





The Graduate School of Biostudies was established So how can you earn your PhD? In order to do that, in 1999 as Japan's first independent graduate you must first find your personal treasure that gets school focused on life science research and you excited. It is like when you were a young child education with the objective of developing and you got all excited about discovering a pretty individuals who can transcend the existing marble or seashell. But when it comes to this frameworks of science, agriculture, pharmacology, treasure, there are some conditions. It should have an element of being the "first in the world," and the and medicine to discover and apply new knowledge related to biological phenomena. As of the end of the method for finding this treasure should be through last academic year, a total of 1,360 students had experimentation. The more experiments you carry earned their master's degree from our school, while out, the faster you will find such a treasure. In 414 had earned their PhD; and these graduates are particular, when you produce an unanticipated result, now contributing to life science research and the you could be closing in on a large treasure, so it is development of industry across life science related important to verify your findings. fields. This is an achievement that brings If you find your treasure, next you should teach others about it. That entails writing papers. Writing papers requires a bit of hard work, but you can ask senior students and professors in your lab to advise you, so there is absolutely no need to worry. After the paper has been presented, if you write your doctoral

tremendous joy to all of the faculty members who have been involved in research and teaching at the Graduate School of Biostudies since its inception. From this fiscal year (2018), we set up two research centers, Radiation Biology Center and Research Center for Dynamic Living System, in our graduate thesis based on that and successfully defend it, you school, aiming for a new education and research will receive your PhD, making you qualified to work at system toward 21st century biology and life science. universities and research institutes around the world. I believe that the greatest mission of this graduate You will then use your experience to steadily find new school is to train exceptional PhDs. Since the majority treasures and write more papers. That is the work of a of those who are reading this message are probably researcher. It is fun! Even if you do not become a hoping to enroll in our school, I would like to offer my researcher, I can assure you that the experience and personal thoughts on earning a PhD (doctoral degree). confidence you will gain from discovering something that nobody else in the world knew about will serve When I was a student in the medical school, I had a you well no matter what type of work you do. For that strong desire to work overseas in the future. Since a reason, I hope that as you begin your graduate studies, Japanese medical license is not accepted overseas, you will devote all of your efforts to conducting lots of I thought about going abroad as a researcher. To do experiments and discovering your treasure. Then, so, I realized I would need to earn a PhD, so after once you have discovered your treasure, you can move completing my undergraduate degree, I immediately on to your doctoral program with your mind at ease, went on to graduate school and earned my PhD. further polish your skills, and obtain your PhD. Waiting When I explain what a PhD is, I tend to compare it to on the other side of that goal line, you will find an a driver' s license. For example, if you have an F1 exciting life that far exceeds your expectations. By all license, you are allowed to race F1 cars on circuits means, I hope that many of you will join our graduate throughout the world. Similarly, if you have a PhD, you school and will build the foundation for your future life. are allowed to carry out research at universities and We, the members of the faculty, will dedicate ourselves research institutes around the world. I believe there is no other qualification that enables you to so freely do to supporting your efforts and your growth. what you like. After I received my PhD, I was hired for Dean, MD, PhD. KAKIZUKA, Akira a postdoctoral position at the Salk Institute for Biological Studies in the United States, where I was able to enjoy living abroad as I had hoped and to gain irreplaceable experiences. That was one of the most enjoyable times of my life.

Graduate School of BIOSTUDIES, Kyoto University

# Let's Find Your Treasure!

Ahir Kahiyaka

### **MISSIONS of our GRADUATE SCHOOL**

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Provide education for pursuing the new biostudies at the world's top level

To meet the demands of the industry, college, research institutes and administrative organizations, individuals are educated in the life sciences and master the techniques for the society needs.

Train individuals to apply the new life sciences for the protection of the global environment and for human welfare

Integrate the knowledge and technology in the old fields of science, agriculture, medicine and pharmacology, and nurture individuals who can contribute to the human society in the 21st century.

Nurture individuals who can understand the various vital phenomena of the living organisms as a systemic function, and pursue these systemic functions

Nurture individuals who will be leaders in the human society to pursue their activities for the welfare and happiness of humans in the 21st century, where humans will be living in harmony with other living beings.



### **OPERATION POLICIES of our GRADUATE SCHOOL**

Training of individuals with the most advanced knowledge of the life sciences for the next generation

The graduate student studies a higher level of life sciences beyond the structures of past life science - related fields at each undergraduate level to understand the integrated life sciences. The goal is to nurture a new type of individual with creative and innovative abilities to cope with the various unknown themes to be confronted by human beings in the next generation.

### Activation and flexibility of staff in the human relations

Research is pursued by each staff member independently to develop a new life science based on active exchange among the various laboratories in the graduate school.

### Training to establish self for society

In the Graduate School of Biostudies, individuals are trained to make a healthy and fair judgment based on the academic background of the staff and their prospects for the future; and, establish a new system to evaluate the effects of education from multiple aspects from the past.

Use of current post-doctoral system and evaluation of academic activities

Full use should be made of the current system, to provide the increasing necessary number of instructors per student, for the intensive training to become life scientists at an international level, for true development of a new research field.

### **Mission and Desired Student Profile**

As an advanced discipline that holds the key to the future of humankind, the life sciences are currently undergoing a major evolutionary change. The Graduate School of Biostudies was inaugurated in 1999 as the first independent school of its kind in Japan with the mission of accelerating this global trend, building a world-class center for research, and training the human resources to lead the life sciences field into the next generation. Our school has engineered a fusion of cutting-edge areas in several existing fields and harnessed the common languages of cellular and molecular biology and genetics that together articulate the principles of life. Furthermore, it has developed an integrated understanding of diverse life forms and the environments they help shape, and has launched innovative efforts in research and education that will define a new set of values for the future and dignity of life.

To meet the diverse expectations of society for advances in life science, which is becoming increasingly sophisticated and complex, the Graduate School of Biostudies endeavors to cultivate human resources with the following attributes.





### **Admissions Policy**

- 1. Researchers ready to shed fresh light on, and discover, the fundamental principles of life and pursue world-class research in new areas of the life sciences
- 2. Researchers and advanced engineers committed to global environmental conservation and gains in human health, welfare, and well-being, and ready to make social contributions through roles in public and private research institutions
- 3. Educators and working professionals with a broad-based understanding of the varied phenomena of life in general and ready to make social contributions through roles in education, industry, the news media, and government

We seek students from a broad spectrum of backgrounds who share our values and desire to continue their education through our programs. We especially welcome students who are both knowledgeable and free of preconceptions, and possess the pioneering spirit to help propel the comprehensive and advanced branches of the life sciences into new territory, while appreciating the dignity of life.

### Policy

**Curriculum Policies** 

1. The master's program provides a broad education spanning all domains of the life sciences, and cultivates a foundation of competence for occupations that demand research abilities and advanced expertise in specialized fields.

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- 2. The doctoral program endeavors to impart cutting-edge specialist knowledge backed by diversified academic research, and to cultivate independent researchers who can perform well in an international setting. Additionally, it equips advanced professionals with the knowledge and skills required for occupations in specialized fields as well as the ability to integrate those strengths and assume leading roles.
- 3. Students develop the ability to accurately place their own research into perspective with their specialization, discuss and debate the findings and their significance in an international setting, and build frameworks for collaboration, as necessary.
- 4. The curriculum is organized and implemented so that students can apply broad visions to put their own research into perspective, build systems of knowledge, and pursue cross-disciplinary study unencumbered by existing fields of specialization. This approach lays the groundwork for the creation of new knowledge with which students will be ready to tackle unknown fields with a tireless spirit of innovation.
- 5. As they pursue their research at deeper levels, students develop the power to reflect on their own research with firm ethical integrity and a strong sense of responsibility, and continually inquire whether it is consistent with the harmonious coexistence of humanity and nature.

### **Requirements for** completing the Doctoral program

- "The Life-Science Special Exercises" (8 credits : compulsory)
- Common Compulsory Subject (1 credit)
- Common Elective Subjects (at least 1 credit) For graduation, the student must have enrolled for at least three years and have completed at least 10 credits. It is also required to pass the probation and the examination (thesis defense) upon completion of a Doctoral thesis written under the supervision of faculty.

### Requirement for completing the Master's program

- The Life-Science Experiments and Exercises (20 credits : compulsory)
- Common Compulsory Subject (1 credit)
- Common Elective Subjects (at least 9 credits) For graduation, the student must have enrolled for at least two years and have completed at least 30 credits. It is also required to pass the probation and an examination upon completion of the Master's thesis written under the supervision of faculty.

### Features of Education

### Features of Education

From 2006 to 2007, we conducted the "Biostudies Career-Development Program" supported by the Ministry of Education, Culture, Sports, Science and Technology. From 2008, we have launched the "Program for Developing Pharmaceutical Strategists" as one of the projects of "Reforming Programs in Education" at Kyoto University. This program, in cooperation with the Graduate School of Pharmaceutical Sciences, is aimed to reform the educational system of graduate schools in our university. Launched in 2011, we are conducting a new program named "Global Frontier in Life Science". In 2012-2013, we were selected as one of the schools of the "MEXT Excellent Graduate School Hub Formation Project " and supported our Doctoral students with the subsidy. We are hoping that our students will understand the essential aspects of the programs and cooperate with us in achieving their goals.

### **Outline of Reforming Programs in Education** 1. Lectures

In our Master's program, the curriculum is designed to make the students systematically understand life science and its related fields. We offer a broad range of lectures for understanding, revealing, and cultivating the relationship between life science and our society. In our Doctoral program, advanced courses in life science are offered in addition to the seminars at the lab where each student belongs. We gear the program to provide the requisite knowledge and experience for the students' future careers in various fields of Industry, Government, and Academia, at home and internationally.

2. Emphasis on English communication for life science, with support for attendance at international scientific meetings It is now very important to give seminars in English, especially scientific presentations at international meetings. Historically, however, the graduate schools in our country scarcely cared about the development of English communication skills for students. Our school has been emphasizing the development of communication skills in English. We encourage and financially support our students to give talks at international conferences abroad. We also give them advice for their presentation skills.

### 3. Workshops organized by students

Students in life science fields tend to stay in their labs because they are busy working at the bench. However, it is highly important to communicate with other students studying life science inside and outside of our school during the course of education. We encourage and financially support the students to organize and conduct workshops by themselves.

### 4. Guidance by multiple supervisors

Heretofore, students who were assigned to their laboratories studied under the supervision of one faculty member. However, it would be highly stimulating for the students if they could have opportunities to discuss their research and other matters with other faculty members. In our school, each student is strongly encouraged to consult with two additional supervisors for his/her current research and also career objectives. We hope that the practice widens their vision on life science and on their future plans.

### 5. Global Frontier in Life Science (Program conducted in English)

The Ministry of Education, Culture, Sports, Science and Technology launched the "Global 30" Project for Establishing Core Universities for Internationalization, for the purpose of selecting universities that will function as core schools for receiving and educating international students. In 2009, thirteen universities including Kyoto University were selected. These core universities are playing a major role in dramatically boosting the number of international students educated in Japan as well as Japanese students studying abroad.



### **Composition of Departments**

### Research Laboratories in the Graduate School of Biostudies

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### **Division of Integrated Life Science**

In this division, education and research are focused on the elucidation of basic mechanisms regulating the chromosome transmission, chromosome replication, RNA architecture, cell cycle, cellular transport, cell polarity, signal transduction, growth and development, developmental plasticity, bioconversion, and environmental adaptation. Experimental approaches are taken with microorganisms, plants, and animals. We pursue education and research to elucidate the molecular aspects of Integrative Life Science.

Dept. of Gene Mechanisms Chromosome Transmission/Gene Biodynamics/Cell Cycle Regulation — Major interest is the molecular mechanism of higher order phenomena (cell proliferation, morphogenesis, canceration, aging, etc.) and the cellular function (cell cycle, chromosome replication, segregation, maintenance and repair, etc.) in unicellular and multicellular organisms.

