University of Tsukuba 筑波大学

9th Summer Research Program in Tsukuba

July 23- August 3, 2018

List of Laboratories
University of Tsukuba

筑波大学生命環境系
Faculty of Life and Environmental Sciences
University of Tsukuba

IMAGINE THE FUTURE.

FACULTY OF MEDICINE Med UNIVERSITY OF TSUKUBA

IIIS
INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE

Participating Laboratories

Medical Sciences

1. **Shigeru Chiba** - *Hematology*
2. **Manabu Fujimoto** - *Dermatology*
3. **Koji Hisatake** - *Gene Regulation*
4. **Kiong Ho** - *Molecular Parasitology*
5. **Kenji Irie** - *Molecular Cell Biology*
6. **Mitsuyasu Kato** - *Experimental Pathology*
7. **Atsushi Kawaguchi** - *Infection Biology (Virology)*
8. **Makoto Kobayashi** - *Molecular and Developmental Biology*
9. **Yoshito Kumagai** - *Environmental Biology*
10. **Michael Lazarus** - *Systems Sleep Biology*
11. **Kazuya Morikawa** - *Infection Biology (Microbiology)*
12. **Masafumi Muratani** - *Genome Biology*
13. **Michio Nagata** - *Kidney and Vascular Pathology*
14. **Masayuki Noguchi** - *Diagnostic Surgical Pathology*
15. **Norihiko Ohbayashi** - *Physiological Chemistry*
16. **Osamu Ohneda** - *Regenerative Medicine and Stem Cell Biology*
17. **Akira Shibuya** - *Immunology*
18. **Hitoshi Shimano** - *Endocrinology and Metabolism*
19. **Fumihiro Sugiyama** - *Laboratory Animal Science*
20. **Satoru Takahashi** - *Anatomy and Embryology/ Laboratory Animal Resource Center*
21. **Peter ten Dijke** - *Cancer Signaling*
22. **Hiromi Yanagisawa** - *Matrix and Stem Cell Biology*
23. **Masashi Yanagisawa** - *Molecular Pharmacology*

Life and Environmental Sciences

24. **Shigeyuki Betsuyaku** - *Plant Immune Dynamics*
25. **Toshiharu Enomae** - *Paper device and eco-friendly materials*
26. **Hiroshi Ezura** - *Olericulture and Floriculture*
27. **Louis John Irving** - *Plant Ecophysiology*
28. **Yasuhiro Ishiga** - *Molecular Plant Pathology*
29. **Yooichi Kainoh** - *Applied Entomology and Zoology*
30. **Yutaka Kitamura** - *Food and Biomass Process Engineering*
31. **Yuichi Onda** - *Isotope Hydrogeomorphology and Radioecology*
32. **Sumiko Sugaya** - *Pomology*

1. Hematology

Principal Investigator **Shigeru Chiba**
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Other Faculty Members

Associate Professor, Yuichi Hasegawa
Associate Professor, Naoshi Obara
Associate Professor, Mamiko Sakata-Yanagimoto
Associate Professor, Hidekazu Nishikii
Assistant Professor, Yasuhisa Yokoyama
Assistant Professor, Naoki Kurita
Assistant Professor, Takayasu Kato
Assistant Professor, Manabu Kusakabe

Major Scientific Interests

Our research aim is to understand molecular mechanisms underlying hematologic malignancies and, on the bases of those, develop new clinical approaches in diagnostics and treatment. We are using patient-derived samples and genetically modified mice to analyze genetics, epigenetic, metabolism, cell biology, and disease biology. The results are sometimes directly translated in clinical trials in our hospital ward.

Projects for Regular Students in Doctoral or Master's Programs

1) Analysis of molecular mechanisms in hematologic malignancies
2) Analysis of bone marrow stromal cells involved in normal and malignant hmeatopoiesis

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

1) Training in hematopoietic cell culture, flow cytometry, and epigenetic approaches
2) Training in sequence procedure using a second generation sequencer
3) Training in immunostaining procedure

Recent Publications

1) Suehara Y, Sakata-Yanagimoto M, Hattori K, Nanmoku T, Itoh T, Kaji D, Yamamoto G, Abe Y, Narita K, Takeuchi M, Matsue K, Sato T, Noguchi M, Baba N, Sakamoto T, Kusakabe M, Kurita N, Kato T, Yokoyama Y, Nishikii H, Obara N, Hasegawa Y, **Chiba S**. Liquid biopsy for the identification of intravascular large B-cell lymphoma. ***Haematologica***. (doi: 10.3324/haematol.2017.178830.) [Epub ahead of print]
2) Fujisawa M, Sakata-Yanagimoto M, Nishizawa S, Komori D, Gershon P, Kiryu M, Tanzima S, Fukumoto K, Enami T, Muratani M, Yoshida K, Ogawa S, Matsue K, Nakamura N, Takeuchi K, Izutsu K, Fujimoto K, Teshima T, Miyoshi H, Gaulard P, Ohshima K, **Chiba S**. Activation of RHOA-VAV1 signaling in angioimmunoblastic T-cell lymphoma. ***Leukemia***. 2017 (doi: 10.1038/leu.2017.273.) [Epub ahead of print]
3) Pierini A, Nishikii H, Baker J, Kimura T, Kwon HS, Pan Y, Chen Y, Alvarez M, Strober W, Velardi A, Shizuru JA, Wu JY, **Chiba S**, Negrin RS. Foxp3+ regulatory T cells maintain the bone marrow microenvironment for B cell lymphopoiesis. ***Nat Commun***. 8:15068, 2017
4) Nguyen TB, Sakata-Yanagimoto M, Asabe Y, Matsubara D, Kano J, Yoshida K, Shiraishi Y, Chiba K, Tanaka H, Miyano S, Izutsu K, Nakamura N, Takeuchi K, Miyano H, Ohshima K, Minowa T, Ogawa S, Noguchi M, **Chiba S**. Identification of cell-type-specific mutations in nodal T-cell lymphomas. ***Blood Cancer J***. 7:e516, 2017
5) Makishima H, Yoshizato T, Yoshida K, Sekeres MA, Radivoyevitch T, Suzuki H, Przychodzen B, Nagata Y, Meggendorfer M, Sanada M, Okuno Y, Hirsch C, Kuzmanovic T, Sato Y, Sato-Otsubo A, LaFramboise T, Hosono N, Shiraishi Y, Chiba K, Haferlach C, Kern W, Tanaka H, Shiozawa Y, Gómez-Seguí I, Husseinzadeh HD, Thota S, Guinta KM, Dienes B, Nakamaki T, Miyawaki S, Sauntharajah Y, **Chiba S**, Miyano S, Shih LY, Haferlach T, Ogawa S, Maciejewski JP. Dynamics of clonal evolution in myelodysplastic syndromes. ***Nat Genet***. 49(2):204-12, 2017
6) Nishikii H, Kim BS, Yokoyama Y, Chen Y, Baker J, Pierini A, Alvarez M, Mavers M, Maas-Bauer K, Pan Y, **Chiba S**, Negrin RS. DR3 signaling modulates the function of Foxp3+ regulatory T cells and the severity of acute graft versus host disease. ***Blood***. 128(24):2846-58, 2016

2. Dermatology

Principal Investigator **Manabu Fujimoto**
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Other Faculty Members
Assistant Professor: Yasuhiro Fujisawa (fujisan@md.tsukuba.ac.jp)
Assistant Professor: Naoko Okiyama (naoko.okiyama@md.tsukuba.ac.jp)
Assistant Professor: Rei Watanabe (rwatanabe@md.tsukuba.ac.jp)
Assistant Professor: Yosuke Ishitsuka (yosuke.ishitsuka@md.tsukuba.ac.jp)
Assistant Professor: Yoshiyuki Nakamura (ynakamura-tuk@umin.ac.jp)

Major Scientific Interests

We are working on revealing the function of skin from the aspect of barrier and immune system through mouse models of inflammatory skin diseases and skin tumors, and actual human disease samples.

Projects for Regular Students in Doctoral or Master's Programs

1) Research on immune reaction in inflammatory skin disorders
2) Research on immune reaction in malignant skin tumors

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

1) Learn procedures for immunofluorescence analyses of human and mouse skin.
2) Learn procedures for flow cytometry analyses of human and mouse immune cells.

Recent Publications

1. Saito A, Okiyama N, Kubota N, et al. Blockade of granzyme B remarkably improves mucocutaneous diseases with keratinocyte death in interface dermatitis. ***J Invest Dermatol.*** *in press.*
2. Fujisawa Y, Yoshino K, Otsuka A, et al. Baseline neutrophil to lymphocyte ratio combined with serum LDH level associated with outcome of nivolumab immunotherapy in a Japanese advanced melanoma population. ***Br J Dermatol.*** *in press.*
3. Nakamura Y, Fujisawa Y, Okiyama N, et al. Surgical damage to the lymphatic system promotes tumor growth via impaired adaptive immune response. J Dermatol Sci. 90:46-51, 2018.
4. Ishitsuka Y, Huebner AJ, Rice RH, et al. Lce1 family members are Nrf2-Target genes that are induced to compensate for the loss of loricrin. ***J Invest Dermatol.*** 136:1656-63, 2016.
5. Fujimoto M, Watanabe R, Ishitsuka Y and Okiyama N. Recent advances in dermatomyositis-specific autoantibodies. ***Curr Opin Rheumatology.*** 28:636-44, 2016.
6. Watanabe R, Gehad A, Yang C, et al. Human skin is protected by four functionally and phenotypically discrete populatios of resident and recirculating memory T cells. ***Sci Transl Med.*** 7:279ra39, 2015.

3. Gene Regulation

Principal Investigator **Koji Hisatake**
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Major Scientific Interests

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) Identification and functional analyses of transcription factors involved in adipocyte commitment.
4) Role of non-coding RNA in epigenetic regulation during adipocyte differentiation.

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

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

Recent Publications

1) Nishimura K, Aizawa S, Nugroho FL, Shiomitsu E, Tran YT, 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)
2) 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, and 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)
3) 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.*** pii: jbc.M115.688317. (2015)
4) 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*** Vol. 3(5), 915-929 (2014)
5) 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).
6) Wakao H, Yoshikiyo K, Koshimizu U, Furukawa T, Enomoto K, Matsunaga T, Tanaka T, Yasutomi Y, Yamada T, Minakami H, Tanaka J, Oda A, Sasaki T, Wakao R, Lantz O, Udagawa T, Sekiya Y, Higuchi K, Harada N, Nishimura K, Ohtaka M, Nakanishi M, Fujita H: Expansion of Functional Human Mucosal-Associated Invariant T Cells via Reprogramming to Pluripotency and Redifferentiation. ***Cell Stem Cell*** 12, 546-558 (2013).
7) Nishimura T, Kaneko S, Kawana-Tachikawa A, Tajima Y, Goto H, Zhu D, Nakayama-Hosoya K, Iriguchi S, Uemura Y, Shimizu T, Takayama N, Yamada D, Nishimura K, Ohtaka M, Watanabe N, Takahashi S, Iwamoto A, Koseki H, Nakanishi M, Eto K, Nakauchi H: Generation of rejuvenated antigen-specific T cells by reprogramming to pluripotency and redifferentiation. ***Cell Stem Cell*** 12, 114-126 (2013).

