生命医科学域

Anatomy and Embryology

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Major Scientific Interests of the Group

We are working on the functional analysis of transcription factors in the body by employing developmental engineering techniques such as the generation of transgenic mice.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanism of the development of pancreatic endocrine cells and macrophages. We are researching the molecular mechanisms of the development of pancreatic endocrine cells and macrophages by analyzing the function of the large Maf family of transcription factors. In both human and mouse, four large Maf transcription factors, MafA, MafB, c-Maf and Nrl, have been identified.
2) Analysis about in vivo functions of sugar chains on molecules. In addition to these themes, we are also analyzing functions of sugar chains on molecules in vivo by using genetically manipulated mice.

Study Programs for Short Stay Students (one week – one trimester)

1) Histological analysis of genetically manipulated mice.
2) Handling skill for mouse embryos.

Selected Publications

1) Tran MTN**,** et al**.** MafB is a critical regulator of complement component C1q. ***Nat Commun.*** 8, 1700, 2017.
2) Hamada M, et al**.** MafB promotes atherosclerosis by inhibiting foam-cell apoptosis. ***Nat Commun.*** 5, 3147, 2014.

Anatomy and Neuroscience

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Major Scientific Interests of the Group

Our goal is to elucidate the pathogenesis and pathophysiology of schizophrenia and autism. In these illnesses, neuronal morphology and function are affected by a combination of genetic and environmental factors. A better understanding of the molecular mechanisms underlying these illnesses is important as it will lead to the future development of novel methods of treatment and prevention. Our current research is focusing on neuronal cytoskeletons and immunological systems related to these mental illnesses.

Projects for Regular Students in Doctoral or Master's Programs

1) A mouse model of mental illnesses caused by immunological abnormalities.
2) Brain abnormalities caused by maternal immune activation during pregnancy.
3) Mental illnesses based on the disruption of intracellular transport machinery.
4) A common marmoset model of mental illnesses.

Study Programs for Short Stay Students (one week – one trimester)

1) Basic methods in Cellular and molecular biology.
2) Immunocytochemistry and immunohistochemistry.

Selected Publications

1) R. Koshida, S. Tome, **Y. Takei**: Myosin Id localizes in dendritic spines through the tail homology 1 domain. Experimental Cell Research 367, 65-72, 2018
2) K. Mitsumori, **Y. Takei**, N. Hirokawa: Components of RNA granules affect their localization and dynamics in neuronal dendrites. Molecular Biology of the Cell. 28, 1412-1417, 2017
3) **Y. Takei**, Y. S. Kikkawa, N. Atapour, T. K. Hensch, N. Hirokawa: Defects in synaptic plasticity, reduced NMDA-receptor transport, and instability of postsynaptic density proteins in mice lacking microtubule-associated protein 1A. Journal of Neuroscience. Vol. 35, 15539-15554, 2015
4) M. Kondo, **Y. Takei**, N. Hirokawa: Motor protein KIF1A is essential for hippocampal synaptogenesis and learning enhancement in an enriched environment. Neuron, Vol. 73, 743-757, 2012
5) X. Yin, **Y. Takei**, M. Kido, N. Hirokawa: Molecular Motor KIF17 Is fundamental for Memory and Learning via Differential Support of Synaptic NR2A/2B Levels. Neuron, 70, 310-325, 2011
6) R. Midorikawa, **Y. Takei**, N. Hirokawa: Kinesin superfamily protein 4 (KIF4) regulates activity-dependent neuronal survival by suppressing PARP-1 enzymatic activity. Cell, Vol. 125, 371-383, 2006
7) N. Homma, **Y. Takei**, Y. Tanaka, T. Nakata, S. Terada, M. Kikkawa, Y. Noda,, N. Hirokawa: Kinesin Superfamily Protein 2A (KIF2A) Functions in Suppression of Collateral Branch Extension. Cell, Vol. 114, 229-239, 2003
8) **Y. Takei**, J. Teng, A. Harada, N. Hirokawa: Defects in axonal elongation and neuronal migration in mice with disrupted tau and map1b genes. Journal of Cell Biology, Vol. 150, 989-1000, 2000

9) **Y. Takei**, S. Kondo, A. Harada,S. Inomata, T. Noda, N. Hirokawa: Delayed development of nervous system in mice homozygous for disrupted microtubule-associated protein 1B (MAP1B) gene. Journal of Cell Biology, Vol. 137, 1615-1626, 1997

10) **Y. Takei**, A. Harada, S. Takeda, K. Kobayashi, S. Terada, T. Noda, T. Takahashi, N. Hirokawa: Synapsin I deficiency results in the structural change in the presynaptic terminals in the murine nervous system. Journal of Cell Biology, Vol. 131, 1789-1800, 1995

Neurobiology

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Major Scientific Interests of the Group

We are examining the mechanisms underlying the formation of neural network by multidisciplinary approaches from molecules to behavior, using mouse and rat.

Projects for Regular Students in Doctoral or Master's Programs

(1) Monoamines in the dendrite formation and synaptogenesis
(2) Environmental factors affecting development of brain and behavior
(3) Axon guidance mechanisms with special reference to axon guidance molecules

Study Programs for Short Stay Students (one week – one trimester)

1) Anaysis of mouse behavior (spatial memory, anxiety and depression)
2) Quantitative RT-PCR of mRNA in brain regions (5-HT receptors etc)

Selected Publications

1) Li H, Ishikawa C, Shiga T. Effects of postnatal handling on adult behavior and brain mRNA expression of serotonin receptor, brain-derived neurotrophic factor and GABA-A receptor subunit. Int J Dev Neurosci. 68(2018)17-25.
2) Ishikawa C, Shiga T. The postnatal 5-HT_{1A} receptor regulates adult anxiety and depression differently via multiple molecules Progress in neuro-psychopharmacology and biological psychiatry. 78(2017)66-74.
3) Ishikawa C, Li H, Ogura R, Yoshimura Y, Kudo T, Shirakawa M, Shiba D, Takahashi S, Morita H, and Shiga T. Effects of gravity changes on gene expression of BDNF and serotonin receptors in the mouse brain. Plos One. 12(6):e0177833
4) Kozono N, Ohtani A, Shiga T. Roles of the serotonin 5-HT4 receptor in dendrite formation of the rat hippocampal neurons in vitro. Brain Res.1655(2017)114-121.
5) Ishiwata H, Shiga T, and Okado N. Selective serotonin reuptake inhibitor treatment of early postnatal mice reverses their prenatal stress-induced brain dysfunction. Neuroscience 133 (2005) 893-9015)
6) Inoue K, Ozaki S, Shiga T, et al. (2002) *Runx3* controls the axonal projection of proprioceptive dorsal root ganglion neurons. Nature Neurosci. 5 (2002) 946-954.

Diagnostic Surgical Pathology

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Major Scientific Interests of the Group

1) Molecular pathology of multistep carcinogenesis
2) Studies of the initial genetic alterations of precancerous lesions and early carcinoma
3) Studies of the interactions between cancer cells and interstitial cells

Projects for Regular Students in Doctoral or Master's Programs

1) Analysis for the molecular mechanisms of pulmonary adenocarcinogenesis. Screening of the differentially expressed genes and proteins between early adenocarcinoma of the lung (*in situ* adenocarcinoma) and early advanced tumors.
2) Produce monoclonal antibodies against fetal swine to screen for specific antibodies against human carcinomas.
3) *In vitro* and *in vivo* studies of the molecular mechanisms of the reproduction of liver tissue.

Study Programs for Short Stay Students (one week – one trimester)

1) Basic techniques of immunohistochemistry, *in situ* hybridization, and FISH
2) Basic techniques of tissue micro-dissection

Selected Publications

1) Shiba-Isii A, Noguchi M, et al. SFN inhibits SCFFWB7 formation and block ubiquitination of oncoprotein during the course of lung adenocarcinogenesis. *Clin Cancer Res* (*in press*)
2) Kosibaty Z, Noguchi M et al. Cytoplasmic expression of epithelial cell transforming sequence 2 (ECT2) in lung adenocarcinoma and its implication for malignant progression. *Lab Invest*, Epub ahead of print, 2018
3) Kim Y, Shiba-Ishii A, Noguchi M, et al. Stratifin regulates stabilization of receptor tyrosine kinases via interaction with ubiquitin-specific protease 8 in lung adenocarcinoma. *Oncogene* 37:5387-5402, 2018

Experimental Pathology

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Major Scientific Interests of the Group

The roles of transforming growth factor-β related molecules (TMEPAI, MAFK, GPNMB, THG-1) in cancer stem cells.
Establishment of cancer stem cell targeting therapies using macrocyclic peptides.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanisms of TGF-β related molecules (TMEPAI, MafK, GPNMB, THG-1) in stem cell dynamics and carcinogenesis.
2) Quantitative live imaging of cancer stem cell dynamics.
3) Macrocyclic peptide screening for the establishment of cancer stem cell targeting therapy.

Study Programs for Short Stay Students (one week – one trimester)

1) Tissue preparation, Immunohistochemistry and 3D reconstruction
2) *In vitro* assay of tumorigenic activities (cell proliferation, colony formation, sphere formation, Matrigel invasion assay, *etc*.) of TMEPAI, MAFK, GPNMB, THG-1 and stem cell imaging.