**Dept. of Cell and Developmental Biology** Cell Recognition and Pattern Formation/Signal Transduction — 1 We are studying signal transduction mechanisms that control organogenesis and animal growth in response to nutrition and growth factors. We are also dissecting operating principles of neuronal circuits that evoke behaviors to sensory stimuli.

Dept. of Plant Gene and Totipotency Plant Molecular Biology/Molecular and Cellular Biology of Totipotency — 13 The department pursues the basic research and application of molecular and cellular principles related to plant growth and development. We take approaches by cell biology, chemical biology, molecular and cellular biology, molecular genetics, and genomics.

 Dept. of Applied Molecular Biology
 Biosignals and Response/Applied Molecular Microbiology/
 1

 Signal response mechanisms have evolved in organisms through adaptations to fluctuations or changes in the natural environment. These mechanisms are being elucidated using various model organisms at different levels (individual, organ, tissue, cell, molecule and gene), and directing this knowledge toward applications with benefits to human welfare is a priority.

**Dept. of Responses to Environmental Signals and Stresses**Plant Developmental Biology/ Plasma Membrane and Nuclear Signaling — 1
We aim at understanding fundamental systems underlying environmental responses by organisms through
structural-functional study of information molecules involved in environmental responses and study of
regulatory mechanisms of development in response to environmental signals.

**Dept. of Molecular and Developmental Biology** Developmental Neurobiology/Biochemical Cell Dynamics — 20 The development, function, and maintenance of tissues and organs are regulated by a coordinated interplay of cell-intrinsic programs and intercellular signals. We seek their mechanisms at cellular, organellar and molecular mechanisms using various model systems, including the brain and immune systems.

 Dept. of Molecular and Cellular Biology
 Molecular and Cellular Immunology/Mammalian Molecular Biology
 21

 We study on mammalian development, differentiation, aging and viral immunity. We utilize molecular biology and developmental engineering as tools of analyses to elucidate mechanisms at molecular, cellular and animal levels.
 21

 Radiation Biology Center
 Radiation System Biology/Mutagenesis/Late Effects Studies/Genome Repair Dynamics/

 Our center is trying to elucidate basic mechanisms behind biological responses to irradiation as well as chromosomal damages, and thereby pursue fundamental basis for evaluation of radiation exposure risks and for efficacious radiation therapy. To achieve the goals, our center is acting as a joint usage research center to promote collaborations among researchers in the community.

Research Center for Dynamic Living Systems <sup>Cutting-edge Bioimaging/Data-driven Modeling/Multiscale Biomechanics/Develop-\_\_\_43 We aim at understanding the life as dynamic living systems. We observe the dynamic behavior of molecules and cells with cutting-edge technologies of microscopy, optogenetics, and mouse genomics. Based on the accumulated multidimensional data, we will uncover the working principles of life by the approaches of mathematics and informatics.</sup>

### **Division of Systemic Life Science** In this division, education and research are focused systemic biology, cell biology and immunology. Exp microorganisms, cultured cells and animals. We put aspects of Systemic Life Science. Dept. of Molecular and System Biolog We will challenge direct viewing of biomolecula super-resolution microscopy IRIS. By elucidatin drugs, we will pursue principles in biology and s Dept. of Animal Development and Phy The objectives of our studies are to clarify the n cells, tissues, organs, at the molecular, cellular, differentiation, cell death, cell-cell interactions, Dept. of Signal Transductions Molect Cancer, autoimmune diseases, and life-style rela aberrant response mechanisms. We aim to reve cancer, and immunological, genetic diseases. Dept. of Functional Biology Functional Using animal models of human diseases, such diseases, and using metabolite imaging technic and develop new strategies to cure or prevent the Dept. of Biology Education and Heredi Development of effective teaching materials for Dept. of Systems Biology Bioimaging an By the use of cutting-edge technologies of micr information that living organism perceive. Base built to understand systematically the mechani Dept. of Genome Biology Genome and epigenome information are mainta exogenous and endogenous perturbations. We human disorders. Dept. of Mammalian Regulatory Netw Laboratories consisting of this Department stud to the integrity of higher organisms. Studies als biomaterials, serving to establish basic principl

Attached Research Centers



d on the elucidation of the fundamentals of molecular and perimental approaches are taken with viruses, Irsue education and research to elucidate the molecular	
<b>gy</b> Single-Molecule Cell Biology r dynamics using single-molecule imaging and multi-target g the molecular basis of morphogenesis and the action of seeds for drug development.	- 23
Molecular and Cellular Biology/Immunobiology/ Molecular Cell Biology and Development nechanisms that regulate hierarchical structures composing and individual levels, especially about cell growth, and histogenesis.	- 24
ular Neurobiology/Genetics	- 26
l Biology as neurodegenerations, cancers, and obesity-related ques, we aim to elucidate molecular bases of such diseases hem.	- 28
ty Science Communication and Bioethics/Science Communication/ Bioeducation/Chromosome Function and Inheritance r biological sciences.	- 29
d Cell Signaling/Theoretical Biology/Brain Development and Regeneration — roscopy, optogenetics, and chemical biology, we will study the ed on the accumulated information, mathematical models are sm of information processing of living organisms.	- 32
tenance/Genome Damage Signaling/Cancer Cell Biology/ gulatory Network	- 34
ained by an intricate molecular system acting against aim to study defects in these mechanisms that result in	
Cell Regulation and Molecular Network/RNA Viruses/ Cell Division and Differentiation/Genetic Information/ Cellular and Molecular Biomechanics dy multi-dimensional networks of life signals that contribute so include those utilizing viruses, animal models, and es in life science.	- 38

### Division of Integrated Life Science | Department of Gene Mechanisms

Laboratory of Chromosome Transmission

Assoc. Prof. NAKASEKO, Yukinobu



### Main theme

We are focusing on analyzing the genes involved in regulation of chromosome function. Especially, the genes essential for mitosis have been studied. Fission yeast Schizosaccharomyces pombe is used as a model system. This yeast has all basic features essential for eukaryotic cell division. Many genes have been identified which regulate the cell cycle of this yeast. Also, their functions as well as their primary structure have been shown to be conserved among all eukaryotic cells. We are trying to characterize these genes and their functions by genetical approach.

Elucidation of whole functional network of these genes is one of a goal in our research.





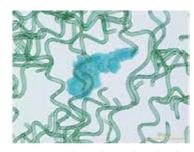
Assoc. Prof. SHIRAISHI, Hideaki

### Main theme

We are interested in the mechanism of growth, development and evolution of photosynthetic microorganisms and currently focusing on the study of the edible cyanobacterium Arthrospira (Spirulina) platensis. A. platensis is a filamentous alkalophilic cyanobacterium that has been traditionally consumed as food by people living along the shores of alkaline lakes in several regions in the world. Because it can be cultured under alkaline conditions where growth of other microalgae is suppressed, it can be produced in mass cultures outdoors as an almost single algal strain. Because of its easiness of mass culture, it is commercially produced in many subtropical areas in the



world and consumed worldwide as food, food additives, and feed for animals and fishes. We are currently focusing on developing tools for molecular genetic studies of this cyanobacterium.



Filamentous cyanobacterium Arthrospira platensis and the aggregated expolysaccharides produced by



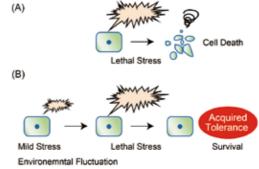


### Main theme

Stable maintenance of genetic information is essential for cell viability. Genetic instability, a condition in which the genome is not properly maintained, causes numerous pathologies including cancer and aging. Telomeres, the ends of chromosomes, play a pivotal role in this process. We are interested in how telomeres protect genetic information from intrinsic and extrinsic insults. Aging can be defined as the accumulation of damaged cells caused by various stresses. Stress is generally considered to be non-adaptive. However, low-dose stress can act in an adaptive role by fostering cell resistance to prospective lethal stresses. This process is termed acquired tolerance (or hormesis) and its molecular mechanisms remain largely unknown. We are trying to understand how acquired tolerance is induced molecularly. Arguably, cancer cells

in vivo acquire stress resistance through experiencing ever-lasting environmental changes. As such, inhibiting the acquired tolerance in cancer cells may lead to fragility of cancers to various stresses, including iatrogenic ones.

- Molecular understanding of how yeast and mammals.
- conditions. Mechanism of retrotransposition and
- mammalian genome. · Development of therapeutic strategies
- for cancer by elucidating the mechanisms of cellular senescence.
- · Mechanism of genomic instability induced by chromosome end-to-end fusions



Ingeneral, cells exposed to lethal stress undergo cell death (A). However, cells preconditioned with mild stress can become resistant to subsequent lethal stresses (B). This process is called acquired tolerance or hormesis: an adaptive behavior that is crucial for survival in an ever-changing environment. In vivo, cancer cells can experience environmental changes such as hypoxia and iatrogenic stress. This is in contrast to normal cells that live in a stable niche given by the tissue. It is possible that cancer cells are pre-conditioned by the environmental changes to prepare for the prospective lethal stress. Therefore, inhibition of this acquired tolerance may make cancer cells sensitive to anti-cancer therapeutics.

http://www.fish.lif.kyoto-u.ac.jp/ Lab U

### Division of Integrated Life Science | Department of Gene Mechanisms

telomeres protect DNA ends in fission

• Functional roles of acquired tolerance in various physiological and pathological

its impact on genomic instability in the

# Professor

Laboratory of

Cell Cycle

Regulation

### ISHIKAWA, Fuyuki

### Assoc. Prof. MIYOSHI, Tomoichiro



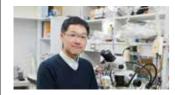


### Division of Integrated Life Science | Department of Cell and Developmental Biology

### Laboratory of **Cell Recognition and Pattern Formation**

### Professor UEMURA, Tadashi

Lecturer USUI, Tadao



Assist. Prof. HATTORI, Yukako



Program-Specific Assist. Prof. KONDO, Takefumi



Program-Specific Assist. Prof. TSUYAMA. Taiichi



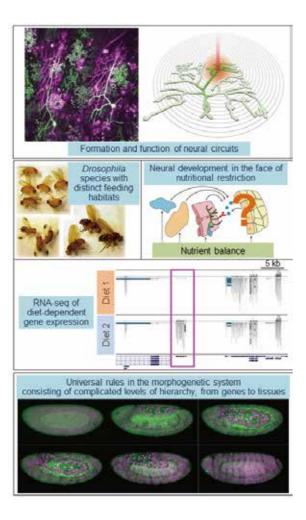




### Main theme

Diet is a critical environmental determinant that affects life-history traits. We are studying dietary responses that govern animal growth. We are also dissecting neuronal circuits that evoke selective behaviors in response to

sensory stimuli. Furthermore, we are finding the universal rule(s) in the morphogenetic system of multicellular organs consisting of complicated levels of hierarchy, from genes, cells to tissues.

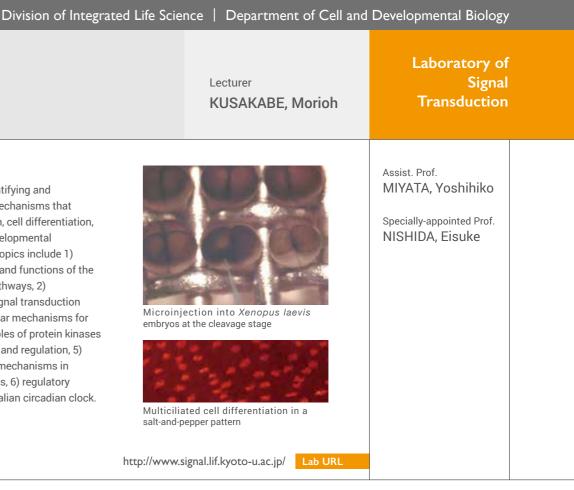


Lab URL http://www.cellpattern.lif.kyoto-u.ac.jp/

### Main theme

We are interested in identifying and elucidating molecular mechanisms that regulate cell proliferation, cell differentiation, cell cycle, aging and developmental processes. The current topics include 1) regulatory mechanisms and functions of the MAP kinase cascade pathways, 2) identification of novel signal transduction mechanisms, 3) molecular mechanisms for life span regulation, 4) roles of protein kinases in cell cycle progression and regulation, 5) growth factor signaling mechanisms in developmental processes, 6) regulatory mechanisms for mammalian circadian clock.