4. Molecular Parasitology

Principal Investigator **Kiong Ho**
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Major Scientific Interests

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 the mechanism of RNA repair and recombination. RNA ligase is the key enzyme that joins the broken RNAs together. We are 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 Graduate Students

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

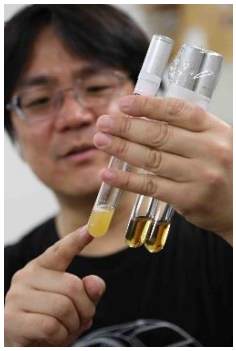
Study Programs for Short Stay Students

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

5. Molecular Cell Biology



Principal Investigator **Kenji Irie**
E-mail address kirie@md.tsukuba.ac.jp
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Other Faculty Members
Assistant Professor Tomoaki Mizuno: mizuno@md.tsukuba.ac.jp
Assistant Professor Yasuyuki Suda: ysuda@md.tsukuba.ac.jp

Major Scientific Interests

- Post-transcriptional regulation of gene expression by RNA-binding proteins
- Molecular mechanism of mRNA localization and local translation regulating cell polarity, asymmetric cell division, and cell-fate
- Regulation of the endoplasmic reticulum stress response by protein kinases
- Prospore membrane formation by vesicle docking

Projects for Regular Students in Doctoral or Master's Programs

1) Post-transcriptional regulation of gene expression by the Ccr4-Not complex in yeast.
2) Regulation of the endoplasmic reticulum stress response by protein kinases.
3) Roles of yeast Ataxin-2 ortholog, Pbp1, in the control of mRNA stability and translation.
4) Roles of decapping activators in the control of mRNA stability and translation.

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

1) Yeast genetic approaches including the isolation and characterization of mutants, tetrad analysis, complementation, and mitotic recombination.
2) Molecular genetic techniques including yeast transformation, gene knockout, and generation of mutations in cloned genes.
3) Molecular biology and biochemistry techniques analyzing gene expression including Northern blotting, RT-PCR, and Western blotting.
4) Imaging yeast cells using indirect immunofluorescence and GFP-protein fusions.

Recent Publications

1) 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).
2) 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.
3) 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.
4) 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.
5) 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.
6) 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).
7) 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.
8) Kimura Y, Irie K, Irie K. Pbp1 is involved in Ccr4- and Khd1-mediated regulation of cell growth through association with ribosomal proteins Rpl12a and Rpl12b. Eukaryot Cell. 2013 Jun;12(6):864-74.

6. Experimental Pathology

Principal Investigator **Mitsuyasu Kato**
E-mail address mit-kato@md.tsukuba.ac.jp
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Other Faculty Members
Associate Professor Hiroyuki Suzuki: h-suzuki@md.tsukuba.ac.jp
Assistant Professor Yukihide Watanabe: y-watanabe@md.tsukuba.ac.jp
Assistant Professor Yukari Okita: yukari-okita@md.tsukuba.ac.jp

Major Scientific Interests

Experimental studies using cultured cells and murine models, for elucidation of the roles of transforming growth factor-β related molecules in stem cell biology and carcinogenesis. Our aim is to establish novel molecular targeting therapies useful for relapse-free therapy and prevention of cancer by targeting dormant cancer stem cells.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanisms of TGF-β related molecules (TMEPAI, MafK, GPNMB etc.) in stem cell kinetics and carcinogenesis using gene-edited mice and cells with three dimensional histopathological analysis.
2) Molecular mechanisms of TGF-β1 stimulated clone 22 related molecules (TSC22, THG-1) in squamous cell carcinoma development
3) Establishment of Novel Anti-cancer drugs by using Macrocyclic peptide technologies

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

1) In vitro tumorigenic assays and gene expression (cell proliferation, sphere forming assay, matrigel invasion assay, and immunofluorescent staining, qPCR, Western blotting etc.)
2) Pathological tissue preparation, Immunohistochemistry and 3D quantitative analysis

Recent Publications

1) Zheng L, **Suzuki H**, Nakajo Y, Nakano A, **Kato M**. Regulation of c-MYC transcriptional activity by transforming growth factor-beta 1-stimulated clone 22. **Cancer Sci**.109: 395-402, 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, **Kato M**. The transcription factor MAFK induces EMT and malignant progression of triple-negative breast cancer cells through its target GPNMB. **Sci. Signal.** 10 (474), eaak9397, 2017.
3) **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.
4) Nakano N, **Kato M**, Itoh S. Regulation of the TMEPAI promoter by TCF7L2: the C-terminal tail of TCF7L2 is essential to activate the TMEPAI gene. **J Biochem.** 159: 27-30, 2016.
5) Azami S*, Vo Nguyen TT*, **Watanabe Y** and **Kato M**. Cooperative induction of transmembrane prostate androgen induced protein TMEPAI/PMEPA1 by transforming growth factor-β and epidermal growth factor signaling. **Biochem Biophys Res Commun.** 456: 580-585, 2015 (*equal contribution)
6) 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.
7) Nakano N, Itoh S, **Watanabe Y**, Maeyama K, Itoh F, and **Kato M**. Requirement of TCF7L2 for TGF-β -dependent transcriptional activation of the TMEPAI gene. **J Biol Chem**. 285: 38023-38033, 2010.
8) **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.

7. Infection Biology (Virology)

Principal Investigator **Atsushi Kawaguchi**
E-mail address ats-kawaguchi@md.tsukuba.ac.jp
URL http://www.md.tsukuba.ac.jp/basic-med/infectionbiology/virology/index_english.html
Other Faculty Members
Associate Professor Mitsuru Okuwaki
Assistant Professor Shoko Saito, Kohsuke Kato

Major Scientific Interests

The research aim of this group is to understand the molecular mechanism of replication and pathogenicity of animal viruses such as influenza virus, adenovirus, etc. The structure and function of virus-encoded factors and host cell-derived factors involved in the above processes are being studied at the atomic, molecular, cellular, and body levels. In addition, we are particularly interested in clarifying the physiological function of identified host factors such as chromatin regulators, molecular chaperones, etc. as well as their roles in infection.

Projects for Regular Students in Doctoral or Master's Programs

1) Identification of novel factors in virus replication and host immune system.
2) Control of virus diseases based on the knowledge of host defense systems, or through development of novel anti-viral drugs
3) Regulatory mechanism for the structure and function of chromatin
4) Leukemogenic mechanism by chromosomal translocation

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

1) Molecular mechanism of host factors involved in influenza virus replication
2) Molecular mechanism of host inflammatory responses against influenza virus infection
3) Action mechanism of an anti-virus drug

Selected Recent Publications

1) Asaka MN, Kawaguchi A, Sakai Y, Mori K, Nagata K. Polycomb repressive complex 2 facilitates the nuclear export of the influenza viral genome through the interaction with M1. ***Sci. Rep.***, 2016; 6: 33608.
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: 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, Asaka MN, Matsumoto K, Nagata K. Centrosome maturation requires YB-1 to regulate dynamic instability of microtubules for nucleus reassembly. ***Sci. Rep.***, 2015; 5: 8768.
5) Kawaguchi A, Matsumoto K, Nagata K. YB-1 functions as a porter to lead influenza virus ribonucleoprotein complexes to microtubules. ***J. Virol.***, 2012; 86: 11086-11095.
6) Sugiyama K, Obayashi E, Kawaguchi A, Tame JRH, Nagata K, Park SY. Structural insight into a novel subunit contact within influenza virus RNA polymerase. ***EMBO J.***, 2009; 28: 1803-1811.
7) Obayashi E, Yoshida H, Kawai F, Shibayama N, Kawaguchi A, Nagata K, Tame JRH, Park SY. The structural basis for an essential subunit interaction in influenza virus RNA polymerase. ***Nature***, 2008; 454: 1127-1131.

8. Molecular and Developmental Biology

Principal Investigator **Makoto Kobayashi**
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URL http://www.md.tsukuba.ac.jp/MDBiology/mdbiol.index.html

Major Scientific Interests

- Epigenetic regulation in the cell-fate determination
- Stress response and gene regulation in the cellular defense system

Projects for Regular Students in Doctoral or Master's Programs

1) Development of hematopoietic stem cells
2) Development of internal organs: liver, pancreas, gill, ...
3) Defense against a variety of stresses: oxidative stress, ER stress, autophagy defect, heavy metals, ...
4) Functional foods and healthy life expectancy

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

1) Whole body expression analyses of anti-stress or hematopoietic genes in zebrafish
2) Investigation of hematopoietic stem cell generation using transgenic GFP zebrafish
3) Examination of toxicity/medicinal effects of active ingredients in foods or drugs using zebrafish

Recent Publications

1) Mukaigasa K, Tsujita T, Nguyen TV, Li L, Yagi H, Fuse Y, Nakajima-Takagi Y, Kato K, Yamamoto M & Kobayashi M. (2018) Nrf2 activation attenuates genetic endoplasmic reticulum stress induced by a mutation in the phosphomannomutase 2 gene in zebrafish. ***Proc Natl Acad Sci USA*** in press.
2) Fuse Y, Endo Y, Araoi S, Daitoku H, Suzuki H, Kato M & Kobayashi M. (2018) The possible repositioning of an oral anti-arthritic drug, auranofin, for Nrf2-activating therapy: The demonstration of Nrf2-dependent anti-oxidative action using a zebrafish model. ***Free Rad Biol Med*** 115:405-411.
3) Fuse Y & Kobayashi M. (2017) Conservation of the Keap1-Nrf2 system: An Evolutionary Journey through Stressful Space and Time. ***Molecules*** 22: 436.
4) Fuse Y, Nguyen VT & Kobayashi M. (2016) Nrf2-dependent protection against acute sodium arsenite toxicity in zebrafish. ***Toxicol Appl Pharmacol*** 305: 136-142.
5) Nguyen TV, Fuse Y, Tamaoki J, Akiyama S, Muratani M, Tamaru Y & Kobayashi M. (2016) Conservation of the Nrf2-mediated gene regulation of proteasome subunits and glucose metabolism in zebrafish. ***Oxid Med Cell Longev*** 2016: 5720574
6) Takeuchi M, Fuse Y, Watanabe M, Andrea CS, Takeuchi M, Nakajima H, Ohashi K, Kaneko H, Kobayashi-Osaki M, Yamamoto M & Kobayashi M. (2015) LSD1/KDM1A promotes hematopoietic commitment of hemangioblasts through downregulation of Etv2. ***Proc Natl Acad Sci USA*** 112: 13922-13927.
7) Fuse Y, Nakajima H, Nakajima-Takagi Y, Nakajima O & Kobayashi M. (2015) Heme-mediated inhibition of Bach1 regulates the liver specificity and transience of the Nrf2-dependent induction of zebrafish heme oxygenase 1. ***Genes Cells*** 20: 590-600.
8) Mukaigasa K, Nguyen LTP, Li L, Nakajima H, Yamamoto M & Kobayashi M. (2012) Genetic evidence of an evolutionarily conserved role for Nrf2 in the protection against oxidative stress. ***Mol Cell Biol*** 32: 4455-4461.

9. Environmental Biology

Principal Investigator **Yoshito Kumagai**
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Other Faculty Members Assistant Professors, Yasuhiro Shinkai, Yumi Abiko, and Masahiro Akiyama .