Selected Publications

1) Chen C, Okita Y, Watanabe Y, Abe F, Fikry MA, Ichikawa Y, Suzuki H, Shibuya A, **Kato M**. Glycoprotein nmb is exposed on the surface of dormant breast cancer cells and induces stem cell-like properties. **Cancer Res.** 78(22): 6424-6435, 2018.
2) Okita Y, Kimura M, Xie R, Chen C, Shen LTW, Kojima Y, Suzuki H, Muratani M, Saitoh M, Semba K, Heldin C-H, and **Kato M**. The transcription factor MAFK induces EMT and malignant progression of triple-negative breast cancer cells through its target GPNMB. **Science Signal.** 10, eaak9397, 2017.
3) Vo Nguyen TT, Watanabe Y, Shiba A, Noguchi M, Itoh S and **Kato M**. TMEPAI/PMEPA1 enhances tumorigenic activities in lung cancer cells. **Cancer Sci.** 105: 334-341, 2014.
4) Okita Y, Kamoshida A, Suzuki H, Itoh K, Motohashi H, Igarashi K, Yamamoto M, Ogami T, Koinuma D, and **Kato M**. Transforming Growth Factor-β induces transcription factors MafK and Bach1 to suppress expression of the heme oxygenase-1 gene. **J. Biol Chem**, 288: 20658-20667, 2013.
5) Watanabe Y, Itoh S, Goto T, Ohnishi E, Inamitsu M, Itoh F, Satoh K, Wiercinska E, Yang W, Shi L, Tanaka A, Nakano N, Mommaas AM, Shibuya H, ten Dijke P, and **Kato M**. TMEPAI, a transmembrane TGF-β-inducible protein, sequesters Smad proteins from active participation in TGF-β signaling. **Mol. Cell** 37: 123-134, 2010.

Kidney and Vascular Pathogy

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Major Scientific Interests of the Group

Understand the common mechanism of kidney disease progression, particularly cell to cell interaction among glomerular resident cells. Podocyte pathobiology and its response are the main focus to understand segmental nature of glomerulosclerosis.

Projects for Regular Students in Doctoral or Master's Programs

1) Mechanism of podocyte loss.
2) Molecular dynamics and the roles of cytokine/chemokine-receptors determining parietal cell migration.
3) Establishment of one nephrotic two kidney model.

Study Programs for Short Stay Students (one week – one trimester)

1) Renal biopsy diagnosis.
2) Observation of glomerular structures by Low-vacuum scanning electron microscopy.

Selected Publications

1) Podocyte Injury and Its Consequences Kidney Int. 2016, Jun;89(6):1221-30.
2) Podocyte injury-driven intracapillary PAI-1 accelerates podocyte loss via uPAR mediated beta 1 integrin endocytosis. Am J Physiol Renal Physiol. 2015 Mar 15;308(6):F614-26
3) Podocyte injury-driven lipid peroxidation accelerates the infiltration of glomerular foam cells in focal segmental glomerulosclerosis. Am J Pathol. 2015 Aug;185(8):2118-31.
4) Genetic podocyte lineage reveals progressive podocytopenia with parietal cell hyperplasia in a murine model of focal segmental glomerulosclerosis. Am J Pathol. 2009May;174(5):1675-82.
5) Abberant Notchi-1-dependent migration and dedifferentiation of parietal epithelal cells promote collapsing focal segmental glomerulosclerosis with progressive podocyte loss. Kidney Int. 2013; 83,1065-1075.

Cognitive and Behavioral Neuroscience

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Major Scientific Interests of the Group

The goal of our research is to understand neural mechanisms underlying cognition such as attention, memory, prediction, learning and decision-making. In particular, we are investigating the role of monoamine systems, such as dopamine and serotonin, in cognitive functions. Experiments in our laboratory center on the brain of awake behaving monkeys as a model for similar systems in the human brain. Using electrophysiological, pharmacological and optogenetic techniques, we examine what signals monoamine neurons convey while monkeys are performing cognitive tasks and how the signals, released monoamine, work in targeted brain areas to achieve the tasks. These studies will provide more mechanistic accounts of cognitive disorders.

Projects for Regular Students in Doctoral or Master's Programs

1) Roles of monoamine systems in cognitive functions including attention, memory, response inhibition, and decision-making

Selected Publications

1) Ogasawara T, Nejime M, Takada M, Matsumoto M, Primate nigrostriatal dopamine system regulates saccadic response inhibition. *Neuron*, 100, p1513-1526, 2018
2) McCairn KW, Nagai Y, Hori Y, Kikuchi E, Ninomiya T, Suhara T, Lee JY, Iriki A, Minamimoto M, Takada M, Isoda M, Matsumoto M, A primary role for nucleus accumbens and related limbic network in vocal tics. *Neuron*, 89, p300-307, 2016
3) Kawai T, Yamada H, Sato N, Takada M, Matsumoto M, Roles of the lateral habenula and anterior cingulate cortex in negative outcome monitoring and behavioral adjustment in nonhuman primates. *Neuron*, 88, p792-804, 2015
4) Inoue KI, Takada M, Matsumoto M, Neuronal and behavioural modulations by pathway-selective optogenetic stimulation of the primate oculomotor system. *Nature Communications*, 6, 8378, 2015
5) Matsumoto M, Takada M. Distinct representations of cognitive and motivational signals in midbrain dopamine neurons. *Neuron*, 79, p1011-1024, 2013
6) Matsumoto M, Hikosaka O, Two types of dopamine neuron distinctly convey positive and negative motivational signals. *Nature*, 459, p837-841, 2009
7) Matsumoto M, Hikosaka O, Lateral habenula as a source of negative reward signals in dopamine neurons. *Nature*, 447, p1111-1115, 2007

Molecular Behavioral Physiology

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Major Scientific Interests of the Group

We have particular interest in the elucidation of neural circuits and mechanisms that play an essential role in regulating homeostatic processes and various animal behavior patterns, including many of our most basic functions, such as eating, drinking, reacting to fear and pleasure, sleeping and forming memories.

Projects for Regular Students in Doctoral or Master's Programs

1) Decipher physiological roles of neuropeptides
2) Delineating the neuronal circuits that regulate emotion, arousal, and sleep/wakefulness states.

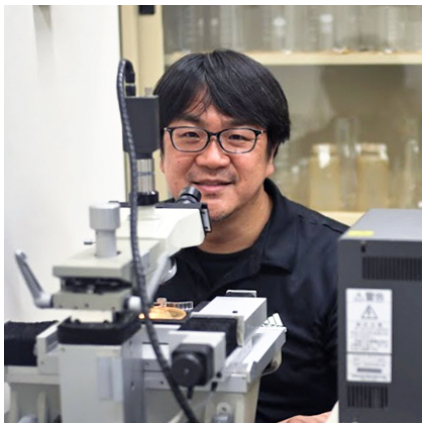
Study Programs for Short Stay Students (one week – one trimester)

1) Learning basic techniques about opto/pharmacogenetics
2) Neuronal circuit tracings using viral vectors

Selected Publications

1. Soya, S., Takahashi, T.M., McHugh, T.J., Maejima, T., Herlitze, S., Abe, M., Sakimura, K., and Sakurai, T. Orexin modulates behavioral fear expression through the locus coeruleus. ***Nat Commun.*** 2017;8(1):1606.
2. Mieda, M., Ono, D., Hasegawa, E., Okamoto,H., Honma, K., Honma, S., Sakurai, T. Cellular Clocks in AVP Neurons of the SCN Are Critical for Interneuronal Coupling Regulating Circadian Behavior Rhythm. ***Neuron***, 2015, 85(5): 1103–1116.
3. Sakurai T, et al. Input of Orexin/Hypocretin Neurons Revealed by a Genetically Encoded Tracer in Mice. ***Neuron*** 46(2):297-308,2005
4. Hara J, BeuckmannCT, Nambu T, Willie JT, Chemelli RM, Sinton CM, Sugiyama F, Yanagi K, Goto K, Yanagisawa M, Sakurai T. Genetic Ablation of Orexin Neurons in Mice Results in Narcolepsy, Hypophagia and Obesity. ***Neuron*** 30:345-354, 2001
5. Sakurai T, et al. Orexins and orexin receptors: A family of hypothalamic neuropeptides and G protein-coupled receptors that regulate feeding behavior. ***Cell*** 92:573-585, 1998

Molecular Cell Biology



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Major Scientific Interests of the Group

1) Post-transcriptional regulation of gene expression by RNA-binding proteins.
2) Molecular mechanism of mRNA localization and local translation regulating cell polarity, asymmetric cell division, and cell-fate.
3) Signaling pathway for the regulation of the endoplasmic reticulum stress response.
4) Developmental regulation for membrane traffic in meiosis.

Projects for Regular Students in Doctoral or Master's Programs

1) Post-transcriptional regulation of gene expression by Khd1, Ccr4, and Pbp1 in yeast.
2) Stability control of *LRG1* mRNA by RNA-binding proteins.
3) Regulation of the endoplasmic reticulum stress response by protein kinases.

Selected Publications

1) Valderrama AL, Fujii S, Duy DL, Irie K, Mizuno T, Suda Y, Irie K. Pbp1 mediates the aberrant expression of genes involved in growth defect of ccr4 and pop2 mutants in yeast Saccharomyces cerevisiae. Genes Cells. 2021 Mar 25.
2) Mizuno T, Muroi K, Irie K. Snf1 AMPK positively regulates ER-phagy via expression control of Atg39 autophagy receptor in yeast ER stress response. PLoS Genet. 2020 Sep 28;16(9):e1009053.
3) Lien PTK, Viet NTM, Mizuno T, Suda Y, Irie K. Pop2 phosphorylation at S39 contributes to the glucose repression of stress response genes, HSP12 and HSP26. PLoS One. 2019 Apr 11;14(4):e0215064.
4) Viet NTM, Duy DL, Saito K, Irie K, Suda Y, Mizuno T, Irie K. Regulation of *LRG1* expression by RNA-binding protein Puf5 in the budding yeast cell wall integrity pathway. Genes Cells. 2018 Dec;23(12):988-997.
5) Mizuno T, Nakamura M, Irie K. Induction of Ptp2 and Cmp2 protein phosphatases is crucial for the adaptive response to ER stress in *Saccharomyces cerevisiae*. Sci Rep. 2018 Aug 30;8(1):13078.
6) Suda Y, Tachikawa H, Inoue I, Kurita T, Saito C, Kurokawa K, Nakano A, Irie K. Activation of Rab GTPase Sec4 by its GEF Sec2 is required for prospore membrane formation during sporulation in yeast Saccharomyces cerevisiae. FEMS Yeast Res. 2018 Feb 1;18(1).
7) Kimura Y, Irie K, Mizuno T. Expression control of the AMPK regulatory subunit and its functional significance in yeast ER stress response. Sci Rep. 2017 Apr 21;7:46713.
8) Duy DL, Suda Y, Irie K. Cytoplasmic Deadenylase Ccr4 is Required for Translational Repression of *LRG1* mRNA in the Stationary Phase. PLoS One. 2017 Feb 23;12(2):e0172476.
9) Ito Y, Kitagawa T, Yamanishi M, Katahira S, Izawa S, Irie K, Furutani-Seiki M, Matsuyama T. Enhancement of protein production via the strong *DIT1* terminator and two RNA-binding proteins in *Saccharomyces cerevisiae*. Sci Rep. 2016 Nov 15;6:36997.
10) Lien PT, Izumikawa K, Muroi K, Irie K, Suda Y, Irie K. Analysis of the Physiological Activities of Scd6 through Its Interaction with Hmt1. PLoS One. 2016 Oct 24;11(10):e0164773.
11) Li X, Ohmori T, Irie K, Kimura Y, Suda Y, Mizuno T, Irie K. Different Regulations of *ROM2* and *LRG1* Expression by Ccr4, Pop2, and Dhh1 in the Saccharomyces cerevisiae Cell Wall Integrity Pathway. mSphere. 2016 Sep 28;1(5).
12) Mizuno T, Masuda Y, Irie K. The Saccharomyces cerevisiae AMPK, Snf1, Negatively Regulates the Hog1 MAPK Pathway in ER Stress Response. PLoS Genet. 2015 Sep 22;11(9):e1005491.

