substances to maintain life in the tiny space of 1/100,000 to 1/10,000,000 microliters? What is life? It is very mysterious. Biochemistry is a chemical approach to these questions, and Molecular Genetics is an approach based on the genetic information encoded in DNA. We aim to understand cells and, beyond that, to understand life and disease using biochemistry and molecular genetics.

(2) Research

We aim to understand the biological functions of cells. Abnormalities in critical cellular processes are always associated with the development of disease. We conduct research to identify genes and molecules that are "actually" involved in cellular functions through non-bias screening using forward genetics and biochemistry and to clarify the functions of the identified molecules in vivo and their pathological significance through mutation analysis in mouse models and humans. We are currently conducting the following research.

(3) Publications

[Misc]

1. Yugo Miyata, Katsumori Segawa, . Asymmetry and vulnerability on phospholipids in the plasma membrane 2023.04; 32(2); 11-16

RIKEN Molecular and Chemical Somatology

Visiting Professor	Ichiro Taniuchi	
Visiting Professor	Mikiko Sodeoka	
Visiting Professor	Kazuyoshi Ishigaki	
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	Shusuke Egoshi	
Visiting Lecturer	Ryo Endo	
Visiting Lecturer	Hideyuki Yoshida	
Visiting Lecturer	Nicolas Gailhouste	
Visiting Lecturer	Takashi Nomura	
Visiting Lecturer	Shunsuke Tagami	
Visiting Lecturer	Jun Ando	
Graduate Students	D3	Nayan Suryawanshi
	D3	Chang Jingjie
	D2	Shingo Tamai
	D1	Jyunji Harada
	D1	Qin Zhizhen
	D1	Yuxin Chen

(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 interdisciplinary study for developing a new technology to measure bio-molecules at single molecular level. Our studies will also aim to apply our findings 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

- Molecular basis of neurodegenerative disorders and psychiatric diseases

6) Digital Biology

- Development of new technology to detect bio-molecules at single molecular level and its application for rapid disease diagnosis.

(3) Publications

[Original Articles]

1. Chang J, Yamashita M, Padhi AK, Zhang KYJ, Taniuchi I. Impaired tissue homing by the *Ikzf3*^{N159S} variant is mediated by interfering with Ikaros function. ***Front. Immunol.*** 14:1239779. (2023).
2. Endo R, Chen YK, Burke J, Takashima N, Suryawanshi N, Hui KK, Miyazaki T, Tanaka M. Dysregulation of ribosome-associated quality control elicits cognitive disorders via overaccumulation of TTC3. ***Proc Natl Acad Sci USA.*** 120(12): e2211522120 (2023)

[Review Articles]

1. Suryawanshi N, Tanaka M. DISC1 protein aggregates in cerebrospinal fluid as a potential diagnostic biomarker for first-episode psychosis. *Psychiatry Clin Neurosci*.

[Books]

[Conference Activities & Talks]

1. Ichiro Taniuchi “Pathogenesis of immune disorders by dysregulation of the transcription factor function.” The 2nd International Symposium of Clinical Immunology. May 19, 2023、Kamakura, Japan.
2. Suryawanshi N, Tanaka M. “Activity-dependent translome analysis reveals novel non-canonical translation.” RIKEN-A*STAR joint research workshop. Nov 22nd, 2023. A*STAR, Singapore, Singapore
3. Shingo Tamai “Structural and functional properties for the fuzzy coat region of AD-relevant full-length tau strain fibrils.” Mini-symposium on amyloids and neurological disease, may 17, 2023. Academia sinica, Genomics Research Center, Taiwan.

[Poster presentation]

1. Shingo Tamai, Takashi Nomura, Ryohei Kojima, Atsushi Yamagata, John W. Burke, Mikako Shirouzu, Takeshi Fukuma, Motomasa Tanaka. “Disaggregation of AD-fold tau filaments by molecular chaperones.” THE 27TH BIOPHYSICS CONFERENCE, 2023.5.18 (Tzu Chi University, Taiwan)
2. Shingo Tamai, Takashi Nomura, Ryo Fujioka, John W. Burke, Atsushi Yamagata, Mikako Shirouzu, Hiroki Sasaguri, Motomasa Tanaka.”Structure-dependent seeding activity of tau fibrils.” APPS 2023, 2023.11.9 (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
Visiting Lecturer	Naoto TSUCHIYA
Visiting Lecturer	Ken-ichi YOSHIOKA
Visiting Lecturer	Bunsyo SHIOTANI
Visiting Lecturer	Keisuke SEKINE
Visiting Lecturer	Rieko OHKI
Graduate Students	D3 Yamato OGIWARA Akira SAKAI Norio SHINKAI Takahiro SHIRAI D2 Yuri YAMASU M2 Haruka ASAI Yuya MANAKA Megumi KATO Shoju ENDO Ta-Chun LIN Takumi YAMADA M1 Naoya KOBAYASHI Masayuki SHINDO

(1) Research

1. Carcinogenesis and molecular mechanism
2. Functions of cancer-associated genes and their alterations
3. Genomic, epigenomic and proteomic analysis of cancer and personalized medicine
4. Tumor microenvironment

5. Cancer stem cells/non-coding RNA/signaling pathway
6. Molecular target/drug delivery/diagnosis and therapy

(2) Education

To learn knowledge and skill for cancer research, students attend lectures and seminars, and attend and/or practice research meeting, journal club, scientific meeting, etc. These practices will enable students to develop an ability to conduct their studies as an independent cancer researcher in the future. To obtain good skills to carry out experiments that are required for cancer research, students belong to one of our research groups, and conduct their own studies under the guidance of the instructor and/or staff. Students perform various experiments involved in genetics, gene technology, biochemistry, cellular biology, molecular biology, physiology, experimental animal, pathology, genomic/epigenomic/proteomic analysis, imaging, next generation sequencing, etc.

(3) Publications

[Original Articles]

1. Ikari N, Arakawa H. Identification of a mitochondrial targeting sequence in cathepsin D and its localization in mitochondria. *Biochemical and Biophysical Research Communications*. 655: 25-34, 2023.
2. Matsuda Y, Ye J, Yamakawa K, Mukai Y, Azuma K, Wu L, Masutomi K, Yamashita T, Daigo Y, Miyagi Y, Yokose T, Oshima T, Ito H, Morinaga S, Kishida T, Minamoto T, Kojima M, Kaneko S, Haba R, Kontani K, Kanaji N, Okano K, Muto-Ishizuka M, Yokohira M, Saito K, Imaida K, Suizu F. Association of longer telomere length in cancer cells and cancer-associated fibroblasts with poor prognosis. *J Natl Cancer Inst*. 115: 208-218, 2023.
3. Niwa T, Tahara T, Chase CE, Fang FG, Nakaoka T, Irie S, Hayashinaka E, Wada Y, Mukai H, Masutomi K, Watanabe Y, Cui Y, Hosoya T. Synthesis of ¹¹C-Radiolabeled Eribulin as a Companion Diagnostics PET Tracer for Brain Glioblastoma. *Bull Chem Soc Jpn*. 96: 283–290, 2023
4. Machino H, Dozen A, Konaka M, Komatsu M, Nakamura K, Ikawa N, Shozu K, Asada K, Kaneko S, Yoshida H, Kato T, Nakayama K, Saloura V, Kyo S, Hamamoto R. Integrative analysis reveals early epigenetic alterations in high-grade serous ovarian carcinomas. *Exp Mol Med*. 55(10): 2205-2219, 2023

5. Igarashi T, Mazevet M, Yasuhara T, Yano K, Mochizuki A, Nishino M, Yoshida T, Yoshida Y, Takamatsu N, Yoshimi A, Shiraishi K, Horinouchi H, Kohno T, Hamamoto R, Adachi J, Zou L, Shiotani B. An ATR-PrimPol pathway confers tolerance to oncogenic KRAS-induced and heterochromatin-associated replication stress. *Nat Commun.* 4(1): 4991, 2023
6. Ohata H, Shiokawa D, Sakai H, Kanda Y, Okimoto Y, Kaneko S, Hamamoto R, Nakagama H, Okamoto K. PROX1 induction by autolysosomal activity stabilizes persister-like state of colon cancer via feedback repression of the NOX1-mTORC1 pathway. *Cell Rep.* 42(6): 112519, 2023
7. Hayashi T, Takasawa K, Yoshikawa T, Hashimoto T, Sekine S, Wada T, Yamagata Y, Suzuki H, Abe S, Yoshinaga S, Saito Y, Kouno N, Hamamoto R. A discrimination model by machine learning to avoid gastrectomy for early gastric cancer. *Ann Gastroenterol Surg.* 7(6): 913-921, 2023
8. Koganemaru S, Fuchigami H, Yamashita H, Morizono C, Sunakawa H, Kawazoe A, Nakamura Y, Kuboki Y, Shitara K, Yano T, Doi T, Yasunaga M. Quantitative Analysis of the Concentration of Trifluridine in Tumor Hypoxic Regions Using a Novel Platform Combining Functional Endoscopy and Mass Spectrometry. *Clin Pharmacol Ther.* 115(1):62-7, 2023.
9. Tsumura R, Haruta M, Kuwano M, Yasunaga M. Expansion of mixed immune cells using CD3/CD161 co-stimulation for the treatment of cancer. *Sci Rep.* 13(1):6803, 2023.
10. Chromatographic analysis of N-glycan profile on therapeutic antibodies using FcγRIIIa affinity column chromatography. Hiranyakorn M, Iwamoto S, Hoshino A, Tsumura R, Takashima H, Yasunaga M, Manabe S, *ACS Omega*, 8(18):16513–16518. 2023
11. Fujii T, Ito K, Takahashi K, Aoki T, Takasugi R, Seki T, Iwai Y, Watanabe T, Hirama R, Tsumura R, Fuchigami H, Yasunaga M, Matsuda Y. Bispecific Antibodies Produced via Chemical Site-Specific Conjugation Technology: AJICAP Second-Generation. *ACS Med Chem Lett.* 14(12):1767-1773.2023.
12. 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 Pharmaceut*, 20(2):1156-1167, 2023.
13. Fukuoka S, Koga Y, Yamauchi M, Koganemaru S, Yasunaga M, Shitara K, Doi T, Yoshino T, Kuronita T, Elenbaas B, Wahra P, Zhang H, Crowley L, Jenkins MH, Clark A, Kojima T. p70S6K/Akt dual inhibitor DIACC3010 is efficacious in preclinical models of gastric cancer alone and in combination with trastuzumab. *Sci Rep*, 13(1):16017, 2023.
14. Ueda T, Shiina S, Iriguchi S, Terakura S, Kawai Y, Kabai R, Sakamoto S, Watanabe A, Ohara K, Wang B, Xu H, Minagawa A, Hotta A, Woltjen K, Uemura Y, Kodama Y, Seno H,

Nakatsura T, Tamada K, Kaneko S. Optimization of the proliferation and persistency of CAR T cells derived from human induced pluripotent stem cells. *Nat Biomed Eng.* 2023 Jan;7(1):24-37

15. Nakatsuka R, Kato T, Zhang R, Uemura Y, Sasaki Y, Matsuoka Y, Shirouzu Y, Fujioka T, Yamashita H, Hattori F, Nozaki T, Ogata H, Hitomi H. The Induction of Parathyroid Cell Differentiation from Human Induced Pluripotent Stem Cells Promoted Via TGF- α /EGFR Signaling. *Stem Cells Dev.* 2023 Nov;32(21-22):670-680.
16. Wu L, Gao Y, Xie S, Ye W, Uemura Y, Zhang R, Yu Y, Li J, Chen M, Wu Q, Cui P, Liu H, Mu S, Li Y, Wang L, Liu C, Li J, Zhang L, Jiao S, Zhang G, Liu T. The level of macrophage migration inhibitory factor is negatively correlated with the efficacy of PD-1 blockade immunotherapy combined with chemotherapy as a neoadjuvant therapy for esophageal squamous cell carcinoma. *Transl Oncol.* 2023 Nov;37:101775.
17. Suzuki, M., Fujimori, H., Wakatsuki, K., Manaka, Y., Asai, H., Hyodo, M., Matsuno, Y., Kusumoto-Matsuo, R., Shiroishi, M., and Yoshioka, K., Genome Destabilization-Associated Phenotypes Arising as a Consequence of Therapeutic Treatment are Suppressed by Olaparib. *PLoS ONE*, 18 (2023) e0281168.

[Reviews Articles]

1. Giulivi C, Zhang K, Arakawa H. Recent advances and new perspectives in mitochondrial dysfunction. *Scientific Reports.* 13: 7977, 2023.
2. Hamamoto R, Takasawa K, Shinkai N, Machino H, Kouno N, Asada K, Komatsu M, Kaneko S. Analysis of super-enhancer using machine learning and its application to medical biology. *Brief Bioinform.* 24(3): bbad107, 2023
3. Koga Y, Takashima H, Koganemaru S. Special Issue: Evaluation of the Antitumor Mechanism of Armed Antibodies. *Pharmaceuticals*, 16:1690, 2023.
4. Fukushima S, Miyashita A, Kuriyama H, Kimura T, Mizuhashi S, Kubo Y, Nakahara S, Kanemaru H, Tsuchiya N, Mashima H, Zhang R, Uemura Y. Future prospects for cancer immunotherapy using induced pluripotent stem cell-derived dendritic cells or macrophages. *Exp Dermatol.* 2023 Mar;32(3):290-296

[Book]

1. Arakawa H. MLOs and control of metabolic pathways. *Uversky V. Droplets of life.* Elsevier. Chapter 14. 431-446, 2023.

[Conference Activities & Talks]

1. Hirofumi Arakawa. Warburg effect as an anti-apoptotic strategy for cancer cells and membrane-less organelles involved in cardiolipin metabolism. KSMRM (Korean Society for Mitochondrial Research and Medicine) 2023, Wonju, Korea. September 2023.
2. Machitani M, Nomura A, Yamashita T, Ueno T, Yamashita A, Taniguchi T, Kaneko S, Kato Y, Mano H, Masutomi K. Maintenance of R-loop structures by phosphorylated hTERT to preserve genome integrity. CSHL Meeting-Telomeres & Telomerase-, May 2023
3. Ryuji Hamamoto. Cancer Research in the Big Data Era: Medical AI Research for Clinical Application、 International Symposium on Tumor Biology in Kanazawa 2023, July 2023.

Department of 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]

1. Tamara A M Chessa, Piotr Jung, Arqum Anwar, Sabine Suire, Karen E Anderson, David Barneda, Anna Kielkowska, Barzan A Sadiq, Ieng Wai Lai, Sergio Felisbino, Daniel J Turnham, Helen B Pearson, Wayne A Phillips, Junko Sasaki, Takehiko Sasaki, David Oxley, Dominik Spensberger, Anne Segonds-Pichon, Michael Wilson, Simon Walker, Hanneke Okkenhaug, Sabina Cosulich, Phillip T Hawkins, Len R Stephens. PLEKHS1 drives PI3Ks and remodels pathway homeostasis in PTEN-null prostate. *Mol Cell*. 2023.08; 83(16); 2991-3009.e13
2. Dang Minh Tran, Nozomu Yoshioka, Norihisa Bizen, Yukiko Mori-Ochiai, Masato Yano, Shogo Yanai, Junya Hasegawa, Satoshi Miyashita, Mikio Hoshino, Junko Sasaki, Takehiko Sasaki, Hirohide Takebayashi. Attenuated cerebellar phenotypes in Inpp4a truncation mutants with preserved phosphatase activity. *Dis Model Mech*. 2023.07; 16(7);
3. Akihiro Iguchi, Sho Takatori, Shingo Kimura, Hiroki Muneto, Kai Wang, Hayato Etani, Genta Ito, Haruaki Sato, Yukiko Hori, Junko Sasaki, Takashi Saito, Takaomi C Saido, Tsuneya Ikezu, Toshiyuki Takai, Takehiko Sasaki, Taisuke Tomita. INPP5D modulates TREM2 loss-of-function phenotypes in a β -amyloidosis mouse model. *iScience*. 2023.04; 26(4); 106375
4. Yusuke Kiyoki, Takayasu Kato, Sakura Kito, Takashi Matsuzaka, Shin Morioka, Junko Sasaki, Kenichi Makishima, Tatsuhiro Sakamoto, Hidekazu Nishikii, Naoshi Obara, Mamiko Sakata-Yanagimoto, Takehiko Sasaki, Hitoshi Shimano, Shigeru Chiba. The fatty acid elongase Elovl6 is crucial for hematopoietic stem cell engraftment and leukemia propagation. *Leukemia*. 2023.03;
5. Takahito Miyake, Yuichi Inoue, Xinyan Shao, Takehito Seta, Yuto Aoki, Khanh Tien Nguyen Pham, Yuichi Shichino, Junko Sasaki, Takehiko Sasaki, Masahito Ikawa, Yoshiaki Yamaguchi, Hitoshi Okamura, Shintaro Iwasaki, Masao Doi. Minimal upstream open reading frame of Per2 mediates phase fitness of the circadian clock to day/night physiological body temperature rhythm. *Cell Rep*. 2023.02; 112157

[Conference Activities & Talks]

1. 柳井翔吾、佐々木純子、長谷川純矢、佐々木雄彦. ホスファチジルイノシトール-3,4,5-三リン酸 (PIP3) は性分化期における精巢形成に必要である. 第 46 回分子生物学会 2023.12.08 神戸, 兵庫
2. 柳井翔吾、佐々木純子、佐々木雄彦. 性維持機構におけるイノシトールリン脂質の機能の解明. 第 20 回生命科学研究会 2023.10.27 東京大学, 東京
3. Yanai, Shogo; Sasaki Junko, Sasaki, Takehiko. The Role of Phospholipid Metabolism in Gonadal Maintenance. The 18th international Symposium of the institute Network for Biomedical Science 2023.10.06 TMDU, Tokyo
4. Junko Sasaki, Toshiyoshi Yamamoto, Takehiko Sasaki. Phosphoinositide profiling in cancer cells and tissues.. BIOCHEMICAL SOCIETY, The PI3K-AKT-mTOR-PTEN pathway: a new era in basic research and clinical translation 2023.09.14 Barcelona, Spain
5. Junko Sasaki, Takehiko Sasaki. Structural and Functional Dissection of Phosphoinositides. Babraham Institute seminar 2023.09.12
6. Junko Sasaki, Shogo Yanai, Toshiyoshi Yamamoto, Takehiko Sasaki. Structural and Functional Dissection of Phosphoinositides.. University College London seminar 2023.09.11 London, UK
7. Yusuke Kiyoki, Takayasu Kato, Sakura Kito, Takashi Matsuzaka, Shin Morioka, Junko Sasaki, Kenichi Makishima, Tatsuhiro Sakamoto, Hidekazu Nishikii, Naoshi Obara, Mamiko Sakata-Yanagimoto, Takehiko Sasaki, Hitoshi Shimano, and Shigeru Chiba. ELOVL6 regulates engraftment of hematopoietic cells through the PI3K pathway.. The 28th European Hematology Association Congress 2023.06.08 Frankfurt, Germany
8. Aya Toyoshima , Natsuko Noguchi , Junko Sasaki , TakehikoSasaki, Motomu Manabe , Shin-Ichi Osada. Selective blockade of phosphatidylinositol-3 kinase γ suppresses the development of cutaneous squamous cell carcinoma. FIRST INTERNATIONAL SOCIETIES FOR INVESTIGATIVE DERMATOLOGY MEETING 2023.05.10 Keio Plaza Hotel Tokyo, Japan

Interdisciplinary Sciences

Prof. Mitsunori Hieda (Physics)
Prof. Kazuyoshi Yagishita (Physical Well-being)
Prof. Jun Nakabayashi (Mathematics)
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. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Kinesiophobia Is Negatively Associated With Psychological Readiness to Return to Sport in Patients Awaiting Anterior Cruciate Ligament Reconstruction. *Arthroscopy*. 2023.09; 39(9); 2048-2055
2. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. *Orthop Traumatol Surg Res*. 2023.02; 109(1); 103147
3. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Sho Mitomo, Toshiyuki Ohara, Kazuyoshi Yagishita. Biomechanical characteristics of the lower extremities during running in male long-distance runners with a history of medial tibial stress syndrome: a case control study. *BMC Musculoskelet Disord*. 2023.02; 24(1); 103
4. Airi Kaneko, Junko Taniguchi, Masaru Suzuki, Mitsunori Hieda. Simultaneous Measurements of 4He Confined in an Oriented Porous Membrane by 32 and 100 kHz Tuning Forks Proceedings of the 29th International Conference on Low Temperature Physics (LT29). 2023; (38); 011005
5. Murofushi Koji, Oshikawa Tomoki, Akuzawa Hiroshi, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Kaneoka Koji, Yagishita Kazuyoshi. Trunk muscle activation in side plank exercises with and without external-focus instruction *ISOKINETICS AND EXERCISE SCIENCE*. 2023; 31(1); 29-36
6. Koji Murofushi, Daisuke Yamaguchi, Koji Kaneoka, Tomoki Oshikawa, Hiroki Katagiri, Kenji Hirohata, Hidetaka Furuya, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity. *J Med Invest*. 2023; 70(1.2); 208-212
7. Kumiko Kasashi, Ayaka Sato, Mark Stuart, Una Hollywood, Marina Kawaguchi-Suzuki, Kazuyoshi Yagishita, Takao Akama. The Tokyo 2020 Olympic and Paralympic pharmacy services during the COVID-19 pandemic. *J Am Pharm Assoc (2003)*. 2023; 63(4); 1156-1161

8. Norihiro Kuroki, Kazuyoshi Yagishita, Keiki Shimizu, Sachiko Okuaki, Yuuri Doi, Yuki Arakawa, Tomotsugu Nakano, Takao Akama. Emergency department activities at the Athletes' Village during the Tokyo 2020 Olympic and Paralympic Games. *Acute Med Surg.* 2023; 10(1); e905

[Conference Activities & Talks]

1. Azimjon A. Temurjonov, 宮内雄也, 清水康弘, 伊藤正行, 小林義明, 檜枝光憲, 和田信雄, 松下琢. ナノトンネル中に形成した 1 次元 ^3He 流体のスピン拡散 II. 第 78 回年次大会 (2023 年) 2023.09
2. Azimjon A. Temurjonov, 松下琢, 檜枝光憲, 和田信雄. ナノ多孔体熱交換器の性能評価 II. 第 78 回年次大会 (2023 年) 2023.09
3. Azimjon Temurjonov, Yuya Miyauchi, Yasuhiro Shimizu, Masayuki Itoh, Yoshiaki Kobayashi1, Mitsunori Hieda, Nobuo Wada, Taku Matsushita. Spin diffusion of dilute ^3He fluid in ^4He -precoated 1D nanochannels. International Symposium on Quantum Fluids and Solids, QFS2023 2023.07
4. Azimjon Temurjonov, Taku Matsushita, Mitsunori Hieda, Nobuo Wada. Performance Evaluation of the Nanopore Heat Exchanger. International Symposium on Quantum Fluids and Solids, QFS2023 2023.07
1. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
2. Kaito Togawa, Hiroshi Churei, Kairi Hayashi, Yumi Takahashi, Shintaro Shimizu, Yoko Hotta, Takahisa Haraguchi, Tomohiko Tateishi, Kazuyoshi Yagishita, Gen Tanabe, Toshiaki Ueno. An case of a professional futsal player who is able to continue competitive life by using a custom-made faceguard. 34th congress of Japanese society of clinical sports medicine 2023.11.11
3. Nakagawa K, Mizutani K, Watanabe K, Saito N, Takemura S, Sakaniwa E, Mikami R, Kido D, Takeda K, Kominato H, Hattori A, Iwata T. Comprehensive gene expression analysis during the healing phase of ligature-induced experimental periodontitis in diabetic rats. 2023.05.26

Department of Data Science Algorithm Design and Analysis

Professor BANNAI Hideo
Assistant Professor

DIPTARAMA HENDRIAN
Assistant Professor
KOEPL 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. Yuta Fujishige, Yuki Tsujimaru, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Linear-time computation of DAWGs, symmetric indexing structures, and MAWs for integer alphabets Theoretical Computer Science. 2023.09; 973; 114093
2. Aaron Hong, Marco Oliva, Dominik Köppl, Hideo Bannai, Christina Boucher, Travis Gagie. Acceleration of FM-Index Queries Through Prefix-Free Parsing Proc. 23rd International Workshop on Algorithms in Bioinformatics (WABI 2023). 2023.09; 273; 13:1-13:16
3. Kouta Okabe, Takuya Mieno, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai. Linear-Time Computation of Generalized Minimal Absent Words for Multiple Strings Proc. 30th International Symposium on String Processing and Information Retrieval (SPIRE 2023). 2023.09; 14240; 331-344
4. Hideo Bannai, Jonas Eller. Lyndon Arrays in Sublinear Time Proc. 31st Annual European Symposium on Algorithms (ESA 2023). 2023.09; 274; 14:1-14:16
5. Haruki Ideguchi, Diptarama Hendrian, Ryo Yoshinaka, Ayumi Shinohara. Efficient Parameterized Pattern Matching in Sublinear Space Proceedings of the 30th International Symposium on String Processing and Information Retrieval (SPIRE 2023). 2023.09; 271-283
6. Bannai Hideo, Tomohiro I, Koeppl Dominik. Longest bordered and periodic subsequences INFORMATION PROCESSING LETTERS. 2023.08; 182;

7. Yutaro Numaya, Diptarama Hendrian, Ryo Yoshinaka, Ayumi Shinohara. Identification of Substitutable Context-Free Languages over Infinite Alphabets from Positive Data Proceedings of the 16th International Conference on Grammatical Inference (ICGI 2023). 2023.07; 23-34
8. Hideo Bannai, Mitsuru Funakoshi, Kazuhiro Kurita, Yuto Nakashima, Kazuhisa Seto, Takeaki Uno. Optimal LZ-End Parsing Is Hard Proc. 34th Annual Symposium on Combinatorial Pattern Matching (CPM 2023). 2023.06; 3-11
9. Hideo Bannai, Tomohiro I, Tomasz Kociumaka, Dominik Köppl, Simon J. Puglisi. Computing Longest Lyndon Subsequences and Longest Common Lyndon Subsequences Algorithmica. 2023.04;
10. Inferring Strings from Position Heaps in Linear Time 2023.03; 115-126
11. Benedikt Kirsch-Gerweck, Leonard Bohnenkämper, Michel T Henrichs, Jarno N Alanko, Hideo Bannai, Bastien Cazaux, Pierre Peterlongo, Joachim Burger, Jens Stoye, Yoan Diekmann. HaploBlocks: Efficient Detection of Positive Selection in Large Population Genomic Datasets Molecular Biology and Evolution. 2023.02; 40(3);
12. Yuuki Yonemoto, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai. Space-Efficient STR-IC-LCS Computation Lecture Notes in Computer Science. 2023.01; 372-384
1. Space-efficient Huffman codes revisited 2023.01; 179; 106274

Pathology and Anatomical Sciences

(Previous Department of Anatomy and Physiological Sciences)

Professor Osamu Hoshi

Assistant Professor Hitomi Fujishiro

(Master's Programs) Nanami Seshimo, Maki Tejima, Mayu Funabashi, Yuho Shishido

(Previous Department of Molecular Pathology)

Junior Associate Professor(Career Track) Yurie Soejima

Master's Program Nozomi Takahashi, Miiko Nakahori, Fumina Fujii

(1) Outline

(Previous Department of Anatomy and Physiological Sciences)

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.