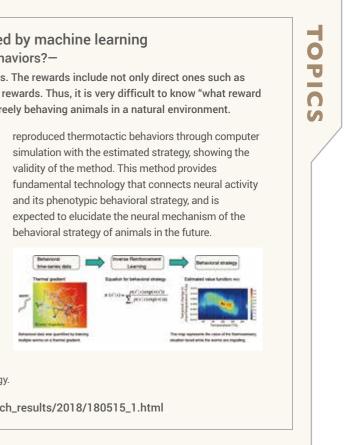




Animal behavioral strategy was unpacked by machine learning -What reward do animals pursue in their behaviors?-Animals behave with a strategy to acquire more rewards. The rewards include not only direct ones such as foods, but also indirect ones associated with the direct rewards. Thus, it is very difficult to know "what reward animals pursue in their behaviors", only by observing freely behaving animals in a natural environment.

The laboratory of Naoki Honda developed a new machine learning method to inversely estimate reward-based strategy from behavioral time-series data. By collaborating with Nagoya University, they applied this method to food-searching behaviors of C. elegans; after cultivation at a constant temperature with or without food, fed worms prefer, while starved worms avoid the cultivation temperature on a thermal gradient. Their method discovered that fed and starved worms pursue reward based on distinct thermosensory information. The fed worms sensed not only the absolute temperature, but also its temporal differentiation, whereas the starved worms used only the absolute temperature. In addition, they

The findings were published in PLoS Computational Biology. For further information, please visit the URL below. URL: https://www.kyoto-u.ac.jp/en/research/research\_results/2018/180515\_1.html

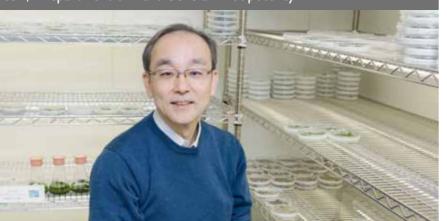


### Division of Integrated Life Science | Department of Plant Gene and Totipotency

Main theme

Laboratory of Plant Molecular Biology

Professor



# Assoc. Prof.

KOHCHI, Takayuki



Assist. Prof. YAMAOKA, Shohei

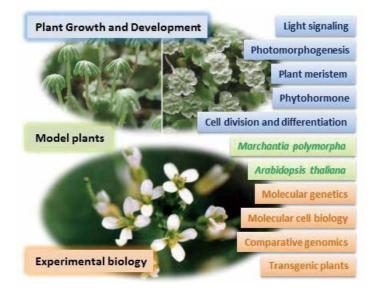


Program-Specific Assist. Prof. YOSHITAKE, Yoshihiro



Research in this laboratory focuses on the adaptive regulation of growth and development to environmental conditions and its evolution by using model photosynthetic organisms. Especially with the liverwort Marchantia polymorpha, which is a basal land plant ideal for comparative evolutionary

studies and amenable to molecular genetic manipulation, we aim to elucidate principles and ancestral molecular mechanisms of photomorphogenesis, growth phase transition, phytohormone signaling, meristem function, cell division, and cell differentiation in land plants.



### Lab URL http://www.plantmb.lif.kyoto-u.ac.jp//

Main theme

Molecular and cellular biological studies on totipotency in plant cells have been carried out in this laboratory using in vitro cultured cells and transgenic plants. Especially, cell/organ differentiation from undifferentiated cells, functional differentiations, e.g. secondary metabolite production, such as biosynthesis of isoquinoline alkaloids, oxygen evolving complex in photosystem II, cyclic electron transfer and gene regulation in chloroplast, have been investigated to understand the totipotent functions in plant cells. Development of novel genetic engineering

techniques such as genome editing, metabolic engineering and synthetic biology of secondary metabolism for industrial application have been also investigated.



### identification of the cell surface ligand Sas that recognizes oncogenic cells The study was published in Nature at 1 a.m. on January 17, 2018

The research group of Professor Tatsushi Igaki, graduate student Masatoshi Yamamoto, and Associate Professor Shizue Ohsawa conducted a genetic screen for genes required for elimination of oncogenic cells from Drosophila eye imaginal epithelium. They found that Sas, the cell surface ligand, is required for elimination of oncogenic cells from epithelium. In response to the emergence of oncogenic cells, Sas on the normal epithelial cell binds to its receptor PTP10D on its neighboring oncogenic cells, thereby suppresses cell proliferation and promotes cell death of oncogenic cells.

### Comments from the research group:

Oncogenic cells are eliminated from the epithelial tissue by 'cell competition' when surrounded by normal cells. This phenomenon is thought to be a novel mechanism of tumor suppression. Using a Drosophila

### Division of Integrated Life Science | Department of Plant Gene and Totipotency

Laboratory of Molecular and Cellular **Biology of Totipotency** 

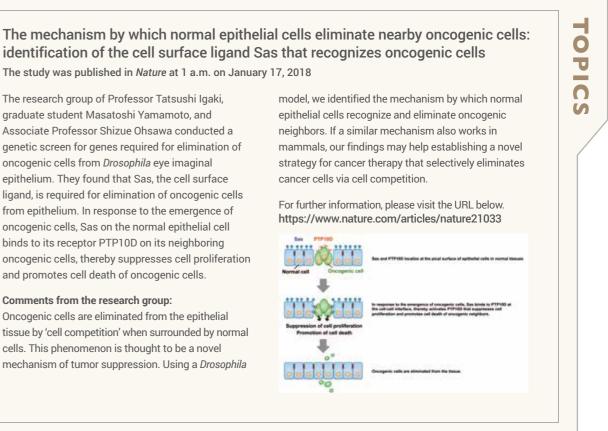


http://www.callus.lif.kyoto-u.ac.jp

Lab URL







### Division of Integrated Life Science | Department of Applied Molecular Biology

Laboratory of **Biosignals and** Response

### Professor NAGAO, Masaya

Assoc. Prof. KAMBE, Taiho



Assist. Prof. NISHINO, Katsutoshi

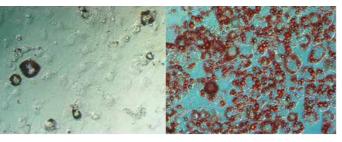




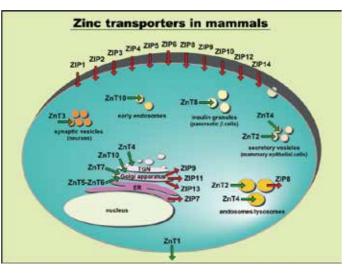
### Main theme

Bio-prospecting, a research strategy searching for compounds that possess beneficial activity for health from natural sources, is one of the projects in this laboratory. Especially, compounds that are useful for treatment of lifestyle-related diseases and cancer are the main targets of our bio-prospecting.

We are also studying how organisms perceive environmental signals and transduce these signals into changes in gene expression, focusing mainly on the molecular and cellular basis of zinc metabolism (such as uptake, storage, delivery, and maintenance of metal concentration in cells) in mammal.

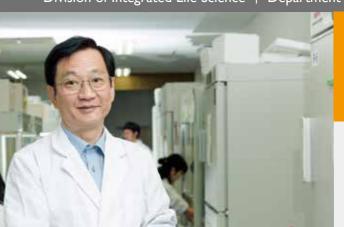


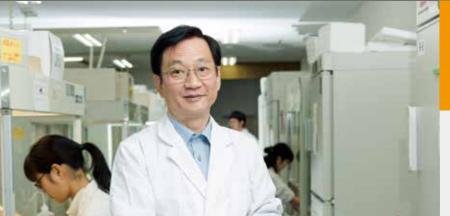
Stimulation of lipid accumulation by plant extracts











### Main theme

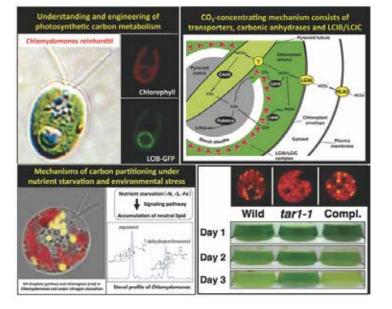
We are focusing on the molecular bases of biological functions of microalgae contributing to production of food, biofuel and industrial materials, and also to environmental remediation by photosynthesis. Especially we employ a green alga, Chlamydomonas reinhardtii, as a model eukaryotic photosynthetic microorganism using its genomic information, mutants, and molecular/biochemical techniques. The current projects are

(1) Molecular characterization of the carbon-concentrating mechanism supporting photosynthetic carbon fixation, biofuel production, and cell proliferation,

(2) Elucidation of regulatory systems changes of levels in CO2 concentration, light and nutrient starvation.

(4) Molecular control and signaling of sexual reproduction by nutrient starvation.

(5) Identification of factors essential for intracellular signal transduction such as calcium and DYRK family of protein kinases supporting cell survival.



http://www.molecule.lif.kyoto-u.ac.jp/ Lab U

### Division of Integrated Life Science | Department of Applied Molecular Biology

controlling photosynthesis and carbon metabolisms by sensing environmental factors including

(3) Metabolic engineering for production of industrial important fatty acids, glycerolipids and carbohydrates.

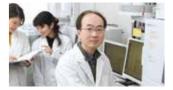
Laboratory of **Applied Molecular** Microbiology

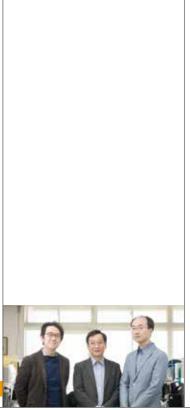
### Professor FUKUZAWA, Hideya

Assist. Prof. YAMANO, Takashi



Assist. Prof. KAJIKAWA, Masataka





### Division of Integrated Life Science | Department of Applied Molecular Biology

Laboratory of Molecular Biology of Bioresponse



### Professor KATAYAMA, Takane

Assoc. Prof. MASUDA, Seiji



Assist. Prof. KATOH. Toshihiko



### Main theme

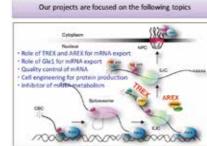
The aim of our laboratory is to understand the fundamental life processes of microbes and human, and to develop food- and health-oriented application research. The research activities mainly include (1) elucidation of the molecular mechanism underlying symbiosis and co-evolution between gut microbes and host, and (2) elucidation of the mechanism of mRNA processing, export and quality control in the nucleus in human and its industrial applications.

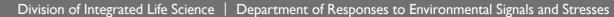
(1) Recent studies have shown that the consortium of gut microbes exerts a considerable influence on host health. Most researchers approach this topic from "host" side using a mouse model, but we believe that approaches from "microbe" side are

equally needed to understand the symbiosis between them. To this end, we are genetically and enzymatically analyzing unique metabolic pathways in gut microbes, which should uncover the cross-kingdom communications between bacteria and host in intestine.

(2) The main projects are (i) the role of TREX and AREX, which couple transcription and export of mRNA, (ii) the molecular mechanism of RNA quality control in the nucleus, (iii) cell engineering for the protein production using mRNA export mechanism in mammalian cells to apply to industrial applications and (iv) identifying the active compounds which inhibit the mRNA matabolism to apply to medical care.

cteria-rich mie infant intestin







### Main theme

We are interested in molecular mechanisms underlying plant's responses to environment. Plants have evolved plastic developmental programs with both genetic and epigenetic basis to adapt their sessile mode of life to changing environment. Using an angiosperm, Arabidopsis thaliana and a liverwort, Marchantia polymorpha as

model systems, we have been investigating (1) regulation of growth phase transition (especially, flowering) in response to environmental signals, (2) long-distance systemic signaling in the control of development, (3) sexual reproduction processes (especially, male gametogenesis and fertilization), and (4) origin and evolution of regulatory systems for plastic development.