Major Scientific Interests

We focus on preventive medicine through reduction of environmental risks and elucidation of signaling alterations by environmental electrophiles and regulatory mechanisms.

Projects for Regular Students in Doctoral and Master's Programs

1) Elucidation of biological response systems elicited by environmental electrophiles and mechanisms underlying disruption of these systems.
2) Elucidation of mechanisms regulating the threshold of redox signaling activated by environmental electrophiles.

Study Programs for Short Stay Students

1) Assays to evaluate existence of reactive sulfur species to capture environmental electrophiles.
2) Analysis of *S*-modification of protein by electrophiles using UPLC-MS/MS

Recent Publications

1. 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. ***PNAS*** 111: 7606-7611, 2014.
2. Abiko Y, Mizokawa M, **Kumagai Y**. Activation of the Keap1/Nrf2 pathway through covalent modification of the 2-alkenal group of aliphatic electrophiles in Coriandrum sativum L. ***J Agric Food Chem*** 62: 10936-10944,2014.
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. Abiko Y, Sha L, Shinkai Y, Unoki T, Luong NC Tsuchiya Y, Watanabe Y, Hirose R, Akaike T, **Kumagai Y**. 1,4-Naphthoquinone activates the HSP90/HSF1 pathway through the S-arylation of HSP90 in A431 cells: Negative regulation of the redox signal transduction pathway by persulfides/polysulfides. ***Free Radic Biol Med*** 104: 118-128, 2017.
5. Shinkai Y, Masuda A, Akiyama M, Xian M, **Kumagai Y**. Cadmium-mediated activation of the HSP90/HSF1 pathway regulated by reactive persulfides/polysulfides. ***Toxicol Sci*** 156: 412-421, 2017.
6. Abiko Y, Shinkai Y, Unoki T, Hirose R, Uehara T, **Kumagai Y**. Polysulfide Na_2S_4 regulates the activation of PTEN/Akt/CREB signaling and cytotoxicity mediated by 1,4-naphthoquinone through formation of sulfur adducts. ***Sci Rep*** 7: 4814, 2017.
7. 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.
8. **Akiyama M**, **Shinkai Y**, **Unoki T**, Shim I, Ishii I, **Kumagai Y.** Capture of cadmium by reactive polysulfides attenuates cadmium-induced adaptive response and hepatotoxicity. ***Chem Res Toxicol*** 30: 2209-2217, 2017.
9. **Kumagai Y**, Abiko Y. Environmental electrophiles: protein adducts, modulation of redox signaling and interaction with persulfides/polysulfides. ***Chem Res Toxicol*** 30: 203-219, 2017.

10. Systems Sleep Biology

Principal Investigator **Michael Lazarus**
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Other Faculty Members
Assistant Professor Yo Oishi: oishi.yo.fu@u.tsukuba.ac.jp

Major Scientific Interests
The investigative focus of our laboratory is the cellular and synaptic basis by which the brain regulates sleep and wakeful consciousness. Our experiments seek to link the activity of defined sets of neurons with neurobehavioral and electroencephalographic outcomes in behaving animals by using innovative genetically or chemically engineered systems (optogenetics, chemogenetics or optopharmacology) in conjunction with recording of the electrical activity produced by the brain or in-vivo imaging (*in-vivo* electrophysiology or fiber-optic endomicroscopy).

Projects for Regular Students in Doctoral or Master's Programs

1) Use of genetically engineered systems to dissect neural circuitry regulating sleep and wakefulness
2) Development of optopharmacologic tools to control sleep
3) Role of brainstem neurons in linking REM sleep to the consumption of weight promoting foods

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

1) EEG/EMG electrode implantation and recording in mice
2) Engineering and production of adeno-associated viruses
3) Optogenetic and chemocogenetic modulation of neural circuitry by using stereotaxic microinjections of viral vectors
4) Immunohistochemistry and hybridization of brain tissue

Selected Publications

1) Oishi Y, Xu Q, Wang L, Zhang BJ, Takahashi K, Takata Y, Luo YJ, Cherasse Y, Schiffmann SN, de Kerchove d'Exaerde A, Urade Y, Qu WM, Huang ZL, Lazarus M. Slow-wave sleep is controlled by a subset of nucleus accumbens core neurons in mice. Nat Commun, 8: article 734, 2017.
2) Valencia Garcia S, Brischoux F, Clement F, Libourel PA, Arthaud S, Lazarus M, Luppi PH, Fort P. Genetic inactivation of ventromedial medulla inhibitory neurons induces REM sleep without atonia and REM sleep behavior disorder. Nat Commun, 9: article 505, 2018.
3) Kaur S, Wang JL, Ferrari L, Thankachan S, Kroeger D, Venner A, Lazarus M, Wellman A, Arrigoni E, Fuller PM, Saper CB. A Genetically defined circuit for arousal from sleep during hypercapnia. Neuron, 96:1153-1167, 2017.
4) McEown K, Takata Y, Cherasse Y, Nagata N, Aritake K, Lazarus M. Chemogenetic inhibition of the medial prefrontal cortex reverses the effects of REM sleep loss on sucrose consumption. eLife, 5: e20269, 2016
5) Lazarus M, Huang Z-L, Lu J, Urade Y, Chen J-F. How do the basal ganglia regulate sleep-wake behavior? Trends Neurosci, 35: 723-732, 2012.
6) Lazarus M, Shen HY, Cherasse Y, Qu WM, Huang ZL, Bass C, Winsky-Sommerer R, Semba K, Fredholm B, Boison D, Hayaishi O, Urade Y, Chen JF. Arousal effect of caffeine depends on adenosine A2A receptors in the shell of the nucleus accumbens. J Neurosci, 31: 10067-10075, 2011.
7) Lazarus M, Yoshida K, Coppari R, Bass CE, Mochizuki T, Lowell BB, Saper CB. EP3 prostaglandin receptors in the median preoptic nucleus are critical for fever responses. Nat Neurosci, 10, 1131-3, 2007.

11. Infection Biology (Microbiology)

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Major Scientific Interests

We are studying evolutionary/adaptation strategies of Gram-positive pathogens. Major research interests include the population heterogeneity, and the acquisition of antibiotics resistance. The main research target is the important human pathogen, *Staphylococcus aureus*, that inhabits in our nasal cavity but can cause a variety of diseases.

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) Interaction of flora and nasal epithelial cells

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

1) Molecular genetic and biochemical techniques in bacteria
2) Single molecule analysis using atomic force microscope

Selected Publications

1) Medrano Romero V, and Morikawa K. *Listeria monocytogenes* σ^H contributes to expression of competence genes and intracellular growth. ***J Bacteriol*** 198, 1207-1217. 2016
2) 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, 587-592. 2016
3) Ushijima Y, Yoshida O, Villanueva MJ, Ohniwa RL, and Morikawa K. Nucleoid clumping is dispensable for the Dps-dependent hydrogen peroxide resistance in *Staphylococcus aureus*. ***Microbiol*** 162, 1822-1828. 2016
4) Maudsdotter L, Imai S, Ohniwa RL, Saito S, and Morikawa K. *Staphylococcus aureus* dry stress survivors have a heritable fitness advantage in subsequent dry exposure. ***Microb Infec*** 17, 456-461. 2015
5) Ushijima Y, Ohniwa RL, Maruyama A, Saito S, Tanaka Y, and Morikawa K. Nucleoid compaction by $MrgA^{Asp56Ala/Glu60Ala}$ does not contribute to staphylococcal cell survival against oxidative stress and phagocytic killing by macrophage. ***FEMS Microbiol Lett*** 360, 144-151. 2014
6) Ohniwa RL, Muchaku H, Saito S, Wada C and Morikawa K. Atomic force microscopy analysis of the role of major DNA-binding proteins in organization of the nucleoid in *Escherichia coli*. ***PLoS One*** 8, e72954. 2013
7) Ohniwa RL, Kitabayashi K, Morikawa K. Alternative cardiolipin synthase Cls1 compensates for stalled Cls2 function in *Staphylococcus aureus* under conditions of acute acid stress. ***FEMS Microbiol Lett*** 338:141-146. 2013
8) 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

12. Genome Biology

Principal Investigator **Masafumi Muratani**
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Major Scientific Interests

We develop methods for genome and epigenome analysis of limited samples. Main area of application is characterization of clinical tissue samples from Tsukuba Human Tissue Bank. We try to link histopathological features of human diseases to regulatory status of the genome.

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 of human and experimental mouse samples at single-cell resolution.

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) Kakran M*, Muratani M*, Tng WJ, Liang H, Trushina DB, Sukhorukov GB, Ng HH, Antipina MN. Layered polymeric capsules inhibiting the activity of RNases for intracellular delivery of messenger RNA. *J. Mater. Chem. B.* Vol.3, 5842-5848, 2015. (*Equal contribution)
3) 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.
4) V. Kumar, M. Muratani, N.A. Rayan, P. Kraus, T. Lufkin, H.H. Ng, S. Prabhakar. Uniform, optimal signal processing of mapped deep-sequencing data. *Nature Biotechnology*, Vol.31(7), 615-22, 2013
5) J.H. Ng*, V. Kumar*, M. Muratani*, P. Kraus, J.C. Yeo, L.P. Yaw, K. Xue, T. Lufkin, S. Prabhakar, H.H. Ng: In vivo epigenomic profiling of germ cells reveals germ cell molecular signatures, *Developmental Cell*, Vol.24(3), 324-33, 2013 (*Equal contribution)

13. Kidney and Vascular Pathology

Principal Investigator **Michio Nagata**
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Major Scientific Interests

Kidney pathology is the main issue in our group.
Current interests include podocyte pathology, pathophysiology of FSGS, systemic vasculitis (ANCA-related) and cystogenesis in polycystic kidney.
Vascular pathology in chronic kidney disease is another focus in our group.

Projects for Regular Students in Doctoral or Master's Programs

1) Pathophysiology and molecular mechanisms of focal segmental glomerulosclerosis from the view of podocyte and parietal cell transdifferentiation.
2) Morphologic investigation in systemic vascular changes and kidney injury.

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

1) Diagnosis of human kidney biopsy samples according to the specific interest.
2) Immunohistochemistry and molecular biologic techniques using podocyte-speciic transgenic animals.