Gene Regulation

Principal Investigator Koji Hisatake

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Major Scientific Interests of the Group

Our group studies the regulation of eukaryotic gene expression, focusing on how transcription regulates cell differentiation. In particular, we are studying the roles of transcription factors and epigenetic changes in regulating iPS cell induction and adipocyte differentiation.

Projects for Regular Students in Doctoral or Master's Programs

1) Mechanistic analyses of the roles for Oct4, Sox2, Klf4 and c-myc during iPS cell induction.
2) Analyses of epigenetic mechanisms of iPS cell induction.
3) Functional analyses of transcription factors involved in adipocyte commitment.
4) In vivo imaging and mechanistic analyses of beige adipocyte differentiation in mouse

Study Programs for Short Stay Students (one week ~ one trimester)

1) Analysis of transcriptional regulation during adipocyte differentiation.
2) Induction of iPS cells using a Sendai virus-based vector.

Recent Publications

1) **Nishimura K**, Ishiwata H, **Sakuragi Y**, **Hayashi Y**, **Fukuda A**, **Hisatake K**: Live-cell imaging of subcellular structures for quantitative evaluation of pluripotent stem cells. **Sci. Reports**, in press (2019).
2) **Tran THY**, **Fukuda A**, **Aizawa S**, **Bui PL**, **Hayashi Y**, **Nishimura K**, **Hisatake K**: Live cell imaging of X chromosome reactivation during somatic cell reprogramming. **Biochem. Biohys. Rep.**, 15:86-92(2018).
3) **Nishimura K**, **Aizawa S**, **Nugroho FL**, **Shiomitsu E**, **Tran YTH**, **Bui PL**, **Borisova E**, **Sakuragi Y**, Takada H, Kurisaki A, **Hayashi Y**, **Fukuda A**, Nakanishi M, **Hisatake K**: A role for KLF4 in promoting the metabolic shift via TCL1 during induced pluripotent stem cell generation. **Stem Cell Reports** 8(3), 787-801 (2017).
4) **Hayashi Y**, Hsiao EC, Sami S, Lancero M, Schlieve CR, Nguyen T, Yano K, Nagahashi A, Ikeya M, Matsumoto Y, **Nishimura K**, **Fukuda A**, **Hisatake K**, Tomoda K, Asaka I, Toguchida J, Conklin BR, Yamanaka S: BMP-SMAD-ID promotes reprogramming to pluripotency by inhibiting p16/INK4A-dependent senescence. **Proc. Natl. Acad. Sci. USA.** 113(46), 13057-13062 (2016).
5) Nakadai T, **Fukuda A**, Shimada M, **Nishimura K**, **Hisatake K**: The RNA binding complexes NF45-NF90 and NF45-NF110 associate dynamically with the c-fos gene and function as transcriptional coactivators. **J. Biol. Chem.** 290(44), 26832-26845 (2015).
6) **Nishimura K**, **Kato T**, **Chen C**, **Oinam L**, **Shiomitsu E**, **Ayakawa D**, Ohtaka M, **Fukuda A**, Nakanishi M, **Hisatake K**: Manipulation of KLF4 expression generates iPSCs paused at successive stages of reprogramming. **Stem Cell Reports** 3(5), 915-929 (2014).
7) **Fukuda A**, Shimada M, Nakadai T, **Nishimura K**, **Hisatake K**: Heterogeneous Nuclear Ribonucleoprotein R Cooperates with Mediator to Facilitate Transcription Reinitiation on the c-Fos Gene. **PLoS ONE** 8(8): e72496. doi:10.1371/journal.pone.0072496 (2013).

Matrix & Stem Cell Biology

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Major Scientific Interests of the Group

The maintenance of a proper extracellular environment comprised of extracellular matrices (ECM), ECM degrading enzymes, cytokines/growth factors, and physical factors, is crucial for normal development and stem cell functions. The long-term goal of our research is to investigate the interactions between extracellular environment and various cell types and elucidate how they modulate intracellular signaling, cellular functions, and cell fate. In particular, we focus on the vessel wall and ECM. We aim to identify novel ECM proteins and characterize their biochemical properties, as well as to investigate pathophysiological functions by taking cellular, molecular biological, and genetic engineering approaches.

Projects for Regular Students in Doctoral or Master's Programs

1) Identification of novel therapeutic targets for genetic aortic aneurysms
2) Molecular mechanism of mechanotransduction in vascular cells.
3) Novel ECM and renal calcification
4) Identification of novel niche for epidermal stem cells
5) Implication of epithelial stem cell aging in age-related diseases

Study Programs for Short Stay Students (one week – one trimester)

1) Genetic and phenotypic identification of mutant mice with defective ECM
2) Preparation of histological sections and expression analysis by immunostaining

Selected Publications

1) Y. Yamashiro, B. Q. Thang, S. Shin, C. A. Lino, T. Nakamura, J. Kim, K. Sugiyama, C. Tokunaga, H. Sakamoto, M. Osaka, E. C. Davis, J. E. Wagenseil, Y. Hiramastu, and H. Yanagisawa: Role of thrombospondin-1 in mechanotransduction and development of thoracic aortic aneurysm in mouse and humans. Circ. Res. 123 (6):660-672 (2018).
2) J. Tsunezumi, H. Sugiura, L. Oinam, A. Ali, B. Q. Thang, A. Sada, Y. Yamashiro, M. Kuro-O, and H. Yanagisawa: Fibulin-7, a heparin binding matricellular protein, promotes renal tubular calcification in mice. Matrix Biol. Dec;74:5-20 (2018).
3) Y. Yamashiro, C. L. Papke, J. Kim, L-J. Ringuette, Q-J. Zhang, Z-P. Liu, H. Mirzaei, J. E. Wagenseil, E. C. Davis and H. Yanagisawa: Abnormal mechanosensing and cofilin activation promote the progression of ascending aortic aneurysms in mice. Sci. Sig. 8(399):ra105 (2015).
4) J. Huang, Y. Yamashiro*, C. L. Papke*, Y. Ikeda*, Y. Lin, M. Patel, T. Inagami, V. P. Le, J. E. Wagenseil and H. Yanagisawa: Angiotensin converting enzyme-induced activation of local angiotensin signaling is required for ascending aortic aneurysms in fibulin-4 deficient mice. Sci. Transl. Med. 5, 183ra58 (2013). * equal contribution second author
5) J. Huang, E. C. Davis, S. L. Chapman, L. Y. Budatha, M., Marmorstein, R. A. Word and H. Yanagisawa: Fibulin-4 deficiency results in ascending aortic aneurysms: a potential link between abnormal smooth muscle cell phenotype and aneurysm progression. Circ Res. 106(3):583-592 (2010).

Molecular Neurobiology

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Assistant Professor: Takuya Okada: okada.takuya.gw@u.tsukuba.ac.jp

Major Scientific Interests of the Group

Our main research focus is to study the molecular mechanisms that regulate the neural circuit formation and higher brain functions. Using integrative approaches including molecular biology, biochemistry, pharmacology, developmental biology, and neuroanatomy, we have been investigating how complex networks are formed in the developing brain and how the mature brain functions are acquired and regulated. We are particularly interested in the molecules that play a role in neural differentiation, cell migration, axon guidance, and synaptogenesis.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular study on neural differentiation
2) Molecular study on axon guidance
3) Molecular study on brain function

Study Programs for Short Stay Students (one week – one trimester)

1) Immunohistochemistry, in situ hybridization, and microscopy
2) Tracing of neural circuits
3) 3D imaging of neural network

Selected Publications

1) Okada T, Keino-Masu K, Suto F, Mitchell KJ, **Masu M**. Remarkable complexity and variability of corticospinal tract defects in adult Semaphorin 6A knockout mice. **Brain Res.** 1710, 209-219, 2019.
2) Okada T et al. Desulfation of heparan sulfate by Sulf1 and Sulf2 is required for corticospinal tract formation. **Sci. Rep.** 7, 13847, 2017.
3) **Masu M**. Proteoglycans and axon guidance: a new relationship between old partners. **J. Neurochem.** 139, 58-75, 2016.
4) Nagamine S et al. Organ-specific sulfation patterns of heparan sulfate generated by extracellular sulfatases Sulf1 and Sulf2 in mice. **J. Biol. Chem.** 287, 9579-9590, 2012.
5) Okada T, Keino-Masu K, and **Masu, M**. Migration and nucleogenesis of mouse precerebellar neurons visualized by *in utero* electroporation of a green fluorescent protein gene. **Neurosci. Res.** 57, 40-49, 2007.
6) Keino-Masu K, **Masu M**, et al. *Deleted in Colorectal Cancer* (*DCC*) encodes a netrin receptor. **Cell** 87, 175-185, 1996.