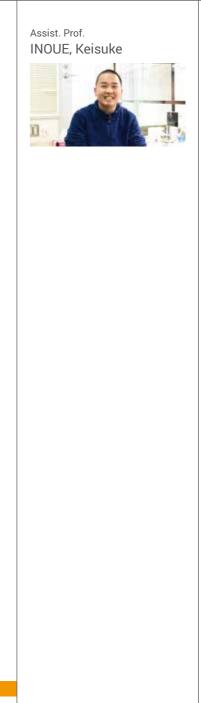


Lab URL http://www.bunshioutou.lif.kyoto-u.ac.jp/

http://www.plantdevbio.lif.kyoto-u.ac.jp/ Lab URL

Laboratory of Plant Developmental Biology

### Professor ARAKI, Takashi



### Division of Integrated Life Science | Department of Responses to Environmental Signals and Stresses

### Laboratory of Plasma Membrane and Nuclear Signaling

Assoc. Prof. YOSHIMURA, Shigehiro



### Main theme



Assist. Prof.

Our laboratory studies dynamic properties of cellular proteins and membrane in cellular environments by using a variety of techniques in biochemistry, cellular biology and biophysical approaches. We are also interested in how those dynamics of cellular architectures are related to diseases. Specific research topics include:

- (1) Cytoskeletal dynamics in cell motility and metastasis: intracellular dynamics of actin cytoskeleton is elucidated by our live-cell nano-imaging technique.
- (2) Molecular mechanism of signal transduction: how plasma membrane and membrane -bound proteins coordinates endocytic process.

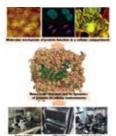
b URL http://www.chrom.lif.kyoto-u.ac.jp/

(3) Virus vs host cell at cell surface: imaging viral particle at the host plasma membrane to elucidate the mechanism of viral infection and proliferation.

(4) Proteins in molecular crowding: dynamic assembly and disassembly of proteins and nucleic acids in cellular environments.

(5) How do cells feel force?: elucidating

molecular mechanism of mechano-sensing and -responses by combining various biophysical approaches

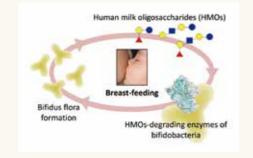




### Molecular basis underlying bifidus flora formation in breast-fed infant intestines

Since the isolation of *Bifidobacterium* sp. from infant stools by Dr. Henri Tissier in 1899, it has been known that bifidobacterial-rich microbiota forms in the gut of breast-fed babies but not formula-fed babies. However, the molecular basis underlying the bifidus flora formation has remained obscure. In the last decade, Prof. Takane Katayama's group has shown that bifidobacteria have gene sets dedicated to assimilate human milk oligosaccharides (HMOs) that collectively constitute the third most abundant component in breast milk. In a paper published in Cell Chemical Biology, he has identified, in collaboration with Prof. Shinya Fushinobu at the University of Tokyo, a key genetic determinant for bifidobacteria to prevail in breast-fed infant intestines. The gene encoding lacto-N-biosidase, which hydrolyzes lacto-N-tetraose (the core structure of HMOs), was found to be enriched in stool DNAs collected from

exclusively breast-fed babies, and the copy number correlated positively with Bifidobacterium longum cell numbers. No such correlation was detected between the two groups in fecal DNAs extracted from mixed-fed babies. The data revealed a mechanistic basis of how bifidobacteria prevail in the gut ecosystem and provided an evolutionary insight into the symbiosis between bifidobacteria and humans.



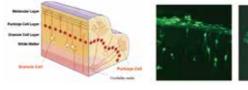
The findings were published in the Journal of "Cell Chemical Biology 24, 515-524 (2017)". For further information, please visit the URL below. http://www.bunshioutou.lif.kyoto-u.ac.jp/katayama/Home.html

# Division of Integrated Life Science | Department of

### Main theme

Neurons in the mammalian brain are orderly arranged in cortices and nuclei for integration into specific neural circuits. During development, neurons directionally migrate from the birthplace to their destination within the cortex, and then arborize well-patterned dendrites and axons to contact with their specific synaptic counterparts. The major goal of our research is to clarity the





http://www.kengaku.



### Main theme

In principle, we identify specific genes involved in the biological phenomenon with our interests. The main approaches are as follows: Expression cloning using cDNA library, functional screening using sgRNA library in a CRISPR/Cas9 system, biochemical approach in combination with mass spectrometry. By establishing the robust experimental systems, we try to understand the biological phenomenon with interests. Currently, we are interested in the biological phenomenon called phospholipid scrambling that regulates blood coagulation, engulfment of dead cells, cell fusion, cancer progression, regulation of brain/bone/muscle functions and so on. In spite of its importance in various biological systems, much is unknown about how phospholipid scrambling is regulated. We are going to

uncover the m Research Top

- Identificatio plasma men
- Identificatio intracellular
- Identificatio scramblases
  - Involvement engulfment
- Understandi scramblase
- · Screening th regulating th
- Exploring th in the above

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f Molecular and Developmental	Biology (Cooperation Course)
Professor KENGAKU, Mineko	Laboratory of Developmental Neurobiology
of cortical lamination and ring of neurons in the brain. We ify the molecular signals uronal migration and dendrite te also aim to develop imaging or real-time observation of d cellular dynamics of neuronal d dendrite patterning to discover nena and rules in neuronal e developing brain.	
u.icems.kyoto-u.ac.jp Lab URL	
Professor SUZUKI, Jun	Laboratory of Biochemical Cell Dynamics
nechanisms of lipid scrambling. opic on of novel scramblases on mbranes on of novel scramblases on r membranes on of regulators or subunits in as it of scramblases on synaptic ding how diseases occur by e deficiency the chemical substances the scramblases ne new phenomenon discovered e projects lus.lif.kyoto-u.ac.jp	

### Division of Integrated Life Science | Department of Molecular and Cellular Biology (Cooperation Course)

Laboratory of Molecular and Cellular Immunology

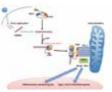
Professor FUJITA, Takashi



### Main theme

Virus infections, such as influenza A epidemic, Ebola hemorrhagic fever, Middle East respiratory syndrom, Zika virus infection are important diseases and outbreaks of newly emerging viruses are serious problems for modern society. Higher animals, including humans, are genetically equipped with mechanisms, collectively known as innate immunity, to counteract viral infections. During the course of replication, many viruses generate double-stranded (ds)RNA, which is virtually absent in normal cells and likely serves as a "foreign molecule" in cells. An RNA helicase, RIG-I, functions as a sensor for viral dsRNA. RIG-I is composed of three domains : a Caspase recruitment domain (CARD), a

DExD/H helicase domain, and a C-terminal domain (CTD)(Figure). CTD senses viral dsRNA produced in the cytoplasm, leading to a conformational change. This conformational change releases CARD, which signals to downstream, resulting in the activation of genes including those for type I interferon and other cytokines. The purpose of our project is to clarify the molecular mechanism underlying the antiviral innate immunity regulated by RIG-I, and to develop new diagnostic and therapeutic means for viral infections.



Optogenetic control of neural stem cells

Induction of

sustained expressi

Asci1

Aucit

Ascl1

Induction of

oscillatory expression

Lab URL http://www.virus.kyoto-u.ac.jp/Lab/bunshiiden2012/English/index.html



Assoc Prof OHTSUKA, Toshiyuki



Assist. Prof. KOBAYASHI, Taeko



### Main theme

We analyze the molecular mechanism of embryonic development by using the most advanced methods such as imaging, optogenetics and transgenic mouse technologies. We evaluate mathematical modeling by using transgenic mice and seek to understand the principles of developmental dynamics. We found that oscillatory gene expression is important for many developmental processes such as brain morphogenesis and somite formation.





### Main theme

Virus infections are accompanied by numerous ultrastructural changes in viral and cellular components. Our laboratory has been investigating the replication mechanism of influenza and Ebola viruses from the ultrastructural point of view, by using different microscopic methods such as electron microscopy and high-speed atomic force microscopy. Visualization and characterization of the virus life cycle at the nano-mesoscopic level give us unique knowledge and novel paradigms, which will advance our understanding of molecular

basis of the replication mechanism.

### ATP maintenance mitigates Parkinson's disease in mice

In a report published in EBioMedicine, Akira Kakizuka and his team from the Graduate School of Biostudies found that regulating of the primary energy source of the body -- ATP -- could be promising avenue for future Parkinson's disease therapy

ATP - chemically known as adenosine triphosphate - is a compound found in all life and powers the body. Decrease in ATP levels in the brain causes neuronal cell death in several pathological conditions, inducing Parkinson's disease (PD). The team developed two types of small compounds, which enhanced ATP production or limited ATP consumption in cells, namely neurons. These compounds were collectively denoted as "ATP Regulators".

Further, when these ATP regulators were administered to two types of PD model mice, the compounds mitigated the loss of neurons involved in PD and moderated the pathological activity resulting from the disease. The results show ATP regulation as a possible avenue for future PD therapy, and opens the door for finding commonalities in other neurodegenerative diseases.

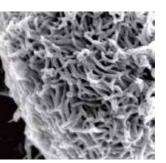
Read the release online

http://www.kyoto-u.ac.jp/ja/research/research\_results/2017/170724\_3.html

### Division of Integrated Life Science | Department of Molecular and Cellular Biology (Cooperation Course)

Professor NODA, Takeshi

### Laboratory of Ultrastructural Virology



Scanning electron micrograph of Ebola viruses budding from cell surface.

Assist. Prof. NAKANO, Masahiro



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https://www.facebook.com/NodaLab/

Lab URL

### Researcher comment

"In neurodegenerative disorders, ATP decrease, or depletion would be a common phenomenon, even though each disease has a unique etiology. Early stage ATP decrease would diminish the function of affected cells or neurons, and further ATP decrease result in neuronal cell death. Our model suggests a potential therapeutic strategy, namely maintenance of ATP levels, to slow or stop neurodegenerative disease progression. Given that many incurable human disorders also

manifest early cell death in the affected organs, ATP maintenance could also provide a strategy for cell protection to these disorders."

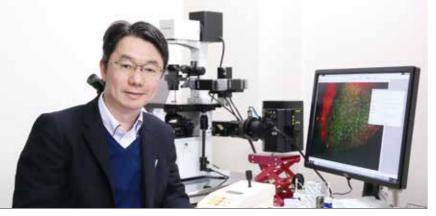


### Division of Systemic Life Science | Department of Molecular and System Biology

### Laboratory of Single-Molecule Cell Biology

Professor

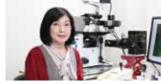
Lecturer



### Main theme

YAMASHIRO, Sawako

WATANABE, Naoki

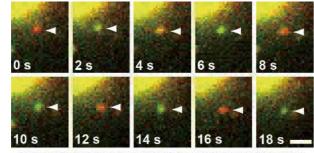


Assist. Prof. MIYAMOTO, Akitoshi

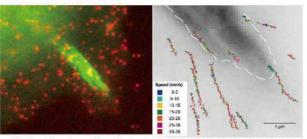


Our laboratory aims at bridging the gap between molecular activities and cell physiology in life systems. We are trying to visualize signal transduction and cell structure remodeling processes directly in living cells by fluorescence single-molecule microscopy. We have also recently invented new

super-resolution microscopy called IRIS, which achieves ultra-high density labeling of multiple targets in a single specimen. By direct viewing using these advanced optical techniques, our laboratory elucidates the mechanism and the dynamics of pathophysiological cell signaling.