Recent Publications

1) Hara S, Kobayashi N, Sakamoto K, Ueno T, Manabe S, Takashima Y, Hamada J, Pastan I, Fukamizu A, Matsusaka T, **Nagata M**. Podocyte injury-driven lipid peroxidation accelerates the infiltration of glomerular foam cells in focal segmental glomerulosclerosis. Am J Pathol. 2015 in press
2) Kobayashi N, Ueno T, Ohashi K, Yamashita H, Takahashi Y, Sakamoto K, Manabe S, Hara S, Takashima Y, Dan T, Pastan I, Miyata T, Kurihara H, Matsusaka T, Reiser J, **Nagata M**. Podocyte injury-driven intracapillary PAI-1 accelerates podocyte loss via uPAR mediated beta 1 integrin endocytosis. Am J Physiol Renal Physiol. 2015 15;308(6):F614-26.
3) Sakamoto K, Ueno T, Kobayashi N, Hara S, Takashima Y, Pastan I, Matsusaka T, **Nagata M**. The direction and role of phenotypic transition between podocytes and parietal epithelial cells in focal segmental glomerulosclerosis. Am J Physiol Renal Physiol. 2014 Jan 1;306(1):F98-F104.
4) Hara S,Umeyama K,Yokoo T,Nagashima, **Nagata M**. Diffuse glomerular nodular lesions in diabetic pigs carrying a dominant-negative mutant hepatocyte nuclear factor 1-alpha, an inheritant diabetic gene in humans. PLoS One.2014 Mar 19;9(3):e92219.
5) Hara S, Kawano M, Mizushima I, Yamada K, Fujita K, Harada K, Matsumura M, Yamagishi M, Sato Y, Yamaguchi Y, Nakanuma Y, **Nagata M**. A condition closely mimicking IgG4-related disease despite the absence of serum IgG4 elevation and IgG4-positive plasma cell infiltration.Mod Rheumatol. 2014 Jun 2:1-6.
6) Iijima K, Sako M, Oba MS, Ito S, Hataya H, Tanaka R, Ohwada Y, Kamei K, Ishikura K, Yata N, Nozu K, Honda M, Nakamura H, **Nagata M**, Ohashi Y, Nakanishi K, Yoshikawa N Cyclosporine C2 monitoring for the treatment of frequently relapsing nephrotic syndrome in children: a multicenter randomized phase II trial.; Japanese Study Group of Kidney Disease in Children. Clin J Am Soc Nephrol. 2014 Feb;9(2):271-8.

14. Diagnostic Surgical Pathology

Principal Investigator **Masayuki Noguchi**
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Assistant Professor Noriaki Sakamoto: n.sakamoto@md.tsukuba.ac.jp

Major Scientific Interests
Molecular pathology of multistep carcinogenesis
Studies of the initial genetic alterations of precancerous lesions and early carcinoma
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 and FISH using human specimens. Statistical analysis on those results and patients prognosis or clinicopathological features.
2) Basic techniques of tissue microdissection

Recent Publications
1) Matsuoka R, Shiba-Ishii A, Nakano N, Togayachi A, Sakashita S, Sato Y, Minami Y, Noguchi M. Heterotopic production of ceruloplasmin by lung adenocarcinoma is significantly correlated with prognosis. ***Lung Cancer***, *in press*.
2) Nakano N, Sakashita S, Matsuoka R, Murata Y, Shiba-Ishii A, Kobayashi N, Sato Y, Noguchi M. Cyclophilin A expression and its prognostic significance in lung adenocarcinoma. ***Pathology International,*** 67(11):555-563, 2017.
3) Sato T, Shiba-Ishii A, Kim Y, Dai T, Husni RE, Hong J, Kano J, Sakashita S, Iijima T, Noguchi M, miR-3941: A novel microRNA that controls IGBP1 expression and is associated with malignant progression of lung adenocarcinoma. ***Cancer Sci*** 108:536-542, 2017.
4) Iyama S, Ono M, Kawai-Nakahara H, Husni RE, Dai T, Shiozaw T, Sakata A, Kohrogi H, Noguchi M. Drebrin: A new oncofetal biomarker associated with prognosis of lung adenocarcinoma. ***Lung Cancer*** 102:74-81, 2016.
5) Shiozawa T, Iyama S, Toshima S, Sakata A, Usui S, Minami, Y, Sato Y, Hizawa N, Noguchi M. Dimethylarginine dimethylaminohydrolase 2 promotes tumor angiogenesis in lung adenocarcinoma. ***Virchows Archiv***. 468:179-190, 2016.
6) Shiba-Ishii A, Kim Y, Shiozawa T, Iyama S, Satomi K, Kano J, Sakashita S, Morishita Y, Noguchi M. Stratifin accelerates progression of lung adenocarcinoma at an early stage. ***Mol Cancer*** 14:142-147, 2015.

15. Physiological Chemistry

Principal Investigator **Norihiko Ohbayashi**
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Assistant Professor, Yuji Funakoshi: funa@md.tsukuba.ac.jp

Major Scientific Interest
Studies on regulatory mechanisms and physiological functions of membrane trafficking systems through small GTP-binding proteins such as Rab and Arf.

Projects for Regular Students in Doctoral or Master's Programs

1) Physiological functions of the small GTP-binding proteins (Rabs and Arf6) and their regulators in tumorigenesis/metastasis, morphogenesis, and neural plasticity.
2) Regulatory mechanisms of ubiquitylation of cargo proteins in the recycling system.
3) Molecular mechanisms of biogenesis of melanin-containing organelles though Rab small GTP-binding proteins.
4) Development of specific agonists/antagonists for certain small GTP-binding proteins.

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

1) Enzyme assay and imaging of molecules regulating membrane trafficking systems.
2) Assays for cell functions such as cell proliferation, cell motility, focal adhesion, secretion, endocytosis, exocytosis, recycling, etc.

Recent Publications:

1) Lin YC, Ohbayashi N, Hongu T, Katagiri N, Funakoshi Y, Lee H, Kanaho Y. Arf6 in lymphatic endothelial cells regulates lymphangiogenesis by controlling directional cell migration. ***Sci Rep***. 7, 11431, (2017).
2) Tsai MT, Katagiri N, Ohbayashi N, Iwasaki K, Ohkohchi N, Ding ST, Kanaho Y, Funakoshi Y. Regulation of HGF-induced hepatocyte proliferation by the small GTPase Arf6 through the PIP2-producing enzyme PIP5K1A. ***Sci Rep***. 7, 9438, (2017).
3) Ohbayashi N, Fukuda M, Kanaho Y. Rab32 subfamily small GTPases: pleiotropic Rabs in endosomal trafficking. ***J Biochem***. 162, 65-71, (2017).
4) Miura Y, Ngo Thai Bich V, Furuya M, Hasegawa H, Takahashi S, Katagiri N, Hongu T, Funakoshi Y, Ohbayashi N, Kanaho Y. The small G protein Arf6 expressed in keratinocytes by HGF stimulation is a regulator for skin wound healing. ***Sci Rep***. 7, 46649, (2017).
5) Marubashi S, Shimada H, Fukuda M, Ohbayashi N. RUTBC1 Functions as a GTPase-activating Protein for Rab32/38 and Regulates Melanogenic Enzyme Trafficking in Melanocytes. ***J Biol Chem***. 291, 1427-40, (2016).
6) Miura Y, Hongu T, Yamauchi Y, Funakoshi Y, Katagiri N, Ohbayashi N, Kanaho Y. ACAP3 regulates neurite outgrowth through its GAP activity specific to Arf6 in mouse hippocampal neurons. ***Biochem J***. 473, 2591-602, (2016).
7) Marubashi S, Ohbayashi N, Fukuda M. A Varp-Binding Protein, RACK1, Regulates Dendrite Outgrowth through Stabilization of Varp Protein in Mouse Melanocytes. ***J Invest Dermatol***. 136, 1672-80, (2016).
8) Okada R, Yamauchi Y, Hongu T, Funakoshi Y, Ohbayashi N, Hasegawa H, Kanaho Y. Activation of the Small G Protein Arf6 by Dynamin2 through Guanine Nucleotide Exchange Factors in Endocytosis. ***Sci Rep***. 27, 14919, (2015).

16. Regenerative Medicine and Stem Cell Biology

Principal Investigator **Osamu Ohneda**
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Dr. Masumi Kuma Nagano (Assistant Professor) naganom@md.tsukuba.ac.jp

Major Scientific Interests

1) Identification and analyses of functional stem cells for cell therapy in human tissues
2) Hypoxic responses in stem cell development and tumor development

Projects for Regular Students in Doctoral or Master's Programs:

1) Analysis of functional stem cells (MSC and EPC) for clinical application
2) Analysis of how hypoxic inducible factors (HIFs) are involved in stem cell development
3) Analysis of how HIFs are involved in tumor development (tumor and tumor endothelial cell)

Summer School Course (2016)

1) Analysis of Mesenchymal Stem Cells
2) Neural Differentiation of human iPS

Recent Publications:

1) Akimoto K, Kimura K, Nagano M, Takano S, Salazar G, Yamashita T, and Ohneda O. Umbilical cord blood-derived mesenchymal stem cells inhibit, but adipose tissue-derived mesenchymal stem cells promote, glioblastoma multiforme proliferation. **Stem Cells and Dev.** 2013; 22: 1370-1386.
2) Tu T, Kimura K, Nagano M, Yamashita T, Ohneda K, Sugimori H, Sato F, Sakakibara Y, Hamada H, Yoshikawa H, Son H , and Ohneda O. Identification of human placenta-derived mesenchymal stem cells involved in re-endothelialization. **J Cell Physiol**. 2011; 226: 224-235.
3) Nagano M, Kimura K, Yamashita T, Ohneda K, Nozawa D, Hamada H, Yoshikawa H, Ochiai N, and Ohneda O. Hypoxia responsive mesenchymal stem cells derived from human umbilical cord blood are effective for bone repair. **Stem Cells and Dev.** 2010; 19: 1195-1210.
4) Yamashita T, Ohneda O, Sakiyama A, Iwata F, Ohneda K, and Fujii-Kuriyama Y. The microenvironment for erythropoiesis is regulated by HIF-2alpha through VCAM-1 in endothelial cells. **Blood** 2008; 112: 1482-1492.
5) Yamashita T, Ohneda K. Nagano M, Miyoshi C, Kaneko N, Miwa Y, Yamamoto M, Ohneda O, and Fujii-Kuriyama Y. HIF-2alpha in endothelial cells regulates tumor neovascularization through activation of ephrin A1. **J Biol Chem** 2008; 283: 18926-18936.
6) Nagano M, Yamashita T, Hamada H, Ohneda K, Kimura K, Nakagawa T, Shibuya M, Yoshikawa H, and Ohneda O. Identification of functional endothelial progenitor cells suitable for the treatment of ischemic tissue using human umbilical cord blood. **Blood** 2007; 110: 151-160.

17. Immunology

Principal Investigator **Akira Shibuya**
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Chigusa Oda, M.D., Ph.D (chigusano@md.tsukuba.ac.jp)
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Kazumasa Kanemaru, M.D., Ph.D. （kazukane.1987@gmail.com）

Major Scientific Interests

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

Recent Publications

1) 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)
2) Nakahashi-Oda C, et al. Apoptotic epithelial cells control regulatory T cell expansion. ***Nature Immunol***, 2016 Feb 8. doi: 10.1038/ni.3345.
3) 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
4) Kim YG, et al. Gut dysbiosis promotes M2 macrophage polarization and allergic airway inflammation via fungi-induced PGE_2. ***Cell Host & Microbe***, 15(1):95–102, 2014
5) Nakahashi-Oda C, et al. Apoptotic cells suppress mast cell inflammatory responses via the CD300a immunoreceptor. ***J. Exp. Med.*** 209, 1493-1503, 2012
6) Nakano-Yokomizo T, et al. The immunoreceptor adapter protein DAP12 suppresses B lymphocyte-driven adaptive immune responses. ***J. Exp. Med.*** 208, 1661-1671, 2011.
7) Hitomi K, et al. An immunoglobulin-like receptor, Allergin-1, inhibits immunoglobulin E-mediated immediate hypersensitivity reactions. ***Nature Immunol.*** 11: 601-607, 2010
8) 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):18593-18598, 20

18. Endocrinology and Metabolism

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Associate Professor: Takashi Matsuzaka (t-matsuz@md.tsukuba.ac.jp)
Assistant Professor: Takafumi Miyamoto (takmi565@md.tsukuba.ac.jp)

Major Scientific Interests

We are 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 metabolomics. We also extend our investigations to develop new therapeutic approaches for obesity, diabetes, and cardiovascular disease.