(Previous Department of Molecular Pathology)

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

(Previous Department of Anatomy and Physiological Sciences)

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.

(Previous Department of Molecular Pathology)

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. Molecular pathological study of cholangiocarcinoma and development of a novel therapy
2. Creation of digital content using cytological images, AI imaging diagnosis
3. Development of pathological diagnosis and pathological technology in developing countries

(3) Education

(Previous Department of Anatomy and Physiological Sciences)

Examination for Technology Stream: Human Anatomy Lecture, Human Anatomy Practicum, Physiology Lecture, Physiology Practicum, General Lecture, Graduate Research Project

Examination for Nursing Stream: Anatomy, Physiology

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

(Previous Department of Molecular Pathology)

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

(Previous Department of Anatomy and Physiological Sciences)

1) Undergraduate education

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.

2) Graduate education

The students will be taught to formulate a hypothesis, conduct experiments to test it, discuss the results, and summarize them in a single paper.

(Previous Department of Molecular Pathology)

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

- In the first 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.
- 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.

· 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

(Previous Department of Molecular Pathology)

In the Pathology department of the TMDU hospital, Soejima participates in the cytological diagnosis and supervises graduate students.

(6) Publications

[Original Articles]

1. Fujishiro H, Nimura A, Azumaya M, Hattori S, Hoshi O, Akita K. Anatomical study of the bone morphology of the anterior talofibular ligament attachment. *Anatomy & cell biology*. 2023.07;

[Conference Activities & Talks]

1. Fujishiro H, Nimura A, Azumaya M, Hattori S, Hoshi O, Akita K.. Anatomical investigation of the bone morphology of the anterior talofibular ligament attachment of fibula.. 10th APICA Congress 2023.11.30
2. Tejima M, Fujishiro H, Nimura A, Hoshi O, Akita K.. Anatomical investigation of the posterior part of the coracohumeral ligament including loose connective tissues.. 10th APICA Congress 2023.11.30
3. Yurie Soejima and Chiara Raggi. ITGB6-knockout affected biological behavior and gene expression of cholangiocarcinoma cells. The 10th Annual Cholangiocarcinoma Foundation Conference 2023 2023.04.12 Salt Lake City
1. Osamu Hoshi, Nobuyuki Takei. The dynamics of ribosomal protein associated with local protein synthesis in axonal growth cones. The 128th Annual Meeting of The Japanese Association of Anatomists 2023.03.20 Sendai

Hematology and Biophysical Systems Analysis

Professor ITO Minami
Associate Professor Miwako Nishio
Assistant Professor HONMA Satoru
Researcher YOSHIMORI Mayumi
Adjunct Lecturer Arai Ayako
Adjunct Lecturer SAEKI Kumiko
Adjunct Lecturer IMADOME Ken-ichi
Adjunct Lecturer NAKAYAMA Yoichi

(1) Outline

A) 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.

B) 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

A)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.

B)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

A)

1) Undergraduate school: After the covid19 situation, a face-to-face lectures and practices were carried out. 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.

B)

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

A) 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.

B) 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

B) 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

B) 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]

1. Takayuki Inoue, Bin Fu, Miwako Nishio, Miyako Tanaka, Hisashi Kato, Masashi Tanaka, Michiko Itoh, Hajime Yamakage, Kozue Ochi, Ayaka Ito, Yukihiro Shiraki, Satoshi Saito, Masafumi Ihara, Hideo Nishimura, Atsuhiko Kawamoto, Shian Inoue, Kumiko Saeki, Atsushi Enomoto, Takayoshi Suganami, Noriko Satoh-Asahara. Novel Therapeutic Potentials of Taxifolin for Obesity-Induced Hepatic Steatosis, Fibrogenesis, and Tumorigenesis. *Nutrients*. 2023.01; 15(2);

[Conference Activities & Talks]

1. Minami Ito, Risa Sugawar, Sayori Sakamoto, Runa Fujii. Exploring individual differences in the material perception in searching material properties.. 第46回日本神経科学学会 2023.08.01 Sendai, Miyagi
2. Bin Fu, Miyako Tanaka, Kozue Ochi, Emi Saita, Michiko Itoh, Miwako Nishio, Atsushi Enomoto, Takayuki Inoue, Noriko Satoh-Asahara, Takayoshi Suganami. Natural bioactive flavonoid Taxifolin prevents the development of hepatic steatosis, fibrogenesis and tumorigenesis in a mouse model of NASH. 第96回日本内分泌学会学術総会 2023.06.01

Clinical Information and Applied Sciences

Professor:	Yuki Sumi, MD, PHD.
Associate Professor:	Miho Akaza, MD, PHD.
Assistant Professor:	Tomoki Kawahara, MD, PHD.
Part-time:	Keiko Hara, MD, PHD, Sayaka Aritake, MT, PHD, Mina Ako, MT, PHD, Osamu Takahashi, MT, PHD, Yoko Soroida, MT, PHD, Jyunji Endo, MD, PHD, Yuri Ichikawa, MT, PHD, Yoshiaki Adachi, PHD, Yuko Kato, MT, PHD, Hiramitsu Shiro, MD, PHD.
Doctoral:	Terutaka Sonohara.
Master's:	Maina Oshige, Yukina Higashiguchi, Yusuke Komabashiri, Sakura Shimooki, Risa Okada.
Students:	Kouki Kawamura, Hiyori Tarui, Satomi Tozato, Jun Ninomiya, Natsumi Iso, Chihiro Kami, Hana Sasaki, Asuka Suzuki, Rena Nakagome, Chiharu Hakkaku.

(1) Outline

We research and educate the physiological function testing which measure and analyze the workings of the living body as an integrated system from the molecular and cellular level to the organ level, clinical medicine, and public health as a human population.

The official name is "Department of Clinical information Applied Sciences, Division of Biomedical Sciences and engineering, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University". 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 in 2018, cardiovascular division separated, and we moved from "Graduate School of Health Care Sciences" to "Graduate School of Medical and Dental Sciences" and were renamed to "Respiratory and Nervous System Science". In 2023 there was an organizational reform in the track of Medical Technology, and we took charge of the field of public health. We were renamed to the "Department of Clinical information Applied Sciences".

(2) Research

Each research is conducted independently, and each staff is the principal investigator. We have expanded on its original specialized fields of respiratory medicine, neurology, and pediatrics. In the respiratory field, Sumi is researching the clinical significance of new pulmonary function tests, the mechanism and endotype classification of bronchial asthma, gene therapy for lung diseases, image diagnosis using AI, and clinical diagnosis using AI. Akaza is conducting electroencephalogram (EEG) research and epilepsy research in the central nervous system, and developing new peripheral nerve activity measuring methods in the peripheral nerve. Kawahara conducts researches in the field of public health.

(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. Sumi also teaches medical students.

1) Undergraduate student education

In the 1st year, a lectures was given on Advanced Laboratory Sciences. Second-year students have the fundamentals of clinical medicine are taught in the Clinical Medicine 1 lecture. In the second semester of the second year and the first semester of the third year, lectures and practical training in Clinical Physiological Laboratory Science 1 cover the basics of clinical physiological testing, including electroencephalography, pulmonary function tests, electrocardiography, and ultrasonic examination, as well as the theory and practice of basic clinical skills such as collecting specimens and intravenous catheterization, which are newly required of medical technologists in task shifts. In the second semester of the second year, students learn more advanced physiological function tests such as neurological examination, respiratory examination, cardiovascular system tests, various ultrasonography, image analysis, thermography, balance function tests, and fundus examination, as well as clinical examination techniques such as vital signs, and emergency care. In the second half of the third and fourth years, students conduct their graduation research. In the second half of the fourth year, students undergo on-site training. During the on-site training, they learn practical pulmonary function tests including arterial blood gas analysis interpretation, electroencephalography, and evoked potential testing.

Sumi also provides medical education to medical students and residents. He teaches MIC (Medical Introductory Course) lecture to first-year medical students, respiratory physiology to second-year students, chest imaging to third-year students, bronchial anatomy for chest X-ray diagnosis to fourth-year students, and CC (Clinical Clerkship) including lecture to small group medical fifth-year students about abnormal findings of respiratory disease. Evening Seminar lectures are given to 6th year students and residents. Furthermore, he participates in AI education for all students. In the "AI Strategy 2019," the Ministry of Education, Culture, Sports, Science and Technology (MEXT) set the target year of 2025 as 1) all university students, regardless of their background, should acquire elementary level competency and 2) university students should acquire advanced competency in their own specialized fields. The Tokyo Medical and Dental university aimed to develop a model curriculum and teaching tools for mathematics, Data Science, and Artificial Intelligence (AI) education to all medical and dental schools in Japan. In the Tokyo Medical and Dental university, we have newly established "Introduction to AI and Big Data with Medicine" starting in FY2021 as a university-wide common course. From FY2023 "Applied AI and Big Data with Medicine" was prepared for all medical and dental students as the required courses. In addition, "AI Practical Exercise" was offered as an elective course.

2) Graduate education

In the Master's course, we are in charge of "Medical Technology II", "Basic Human Pathology for Graduate Students", "Seminar of Clinical information Applied Sciences", "Practice of Clinical information Applied Sciences", "Clinical information Applied Sciences Analysis Research for Thesis", "Seminar of Respiratory and Nervous System Science Analysis", "Practice of Respiratory and Nervous System Science", and "Respiratory and Nervous System Science Analysis Research for Thesis". 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. "Basic Human Pathology for Graduate Students" is the course to study diseases for university graduates who did not specialize in medicine. In each lecture of "Clinical information Applied Sciences" and "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", "Clinical information Applied Sciences", and "Clinical information Applied Sciences Lab". In the "Clinical Reasoning", we aim to cultivate the clinical laboratory technologists who can understand pathological conditions from examination data. In the "Clinical information Applied Sciences", we aim to teach the theory and techniques to research. In particular, students learn the cutting edge medical knowledge in the research area, the methodology to analyze.

(4) Lectures & Courses

What is important in education is to motivate students to learn. Especially in the lower grades of undergraduate studies, many students do not understand how basic learning is useful, and are not motivated to learn, despite its importance. For this reason, we are trying to increase the amount of practical training and early exposure so that students can understand how it is needed in clinical settings. They are thirsty for learning and aim for education like water seeping into dry sand.

In particular, as the physiological function testing is a clinical front line that is conducted in direct contact with patients, we educate from the standpoint of clinical medicine. The goal is that students learn theories and techniques of clinical physiological examinations in nerves, respiration, cardiovascular, digestive organs, and diagnostic imaging, and be able to apply them to researches. Physiological function testing involves not only device operation, safety measures, recording of biological phenomena, data organization / analysis techniques and knowledge, but also testing directly in contact with humans. Therefore, 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 for patient. 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 grade medical students, at PCC (Preparation for Clinical Clerkship) in respiratory internal medicine for 4th year undergraduate medical students, at Respiratory Internal medicine for 3rd year undergraduate medical students, at Respiratory physiology for 2nd year undergraduate medical students, and at MIC (Medical Introductory Course) for 1st year undergraduate medical students.

The neurologist, Dr. Akaza, is familiar with peripheral neuropathy in addition to neurological diseases in general, and plays a central role in performing peripheral nerve tests and evaluating results in medical hospitals.

Dr. Kawahara is conducting various surveys to collect public health research data.

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. Funaita C, Furuie W, Koike F, Oyama S, Endo J, Otani Y, Ichikawa Y, Ito M, Nakamura Y, Komatuzaki K, Hirata A, Miyazaki Y, Sumi Y. Pattern recognition of forced oscillation technique measurement results using deep learning can identify asthmatic patients more accurately than setting reference ranges. *Scientific reports*. 2023.12; 13(1); 21608
2. Sato S, Akaza M(co-first author), Sasaki T, Tanaka Y, Hashimoto J, Watanabe T, Miyano Y, Kim S, Kaminaka S, Sekihara K, Adachi Y, Kawabata S.. Evaluation of electrical activity at the carpal tunnel area in response to median nerve elbow stimulation using magnetoneurography *Clinical Neurophysiology*. 2023.12; 156; 89-97

3. Tani Y*, Matsuyama Y, Yamaoka Y, Matsukura H, Kawahara T, Fujiwara T. Change of human flourishing during the COVID-19 pandemic in Japan: Results from population-based U-CORONA study. *SSM Popul Health*. 2023.09; 23; 101430
4. Kanda K, Nishimura H, Koiso T, Takemoto K, Nakagoe K, Yamada T, Takahashi M, Hanafusa M, Kawahara T, Yanagida Y, Kuramochi J, Fujiwara T. Applying negative ions and an electric field to countermeasure droplets/aerosol transmission without hindering communication. *Scientific reports*. 2023.08; 13(1); 13965
5. Kawahara T, Doi S, Isumi A, Ochi M, Fujiwara T*. Interventions to change parental parenting behaviour to reduce unintentional childhood injury: a randomised controlled trial. *Inj Prev*. 2023.04; 29(2); 126-133
6. 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. *J Med Virol*. 2023.01; 95(1); e28168
7. Isamu Ozaki, Miho Akaza, Taishi Watanabe, Yuki Miyano, Yoshiaki Adachi, Shigenori Kawabata. Detailed magnetoelectric analysis of a nerve impulse propagation along the brachial plexus. *Clin Neurophysiol*. 2023.01; 145; 129-138
8. Kajihara Akiko, Morita Takayoshi, Kato Yasuhiro, Konaka Hachiro, Murakami Teruaki, Yamaguchi Yuta, Koyama Shohei, Takamatsu Hyota, Nishide Masayuki, Maeda Yuichi, Watanabe Akane, Nishida Sumiyuki, Hirano Toru, Shima Yoshihito, Narazaki Masashi, Kumanogoh Atsushi. The proliferative activity levels of each immune cell population evaluated by mass cytometry are linked to the clinical phenotypes of systemic lupus erythematosus(タイトル和訳中) *International Immunology*. 2023.01; 35(1); 27-41
9. Takada Kayoko, Yamamoto Isamu, Sasano Tetsuo, Sumi Yuki. Single nucleotide polymorphisms in paraoxonase 1 and adiponectin are associated with atherosclerotic effects in young healthy subjects(タイトル和訳中) *Journal of Medical and Dental Sciences*. 2023; 70; 37-47

Department of Clinical and Diagnostic Laboratory Science

Professor

Sei Kakinuma, M.D., Ph.D.

Associate Professor

Yu Matsuzawa, 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.

(in collaboration with Department of Gastroenterology and Hepatology, Medical and Dental Science Track)

Graduate Students, Master Program.

Rion Kamimae, Shusuke Sanada(Apr. 2023-), Kyoko Chino(Apr. 2023-).

Undergraduate Students.

4th grade, Minori Kurata, Minori Sato, Hoshie Hirayama, Kaho Yamada, Ayaka Suga.

3rd grade, Moeka Ikoma, Kanau Oshima, Ryutaro Kobayashi, Nanako Seki, Miku Takizawa, Moe Toshioka.

(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 disease, 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 diagnostic strategy established upon basic research are required.

Our department is founded in 2020 under pandemic COVID-19 infection, which is standing by such principles. Our research projects focus on hepatobiliary diseases (Dr. Kakinuma), intestinal diseases (Dr. Matsuzawa), and cardiovascular diseases (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 pathophysiology and medical technology in such diseases.

(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. Matsuzawa aims to elucidate the pathophysiology of inflammatory bowel diseases including Crohn's disease by focusing on the molecular pathogenesis of Crohn's disease responsible genes and other factors, and to develop therapeutic target molecules. Dr. Matsuzawa tries to elucidate the molecular mechanisms regulating intestinal immunity and cell death of intestinal cells through the interaction between immune cells and epithelial cells, using molecular and cell biological approaches, which are partly supported by AMED-PRIME project.

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, intestinal, and cardiovascular diseases
- (3) Development of hepatobiliary and intestinal disease models using organoid culture systems
- (4) Molecular mechanisms regulating homeostasis of stem/progenitor cells in gastrointestinal, hepatobiliary, and pancreatic tissues
- (5) Research on molecular mechanisms regulating liver regeneration and hepatic fibrosis
- (6) Research on molecular pathogenesis in inflammatory bowel disease focused on Paneth cells
- (7) Analysis of the molecular mechanism regulating cell death in gastrointestinal cells
- (8) Analysis on cell communication and signaling in the process of myocardial remodeling.
- (9) Development of a novel treatment for cardiac/limb ischemia using biocompatible and bioabsorbable materials
- (10) Development of low-/non-invasive health monitoring devices

(3) Education

Undergraduate students.

We are teaching the courses of Clinical and Physiological Laboratory, Clinical Pathophysiology, and Medical Genetics/Human Genome Science for undergraduate students of medical technologists in School of Medicine, TMDU. We also teach about basic techniques and scientific thinking necessary to progress 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, intestinal, and 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 and Physiological Laboratory Science (I)

Clinical Medicine (II)
 # Advanced physiological function
 # Analysis of Electrocardiogram
 # Medical Genetics and Human Genome Science

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 Medicine in graduate course. We also educate residents and medical technologists in Medical Hospital of TMDU.

Goals for education in scientific research

- #1. Students should master the strategy of research for molecular and cellular biology to reveal the pathophysiology of Hepato-Biliary, Intestinal, and Cardiovascular diseases.
- #2. Students should master the theory and techniques about physiological laboratory and diagnostic imaging in the field of Hepato-Biliary, Intestinal, and Cardiovascular diseases.
- #3. Students should learn about the research strategy to develop a novel diagnostic and therapeutic strategies.

(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 eradication 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 (Councilor), the Japanese Society of Hepatology (Councilor), and the Japanese Society for the Research of Hepatic cells.

Dr. Matsuzawa contributes to the academic meetings held by the Japanese Society of Immunology and the Japanese Society of Clinical Immunology, and cooperates in the management of these scientific meetings and journals.

Dr. Yamaguchi contributes to the academic meetings held by the American Heart Association and the Japanese Circulation Society, and cooperates in the management of these scientific meetings and journals.