Molecular Virology

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Assistant Professor Takeshi SEKIYA

Major Scientific Interests of the Group

The research aim of this group is to understand the molecular mechanism of replication and pathogenicity of animal viruses such as influenza virus. The structure and function of virus-encoded factors and host cell-derived factors involved in virus replication are being studied at the atomic, molecular and body levels. We also focus on the host innate immune responses against virus infection.

Projects for Regular Students in Doctoral or Master's Programs

1) Identification and characterization of novel factors in virus replication
2) Molecular mechanism of host innate immune responses to virus infection
3) Control of virus infections through development of novel anti-viral drugs

Study Programs for Short Stay Students (one week – one trimester)

1) Molecular mechanism of host factors involved in influenza virus replication
2) Action mechanism of anti-virus drugs

Selected Publications

1) Lee S, Hirohama M, Noguchi M, Nagata K, **Kawaguchi A**. Influenza A virus infection triggers pyroptosis and apoptosis of respiratory epithelial cells through the type I interferon signaling pathway in a mutually exclusive manner. ***J. Virol.***, 2018; 92(14): e00396-18.
2) **Kawaguchi A**, Hirohama M, Harada Y, Osari S, Nagata K. Influenza virus induces cholesterol-enriched endocytic recycling compartments for budozone formation via cell cycle-independent centrosome maturation. ***PLoS Pathog.***, 2015; 11(11): e1005284.
3) Sugiyama K, **Kawaguchi A**, Okuwaki M, Nagata K. pp32 and APRIL are host cell-derived regulators of influenza virus RNA synthesis from cRNA. ***eLife***, 2015; 4: e08939.
4) **Kawaguchi A**, Matsumoto K, Nagata K. YB-1 functions as a porter to lead influenza virus ribonucleoprotein complexes to microtubules. ***J. Virol.***, 2012; 86(20): 11086-95.
5) Obayashi E, Yoshida H, Kawai F, Shibayama N, **Kawaguchi A**, Nagata K, Tame JR, Park SY. The structural basis for an essential subunit interaction in influenza virus RNA polymerase. ***Nature***, 2008; 454(7208): 1127-31.
6) **Kawaguchi A**, Nagata K. De novo replication of the influenza virus RNA genome is regulated by DNA replicative helicase, MCM. ***EMBO J.***, 2007; 26(21): 4566-75.

Microbiology

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Major Scientific Interests of the Group

We aim to understand fundamental biological systems of bacteria, which are distinct from eukaryotic/ multi-cellular organisms. Our research covers both Gram-positive (Staphylococcus, Listeria, Lactobacillus) and Gram-negative bacteria (Salmonella, Escherichia coli), with a focus on evolutionary adaptation strategies and regulatory mechanisms of gene expression.

Projects for Regular Students in Doctoral or Master's Programs

1) Natural genetic competence in Gram-positive pathogens
2) Population heterogeneity
3) Dynamics of cellular structures: nucleoid and membrane
4) Functional RNA and gene regulation in Salmonella

Study Programs for Short Stay Students (one week – one trimester)

1) Molecular genetic and biochemical techniques
2) Analysis of gene regulation

Selected Publications

1) Nguyen Thi LT, Takemura AJ, Ohniwa RL, Saito S, and Morikawa K. Sodium Polyanethol Sulfonate modulates natural transformation of SigH-expressing *Staphylococcus aureus*. ***Curr Microbiol*** 75, 499. 2017.
2) Mizuno K, Mizuno M, Yamauchi M, Takemura AJ, Medrano Romero V, and Morikawa K. Adjacent-possible ecological niche: growth of *Lactobacillus* species co-cultured with *Escherichia coli* in a synthetic minimal medium. ***Sci Rep*** 7, 12880. 2017.
3) Ushijima Y, Ohniwa RL, and Morikawa K. Identification of nucleoid associated proteins (NAPs) under oxidative stress in *Staphylococcus aureus*. ***BMC Microbiol*** 17, 207. 2017
4) Cafini F, Nguyen le TT, Higashide M, Román F, Prieto J, and Morikawa K. Horizontal Gene Transmission of *cfr* gene to MRSA and *Enterococcus*: role of *S. epidermidis* as reservoir and alternative pathway for the spread of linezolid resistance. ***J Antimicrob Chemother*** 71, 587. 2016
5) Miyakoshi M, Chao Y, and Vogel J. Regulatory small RNAs from the 3′ regions of bacterial mRNAs. ***Curr Opin Microbiol*** 24, 132. 2015.
6) Miyakoshi M, Chao Y, and Vogel J. Cross talk between ABC transporter mRNAs via a target mRNA-derived sponge of the GcvB small RNA. ***EMBO J*** 34, 1478. 2015.
7) Morikawa K, Takemura A, Inose Y, Tsai M, Nguyen Thi le T, Ohta T and Msadek T. Expression of a cryptic secondary sigma factor gene unveils natural competence for DNA transformation in *Staphylococcus aureus*. ***PLoS Pathog*** 8:e1003003. 2012
8) Tsai M, Ohniwa RL, Kato Y, Takeshita SL, Ohta T, Saito S, Hayashi H, and Morikawa K. *Staphylococcus*

aureus requires cardiolipin for survival under conditions of high salinity. ***BMC Microbiol*** 11, 13. 2011.

Molecular Parasitology

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Major Scientific Interests of the Group

Our primary research interest is to understand the gene expression of eukaryotic parasites with a goal in identifying parasite-specific processes that can be exploited as targets for novel therapeutic interventions. We have focused on how messenger RNA acquire 5' cap in the protozoan parasites that responsible for malaria and sleeping sickness. The structure and mechanism of protozoan capping enzyme is completely different from human host, and thus, capping is an attractive target for anti-protozoal drug discovery. We are also investigating how RNAs are repair and recombination. RNA ligase is the key enzyme that joins the broken RNAs together. We have characterized three separate types of RNA ligases from various species and our immediate goal is to define how these ligases recognize the breaks in the RNA and to identify what types of RNA are repaired in the cell.

Projects for Regular Students in Doctoral or Master's Programs

1) Dissecting the mechanism of hypermethylated cap 4 synthesis in Trypanosome brucei.
2) Characterization of T.brucei capping enzyme complex with transcription and processing factors.
3) Defining the physiological targets for RNA ligase through genome wide screening.

Study Programs for Short Stay Students (one week – one trimester

1) Screening of small molecule inhibitor against malaria and sleeping sickness.
2) Regulation of gene expression by cytoplasmic mRNA recapping.
3) Defining the optimal RNA substrates for RNA ligase.

Selected Publications

1) Yoshinari S, Liu Y, Gollnick PG and Ho CK. (2017) Cleavage of 3'-terminal adenosine by archaeal ATP-dependent RNA ligase. Scientific Reports 7:11662.
2) Gu H, Yoshinari S, Ghosh R, Murakami KS, Ignatochkina AV, Gollnick P and Ho CK. (2016) Structural and Mutational Analysis of Archaeal ATP-dependent RNA ligase Identifies Amino Acid Required for RNA Binding and Catalysis. Nucleic Acid Res. 44: 2337 - 2347.
3) Smith P, Ho CK, Takagi Y, Djaballah H, and Shuman S. (2016) Nanomolar Inhibitors of Trypanosoma brucei RNA Triphosphatase. mBIO 7: e000058-16
4) Ignatochkina AV, Takagi Y, Liu Y, Nagata K, and Ho CK. (2015) The Messenger RNA Decapping and Recapping Pathway in Trypanosoma. Proc. Natl. Acad. Sci. USA
5) Torchea C, Takagi Y and Ho CK. Archaea RNA Ligase is a Homodimeric Protein that Catalyzes Intramolecular Ligation of Single-Stranded RNA and DNA. (2008) Nucleic Acid Res. 36: 6218 - 6227.
6) Takagi Y, Sindkar S, Ekonomidis D, Hall MP and Ho CK. (2007) Trypanosoma brucei Encodes a Bifunctional Capping Enzyme Essential for Cap 4 Formation on the Spliced Leader RNA. J. Biol. Chem; 282: 15995-16005.
7) Pfeffer S, Sewer A, Lagos-Quintana M, Sheridan R, Sander C, Grässer FA, van Dyk LF, Shuman S, Ho CK, Chien M, Russo JJ, Ju J, Randall G, Lindenbach BD, Rice CM, Simon V, Ho DD, Zavolan M, and Tuschl T. Identification of the MicroRNAs of the Herpesvirus Family. Nature Method 2005; 2: 269-276.

Immunology

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Major Scientific Interests of the Group

The molecular mechanisms of tumor immunity, autoimmunity, infectious immunity and allergy and clinical applications of our basic research findings

Projects for Regular Students in Doctoral or Master's Programs

1) In vivo and in vitro function of the immunoreceptors DNAM-1, Fca/mR, MAIR-I, MAIR-II, and Allergin-1, all of which were identified in our laboratory, in immune responses
2) The pathophysiological roles of the immunoreceptors in tumors, autoimmune diseases, allergy and infectious disease

Study Programs for Short Stay Students (one week – one trimester)

1) Generation of monoclonal antibodies and their application for expression analyses by flow cytometry and immunohistochemistry
2) Cell separation by sorting on flow cytometry or magnetic beads and analyses of cytokine production or proliferation upon antigen stimulation

Selected Publications

1) Shibuya A, Shibuya K. Exploring the gut fungi-lung allergy axis. Cell Host & Microbe 24(6):755-757, 2018
2) Honda, et al. Marginal zone B cells exacerbate endotoxic shock via interleukin-6 secretion induced by Fca/mR-coupled TLR4 signaling. Nature Commun, in press (2016)
3) Nakahashi-Oda C, et al. Apoptotic epithelial cells control regulatory T cell expansion. Nature Immunol, 2016 Feb 8. doi: 10.1038/ni.3345.
4) Totsuka N, et al. Toll-like receptor 4 and MAIR-II/CLM-4/LMIR2 immunoreceptor regulate VLA-4-mediated inflammatory monocyte migration. Nature Commun, 5:4710, 2014
5) Kim YG, et al. Gut dysbiosis promotes M2 macrophage polarization and allergic airway inflammation via fungi-induced PGE2. Cell Host & Microbe, 15(1):95–102, 2014
6) Nakahashi-Oda C, et al. Apoptotic cells suppress mast cell inflammatory responses via the CD300a immunoreceptor. J. Exp. Med. 209, 1493-1503, 2012
7) Nakano-Yokomizo T, et al. The immunoreceptor adapter protein DAP12 suppresses B lymphocyte-driven adaptive immune responses. J. Exp. Med. 208, 1661-1671, 2011.