Rotation of mDia1 along the actin helix during processive polymerization Hiroaki Mizuno et al. Science 331, 80-83, 2011

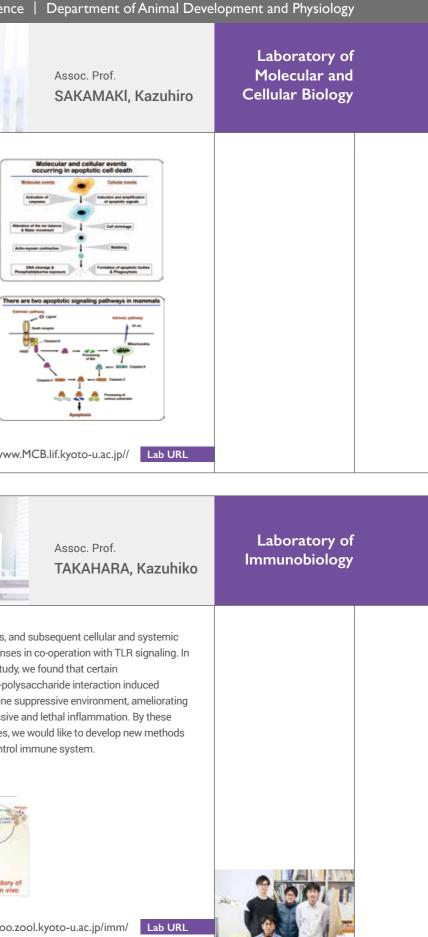


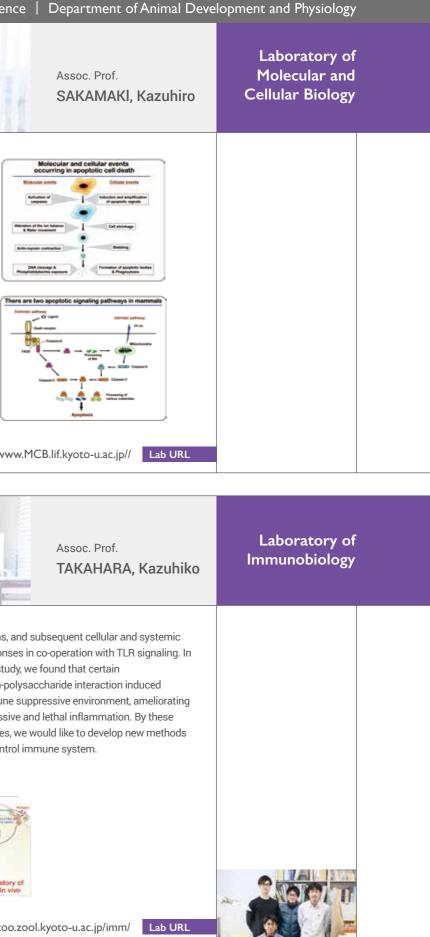
Single-molecule speckles of new nanometer-scale tracking of retro -grade actin flow near focal adhesions DL-labeled photostable actin Sawako Yamashiro et al. MBoC 25: 1010-1024, 2014

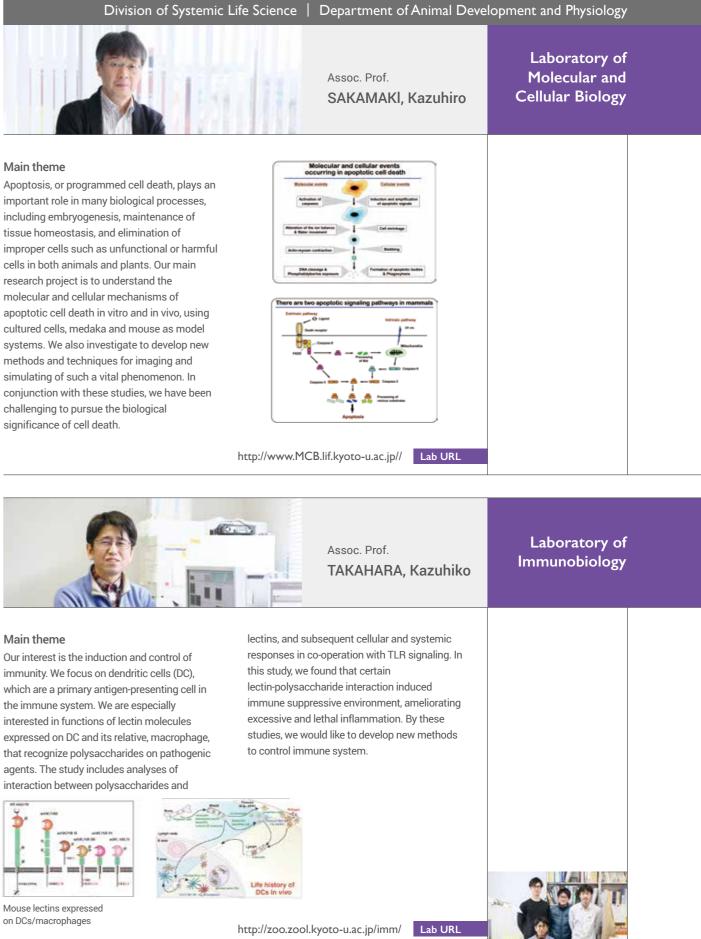


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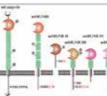
important role in many biological processes, including embryogenesis, maintenance of tissue homeostasis, and elimination of improper cells such as unfunctional or harmful cells in both animals and plants. Our main research project is to understand the molecular and cellular mechanisms of apoptotic cell death in vitro and in vivo, using cultured cells, medaka and mouse as model systems. We also investigate to develop new methods and techniques for imaging and simulating of such a vital phenomenon. In conjunction with these studies, we have been challenging to pursue the biological significance of cell death.

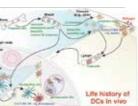






immunity. We focus on dendritic cells (DC), which are a primary antigen-presenting cell in the immune system. We are especially interested in functions of lectin molecules expressed on DC and its relative, macrophage, agents. The study includes analyses of





on DCs/macrophages

### Division of Systemic Life Science | Department of Animal Development and Physiology (Collaboration Course)

GBS's Collaboration Course in the RIKEN KOBE BDR

### Laboratory of Molecular Cell Biology and Development

### Professor MATSUZAKI, Fumio



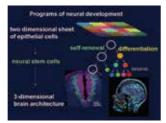
Assoc. Prof.

KITAJIMA, Tomoya

All the vertebrate brains develop from a single layer of epithelial cells that function as neural stem cells, which go through common processes: the initial proliferative phase, and the subsequent neurogenic phase, at which neural stem cells undergo asymmetric cell divisions to generate self-renewing and differentiating daughter cells. Especially, the mammalian brain has rapidly evolved to explosively increase the neuron number and brain size, leading to gyrification. We explore both the principles underlying common

Main theme

processes for brain formation as well as specific mechanisms that allowed the mammals to develop into such complex brains, ultimately enabling human to gain intelligence. We use Drosophila, mouse and ferret that form the folded brain as models.



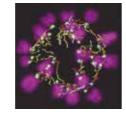


Main theme

### Meiosis in oocytes is prone to chromosome segregation errors and thus frequently produces aneuploid eggs. The aneuploidy of eggs is a leading cause of pregnancy loss and congenital diseases such as Down syndrome. We aim to understand the causes of chromosome segregation errors in oocytes. We will reveal molecular mechanisms of how unique features of oocytes and age-related effects predispose to chromosome segregation errors. The mechanisms in oocytes will be compared with those in eggs and zygotes, by which we will

Lab URL http://www.cdb.riken.jp/lcs/

understand differentiation of intracellular mechanisms through development. By understanding how aging affects chromosome segregation in oocytes, we will provide insights into how events at cell, tissue and organ levels are interconnected at different life stages.



Prometaphase belt of chromosomes

Assoc. Prof. TAKASATO, Minoru



### Main theme

In our previous study, we developed a protocol generating self-organizing kidney organoids from human iPS cells. While these kidney organoids comprise all anticipated renal tissues, they are still far from the real human kidney in terms of their size, tissue complexity, maturity and functionality. We study to achieve the ultimate goal of generating a functional and transplantable three-dimensional kidney. We appreciate knowledge from basic developmental biology that is essential for

such regenerative studies; therefore, we are also highly interested in studies of human embryology. Particularly, we are focusing on uncovering the developmental mechanisms of the human mesoderm and kidney.



A kidney organoid generated from human bluripotent stem cells

Lab URL https://www.bdr.riken.jp/jp/research/labs/takasato-m/index.html



### Main theme

**Outline of Teaching Activities** The laboratory provides seminars which review and discuss recent progress in molecular mechanisms of neuronal functions

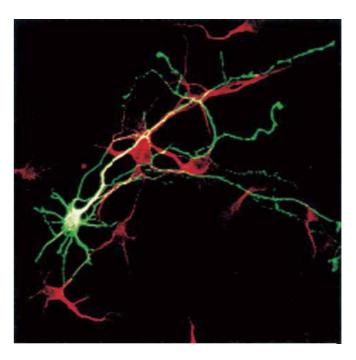
guidance

### **Outline of Research Activities**

The main themes of research in this laboratory are the molecular mechanisms underlying neuronal network formation and neuronal signal transductions. 1. Neuronal functions and signal transductions of GTP-binding proteins 2. Molecular mechanisms for axon

3. Regulatory systems of synaptic transmission

4. Signal transduction of neuronal polarity formation



http://www.negishi.lif.kyoto-u.ac.jp/e/Top.html Lab UR

Laboratory of Molecular Neurobiology

### Professor NEGISHI, Manabu

Assoc. Prof. KATOH, Hironori



### Division of Systemic Life Science | Department of Signal Transductions

Main theme

Our research focuses on the molecular

governs tissue growth, homeostasis, and

basis of cell-cell communication that

cancer. We take advantage of the

powerful genetics of Drosophila.

### Laboratory of Genetics

Professor



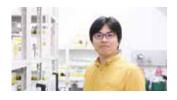
### Assoc. Prof. OHSAWA, Shizue

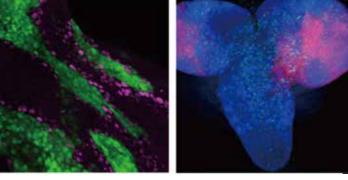


### Assist. Prof. ENOMOTO, Masato



Program-Specific Assist. Prof. TANIGUCHI, Kiichiro





Left: Polarity-deficient cells (green; losers) are eliminated from epithelium by wild-type cells (magenta; winners) through cell competition.

Right:Malignant tumor cells (magenta) are invading and metastasizing from the eye disc to the brain (blue) in Drosophila larva.

### **Research subjects**

- 1. Mechanism of cell competition
- 2. Genetic basis of tissue growth regulation
- 3. Molecular basis of tumor progression and metastasis
- 4. Logic for morphogenesis from folded epithelial sheets

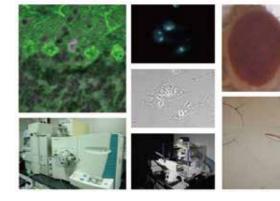


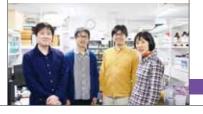
### Main theme

Using animal models of human diseases, such as neurodegenerations, cancers, and obesity-related diseases, and using metabolite imaging techniques, we aim to elucidate molecular bases of such diseases and develop new strategies to cure or prevent them.