Projects for Regular Students in Doctoral or Master's Programs

3) Research on the transcriptional regulation of energy metabolism and metabolic diseases.
4) Research on lipid metabolism and metabolic diseases.

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

3) Learn procedures for analyzing the function of transcription factor.
4) Learn procedures for analyzing energy metabolism in cell and mouse models.
5) Learn procedures for visualization and manipulation of nutrients signaling dynamics.

Recent Publications

1) Shimano H, Sato R. SREBP-regulated lipid metabolism: convergent physiology - divergent pathophysiology. ***Nat Rev Endocrinol.*** 13(12):710-730, 2017.
2) Oishi Y, Spann NJ, Link VM, Muse ED, Strid T, Edillor C, Kolar MJ, Matsuzaka T, Hayakawa S, Tao J, Kaikkonen MU, Carlin AF, Lam MT, Manabe I, Shimano H, Saghatelian A, Glass CK. SREBP1 Contributes to Resolution of Pro-inflammatory TLR4 Signaling by Reprogramming Fatty Acid Metabolism. ***Cell Metab.*** 2017 Feb7;25(2):412-427.
3) Zhao H, Matsuzaka T, Nakano Y, Motomura K, Tang N, Yokoo T, Okajima Y, Han SI, Takeuchi Y, Aita Y, Iwasaki H, Yatoh S, Suzuki H, Sekiya M, Yahagi N, Nakagawa Y, Sone H, Yamada N, Shimano H. Elovl6 Deficiency Improves Glycemic Control in Diabetic db/db Mice by Expanding β-Cell Mass and Increasing Insulin Secretory Capacity. ***Diabetes.*** 66(7):1833-1846, 2017.
4) Takeuchi Y, Yahagi N, Aita Y, Murayama Y, Sawada Y, Piao X, Toya N, Oya Y, Shikama A, Takarada A, Masuda Y, Nishi M, Kubota M, Izumida Y, Yamamoto T, Sekiya M, Matsuzaka T, Nakagawa Y, Urayama O, Kawakami Y, Iizuka Y, Gotoda T, Itaka K, Kataoka K, Nagai R, Kadowaki T, Yamada N, Lu Y, Jain MK, Shimano H. KLF15 Enables Rapid Switching between Lipogenesis and Gluconeogenesis during Fasting. ***Cell Rep.*** 16(9):2373-86, 2016.
5) Nakagawa Y, Oikawa F, Mizuno S, Ohno H, Yagishita Y, Satoh A, Osaki Y, Takei K, Kikuchi T, Han SI, Matsuzaka T, Iwasaki H, Kobayashi K, Yatoh S, Yahagi N, Isaka M, Suzuki H, Sone H, Takahashi S, Yamada N, Shimano H. Hyperlipidemia and hepatitis in liver-specific CREB3L3 knockout mice generated using a one-step CRISPR/Cas9 system. ***Sci Rep.*** 6:27857, 2016.

19. Laboratory Animal Science

Principal Investigator **Fumihiro Sugiyama**
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Major Scientific Interests

Laboratory animals are essential and important bio-resources for the advancement of medical sciences. Gene-modified animals are used very often to study *in vivo* function of genes and proteins in development, homeostasis and disease. In particular, we focus on 1) development of genome editing technology for developmental engineering and 2) creation of mouse models for elucidating biological function and human diseases.

Projects for Regular Students in Doctoral or Master's Programs

1) Elucidating biological function of genes leading to early embryonic lethality.
2) Development of mouse models for *in vivo* imaging.
3) Investigating the novel gene function in germ cell maintenance and maturation.

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

1) Mouse genome editing with the CRISPR/Cas9 system.
2) Live Imaging of early embryonic development

Recent 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.*** 66:437-445. 2017
2) Tokue M, Ikami K, Mizuno S, Takagi C, Miyagi A, Takada R, Noda C, Kitadate Y, Hara K, Mizuguchi H, Sato T, Taketo MM, Sugiyama F, Ogawa T, Kobayashi S, Ueno N, Takahashi S, Takada S, Yoshida S. SHISA6 Confers Resistance to Differentiation-Promoting Wnt/β-Catenin Signaling in Mouse Spermatogenic Stem Cells. ***Stem Cell Reports.*** 14:561-575. 2017
3) 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.*** 65:319-27. 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

20. Anatomy and Embryology/ Laboratory Animal Resource Center

Principal Investigator **Satoru Takahashi**
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Other Faculty Members

Major Scientific Interests

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

Molecular mechanism of the development of organs. We are researching the molecular mechanisms of the development of organs 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. We genetically manipulate mice about these genes and analyze their *in vivo* function.

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

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

Recent Publications

1) Ohmura S, Mizuno S, Oishi H, Ku CJ, Hermann M, Hosoya T, Takahashi S, Engel JD. Lineage-affiliated transcription factors bind the Gata3 Tce1 enhancer to mediate lineage-specific programs. ***J Clin Invest***. 2016 Mar 1;126(3):865-78.
2) Hamada M, Nakamura M, Tran MT, Moriguchi T, Hong C, Ohsumi T, Dinh TT, Kusakabe M, Hattori M, Katsumata T, Arai S, Nakashima K, Kudo T, Kuroda E, Wu CH, Kao PH, Sakai M, Shimano H, Miyazaki T, Tontonz P, Takahashi S. MafB promotes atherosclerosis by inhibiting foam-cell apoptosis. ***Nat Commun***. 5, 3147, 2014.
3) Shinagawa T, Takagi T, Tsukamoto D, Tomaru C, Huynh LM, Sivaraman P, Kumarevel T, Inoue K, Nakato R, Katou Y, Sado T, Takahashi S, Ogura A, Shirahige K, Ishii. Histone variants enriched in oocytes enhance reprogramming to induced pluripotent stem cells. ***Cell Stem Cell***. 14, 217-227,2014.
4) Katsumata T, Oishi H, Sekiguchi Y, Nagasaki H, Daassi D, Ema M, Kudo T, Takahashi S. In vivo monitoring of pancreatic b-cell mass and intrahepatic insulin gene activity in Ins1-luc BAC transgenic mice by bioluminescence imaging. ***Plos One***. 8, e60411, 2013.
5) Hishida T, Nozaki Y, Nakachi Y, Mizuno Y, Okazaki Y, Ema M, Takahashi S, Nishimoto M, Okuda A. Indefinite self-renewal of ES cells through Myc/Max transcriptional complexes-independent mechanisms. ***Cell Stem Cell***. 9, 37-49, 2011.

21. Cancer Signaling

Principal Investigator **Peter ten Dijke**
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Major Scientific Interests

The ten Dijke laboratories, located in the Netherlands and Japan, are interested in the delineation of TGF-β signal transduction in development and disease states such as cancer. Our satellite laboratory at the University of Tsukuba employs platform technologies for the identification of high affinity ligands against key molecules involved in this signaling pathway, which grants us precise control over signaling (mis)regulation. Verified hits are then considered for the development of molecular probes or therapeutics.

Projects for Regular Students in Doctoral or Master's Programs

1) Development of novel platform technologies for the identification of high affinity ligands
2) *In vitro* selection of macrocyclic peptides against serine/threonine kinase receptors
3) *In vitro* selection of macrocyclic peptides against "undruggable" intracellular protein-protein interactions

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

1) Preparation and purification of ribozymes, mRNA, and tRNA
2) *In vitro* translation of mRNA into macrocyclic peptides
3) *In vitro* selection of functional ligands
4) Chemical synthesis of macrocyclic peptide

Recent Publications

1) Sundqvist A, Morikawa M, Ren J, Vasilaki E, Kawasaki N, Kobayashi M, Koinuma D, Aburatani H, Miyazono K, Heldin CH, van Dam H, ten Dijke P. JUNB governs a feed-forward network of TGFβ signaling that aggravates breast cancer invasion. **Nucleic Acids Res.** 46(3):1180-1195 (2018).
2) Astrologo L, Zoni E, Karkampouna S, Gray PC, Klima I, Grosjean J, Goumans MJ, Hawinkels LJAC, van der Pluijm G, Spahn M, Thalmann GN, ten Dijke P, Kruithof-de Julio M. ALK1Fc Suppresses the Human Prostate Cancer Growth in *in Vitro* and *in Vivo* Preclinical Models. **Front Cell Dev Biol.** 20175:104 (2017).
3) Zhang Z, Fan Y, Xie F, Zhou H, Jin K, Shao L, Shi W, Fang P, Yang B, van Dam H, ten Dijke P, Zheng X, Yan X, Jia J, Zheng M, Jin J, Ding C, Ye S, Zhou F, Zhang L. **Nat Commun.** 8(1):2116 (2017).
4) Thomsen LH, Fog-Tonnesen M, Nielsen Fink L, Norlin J, García de Vinuesa A, Hansen TK, de Heer E, ten Dijke P, Rosendahl A. Disparate phospho-Smad2 levels in advanced type 2 diabetes patients with diabetic nephropathy and early experimental db/db mouse model. **Ren Fail.** 39(1):629-642 (2017).
5) Chen X, Orriols M, Walther FJ, Laghmani EH, Hoogeboom AM, Hogen-Esch ACB, Hiemstra PS, Folkerts G, Goumans MTH, ten Dijke P, Morrell NW, Wagenaar GTM. Bone Morphogenetic Protein 9 Protects against Neonatal Hyperoxia-Induced Impairment of Alveolarization and Pulmonary Inflammation. **Front Physiol.** 8:486 11. (2017).
6) Leenheer D, ten Dijke P, John Hipolito C. A current perspective on applications of macrocyclic-peptide-based high-affinity ligands. **Biopolymers**. 106(6):889-900. (2016).

22. Matrix and Stem Cell Biology

Principle Investigator **Hiromi Yanagisawa**
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Other Faculty Members **Yoshito Yamashiro and Aiko Sada**

Major Scientific Interests:

The extracellular environment, which is comprised of extracellular matrices (ECM), ECM degrading enzymes, cytokines/growth factors, and physical factors, is crucial for normal development and cellular functions. The long-term goal of my laboratory is to elucidate how extracellular environment modulates intracellular signaling, cellular functions, and stem cell maintenance. In particular, we focus on the vessel wall and the skin. We aim to 1) identify novel ECM proteins and characterize their biochemical and physiological functions by taking molecular, biochemical, and genetic engineering approaches, and 2) elucidate the effects of alteration of ECM in maintenance of epidermal stem cell functions.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanism of aortic aneurysm
2) Identification of vascular and skin niche for stem/progenitor cells

Study Programs for Short Stay Students

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

Recent Publications:

1) Y. Yamashiro and H. Yanagisawa: Crossing Bridges between Extra- and Intra-cellular Events in Thoracic Aortic Aneurysms. *Invited review to* ***J. Atheroscler and Thromb***, 25 (2): 99-110 (2018).
2) A. Sada, F. Jacob, E. Leung, S. Wang, B.S. White, D. Shalloway, and T. Tumber: Defining the cellular lineage hierarchy in the interfollicular epidermis of adult skin. ***Nat Cell Biol***. 18 (6): 619-631 (2016).
3) Y. Yamashiro, C.L. Papke*, J. Kim*, L.-J. Ringuette*, Q.-J. Zhang, Z.-P. Liu, H. Mirzaei, J. Wagenseil, E.C. Davis, and H. Yanagisawa: Abnormal mechanosensing and cofilin activation promotes the progression of ascending aortic aneurysms in mice. ***Science Signaling***, 8(399): ra105 (2015).
4) C. L. Papke and H. Yanagisawa: Fibulin-4 and fibulin-5 in elastogenesis and beyond: insights from mouse and human studies. *Invited mini review to* ***Matrix Biology***. 37:142-9. (2014).
5) J. Huang, Y. Yamashiro*, C. L. Papke*, Y. Ikeda*, Y. Lin, M. Patel, T. Inagami, V. P. Le, 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. ***Science Transl. Med.*** 5, 183ra58 (2013).