8) Hitomi K, et al. An immunoglobulin-like receptor, Allergin-1, inhibits immunoglobulin E-mediated immediate hypersensitivity reactions. Nature Immunol. 11: 601-607, 2010
9) Nabekura T, et al. Critical role of DNAX accessory molecule-1 (DNAM-1) in the development of acute graft-versus-host disease in mice. Proc Natl Acad Sci USA, 107(43):18593-18,

Medical Genetics

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Major Scientific Interests of the Group

Differences in our DNA sequence are responsible for the differences in our appearance, susceptibility to diseases, and variability to drug response. The focus of our research was to identify novel genetic variants associated with allergic diseases/immune-related diseases and to elucidate the associated pathways by genome analysis. Big genetic data has been generated by next generation sequencing and array-based genotyping technique in recent years. Using this big data, we aim to improve our ability to predict common diseases and new treatments.

Projects for Regular Students in Doctoral or Master's Programs

1) Identification of susceptibility genes for allergic diseases
2) HLA-peptide binding assay for immune-related diseases

Selected Publications

1) Koseki T, Morii W, Noguchi E, Ishikawa M, Yang L, Yamamoto-Hanada K, Narita M, Saito H, Ohya Y. Effect of filaggrin loss-of-function mutations on atopic dermatitis in young age: a longitudinal birth cohort study. J Hum Genet, 2019
2) Morii W, Sakai A, Ninomiya T, Kidoguchi M, Sumazaki R, Fujieda S, Noguchi E. Association of Japanese cedar pollinosis and sensitization with HLA-DPB1 in the Japanese adolescent. Allergol Int, 67: 61-66, 2018
3) Miyadera H, Ohashi J, Lernmark Å, Kitamura T, Tokunaga K. Cell-surface MHC density profiling reveals instability of autoimmunity-associated HLA. J Clin Invest. 2015, 125: 275–291
4) Noguchi E, Sakamoto H, Hirota T, Ochiai K, Imoto Y, Sakashita M, Kurosaka F, Akasawa A, Yoshihara S, Kanno N, Yamada Y, Shimojo N, Kohno Y, Suzuki Y, Kang M J, Kwon J W, Hong S J, Inoue K, Goto Y, Yamashita F, Asada T, Hirose H, Saito I, Fujieda S, Hizawa N, Sakamoto T, Masuko H, Nakamura Y, Nomura I, Tamari M, Arinami T, Yoshida T, Saito H, Matsumoto K. Genome-Wide Association Study Identifies HLA-DP as a Susceptibility Gene for Pediatric Asthma in Asian Populations. PLos Genet, 7: e1002170, 2011

Molecular and Genetic Epidemiology

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Major Scientific Interests of the Group

Our laboratory is interested in genetics and genomics of human autoimmune rheumatic diseases such as ANCA-associated vasculitis, systemic lupus erythematosus, rheumatoid arthritis and systemic sclerosis. We are taking both genome-wide and candidate gene approaches to find genomic variations associated with development of the rheumatic diseases, as well as those associated with their serious clinical manifestations such as interstitial lung disease. These studies will eventually lead to understanding the pathogenesis of the intractable diseases, identification of molecular targets and biomarkers.

Projects for Regular Students in Doctoral or Master's Programs

1) Identification of genomic variations associated with autoimmune rheumatic diseases
2) Biologic and bioinformatic analyses of the variations associated with autoimmune rheumatic diseases

Study Programs for Short Stay Students (one week – one trimester)

Genome database (tutorial), SNP typing (laboratory).

Selected Publications

1) **Namba N**, **Kawasaki A**, Sada K-e, Hirano F, Kobayashi S, Yamada H, **Furukawa H**, Shimada K, Hashimoto A, Matsui T, Nagasaka K, et al.. Association of *MUC5B* promoter polymorphism with interstitial lung disease in myeloperoxidase - antineutrophil cytoplasmic antibody - associated vasculitis. ***Ann Rheum Dis*** 2019; doi: 10.1136/annrheumdis-2018-214263.
2) Juge P-A, Lee JS, Ebstein E, **Furukawa H,** Dobrinskikh E, Gazal S, Kannengiesser C, Ottaviani S, **Oka S**, Tohma S, **Tsuchiya N**, et al. *MUC5B* promoter variant and rheumatoid arthritis with interstitial lung disease. ***N Engl J Med*** 2018; 379:2209-19.
3) Terao C, Kawaguchi T, Dieude P, Varga J, Kuwana M, Hudson H, Kawaguchi Y, Matucci-Cerinic M, Ohmura K, Riemekasten G, **Kawasaki A,** et al. Transethnic meta-analysis identifies *GSDMA* and *PRDM1* as susceptibility genes to systemic sclerosis. ***Ann Rheum Dis*** 2017;76:1150-8.
4) **Kawasaki A**, **Hasebe N, Hidaka M**, Hirano F, Sada K-e, Kobayashi S, Yamada H, **Furukawa H**, Yamagta K, Sumida T, Miyasaka N, et al. Protective role of *HLA-DRB1*13:02* against microscopic polyangiitis and MPO-ANCA positive vasculitides in a Japanese population: a case-control study. ***PLoS One*** 2016;11:e0154393.
5) **Furukawa H**, **Oka S**, Shimada K, Rheumatoid Arthritis associated Interstitial Lung Disease (RA-ILD) Study Consortium, **Tsuchiya N**, Tohma S. *HLA-A*31:01* and methotrexate-induced interstitial lung disease in Japanese rheumatoid arthritis patients: a multi-drug hypersensitivity marker? ***Ann Rheum Dis*** 2013;72:153-5.
6) **Furukawa H, Oka S**, Shimada K, Sugii S, **Ohashi J**, Matsui T, Ikenaka T, Nakayama H, Hashimoto A, Takaoka H, Arinuma Y, et al. Association of human leukocyte antigen with interstitial lung disease in rheumatoid arthritis: A

protective role for shared epitope. ***PLoS One*** 2012;7: e33133.

7) **Kawasaki A, Furukawa H,** Kondo Y, Ito S, Hayashi T, Kusaoi M, Matsumoto I, Tohma S, Takasaki Y, Hashimoto H, Sumida T, et al. *TLR7* single-nucleotide polymorphisms in the 3' untranslated region and intron 2 independently contribute to systemic lupus erythematosus in Japanese women: a case-control association study. ***Arthritis Res Ther*** 2011;13:R41.
8) **Kawasaki A, Kyogoku C**, **Ohashi J, Miyashita R, Hikami K**, Kusaoi M, **Tokunaga K,** Takasaki Y, Hashimoto H, Behrens TW, **Tsuchiya N**. Association of *IRF5* polymorphisms with systemic lupus erythematosus in a Japanese population. Support for a crucial role of intron 1 polymorphisms ***Arthritis Rheum*** 2008;58: 826–34.
9) **Kyogoku C**, Dijstelbloem HM, **Tsuchiya N**, **Hatta Y, Kato H, Yamaguchi A**, Fukazawa T, Jansen MD, Hashimoto H, van de Winkel JGJ, Kallenberg CGM, et al. Fc□ receptor gene polymorphisms in Japanese patients with systemic lupus erythematosus: Contribution of *FCGR2B* to genetic susceptibility. ***Arthritis Rheum*** 2002;46:1242-54.
10) **Tsuchiya N,** Husby G, Williams RCJr, Stieglitz H, Lipsky PE, Inman RD. Autoantibodies to HLA-B27 sequence cross-react with the hypothetical sequence of arthritis-associated *Shigella* plasmid. ***J Clin Invest*** 1990;86:1193-203.

Genome Biology

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Major Scientific Interests of the Group

The main research interests in our group is genomics and epigenomics in space life science and clinical research, with particular focus on development of technologies for limited sample analysis. We also collaborate with clinicians and industry partners to implement our methods to personalized medicine and automated laboratory testing using AI and robotics.

Projects for Regular Students in Doctoral or Master's Programs

1) Clinical sample analysis using chromatin immunoprecipitation combined with 2nd generation sequencing (ChIPseq) and RNAseq, data analysis and validation of potential disease biomarkers.
2) Genomics and epigenomics analysis in space research projects

Study Programs for Short Stay Students (one week – one trimester)

1) Access to genomics databases, integrative analysis of regulatory regions, gene expression and genetic variations.
2) Genomics and epigenomics assays, chromatin immunoprecipitation, RNA assays and genotyping.

Selected Publications

1) Kumar V*, Rayan NA*, Muratani M*, Lim S, Elanggovan B, Lixia X, Lu T, Makhija H, Poschmann J, Lufkin T, Ng HH, Prabhakar S. Comprehensive benchmarking reveals H2BK20 acetylation as a distinctive signature of cell-state-specific enhancers and promoters. *Genome Res.* pii: gr.201038.115, 2016. (*Equal contribution)
2) Muratani M, Deng N, Ooi WF, Lin SJ, Xing M, Xu C, Qamra A, Tay ST, Malik S, Wu J, Lee MH, Zhang S, Tan LL, Chua H, Wong WK, Ong HS, Ooi LL, Chow PK, Chan WH, Soo KC, Goh LK, Rozen S, Teh BT, Yu Q, Ng HH, Tan P. Nanoscale chromatin profiling of gastric adenocarcinoma reveals cancer-associated cryptic promoters and somatically acquired regulatory elements. *Nat Commun.* 5:4361, 2014.