(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 studies 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]

1. Yamaguchi J, Takigawa M, Goya M, Yamamoto T, Ikenouchi T, Iwakawa H, Negishi M, Goto K, Shigeta T, Nishimura T, Takamiya T, Tao S, Miyazaki S, Sasano T. Safety verification of a novel irrigation catheter with flexible tip of laser-cut kerfs and contact force sensor. *Pacing and clinical electrophysiology : PACE*. 2023.12; 46(12); 1536-1545
2. Shun Kaneko, Yasuhiro Asahina, Miyako Murakawa, Shunsuke Ueyama, Chiaki Maeyashiki, Hideki Watanabe, Akiko Kusano-Kitazume, Ayako Sato, Kozue Uchidate, Takehito Asakawa, Sho Watanabe, Yasuhiro Iizuka, Isamu Shibata, Shinya Oooka, Yuko Karakama, Takashi Fujii, Taro Watabe, Keiichi Akahoshi, Minoru Tanabe, Kento Inada, Tomohiro Mochida, Keiya Watakabe, Taro Shimizu, Jun Tsuchiya, Masato Miyoshi, Fukiko Kitahata-Kawai, Sayuri Nitta, Mina Nakagawa, Sei Kakinuma, Ryuichi Okamoto, . Prognostic Significance of C-Reactive Protein in Unresectable Hepatocellular Carcinoma treated with Atezolizumab and Bevacizumab. *Hepatol Res*. 2023.12; Online ahead of print.;
3. Iwakawa H, Takigawa M, Yamaguchi J, Martin CA, Goya M, Yamamoto T, Amemiya M, Ikenouchi T, Negishi M, Kawamura I, Goto K, Shigeta T, Nishimura T, Takamiya T, Tao S, Miyazaki S, Watanabe H, Sasano T. Superiority of the Combination of Input and Output Parameters to the Single Parameter for Lesion Size Estimation. *Circulation journal : official journal of the Japanese Circulation Society*. 2023.11; 87(12); 1757-1764
4. Ikenouchi T, Takigawa M, Goya M, Yamaguchi J, Martin CA, Yamamoto T, Negishi M, Kawamura I, Goto K, Shigeta T, Nishimura T, Takamiya T, Tao S, Miyazaki S, Sasano T. The effect of half-normal saline irrigation on lesion characteristics in temperature-flow-controlled ablation. *Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing*. 2023.11;
5. Takigawa M, Yamamoto T, Amemiya M, Martin CA, Ikenouchi T, Yamaguchi J, Negishi M, Goto K, Shigeta T, Nishimura T, Tao S, Miyazaki S, Goya M, Sasano T. Impact of baseline pool impedance on lesion metrics and steam pops in catheter ablation. *Journal of cardiovascular electrophysiology*. 2023.08; 34(8); 1671-1680
6. Mina Nakagawa, Yasuhiro Asahina, Sei Kakinuma, Ryuichi Okamoto. Impact of eradication of hepatitis C virus on liver-related and -unrelated diseases: morbidity and mortality of chronic hepatitis C after SVR. *J Gastroenterol*. 2023.04; 58(4); 299-310
7. Mina Nakagawa, Yasuhiro Asahina, Sei Kakinuma, Ryuichi Okamoto. Correction: Impact of eradication of hepatitis C virus on liver-related and -unrelated diseases: morbidity and mortality of chronic hepatitis C after SVR. *J Gastroenterol*. 2023.04; 58(4); 311-312
8. Ikenouchi T, Takigawa M, Goya M, Martin CA, Yamamoto T, Yamaguchi J, Goto K, Shigeta T, Nishimura T, Tao S, Miyazaki S, Sasano T. Comparison of lesion characteristics using temperature-flow-controlled versus conventional power-controlled ablation with fixed ablation index. *Journal of cardiovascular electrophysiology*. 2023.03; 34(4); 908-917
9. Yamaguchi J, Takigawa M, Goya M, Martin CA, Yamamoto T, Ikenouchi T, Shigeta T, Nishimura T, Tao S, Miyazaki S, Sasano T. Comparison of Three Different Approaches to Very High-power Short-duration Ablation using the QDOT-MICRO Catheter. *Journal of cardiovascular electrophysiology*. 2023.02; 34(4); 888-897
10. Shun Kaneko, Yasuhiro Asahina, Mina Nakagawa, Miyako Murakawa, Yasunari Miyazaki, Takahiro Asakage, Shohei Fukuda, Takeshi Namiki, Yoshito Kano, Masashi Nagata, Jun Tsuchiya, Masato Miyoshi, Fukiko Kitahata-Kawai, Sayuri Nitta, Yasuhiro Itsui, Sei Kakinuma, Ryuichi Okamoto. Factors associated with liver injury and prognosis in advanced cancer patients treated with immune checkpoint inhibitors. *Hepatol Res*. 2023.01;

[Conference Activities & Talks]

1. Mina Nakagawa, Miyako Murakawa, Masato Miyoshi, Shun Kaneko, Fukiko Kawai-Kitahata, Sayuri Nitta, Sei Kakinuma, Yasuhiro Asahina, Ryuichi Okamoto. Factors associated with HCC development and patients' survival in patients with an SVR. The 3rd JSH International Liver Conference 2023.09.07

2. Sei Kakinuma, Keiya Watakabe, Masato Miyoshi, Mina Nakagawa, Yasuhiro Asahina. Functional analysis of TNFAIP3 in murine hepatic stellate cells. The 3rd JSH International Liver Conference 2023.09.07
3. Junji Yamaguchi, Masateru Takigawa, Tasuku Yamamoto, Takashi Ikenouchi, Kentaro Goto, Takatoshi Shigeta, Takuro Nishimura, Susumu Tao, Shinsuke Miyazaki, Masahiko Goya, and Tetsuo Sasano. Impact of the Tip Design on the Efficacy and Safety of RF Application. The 87th Annual Scientific Meeting of the Japanese Circulation Society (JCS2023) 2023.03.11
4. Junji Yamaguchi, Masateru Takigawa, Tasuku Yamamoto, Takashi Ikenouchi, Kentaro Goto, Takatoshi Shigeta, Takuro Nishimura, Susumu Tao, Shinsuke Miyazaki, Masahiko Goya, and Tetsuo Sasano. Lesion Characteristics of Steam-pops in Very High-power and Short-duration Ablation with QDOT-MICRO Catheter. The 87th Annual Scientific Meeting of the Japanese Circulation Society (JCS2023) 2023.03.10

Clinical Bioanalysis and Molecular Biology

Professor:

- 2023.1-12 : Ryunosuke Ohkawa

Associate Professor:

- 2023.4-12: Nobuharu Suzuki

Assistant Professor:

- 2023.1-3 : Takahiro Kameda
- 2023.5-12 : Akira Yoshimoto

Contract Lecturer

- 2023.4-12 : Yuna Horiuchi
- 2023.4-12 : Susana DE VEGA
- 2023.4-12 : Shunsuke Yaguchi
- 2023.4-12 : Chikako Hayashi
- 2023.5-12 : Takahiro Kameda

Graduate Students:

(Master students)

- 2023.1-3 : Mei Ogino, Rina Kawaguchi, Marino Shibuya, Motoki Nakamura, Takako Yamada, Wakana Okabayashi, Riho Shimizu, Sun Chengman, Motoki Nakamura, Yuna Hakii, Tsunehiro Miyakoshi
- 2023.4-12 : Rina Kawaguchi, Mei Ogino, Wakana Okabayashi, Riho Shimizu, Sun Chengman, Motoki Nakamura, Yuna Hakii, Tsunehiro Miyakoshi, Hinako Saito, Mizuki Fukuhara, Yuwa Someya, Taichi Hashimoto, Reina Ohno, Binri Sasaki, Mio Fujisato

(Doctoral Students)

Adult Graduate Students:

- 2023.1-12 : Azusa Yamazaki, Masamichi Mikame, Takuya Shimura

Under Graduate Students:

(Senior)

- 2023.1-3 : Sayaka Okuma, Yuto Kikuchi, Honoka Sedutu, Yuwa Someya, Taichi Hashimoto
- 2023.4-12: Hanae Akiyama, Nao Igarashi, Mizuki Tanaka, Kotoko Matayoshi, Chisato Banno, Nanako Yamada

(Junior)

- 2023.1-3 : Hanae Akiyama, Nao Igarashi, Mizuki Tanaka, Kotoko Matayoshi
- 2023.11-12 : Haruka Akagi, Saki Izumi, Misaki Tanaka, Yurina Togashi, Tomoka Aoki, Kanoko Mitsunari

(1) Outline

Clinical Bioanalysis and Molecular Biology (2023.4~)

Ohkawa Group (former Analytical Laboratory Chemistry (~2023.3)): Prof. Ohkawa, Assistant Prof. Yoshimoto (from 1st, May), 13 graduate students, and 4 undergraduate students had been conducting research activities in Ohkawa's group. The central mission 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.

In Suzuki's group, Assoc. Prof. Suzuki, 5 graduate students, and 2 undergraduate students were the members and performed various activities in research and education. Regarding our research, our main goal was the elucidation of the molecular mechanism of myelination in the central nervous system. In 2023 particularly, we proceeded 3 main projects, "Elucidation of the molecular mechanism of myelination in the central nervous system", "Development of new animal models of neurological and mental disorders using genetically engineered mice", and "Application of extracellular matrix molecules for the creation of novel cell culture substrates and biomaterials". In terms of education, we taught graduate and undergraduate students at many lectures and laboratory classes of basic and advanced biochemistry/molecular biology. In addition, Suzuki worked as a member of various committees and contributed to their activities.

(2) Research

Ohkawa Group: 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 the above functions. We are further studying the red blood cell-related lipids metabolism.

In 2023, we focused on the truncation of apolipoprotein A-I (apoA-I), main protein of HDL, by sequential modification with myeloperoxidase and chymase, which are released from activated macrophage and mast cells, respectively, and found that the fragment site of the one fragment was C-terminal of Tyr¹⁰⁰ in apoA-I, cross-validated by three different mass spectrometry. This identification of the apoA-I fragment might lead to a new development of biomarker for atherosclerosis (Lai et al. *Biochimie*). We further improved the assay for evaluating cholesterol efflux capacity previously developed in our laboratory (Miyakoshi et al, *Bioscience Reports*, and Mutsuda et al, *Bioscience Reports*).

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
- Molecular mechanism of red blood cell-related lipids metabolism

Suzuki Group: 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 group, 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 2023, we demonstrated the molecular mechanism of axon maintenance after the inhibition of myelination in teneurin-4 deficient mice and reported that at The Japanese Society for Neurochemistry (JSN), The Molecular Biology Society of Japan (MBSJ), and The Japanese Society for myelin study. Further, we focused on the mutations in the teneurin-4 gene and examined the effect on the cell adhesion activity. We also 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 extracellular matrix proteins, fibulin-7 and laminins. We applied for the many research grants and got a couple of grants from public associations and private foundations.

Research Focus

- Elucidation of the molecular mechanism of myelination in the central nervous system

- Development of new animal models of neurological and mental disorders using genetically engineered mice
- Application of extracellular matrix molecules for the creation of novel cell culture substrates and biomaterials

(3) Lectures & Courses

Undergraduate education: (Ohkawa) Main topic is Analytical Laboratory Chemistry which includes Urinalysis & Body Fluid Tests and Clinical Chemistry. In addition, Associate Professor Masayuki Hara from General Isotope Research Division helps to educate radioisotope. We aim to educate student to become a leader of biomedical laboratory scientist in hospital or company. Our final goal is that student develop their creativities to think, solve a problem and improve by themselves.

(Suzuki) For the undergraduate education, Suzuki was a responsible organizer for “Biochemistry” and “Biochemistry, Lecture” for the students of the nursing course and medical technology course, and “Medical Genetics and Human Genome Science, Lecture”, “Biochemistry, Laboratory”, and “Medical Genetics, Laboratory” for the students of the medical technology course. Through these lectures, we educated the students to let them understand fundamental mechanism of the biological phenomena at the molecular levels. In addition, we taught how to make hypotheses, expertized techniques of gene engineering and primary cultures from experimental animals, scientific analyses of the results, and scientific discussions via our research activities of the molecular biology of the central nervous system myelination.

Graduate education: (Ohkawa) 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.

(Suzuki) During the last century, molecular biology has been markedly developed and has contributed to the elucidation of numerous biological phenomena and to clinical applications. The progress has not been stopped and various novel phenomena have been demonstrated. We tried to catch them up and acquire them and to educate students to become leaders for the life scientists at the next generation. Through our research activity of molecular biology of myelination in the central nervous system, we taught how to make hypotheses, expertized experiments of gene recombination techniques, genetically engineered animals, and primary cultures from the animals, and scientific analyses and discussions via our research activities of the molecular biology of the central nervous system myelination. In our laboratory, we taught 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. Moreover, we made efforts for students to have high motivation with their research and study and to enjoy new findings.

(4) Publications

[Original Articles]

1. Masamichi Mikame, Nelson Hirokazu Tsuno, Yoshino Miura, Hideaki Kitazaki, Daisuke Uchimura, Toru Miyazaki, Toru Miyagi, Takayuki Onodera, Wataru Ohashi, Takahiro Kameda, Ryunosuke Ohkawa, Shuichi Kino, Kazuo Muroi. Decreased rate of blood donors with high ABO antibody titers in Japan and the underlying factors: Comparisons between 2010 and 2021. *Transfus Apher Sci.* 2023.12; 62(6); 103812
2. Azusa Yamazaki, Yoko Nukui, Takahiro Kameda, Ryoichi Saito, Yuki Koda, Naoya Ichimura, Shuji Tohda, Ryunosuke Ohkawa. Variation in presepsin and thrombomodulin levels for predicting COVID-19 mortality. *Sci Rep.* 2023.12; 13(1); 21493
3. Masamichi Mikame, Nelson Hirokazu Tsuno, Yoshino Miura, Hideaki Kitazaki, Daisuke Uchimura, Toru Miyagi, Toru Miyazaki, Takayuki Onodera, Wataru Ohashi, Takahiro Kameda, Ryunosuke Ohkawa, Shuichi Kino, Kazuo Muroi. Anti-A and anti-B titers, age, gender, biochemical parameters, and body mass index in Japanese blood donors. *Immunohematology.* 2023.12; 39(4); 155-165

4. Shao-Jui Lai, Takahiro Kameda, Maasa Morita, Yuka Yamagata, Kaoruko Nishizaka, Yuna Horiuchi, Yukihiro Kobayashi, Yoko Usami, Jun-Jen Liu, Takeshi Kasama, Minoru Tozuka, Ryunosuke Ohkawa. Characterization of novel truncated apolipoprotein A-I in human high-density lipoprotein generated by sequential treatment with myeloperoxidase and chymase. *Biochimie*. 2023.09; 218; 34-45
5. Tsunehiro Miyakoshi, Yume Mutsuda, Yuna Horiuchi, Takahiro Kameda, Minoru Tozuka, Ryunosuke Ohkawa. Improvement in bilirubin influence on cholesterol efflux capacity evaluation using the immobilized liposome-bound gel beads method. *Biosci Rep*. 2023.06; 43(6);
6. Yume Mutsuda, Tsunehiro Miyakoshi, Yuna Horiuchi, Takahiro Kameda, Minoru Tozuka, Ryunosuke Ohkawa. Development and validation of novel automatable assay for cholesterol efflux capacity. *Biosci Rep*. 2023.02; 43(2);

[Conference Activities & Talks]

1. Hinako Saito, Riko Takahashi, Mio Fujisato, Yukina Hosoda, Chikako Hayashi, Ryunosuke Ohkawa, and Nobuharu Suzuki. The molecular mechanism of axon maintenance after myelination defect. 第46回日本分子生物学会年会 2023.12.08
2. Chisato Banno, Binri Sasaki, Momona Yamada, Keisuke Hamada, Yuji Yamada, Yamato Kikkawa, Motoyoshi Nomizu, Nobuharu Suzuki. Identification of active peptides from the extracellular matrix protein laminin-411 that promotes the formation of myelin membranes in oligodendrocytes. 第46回日本分子生物学会年会 2023.12.08
3. Reina Ono, Riko Takahashi, Hinako Saito, Mio Fujisato and Nobuharu Suzuki. The RNA-Seq analysis in reactive gliosis by the murine genetical dysmyelination. 第46回日本分子生物学会年会 2023.12.07
4. Binri Sasaki, Chikako Hayashi, and Nobuharu Suzuki. Cell adhesion protein teneurin-4 regulates actin polymerization in oligodendrocytes for CNS myelination. 第46回日本分子生物学会年会 2023.12.07
5. Mio Fujisato, Hinako Saito, Riko Takahashi, Reina Ohno and Nobuharu Suzuki. The expression and function of monocarboxylate transporters for the maintenance of unmyelinated small axons in the CNS. 第46回日本分子生物学会年会 2023.12.07
6. Mizuki Fukuhara, Yuki Munakata, Reina Ohno, Nanako Yamada, Momona Yamada, Chikako Hayashi, and Nobuharu Suzuki. Evaluation of cell adhesion activity of mutant teneurin-4 and its effect on the diseases. 第46回日本分子生物学会年会 2023.12.06
7. Miyakoshi T., Horiuchi Y., Araki M., Yonetsu T., Watanabe M., Nakamura M., Kameda T., Yoshimoto A., Ichimura N., Tohda S., Tozuka M., Sasano T., Ohkawa R. Association between CEC measured by immobilized liposome-bound gel beads method and the size of lipid-rich coronary artery plaque. Scientific Session of the American Heart Association 2023.11.09
8. Horiuchi Y., Kameda T., Ogura M., Miida T., Tozuka M., Ohkawa R. Search for standardizable references in cell-free cholesterol efflux assay using immobilized liposome-bound gel beads. the 12th International Congress on Lipid & Atherosclerosis with Asia-Australia Vascular Biology Meeting (ICoLA 2023 in conjunction with AAVBM) 2023.09.15 Seoul
9. Ohkawa R.. Structural and Functional Analysis of Modified HDL. Lunchtime Seminar at Chulalongkorn University 2023.08.18 Bangkok
10. Miyakoshi T., Mutsuda Y., Horiuchi Y., Kameda T., Tozuka M., Ohkawa R. Application of bilirubin oxidase for improvement of false positive error caused by bilirubin on cholesterol efflux capacity assay by immobilize liposome-bound gel beads method. American Association for Clinical Chemistry (AACC) 2023 AACC Annual Scientific Meeting & Clinical Lab Expo 2023.07.24 Anaheim
11. Yamazaki A., Nukui Y., Kameda T., Saito R., Koda Y., Ichimura N., Tohda S., Ohkawa R.. Usefulness of presepsin and thrombomodulin measurements for predicting COVID-19 mortality. American Association for Clinical Chemistry (AACC) 2023 AACC Annual Scientific Meeting & Clinical Lab Expo 2023.07.24 Anaheim
12. Hinako Saito, Riko Takahashi, Mio Fujisato, Yukina Hosoda, Chikako Hayashi, and Nobuharu Suzuki. The molecular mechanism of axonal survival in the murine dysmyelination. 第66回日本神経化学会大会 2023.07.08

13. Mizuki Fukuhara, Chikako Hayashi, Yuki Munakata, Reina Ohno, Nanako Yamada, Momona Yamada, and Nobuharu Suzuki. The molecular mechanism of CNS myelination through the cell adhesion of teneurin-4 and its effect on the diseases. 第66回日本神経化学学会大会 2023.07.08
14. Mikame M., Tsuno N.H., Miura Y., Kitazaki H., Uchimura D., Miyagi T., Miyazaki T., Onodera T., Ohashi W., Kameda T., Ohkawa R., Kino S., Muroi K. Correlation of ABO antibody titers with physiological/biochemical parameters in Japanese blood donors, and comparison between donors of 2010 and 2021. 33rd Regional Congress of the ISBT 2023.06.17 Gothenburg
15. Kawaguchi R., Kameda T., Yoshimoto A., and Ohkawa R. Usefulness of Apolipoprotein B-Depleted Serum in Paraoxonase 1 Assessment. Worldlab EuroMedLab Roma 2023 2023.05.21 Roma
16. Ohkawa R.. Japanese Medical Technology Education - Connection Potential for Cooperation Between Japan and Vietnam Schools/Association -. The Workshop On the Diamond Jubilee Celebration of the 60 years of Da Nang University of Medical Technology and Pharmacy (DUMTP) 2023.04.14 Da Nang City (Vietnam)
1. Nobuharu Suzuki, Momona Yamada, Binri Sasaki, Susana de Vega. The Functional Analysis of ECM Proteins in Oligodendrocyte Development and Differentiation. The 7th Annual Meeting of the Japan Myelin Society 2023.02.11

[Social Contribution]

1. Nobuharu Suzuki, Frontiers in Cell and Developmental Biology:Topic Editor, 2021.09.01 - Now
2. Nobuharu Suzuki, Cells:Topical Advisory Panel, 2021.09.01 - Now
3. Ryunosuke Ohkawa,Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine (APFCB),Communication and Publication Committee member, 2023.02.10 - Now
4. Nobuharu Suzuki, Frontiers in Cell and Developmental Biology:Review Editor, 2023.09.01 - Now
5. Nobuharu Suzuki, Neurology International:Editorial Board, 2023.09.01 - Now

Department of Molecular Microbiology and Immunology

Professor: Ryoichi Saito

Associate Professor: Yukie Tanaka

Assistant Professor: Yusuke Ota

Graduate Student (doctor's course): Samiratu Mahazu, Frederick Ofosu Appiah, Mika Nagata, Shu Hagiwara, Runa Furuya

Graduate Student (master's course): Taira Kawamura, Miho Matsuba, Yikeshan Yalikun, Tomoko Oshiro, Ayaha Suzuki, Nanako Minami

(1) Outline

Our department is engaged in both lecture and practical course for medical microbiology and immunology. 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.

In the immunology section, students learn basic immunology to understand various aspects of immune response in the human body, and through this, acquire the ability to properly perform tests related to immune diseases, including infectious diseases, and to accurately evaluate the results. Regarding our research, we are interested in immune mechanisms in hematopoietic stem cell transplantation and the development of immunotherapy for refractory viral infections.

(2) Research

Research Interests involved in Molecular Microbiology:

1. Evolution and diversity of multidrug-resistant bacteria
2. Regulation system of virulence in pathogenic bacteria
3. Environmental microbiome dynamics and interactions for AMR transmission
4. Development of molecular biological and bacteriological methods for rapid identification and typing of pathogenic bacteria

Research Interests involved in immunology:

1. Multi-virus-specific T-cell therapy for patients with opportunistic infections after transplantation.
2. Analysis of HTLV-1-specific cytotoxic stem-cell memory like T-cells.
3. Research on the mechanism of hematopoietic stem cell mobilization using CXCR4 antagonists
4. Development of novel therapies for hematopoietic tumors.

(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, antimicrobial susceptibility testing, and immunological testing which are performed in the clinical laboratory at medical facilities.

(4) Publications

[Original Articles]

1. Azusa Yamazaki, Yoko Nukui, Takahiro Kameda, Ryoichi Saito, Yuki Koda, Naoya Ichimura, Shuji Tohda, Ryunosuke Ohkawa. Variation in presepsin and thrombomodulin levels for predicting COVID-19 mortality. *Sci Rep.* 2023.12; 13(1); 21493
2. Akira Nishimura, Kazuaki Yokoyama, Takuya Naruto, Chika Yamagishi, Toshihiko Imamura, Hiroto Nakazono, Shunsuke Kimura, Mieko Ito, Maiko Sagisaka, Yukie Tanaka, Jinhua Piao, Yui Namikawa, Masakatsu Yanagimachi, Takeshi Isoda, Akinori Kanai, Hirotaka Matsui, Tomoya Isobe, Aiko Sato-Otsubo, Naoko Higuchi, Akiko Takada, Haruna Okuno, Shoji Saito, Shuhei Karakawa, Shogo Kobayashi, Daisuke Hasegawa, Hiroyuki Fujisaki, Daiichiro Hasegawa, Kazutoshi Koike, Takashi Koike, Shinya Rai, Katsutsugu Umeda, Hideki Sano, Yujin Sekinaka, Atsushi Ogawa, Akitoshi Kinoshita, Norio Shiba, Mizuka Miki, Fumihiko Kimura, Hideki Nakayama, Yozo Nakazawa, Takashi Taga, Tomohiko Taki, Souichi Adachi, Atsushi Manabe, Katsuyoshi Koh, Yasushi Ishida, Junko Takita, Fumihiko Ishikawa, Hiroaki Goto, Tomohiro Morio, Shuki Mizutani, Arinobu Tojo, Masatoshi Takagi. Myeloid/natural killer (NK) cell precursor acute leukemia as a distinct leukemia type. *Sci Adv.* 2023.12; 9(50); ead4407
3. Hideyuki Takahashi, Masatomo Morita, Hajime Kamiya, Munehisa Fukusumi, Mitsuru Yasuda, Masatomi Sunagawa, Haruna Nakamura-Miwa, Yuki Ohama, Ken Shimuta, Makoto Ohnishi, Ryoichi Saito, Yukihiro Akeda. Emergence of ciprofloxacin- and penicillin-resistant *Neisseria meningitidis* isolates in Japan between 2003 and 2020 and its genetic features. *Antimicrob Agents Chemother.* 2023.11; 67(11); e0074423
4. Yusuke Ota, Isaac Prah, Samiratu Mahazu, Yoshiaki Gu, Yoko Nukui, Ryuji Koike, Ryoichi Saito. Novel insights into genetic characteristics of bla_{GES}-encoding plasmids from hospital sewage *Frontiers in Microbiology.* 2023.08; 14; 1209195
5. Yusuke Ota, Kazuki Furuhashi, Nachi Hirai, Yuki Nagao, Jinko Ishikawa, Osanori Nagura, Keita Yamashita, Masato Maekawa. Utility of the MBT STAR-Cepha kit in detecting extended-spectrum β -lactamase producers in clinical urine samples and positive blood cultures using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry *Journal of Microbiological Methods.* 2023.06; 211; 106756
6. Yusuke Ota, Reina Okada, Hideyuki Takahashi, Ryoichi Saito. A mismatch amplification mutation assay for specific detection of ciprofloxacin-resistant *Neisseria meningitidis* *Journal of Infection and Chemotherapy.* 2023.05; 29(5); 562-564
7. Yusuke Ota, Reina Okada, Hideyuki Takahashi, Ryoichi Saito. A mismatch amplification mutation assay for specific detection of ciprofloxacin-resistant *Neisseria meningitidis*. *J Infect Chemother.* 2023.05; 29(5); 562-564
8. Takatsuki Y., Takahashi Y., Nakajima J., Iwasaki Y., Nagano K., Tani-Sassa C., Yuasa S., Kanehira S., Sonobe K., Nukui Y., Takeuchi H., Tanimoto K., Tanaka Y., Kimura A., Ichimura N., and Tohda S.. Viral load of SARS-CoV-2 Omicron BA.5 is lower than that of BA.2 despite higher infectivity of BA.5. *Immunity, Inflammation and Disease.* 2023.02; 11; e783
9. Ota Y, Prah I, Mahazu S, Gu Y, Nukui Y, Koike R, Saito R. Novel insights into genetic characteristics of bla_(GES)-encoding plasmids from hospital sewage. *Frontiers in microbiology.* 2023; 14; 1209195
10. Taira Kawamura, Isaac Prah, Samiratu Mahazu, Anthony Ablordey, Ryoichi Saito. Types A and F *Clostridium perfringens* in healthcare wastewater from Ghana. *Appl Environ Microbiol.* 2023.12; e0161923
1. Yohei Sonoya, Osamu Fukuda, Yusuke Ota, Ryoichi Saito, Yoshiyuki Sumita, Yukihiro Kaneko, Makoto Sata. A case of Infective endocarditis due to *Lactacisbacillus paracasei* successfully managed with appropriate usage of antibacterial agents guided by Blood culture Gram stain. *The Journal of the Japanese Society for Clinical Microbiology.* 2023.09; 33(4); 275-279