23. Molecular Pharmacology

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Major Scientific Interests

1) Exploring genes regulating sleep/wake
2) Real-time visualization and manipulation of neuronal mechanisms controlling sleep/wake
3) Finding new drugs for sleep disorders

Projects for Regular Students in Doctoral or Master's Programs

1) Large-scale, forward genetic screening of genes responsible for sleep/wake regulation in mutagenized mice
2) Screening for orexin receptor agonists
3) Analysis of sleep and wakefulness in genetically modified mice
4) in vivo real-time imaging of neuronal activities in hypothalamus and other deep brain structures in freely behaving mice

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

1) EEG/EMG electrode implantation and recording in mice
2) patch clamp recording in cells and brain slices
3) imaging of nerve cell activities in brain slices

Recent Publications

1) Funato, H., Tsai, A.L., Willie, J.T., Kisanuki, Y., Williams, S.C., Sakurai, T., Yanagisawa, M. Enhanced orexin receptor-2 signaling prevents diet-induced obesity and improves leptin sensitivity. *Cell Metab.* 9: 64-76, 2009.
2) Funato, H., Sato, M., Sinton, C.M., Gautron, L., Williams, S.C., Skach, A., Elmquist, J.K., Skoultchi, A.I., Yanagisawa, M. Loss of Goosecoid-like and DiGeorge syndrome critical region 14 in interpeduncular nucleus results in altered regulation of rapid eye movement sleep. *Proc. Natl. Acad. Sci. USA* 107: 18155-18160, 2010.
3) Suzuki, A., Sinton, M.C., Green, W.R., Yanagisawa, M. Behavioral and biochemical dissociation of arousal and homeostatic sleep need influenced by prior wakeful experience in mice. *Proc. Natl. Acad. Sci. USA* 110: 10288-10293, 2013.
4) Ikeda, Y., Kumagai, H., Skach, A., Sato, M., Yanagisawa, M. Modulation of circadian glucocorticoid oscillation through adrenal opioid-CXCR7 signaling alters emotional behavior. *Cell* 155: 1323-1336, 2013.
5) Wei, W., Motoike, T., Krzeszinski, J.Y., Jin, Z., Xie, X., Dechow, C.P., Yanagisawa, M., Wan. Y. Orexin regulates bone remodeling via a dominant positive central action and a subordinate negative peripheral action. *Cell Metab*. 19: 927-240, 2014.
6) Lee, I.T., Chang, A.S., Manandhar, M., Shan, Y., Fan, J., Izumo, M., Ikeda, Y., Motoike, T., Dixon, S., Seinfeld, E.J., Takahashi, S.J., Yanagisawa, M. Neuromedin S-Producing Neurons Act as Essential Pacemakers in the Suprachiasmatic Nucleus to Couple Clock Neurons and Dictate Circadian Rhythms. *Neuron* 85: 1086-1102, 2015.
7) Nagahara, T., Saitoh, T., Kutsumura, N., Irukayama-Tomobe, Y., Ogawa, Y., Kuroda, D., Gouda, H., Kumagai, H., Fujii, H., Yanagisawa, M., Nagase, H. Design and Synthesis of Non-Peptide, Selective Orexin Receptor 2 Agonists. *J. Med. Chem.* 58: 7931–7937, 2015.
8) Funato H., Miyoshi C., Fujiyama T., Kanda T., Sato M., Wang Z., Ma J., Nakane S., Tomita J., Ikkyu A., Kakizaki M., Hotta N., Kanno S., Komiya H., Asano F., Honda T., Kim J.S., Harano K., Muramoto H., Yonezawa T., Mizuno S., Miyazaki S., Connor L., Kumar V., Miura I., Suzuki T., Watanabe A., Abe M., Sugiyama F., Takahashi S., Sakimura K., Hayashi Y., Liu Q., Kume K., Wakana S., Takahashi J.S., Yanagisawa M. Forward genetic analysis of sleep in randomly mutagenized mice. *Nature* 539: 378-383, 2016
9) Ogawa, Y., Irukayama-Tomobe, Y., Murakoshi, N., Kiyama, M., Ishikawa, Y., Hosokawa, N., Tominaga, H., Uchida, S., Kimura, S., Kanuka, M., Morita, M., Hamada, M., Takahashi, S., Hayashi, Y., Yanagisawa, M. Peripherally administered orexin improves survival of mice with endotoxin shock. *eLife* DOI: 10.7554/eLife.21055, 2016
10) Nagase, H., Yamamoto, N., Yata, M., Ohrui, S., Okada, T., Saitoh, T., Kutsumura, N., Nagumo, Y., Irukayama-Tomobe, Y., Ishikawa, Y., Ogawa, Y., Hirayama, S., Kuroda, D., Watanabe, Y., Gouda, H., Yanagisawa, M. Design and Synthesis of Potent and Highly Selective Orexin 1 Receptor Antagonists with a Morphinan Skeleton and Their Pharmacologies. *J. Med. Chem* 60: 1018–1040, 2017

24. Plant Immune Dynamics

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Nomura ERATO Laboratory; Professor Nobuhiko Nomura
Associate Professor Andrew Utada, Assistant Professor Nozomu Obana

Major Scientific Interests

The aim of our group is to unravel the basic principles that govern the spatiotemporal regulation of plant immune responses. Upon microbial infections, plants mount a battery of defense responses around the infection sites. Recently, we have identified that, using intravital imaging, two phytohormone signaling pathways in a mutually inhibitory relationship are activated in distinct concentric domains around the infection foci in Arabidopsis, thus providing, for the first time, compelling evidence for the existence of a "plant immune field" around the infection site (Betsuyaku et al, in prep.). We are currently deepening our understanding of the plant immune field formation with the aid of multidiscipline approaches.

Projects for Regular Students in Doctoral or Master's Programs

1) Functional analysis of the genes required for salicylic acid production during effector-triggered immunity (ETI)
2) Systems understanding of plant immunity through various single-cell technologies
3) Functional analysis of the negative regulators involved in "plant immune field" formation
4) Live imaging-based analysis of virulence-related genes of *Pseudomonas syringae* isolates

Study Programs for Short Stay Students

1) *in planta* live imaging analysis of defense-related promoter reporter activities in ETI
2) Live single-cell imaging analysis of defense-related promoter reporter activities upon stimuli

Selected Recent Publications

1) Inada N, Betsuyaku S, Shimada TL, Ebine K, Ito E, Kutsuna N, Hasezawa S, Takano Y, Fukuda H, Nakano A, Ueda T. Modulation of Plant RAB GTPase-Mediated Membrane Trafficking Pathway at the Interface Between Plants and Obligate Biotrophic Pathogens. Plant Cell Physiol. 57(9):1854-64,2016.
2) Endo S, Betsuyaku S, Fukuda H. Endogenous peptide ligand-receptor systems for diverse signaling networks in plants. Current Opinion in Plant Biology. 2014 Oct; 21:140-6.
3) Betsuyaku S, Sawa S, Yamada M. The Function of the CLE Peptides in Plant Development and Plant-Microbe Interactions. The Arabidopsis Book. 2011;9:e0149. doi: 10.1199/tab.0149.
4) Betsuyaku S*#, Takahashi F*, Kinoshita A, Miwa H, Shinozaki K, Fukuda H, Sawa S. Mitogen-activated protein kinase regulated by the CLAVATA receptors contributes to shoot apical meristem homeostasis. Plant & Cell Physiology. 2011 Jan;52(1):14-29. *Co-First Authors, #Corresponding Author
5) Azevedo C*, Betsuyaku S*, Peart J, Takahashi A, Noël L, Sadanandom A, Casais C, Parker J, Shirasu K. Role of SGT1 in resistance protein accumulation in plant immunity. The EMBO Journal. 2006 May 3;25(9):2007-16. *Co-First Authors

25. Paper device and eco-friendly materials

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Major Scientific Interests

For effective utilization of bio-materials and new technology derived from paper science, "super paper-application" is a promising field into the future. Paper is a simple and familiar material, and thus greatly expected to be applied to electronics, biosensors, and power generators. Technologies of papermaking processes can alter paper properties and provide superior performances. In addition, we proposed a simple method-immersion in salt water- for flood-damaged important books and documents to rescue them by inhibiting mold growth.

Projects for Regular Students in Doctoral or Master's Programs

1) Power generator to convert from paper vibration by sound and noise to electricity
2) Nanocellulose-reinforced cellulosic adsorbent for copper recovery from agricultural water
3) Nanocellulose-reinforced cellulosic membrane to separate oil/water mixture in food waste
4) Comfortable feeling of toilet tissue and creation of comfortable paper for wearable devices

Study Programs for Short Stay Students

1) Pulp fiber geometry characterization and surface profile of paper
2) Paper mechatronics —Application of drying shrinkage to intentional shaping of paper
3) Fabrication of paper-based electronics with conductive ink by ink jet printing

Recent Publications

1) Xu, Y., Enomae, T., "Development of a paper-based sensor for the qualitative and quantitative detection of Cu^{2+} in water", **Nordic Pulp & Paper Research Journal**, 32, 2, 237-243 (2017).
2) Srimongkon, T., Buerkle. M., Enomae, T., Ushijima, H., Fukuda, N., "Study of the electrical response of culture media during bacterial growth on a paper-based device", **Japanese Journal of Applied Physics**, 56, 5S2, 05EC04 (2017).
3) Oktavia, E., Morii, M., Enomae, T., "Triboelectric power generation from paper vibration induced by sonic waves, **Energy Harvesting and Systems**, 3(2), 189-196 (2016).
4) Srimongkon, T., Mandai, S., Enomae, T., "Application of biomaterials and inkjet printing to develop bacterial culture system", **Advances in Materials Sci & Eng**, Vol. 2015, 290790(2015).
5) Bunyaphiphat, T., Nakagawa-Izumi, A., Enomae, T., "Influences of saltwater immersion on properties of wood-cellulosic paper", **Carbohydrate polymers**, 116, 255-260 (2015).
6) Srimongkon, T., Ishida, T., Igarashi, K., Enomae, T., "Development of a bacterial culture system using a paper platform to accommodate media and an ink-jet printing to dispense bacteria", **Am. J. Biochem Biotechnol**, 10, 81-87(2014).
7) Xu, Y., Enomae, T., "Paper substrate modification for rapid capillary flow in microfluidic paper-based analytical devices", **RSC Advances**, 4, 12867-12872(2014).
8) Dogome, K., Enomae, T., Isogai, A., "Method for controlling surface energies of paper substrates to create paper-based printed electronics", **Chem Eng Proces: Process Intens**, 68, 21-25(2013).
9) Higashijima, K., Hori, C., Igarashi, K., Enomae, T., Isogai, A., "First aid for flood-damaged paper using saltwater: The inhibiting effect of saltwater on mold growth", **Studies in Conservation**, 57(3), 164-171(2012).
10) Enomae,T., Dogome, K. and Isogai, A., "Evaluation of absorption of micro-droplets on paper for creation of paper-based microstructures", **Journal of Materials Science**, 47, 8, 3554-3563(2012).

