Laboratory list for KIBI-Tsukuba Research Training Program 2022

1. **Anatomy and Embryology**
2. **Animal Sciences**
3. **Experimental Pathology**
4. **Gene Regulation**
5. **Genome Biology**
6. **Metabolism and Endocrinology**
7. **Microbiology**
8. **Molecular Cell Biology**
9. **Molecular Parasitology**
10. **Molecular Virology**
11. **Regenerative Medicine and Stem Cell Biology**

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.

Laboratory Animal Science
Laboratory Animal Resource Center

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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.

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.

Gene Regulation

Principal Investigator Koji Hisatake

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Other Faculty Members

Associate Professor: Aya Fukuda
Associate Professor: Ken Nishimura

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).

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.

Metabolism and Endocrinology

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Major Scientific Interests of the Group

We have been working to understand the molecular mechanisms of energy metabolism using the newest technologies, such as molecular and cellular biology, gene-engineered animals, genome informatics and trans-omics including lipidomics. We especially focus on lipid metabolism with our original molecular targets: SREBPs, CREBH, Elovl6, CtBP2, and KLF15 (see details in each section) develop new therapeutic approaches for preventing obesity, diabetes, and cardiovascular disease. We reveal that these factors regulate organ lipids in both quantity and quality aspects and energy metabolism, and thus, play pivotal roles in a wide variety of biological and pathological events. Our lab motto is “BREAK the DOGMA”. We always try to open up a new world of science with pieces of novel wisdom to contribute to future therapy for inflammation, cancer, and brain sciences beyond endocrinological and metabolic diseases.

Projects for Regular Students in Doctoral or Master’s Programs

1) Energy metabolism and transcription factors with our main target factors: SREBPs, CREBH, Elovl6, CtBP2, and KLF15 relating to the following projects.
2) Lipid metabolism for various metabolic diseases
3) Pathogenic mechanisms and treatment of diabetes
4) Pathogenic mechanisms and treatment of atherosclerosis

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

1) Transfection and Luciferase assay for analyzing the function of transcription factors
2) Experimental procedures for mouse metabolic disease model. Petting obesity mice and measure blood sugar.

Selected Publications

1) Shimano H, et al. SREBP-regulated lipid metabolism: convergent physiology - divergent pathophysiology. ***Nat Rev Endocrinol.*** **2017** Dec; 13(12):710-730.
2) Oishi Y, et al. SREBP1 Contributes to Resolution of Pro-inflammatory TLR4 Signaling by Reprogramming Fatty Acid Metabolism. ***Cell Metab***. 2017 Feb 7; 25(2): 412-427
3) Zhao H, et al. Elovl6 Deficiency Improves Glycemic Control in Diabetic db/db Mice by Expanding β-Cell Mass and Increasing Insulin Secretory Capacity. ***Diabetes***. 2017 Jul; 66(7): 1833-1846.

4) Takeuchi Y, et al. KLF15 Enables Rapid Switching between Lipogenesis and Gluconeogenesis during Fasting. ***Cell Rep***. **2016** Aug 30; 16(9): 2373-2386.
5) Nakagawa Y, et al. Hepatic CREB3L3 Controls Whole-Body Energy Homeostasis and Improves Obesity and Diabetes. ***Endocrinology***. **2014** Dec; 155(12): 4706-4719.
6) Sunaga H, et al. Deranged fatty acid composition causes pulmonary fibrosis in Elovl6-deficient mice. ***Nat Commun***. **2013**; 4: 2563.
7) Izumida Y, et al. Glycogen shortage during fasting triggers liver-brain-adipose neurocircuitry to facilitate fat utilization. ***Nat Commun***. **2013**; 4: 2316.
8) Matsuzaka T, et al. Elovl6 promotes nonalcoholic steatohepatitis in mice and humans. ***Hepatology***. **2012** Dec; 56(6): 2199-2208.
9) Matsuzaka T, et al. Crucial role of a long-chain fatty acid elongase, Elovl6, in obesity-induced insulin resistance. ***Nat Med*** 2007 Oct; 13(10): 1193-1202.
10) Kato T, et al. Granuphilin is activated by SREBP-1c and involved in impaired insulin secretion in diabetic mice. ***Cell Metab*** 4(2): 143-54, 2006 Aug
11) Nakagawa Y, et al. TFE3 transcriptionally activates hepatic IRS-2, participates in insulin-signaling and , ameliorates diabetes. ***Nat Med*** 12(1): 107-13, 2006 Jan__
12) Ide T, et al. SREBPs suppress IRS-2-mediated insulin signaling in the liver. ***Nature Cell Biology*** 6(4): 351-7, 2004 Apr

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)

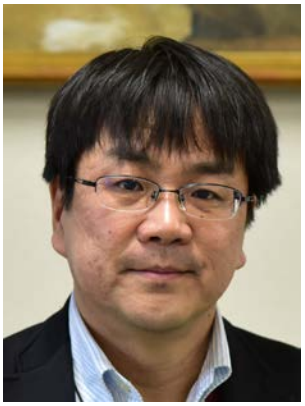
1) Molecular genetic and biochemical techniques
2) Analysis of gene regulation

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 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) 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.
2) 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.
3) 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).
4) 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.
5) 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.
6) 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.
7) 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.
8) 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).
9) 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.

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.

Molecular Virology

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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.
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Regenerative Medicine and Stem Cell Biology

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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.