One of the main features of life science research in the coming years will be that the results obtained from fundamental research should ideally be directly connected to the good of society. From this standpoint, in addition to handling

of treatments for neurodegenerative diseases, cancers, and obesity-related diseases from our research results. We hold the same view on scientific education, and through training logically yet effectively, as well as by nurturing their creativity, in addition to strengthening their practical research standing at the core of life science research in the 21st century.





http://www.funcbiol.lif.kyoto-u.ac.jp/ Lab URL

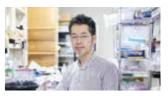
Laboratory of Functional **Biology** 

### Professor KAKIZUKA, Akira

topics with high scientific significance, we aim to contribute to the development individuals to communicate their ideas skills, we aim to cultivate opinion leaders



Assoc. Prof. IMAMURA, Hiromi



Assist. Prof. SASAOKA, Norio



Program-Specific Assist. Prof. YOSHIDA, Tomoki



### Division of Systemic Life Science | Department of Biology Education and Heredity

Laboratory of Science Communication

**HEJNA**, James Alan

Professor

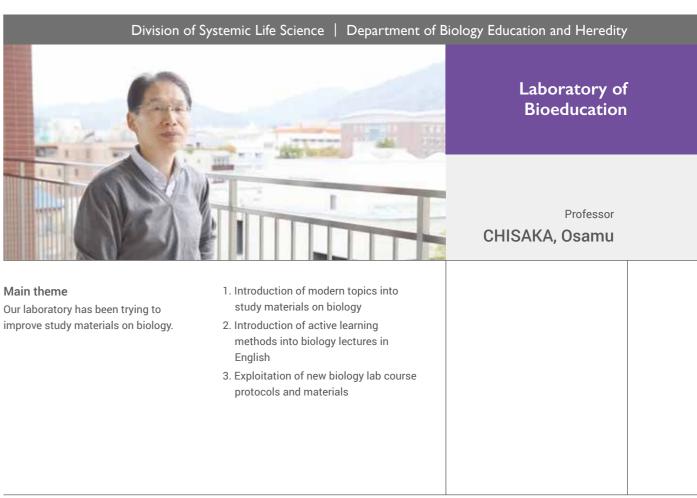


### Main theme

Our laboratory engages in the development and implementation of new approaches to the internationalization of science education and communication, based on principles of active learning. The particular challenges we are addressing often involve overcoming the differences in culture and pedagogical traditions between Japanese and Western societies. Our efforts are chiefly in the educational arena, aimed at training the next generation of scientists to communicate their knowledge and expertise not only to the international scientific community but locally to the citizens who ultimately

support basic research. Our activities entail the following:

- 1. Increasing the exposure of Japanese students to foreign peers. We are forging new partnerships with foreign universities to foster joint courses, using live Internet connections, with active student participation in English.
- 2. Establishing partnerships with foreign universities to encourage short-term reciprocal exchanges of graduate students for collaborative research.
- 3. Expanding the opportunities for students to present their research in English to a broad audience.



improve study materials on biology.

### Difference in Dachsous cadherin levels between migrating cells directs collective migration

In normal development, groups of cells migrate directionally and generate functional organs. Masaki Arata of Laboratory of Cell Recognition and Pattern Formation (Uemura lab), in collaboration with Kaoru Sugimura (WPI-iCeMS, Kyoto Univ.), studied the collective cell migration along a body axis of Drosophila. They employed quantitative imaging of live pupae and propose a mechanism where difference in the amount of an atypical cadherin Dachsous between migrating cells coordinate the migratory direction. Dachsous cadherin is evolutionally conserved and required for the morphogenesis of a number of organs including human heart valve formation; however, its driving mechanism was largely unknown. Arata's study

The findings were published in the Journal of "Developmental Cell." For further information, please visit the URL below. http://www.kyoto-u.ac.jp/ja/research/research\_results/2017/170912\_1.html

### The genome of the liverwort Marchantia polymorpha reveals features of the common ancestor of land plants

Prof. Takayuki Kohchi and his colleagues in Plant Molecular Biology Laboratory revealed the genome of the liverwort Marchantia polymorpha, in an international collaboration with researchers in 38 other universities and institutes. The paper was published in the journal Cell on 5th October, 2017.

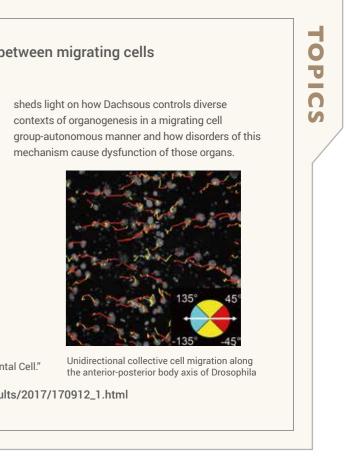
All land plants, from bryophytes to flowering plants, including crops and vegetables, evolved from a common ancestral algal species and colonized land ca. 500 million years ago. Liverworts are a lineage of bryophytes that diverged from other plants in the earliest stage of land plant evolution and possess ancestral characteristics of land plants. Prof. Kohchi and the international research community determined the entire structure of the Marchantia genome, and showed that it has an ancestral version of molecular

mechanisms for plant development and physiology. By this study, Marchantia has now been established as a new model plant, in which a wide variety of molecular genetic techniques, including genome editing, are available. Future analysis of Marchantia will reveal

novel molecular mechanisms fundamental to all land plants and will provide new strategies for agriculture and plant breeding technologies.



For further information, please visit the URL below. https://doi.org/10.1016/j.cell.2017.09.030 http://www.kyoto-u.ac.jp/cutting-edge/cutting\_edge/page121.html https://www.kyoto-u.ac.jp/en/research/research\_results/2017/171006\_2.html



### Division of Systemic Life Science | Department of Biology Education and Heredity

Laboratory of **Chromosome Function** and Inheritance

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Assoc. Prof. CARLTON, Peter



### Main theme

To create haploid gamete cells (sperm or egg cells) from diploid precursors in meiosis, homologous chromosomes must pair, recombine, and then separate from each other, reducing the genome by half.

Recombination between homologous chromosomes is initiated in meiotic prophase by programmed DNA double-strand breaks; these breaks are then repaired through homologous recombination, giving rise to genetic crossovers that link homologous chromosomes until they divide. Using the model organism Caenorhabditis elegans, we are working to determine the molecular mechanisms of recombination initiation and repair in the context of chromosome dynamics,

combining molecular genetics, biochemistry and cytology with high-resolution microscopy and quantitative image analysis. Since errors during meiosis are common in humans and can lead to infertility and developmental defects, understanding these mechanisms is important for achieving improvements in human reproductive health.

Our current research focuses on the following areas:

- Understanding mechanisms of chromosome dynamics and regulation during meiosis
- Phosphoregulation of the synaptonemal complex
- Analysis of chromosome structures using super-resolution microscopy



Lab URL http://www.carltonlab.org

https://www.kyoto-u.ac.jp/en/research/research\_results/2017/171208\_1.html



Meiosis is the sequence of two cell divisions that produces haploid cells such as sperm or eggs from diploid precursor cells. In a recent study in the Journal of Cell Biology, the Carlton laboratory has used the model roundworm C. elegans to show that phosphorylation of a protein called SYP-1 is required for proper segregation of chromosomes in meiosis. SYP-1 is a component of the synaptonemal complex, a protein matrix that holds maternal and paternal chromosomes together during meiosis and promotes genetic recombination. The study found that phosphorylation of SYP-1 starts out evenly distributed along the chromosome, but once recombination occurs, phosphorylated SYP-1 becomes restricted to the region of the chromosome between the recombination site and the closest chromosome end. This chromosome region normally becomes marked as the site where chromosomes separate in the first division of meiosis. Without

phosphorylation of SYP-1, however, this region loses its identity, and chromosomes cannot segregate normally. The team thinks that the ability of SYP-1 to sense distance along the chromosome is critical for its role in promoting chromosome segregation, and is currently working to determine how this sensing mechanism works.

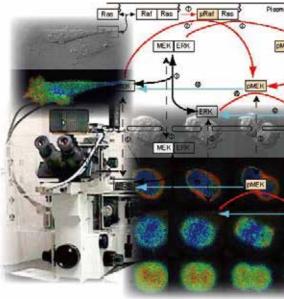


Image: Visualization of chromosome axis dynamics and sites of crossover recombination in C. elegans oocytes

### Main theme

We are visualizing the growth signal transduction cascades in living cells by using biosensors based on the principle of Foerster resonance energy transfer (FRET). These FRET videos are used to characterize the property of each signaling molecule. We are also

FRET biosensors to observe the signaling status in living mice with of mouse brain.

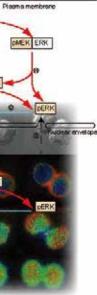


http://www.fret.lif.kyoto-u.ac.jp/mi.htm Lab UR

For details, please see



developing transgenic mice expressing two-photon excitation microscopes. We also study development and plasticity of nervous system by using in vivo imaging



Division of Systemic Life Science | Department of Systems Biology

Laboratory of **Bioimaging and Cell Signaling** 

### Professor MATSUDA, Michiyuki

Assoc. Prof. TERAI, Kenta



Assist. Prof. IMAJO, Masamichi





### Division of Systemic Life Science | Department of Systems Biology

Laboratory of **Theoretical** Biology

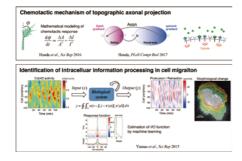
Assoc. Prof. HONDA, Naoki



### Main theme

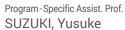
Our laboratory aims to elucidate theoretical logic of dynamic living systems. By developing and simulating mathematical models, we are trying to understand mechanisms underlying phenomena in a bottom-up manner. We are also utilizing machine learning to extract hidden rules of dynamic, complicated phenomena from experimental quantitative data in a top-down manner. By means of these theoretical approaches, we are studying neuronal wiring in the brain, emotional neural dynamics, noise-resistant embryonic development, mechano-chemical mechanism of collective

cell migration, cytoskeleton-based cellular morphogenesis, identification of intracellular information processing and animal behavioral strategy.



### Lab URL https://sites.google.com/view/theoretical-biology/

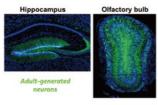






Main theme

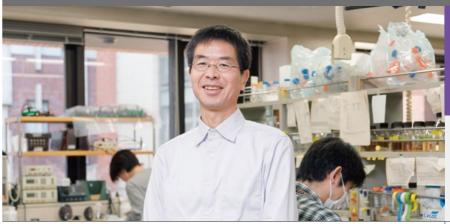
Our laboratory aims at understanding the mechanisms of development and regeneration processes in the mammalian brain, and their functional outcomes on neural circuits, higher brain functions, and animal behaviors. We are focusing on the regulatory mechanism of cell growth, differentiation, and quiescence of neural stem cells. We are also focusing on the functional contribution of newly-generated neurons to neural circuits and animal behaviors. Our laboratory is also developing novel optogenetic tools that can manipulate gene expression of cells by light.



Imayoshi, I., et al., (2008) Nature Neuroscience 11: 1153-1161. Sakamoto, M., et al., (2014) The Journal of Neuroscience 34: 5788-5794



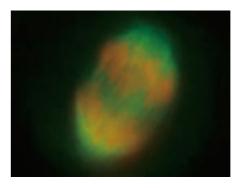
Lab URL https://brainnetworks.jimdofree.com



### Main theme

The spindle checkpoint, our major research subject, is a surveillance mechanism to regulate cellular apparatus for compliance with this rule. It is a unique negative feedback that converts/amplifies a physical signal sensed by kinetochores (attachment of the spindle and/or tension) and regulates the timing of the sister chromatid separation. Mad2, a signal

in the spindle checkpoint. It is specifically localized at unattached the activity of Mad2.



http://www.rbc.kyoto-u.ac.jp/radiation\_system/ Lab UR



carrier of this feedback, plays a vital role kinetochores that are the origin of the checkpoint signal. Mad2 targets CDC20 and inhibits its activity to promote sister chromatid separation. We study Mad2, a central player of the spindle checkpoint, to reveal mechanisms, which regulate

Laboratory of Genome Maintenance

Professor MATSUMOTO, Tomohiro









Laboratory of Genome Damage Signaling



Program-Specific Assist. Prof.