26. Olericulture and Floriculture

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Other Faculty Member:
Professor Chiaki Matsukura, Ph.D.,
Associate Professors Naoya Fukuda, Ph.D., Kang Seungwon, Ph.D. Tohru Ariizumi, Ph.D., Kyoko Tanase-Hiwasa Ph.D.
Assistant Professors Satoko Nonaka, Ph.D., Ken Hoshikawa, Ph.D., Ryoichi Yano Ph.D., Yoshihiro Okabe Ph.D., Naomichi Fujiuchi

Major Scientific Interests
Exploring genes regulating tomato fruit development
Analysis of the mechanism for sugar and GABA metabolism in tomato
Creation of genetic modified tomato accumulating functional materials benefit for human health
Innovating crop transgenic and genome editing technologies for crop breeding
Improving cultivation method for increasing sugar accumulation in tomato fruit
Development of advanced plant factory equipped with AI and robotics

Projects for Regular Students in Doctoral or Master's Programs
1) Forward genetic screening of genes that influence fruit development in tomato
2) Reverse genetic screening of novel mutations that increase fruit shelf-life of tomato
3) Functional analysis of GABA metabolism genes in tomato

Study Programs for Short Stay Students (one week)
1) DNA/RNA purification from plants
2) DNA amplification by PCR reaction, digestion by restriction enzymes, and electrophoresis
3) cDNA synthesis and RT-PCR reaction

Recent Publications
1) Ueta R, Abe C, Watanabe T, Sugano S, Ishihara R, Ezura H, Osakabe Y, Osakabe K. (2017) Rapid breeding of parthenocarpic tomato plants using CRISPR/Cas9. ***Scientific Reports.*** 7(1):507.
2) Shimatani Z, Kashojiya S, Takayama M, Terada R, Arazoe T, Ishii H, Teramura H, Yamamoto T, Komatsu H, Miura K, Ezura H, Nishida K, Ariizumi T, Kondo A (2017) Targeted base editing in rice and tomato using a CRISPR-Cas9 cytidine deaminase fusion. ***Nature Biotechnology***. doi: 10.1038/nbt.3833
3) Nonaka S, Someya T, Zhou S, Takayama M, Nakamura K, Ezura H (2017). An *Agrobacterium tumefaciens* strain with gamma-aminobutyric acid transaminase activity shows an enhanced genetic transformation ability in plants. ***Scientific Reports.*** **7**, Article number: 42649
4) Shikata M, Hoshikawa K, Ariizumi T, Fukuda N, Yamazaki Y, Ezura H (2016) TOMATOMA Update: Phenotypic and metabolite information of Micro-Tom mutant resource. ***Plant Cell Physiol.*** 57(1): 1-10.
5) Takayama M, Koike S, Kusano M, Matsukura C, Saito K, Ariizumi T, Ezura H. (2015) Tomato glutamate decarboxylase genes SlGAD2 and SlGAD3 play key roles in regulation of γ-aminobutyric acid level in tomato (*Solanum lycopersicum*). ***Plant Cell Physiol.*** 56(8): 1533-1545.
6) Shinozaki Y, Hao S, Kojima M, Sakakibara H, Oseki-Iida Y, Zhen Y, Fei Z, Zhong S, Giovannoni J, Rose JKC, Okabe Y, Heta Y, Ezura H, Ariizumi T. (2015) Ethylene suppresses tomato fruit set through modification of gibberellin metabolism. ***Plant J***. 83(2): 237-251.
7) Ariizumi T, Kishimoto S, Kakami R, Maoka T, Hirakawa H, Suzuki Y, Ozeki Y, Shirasawa K, Bernillon S, Okabe Y, Moing A, Asamizu E, Rothan C, Ohmiya A, Ezura H (2014) Identification of the Carotenoid Modifying Gene *PALE YELLOW PETAL 1* as an Essential Factor in Xanthophyll Esterification and Yellow Flower Pigmentation in Tomato (*Solanum lycopersicum*). ***Plant J*** 79:453-465

27. Plant Ecophysiology

Principal Investigator **Louis John Irving**
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URL

Major Scientific Interests

- Effect of parasitic plants on host growth and metabolism
- Allocation of carbon to roots in nutrient rich patches
- Cs uptake and allocation in rice
- Importance environmental factors controlling water uptake and seed germination rates

Projects for Regular Students in Doctoral or Master's Programs

1) Factors determining the abstraction of C and N by parasitic plants
2) Environmental drivers of root growth, maintenance and death in grasses
3) Effects of nutrient status on Cs uptake and partitioning in rice
4) Environmental drivers of seed germination rate in wheat

Study Programs for Short Stay Students (one week)

1) Measuring nutrient abstraction from host plants using stable isotopes
2) Quantifying effects of nutrient status on plant leaf chemistry and photosynthesis
3) Determining nutrient uptake by plants using 15N as a tracer
4) Influence of NaCl / PEG in determining water uptake in wheat seeds

Recent Publications

1) Yamori W, Irving LJ, Adachi S, Busch FA (2016) Strategies for optimizing photosynthesis with biotechnology to improve crop photosynthesis. *Handbook of Photosynthesis* 741 – 759
2) Irving LJ (2015) Carbon assimilation, biomass partitioning and productivity in grasses. *Agriculture* **5** 1116 – 1134
3) Khaembah EN, Irving LJ, Thom ER, Faville MJ, Easton HS, Matthew C (2013) Leaf Rubisco turnover in a perennial ryegrass (*Lolium perenne* L.) mapping population: genetic variation, identification of associated QTL, and correlation with plant morphology and yield. *Journal of Experimental Botany* **64** (5) 1305 – 1316
4) Zhang HX, McGill CR, Irving LJ, Kemp PD, Zhou D (2013) A modified thermal time model to predict germination rate of ryegrass and tall fescue at constant temperatures. *Crop Science* **53** 1 – 10
5) Irving LJ, Cameron DD (2009) You are what you eat: interactions between root parasitic plants and their hosts. *Advances in Botanical Research* **50** 87 – 138

28. Molecular Plant Pathology

Principal Investigator **Yasuhiro Ishiga**
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Other Faculty Members

Plant Parasitic Mycology Laboratory; Professor Yuichi Yamaoka Associate Professor Izumi Okane, Assistant Professor Junichi P Abe

Major Scientific Interests

The research aim of our group is to understand the molecular mechanisms of plant immunity and pathogenicity of plant pathogens in the interactions of plant and microbes. Our primary target pathosystem is soybean and soybean rust interactions. Soybean rust caused by *Phakopsora pachyrhizi* is one of the most devastating foliar diseases affecting soybean production worldwide. In addition, we are interested in bacterial pathosystem, such as *Pseudomonas syringae*-tomato interactions. By working on the molecular basis of plant-microbe interactions, we are trying to establish the sustainable disease control strategies.

Projects for Regular Students in Doctoral or Master's Programs

1) Multi-omics approached to study host-resistance on soybean against soybean rust using *Rpp* near-isogenic lines (NILs)
2) Development of Host Induced Gene Silencing (HIGS) in the interactions of soybean and soybean rust towards crop protection
3) Functional analysis of retrograde signaling in plant immunity
4) Reactive Oxygen Species (ROS)-mediated plant-microbe interactions

Study Programs for Short Stay Students

1) Molecular mechanism of plant immunity against fungal and bacterial pathogens
2) Functional analysis of pathogenicity related genes in bacterial and fungal pathogens.

Selected Recent Publications

1) **Ishiga, Y.**, Ishiga, T., Ikeda, Y., Matsuura, T. and Mysore, K.S. (2016) NADPH-dependent thioredoxin reductase C plays a role in nonhost disease resistance against Pseudomonas syringae pathogens by regulating chloroplast-generated reactive oxygen species. ***PeerJ***.
2) **Ishiga, Y.** and Ichinose, Y. (2015) Pseudomonas syringae pv. tomato OxyR is required for virulence in tomato and Arabidopsis. ***Mol. Plant-Microbe Interact.*** 29:119-31.
3) **Ishiga, Y.**, Uppalapati, S.R., Gill, U.S., Huhman, D., Tang, Y. and Mysore, K.S. (2015) Transcriptomic and metabolomic analyses identify a role for chlorophyll catabolism and phytoalexin during Medicago nonhost resistance against Asian soybean rust. ***Scientific Reports*** 12;5:13061
4) **Ishiga, Y.**, Ishiga, T., Uppalapati, S.R. and Mysore, K.S. (2013) Jasmonate ZIM-domain (JAZ) protein regulates host and nonhost pathogen-induced cell death in tomato and *Nicotiana benthamiana*. ***PLoS ONE*** 8: e75728.
5) Uppalapati, S.R., **Ishiga, Y.**, Doraiswamy, V., Bedair, M., Mittal, S., Chen, J., Nakashima, J., Tang, Y., Tadege, M., Ratet, P., Chen, R., Schultheiss, H. and Mysore K.S. (2012) Loss of abaxial leaf epicuticular wax in *Medicago truncatula irg1/palm1* mutants results in reduced spore differentiation of anthracnose and nonhost rust pathogens. ***The Plant Cell*** 24: 353-370.
6) **Ishiga, Y.**, Ishiga, T. Wangdi, T., Mysore, K.S. and Uppalapati, S.R. (2012) NTRC and chloroplast-generated reactive oxygen species regulate *Pseudomonas syringae* pv. *tomato* disease development in tomato and Arabidopsis. ***Mol. Plant-Microbe Interact.*** 25: 294-306.

29. Applied Entomology and Zoology

Principal Investigator **Yooichi Kainoh**
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Other Faculty Members
Professor DeMar Taylor: taylor.de.mar.ge@u.tsukuba.ac.jp
Associate Professor Seiichi Furukawa: furukawa.seiichi.ew@u.tsukuba.ac.jp

Major Scientific Interests

Experimental studies using insects, spiders and ticks for elucidation of behavioral and physiological mechanisms underlining host location behavior, physiology of reproduction and immunity, innate immune response to various infections, and molecular mechanisms inducing the release of plant volatiles from herbivore-infested plants.

Projects for Regular Students in Doctoral or Master's Programs

1) Flight response of parasitic wasps to the plant infested by host insect.
2) Endocrinological and gene regulatory mechanisms of tick and spider ecdysis, reproduction and immunity.
3) Molecular mechanisms in the regulation of insect immunity.
4) Molecular mechanisms in the plant induction caused by herbivorous infestation.