[Conference Activities & Talks]

1. Nishimura A, Sasaki M, Muhaimin R, Tanaka Y, Morio T, Takagi M, Isoda T.. Non-coding RNA transcription and super-enhancer activation facilitate 3D genome structure. 2023.10.04 Tokyo
2. Y Nukui, C Yamamoto, T Inaba, Y Aiso, J Nakajima, S Kanehira, K Sonobe, S Tohda, Y Ota, and R Saito. Genetic Analysis of Antimicrobial Resistant Enterobacteriaceae in Travelers and Patients Who Were Treated Overseas . AMS Microbe 2023 2023.06.15 Houston, TX
3. Y Nukui, C Yamamoto, T Inaba, Y Aiso, J Nakajima, S Kanehira, K Sonobe, S Tohda, Y Ota, R Saito. . Genetic Analysis of Antimicrobial Resistant Enterobacteriaceae in Travelers and Patients Who Were Treated Overseas. ASM microbe 2023.06.05 Houston
4. Yusuke Ota, Isaac Prah, Samiratu Mahazu, Yoshiaki Gu, Ryuji Koike, Ryoichi Saito. Molecular characterization of blaGES-encoding plasmids from hospital sewage in Japan. 33rd European Congress of Clinical Microbiology and Infectious Diseases 2023.04 Copenhagen, Denmark
5. Miho Matsuba, Yusuke Ota, Samiratu Mahazu, Isaac Prah, Hideyuki Takahashi, Ryoichi Saito. Development of a rapid and simple assay for identification and serotyping of *Neisseria meningitidis*. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04 Copenhagen, Denmark
6. Taira Kawamura, Akari Samejima, Yukino Usui, Isaac Prah, Samiratu Mahazu, Yusuke Ota, Ryoichi Saito. Loss of GdpP function leads to reduced vancomycin susceptibility in *Clostridioides difficile*. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04 Copenhagen, Denmark
7. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Masato Suzuki, Yoshihiko Hoshino, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Chromosomal mcr-3-related lipid A phosphoethanolamine transferases conferring colistin resistance in *Aeromonas* species from river water samples. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04
8. Yusuke Ota, Isaac Prah, Samiratu Mahazu, Yoshiaki Gu, Ryuji Koike, Ryoichi Saito. Molecular characterization of blaGES-encoding plasmids from hospital sewage in Japan. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04 Copenhagen, Denmark
9. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Masato Suzuki, Yoshihiko Hoshino, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Chromosomal mcr-3-related lipid A phosphoethanolamine transferases conferring colistin resistance in *Aeromonas* species from river water samples. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04 Copenhagen, Denmark
10. Taira Kawamura, Akari Samejima, Yukino Usui, Isaac Prah, Samiratu Mahazu, Yusuke Ota, Ryoichi Saito. Loss of GdpP function leads to reduced vancomycin susceptibility in *Clostridioides difficile*. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04 Copenhagen, Denmark
11. Miho Matsuba, Yusuke Ota, Samiratu Mahazu, Isaac Prah, Hideyuki Takahashi, Ryoichi Saito. Development of a rapid and simple assay for identification and serotyping of *Neisseria meningitidis*. The 33rd European Congress of Clinical Microbiology & Infectious Diseases 2023.04 Copenhagen, Denmark
12. Isaac Prah, Ayaha Suzuki, Samiratu Mahazu, Yusuke Ota, Anthony Ablordy, Ryoichi Saito. Molecular characterization of carbapenem resistant isolates from hospital sewage samples in Ghana. 第34回日本臨床微生物学会総会・学術集会 2023.02.04 横浜
13. Samiratu Mahazu, Isaac Prah, Yusuke Ota, Takaya Hayashi, Yoko Nukui, Masato Suzuki, Yoshihiko Hoshino, Yukihiro Akeda, Toshihiko Suzuki, Tomoko Ishino, Anthony Ablordey, Ryoichi Saito. Genetic analysis of carbapenemase-producing *Enterobacter cloacae* and *Klebsiella* species . 第34回日本臨床微生物学会総会・学術集会 2023.02.04 横浜
14. Yikeshan Yalikun, Isaac Prah, Samiratu Mahazu, Yusuke Ota, Ryoichi Saito. Genomic and population insight of ESBL-producing *Klebsiella pneumoniae* from Ghana. 第34回日本臨床微生物学会総会・学術集会 2023.02.03
15. Yikeshan Yalikun, Isaac Prah, Samiratu Mahazu, Yusuke Ota, Ryoichi Saito. Genomic and population insight of ESBL-producing *Klebsiella pneumoniae* from Ghana. 第34回日本臨床微生物学会総会・学術集会 2023.02.03 横浜

1. Analysis of the biological function of carbohydrate-binding proteins in a pneumococcal infection. The 96th Annual Meeting of Japanese society for bacteriology 2023.03.16 Himeji

[Awards & Honors]

1. Kayo Yamada, The Biomedical Research Award (Master's Program), Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, 2023.03

Department of Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA
Junior Associate Professor Yasuo TAKEUCHI
Specially Appointed Assistant Professor Masayuki TOI
Specially Appointed Assistant Professor Hiromi NIIMI

(1) Outline

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care. Regarding research, the effects of the functional waters to organism and clinical application of them were investigated.

(2) Research

- 1) Clinical and basic studies on Ozone ultrafine bubble water (OUFBW) :antimicrobials activity and effects to eukaryotic cells (induction of anti-oxidant 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 oral pathology and oral health promotion, and are trained to master the modality of oral health care.

(4) Lectures & Courses

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care.

(5) Clinical Services & Other Works

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

(6) Clinical Performances

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

(7) Publications

[Original Articles]

1. Yuichi Ikeda, Otofumi Chigasaki, Koji Mizutani, Yoshiyuki Sasaki, Norio Aoyama, Risako Mikami, Misa Gokyu, Makoto Umeda, Yuichi Izumi, Akira Aoki, Yasuo Takeuchi. The Potential of a Saliva Test for Screening of Alveolar Bone Resorption healthcare. 2023.06; 11(13); 1822
2. Hayashi S, Takeuchi Y, Hiratsuka K, Kitanaka Y, Toyoshima K, Nemoto T, Aung N, Hakariya M, Ikeda Y, Iwata T, Aoki A. Effects of various light-emitting diode wavelengths on periodontopathic bacteria and gingival fibroblasts: An in vitro study. Photodiagnosis and Photodynamic Therapy. 2023.10; 44; 103860
3. Hirasawa I, Odagiri H, Park G, Sanghavi R, Oshita T, Togi A, Yoshikawa K, Mizutani K, Takeuchi Y, Kobayashi H, Katagiri S, Iwata T, Aoki A. Anti-inflammatory effects of cold atmospheric plasma irradiation on the THP-1 human acute monocytic leukemia cell line. PloS one. 2023.10; 18(10); e0292267
4. Takeuchi Y, Nemoto T, Kitanaka Y, Aoki A, Izumi Y, Iwata T, Arakawa S. Antibacterial activity of lysozyme-chitosan oligosaccharide conjugates on two periodontal bacteria Oral diseases. 2023.08; 30(4); 2728-2735
5. Shiba T, Komatsu K, Watanabe T, Takeuchi Y, Nemoto T, Ohsugi Y, Katagiri S, Shimogishi M, Marukawa E, Iwata T. Peri-implantitis management by resective surgery combined with implantoplasty and Er:YAG laser irradiation, accompanied by free gingival graft: a case report. Therapeutic advances in chronic disease. 2023.06; 14; 20406223231174816
6. Masayuki Tooi, Yuhei Matsuda, Hui Zhong, Shinichi Arakawa. Association between Clinical Periodontal Features and Glycated Hemoglobin in Patients with Diabetes and Controlled Periodontitis: A Cross-Sectional Study. Healthcare (Basel). 2023.04; 11(7);
1. Shinichi Arakawa. A new functional water as a mouthwash that dental hygienists should know in this super-aging society Journal of the Japanese Society of Periodontology. 2023.04; 65(1); 26-34
2. Risako Mikami, Koji Mizutani, Norio Aoyama, Takanori Matsuura, Tomonari Suda, Kohei Takeda, Natsumi Saito, Shinichi Arakawa, Yuichi Izumi, Takanori Iwata, Jun Aida. Income-related inequalities in the association of smoking with periodontitis: a cross-sectional analysis in Tokyo Metropolitan Districts Clinical Oral Investigations. 2023.02; 27(2); 519-528

[Misc]

1. Takeuchi Y, Aoki A, Hiratsuka K, Chui C, Ichinose A, Aung N, Kitanaka Y, Hayashi S, Toyoshima K, Iwata T, Arakawa S. Application of different wavelengths of LED lights in antimicrobial photodynamic therapy for the treatment of periodontal disease. Antibiotics (Basel). 2023.11; 12(12);

[Conference Activities & Talks]

1. 遠井 政行, 近藤 真啓, 荒川 真一. 閉所ストレス負荷を受けたショウジョウバエは糖質摂食行動を促進させる. 第46回日本分子生物学会年会 2023.12.06 神戸
2. Shimizu S, Hayashi K, Takeuchi Y, Tanabe G, Churei H, Kobayashi H, Ueno T, Fueki K. Effect of Administration of Sonicated P. gingivalis on skeletal muscle injury healing using a rat model. . ECSS Paris 2023 2023.07.04 Paris

1. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Hiroshi Churei, Kenji Fueki. The effect of antigen of periodontitis to sports related muscle reaction. 88th congress of Stomatological society Japan 2023.12.02
2. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Zhu Qiushuang, Li Zequn, Gen Tanabe, Hiroshi Churei, Toshiaki Ueno. The effect of *P. gingivalis* administration to PGC-1 α and TNF α expression in skeletal muscle after endurance training in vivo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
3. Matsuda S, Sugaya T, Kato S, Nemoto E, Takeuchi Y, Yamashita K, Numabe Y, Nishida T, Ogata Y, Shin K, Nagano T, Morozumi T, Komatsu Y, Dewake N, Goto R, 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- 2nd report. The 66th Spring Meeting of the Japanese Society of Periodontology 2023.05.27

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, 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.

(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

[Original Articles]

1. Ito K, Tokura S, Takazawa I, Yoshida N, Nakanishi T, Akiyama K, Onuma Y, Adachi T, Harada H, Nojima H, Miura M, Yoshimura R, Kabasawa Y. Clinical investigation of use of Episil® oral solution in oral mucositis during radiotherapy for head and neck cancer. *Heliyon*. 2023.06; 9(6); e15869
2. Lin YC, Lin PC, Lin PC, Lin CY, Kabasawa Y, Choi YK, Huang HL. Combining augmented and virtual reality simulation training to improve geriatric oral care performance in healthcare assistants: A randomized controlled trial. *Digital health*. 2023.01; 9; 20552076231203891

[Conference Activities & Talks]

1. Kanako Noritake, Yuji Kabasawa, Yohei Hama, Ken-ichi Tonami, Arata Ebihara, Masayuki Hideshima, Sachi Umemori, Yuna Kanamori, Hirohito Miki, Daisuke Kido, Akira Nishiyama, Hiroshi Nitta.. Newly introduced training contents in the clinical training programs for dental residents at Tokyo Medical and Dental University Hospital. 2023.07.15

Department of Preventive Oral Health Care Sciences

(1) Publications

[Original Articles]

1. Hitomi Suzuki, Kumiko Sugimoto, Naoko Adachi, Natsumi Tsuchihashi, Ayako Kubota-Miyazawa, Itsuki Takazawa, Naomi Yoshida. A cross-sectional study on eating behavior of nursery school children and parents' perceptions of their children's eating problems Journal of Medical and Dental Sciences. 2023.10; 70; 49-58
2. Naoko Adachi, Kumiko Sugimoto, Kayoko Shinada. Association between tooth loss and adherence to oral maintenance in a dental clinic: A retrospective study more than 20 years. International Journal of Dental Hygiene. 2023.08; 00; 1-8
3. 西 真紀子, 安達 奈穂子, 品田 佳世子, 仲川 隆之, ドーベン・ビルクヘッド. 加工でんぷんスナック製品 (PSSP) とう蝕 ナラティブレビュー (Processed starch snack products(PSSPs) and dental caries: a narrative review) 日本歯科衛生学会雑誌. 2023.08; 18(1); 28-42
4. 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. 2023.07; 18(3); 1094-1102

[Misc]

1. NISHI Makiko, ADACHI Naoko, SHINADA Kayoko, NAKAGAWA Takayuki, BIRKHED Downen. Processed starch snack products (PSSPs) and dental caries: a narrative review. The Journal of Japan Society for Dental Hygiene. 2023.08; 18(2); 28-42
2. Kanako Toda, Koji Mizutani, Kayoko Shinada. Oral Health Instruction Improves glycaemic Control as Minimally Invasive Periodontal Therapy in Patients with Diabetes:A Systematic Review Journal of Dental Sciences. 2023.01; 11(1); 1-15

[Conference Activities & Talks]

1. Kyoko Kajitani, Atsushi Oyama, Naoko Adachi, Kayoko Shinada. A qualitative study of patients' regular dental visits and dental hygienists' involvement. 第 88 回 口腔病学会学術大会 2023.12.02
2. Ran WANG, Yui IWASAKI, Atsushi OHYAMA, Naoko ADACHI, Kayoko SHINADA. Research on oral health and dental examination behavior of foreign students in Japan. 第 88 回 口腔病学会学術大会 2023.12.02

Oral Health Sciences for Community Welfare

Professor Koichiro MATSUO
Senior Assistant Professor Rena HIDAHA
Graduate Student Misaki TANAKA
Tomoka MARUYAMA
Amika SUGITA

(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

Asian Association of Dentistry and Oral Health: Board member

International Association of Dentistry and Oral Health: Councilor, International Advisory Committee

(6) Publications

[Original Articles]

1. Suzuki H, Furuya J, Nakagawa K, Hidaka R, Nakane A, Yoshimi K, Shimizu Y, Saito K, Itsui Y, Tohara H, Minakuchi S. Factors influencing the selection of oral healthcare providers in multidisciplinary Nutrition Support Team for malnourished inpatients: A cross-sectional study. *Journal of oral rehabilitation*. 2023.08; 50(12); 1446-1455
2. Stading M, Miljkovic A, Andersson J, Matsuo K. Bolus rheology of texture adjusted food—Effect of age *Journal of Texture Studies*. 2023.07;
3. A Sakai, K Matsuo, Y Sekimoto, R Hidaka, A Yoshihara. Changes in oral health status with dental intervention during the acute to subacute stages of stroke *Gerodontology*. 2023.07;
4. R Hidaka, Y Masuda, K Ogawa, T Tanaka, M Kanazawa, K Suzuki, M Stading, K Iijima, K Matsuo. Impact of oral frailty prevention program with textured lunch gatherings on attitude and behavior towards eating habits and improving oral frailty: The Comprehensive Awareness Modication of Mouth, Chewing And Meal (CAMCAM) program *The Journal of Nutrition Health and Aging*. 2023.04; 27(5); 340-347
5. R Hidaka, K Matsuo, T Maruyama, K Kawasaki, I Tasaka, M Arai, S Sakoda, K Higuchi, E Jinno, T Yamada and S Minakuchi. Impact of COVID-19 on the Surrounding Environment of Nursing Home Residents and Attitudes towards Infection Control and Oral Health Care among Nursing Home Staff in Japan *Journal of Clinical Medicine*. 2023.03; 12(5); 1944
6. C Matsuda, T Shimizu, Y Nakayama, M Haraguchi, C Hakuta, R Hidaka, A Nishiyama, T Numayama. Clinical relevance of macroglossia to disease progression in ventilation dependent patients with advanced ALS *Neurol Sci* . 2023.01; 44(6); 2025-2031

[Misc]

1. Matsuo K, Palmer JB. Anatomy and physiology of feeding and swallowing: normal and abnormal *Clinics in Integrated Care*. 2023.02; 16; 100139

[Conference Activities & Talks]

1. Koichiro Matsuo, Kenji Suzuki, Rena Hidaka, Johanna Andersson, Mats Stading. Sound based analysis of oral processing and swallowing time in the Test of Masticating and Swallowing Solids (TOMASS) using a portable neck-worn swallowing sounds monitoring device. *ESSD* 2023.12.01 Toulouse
2. Koichiro Matsuo. Multi-disciplinary approach for postoperative dysphagia rehabilitation. *PENSA* 2023.10.20 Taipei
3. koichiro matsuo. Multidisciplinary approach to oral health care and dysphagia management. . Annual meeting of Taiwan Association of Disability and Oral Health, 2023.08.06 Taipei
4. koichiro matsuo. Perioperative oral function and hygiene management to prevent postoperative complications. *IAGG-AOR* 2023 Yokohama 2023.06.15 Yokohama

5. K Matsuo, Y Masuda, R Hidaka, K Ogawa, T Tanaka, M Kanazawa, K Suzuki, M Stading, K Iijima.. Impact of oral frail prevention program including textured lunch gatherings on attitude and behavior for eating habit and oral frailty.. IAGG Asia/Oseania Regional Congress 2023 2023.06.13 Yokohama
6. K Matsuo, Y Masuda, R Hidaka, K Ogawa, T Tanaka, M Kanazawa, K Suzuki, M Stading, K Iijima.. Impact of oral frail prevention program including textured lunch gatherings on attitude and behavior for eating habit and oral frailty.. IAGG Asia/Oseania Regional Congress 2023 2023.06.13 Yokohama
7. Rena Hidaka. Oral health management for patients with stroke. IAGG Asia/Oseania Regional Congress 2023 2023.06.12 Yokohama
8. Rena Hidaka, Itsuki Tasaka, Yasuyuki Iwasa, Tomohisa Ohno, Daisuke Kanamori, Masako Kijima, Satoshi Teranaka, Junichi Furuya, Koichiro Matsuo. Association between oral function and malnutrition in subacute stroke patients admitted to a convalescent rehabilitation unit - a multicenter prospective study -. IAGG Asia/Oseania Regional Congress 2023 2023.06.12 Yokohama
9. koichiro matsuo. Current updates and future directions on basic science/human work for chewing and swallowing in adults,. 3rd World Dysphagia Summit 2023.03.13 San Francisco, California,

[Awards & Honors]

1. Outstanding Poster Presentation Award At the 12th IAGG Asia, Oceania Regional Congress 2023 held in Yokohama, 2023.06

Oral Health Care Education

Professor Naomi Yoshida

Assistant Professor

Graduate Students

Nana Yoshida

Hitomi Suzuki

Itsuki Takazawa

(1) Research

- 1) Research on oral health behavior
- 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 theoretic and skill for health promotion to contribute to the development of the health. Educational objects of Oral health care education in the graduate course is to foster human resources who will be able to implement health promotion program in collaboration with other career or residents in many fields.

(3) Clinical Services & Other Works

In oral health care clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases for the patients to maintain the their oral and general health in the entire lifetime.

(4) 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 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 first-year dental students at a Japanese university. Journal of oral science. 2022.01; 64(1); 85-90
4. Suzuki Hitomi, Sugimoto Kumiko, Kubota-Miyazawa Ayako, Noritake Kanako, Umemori Sachi, Araki Kouji, Adachi Naoko, Otsuka Hiromi, Yoshida Naomi. 日本の大学の歯科学学生1年生を対象とした口腔健康状態、主観的口腔症状、口腔保健行動の調査 (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

5. 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(タイトル和訳中) Journal of Medical and Dental Sciences. 2022; 69; 21-28

[Misc]

1. 吉田 直美, 新田 浩, うさっぱ, 磯村 毅. マンガで学ぶ はじめよう MI (第1回) 言い方ひとつで患者さんのやる気が大違い! 歯科衛生士. 2022.04; 46(4); 50

[Conference Activities & Talks]

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 2022.12.04 東京
2. 高澤維月、鈴木瞳、杉本久美子、樺沢勇司、吉田直美. 本学病棟における口腔ケア実施状況と実践に関連する要因の検討. 第87回 口腔病学会学術大会 2022.12.04
3. 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
4. 高澤維月, 鈴木瞳, 杉本久美子, 樺沢勇司, 吉田直美. 本学病棟における口腔ケア実施状況と実践に関連する要因の検討. 第87回 口腔病学会学術大会 2022.12.03
5. 高澤維月, 鈴木瞳, 杉本久美子, 橋爪顕子, 矢野貴子, 伊藤 奏, 安達奈穂子, 日高 玲奈, 吉田直美. 新入職看護師における口腔ケア関連知識の理解度および口腔ケア研修の効果に関する調査. 第28回日本摂食嚥下リハビリテーション学会 2022.09.23 千葉

Department of Basic Oral Health Engineering

Professor Kazuhiro AOKI
Associate Professor
OKI Meiko
Assistant Professor
KAMIJO Shingo
Visiting Lecturer
FUMI Yoshioka
Visiting Lecturer
HIROKI Nikawa
Visiting Lecturer
Ozawa Shogo

(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 was included in doctoral program at Biomedical Sciences and Engineering in 2023.

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) Development of scaffold materials for vertical bone augmentation by injection method
- 2) Development of novel bone anabolic agents that bind to RANKL molecules
- 3) Standardization of biomarkers of well-being in saliva and analysis of their relationship with cancer markers and oral microflora
- 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

(3) Lectures & Courses

Basic Oral Health Engineering is a department of oral health engineering which deals with the basic oral health sciences to perform evidence-based oral health care and prosthetic treatments to support people to promote oral health and improve quality of life. Main objective of Basic Oral Health Engineering in the undergraduate

course is to provide students opportunity to study the structure and function of the human body, pharmacology, fabrication of dental and maxillofacial prostheses, dental CAD/CAM technology and research process.