KATSUKI, Yoko

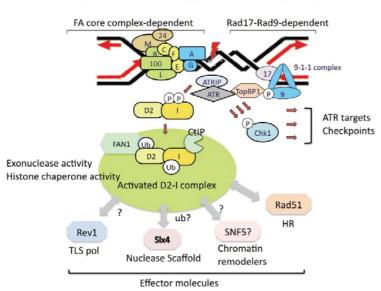
Professor

### Main theme

DNA damage response (DDR) is the fundamental mechanism that stabilizes our genome. Genome stability underlies all biological processes. We try to identify molecules involved in genome

stability/ replication stress/DDR by methods such as screening mutations in human patients, and further analyze their function using genome engineering in various cell lines, iPS cells, and model organisms.

### Replication stress triggers DNA damage response





### Main theme

Cells maintain their function and morphology by exploiting a suitable adaptive response system to diverse and complex tissue microenvironments. Several lines of evidence have suggested that hypoxic, acidic and nutrients-depleted microenvironments exist in solid tumors and induce malignant phenotypes and chemo/radioresistance of cancer cells (Figure 1). We aim at elucidating molecular mechanisms responsible for cellular

adaptive responses to the tumor-specific microenvironments and malignant progression of cancer cells (Figure 2). · Cellular adaptive responses to diverse

and complex tissue microenvironments · Molecular mechanisms underlying

- malignant progression and radioresistance of cancer cells
- · Regulatory mechanisms of carbohydrate metabolic pathway

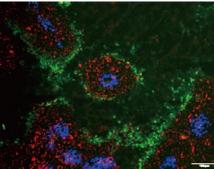


Figure 1: Hypoxic tumor cells (green) distant from blood vessels (blue) are resistant to radiation-induced DNA damage (red).

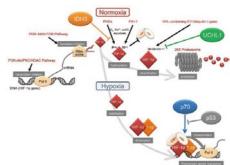
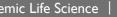


Figure 2: HIF-1-mediated gene networks responsible for both adaptive responses to hypoxia and malignant progression of cancer cells.

http://www.rbc.kyoto-u.ac.jp/cancer\_biology/ Lab URL



Division of Systemic Life Science | Department of Genome Biology

### Laboratory of Cancer Cell Biology

### Professor HARADA, Hiroshi





### Division of Systemic Life Science | Department of Genome Biology

Laboratory of Chromatin **Regulatory Network** 

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Assoc. Prof. IKURA, Tsuyoshi

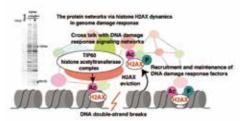


### Main theme

The purpose of our research is to clarify the role of chromatin dynamics, which is required for the DNA metabolisms such as transcription, DNA replication, and DNA repair. In particular, we focus on the molecular mechanisms by which histone modifier complexes regulate the histone eviction as chromatin remodeling machinery upon DNA damage induced by ionizing radiation. Our goal is to understand how histone eviction activates DNA damage signaling pathways and functions as an anti-cancer signaling.

### Main research topics

- · Memory of genomic damage
- Cellular robustness in genomic stress
- response
- Solution of energy metabolism mechanism in specific cancer cell



### http://house.rbc.kyoto-u.ac.jp/mutagenesis2/index1 l ah LIRI

The mechanism how cancer cells proliferates under DNA damage stress

Dr. Kanii FURUYA and his colleagues in the Laboratory of Genome Maintenance, in collaboration with Dr. Tsuyoshi IKURA, the Laboratory of Chromatin Regulatory Network, found that a novel phosphor-signaling pathway that promotes cancer cell proliferation. The paper was published in the journal "eLIFE" on Dec 19, 2017.

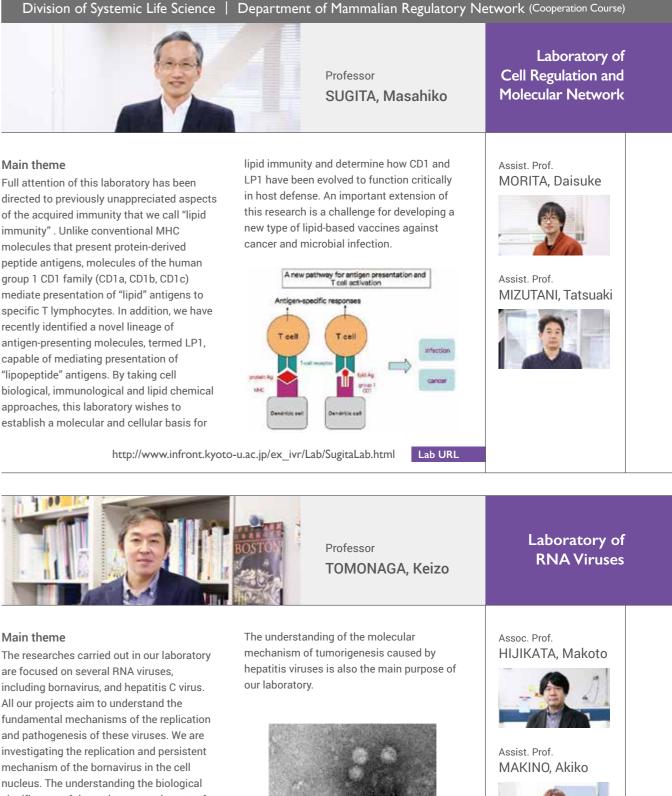
Cancer cells are immortal and possesses high proliferation ability. In contrast, normal cells have cellular network system that prevents these abnormal proliferation, and one of the mechanism is the DNA checkpoint. DNA checkpoint detects genomic DNA damage and is activated when cells are exposed to genotoxic stresses such as radiations. The phosphor-signaling pathway via PLK1, that we identified, suppresses DNA damage detection machinery so as to inactivate DNA checkpoints. PLK1 is frequently over-expressed in cancer cells, and our results explains how cancer cells keep proliferation rate even under DNA

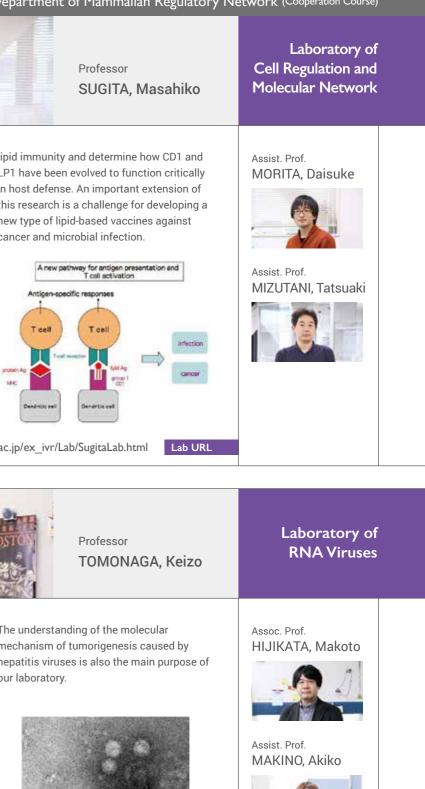
For further information, please visit the URL below. https://elifesciences.org/articles/29953

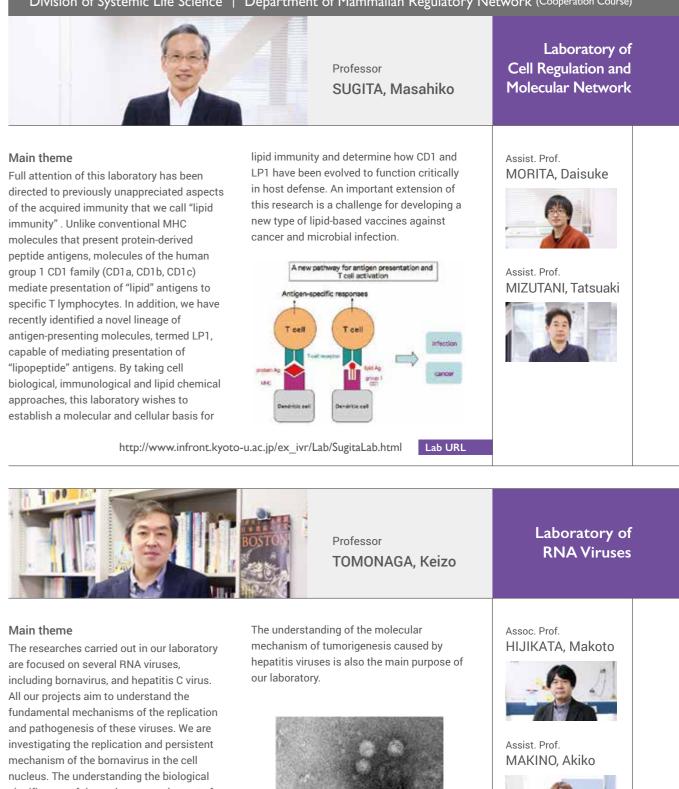
damage stress, and also explains why cancer cells accumulates genomic mutations.

Cancer Cell Proliferation =Aquisition of tolerance to DNA damage Normal Cel PLK1-signaling ON "PLK1-signaling OFF"









significance of the endogenous element of bornaviruses in mammalian genomes is one of the main focuses of bornavirus researches. We also aim to develop a novel RNA virus vector using bornavirus, which can express stably functional small RNAs.



https://t.rnavirus.virus.kyoto-u.ac.jp/

Lab URL

### Division of Systemic Life Science | Department of Mammalian Regulatory Network (Cooperation Course)

### Laboratory of Cell Division and Differentiation

Professor TOYOSHIMA, Fumiko



### Asst. Prof. ODA, Yukako

Assist, Prof.

ISHIBASHI, Riki

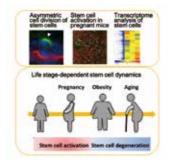


### Main theme

How adult tissue stem cells adapt to physiological changes is a fundamental question in stem cell biology. Balance between self-renewal and differentiation of stem cells via symmetric/asymmetric cell division is essential for steady state homeostasis. Biased stem cell self-renewal or differentiation leads to changes in tissue organization and in organ size. Our group focuses on the mechanisms of symmetric/asymmetric stem cell division, stem cell differentiation, and cell lineage-commitment in tissues metabolism and regeneration. We further research on the stem cell regulation in response to the physiological changes of the body, including pregnancy, obesity and aging.

### **Research subjects**

- 1. Symmetric and asymmetric stem cell division in tissue homeostasis
- 2. Maternal tissue stem cell dynamics during pregnancy
- 3. Obesity- and age-related stem cell degeneration



Lab URL http://www.virus.kyoto-u.ac.jp/Lab/toyoshima.html

### Main theme

Our research group aims to clarify the mechanisms by which cells sense mechanical stimuli and regulate their activities in tissue adaptation, regeneration and stem cell differentiation in morphogenesis. To better understand the mechano-regulation of these dynamical processes through the complex hierarchical structure-function relationships, bridging spatial and temporal scales from microscopic molecular/cellular activities to macroscopic tissue behaviors is very important. Based on multiscale biomechanics, our group is involved in the integrated biomechanics and mechanobiology researches of modeling and simulation combined with experiments, focusing on mechano-biochemical couplings in the system dynamics.

1. Biomechanics and mechanobiology studies on stem

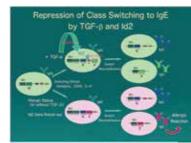
http://www.infront.kyoto-u.a

### Laboratory of Genetic Professor Information SHIMIZU, Akira Main theme Major goal of research in this laboratory is to understand molecular and cellular mechanisms underlying highly systemic aenes functions of living things, such as immune and neural systems. For this purpose, structure and regulation of genetic information responsible for such systemic functions are being analyzed using model animals, for example, transgenic or gene disrupted mice. Our research is focused on the following subjects: 1. Analysis of molecular mechanisms and regulation of chromatin modification, gene expression, gene rearrangements and RNA

processing during lymphocyte

differentiation.

- 2. Making and characterization of model mice of immunodeficiency or autoimmune by introduction of, or targeted disruption of interleukin, immunoglobulin or other
- 3. Analysis of molecular and cellular mechanism for lymphocyte mobility and formation of immunomicroenvironment during development and immune reaction.