Regenerative Medicine and Stem Cell Biology

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Assistant Professor, Mizuho Fukushige

Major Scientific Interests of the Group

1) Identification and analysis of functional human adult stem cells for therapy
2) Hypoxic responses in stem cell and tumor development
3) Studying the relation between human adult stem cells and cancer cells

Projects for Regular Students in Doctoral or Master's Programs

1) Effects of diseases and aging on the functions of human adult stem cells
2) Functional analysis of human adult stem cell-derived microvesicles
3) Studying the regulation of beige adipogenesis in human mesenchymal stem cells
4) The roles of hypoxic inducible factors (HIFs) in stem cell and cancers
5) The roles of human mesenchymal stem cells in cancer development

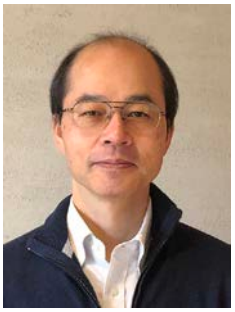
Study Programs for Short Stay Students (one week – one trimester)

1) Effects of diseases and aging on human adult stem cells
2) Human adult stem cell-derived microvesicles for non-cell therapy
3) Interaction between human mesenchymal stem cells and cancer cells

Selected Publications

1) Carolina E, Kato T, Khanh VC, Moriguchi K, Yamashita T, Takeuchi K, Hamada H, **Ohneda O.** Glucocorticoid Impaired the Wound Healing Ability of Endothelial Progenitor Cells by Reducing the Expression of CXCR4 in the PGE2 Pathway. Front Med (Lausanne). 2018 Sep 28;5:276.
2) Kato T, Khanh VC, Sato K, Kimura K, Yamashita T, Sugaya H, Yoshioka T, Mishima H, **Ohneda O.** Elevated Expression of Dkk-1 by Glucocorticoid Treatment Impairs Bone Regenerative Capacity of Adipose Tissue-Derived Mesenchymal Stem Cells. Stem Cells Dev. 2018 Jan 15;27(2):85-99.
3) Khanh VC, Ohneda K, Kato T, Yamashita T**,** Sato F, Tachi K, **Ohneda O .** Uremic Toxins Affect the Imbalance of Redox State and Overexpression of Prolyl Hydroxylase 2 in Human Adipose Tissue-Derived Mesenchymal Stem Cells Involved in Wound Healing. Stem Cells Dev. 2017 Jul 1;26(13):948-963.
4) Shiraishi A, Tachi K, Essid N, Tsuboi I, Nagano M, Kato T, Yamashita T, Bando H, Hara H, **Ohneda O**. Hypoxia promotes the phenotypic change of aldehyde dehydrogenase activity of breast cancer stem cells. Cancer Sci. 2017 Mar; 108(3): 362–372.
5) Trinh NT, Yamashita T, Ohneda K, Kimura K, Salazar G, Sato F, **Ohneda O**. Increased expression of EGR-1 in diabetic human adipose tissue-derived mesenchymal stem cells reduces their wound healing capacity. Stem Cells Dev. 2016 May 15; 25(10): 760–773.
6) Tsuboi I, Yamashita T, Nagano M, Kimura K, To'a Salazar G, **Ohneda O.** Impaired expression of HIF-2α induces compensatory expression of HIF-1α for the recovery from anemia. J Cell Physiol. 2015 Jul;230(7):1534-48.

Biomedical Engineering



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Major Scientific Interests of the Group

Development of bioartificial organs by using tissue engineering approach. Establishment of novel 3D culture methods mimicking in vivo microenvironment.

Projects for Regular Students in Doctoral or Master's Programs

1) Development of ex vivo expansion system of hematopoietic stem cells
2) Development of bioartificial livers
3) Establishment of novel bioreactor systems applicable to bioartificial organs

Study Programs for Short Stay Students (one week – one trimester)

1) 3D culture techniques including preparation of 3D scaffolds, cell seeding into the scaffolds, cryopreservation of 3D culture cells, and assays of the cells.

Selected Publications

1) **Miyoshi H**, Sato C, Shimizu Y, Morita M. Expansion of mouse hematopoietic stem/progenitor cells in three-dimensional cocultures on growth-suppressed stromal cell layer. *Intern J Artif Organs*, 2019. DOI:10.1177/0391398819827596.
2) **Miyoshi H**, Morita M, Ohshima N, Sato C. Expansion of mouse hematopoietic progenitor cells in three-dimensional cocultures on frozen-thawed stromal cell layers formed within porous scaffolds. *Exp Hematol*, 43: 115-124, 2015.
3) **Miyoshi H**, Ohshima N, Sato C. Three-dimensional culture of mouse bone marrow cells on stroma formed within a porous scaffold: influence of scaffold shape and cryopreservation of the stromal layer on expansion of haematopoietic progenitor cells. *J Tissue Eng Regen Med*, 7: 32-38, 2013.
4) **Miyoshi H**, Ehashi T, Kawai H, Ohshima N, Suzuki S. Three-dimensional perfusion cultures of mouse and pig fetal liver cells in a packed-bed reactor: effect of medium flow rate on cell numbers and hepatic functions. *J Biotechnol*, 148: 226-232, 2010.
5) Koyama T, Ehashi T, Ohshima N, **Miyoshi H**. Efficient proliferation and maturation of fetal liver cells in three-dimensional culture by stimulation of oncostatin M, epidermal growth factor, and dimethyl sulfoxide. *Tissue Eng A*, 15: 1099-1107, 2009.

Laboratory Animal Science
Laboratory Animal Resource Center

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Assistant Professor Dinh Thi Huong Tra

Major Scientific Interests of the Group

Comparative analyses of mouse and human genomes have strongly guided the importance of mutant mice for understanding the mechanism of human diseases. Our main task are the development and characterization of new gene-modified mouse (GMM) models for human diseases. Further, we investigate a new strategy for genome modification and create novel mouse resources for analyzing gene function in vivo. Moreover, we study spermatogenesis and oogenesis using GMMs.

Projects for Regular Students in Doctoral or Master's Programs

1）Development of a mouse model for human diseases
2）Creation of a new strategy for analyzing gene function in mice
3）Investigation of spermatogenesis and oogenesis in mice

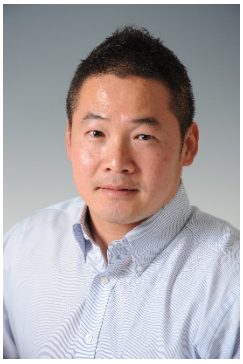
Study Programs for Short Stay Students (one week – one trimester)

1）Manipulation of mouse embryos
2）Genome manipulation using the CRISPR/Cas9 system

Selected Publications

1) Hoshino Y, Mizuno S, Kato K, Mizuno-Iijima S, Tanimoto Y, Ishida M, Kajiwara N, Sakasai T, Miwa Y, Takahashi S, Yagami K, Sugiyama F. Simple generation of hairless mice for in vivo imaging. Exp Anim. 66(4):437-445, 2017.
2) Hasegawa Y, Hoshino Y, Abdelaziz E. Ibrahim, Kato K, Daitoku Y, Tanimoto Y, Ikeda Y, Oishi H, Takahashi S, Yoshiki A, Yagami K, Iseki H, Mizuno S, Sugiyama F. Generation of CRISPR/Cas9-mediated bicistronic knock-in Ins1-cre driver mice. Exp Anim. 65(3):319-327, 2016.
3) Al-Soudy AS, Nakanishi T, Mizuno S, Hasegawa Y, Shawki HH, Katoh MC, Basha WA, Ibrahim AE, El-Shemy HA, Iseki H, Yoshiki A, Hiromori Y, Nagase H, Takahashi S, Oishi H, Sugiyama F. Germline recombination in a novel Cre transgenic line, Prl3b1-cre mouse. Genesis. 54(7):389-397, 2016.
4) Mizuno S, Takami K, Daitoku Y, Tanimoto Y, Dinh TT, Mizuno-Iijima S, Hasegawa Y, Takahashi S, Sugiyama F (Corresponding author), Yagami K. Peri-implantation lethality in mice carrying megabase-scale deletion on 5qc3.3 is caused by Exoc1 null mutation. Sci Rep. 5:13632, 2015.
5) Mizuno S, Dinh TT, Kato K, Mizuno-Iijima S, Tanimoto Y, Daitoku Y, Hoshino Y, Ikawa M, Takahashi S, Sugiyama F (corresponding author), Yagami K., Simple generation of albino C57BL/6J mice with G291T mutation in the tyrosinase gene by the CRISPR/Cas9 system. Mamm Genome. 25:327-343, 2014.

Chemical Biology & Computational Drug Discovery



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Major Scientific Interests of the Group

We propose the supporting and developing of chemical biology and *in silico* drug discovery using molecular modeling and simulation based on fundamental technologies such as homology modeling, docking simulation, cheminformatics and molecular dynamics simulation. Our goal is to achieve in silico drug discovery technology having high practicability for translational research in relationships between pharmaceutical industry and academia.

Projects for Regular Students in Doctoral or Master's Programs

1) Computational molecular docking and dynamics simulation for understanding the molecular function, structure-activity relationship analysis and drug discovery.
2) Molecular dynamics simulation of binding pathway of the ligands to drug target proteins.
3) Development of software for structure-based drug discovery and its applications

Study Programs for Short Stay Students (one week – one trimester)

1) Hands on training of bioinformatics and cheminformatics for beginers.