(4) Clinical Services & Other Works

Clinical activities

- Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects
- Making dental and maxillofacial prostheses

(5) Publications

[Original Articles]

1. [Department of Basic Oral Health Engineering : OKI Meiko] Aiko Hoshiai, Meiko Oki, Taiji Hoshiai, Toshiaki Iida, Yuka I Sumita, Shigeru Watanabe. Oral Health Management of Three Head and Neck Cancer Patients Performed by Dental Hygienists - A Case Report HEALTH. 2023.12; 15(12);
2. [Department of Basic Oral Health Engineering : OKI Meiko] Meiko Oki, Mirai Nakayama, Yumi Tsuchida, Shingo Kamijo, Kazuhiro Aoki. Objective evaluation of tooth carving using homologous models Journal of Dental Education. 2023.11;
3. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Katada H, Inokoshi M, Kamijo S, Liu H, Xu K, Kawashita M, Yokoi T, Shimabukuro M, Minakuchi S. Effects of multiple firings on the translucency, crystalline phase, and mechanical strength of highly translucent zirconia. Dent Mater J. 2023.11;
4. [Department of Basic Oral Health Engineering : KAMIJO Shingo] Linn Htat H, Takaichi A, Kajima Y, Kittikundecha N, Kamijo S, Hanawa T, Wakabayashi N. Influence of stress-relieving heat treatments on the efficacy of Co-Cr-Mo-W alloy copings fabricated using selective laser melting. Journal of prosthodontic research. 2023.07;
5. [Department of Oral Pathology : XIE Cangyou] Cangyou Xie, Fatma Rashed, Yosuke Sasaki, Masud Khan, Jia Qi, Yuri Kubo, Yoshiro Matsumoto, Shinichi Sawada, Yoshihiro Sasaki, Takashi Ono, Tohru Ikeda, Kazunari Akiyoshi and Kazuhiro Aoki. Comparison of Osteoconductive Ability of Two Types of Cholesterol-Bearing Pullulan (CHP) Nanogel-Hydrogels Impregnated with BMP-2 and RANKL-Binding Peptide: Bone Histomorphometric Study in a Murine Calvarial Defect Model 2023.06; 24(11);
6. [Department of Basic Oral Health Engineering : OKI Meiko] Meiko OKI, Maho SHIOZAWA, Shuma AOKI, Yumi TSUCHIDA, Tetsuya SUZUKI, Hidekazu TAKAHASHI. Digitally creating three-dimensional standard shapes of complete dentures by using homologous models: A pilot study Journal of Digital Dentistry. 2023.06; 1(1); 26-32
7. [Faculty of Dentistry : SASAKI Yoshiyuki] Shibata M, Takahara N, Kaneko T, Oki M, Sasaki Y, Tomomatsu N, Kurasawa Y, Nakakuki K, Yoda T. Risk factors for postoperative facial swelling at 1 week after bimaxillary orthognathic surgery in Class III patients. Journal of stomatology, oral and maxillofacial surgery. 2023.05; 124(5); 101516
8. [Department of Periodontology : YAMAKI Daichi] Shunsuke Takeuchi, Shunsuke Fukuba, Munehiro Okada, Kohei Nohara, Ryo Sato, Daichi Yamaki, Takanori Matsuura, Shu Hoshi, Kazuhiro Aoki, Takanori Iwata. Preclinical evaluation of the effect of periodontal regeneration by carbonate apatite in a canine one-wall intrabony defect model. Regen Ther. 2023.03; 22; 128-135
9. [Department of Basic Oral Health Engineering : Kazuhiro AOKI] Matsuno H, Li B, Okawara H, Toyoshima Y, Xie C, Khan M, Murakami N, Aoki K, Wakabayashi N. Effect of tension and compression on dynamic alveolar histomorphometry. Journal of the mechanical behavior of biomedical materials. 2023.02; 138; 105666
10. [Department of Basic Oral Health Engineering : OKI Meiko] Takahashi K, Amano H, Urano T, Li M, Oki M, Aoki K, Amizuka N, Nakayama KI, Nakayama K, Udagawa N, Higashi N. p57Kip2 is an essential regulator of vitamin D receptor-dependent mechanisms PLOS ONE. 2023.02; 18(2); e0276838

[Conference Activities & Talks]

1. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Xu K, Inokoshi M, Yoshihara K, Kakehata M, Yashiro H, Takahashi R, Yamatomo M, Kamijo S, Ikeda M, Minakuchi S. Bonding efficacy to femtosecond laser irradiated lithium disilicate glass-ceramic. IADR-ANZ Conference 2023 2023.09.29 Sydney
2. [Department of Basic Oral Health Engineering : Kazuhiro AOKI] Yuri Kubo, Qi Jia, Cangyou Xie, Yoshiro Matsumoto, Takashi Ono, Tohru Ikeda, and Kazuhiro Aoki. Development of novel anabolic reagents for local bone formation. International Summer Program 2023 2023.08.01 Tokyo, Japan
1. [Prosthodontics : TAKAICHI Atsushi] Qu Wenrui, Takaichi Atsushi, Kajima Yuka, Kamijo Shingo, Wakabayashi Noriyuk. Effect of build orientation on trueness and adaptation of maxillary complete denture frameworks fabricated by selective laser melting. Japan Dental Science and Engineering Society Kinki/Chushikoku Regional Meeting Seminar 2023.10.29 Osaka

Department of Digital Dentistry

Professor: KANAZAWA Manabu
Associate Professor: IWAKI Maiko
Assistant Professor: TSUCHIDA Yumi
RPD: HADA Tamaki

Graduate Students (Master)
NAKAYAMA Mirai
HAYASHI Nanaka
PIAO Yuanhua (Apr-)
LI Haoyu (Apr-)

Graduate Students (PhD)
WANG Jingrong (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.

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

[Original Articles]

1. Akiyama Y, Iwaki M, Komagamine Y, Minakuchi S, Kanazawa M. Effect of spindle speed and feed rate on surface roughness and milling duration in the fabrication of milled complete dentures: an in vitro study. *Appl Sci.* 2023.12; 13(24); 13338
2. Kashiwazaki K, Komagamine Y, Namano S, Park JM, Iwaki M, Minakuchi S, Kanazawa M. Prediction accuracy of incisal points in determining occlusal plane of digital complete dentures. *J Adv Prosthodont.* 2023.12; 15(6); 281-289
3. Huang Y, Wang J, Zhu L, Liu L, Gao S. The optimal design and three-dimensional finite element analysis of CAD/CAM integrated roach attachment. *Heliyon.* 2023.12; 16(10);
4. Oki M, Nakayama M, Tsuchida Y, Kamijo S, Aoki K. Objective evaluation of tooth carving using homologous models. *J Dent Educ.* 2023.11;
5. Kashiwazaki K, Komagamine Y, Shanglin W, Ren X, Hayashi N, Nakayama M, Namano S, Kanazawa M, Minakuchi S. Improvements in Maximum Bite Force with Gum-Chewing Training in Older Adults: A Randomized Controlled Trial. *J Clin Med.* 2023.10; 12(20);
6. Wang J, Jin C, Dong B, Yue L, Gao S. Fully digital workflow for replicating treatment dentures: A technique for jaw relation transfer and dynamic occlusal adjustment. *J Prosthet Dent.* 2023.09; 130(3); 288-294
7. Komagamine Y, Kanazawa M, Miyayasu A, Uehara Y, Watanabe M, Sahaprom N, Huyen TBN, Iwaki M, Sato D, Minakuchi S. The effect of single-implant overdentures on cognitive function in older adults: A 3-year follow-up report. *Journal of dentistry.* 2023.09; 136; 104632
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10. Komagamine, Y; Suzuki, H; Iwaki, M; Minakuchi, S; Kanazawa, M. Effect of New Complete Dentures and Simple Dietary Advice on Cognitive Screening Test among Edentulous Older Adults: A Randomized Controlled Trial *JOURNAL OF CLINICAL MEDICINE.* 2023.07; 12(14);
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12. 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. *J Prosthodont Res.* 2023.07; 67(3); 430-436
13. Oki M, Shiozawa M, Aoki S, Tsuchida Y, Suzuki T, Takahashi H. Digitally creating three-dimensional standard shapes of complete dentures by using homologous models: A pilot study. *Journal of Digital Dentistry.* 2023.06; 1(1); 26-32
14. Chaiamornsup P, Shiozawa M, Tsuchida Y, Takahashi H. Digital technique for placing markings on removable denture. *J Digital Dent.* 2023.06; 1(1); 41-44
15. Tsuchida Y, Shiozawa M, Handa K, Takahashi H, Nikawa H. Comparison of the accuracy of different handheld-type scanners in three-dimensional facial image recognition. *J Prosthodont Res.* 2023.04; 67(2); 222-230
16. Chaiamornsup P, Katheng A, Ha R, Tsuchida Y, Kanazawa M, Uo M, Minakuchi S, Suzuki T, Takahashi H. Effects of build orientation and bar addition on accuracy of complete denture base fabricated with digital light projection: An in vitro study. *J Prosthodont Res.* 2023.04;
17. R Hidaka, Y Masuda, K Ogawa, T Tanaka, M Kanazawa, K Suzuki, M Stading, K Iijima, K Matsuo. Impact of oral frailty prevention program with textured lunch gatherings on attitude and behavior towards eating habits and improving oral frailty: The Comprehensive Awareness Modication of Mouth, Chewing And Meal (CAMCAM) program *The Journal of Nutrition Health and Aging.* 2023.04; 27(5); 340-347
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20. 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. *Dent Mater J.* 2023.01; 42(1); 64-71
21. Tabira K, Kawaguchi R, Mine Y, Iwaguro S, Peng TY, Tsuchida Y, Takayama Y, Okazaki S, Taji T, Murayama T. An in vitro study of digital impressions and three-dimensional printed models of orbital defects using mobile devices and monoscopic photogrammetry. *J Oral Sci.* 2023; 65(2); 127-130
22. Akiyama Y, Kanazawa M, Iwaki M, Hada T, Soeda Y, Otake R, Kashiwazaki K, Komagamine Y, Murakami N, Takaichi A, Wakabayashi N, Minakuchi S. Fabrication of milled removable partial dentures using a custom plate with prefabricated artificial teeth. *J Prosthodont Res.* 2023.10; 67(4); 647-651

[Misc]

1. Kanazawa M. Digital transformation of removable dentures. *J Prosthodont Res.* 2023.10; 67(4); 7-8

[Conference Activities & Talks]

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3. Qi K, Kanazawa M, Hada T, Sahaprom N, Ren X, Akiyama Y, Minakuchi S. Effect of silanization on SLA resin enhanced by 3Y-TZP nanoparticles. The 101st General Session & Exhibition of the IADR 2023.06.23 Bogota
4. Hayashi N, Akiyama Y, Kashiwazaki K, Komagamine Y, Iwaki M, Minakuchi S, Kanazawa M. Effects of the offset values of fixed part of metal framework on accuracy in milled removable partial denture using custom plate. IAGG Asia/Oceania Regional Congress 2023. 2023.06.14 Yokohama
5. Qi K, Kanazawa K, Soeda Y, Akiyama Y, Hada T, Sahaprom N, Komagamine Y, Iwaki M, Shibata S, Mizokoshi N, Takeyama J, Shinpo H, Okubo C, Minakuchi S. The oral health-related quality of life and patient satisfaction of 3D-printed and conventional complete denture: The interim report of the randomized cross-over clinical trial. 日本補綴歯科学会第 132 回学術大会 2023.05.19 Yokohama
6. Wu S, Kanazawa M, Akiyama Y, Soeda Y, Hada T, Qi K, Sahaprom N, Komagamine Y, Iwaki M, Shibata S, Mizokoshi N, Takeyama J, Shinpo H, Okubo C, Minakuchi S. Comparison of the occlusal contact area and masticatory function between 3D-printed and conventional complete dentures: a randomized, cross-over clinical trial evaluating. the 14th Japan Academy of Digital Dentistry 2023.04.22 神奈川
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8. Manabu Kanazawa. Present and future of Digital Complete Denture. 30th Malaysian Dental Association SCATE2023. 2023.02.17
9. Manabu Kanazawa. The cutting edge of digital dentures. Japan Dental Tour 2023: Dentayori in collaboration with JDP 2023.02.15
10. Manabu Kanazawa. The cutting edge of digital dentures. International Academy for Digital Dental Medicine 2023.02.12
1. Retention Force Comparison of 3D Multiple Layer Mouthguard and Conventional Mouthguard via Cycle-loading Durability Fatigue Test. 2023.11.19
2. Yuna Kanamori, Kanako Noritake, Yumi Tsuchida, Maiko Iwaki, Manabu Kanazawa, Hiroshi Nitta. Comparison of quantitative evaluation and self-evaluation by trainee residents at Tokyo Medical and Dental University (TMDU) Hospital in abutment tooth preparation. The 42nd Annual Meeting of Japanese Dental Education Association 2023.07.17 Web

Department of Oral Biomedical Engineering

Professor IKEDA Masaomi

Junior Associate Professor

SATO Takaaki

Assistant Professor

NAKAGAWA Hisaichi

Assistant Professor

SHIOZAWA Maho

(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. Nami Tsuchiyama, Yukihiro Tamura, Tadamu Gondo, Masaomi Ikeda, Yasushi Shimada. The effect of ions used in bioactive dental materials on proliferation and differentiation of MC3T3-E1 cells Asian Pacific Journal of Dentistry. 2023.10; 23(2); 15-19
2. Tabata T, Nakagawa H, Kobayashi K, Takeuchi A, Fujimori R, Dohi K, Nakamura R, Iwabuchi H, Gondo T, Tsuji Y, Chen X, Sato T, Inoue G, Shimada Y. Diagnosis of occlusal caries using optical coherence tomography in a real clinical situation. Asian Pacific Journal of Dentistry. 2023.10; 23(2); 24-27
3. Kitasako, Y; Tanabe, T; Koeda, M; Momma, E; Hoshikawa, Y; Hoshino, S; Kawami, N; Ikeda, M; Iwakiri, K. Patients with gastroesophageal reflux disease (both reflux oesophagitis and non-erosive reflux disease): Prevalence and severity of erosive tooth wear and saliva properties JOURNAL OF ORAL REHABILITATION. 2023.09; 51(2); 305-312
4. Takaaki Sato, Tomoko Tabata, Koudai Akabane, Mengtian Zhao, Abu Hasan Mohammad Khaled, Noriko Hiraishi, Yasunori Sumi, Junji Tagami, Yasushi Shimada. Noninvasive diagnostic method using optical coherence tomography detected a vulnerable dentin enamel junction created by phosphoric acid etching. Dental Materials Journal. 2023.08; 42(4); 552-558
5. Seung-Hoon Han, Yasushi Shimada, Alireza Sadr, Tomoko Tabata, Hisaichi Nakagawa, Takaaki Sato, Ji-Eun Byun, Sung-Ho Park. Effect of Attenuated Light Through Translucent Zirconia on the Interfacial Adaptation and Polymerization of Resin Cements. The Journal of Adhesive Dentistry. 2023.08; 25(1); 219-230
6. Meiko OKI, Maho SHIOZAWA, Shuma AOKI, Yumi TSUCHIDA, Tetsuya SUZUKI, Hidekazu TAKAHASHI. Digitally creating three-dimensional standard shapes of complete dentures by using homologous models: A pilot study Journal of Digital Dentistry. 2023.06; 1(1); 26-32
7. Patcharanun Chaiamornsap, Maho Shiozawa, Yumi Tsuchida, Hidekazu Takahashi. Digital technique for placing markings on removable denture Journal of Digital Dentistry. 2023.06; 1(1); 41-44
8. Ayaka Sato, Takaaki Sato, Masaomi Ikeda, Tomohiro Takagaki, Toru Nikaido, Junji Tagami, Yasushi Shimada. Influence of different tooth etchants on bur-cut and uncut enamel. Dental Materials Journal. 2023.05; 42(3); 311-318
9. Tsuchida Y, Shiozawa M, Handa K, Takahashi H, Nikawa H. Comparison of the accuracy of different handheld-type scanners in three-dimensional facial image recognition. J Prosthet Res. 2023.04; 67(2); 222-230
10. Zandinejad A, Khanlar LN, Barmak AB, Ikeda M, Tagami J, Masri R. Shear bond strength of porcelain to milled and stereolithography additively manufactured zirconia with and without surface treatment: An in vitro study. The Journal of prosthetic dentistry. 2023.03;
11. Rose Y Kumagai, Tomohiro Takagaki, Takaaki Sato, Toru Nikaido, Marcelo Giannini, Andre Reis, Junji Tagami. Resin Cement/Enamel Interface: A Morphological Evaluation of the Acid-Base Resistant Zone, Enamel Etching Pattern, and Effect of Thermocycling on the Microshear Bond Strength. The Journal of Adhesive Dentistry. 2023.03; 25(1); 71-78
12. Chen X, Inoue G, Ikeda M, Sadr A, Shimada Y. Time-dependent structural changes and hypermineralisation of artificially demineralised dentine following treatment with silver diammine fluoride and glass ionomer cement. Journal of dentistry. 2023.02; 131; 104452
13. Takaaki Sato, Jirun Sun, Xiaohong Wang, Shozo Takagi, Yoshikazu Teranishi, Go Inoue, Tomohiro Takagaki, Toru Nikaido, Junji Tagami, Yasushi Shimada. Analysis of reaction products on hydroxyapatite created by tooth etchants with different compositions. Journal of Oral Science. 2023.01; 65(1); 53-56
14. Shimizu S, Kusakabe S, Toyama M, Takagaki T, Kitada N, Yamamoto K, Ikeda M, Ichimura Y, Burrow MF, Hotta M, Nikaido T. Bacterial adhesion and antibacterial property of coating materials containing theobromine and S-PRG filler. Dental materials journal. 2023.01; 42(1); 112-120

15. Hoshikawa Yoshimasa, Momma Eri, Kawami Noriyuki, Ikeda Masaomi, Kuribayashi Shiko, Iwakiri Katsuhiko. Starlet システムを使用し追加の手技を併用する高解像度マノメトリー 問題となる食道胃接合部通過障害に関する正常閾値と診断率 (High-resolution manometry with additional maneuvers using the Starlet system: normative thresholds and diagnostic yields for relevant esophagogastric junction outflow disorders) *Esophagus*. 2023.01; 20(1); 150-157
16. 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 *The Spine Journal*. 2023;

[Misc]

1. Tomoko TABATA, Hisaichi NAKAGAWA, Khairul MATIN Masayuki OTSUKI, Akira AOKI and Yasushi SHIMADA. Biofilm Studies Using Optical Coherence Tomography (OCT): Review *Journal of Japanese Society for Laser Dentistry*. 2023.09; 33(1); 11-17

[Conference Activities & Talks]

1. Go Inoue, Masaomi Ikeda, Yasushi Shimada. Composite resin restoration with injection technique on severe eroded teeth. The 71st Annual Meeting of Japanese Association for Dental Research 2023.11.25 Sendai
2. Xu K, Inokoshi M, Yoshihara K, Kakehata M, Yashiro H, Takahashi R, Yamatomo M, Kamijo S, Ikeda M, Minakuchi S. Bonding efficacy to femtosecond laser irradiated lithium disilicate glass-ceramic. IADR-ANZ Conference 2023 2023.09.29 Sydney
3. Tomoko Tabata, Hisaichi Nakagawa, Takaaki Sato, Go Inoue, Masaomi Ikeda, Yasushi Shimada. Clinical evaluation of optical coherence tomography in the diagnosis of occlusal enamel caries using ICDAS codes. the 2nd General Meeting of Asian-Oceanian Federation of Conservative Dentistry 2023 (ConsAsia 2023) 2023.09.02 Taipei, Taiwan
4. Go Inoue, Hisaichi Nakagawa, Takaaki Sato, Tomoko Tabata, Masaomi Ikeda, Yasushi Shimada. Clinical assessment of diagnosis of enamel caries ICDAS codes using optical coherence tomography. the 2nd General Meeting of Asian-Oceanian Federation of Conservative Dentistry 2023 2023.09.02 Taipei
5. Mustafa Ata ÇAKALOĞLU, Takaaki SATO, Noriko HIRAISHI, Yasushi SHIMADA. NON-INVASIVE EVALUATION OF MARGINAL ADAPTATION OF DENTIN-GLASS IONOMER CEMENT INTERFACE USING SWEPT SOURCE OPTICAL COHERENCE TOMOGRAPHY. The 7th International Congress on Adhesive Dentistry 2023.06.01 Konya, Turkey
6. Hitoshi Miki, Hirofumi Tashiro, Junji Tagami, Tomohiro Takagaki, Keiichi Hosaka, Takaaki Sato, Takashi Hatayama, Yasushi Shimada. Clinical effectiveness of the mono-block direct composite crown restoration. The 7th International Congress on Adhesive Dentistry 2023.06.01 Konya, Turkey
7. Takaaki Sato. Deep caries treatment. UP College of Dentistry – Tokyo Medical and Dental University Research Mini-Symposium, PHILIPPINES MANILA 2023.05.15 Manila, Philippines
8. Xu K, Inokoshi M, Yoshihara K, Ikeda M, Liu H, Minakuchi S. Influence of femtosecond laser irradiation on biaxial flexural strength of lithium disilicate glass-ceramic. 第 81 回日本歯科理工学会学術講演会 2023.04.15 東京

[Awards & Honors]

1. Prof, Dr. NAKABAYASHI AWARD, The 7th International Congress on Adhesive Dentistry, 2023.06

Department of Nutrition and Metabolism in Cardiovascular Disease

Makiko Egawa
Maki Gau

(1) Outline

This course was established as a donated research division attached to the Department of Life Sciences and Medical Ethics.

The main themes are investigating the mechanism of arteriosclerosis development, which are one of the main causes of lifestyle-related diseases such as cardiovascular diseases and diabetes. This course also has been interested in the treatment and prevention of atherosclerosis and its relationship toward pregnancy in women. Our education is being developed with the aim of training excellent researchers and highly specialized professionals with specialized knowledge and abilities capable of playing an active role in the international community.

(2) Publications

[Original Articles]

1. Yamashita M, Tomoda T, Mizuo A, Isoda T, Egawa M, Yoshida M, Toki T, Kudo K, Terui K, Ito E, Morio T, Takagi M. Transient erythroblastopenia due to a GATA1 variant in an infant female. *Pediatric blood & cancer*. 2023.12; e30834
2. Yogi A, Iemura R, Nakatani H, Takasawa K, Gau M, Yamauchi T, Yoshida M, Moriyama K, Ishii T, Hosokawa S, Yamada M, Suzuki H, Kosaki K, Kashimada K, Morio T. BMP2 is a potential causative gene for isolated dextrocardia situs solitus. *European journal of medical genetics*. 2023.08; 66(9); 104820
3. Egawa M, Kanda E, Ohtsu H, Nakamura T, Yoshida M. Hypertensive Disorders of Pregnancy are Associated with Cardiovascular Disease in Middle- and Older-Aged Japanese Women. *Journal of atherosclerosis and thrombosis*. 2023.01; 30(10); 1420-1426
4. Shizuka Kirino, Analia Yogi, Eriko Adachi, Hisae Nakatani, Maki Gau, Ryosei Iemura, Haruki Yamano, Toru Kanamori, Takayasu Mori, Eisei Sohara, Shinichi Uchida, Kentaro Okamoto, Tomohiro Udagawa, Kei Takasawa, Tomohiro Morio, Kenichi Kashimada. Phenotypic Variation in 46,XX Disorders of Sex Development due to the Fourth Zinc Finger Domain Variant of WT1: A Familial Case Report. *Sex Dev*. 2023; 17(1); 51-55

[Conference Activities & Talks]

1. Masayuki Yoshida, Eriko Takamine, Hiroko Kohbata, Sayako Takahashi, Mariko Komine, Yusuke Ebana, Makiko Egawa, Sadakatsu Ikeda, Kana Kobori, Takuto Matura, Atsushi Tajima, Yu Oyama.. Clinical usefulness of multi-gene panel testing in hereditary cancer analysis in Japan -INSIGNIA study. *ASHG Annual Meeting 2023* 2023.11.01
2. Eriko Adachi, Ryuichi Nakagawa, Atsumi Tsuji-Hosokawa, Maki Gau, Shizuka Kirino, Analia Yogi, Hikase Nakatani, Tomomi Yamaguchi, Masanori Murakami, Toshihiro Tajima, Tomonobu Hasegawa, Tetsuya Yamada, Tomohiro Morino, Osamu Ohara, Kenichi Kashimada. Development of a clinically applicable one-step PCR-based CYP21A2 analysis using long read sequences.. *Human Genetics Asia 2023*(68th

Annual Meeting of Japan Society of Human Genetics/ 14th Asia Pacific Conference on Human Genetics/
22nd Annual meeting of East Asian Union of human Genetics Societies) 2023.10.14 Tokyo Japan

3. Masatoshi Takagi, Motoi Yamashita, Takahiro Tomoda, Takeshi Isoda, Makiko Egawa, Masayuki Yoshida, Tsutomu Toki, Ko Kudou, Kiminori Terui, Etsuro Ito, Tomohiro Morio. Transient erythroblastopenia by GATA1 variant in female. Human Genetics Asia 2023 2023.10.13
4. Shizuka Kirino, Ryuichi Nakagawa, Kei Takasawa, Maki Gau, Atsumi Tsuji-Hosokawa, Liang Zhao, Josephine Bowles, Peter Koopman, Tomohiro Morio, Kenichi Kashimada.. Application of Cap analysis of gene expression (CAGE) in genetic analysis of mouse sex differentiation. Ninth International Symposium on the Biology of Vertebrate Sex Determination 2023.04.19 Kailua-Kona, HAWAII
5. Satoru Aoyama, Takashi Kamatani, Kousuke Tanimoto, Junko Yokobori, Eriko Takamine, Makiko Egawa, Yuki Kato, Susumu Kirimura, Ichiro Ohnishi, Kouichiro Kimura, Takahiro Asakage, Sadakatsu Ikeda. Case report: Myxofibrosarcoma in the head and neck region with rare TP53 aberration in the background of retinoblastoma.. 2023 the Japanese Society of Medical Oncology Annual Meeting 2023.03.17

Department of Lifetime Clinical Immunology

MORI Masaaki
YAMAMOTO Akiou
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. Finally, 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 Rheumatology 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

[Original Articles]