Study Programs for Short Stay Students

1. Head space volatile collection from herbivore-infested plants and its chemical analysis.
2. Behavioral study of insect parasitoids responding to plant volatiles.
3. Measurement of insect immune activity against infection by molecular techniques.

Recent Publications:

1. Nurkomar, I.; Pudjianto; S. Manuwoto; D. Buchori; S. Matsuyama; D. Taylor; Y. Kainoh (2018) (E,E)-α-Farnesene as one cucumber plant volatile that attracts Apanteles taragamae (Hymenoptera: Braconidae) to the host-infested habitat. Biocontrol Science and Technology 28:34-48.
2. Piyasaengthong, N.; N. Kinoshita; Y. Sato; Y. Kainoh (2016) Sex-specific elicitor of Adoxophyes honmai (Lepidoptera: Tortricidae) on tea leaf arrests the egg–larval parasitoid Ascogaster reticulata (Hymenoptera: Braconidae). Applied Entomology and Zoology 51:353-362.
3. Honda, Y., Ishiguro, W., Ogihara, M.H., Kataoka H. and Taylor, D. (2017) Identification and expression of nuclear receptor genes and ecdysteroid titers during nymphal development in the spider Agelena silvatica. General and Comparative Endocrinology, 247: 183-198.
4. Ogihara, M.H., Hikiba, J., Suzuki, Y., Taylor, D. and Kataoka, H. (2015) Ovarian ecdysteroids in both immature and mature stages of an Acari, Ornithodoros moubata. PLoS ONE 10(4): e0124953.
5. Furukawa, S., Tanaka, H., Sagisaka, A., Ishibashi, J. and Yamakawa, M. (2012) Both □B and C/EBP binding sites are indispensable for full expression of a nitric oxide synthase gene in the silkworm, Bombyx mori. J. Seric. Sci. Jpn. 81:13-20.
6. Furukawa, S., Tanaka, K., Ikeda, T., Fukatsu, T. and Sasaki, T. (2012) Quantitative analysis of the lytic cycle of WO phages infecting Wolbachia. Appl. Entomol. Zool. 47:449-456.

30. Food and Biomass Process Engineering

Principal Investigator **Yutaka Kitamura**
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Other Faculty Member Assistant Professor Mito Kokawa

Major Scientific Interests

Focusing on agricultural products, food, unused resources and biomass as local biological materials, process development and characteristics for utilization and conversion of these resources are investigated to produce food, energy and industrial materials. By implementing the advanced technology for the local biological resources, we have the goal to contribute widely to the promotion of agriculture, energy conservation, environmental protection and industry creation in local and global view point.

Projects for Regular Students in Doctoral or Master's Programs

1) Monitoring of beef aging with electrical impedance
2) Processing of orange juice (*Citrus sinensis*) powder by micro wet milling and vacuum spray drying Process
3) Processing of rice bread and rice pasta from rice gel
4) Processing of fermented rice milk products
5) Monitoring of fruit and vegetable freshness and ripening with the fluorescence fingerprint

Study Programs for Short Stay Students

1) Processing of rice milk and rice milk products
2) Processing of rice gel products

Recent Publications

1) Dheni Mita Mala, Masatoshi Yoshimura, Susumu Kawasaki, Mizuki Tsuta, Mito Kokawa, Vipavee Trivittayasil, Junichi Sugiyama, Yutaka Kitamura, Fiber optics fluorescence fingerprint measurement for aerobic plate count prediction on sliced beef surface, LWT - Food Science and Technology, 68, 14- 20, 2016
2) M.Z. Islam, Yutaka Kitamura, Yoshitsugu Yamano, Mai Kitamura, Effect of vacuum spray drying on the physicochemical properties, water sorption and glass transition phenomenon of orange juice powder, Journal of Food Engineering, 169, 131-140, 2016
3) Masaru Koyama, Yutaka Kitamura, Development of a new rice beverage by improving the physical stability of rice slurry, Journal of Food Engineering, 131, 89-95, 2014
4) Kenji Takisawa, Kazuyo Kanemoto, Tatsuo Miyazaki, Yutaka Kitamura, Hydrolysis for direct esterification of lipids from wet microalgae, Bioresource Technology, 144, 38-43, 2013
5) C. Song, Y. Kitamura, S. Li, J. Lu. Deposition CO2 Capture Process Using a Free Piston Stirling Cooler. Industrial & Engineering Chemistry Research, 52 (42), 14936–14943, 2013
6) Chunfeng Song, Yutaka Kitamura, Shuhong Li. Energy analysis of the cryogenic CO2 capture process based on Stirling coolers. Energy. 65, 580-589, 2014

31. Isotope Hydrogeomorphology and Radioecology

Principal Investigator **Yuichi Onda**
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Other Faculty Member
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Assistant Professor Junko Takahashi, takahashi.junko.ka@u.tsukuba.ac.jp

Major Scientific Interests

1) Transfer of radionuclides in terrestrial environment after the Fukushima Daiichi NPP accident
2) Interaction between subsurface water movement and sediment yield
3) Development of innovative technologies for increasing in watershed runoff and improving river environment by the management practice of devastated forest plantation

Projects for Regular Students in Doctoral or Master's Programs

1) Monitoring and modeling radionuclides migrated with water and sediment
2) Transfer mechanism of radionuclides in the forest and soil
3) Estimation of surface soil erosion and sources of sediment production using radionuclides

Study Programs for Short Stay Students

1) Studying the method of Radiocesium analysis of water, soils and litter
2) Lab studies on physical and chemical properties of soil and water
3) Field work of monitoring and sampling of radiocesium in Fukushima
4) Experiencing hillslope hydrological monitoring in Tochigi

Recent Publications

1) Kato, H., Onda, Y., Hisadome, K., Loffredo, N., Kawamori, A. (2017) Temporal changes in radiocesium deposition in various forest stands following the Fukushima Dai-ichi Nuclear Power Plant accident. Journal of Environmental Radioactivity, 166, Part 3, 449-457.
2) Iwagami, S., Tsujimura, M., Onda, Y., Nishino, M., Konuma, R., Abe, Y., Hada, M., Pun, I., Sakaguchi, A., Kondo, H., Yamamoto, M., Miyata, Y., Igarashi, Y. (2017) Temporal changes in dissolved 137Cs concentrations in groundwater and stream water in Fukushima after the Fukushima Dai-ichi Nuclear Power Plant accident. Journal of Environmental Radioactivity, 166, Part 3, 458-465.
3) Iwagami, S., Onda, Y., Tsujimura, M. and Abe, Y. (2017) Contribution of Radioactive ^{137}Cs discharge by Suspended Sediment, Coarse Organic Matter, and Dissolved Fraction from a Headwater Catchment in Fukushima after the Fukushima Dai-ichi Nuclear Power Plant Accident, Journal of Environmental Radioacivity, 166, Part 3, 466-474.
4) Yoshimura, K., Onda, Y., Wakahara, T. (2016) Time dependence of the ^{137}Cs concentration in particles discharged from rice paddies to freshwater bodies after the Fukushima Daiichi NPP accident, Environmental Science & Technology, DOI: 10.1021/acs.est.5b05513
5) Sun, X., Onda, Y., Otsuki, K., Kato, H., Gomi, T. (2016) The effect of strip thinning on forest floor evaporation in a Japanese cypress plantation. Agriculture and Forest Meteorology, 216, 48-57.
6) Onda, Y., Kato, H., Hoshi, M., Takahashi, K., Saito, K., and Ngyuen, L. M. (2015) Soil sampling and analytical strategies for mapping fallout in nuclear emergencies. Journal of Environmental Radioactivity, 139, 300-307.
7) Takahashi, J., Tamura, K., Suda, T., Matsumura, R., and Onda, Y. (2015) Vertical distribution and temporal changes of ^{137}Cs in soil profiles under various land uses after Fukushima Dai-ichi Nuclear Power Plant Accident. Journal of Environmental Radioactivity, 139, 351-361.

32. Pomology

Principal Investigator **Sumiko Sugaya, Ph.D.**
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Other Faculty Member
Assistant Professor Yoshihiko Sekozawa, Ph.D.

Major Scientific Interests

1) Molecular mechanism underlying fruit quality involving coloring, taste and flavor in fruit trees.
2) Mechanism of bud dormancy in deciduous trees and role of chilling in winter.
3) Postharvest physiology in fruits to develop technologies for prolonging shelf life.

Projects for Regular Students in Doctoral or Master's Programs

1) Carbohydrate metabolism in dormancy of Japanese pear under mild winter condition.
2) Effects of the joint training system on phytohormone metabolism and flowering in fruit trees.
3) Effects of heat treatment on ripening and quality during storage of fruits.

Study Programs for Short Stay Students (one week)

1) Determination of fruit quality with sugar analysis in fruits.
2) Analysis of flavor compounds in fruits.
3) Extraction of DNA/RNA from fruits and amplification by PCR.

Recent Publications

1) Chutinanthakun,T., J.S. Maninang, Sugaya Sumiko, Y. Sekozawa, Gemma H. 2014.Tree jointing and branch bending influence endogenous levels of hormones and flowering in Japanese plum 'Kiyo'. ***Acta Horticulturae*** 1042: 57-63.
2) Yooyongwech, S., A. K. Horigane, M. Yoshida, Y. Sekozawa, S. Sugaya, S. Cha-um and H. Gemma. 2012. Hydrogen cyanamide enhances MRI-measured water status in flower buds of peach (*Prunus persica* L.) during winter. ***Plant Omics Journal*** 5: 400-404.
3) Boonkorn, P., H. Gemma, S. Sugaya, S. Setha, J. Uthaibulta and K. Wangchai. 2012. Impact of high-dose, short periods of ozone exposure on green mold and antioxidant enzyme activity of tangerine fruit. ***Postharvest Biology and Technology*** 67: 25-28.
4) Kondo, S., S. Sugaya, S. Sugawa, M. Ninomiya, M. Kittikorn, K. Okawa, H. Ohara, K. Ueno, Y. Todoroki,
5) M. Mizutani and N. Hirai. 2012. Dehydration tolerance in apple seedlings is affected by an inhibitor of ABA 8' -hydroxylase CYP707A. ***Journal of Plant Physiology*** 169: 234-241.
6) Maninang, J. S., C. Wong-Aree, S. Kanlayanarat, S. Sugaya, and H. Gemma. 2011. Influence of maturity and postharvest treatment on the volatile profile and physiological properties of the durian (*Durio zibethinus* Murray) fruit. ***International Food Research Journal*** 18: 1067-1075.
7) Pongprasert, N., Y. Sekozawa, S. Sugaya and H. Gemma. 2011. A novel postharvest UV-C treatment to reduce chilling injury (membrane damage, browning and chlorophyll degradation) in banana peel. ***Scientia Horticulturae*** 130: 73-77.
8) Pongprasert, N., Y. Sekozawa, S. Sugaya and H. Gemma. 2011. The role and mode of action of UV-C hormesis in reducing cellular oxidative stress and the consequential chilling injury of banana fruit peel. ***International Food Research Journal*** 18: 741-749.
9) Pathirana, U. A. P., Y. Sekozawa, S. Sugaya and H. Gemma. 2011. Effect of combined application of 1-MCP and low oxygen treatments on alleviation of chilling injury and lipid oxidation stability of avocado (*Persea americana* Mill.) under low temperature storage. ***Fruits*** 66: 161-170.