Selected Publications

1) Shiba-Ishii A, Hong J, **Hirokawa T**, Kim Y, Nakagawa T, Sakashita S, Sakamoto N, Kozuma Y, Sato Y, Noguchi M. Stratifin Inhibits SCFFBW7 Formation and Blocks Ubiquitination of Oncoproteins during the Course of Lung Adenocarcinogenesis. **Clin Cancer Res**. 25(9): 2809-2820, 2019.
2) Toyoda Y, Morimoto K, Suno R, Horita S, Yamashita K, Hirata K, Sekiguchi Y, Yasuda S, Shiroishi M, Shimizu T, Urushibata Y, Kajiwara Y, Inazumi T, Hotta Y, Asada H, Nakane T, Shiimura Y, Nakagita T, Tsuge K, Yoshida S, Kuribara T, Hosoya T, Sugimoto Y, Nomura N, Sato M, **Hirokawa T**, Kinoshita M, Murata T, Takayama K, Yamamoto M, Narumiya S, Iwata S, Kobayashi T. Ligand binding to human prostaglandin E receptor EP4 at the lipid-bilayer

interface. **Nat Chem Biol**. 15(1):18-26, 2019.

3) Sakai Y, Kawaguchi A, Nagata K, **Hirokawa T**. Analysis by metadynamics simulation of binding pathway of influenza virus M2 channel blockers. **Microbiol Immunol**. 62(1): 34-43, 2018.
4) Wakui N, **Yoshino** R, Yasuo N, Ohue M, Sekijima M. Exploring the selectivity of inhibitor complexes with Bcl-2 and Bcl-XL: A molecular dynamics simulation approach. **J Mol Graph Model**. 79:166-174, 2018.
5) **Yoshino R**, Yasuo N, Hagiwara Y, Ishida T, Inaoka DK, Amano Y, Tateishi Y, Ohno K, Namatame I, Niimi T, Orita M, Kita K, Akiyama Y, Sekijima M. In silico, in vitro, X-ray crystallography, and integrated strategies for discovering spermidine synthase inhibitors for Chagas disease. **Sci Rep**. 7(1): 6666, 2017.
6) Sayama M, Inoue A, Nakamura S, Jung S, Ikubo M, Otani Y, Uwamizu A, Kishi T, Makide K, Aoki J, **Hirokawa T**, Ohwada T. Probing the Hydrophobic Binding Pocket of G-Protein-Coupled Lysophosphatidylserine Receptor GPR34/LPS1 by Docking-Aided Structure-Activity Analysis. **J Med Chem**. 60(14): 6384-6399, 2017.
7) **Yoshino R**, Yasuo N, Inaoka DK, Hagiwara Y, Ohno K, Orita M, Inoue M, Shiba T, Harada S, Honma T, Balogun EO, da Rocha JR, Montanari CA, Kita K, Sekijima M. Pharmacophore modeling for anti-Chagas drug design using the fragment molecular orbital method. **PLoS One**. 10(5): e0125829, 2015.
8) Sato M, **Hirokawa T**. Extended template-based modeling and evaluation method using consensus of binding mode of GPCRs for virtual screening. **J Chem Inf Model**. 54(11):3153-61, 2014.

Bioinformatics

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Major Scientific Interests of the Group

Bioinformatics is the research field of thinking on and solve biomedical problems thorough computers and massive data. Our lab develops bioinformatic methods to solve the biomedical problems and to interpret complicated massive data with the help of computers and AI. In addition, we apply informatics and statistics to biological and disease research.

Projects for Regular Students in Doctoral or Master's Programs

1) Machine learning-based prediction functions of genome sequences
2) Single-cell informatics (informatics for single-cell omics data)
3) Integrative analyses of massive biomedical datasets

Study Programs for Short Stay Students (one week – one trimester)

1) Basic python programming for unsupervised learning
2) Basic python programming for supervised learning

Selected Publications

1) Takeuchi M, Ozaki H*, Hiraoka S, Kamagata Y, Sakata S, Yoshioka H, Iwasaki W. Possible cross-feeding pathway of facultative methylotroph *Methyloceanibacter caenitepidi* Gela4 on methanotroph *Methylocaldum marinum* S8. ***PLOS ONE***. 2019;14(3):e0213535.
2) Hayashi T, Ozaki H*, Sasagawa Y, Umeda M, Danno H, Nikaido I. Single-cell full-length total RNA sequencing uncovers dynamics of recursive splicing and enhancer RNAs. ***Nature Communications***. 2018;9(1):619.
3) Terajima H, Yoshitane H, Ozaki H, Suzuki Y, Shimba S, Kuroda S, Iwasaki W, Fukada Y. ADARB1 catalyzes circadian A-to-I editing and regulates RNA rhythm. ***Nature Genetics***. 2017;49(1):146.
4) Ozaki H, Iwasaki W. MOCCS: Clarifying DNA-binding motif ambiguity using ChIP-seq data. ***Computational biology and chemistry.*** 2016;63:62-72.
5) Ishizu H, Iwasaki YW, Hirakata S, Ozaki H, Iwasaki W, Siomi H, Siomi MC. Somatic primary piRNA biogenesis driven by cis-acting RNA elements and trans-acting Yb. ***Cell reports***. 2015;12(3):429-40.
6) Hirase S, Ozaki H*, Iwasaki W. Parallel selection on gene copy number variations through evolution of three-spined stickleback genomes. ***BMC Genomics***. 2014;15(1):735.
7) Yoshitane H, Ozaki H*, Terajima H, Du NH, Suzuki Y, Fujimori T, Kosaka N, Shimba S, Sugano S, Takagi T, Iwasaki W. CLOCK-controlled polyphonic regulation of circadian rhythms through canonical and noncanonical E-boxes. ***Molecular and Cellular Biology***. 2014;34(10):1776-87.

Stem Cell Therapy Major Scientific Interests of the Group

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Major Scientific Interests of the Group

1) Elucidation of regulatory mechanisms underlying self-renewal and differentiation of stem cells. (Especially focusing on blood stem cells.)
2) A study on the efficient utilization of intra-placental injection in a murine model.
3) Analysis of mammalian embryonic development mechanism using developmental engineering techniques

Projects for Regular Students in Doctoral or Master's Programs

Regulation of stem cell self-renewal and differentiation.

1) Generation of allogeneic/xenogeneic hematopoietic chimera mouse model
2) Analysis of reprogramming mechanism using cloned embryos and development of new embryo manipulation technology

Study Programs for Short Stay Students (one week – one trimester)

1) Understanding of ex vivo somatic cells expansion.
2) Practice and understanding of a mouse model of in utero transplantation
3) Practice of embryo manipulation using a micromanipulator

Selected Publications

1) **Long-term ex vivo expansion of mouse hematopoietic stem cells.** Wilkinson AC, Ishida R, Nakauchi H, **Yamazaki S.** Nat Protoc. 2020 Feb;15(2):628-648. doi: 10.1038/s41596-019-0263-2. Epub 2020 Jan 8.
2) **Long-term ex vivo haematopoietic-stem-cell expansion allows nonconditioned transplantation.** Wilkinson AC, Ishida R, Kikuchi M, Sudo K, Morita M, Crisostomo RV, Yamamoto R, Loh KM, Nakamura Y, Watanabe M, Nakauchi H, **Yamazaki S.** Nature. 2019 Jul;571(7763):117-121. doi: 10.1038/s41586-019-1244-x. Epub 2019 May 29.
3) **Depleting dietary valine permits nonmyeloablative mouse hematopoietic stem cell transplantation.** Taya Y, Ota Y, Wilkinson AC, Kanazawa A, Watarai H, Kasai M, Nakauchi H, **Yamazaki S.** Science. 2016 Dec 2;354(6316):1152-1155. doi: 10.1126/science.aag3145. Epub 2016 Oct 20.
4) **Hoxb5 marks long-term haematopoietic stem cells and reveals a homogenous perivascular niche.** Chen JY, Miyanishi M, Wang SK, **Yamazaki S**, Sinha R, Kao KS, Seita J, Sahoo D, Nakauchi H, Weissman IL. Nature. 2016 Feb 11;530(7589):223-7. doi: 10.1038/nature16943.
5) **Nonmyelinating Schwann cells maintain hematopoietic stem cell hibernation in the bone marrow niche.Yamazaki S**, Ema H, Karlsson G, Yamaguchi T, Miyoshi H, Shioda S, Taketo MM, Karlsson S, Iwama A, Nakauchi H. Cell. 2011 Nov 23;147(5):1146-58. doi: 10.1016/j.cell.2011.09.053.

Medical Physics

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Major Scientific Interests of the Group
Medical application of physics and engineering, Particle therapy

Projects for Regular Students in Doctoral or Master's Programs
1) Proton therapy, QA, QC, BNCT, 2) Diagnostic technology

Study Programs for Short Stay Students (one week – one trimester)
1) One week training for medical staffs (medical physics)