1. Takuji Itakura, Hirokazu Sasaki, Tadashi Hosoya, Taiki Yamaguchi, Erika Mimori, Yukino Saimon, Hideyuki Iwai, Natsuka Umezawa, Daisuke Kawata, Naoki Kimura, Morito Kurata, Masaki Shimizu, Shinsuke Yasuda. A novel gain-of-function missense variant in PLCG2 associated with autoinflammation and hypergammaglobulinaemia. *Rheumatology (Oxford)*. 2023.11; 62(11); e319-e321
2. Susumu Yamazaki, Kazushi Izawa, Masakazu Matsushita, Akinori Moriichi, Dai Kishida, Hajime Yoshifuji, Ken Yamaji, Ryuta Nishikomori, Masaaki Mori, Takako Miyamae. Promoting awareness of terminology related to unmet medical needs in context of rheumatic diseases in Japan: a systematic review for evaluating unmet medical needs. *Rheumatol Int*. 2023.11; 43(11); 2021-2030
3. Masaaki Mori, Kanako Yoshizaki, Shinichi Watabe, Mika Ishige, Akinari Hinoki, Takuya Kondo, Tomoaki Taguchi, Hisaya Hasegawa, Tomoko Hatata, Naoyuki Tanuma, Kosuke Kirino, Akihiro Hirakawa, Takuya Naruto, Minoru Imai, Ryuji Koike, Kenichiro Hosoi, Satoshi Kusuda. Safety, efficacy and pharmacokinetics of palivizumab in off-label neonates, infants, and young children at risk for serious respiratory syncytial virus infection: a multicenter phase II clinical trial. *Lancet Reg Health West Pac*. 2023.10; 39; 100847
4. Masaaki Mori, Tomoyo Matsubara. Overview of Guidelines for the Medical Treatment of Acute Kawasaki Disease in Japan (2020 Revised Version) and Positioning of Plasma Exchange Therapy in the Acute Phase. *Pediatr Infect Dis J*. 2023.09; 42(9); e328-e332
5. 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, Shuichi 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*. 2023.08; 33(5); 1021-1029
6. Athimalaipet V Ramanan, Pierre Quartier, Nami Okamoto, Ivan Foeldvari, Alberto Spindler, Šárka Fingerhutová, Jordi Antón, Zhongkai Wang, Gabriella Meszaros, Joana Araújo, Ran Liao, Stuart Keller, Hermine I Brunner, Nicolino Ruperto, , . Baricitinib in juvenile idiopathic arthritis: an international, phase 3, randomised, double-blind, placebo-controlled, withdrawal, efficacy, and safety trial. *Lancet*. 2023.08; 402(10401); 555-570
7. Mari Kamiya, Naoki Kimura, Natsuka Umezawa, Hisanori Hasegawa and Shinsuke Yasuda. Muscle fiber necroptosis in pathophysiology of idiopathic inflammatory myopathies and its potential as target of novel treatment strategy *Frontiers in Immunology*. 2023.07; 14; 1191815
8. 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 developed during treatment of juvenile dermatomyositis and macrophage activation syndrome: A case report. *Mod Rheumatol Case Rep*. 2023.06; 7(2); 404-409

9. Shuya Kaneko, Masaki Shimizu, Asami Shimbo, Hitoshi Irabu, Koji Yokoyama, Kenji Furuno, Takayuki Tanaka, Kazuyuki Ueno, Shuhei Fujita, Naomi Iwata, Junya Fujimura, Keiji Akamine, Mao Mizuta, Yasuo Nakagishi, Toshinori Minato, Kenichi Watanabe, Anna Kobayashi, Takuya Endo, Katsuhiko Tabata, Masaaki Mori, Tomohiro Morio. Clinical significance of serum cytokine profiles for differentiating between Kawasaki disease and its mimickers. *Cytokine*. 2023.06; 169; 156280
10. Natsuka Umezawa, Fumitaka Mizoguchi, Yasuhiro Maejima, Naoki Kimura, Hisanori Hasegawa, Tadashi Hosoya, Minoru Fujimoto, Hitoshi Kohsaka, Tetsuji Naka, Shinsuke Yasuda. Leucine-rich alpha-2 glycoprotein as a potential biomarker for large vessel vasculitides. *Front Med (Lausanne)*. 2023.05; 10; 1153883
11. Masaki Shimizu, Kenichi Nishimura, Naomi Iwata, Takahiro Yasumi, Hiroaki Umebayashi, Yasuo Nakagishi, Yuka Okura, Nami Okamoto, Noriko Kinjo, Mao Mizuta, Masato Yashiro, Junko Yasumura, Hiroyuki Wakiguchi, Tomohiro Kubota, Mariko Mouri, Utako Kaneko, Masaaki Mori. Treatment for macrophage activation syndrome associated with systemic juvenile idiopathic arthritis in Japan. *Int J Rheum Dis*. 2023.05; 26(5); 938-945
12. Xavier Carbonell-Estrany, Eric Af Simões, Louis J Bont, Bosco A Paes, . Prioritising respiratory syncytial virus prevention in low-income and middle-income countries. *Lancet Glob Health*. 2023.05; 11(5); e655-e657
13. Shuya Kaneko, Masaki Shimizu, Futaba Miyaoka, Asami Shimbo, Hitoshi Irabu, Mao Mizuta, Yasuo Nakagishi, Naomi Iwata, Junya Fujimura, Masaaki Mori, Tomohiro Morio. The dynamics of laboratory markers reflecting cytokine overproduction in macrophage activation syndrome complicated with systemic juvenile idiopathic arthritis. *Clin Immunol*. 2023.03; 248; 109270
14. 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*. 2023.01; 33(1); 21-35
15. Ryosuke Wakatsuki, Masaki Shimizu, Asami Shimbo, 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*. 2023.01; 7(1); 65-67
16. Masaki Shimizu, Hitoshi Irabu, Asami Shimbo, Shuya Kaneko, Masaaki Mori. Monthly intravenous immunoglobulin for refractory intestinal IgA vasculitis. *Pediatr Int*. 2023.01; e15470
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18. Megumi Matsumoto, Susumu Yamazaki, Eisuke Inage, Keisuke Jimbo, Mitsuyoshi Suzuki, Masaaki Mori, Toshiaki Shimizu. TAFRO syndrome in an adolescent with acute hepatitis-like imaging findings. *Pediatr Int*. 2023; 65(1); e15695

Department of Child Health and Development

Professor: Hirokazu KANEGANE
Junior Assistant Professor: Akihiro Hoshino

(1) Outline

In addition to acute diseases of medicine and child health care, “growth and medical care” include transition to the chronic phase, long-term medical treatment of patients with intractable diseases, medicine encompassing healthy growth of children. As a philosophy of “growth and medical care”, we establish a developmental and medical system closely related to regional medical care in the suburbs of the metropolitan area, and to foster human resources of pediatricians responsible for next-generation medical care.

(2) Research

We conduct survey research and education based on the organic collaboration between Tokyo Medical and Dental University and Kashiwa City Kashiwa Hospital.

The current main projects are the following.

- 1.Establishment of pediatric medical system in Kashiwa city.
- 2.Study of primary immunodeficiency (PID) predisposing to Epstein-Barr virus infection
- 3.Study of primary antibody deficiency
- 4.Etiologic and pathophysiological analysis of cytokine storm syndrome, especially of macrophage activation syndrome.
- 5.Etiologic and pathophysiological analysis of juvenile idiopathic arthritis (JIA), the most common type of pediatric rheumatic diseases.
- 6.Registry study on pediatric kidney disease in Kashiwa city.

(3) Education

We conduct a broader range of more specialized clinical education for acquiring pediatric specialists at the University Hospital.

(4) Lectures & Courses

We mainly train young pediatric researchers and specialists. We make them to be familiar with chronic diseases and intractable diseases of childhood and to be responsible for next generation medical care.

(5) Clinical Services & Other Works

We treat children with PID, hematological malignancies, hematological disorders, and malignant solid tumors in the University Hospital.

At Kashiwa City Kashiwa Hospital, we provide pediatric medicine mainly for acute diseases, cooperating with medical facilities in the suburbs, and establish a reliable medical system for children in the local residents.

(6) Clinical Performances

We provide diagnosis, treatment of pathological analysis of primary immunodeficiency (PID) and hematological malignancies, and perform hematopoietic cell transplantation for refractory diseases. Especially, we treat the largest number of patients with PID in Japan.

Our university hospital is one of the largest core centers for pediatric rheumatic diseases in Japan. Pediatric rheumatologists, adult rheumatologists, pediatric orthopedic surgeons and pediatric ophthalmologists cooperatively provide seamless medical cares for pediatric rheumatic diseases from children to adults.

(7) Publications

[Original Articles]

1. Kunihiko Moriya, Kanako Mitsui-Sekinaka, Yujin Sekinaka, Akifumi Endo, Hirokazu Kanegane, Tomohiro Morio, Kohsuke Imai, Shigeaki Nonoyama. Clinical practice guideline for activated phosphatidylinositol 3-kinase-delta syndrome in Japan. *Immunol Med.* 2023.12; 46(4); 153-157
2. Aidé Tamara Staines-Boone, Pandiarajan Vignesh, Miyuki Tsumura, Germán de la Garza Fernández, Reva Tyagi, Amit Rawat, Jhumki Das, Dan Tomomasa, Takaki Asano, Atsushi Hijikata, Yuridia Salazar-Gálvez, Hirokazu Kanegane, Satoshi Okada, Saul O Lugo Reyes. Fatal COVID-19 Infection in Two Children with STAT1 Gain-of-Function. *J Clin Immunol.* 2023.12; 44(1); 20
3. Takuro Nishikawa, Takahiro Tomoda, Aki Nakamura, Jun Nagahama, Akihito Tanaka, Shuji Kanmura, Mari Kirishima, Akihide Tanimoto, Tsubasa Okano, Takahiro Kamiya, Kentaro Okamoto, Susumu Kirimura, Tomohiro Morio, Yasuhiro Okamoto, Hirokazu Kanegane. Case Report: The leopard sign as a potential characteristic of chronic granulomatous disease-associated colitis, unrelated to colitis severity. *Front Immunol.* 2023.12; 14; 1208590
4. Akira Nishimura, Ramya Uppuluri, Revathi Raj, Venkateswaran Vellaichamy Swaminathan, Yifei Cheng, Rolla F Abu-Arja, Bin Fu, Alexandra Laberko, Michael H Albert, Fabian Hauck, Giorgia Bucciol, Venetia Bigley, Suzanne Elcombe, Gaurav Kharya, Cornelis Jan H Pronk, Claudia Wehr, Bénédicte Neven, Klaus Warnatz, Isabelle Meyts, Tomohiro Morio, Andrew R Gennery, Hirokazu Kanegane. An International Survey of Allogeneic Hematopoietic Cell Transplantation for X-Linked Agammaglobulinemia. *J Clin Immunol.* 2023.11; 43(8); 1827-1839
5. Masatoshi Takagi, Akihiro Hoshino, Kristine Bousset, Jule Röddecke, Hanna Luisa Martin, Iulia Folcut, Dan Tomomasa, Xi Yang, Junya Kobayashi, Naoki Sakata, Kenichi Yoshida, Satoru Miyano, Seishi Ogawa, Seiji Kojima, Tomohiro Morio, Thilo Dörk, Hirokazu Kanegane. Bone Marrow Failure and Immunodeficiency Associated with Human RAD50 Variants. *J Clin Immunol.* 2023.11; 43(8); 2136-2145
6. Rintaro Ono, Kenichi Sakamoto, Takehiko Doi, Ryu Yanagisawa, Akira Morimoto, Hirokazu Kanegane, Yozo Nakazawa, Yoko Shioda. Dexamethasone palmitate as an etoposide-free treatment for children with hemophagocytic lymphohistiocytosis after hematopoietic cell transplantation. *Bone Marrow Transplant.* 2023.11; 58(11); 1286-1288
7. Keisuke Ogasawara, Makoto Ono, Keita Tamanuki, Ryosuke Wakatsuki, Kento Inoue, Yoshinori Tateishi, Rentaro Oda, Shogo Shirane, Hiraku Funakoshi, Hirokazu Kanegane, Yoshiho Hatai. Respiratory Symptoms are the First Presentation of Liver Abscess. *Pediatr Infect Dis J.* 2023.11;
8. Shuya Kaneko, Fumiaki Sakura, Kay Tanita, Asami Shimbo, Ryusuke Nambu, Masashi Yoshida, Shuichiro Umetsu, Ayano Inui, Chizuru Okada, Miyuki Tsumura, Mamiko Yamada, Hisato Suzuki, Kenjiro

- Kosaki, Osamu Ohara, Masaki Shimizu, Tomohiro Morio, Satoshi Okada, Hirokazu Kanegane. Janus kinase inhibitors ameliorate clinical symptoms in patients with STAT3 gain-of-function. *Immunotherapy Advances*. 2023.11;
9. Daisuke Kurita, Norio Shiba, Takashi Ohya, Ayako Murase, Yuko Shimosato, Masahiro Yoshitomi, Seira Hattori, Koji Sasaki, Kenichi Nishimura, Shin-Ichi Tsujimoto, Masanobu Takeuchi, Reo Tanoshima, Hirokazu Kanegane, Norihiko Kitagawa, Shuichi Ito. Severe RAS-Associated Lymphoproliferative Disease Case with Increasing $\alpha\beta$ Double-Negative T Cells with Atypical Features. *J Clin Immunol*. 2023.11; 43(8); 1992-1996
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 14. Ryosuke Wakatsuki, Yoshiho Hatai, Kentaro Okamoto, Shuya Kaneko, Asami Shimbo, Hitoshi Irabu, Masaki Shimizu, Hirokazu Kanegane, Makoto Ono. An infant with A20 haploinsufficiency presenting with periodic fever syndrome: A case report. *Int J Rheum Dis*. 2023.05; 26(5); 973-976
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 16. Dan Tomomasa, Motoi Yamashita, Takahiro Kamiya, Tomohiro Morio, Hirokazu Kanegane. Maternal Gonosomal Mosaicism Causes XIAP Deficiency. *J Clin Immunol*. 2023.04; 43(3); 525-527
 17. Kana Unuma, Dan Tomomasa, Kosuke Noma, Kouhei Yamamoto, Taka-Aki Matsuyama, Yohsuke Makino, Atsushi Hijikata, Shuheng Wen, Tsutomu Ogata, Nobuhiko Okamoto, Satoshi Okada, Kenichi Ohashi, Koichi Uemura, Hirokazu Kanegane. Case Report: Molecular autopsy underlie COVID-19-associated sudden, unexplained child mortality. *Front Immunol*. 2023.04; 14; 1121059
 18. Fumiaki Sakura, Kosuke Noma, Takaki Asano, Kay Tanita, Etsushi Toyofuku, Kentaro Kato, Miyuki Tsumura, Hiroshi Nihira, Kazushi Izawa, Kanako Mitsui-Sekinaka, Ryo Konno, Yusuke Kawashima, Yoko Mizoguchi, Shuhei Karakawa, Seiichi Hayakawa, Hiroshi Kawaguchi, Kohsuke Imai, Shigeaki Nonoyama, Takahiro Yasumi, Hidenori Ohnishi, Hirokazu Kanegane, Osamu Ohara, Satoshi Okada. A complementary approach for genetic diagnosis of inborn errors of immunity using proteogenomic analysis. *PNAS Nexus*. 2023.04; 2(4); pgad104
 19. Dan Tomomasa, Takeshi Isoda, Noriko Mitsui, Kento Inoue, Akira Nishimura, Kazuhiro Uda, Toru Uchiyama, Motoi Yamashita, Takahiro Kamiya, Akifumi Endo, Masatoshi Takagi, Kohsuke Imai, Michiko Kajiwarra, Morton J Cowan, Tomohiro Morio, Hirokazu Kanegane. Successful TCR $\alpha\beta$ /CD19-Depleted Hematopoietic Cell Transplantation for a Patient With Artemis Deficiency. *J Pediatr Hematol Oncol*. 2023.03; 45(2); e285-e289

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21. Rintaro Ono, Miyuki Tsumura, Saho Shima, Yusuke Matsuda, Kenji Gotoh, Yurina Miyata, Yuko Yoto, Dan Tomomasa, Takanori Utsumi, Hidenori Ohnishi, Zenichiro Kato, Naruhiko Ishiwada, Aki Ishikawa, Taizo Wada, Hisashi Uhara, Ryuta Nishikomori, Daisuke Hasegawa, Satoshi Okada, Hirokazu Kanegane. Novel STAT1 Variants in Japanese Patients with Isolated Mendelian Susceptibility to Mycobacterial Diseases. *J Clin Immunol.* 2023.02; 43(2); 466-478
22. Hirokazu Kanegane. Patient-derived induced pluripotent stem cells underlie the pathogenesis of the diseases. *Pediatr Int.* 2023.01; 65(1); e15463
23. Takeru Kanazawa, Tatsuyuki Ishida, Madoka Shirai, Daiki Niizato, Takeshi Isoda, Yoshifusa Abe, Hirokazu Kanegane. Wiskott-Aldrich syndrome with normal-sized platelets. *Pediatr Int.* 2023.01; 65(1); e15453
24. Hirokazu Kobushi, Katsutsugu Umeda, Eitaro Hiejima, Kentaro Kato, Mayumi Sugimoto, Hirokazu Kanegane, Junko Takita. Alemtuzumab-based reduced-intensity conditioning for XIAP deficiency. *Pediatr Int.* 2023; 65(1); e15576
25. Sara Konishi, Rintaro Ono, Miyuki Tanaka, Ken-Ichi Imadome, Yozo Nakazawa, Hirokazu Kanegane, Daisuke Hasegawa. Cytokine-based disease monitoring in refractory HLH with primary EBV infection. *Pediatr Int.* 2023; 65(1); e15590
26. Hirokazu Kanegane, Masataka Ishimura, Toshinao Kawai, Satoshi Okada, Nobuaki Okamatsu, Madoka Go, Shinichi Noto. Patient-reported outcomes in patients with primary immunodeficiency diseases in Japan: baseline results from a prospective observational study. *Front Immunol.* 2023; 14; 1244250

[Misc]

1. Holm H Uhlig, Claire Booth, Judy Cho, Marla Dubinsky, Anne M Griffiths, Bodo Grimbacher, Sophie Hambleton, Ying Huang, Kelsey Jones, Jochen Kammermeier, Hirokazu Kanegane, Sibylle Koletzko, Daniel Kotlarz, Christoph Klein, Michael J Lenardo, Bernice Lo, Dermot P B McGovern, Ahmet Özen, Lissy de Ridder, Frank Ruemmele, Dror S Shouval, Scott B Snapper, Simon P Travis, Dan Turner, David C Wilson, Aleixo M Muise. Precision medicine in monogenic inflammatory bowel disease: proposed mIBD REPORT standards. *Nat Rev Gastroenterol Hepatol.* 2023.12; 20(12); 810-828
2. Hirokazu Kanegane, Atsuko Noguchi, Yuki Yamada, Takahiro Yasumi. Rare diseases presenting with hemophagocytic lymphohistiocytosis. *Pediatr Int.* 2023; 65(1); e15516

[Conference Activities & Talks]

1. Hirokazu Kanegane. Flow cytometry use in Primary Immunodeficiency disorders. Mini-symposium: Inborn errors of immunity 2023.10.27 Bangkok
2. Hirokazu Kanegane. NK cell assays. APSID 2023 2023.10.26 Singapore
3. Hirokazu Kanegane. Diagnosis and Management of Primary Atopic Disorder. APAAACI 2023 2023.10.25 Singapore
4. Hirokazu Kanegane. Rare diseases presenting with hemophagocytic lymphohistiocytosis. IEI SCAC 2023 2023.09.15 重慶
5. Satoshi Miyamoto, Daiki Niizato, Takahiro Kamiya, Takeshi Isoda, Masatoshi Takagi, Shohei Azumi, Shinsuke Hirabayashi, Kenichi Sakamoto, Kenji Kishimoto, Takako Miyamura, Katsutsugu Umeda, Masakatsu Yanagimachi, Kaori Kanda, Yasuhiro Ikawa, Kenichiro Watanabe, Tatsuo Ichinohe, Hirotoshi Sakaguchi, Tomohiro Morio, Hirokazu Kanegane. Allogeneic hematopoietic cell transplantation with alemtuzumab in Asian patients with inborn errors of immunity. ICBMT2023 2023.09.01 Busan

6. Dan Tomomasa, Tasuku Suzuki, Ichiro Takeuchi, Kimitoshi Goto, Shin-Ichiro Hagiwara, Dai Keino, Satoshi Saida, Takashi Ishige, Takahiro Kudo, Masataka Ishimura, Motohiro Kato, Yoji Sasahara, Tomohiro Morio, Katsuhiro Arai, Hirokazu Kanegane. Clinical and genetic characteristics of IL10RA deficiency patients in Japan. The 2nd International Symposium of Clinical Immunology 2023.05.19 神奈川
7. Hirokazu Kanegane. HLH associated with inborn errors of metabolism and familial hemophagocytic lymphohistiocytosis in adult. 2nd National Congress of Inborn Errors of Immunity and National Forum on Pediatric Immunology (IEI China 2023 and FOPI) 2023.04.26 Web 開催
8. Mahnaz Jamee, Hirokazu Kanegane. Lung Surgery in STAT3 loss-of-function mutation: is it advisable?. APSID 2023 2023.04.22 香港
1. Allogenic HCT with alemtuzumab in pediatric patients with inborn errors of immunity. 2023.02.12
2. Two cases of late-onset familial hemophagocytic lymphohistiocytosis type 3 presenting with CLIPPERS-like syndrome. 2023.02.12
3. Wiskott-Aldrich syndrome due to chromosomal structural abnormalities. 2023.02.12
4. A case of relapsed AML maintained complete remission by re-transplantation using clofarabine. 2023.02.11
5. Support for adolescent patients and their families by HSC coordinators in fertility preservation. 2023.02.11
6. Comparison of adult and pediatric cases with hyper-IgE syndrome caused by function in STAT3. 2023.02.11
7. Efficacy of JAK inhibitors for patients with gain-of-function mutation of STAT3. 2023.02.11
8. Hematopoietic cell transplantation for patients with inborn errors of immunity. 2023.02.11

Department of 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

[Original Articles]

1. Endo S, Okamoto T, Kawahara T, Anzai T, Takahashi K, Miyazaki Y. Effect of warm and humid days on the positivity rate of anti-Trichosporon asahii antibody test for the diagnosis of summer-type hypersensitivity pneumonitis. Respiratory investigation. 2023.12; 62(1); 150-156
2. Aoki H, Miyazaki Y, Anzai T, Yokoyama K, Tsuchiya J, Shirai T, Shibata S, Sakakibara R, Mitsumura T, Honda T, Furusawa H, Okamoto T, Tateishi T, Tamaoka M, Yamamoto M, Takahashi K, Tateishi U, Yamaguchi T. Deep convolutional neural network for differentiating between sarcoidosis and lymphoma based on [(18)F] FDG maximum-intensity projection images. European radiology. 2023.08; 34(1); 374-383
3. Maruyama S, Furusawa H, Endo S, Kumagai T, Mitsumura T, Shimada S, Yamana T, Sakakibara R, Iijima Y, Shibata S, Honda T, Shirai T, Okamoto T, Tateishi T, Tamaoka M, Kinowaki Y, Ishibashi H, Okubo K, Miyazaki Y. Pulmonary Artery Aneurysm in a Patient with Nontuberculous Mycobacteria Infection. Internal medicine (Tokyo, Japan). 2023.08;

4. Ikeda Tokuji, Ichiba Shingo, Sasaki Takashi, Sato Masaaki, Konoeda Chihiro, Okamoto Tsukasa, Miyazaki Yasunari, Nakajima Jun, Sakamoto Atsuhiko. 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(タイトル和訳中) *Journal of Artificial Organs*. 2023.03; 26(1); 84-88
5. Yamashita Shohei, Okamoto Tsukasa, Kawahara Tatsuo, Tateishi Tomoya, Anzai Tatsuhiko, Takahashi Kunihiro, Fushimi Kiyohide, Miyazaki Yasunari. Database analysis of hypersensitivity pneumonitis in Japan(タイトル和訳中) *Respiratory Investigation*. 2023.03; 61(2); 172-180
6. Tateishi T, Shimada S, Yamana T, Iijima Y, Sakakibara R, Mitsumura T, Shibata S, Honda T, Shirai T, Okamoto T, Tamaoka M, Sasai T, Miyazaki Y. COVID-19 Pneumonia Followed by Anti-signal Recognition Particle Antibody-positive Fibrosing Interstitial Lung Disease: A Case Report. *Internal medicine (Tokyo, Japan)*. 2023.02; 62(9); 1323-1328
7. Yamashita S, Okamoto T, Kawahara T, Tateishi T, Anzai T, Takahashi K, Fushimi K, Miyazaki Y. Database analysis of hypersensitivity pneumonitis in Japan. *Respiratory investigation*. 2023.01; 61(2); 172-180
8. Peljto AL, Blumhagen RZ, Walts AD, Cardwell J, Powers J, Corte TJ, Dickinson JL, Glaspole I, Moodley YP, Vasakova MK, Bendstrup E, Davidsen JR, Borie R, Crestani B, Dieude P, Bonella F, Costabel U, Gudmundsson G, Donnelly SC, Egan J, Henry MT, Keane MP, Kennedy MP, McCarthy C, McElroy AN, Olaniyi JA, O'Reilly KMA, Richeldi L, Leone PM, Poletti V, Puppo F, Tomassetti S, Luzzi V, Kokturk N, Mogulkoc N, Fiddler CA, Hirani N, Jenkins G, Maher TM, Molyneaux PL, Parfrey H, Braybrooke R, Blackwell TS, Jackson PD, Nathan SD, Porteous MK, Brown KK, Christie JD, Collard HR, Eickelberg O, Foster EE, Gibson KF, Glassberg M, Kass D, Kropski JA, Lederer D, Linderholm AL, Loyd J, Mathai SK, Montesi SB, Noth I, Oldham JM, Palmisciano AJ, Reichner CA, Rojas M, Roman J, Schluger N, Shea BS, Swigris JJ, Wolters PJ, Zhang Y, Prele CMA, Enghelmayer JJ, Otaola M, Ryerson CJ, Salinas M, Sterclova M, Gebremariam TH, Myllärniemi M, Carbone R, Furusawa H, Hirose M, Inoue Y, Miyazaki Y, Ohta K, Ohta S, Okamoto T, Kim DS, Pardo A, Selman M, Aranda AU, Park MS, Park JS, Song JW, Molina-Molina M, Planas-Cerezales L, Westergren-Thorsson G, Smith AV, Manichaikul AW, Kim JS, Rich SS, Oelsner EC, Barr RG, Rotter JJ, Dupuis J, O'Connor G, Vasan RS, Cho MH, Silverman EK, Schwarz MI, Steele MP, Lee JS, Yang IV, Fingerlin TE, Schwartz DA, NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium. Idiopathic Pulmonary Fibrosis Is Associated with Common Genetic Variants and Limited Rare Variants. *American journal of respiratory and critical care medicine*. 2023.01; 207(9); 1194-1202
9. Okada K, Sakakibara R, Honda T, Mitsumura T, Shibata S, Shirai T, Okamoto T, Furusawa H, Tateishi T, Miyazaki Y. Tolerability of sotorasib for KRAS positive lung adenocarcinoma patient with pre-existing interstitial pneumonia; A case report. *Respiratory medicine case reports*. 2023; 46; 101929
10. Chida-Nagai A, Masaki N, Maeda K, Sasaki K, Sato H, Muneuchi J, Ochiai Y, Murayama H, Tahara M, Shiono A, Shinozuka A, Kono F, Machida D, Toyooka S, Sugimoto S, Nakamura K, Akagi S, Kondo M, Kasahara S, Kotani Y, Koizumi J, Oda K, Harada M, Nakajima D, Murata A, Nagata H, Yatsunami K, Kobayashi T, Matsunaga Y, Inoue T, Yamagishi H, Nakagawa N, Ohtani K, Yamamoto M, Ito Y, Hosokaki T, Kuwahara Y, Masutani S, Nomura K, Wada T, Sawada H, Abiko M, Takahashi T, Ishikawa Y, Okada S, Naitoh A, Toda T, Ando T, Masuzawa A, Hoshino S, Kawada M, Nomura Y, Ueno K, Ohashi N, Tachibana T, Cao Y, Ueda H, Yanagi S, Koide M, Mitsushita N, Higashi K, Minosaki Y, Hayashi T, Okamoto T, Kuraishi K, Ehara E, Ishida H, Horigome H, Murakami T, Takei K, Ishii T, Harada G, Hirata Y, Maeda J, Tatebe S, Ota C, Hayabuchi Y, Sakazaki H, Sasaki T, Hirono K, Suzuki S, Yasuda M, Takeda A, Sawai M, Miyaji K, Kitagawa A, Nakai Y, Kakimoto N, Agematsu K, Manabe A, Saiki Y. Use of the index of pulmonary vascular disease for predicting long-term outcome of pulmonary arterial hypertension associated with congenital heart disease. *Frontiers in cardiovascular medicine*. 2023; 10; 1212882

Hyperbaric Medical Center

Director and Professor; Kazuyoshi YAGISHITA
Junior Associate Professor ; Takuya OYAIKU (2023.4～)
Assistant Professor ; Takashi HOSHINO
Specially Appointed Assistant Professor ; Masaki AMEMIYA
Senior Resident ; Yasue Niwa(2023.7～), Tatsunobu IKEDA (～2023.6)
Adjunct Lecturer; Yasushi KOJIMA, Toshiyuki OHARA
Researcher; Masaki HORIE, Toshihiro KONDOH, Naohiro MITSUMOTO
Staff Assistant; Kiyomi ITOH

(1) Outline

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in proportion to atmospheric pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute arterial 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 2023, 3,957 times hyperbaric oxygen therapy (HBO) in 330 patients were performed in the university hospital.

(5) Publications

[Original Articles]

1. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Kinesiophobia Is Negatively Associated With Psychological Readiness to Return to Sport in Patients Awaiting Anterior Cruciate Ligament Reconstruction. *Arthroscopy*. 2023.09; 39(9); 2048-2055
2. Atsuyuki Kawabata, Kenichiro Sakai, Kentaro Yamada, Kurando Utagawa, Jun Hashimoto, Shingo Morishita, Yu Matsukura, Takuya Oyaizu, Takashi Hirai, Hiroyuki Inose, Masaki Tomori, Ichiro Torigoe, Hiroaki Onuma, Kazuo Kusano, Kazuyuki Otani, Yoshiyasu Arai, Shigeo Shindo, Atsushi Okawa, Toshitaka Yoshii. The lower Osteotomy Level is Associated With Decreased Revision Surgery Due to Mechanical Complications After Three-Column Osteotomy in Patients With Adult Spinal Deformity: A Multi-Institutional Retrospective Study. *Global Spine J*. 2023.08; 21925682231196449
3. 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. K-Line Tilt is a Predictor of Postoperative Kyphotic Deformity After Laminoplasty for Cervical Myelopathy Caused by Ossification of the Posterior Longitudinal Ligament. *Global Spine J*. 2023.05; 13(4); 1005-1010
4. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. *Orthop Traumatol Surg Res*. 2023.02; 109(1); 103147
5. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Sho Mitomo, Toshiyuki Ohara, Kazuyoshi Yagishita. Biomechanical characteristics of the lower extremities during running in male long-distance runners with a history of medial tibial stress syndrome: a case control study. *BMC Musculoskelet Disord*. 2023.02; 24(1); 103
6. Murofushi Koji, Oshikawa Tomoki, Akuzawa Hiroshi, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Kaneoka Koji, Yagishita Kazuyoshi. Trunk muscle activation in side plank exercises with and without external-focus instruction *ISOKINETICS AND EXERCISE SCIENCE*. 2023; 31(1); 29-36
7. Koji Murofushi, Daisuke Yamaguchi, Koji Kaneoka, Tomoki Oshikawa, Hiroki Katagiri, Kenji Hirohata, Hidetaka Furuya, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity. *J Med Invest*. 2023; 70(1.2); 208-212
8. Kumiko Kasashi, Ayaka Sato, Mark Stuart, Una Hollywood, Marina Kawaguchi-Suzuki, Kazuyoshi Yagishita, Takao Akama. The Tokyo 2020 Olympic and Paralympic pharmacy services during the COVID-19 pandemic. *J Am Pharm Assoc (2003)*. 2023; 63(4); 1156-1161
9. Norihiro Kuroki, Kazuyoshi Yagishita, Keiki Shimizu, Sachiko Okuaki, Yuuri Doi, Yuki Arakawa, Tomotsugu Nakano, Takao Akama. Emergency department activities at the Athletes' Village during the Tokyo 2020 Olympic and Paralympic Games. *Acute Med Surg*. 2023; 10(1); e905

[Conference Activities & Talks]

1. Plasmin activation by tPA or uPA is indispensable for fracture repair.. Orthopaedic Research Society 2023.02.14
2. Progenitor cells derived from iliac crest autograft survive, induce endochondral ossification and contribute to lumbar fusion.. 2023.02.11
1. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19

2. Kaito Togawa, Hiroshi Churei, Kairi Hayashi, Yumi Takahashi, Shintaro Shimizu, Yoko Hotta, Takahisa Haraguchi, Tomohiko Tateishi, Kazuyoshi Yagishita, Gen Tanabe, Toshiaki Ueno. An case of a professional futsal player who is able to continue competitive life by using a custom-made faceguard. 34th congress of Japanese society of clinical sports medicine 2023.11.11
3. Oyaizu T, Kawabata A, Moore-Lotridge S, Egawa S, Yoshii T, Schoenecker J. Progenitor cells derived from iliac crest autograft survive, induce endochondral ossification, and contribute to lumbar fusion.. The 52nd Annual Meeting of the Japanese Society for Spine Surgery and Related Research 2023.04.13

Sports Dentistry

(1) Publications

[Misc]

1. Tanabe G, Ueno T, Li C, Manka-Malara K, K Janicka J, Togawa K, Hayashi K, Churei H, Gonda T, Suzuki H, Nakajima K, Mizuhashi F, Matsumura H, Maeda Y, Yasui T.. Literature review on the advances and applications of digital dentistry in sports mouthguard fabrication. International Journal of Sports Dentistry. 2023.11; 16(1); 15-23

[Conference Activities & Talks]

1. Shimizu S, Hayashi K, Takeuchi Y, Tanabe G, Churei H, Kobayashi H, Ueno T, Fueki K. Effect of Administration of Sonicated P. gingivalis on skeletal muscle injury healing using a rat model. . ECSS Paris 2023 2023.07.04 Paris
1. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Hiroshi Churei, Kenji Fueki. The effect of antigen of periodontitis to sports related muscle reaction. 88th congress of Stomatological society Japan 2023.12.02
2. Yuzuki Komazawa, Gen Tanabe, Tetsuya Hasunuma, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Naoki Moriya, Toshikazu Yasui, Toshiaki Ueno. Assessment of similarity of association between athlete fatigue and subjective oral-maxillofacial symptoms. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
3. Yoko Hotta, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Yumi Takahashi, Shintaro Shimizu, Akihito Kumagai, Norio Hirata, Kazushi Watanabe, Takeshi Negoro, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Questionnaire survey on experiences of maxillofacial trauma during water polo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
4. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
5. Liu Chang, Thida Aung, Kaung Si Thu, Kaito Togawa, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Ryo Sato, Yukio Sasaki, Hiroshi Churei. Effect of CT-slice thickness on defining the maxillofacial fracture area. 2023.11.19
6. Li Chenyuan, Takahiro Wada, Yumi Tsuchida, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Retention force comparison of 3D multiple layer mouthguard and conventional mouthguard via cycle-loading durability fatigue test. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
7. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Zhu Qiushuang, Li Zequn, Gen Tanabe, Hiroshi Churei, Toshiaki Ueno. The effect of P. gingivalis administration to PGC-1 α and TNF α expression in skeletal muscle after endurance training in vivo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
8. Y. Ohara, H. Churei, S. Makino, K. Hayashi, G. Tanabe, G. Kondo, A. Nagai, C. Ichihara, W. Oguchi, T. Ueno. A survey of blind soccer players' attitudes before and after mouthguard use. The 34th Annual Meeting of the Japanese Society of Sports Dentistry 2023.11.19

9. Kaito Togawa, Hiroshi Churei, Kairi Hayashi, Yumi Takahashi, Shintaro Shimizu, Yoko Hotta, Takahisa Haraguchi, Tomohiko Tateishi, Kazuyoshi Yagishita, Gen Tanabe, Toshiaki Ueno. An case of a professional futsal player who is able to continue competitive life by using a custom-made faceguard. 34th congress of Japanese society of clinical sports medicine 2023.11.11
10. Shintaro Shimizu, Gen Tanabe, Tatsuhiko Anzai, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Kunihiro Takahashi, Toshiaki Ueno . Corresponding analysis of sports injury of school life using text mining method. 24th congress of The Japanese Association of Safety Education 2023.09.09
11. C. Liu, K. Hayashi, K. Togawa, Y. Takahashi, S. Shimizu, A. Kumagai, H. Churei. Dental Diseases and Treatments for Patient Education. The 7th Annual Congress of Japanes Society of Medical illustration 2023.03.05
12. C. Liu, K. Hayashi, K. Togawa, Y. Takahashi, S. Shimizu, A. Kumagai, H. Churei. Mouthguards and faceguards for sports. The 7th Annual Congress of Japanes Society of Medical illustration 2023.03.05
13. Kairi Hayashi. Sports Dentistry of Tokyo Medical and Dental University. Seminar of clinical sports dentist course in Aichi Dental Association 2023.03.04

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 : Naoto Aoyama

(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 physiological function tests to not only the medical students and medical technologist students in the faculty of medicine of the university but also those in the other vocational school for medical technologists. We give a labo tour and practice to master course graduate students, too. We gave a general training for clinical laboratory medicine to 15 junior residents of university hospital in 2023.

(4) Clinical Services & Other Works

Clinical laboratory bears an important responsibility for advanced and high quality medical care. Our clinical laboratory is based on the principle of providing the speedy and high quality tests. The highest level of advanced tests, such as qualitative and quantitative analysis of various viral DNA by the PCR method, are also introduced here. In the night time and holidays, the clinical laboratory provides blood products for transfusion in cooperation with the blood transfusion service of the hospital. The updated information on antibiotic sensitivity of the pathogens in each ward is also provided online regularly. Together with the division of infection control and prevention, we monitor the nosocomial transmission of bacteria such as MRSA by genotypic analysis of those. Our clinical laboratory and blood transfusion service have received accreditation of ISO15189 (Medical laboratories - Particular requirements for quality and competence) in June 2014, and renewed it with the latest version in June 2018. It means that the clinical laboratory is an international standard on quality and that our hospital is allowed to conduct the international clinical trials. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

(5) Clinical Performances

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

(6) Publications

[Original Articles]

1. Azusa Yamazaki, Yoko Nukui, Takahiro Kameda, Ryoichi Saito, Yuki Koda, Naoya Ichimura, Shuji Tohda, Ryunosuke Ohkawa. Variation in presepsin and thrombomodulin levels for predicting COVID-19 mortality. *Sci Rep.* 2023.12; 13(1); 21493
2. Noguchi K, Itoh M, Ito C, Tohda S. Effects of MYC Inhibitors on the Growth of Acute Leukaemia Cells. *Anticancer research.* 2023.07; 43(7); 3023-3028

[Conference Activities & Talks]

1. Miyakoshi T., Horiuchi Y., Araki M., Yonetsu T., Watanabe M., Nakamura M., Kameda T., Yoshimoto A., Ichimura N., Tohda S., Tozuka M., Sasano T., Ohkawa R. Association between CEC measured by immobilized liposome-bound gel beads method and the size of lipid-rich coronary artery plaque. Scientific Session of the American Heart Association 2023.11.09
2. Haruka Kumada, Mai Itoh, and Shuji Tohda. Effects of ferroptosis inducers and inhibitors on growth of acute leukemia cells. 52nd annual scientific meeting, International Society of Experimental Hematology 2023.08.19
3. Mai Itoh, Shuji Tohda. Renin-angiotensin system inhibitors suppress the growth of leukemia cells. 52nd annual scientific meeting, International Society of Experimental Hematology 2023.08.19 New York
4. Miyakoshi T., Mutsuda Y., Horiuchi Y., Kameda T., Tozuka M., Ohkawa R. Application of bilirubin oxidase for improvement of false positive error caused by bilirubin on cholesterol efflux capacity assay by immobilize liposome-bound gel beads method. American Association for Clinical Chemistry (AACC) 2023 AACC Annual Scientific Meeting & Clinical Lab Expo 2023.07.24 Anaheim
1. Ayako Nogami, Morito Kurata, Towako Taguchi, Shomi Koyama, Katsutoshi Nagano, Keisuke Tanaka, Kota Yoshifuji, Yoshihiro Umezawa, Naoya Ichimura, Shuji Tohda, and Takehiko Mori. Efficacy of pathological method of identifying causative virus of hemorrhagic cystitis by cell block. The 85th Annual Meeting of the Japanese Society of Hematology 2023.10.13 Tokyo
2. Momoko Chiba, Keisuke Tanaka, Fumihiko Ouchi, Marie Yagi, Hikari Kanai, Takuma Harada, Hiroki Hatsuzawa, Kota Yoshifuji, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Chizuko Sakashita, Toshikage Nagao, Takehiko Mori, Masahide Yamamoto. Evaluation of autologous stem cell transplantation using busulfan-containing conditioning for central nervous system lymphoma. 5th JSTCT Annual Meeting Japanese Society for Transplantation and Cellular Therapy 2023.02.11 Nagoya

Sports Medicine Center

Director and Professor; Kazuyoshi YAGISHITA
Assistant Professor ; Takashi HOSHINO
Specially Appointed Assistant Professor ; Masaki AMEMIYA
Head Physical Therapist ; Kenji HIROHATA
Physical Therapist ; Takehiro OHMI, Shunsuke OHJI, Tomoko KASAKI
Adjunct Lecturer ; Tomohiko TATEISHI, Sho MITOMO
Staff Assistant; Kiyomi ITOH

(1) Publications

[Original Articles]

1. Hao Ding, Hideyuki Koga, Hiroki Katagiri, Shoichi Hasegawa, Tatushiko Anzai, Mai Katakura, Aritoshi Yoshihara, Masaki Amemiya, Takashi Hoshino, Nobutake Ozeki, Tomomasa Nakamura, Yusuke Nakagawa. Low central sensitisation inventory score is associated with better post-operative outcomes of osteotomy around the knee. *Knee Surg Sports Traumatol Arthrosc.* 2023.12; 31(12); 5896-5904
2. Ryuichi Nakamura, Fumiyoshi Kawashima, Masaki Amemiya, Tomoyuki Shimakawa, Akira Okano. Double-Row Root Repair with Bridging Centralization Using Double Nonsliding Anchors for Medial Meniscus Posterior Root Tear. *Arthrosc Tech.* 2023.10; 12(10); e1751-e1756
3. Ryuichi Nakamura, Fumiyoshi Kawashima, Masaki Amemiya, Tomoyuki Shimakawa, Akira Okano. Derotational Hybrid Closed-Wedge High Tibial Osteotomy for Knee Osteoarthritis With Patellar Subluxation Caused by Tibial Torsional Deformity. *Arthrosc Tech.* 2023.10; 12(10); e1687-e1694
4. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Kinesiophobia Is Negatively Associated With Psychological Readiness to Return to Sport in Patients Awaiting Anterior Cruciate Ligament Reconstruction. *Arthroscopy.* 2023.09; 39(9); 2048-2055
5. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. *Orthop Traumatol Surg Res.* 2023.02; 109(1); 103147
6. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Sho Mitomo, Toshiyuki Ohara, Kazuyoshi Yagishita. Biomechanical characteristics of the lower extremities during running in male long-distance runners with a history of medial tibial stress syndrome: a case control study. *BMC Musculoskelet Disord.* 2023.02; 24(1); 103
7. Ryuichi Nakamura, Masaki Amemiya, Fumiyoshi Kawashima, Akira Okano. Flexion Contracture in Knee Osteoarthritis Can Be Fully Eliminated by Hybrid Closed Wedge High Tibial Osteotomy Using a Reduction-Insertion-Compression Handle. *Arthrosc Tech.* 2023.02; 12(2); e247-e253
8. Murofushi Koji, Yamaguchi Daisuke, Kaneoka Koji, Oshikawa Tomoki, Katagiri Hiroki, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. KOJI AWARENESS スコアおよび活動関連疼痛強度に対する矯正エクササイズの効果 (The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity) *The Journal of Medical Investigation.* 2023.02; 70(1-2); 208-212

9. Ryuichi Nakamura, Masaki Amemiya, Tomoyuki Shimakawa, Masaki Takahashi, Kazunari Kuroda, Yasuo Katsuki, Akira Okano. Femoral-varus tibial-valgus osteotomy (FVTVO) for neutrally-aligned knee osteoarthritis with severe joint line obliquity enables return to sports activities: A case series study. *Asia Pac J Sports Med Arthrosc Rehabil Technol.* 2023.01; 31; 11-17
10. Murofushi Koji, Oshikawa Tomoki, Akuzawa Hiroshi, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Kaneoka Koji, Yagishita Kazuyoshi. Trunk muscle activation in side plank exercises with and without external-focus instruction *ISOKINETICS AND EXERCISE SCIENCE.* 2023; 31(1); 29-36
11. Koji Murofushi, Daisuke Yamaguchi, Koji Kaneoka, Tomoki Oshikawa, Hiroki Katagiri, Kenji Hirohata, Hidetaka Furuya, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity. *J Med Invest.* 2023; 70(1.2); 208-212
12. Kumiko Kasashi, Ayaka Sato, Mark Stuart, Úna Hollywood, Marina Kawaguchi-Suzuki, Kazuyoshi Yagishita, Takao Akama. The Tokyo 2020 Olympic and Paralympic pharmacy services during the COVID-19 pandemic. *J Am Pharm Assoc (2003).* 2023; 63(4); 1156-1161
13. Norihiro Kuroki, Kazuyoshi Yagishita, Keiki Shimizu, Sachiko Okuaki, Yuuri Doi, Yuki Arakawa, Tomotsugu Nakano, Takao Akama. Emergency department activities at the Athletes' Village during the Tokyo 2020 Olympic and Paralympic Games. *Acute Med Surg.* 2023; 10(1); e905

[Conference Activities & Talks]

1. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
2. Kaito Togawa, Hiroshi Churei, Kairi Hayashi, Yumi Takahashi, Shintaro Shimizu, Yoko Hotta, Takahisa Haraguchi, Tomohiko Tateishi, Kazuyoshi Yagishita, Gen Tanabe, Toshiaki Ueno. An case of a professional futsal player who is able to continue competitive life by using a custom-made faceguard. 34th congress of Japanese society of clinical sports medicine 2023.11.11

[Awards & Honors]

1. Honorable Mention Award 2022, Society of Physical Therapy Science, 2023.05

Center for Transfusion Medicine and Cell Therapy

Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine/Professor)
Vise Director: Hisako Katano (Center for Stem Cell and Regenerative Medicine/Junior Associate Professor)
until Mar 31, 2023
Vise Director: Hisako Katano (Center for Stem Cell and Regenerative Medicine/ Associate Professor)
from Apr 1, 2023
Vise Director: Michiko Kajiware (Center for Transfusion Medicine and Cell Therapy/Junior Associate Professor)
Quality control manager: Norio Shimizu (Center for Stem Cell and Regenerative Medicine/Associate Professor)
until Mar 31, 2023
Quality control manager: Hisako Katano (Center for Stem Cell and Regenerative Medicine/ Associate Professor)
from Apr 1, 2023
Product manager: Mitsuru Mizuno (Center for Stem Cell and Regenerative Medicine/Project Assistant Professor)
until Apr 30, 2023
Product manager: Mitsuru Mizuno (Center for Stem Cell and Regenerative Medicine/ Assistant Professor)
from May 1, 2023
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
Assistant Section Chief Medical Technologist: Yukiko Ohishi, Chihiro Itoh
Medical Technologist: Tomoko Kamiyama, Misaki Chiba, Akiko Shiraishi, Sumire Fujiki, Akemi Fukuoka,
Nozomi Oda, Eriko Okazaki, Fuka Hirose, Mayumi Yoshimori
Technician: Ayako Tsuji, Yuri Kohno
Clerical Assistant: Jun Kusano, Yuka Shinkai

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 staffs, and cell therapy certified administrators enroll. We cover blood transfusion testing, blood product management, safety measures up to the implementation of blood transfusion including blood transfusion certification, and blood transfusion history management. We perform safe and appropriate blood transfusion therapy and hematopoietic stem cell transplantation.
In the Cell Therapy group, we set up a cell processing facility with the aim of putting the world’s top level of regenerative medicine and cell therapy into practical use. Japan Society of Regenerative Medicine certified doctors and clinical culture specialists process cells for clinical research and trials there. We support the practical application of useful regenerative medicine procedures inside and outside our university.