Selected Publications
1) Onishi Takahiro, Kumada Hiroaki, Takada Kenta, Naito Fujio, Kurihara Toshikazu, Sakae Takeji, Investigation of the neutron spectrum measurement method for dose evaluation in boron neutron capture therapy, APPLIED RADIATION AND ISOTOPES 140, 2018, 5-11
2) Takei Hideyuki, Isobe Tomonori, Kitamura Nozomi, Mori Yutaro, Tomita Tetsuya, Kobayashi Daisuke, Kamizawa Satoshi, Sato Tomoharu, Sakurai Hideyuki, Sakae Takeji, General ion recombination effect in a liquid ionization chamber in high-dose-rate pulsed photon and electron beams, JOURNAL OF RADIATION RESEARCH 59, No.3, 2018, 282-285
3) Terunuma Toshiyuki, Tokui Aoi, Sakae Takeji, Novel real-time tumor-contouring method using deep learning to prevent mistracking in X-ray fluoroscopy, RADIOLOGICAL PHYSICS AND TECHNOLOGY 11, No.1,2018, 43-53
4) Takada Kenta, Sato Tatsuhiko, Kumada Hiroaki, Koketsu Junichi, Takei Hideyuki, Sakurai Hideyuki, Sakae Takeji, Validation of the physical and RBE-weighted dose estimator based on PHITS coupled with a microdosimetric kinetic model for proton therapy, JOURNAL OF RADIATION RESEARCH, 59, No.1, 2018, 91-99
5) Masuda Akihiko, Matsumoto Tetsuro, Takada Kenta, Onishi Takahiro, Kotaki Kohei, Sugimoto Hidenori, Kumada Hiroaki, Harano Hideki, Sakae Takeji, Neutron spectral fluence measurements using a Bonner sphere spectrometer in the development of the iBNCT accelerator-based neutron source, APPLIED RADIATION AND ISOTOPES 127, 2017, 47-51
6) Takada Kenta, Kumada Hiroaki, Liem Peng Hong, Sakurai Hideyuki, Sakae Takeji, Development of Monte Carlo based real-time treatment planning system with fast calculation algorithm for boron neutron capture therapy, PHYSICA MEDICA-EUROPEAN JOURNAL OF MEDICAL PHYSICS 32, No.12, 2016, 1846-1851
7) Mori Yutaro, Isobe Tomonori, Yamaguchi Yoshiki, Takei Hideyuki, Kamizawa Satoshi, Terunuma Toshiyuki, Sato Eisuke, Takada Kenta, Tadano Kiichi, Yoshimura Yousuke, Sakurai Hideyuki, Sakae Takeji, Development of simple high-precision two-dimensional dose-distribution measurement method for proton beam therapy using imaging plate and EBT3, AUSTRALASIAN PHYSICAL & ENGINEERING SCIENCES IN MEDICINE 39, No.3, 2016, 687-696
8) Horiguchi Hironori, Sato Tatsuhiko, Kumada Hiroaki, Yamamoto Tetsuya, Sakae Takeji, Estimation of relative biological effectiveness for boron neutron capture therapy using the PHITS code coupled with a microdosimetric kinetic model, JOURNAL OF RADIATION RESEARCH 56, No.2, 2015, 382-390

Environmental Biology

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Major Scientific Interests of the Group

This laboratory addresses the mechanisms by which environmental electrophiles such as naphthoquinones, (E)-2-alkenals, 1,4-benzoquinone, crotonaldehyde, methylmercury and cadmium affect living systems by interacting with redox sensor proteins with reactive thiols (thiolate ions) through covalent modification. The observations obtained by this group regarding environmental electrophiles have lent new insight into mechanisms of redox-dependent signal transduction pathways that are regulated by reactive sulfur species (persulfides and polysulfides) in the body.

Projects for Regular Students in Doctoral or Master's Programs

1) Activation of redox signal transduction pathways (e.g., PTP1B/EGFR, Keap1/Nrf2, HSP90/HSF1 and PTEN/Akt) during exposure to environmental electrophiles.
2) Isolation and identification of phytochemicals with reactive sulfur species that can capture environmental electrophiles, resulting in inactivation of these chemicals.

Selected Publications

1) **Kumagai Y**, Abiko Y. Environmental electrophiles: protein adducts, modulation of redox signaling and interaction with persulfides/polysulfides. ***Chem Res Toxicol*** 30: 203-219, 2017.
2) Akaike T, Ida T, Fan-Yan Wei FY, Nishida M, **Kumagai Y**, Alam MM, Ihara H, Sawa T, Matsunaga T, Kasamatsu S, Nishimura A, Morita M, Tomizawa K, Nishimura A, Watanabe S, Inaba K, Shima H, Tanuma N, Jung M, Fujii S, Watanabe Y, Ohmuraya M, Nagy P, Feelisch M, Fukuto JM, Motohashi H. Cysteinyl-tRNA synthetase governs cysteine polysulfidation and mitochondrial bioenergetics. ***Nature Commun*** 8: 1177, 2017.
3) Unoki T, Abiko Y, Toyama T, Uehara T, Tsuboi K, Nishida M, Kaji T, **Kumagai Y.** Methylmercury, an environmental electrophile capable of activation and disruption of the Akt/CREB/Bcl-2 signal transduction pathway in SH-SY5Y cells. ***Sci Rep*** 6: 28944, 2016.
4) Ida T, Sawa T, Ihara H, Tsuchiya Y, Watanabe Y, **Kumagai Y**, Suematsu M, Motohashi H, Fujii S, Matsunaga T, Yamamoto M, Ono K, Devarie-Baez NO, Xian M, Fukuto JM, Akaike T. Reactive cysteine persulfides and S-polythiolation regulate oxidative stress and redox signaling. ***Proc Natl Acad Sci USA*** 111: 7606-7611, 2014.
5) **Kumagai Y**, Shinkai Y, Miura T, Cho AK. The chemical biology of naphthoquinones and its environmental implications. ***Annu Rev Pharmacol Toxicol*** 52: 221-247, 2012.
6) Iwamoto N, Sumi D, Ishii T, Uchida K, Cho AK, Froines JR, **Kumagai Y**. Chemical knockdown of protein tyrosine phosphatase 1B by 1,2-naphthoquinone through covalent modification causes persistent transactivation of epidermal growth factor receptor. ***J Biol Chem*** 282: 33396-33404, 2007.

Environmental Microbiology

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Major Scientific Interests of the Group

The aim of our group is to understand the host-pathogen interactions. We are analyzing molecular mechanism of the pathogenicity of paramyxoviruses. We are also interested in applied science. We are developing edible vaccines using virus-like particles (empty virion without genome) of small non-enveloped viruses produced in plants.

Projects for Regular Students in Doctoral or Master's Programs

1) Manipulation of negative-stranded viruses
2) Generation of edible vaccines

Study Programs for Short Stay Students (one week – one trimester)

1) Rescue of recombinant virus from cloned cDNA
2) Expression of virus proteins in *E. coli*.

Selected Publications

1) **Takeuchi K**, Nagata N, Kato SI, Ami Y, Suzaki Y, Suzuki Y, Sato Y, Tsunetsugu-Yokota Y, Mori K, Van Nguyen N, Kimura H, Nagata K. Wild-type measles virus with the hemagglutinin protein of the Edmonston vaccine strain retains wild-type tropism in macaques. ***J Virol.*** 2012; 86:3027-3037. (corresponding author)
2) Kubota M, **Takeuchi K**, Watanabe S, Ohno S, Matsuoka R, Kohda D, Nakakita SI, Hiramatsu H, Suzuki Y, Nakayama T, Terada T, Shimizu K, Shimizu N, Shiroishi M, Yanagi Y, Hashiguchi T. Trisaccharide containing α2,3-linked sialic acid is a receptor for mumps virus. ***Proc Natl Acad Sci U S A.*** 2016; 113(41):11579-11584. (corresponding author)
3) Takada M, Matsuura R, Kokuho T, Tsuboi T, Kameyama KI, **Takeuchi K**. Reciprocal complementation of bovine parainfluenza virus type 3 lacking either the membrane or fusion gene. J Virol Methods. 2017, 249:25-30. (corresponding author)

Occupational and Aerospace Psychiatry

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Major Scientific Interests of the Group

We are interested in the prevention and management of mental health in workplace, and the mechanism how space environmental stress affects stress reaction.

Projects for Regular Students in Doctoral or Master's Programs

1) The mechanism how employment system affect mental health in workplace
2) The survey of mental health in researchers and teachers
3) The effect of environmental adaptation on mental health
4) The impact of sleep problems on job performance
5) The collaborative study with JAXA

Selected Publications

1) Oi, Y., Hirai, Y., Doki, S., Ohtaki, Y., Hori, D., Andrea, C. S., ... & Matsuzaki, I. (2018). Trial of stress-related index measurement under confinement stress. Transactions of the Japan society for aeronautical and space sciences, aerospace technology Japan, 16(6), 476-480.
2) Ohtaki, Y., Oi, Y., Doki, S., Kaneko, H., Usami, K., Sasahara, S., & Matsuzaki, I. (2017). Characteristics of Telephone Crisis Hotline Callers with Suicidal Ideation in Japan. Suicide and Life-Threatening Behavior, 47(1), 54-66.
3) Sakurai, T., Amemiya, A., Ishii, M., Matsuzaki, I., Chemelli, R. M., Tanaka, H., ... & Arch, J. R. (1998). Orexins and orexin receptors: a family of hypothalamic neuropeptides and G protein-coupled receptors that regulate feeding behavior. Cell, 92(4), 573-585.
4) Murakami, M., & Matsuzaki, I. (1984). 11 The physical and chemical environment. Oxford Textbook of Public Health: History, determinates, scope, and strategies, 1, 199.

English for Medical Purposes

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Major Research Interests of the Group

Our main interests are in researching and developing English-language pedagogies in the following areas:

1. English for Medical Purposes (clinical communication, medical terminology)
2. English for Scientific Purposes (scientific presentation, writing for research publication, English for laboratory techniques)
3. English as a Lingua Franca in Academic Settings (international academic collaboration/exchange)

Projects for Regular Students in Doctoral or Master's Programs

1) Development of pedagogies for supporting communication in English for biomedical purposes
2) Data collection, analysis, and international publication for Biomedical Topics (Cardiovascular Science, Immunology, Women's Sports Medicine)

Study Programs for Short Stay Students (one week – one trimester)

1) Basic Editing Skills for Life Sciences Publishing
2) Basic Scientific Review Writing/Drafting/Publication Process
3) Multimedia and Design for Effective Visual Communications in Science

Selected Publications

1) Mayers T, Morikawa K, Ho CK, Ohneda O. An international exchange program for undergraduate medical science students. J Med Eng Educ. 2018;17:7–13.
2) Mayers T. Using comedy sketches to learn medical English. J Med Eng Educ. 2017;15:105–7.
3) Mayers T, Purdue B, Ho CK, Ohneda O. Teaching science and leaning English: an introduction to the Molecular Biology Course in Vietnam. J Med Eng Educ. 2015;14:87–92.
4) Miyamasu F, Tanaka M. e-Learning Systematic Approach to Medical Vocabulary. Tokyo: Kripton; 2010.
5) Miyamasu F. Introducing the medical humanities to Japanese medical students through the English-for-Medical-Purposes class. J Med Eng Educ. 2008;7:106–12.
6) Miyamasu F. Problem-based learning in the English-for-Medical-Purposes class. J Med Eng Educ. 2006;6:45–51.