2) Research

Blood Transfusion group

- .) The practice of safe and appropriate transfusion therapy
(Including prevention of medical accident related transfusion)
- .) Basic and clinical research of hematopoietic stem cell transplantation

· Cell Therapy group

- 1) Development of multi-virus specific T lymphocytes for adoptive immunotherapy
(Department of Pediatrics and Developmental Biology)
- 2) Research on a regeneration system of the cartilage from the synovial membrane
(Department of Orthopedic Surgery)
- 3) Development of organoid-based therapy for inflammatory bowel disease
(Department of Gastroenterology & Hepatology, Advanced Research Institute)
- 4) Promote the development of infrastructure for cell culture processing support
- 5) Development of a novel measure for rapid and sensitive detection of multiple pathogens

(3) Education

· Blood Transfusion group

Transfusion therapy is supplementation of the blood component, but it also has aspects of cell therapy and transplantation. So, it is important to practice safe and appropriate transfusion therapy. Clinical tests of transfusion, such as blood type test, are the most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of the medical treatment. From this point of view, we educate the students of the school of medicine, school of allied health sciences, a graduate school of medical and dental sciences, medical doctors, and co-medicals.

· Cell Therapy group

Center of Cell Therapy assist to prepare standard operation procedure (SOP) and offer on-the-job training for cell processing/ manipulating procedures and that for quality assurance at the center. Facility for the education and training were recently installed at the CPC annex.

(4) Clinical Services & Other Works

· Blood Transfusion services (The result of 2023)

- 1) The number of blood products used
Red cell component products 11,145Units (5,635 bags)
Platelet concentration 27,245 Units (2,311 bags)
Fresh frozen plasma 7,152 Units (3,414 bags)
Allogenic cryoprecipitate 928 Units (232 bags)
- 2) Autologous blood collection and transfusion
Autologous blood collection 186 cases (238 times, 468Units)
Autologous blood transfusion 162 cases (389 Units)
Autologous cryoprecipitate preparation 50 cases, administration 50 cases
- 3) The number of clinical tests of transfusion
Blood typing 10,521
Anti-red blood cell antibody test 7,542
Crossmatch tests 8,558

· Cell Therapy services (The result of 2023)

- 1) Hematopoietic stem cell harvest
Autologous peripheral blood stem cell harvest 8 cases 9 times
Allogenic peripheral blood stem cell harvest 3 cases 3 times
Allogenic bone marrow harvest 10 cases 10 times (Including Japan Marrow Donor Program donors)
- 2) Hematopoietic stem cell transplantation
(The evaluation and preservation of the stem cells were done in our department)
Autologous peripheral blood stem cell transplantation 5 cases 5 times
Allogenic peripheral blood stem cell transplantation 3 cases 3 times
Allogenic bone marrow transplantation 10 cases 10 times
Allogenic umbilical cord blood transplantation 4 case 4 time
- 3) CAR-T therapy
Obtained Kymriah facility certification at the end of October 2019
2023 Autologous peripheral blood mononuclear cell collection 12 cases 12 times

Tisagen Reclucell administration 10 cases 10 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: 8 cases 12 times

#4 Autologous Protein Solution (APS: concentrated Platelet-Rich Plasma) for the hips: 10 cases 10 times

#5 GPS III Platelet Concentration System (PRP for the extraarticular tissues): 7 cases 7 times

#6 Organoid-based therapy for inflammatory bowel disease 2 cases 2 times

#7 Third-party derived multiple virus specific T-cell therapy for virus infection 4 times

(5) Clinical Performances

· Blood Transfusion group

We provide safe and wide of variation transfusion therapy. We cope with highly urgent blood transfusion of critical care center and blood transfusion with a high specialty such as NICU. In the area of hematopoietic stem cell transplantation, we closely cooperate with the clinical department. Transfusion medicine staffs mainly conduct collection, evaluation, processing, and storage of cells.

· Cell Therapy group

Our center in TMDU Medical Hospital was renovated and re-started operation as of March 2015. We have five independent cell processing rooms (class 10,000 clean rooms). All the rooms are equipped with a bio-safety cabinet. The hardware, as well as software used in our center, fulfills all the guidelines that are required for the preparation of cell products of clinical grade.

(6) Publications

[Original Articles]

1. Mitsuru Mizuno, Koki Abe, Takashi Kakimoto, Keiichi Yano, Yukiko Ota, Kengo Tomita, Naoki Kagi, Ichiro Sekiya. Volatile organic compounds and ionic substances contamination in cell processing facilities during rest period; a preliminary assessment of exposure to cell processing operators. *Regen Ther.* 2023.12; 24; 211-218
2. Hisako Katano, Nobutake Ozeki, Mitsuru Mizuno, Kentaro Endo, Noriya Okanouchi 1,2, Jo Fujita, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya. Morphological analysis of three-dimensional MR images of patellofemoral joints in asymptomatic subjects *Sci Rep.* 2023.12; 13(1); 16570
3. 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.* 2023.11; 28(6); 1325-1330
4. Zhen Qu, Hideyuki Koga, Kunikazu Tsuji, Guo Tang, Yang Yang, Aritoshi Yoshihara, Mai Katakura, Hiroki Katagiri, Kazumasa Miyatake, Tomomasa Nakamura, Ichiro Sekiya, Yusuke Nakagawa. Hyaluronic acid sheet transplantation attenuates infrapatellar fat pad fibrosis and pain in a rat arthritis model. *J Orthop Res.* 2023.11; 41(11); 2442-2454
5. Ichiro Sekiya, Hisako Katano, Ali Guermazi, Yugo Miura, Noriya Okanouchi, Makoto Tomita, Jun Masumoto, Yoshio Kitazume, Hideyuki Koga, Nobutake Ozeki. Association of AI-determined Kellgren-Lawrence grade with medial meniscus extrusion and cartilage thickness by AI-based 3D MRI analysis in early knee osteoarthritis. *Sci Rep.* 2023.11; 13(1); 20093
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9. Hideto Furuoka, Kentaro Endo, Ichiro Sekiya. Mesenchymal stem cells in synovial fluid increase in number in response to synovitis and display more tissue-reparative phenotypes in osteoarthritis. *Stem Cell Res Ther.* 2023.09; 14(1); 244
10. Shoichi Hasegawa, Yusuke Nakagawa, Aritoshi Yoshihara, Tomomasa Nakamura, Hiroki Katagiri, Masaya Hayashi, Hideya Yoshimura, Tsuyoshi Nagase, Ichiro Sekiya, Hideyuki Koga. Older Age, Poor Preoperative Quadriceps Muscle Strength, and Residual Pain as Risk Factors for Poor Quadriceps Muscle Strength Recovery at 1 Year After ACL Reconstruction: A TMDU MAKS Study of 402 Patients. *Orthop J Sports Med.* 2023.09; 11(9); 23259671231194593
11. Hiroki Katagiri, Yusuke Nakagawa, Yusuke Amano, Yoshiko Shirakawa, Nobutake Ozeki, Tomomasa Nakamura, Ichiro Sekiya, Hideyuki Koga. Decision regret following opening wedge high tibial osteotomy: Older age as a risk factor. *Knee.* 2023.06; 43; 62-69
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13. Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Nobutake Ozeki, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga. Comparison of Clinical Outcomes after Revision Anterior Cruciate Ligament Reconstruction using a Bone-patellar Tendon-bone Autograft and that Using a Double-Bundle Hamstring Tendon Autograft. *J Knee Surg.* 2023.05; 36(6); 613-621
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15. Misaki Yagi, Kentaro Endo, Keiichiro Komori, Ichiro Sekiya. Comparison of the effects of oxidative and inflammatory stresses on rat chondrocyte senescence. *Sci Rep.* 2023.05; 13(1); 7697
16. Yusuke Nakagawa, Kunikazu Tsuji, Tomomasa Nakamura, Hiroki Katagiri, Nobutake Ozeki, Mikio Shioda, Jae-Sung An, Ryu Yoshida, Ichiro Sekiya, Hideyuki Koga. Association of Infrapatellar Fat Pad Fibrosis at 3 Months After ACL Reconstruction With Short-term Clinical Outcomes and Inflammatory Cytokine Levels in the Synovial Fluid. *Orthop J Sports Med.* 2023.04; 11(4); 23259671231164122
17. Dan Tomomasa, Takeshi Isoda, Noriko Mitsuiki, Kento Inoue, Akira Nishimura, Kazuhiro Uda, Toru Uchiyama, Motoi Yamashita, Takahiro Kamiya, Akifumi Endo, Masatoshi Takagi, Kohsuke Imai, Michiko Kajiwarra, Morton J Cowan, Tomohiro Morio, Hirokazu Kanegane. Successful TCR $\alpha \beta$ /CD19-Depleted Hematopoietic Cell Transplantation for a Patient With Artemis Deficiency. *J Pediatr Hematol Oncol.* 2023.03; 45(2); e285-e289
18. Ozeki N, Mizuno M, Yanada S, Okada T, Kubota R, Kushida Y, Furuoka H, Endo K, Katano H, Nakamura K, Ohya S, Koga H, Sekiya I. Autologous Synovial Mesenchymal Stem Cell Transplantation Suppresses Inflammation Caused by Synovial Harvesting and Promotes Healing in a Micro Minipig Repaired Meniscus Model. *Transplantation proceedings.* 2023.03; 55(2); 470-480
19. Mizuno M, Matsuda J, Watanabe K, Shimizu N, Sekiya I. Effect of disinfectants and manual wiping for processing the cell product changeover in a biosafety cabinet. *Regenerative therapy.* 2023.03; 22; 169-175
20. M Isono, H Koga, Y Nakagawa, T Nakamura, I Sekiya, H Katagiri. Inferior Healing Rate in Isolated Meniscal Repair than that in Meniscal Repair with Concomitant ACL Reconstruction Evaluated with MRI. *Malays Orthop J.* 2023.03; 17(1); 61-69

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22. Hiroki Katagiri, Yusuke Nakagawa, Kazumasa Miyatake, Toshiyuki Ohara, Mikio Shioda, Ichiro Sekiya, Hideyuki Koga. Short-Term Outcomes after High Tibial Osteotomy Aimed at Neutral Alignment Combined with Arthroscopic Centralization of Medial Meniscus in Osteoarthritis Patients. *J Knee Surg*. 2023.02; 36(3); 261-268
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24. Akane Ariga, Yuji Kohno, Yusuke Nakagawa, Toshifumi Watanabe, Hiroki Katagiri, Toshiyuki Ohara, Mikio Shioda, Nobutake Ozeki, Masaki Amemiya, Atsushi Okawa, Ichiro Sekiya, Hideyuki Koga. Simultaneous bilateral total knee arthroplasty is safe and effective for patients in different ages. *J Orthop Sci*. 2023.01; 28(1); 173-179

Clinical Center for Sports Medicine and Sports Dentistry

Clinical Center of Sports Medicine
Director and Professor ; Kazuyoshi YAGISHITA
Junior Associate Professor ; Shunsuke TAKAGI
Assistant Professor; Takashi HOSHINO
Specially Appointed Assistant Professor ; Masaki AMEMIYA
Chief Physiotherapist; Kenji HIROHATA
Physiotherapist; Takehiro OHMI, Shunsuke OHJI, Tomoko KAWASAKI
Staff Assistant; 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

○ 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.
- Soft tissue injuries related with sports activities.

○ Sports Medicine/Dentistry

- 1) Oral health promotion of athletes and sports-active people
- 1)-a Field survey of oral health conditions in athletes and sports-active people
- 1)-b Changes of oral environment associated with physical and sporting activities
- 1)-c Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
- 2)-a Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
- 2)-b Development and innovation of sports mouthguard
- 2)-c Development and innovation of sports faceguard
- 2)-d Development and innovation of scuba diving mouthpiece
- 3) Correlations between occlusion and general motor functions

- 3)-a Biomechanical assessment of motor performance associated with occlusion
- 3)-b Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

(3) Clinical Services & Other Works

Center of Sports Medicine and Sports Dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered traumatic injuries, overuse disorders, disorders related with internal medicine, and dental diseases.

○ Clinical Center of Sports Medicine

Number of patients (From January 2023 to December 2023)

Section of out-patient clinic: 2,162

Section of physiotherapy: 3,986

○ 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

[Original Articles]

1. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. Kinesiophobia Is Negatively Associated With Psychological Readiness to Return to Sport in Patients Awaiting Anterior Cruciate Ligament Reconstruction. *Arthroscopy*. 2023.09; 39(9); 2048-2055
2. Naoki Yamamoto, Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Naoto Watanabe, Hideyuki Koga, Toshitaka Yoshii, Kazuyoshi Yagishita, Atsushi Okawa. Wear rate and osteolysis in two types of second-generation annealed highly cross-linked polyethylene in total hip arthroplasty: A retrospective comparative study with a minimum of five years. *Orthop Traumatol Surg Res*. 2023.02; 109(1); 103147
3. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Sho Mitomo, Toshiyuki Ohara, Kazuyoshi Yagishita. Biomechanical characteristics of the lower extremities during running in male long-distance runners with a history of medial tibial stress syndrome: a case control study. *BMC Musculoskelet Disord*. 2023.02; 24(1); 103
4. Murofushi Koji, Yamaguchi Daisuke, Kaneoka Koji, Oshikawa Tomoki, Katagiri Hiroki, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Koga Hideyuki, Yagishita Kazuyoshi. KOJI AWARENESS スコアおよび活動関連疼痛強度に対する矯正エクササイズの効果 (The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity) *The Journal of Medical Investigation*. 2023.02; 70(1-2); 208-212
5. Murofushi Koji, Oshikawa Tomoki, Akuzawa Hiroshi, Yamaguchi Daisuke, Hirohata Kenji, Furuya Hidetaka, Mitomo Sho, Kaneoka Koji, Yagishita Kazuyoshi. Trunk muscle activation in side plank exercises with and without external-focus instruction *ISOKINETICS AND EXERCISE SCIENCE*. 2023; 31(1); 29-36
6. Koji Murofushi, Daisuke Yamaguchi, Koji Kaneoka, Tomoki Oshikawa, Hiroki Katagiri, Kenji Hirohata, Hidetaka Furuya, Sho Mitomo, Hideyuki Koga, Kazuyoshi Yagishita. The effectiveness of corrective exercises on the KOJI AWARENESS score and activity-related pain intensity. *J Med Invest*. 2023; 70(1.2); 208-212
7. Kumiko Kasashi, Ayaka Sato, Mark Stuart, Úna Hollywood, Marina Kawaguchi-Suzuki, Kazuyoshi Yagishita, Takao Akama. The Tokyo 2020 Olympic and Paralympic pharmacy services during the COVID-19 pandemic. *J Am Pharm Assoc (2003)*. 2023; 63(4); 1156-1161

8. Norihiro Kuroki, Kazuyoshi Yagishita, Keiki Shimizu, Sachiko Okuaki, Yuuri Doi, Yuki Arakawa, Tomotsugu Nakano, Takao Akama. Emergency department activities at the Athletes' Village during the Tokyo 2020 Olympic and Paralympic Games. *Acute Med Surg.* 2023; 10(1); e905

[Misc]

1. Tanabe G, Ueno T, Li C, Manka-Malara K, K Janicka J, Togawa K, Hayashi K, Churei H, Gonda T, Suzuki H, Nakajima K, Mizuhashi F, Matsumura H, Maeda Y, Yasui T.. Literature review on the advances and applications of digital dentistry in sports mouthguard fabrication. *International Journal of Sports Dentistry.* 2023.11; 16(1); 15-23

[Conference Activities & Talks]

1. Sentaro Koshida, Takanori Ishii, Hiroshi Churei, Hiroshi Kubota. MEASUREMENT OF HEAD IMPACTS DURING ACTUAL JUDO PRACTICE IN COLLEGE JUDOKAS: A PRELIMINARY STUDY. International Society of Biomechanics Congress 2023 2023.07.31 Fukuoka
2. Shimizu S, Hayashi K, Takeuchi Y, Tanabe G, Churei H, Kobayashi H, Ueno T, Fueki K. Effect of Administration of Sonicated P. gingivalis on skeletal muscle injury healing using a rat model. . ECSS Paris 2023 2023.07.04 Paris
1. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Hiroshi Churei, Kenji Fueki. The effect of antigen of periodontitis to sports related muscle reaction. 88th congress of Stomatological society Japan 2023.12.02
2. Yuzuki Komazawa, Gen Tanabe, Tetsuya Hasunuma, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Naoki Moriya, Toshikazu Yasui, Toshiaki Ueno. Assessment of similarity of association between athlete fatigue and subjective oral-maxillofacial symptoms. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
3. Yoko Hotta, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Yumi Takahashi, Shintaro Shimizu, Akihito Kumagai, Norio Hirata, Kazushi Watanabe, Takeshi Negoro, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Questionnaire survey on experiences of maxillofacial trauma during water polo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
4. Hiroshi Churei, Hiromi Yoshida, Maya Sugii, Kouta Tsuge, Yuko Sase, Masashi Nagata, Kairi Hayashi, Kaito Togawa, Sachiko Fujino, Kazuyoshi Yagishita. Information sharing on the intraoral local use of glucocorticoids. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
5. Liu Chang, Thida Aung, Kaung Si Thu, Kaito Togawa, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Ryo Sato, Yukio Sasaki, Hiroshi Churei. Effect of CT-slice thickness on defining the maxillofacial fracture area. 2023.11.19
6. Li Chenyuan, Takahiro Wada, Yumi Tsuchida, Kairi Hayashi, Gen Tanabe, Toshiaki Ueno, Hiroshi Churei. Retention force comparison of 3D multiple layer mouthguard and conventional mouthguard via cycle-loading durability fatigue test. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
7. Kairi Hayashi, Shintaro Shimizu, Yasuo Takeuchi, Hiroaki Kobayashi, Zhu Qiushuang, Li Zequn, Gen Tanabe, Hiroshi Churei, Toshiaki Ueno. The effect of P. gingivalis administration to PGC-1 α and TNF α expression in skeletal muscle after endurance training in vivo. 34th congress of Japan Academy of Sports Dentistry 2023.11.19
8. Y. Ohara, H. Churei, S. Makino, K. Hayashi, G. Tanabe, G. Kondo, A. Nagai, C. Ichihara, W. Oguchi, T. Ueno. A survey of blind soccer players' attitudes before and after mouthguard use. The 34th Annual Meeting of the Japanese Society of Sports Dentistry 2023.11.19
9. Kaito Togawa, Hiroshi Churei, Kairi Hayashi, Yumi Takahashi, Shintaro Shimizu, Yoko Hotta, Takahisa Haraguchi, Tomohiko Tateishi, Kazuyoshi Yagishita, Gen Tanabe, Toshiaki Ueno. An case of a professional futsal player who is able to continue competitive life by using a custom-made faceguard. 34th congress of Japanese society of clinical sports medicine 2023.11.11
10. Shintaro Shimizu, Gen Tanabe, Tatsuhiko Anzai, Kaito Togawa, Kairi Hayashi, Hiroshi Churei, Kunihiro Takahashi, Toshiaki Ueno. Corresponding analysis of sports injury of school life using text mining method. 24th congress of The Japanese Association of Safety Education 2023.09.09

11. C. Liu, K. Hayashi, K. Togawa, Y. Takahashi, S. Shimizu, A. Kumagai, H. Churei. Dental Diseases and Treatments for Patient Education. The 7th Annual Congress of Japanes Society of Medical illustration 2023.03.05
12. C. Liu, K. Hayashi, K. Togawa, Y. Takahashi, S. Shimizu, A. Kumagai, H. Churei. Mouthguards and faceguards for sports. The 7th Annual Congress of Japanes Society of Medical illustration 2023.03.05

[Awards & Honors]

1. Honorable Mention Award 2022, Society of Physical Therapy Science, 2023.05

Center for Experimental Animals

Professor Masami Kanai
 Junior Associate Professor Yoshikazu Hirate
 Assistant Professor Naoaki Mizuno
 Assistant Professor Toru Suzuki
 Part-time lecturer Fumitoshi Ishino
 Part-time lecturer Hikaru Ito
 Part-time lecturer Tsutomu Endo
 graduate student Hiroshi Yomokida

(1) Publications

[Original Articles]

1. Ishino F, Itoh J, Irie M, Matsuzawa A, Naruse M, Suzuki T, Hiraoka Y, Kaneko-Ishino T.. Retrovirus-Derived RTL9 Plays an Important Role in Innate Antifungal Immunity in the Eutherian Brain International Journal of Molecular Sciences. 2023.10; 24(19); 14884
2. Mayuko Kano, Naoaki Mizuno, Hideyuki Sato, Takaharu Kimura, Rei Hirochika, Yasumasa Iwasaki, Naoko Inoshita, Hisato Nagano, Mariko Kasai, Hiromi Yamamoto, Tomoyuki Yamaguchi, Hidetaka Suga, Hideki Masaki, Eiji Mizutani, Hiromitsu Nakauchi. Functional calcium-responsive parathyroid glands generated using single-step blastocyst complementation. Proc Natl Acad Sci U S A. 2023.07; 120(28); e2216564120
3. Maki Asami, Brian Y H Lam, Martin Hoffmann, Toru Suzuki, Xin Lu, Naoko Yoshida, Marcella K Ma, Kara Rainbow, Miodrag Gužvić, Matthew D VerMilyea, Giles S H Yeo, Christoph A Klein, Anthony C F Perry. A program of successive gene expression in mouse one-cell embryos. Cell Rep. 2023.01; 42(2); 112023
4. Ito M, Ito H, Miyoshi K, Kanai-Azuma M. Chronic non-discriminatory social defeat stress during the perinatal period induces depressive-like outcomes in female mice. Brain Res. 2023.12; 1825; 148734
5. Maruyama N, Fukunaga I, Kogo T, Endo T, Fujii W, Kanai-Azuma M, Naito K, Sugiura K. Accumulation of senescent cells in the stroma of aged mouse ovary. J Reprod Dev. 2023.12; 69(6); 328-336
6. Melig G, Nobuhisa I, Saito K, Tsukahara R, Itabashi A, Kanai Y, Kanai-Azuma M, Osawa M, Oshima M, Iwama A, Taga T. A Sox17 downstream gene Rasip1 is involved in the hematopoietic activity of intra-aortic hematopoietic clusters in the midgestation mouse embryo. Inflamm Regen. 2023.08; 43(1); 41
7. Yomogita H, Ito H, Hashimoto K, Kudo A, Fukushima T, Endo T, Hirate Y, Akimoto Y, Komada M, Kanai Y, Miyasaka N, Kanai-Azuma M. A possible function of Nik-related kinase in the labyrinth layer of delayed delivery mouse placentas. J Reprod Dev. 2023.02; 69(1); 32-40

[Conference Activities & Talks]

1. Takami S, Uemura M, Miyazaki N, Oiki H, Yoshioka T, Nakazawa A, Higashi M, Kanai-Azuma M, Kanai Y, Fujishiro J. Gallbladder wall with reduced Sox17 expression in biliary atresia: gallbladder-dependent hepatic damage and its better prognosis.. The Pacific Association of Pediatric Surgeons 56th Annual Meeting 2023.09.10 The Westin Hotel Nusa Dua Bali または Online

2. Ito H, Ito M, Miyoshi K, Kanai-Azuma M. Development of a novel depression model in female mice.. The 46th Annual Meeting of the Japan Neuroscience Society 2023.08.01 Sendai International Center
3. Gerel Melig,ikuo Nobuhisa,Kiyoka Saito,Ryota Tsukahara,Ayumi Itabashi,Yoshiakira Kanai,Masami Kanai-Azuma,Tetsuya Taga. Rasip1 helps maintenance of hematopoietic activities of mouse embryonic intra-aortic hematopoietic clusters.. The 44th Annual Meeting of the Japanese Society of Inflammation and Regeneration 2023.07.12 City Plaza Osaka
4. Gerel Melig,ikuo Nobuhisa,Kiyoka Saito,Ryota Tsukahara,Ayumi Itabashi,Yoshiakira Kanai,Masami Kanai-Azuma,Tetsuya Taga. Rasip1 gene functioning downstream of Sox17 maintains the hematopoietic cluster-forming cells in E10.5 mouse embryos.. 20th Stem Cell Symposium 2023.05.19 Awaji Yumebutai International Conference Center