### Modulating functions of another molect Antagonism between twisting and untwi

The actin cytoskeleton has two faces. One side provides a relatively stable scaffold to maintain cell shape, and the other side rapidly changes morphology in response to extracellular stimuli. This is achieved by generating actin filaments (F-actin) with a wide range of lifetimes (from a few seconds to several minutes in cultured cells), but it remains as a mystery how F-actin with such diverse lifetimes can coexist within a single cell. Now Naoki Watanabe, Hiroaki Mizuno, and Sawako Yamashiro of Laboratory of Single-Molecule Cell Biology have found a clue to solve this mystery. They show that mDia1 generates a torgue around the filament axis and untwists the filament. As already reported, mDia1 processively elongates the growing end of F-actin and rotates along the F-actin double helical structure. This helical polymerization-mediated untwisting has turned out to inhibit F-actin disassembly

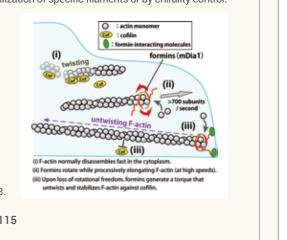
The findings were published in the journal "PNAS" on May 14, 2018. For further information, please visit the URL below. http://www.pnas.org/content/early/2018/05/10/1803415115



### Division of Systemic Life Science | Department of Mammalian Regulatory Network (Cooperation Course)

	Professor ADACHI, Taiji	Laboratory of Cellular and Molecular Biomechanics	
in tissue develo 2. Understanding r and regeneratio 3. Identifying mec adaptation by r 4. Elucidation of r mechanisms ir 5. Nano- and micr combined with		Assoc. Prof. INOUE, Yasuhiro	
	Ile far away : sting determines actin fila induced by the major actin depoly cofilin both in vitro and in cells. Th end-bound molecule can enhance	merizing factor, ius, a single barbed	

end-bound molecule can enhance the stability of a filament over a long distance. The helical polymerization-mediated mechanism may play a role in generating diverse cellular actin architectures either by stabilization of specific filaments or by chirality control.



# Radiation Biology Center (RBC)

Radiation Biology Center, Kyoto University 

### Message from Director of the Center

Takata Minoru

The Radiation Biology Center (RBC) was founded in 1976 to promote basic research on the effects of radiation. As a Joint Usage Research Center, the RBC has been acting as a hub for scientists in radiation and related fields. Now the center is fused with Graduate School of Biostudies and will commence novel and deeper research activities from this privileged position as a part of "Biostudies" looking into the vast areas of life sciences.

### Overview

The research in the RBC is in large part strongly linked with users of Joint Usage Research Center, but at the same time, each member of RBC pursues science with their own research direction.

### Departments

### Dept. of Radiation System Biology

We are pursuing mechanistic understanding of genetic and epigenetic inheritance by analyzing regulation of centromere structure, various cell cycle check points, and stress responses.

[Staff] MATSUMOTO, Tomohiro (Prof.) FURUYA, Kanji (Lecturer)

### Dept. of Late Effects Studies, Lab of DNA Damage Signaling

We are studying (1) cellular and molecular mechanisms in response to endogenous DNA damage and replication stress, and (2) disorders caused by the defects in these mechanisms such as Fanconi anemia and hereditary breast and ovarian cancer. We employ technologies in vitro recapitulation of pathologies with iPS cell lines derived from patients, genome editing, and analysis of human materials.

[Staff] TAKATA, Minoru (Prof.) KATSUKI, Yoko (Program-Specific Assist. Prof.)

### Dept. of Chromosome Function and Inheritance

Using the model organism Caenorhabditis elegans, we are working to determine the molecular mechanisms of recombination initiation and repair in the context of chromosome dynamics. Understanding these mechanisms is important for achieving improvements in human reproductive health problems such as infertility and developmental defects.

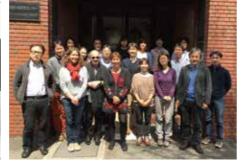
[Staff] CARLTON, Peter (Assoc. Prof.)





Low Dose and Low Dose-rate Irradiation System

Optical In Vivo Imaging System



The 2nd RBC-CEA Joint Workshop



The 33rd International Symposium of Radiation Biology Center, Kyoto University

### Dept. of Mutagenesis, Lab of Chromatin Regulatory Network

How does the cell maintain its integrity in response to various stress such as radiation or UV? What kind of strategy is employed? To solve these questions and to elucidate mechanisms of cancer or lifestyle-related disorders, we focus on chromatin that is the characteristic of eukaryote's genome using proteomics analysis of chromatin regulator protein complexes, bioimaging, and mathematical and statistic approaches.

[Staff] IKURA, Tsuyoshi (Assoc. Prof.)

### Dept. of Genome Repair Dynamics, Lab of Cancer Cell Biology

We are conducting studies on endogenous and exogenous factors that affect cellular radiation sensitivity/resistance such as genetics deficiencies and tissue microenvironments and on the effect of low dose and low dose rate radiation on our body. Our focus is ranging from molecules to individual mice.

[Staff] HARADA, Hiroshi (Prof.) KOBAYASHI, Junya (Assoc. Prof.)

### **Dept. of Stress Response**

We will elucidate what kind of molecular reactions cells would display upon low dose irradiation in terms of stress response. Our main research targets are regulatory mechanisms of chromatin dynamics, translational regulation on ribosomes, acquired resistance mechanisms to low dose irradiation.

> [Staff] ISHIKAWA, Fuyuki (Prof.) MIYOSHI, Tomoichiro (Assoc. Prof.)

# Research Center for Dynamic Living Systems



### Message from Director of the Center Matsuda Michiyuki

Recent advent of biology largely depends on the reductionist's approach that has been deciphering the function of molecules of interest. New functions of molecules are still being discovered, leading to the discovery of new biological phenomena. Meanwhile, it will be also quite important to integrate the huge knowledge accumulated so far and to deduce common principles of biological phenomena. Theoretical biology, mathematical biology, or systems biology are the school of such research area, but their advancement depends on technological break-through of imaging and omics that fuels these theoretical research field with the ground-truth data and tools for validation. With this background, a MEXT-supported project named 'a research and education platform for innovative research on dynamic living systems' were launched by Graduate Schools of Medicine, Biostudies, and Informatics, and by Virus Research Institute and Institute for Frontier Medical Sciences. Here, to further promote this interdisciplinary approach, Research Center for Dynamic Living Systems has launched in 2018. Setting the cutting-edge microscopy as the core of technology, we attempt to understand the biological systems by the collaboration of theoretical researchers and experimental biologists.

### Overview

- Course meeting of developmental biology, cell biology and systems biology. Monthly seminars are given by foreign or domestic top runners and by young researchers. Annual retreat will provide the graduate students with the opportunity to talk and discuss on their data.
- MACS education program: In collaboration with department of mathematics, graduate school of science, a series of lectures will be provided under the title of "Fusion of imaging technology and mathematics".
- Introduction to mathematics, statics, and computational biology. For the graduate students who belongs to the wet laboratories, the basics of mathematics and statistics and the use of mathematical software will be lectured.
- Kyoto University Live Imaging Center. Cutting-edge microscopes including multiphoton microscopes are available for researchers both in and out of Kyoto University. Technicians maintain the microscopes in good condition and help researchers for the operation.

### Laboratories

### Cutting-edge Bioimaging Team (Matsuda Lab)

By using fluorescence biosensors, we will visualize molecular activity and cellular function in the tissue culture cells and the living mice, and thereby decipher the principle of intercellular communication.

> [Staff] MATSUDA, Michiyuki (Prof.) TERAI, Kenta (Assoc. Prof.) IMAJO, Masamichi (Assist. Prof.)

### Multiscale Biomechanics Team (Adachi Lab)

Roles of force in hierarchical living systems from molecular/cellular levels to tissue/organ levels will be clarified by multiscale biomechanics approach through integration of in-vitro and in-silico experiments.

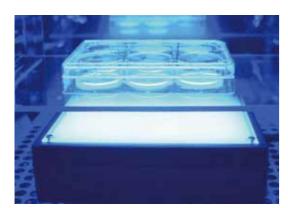
[Staff] ADACHI, Taiji (Prof.) INOUE, Yasuhiro (Assoc. Prof.) KAMEO, Yoshitaka (Assist. Prof.)

### Physiological Network Team (Uemura Lab)

By taking multi-omics and genetic/optogenetic approaches, we will unravel operating principles of physiological mechanisms that control animal life-history traits and neuronal circuits that evoke selective behaviors, in response to nutrient balances or sensory stimuli.

[Staff] UEMURA, Tadashi (Prof.)

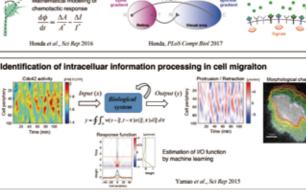
Chemotactic mechanism of topographic axonal projection



Blue light illumination to cultured cells expressing the light-induced gene expression system.



A transgenic mouse expression FRET biosensor (right).



### Data-driven Modeling Team (Honda Lab)

By statistical analysis and machine learning of quantitative experimental data, we will extract hidden patterns and/or rules underlying dynamic and complicated biological phenomena, thereby providing basis for developing mathematical model.

[Staff] HONDA, Naoki (Assoc. Prof.)

### Developmental Dynamics System (Kageyama Lab)

We will elucidate the significance of oscillatory gene expression by live imaging with luminescent and fluorescent reporters and by optogenetic perturbation in cultured cells and tissues.

[Staff] KAGEYAMA, Ryoichiro (Prof.)

### Biological Function Manipulating Team (Imayoshi Lab)

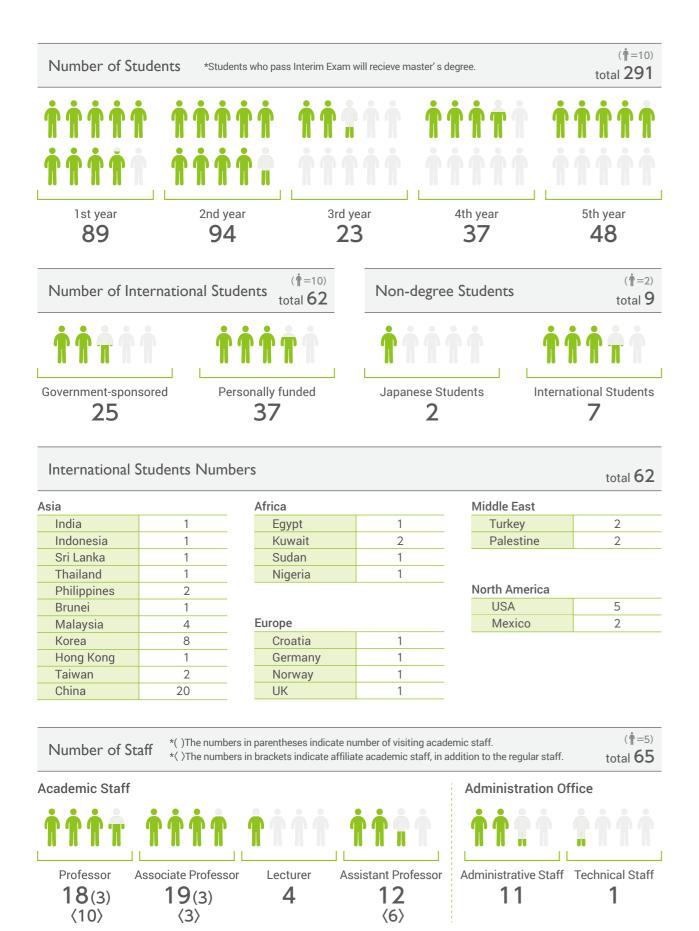
We will develop genetic and virus vector methods for expressing fluorescent proteins and functional molecules in specific cell types of the model organisms, especially mice. We will also develop novel optical methods to manipulate cellular and biological functions. By integrating these cutting-edge technologies, we will unveil the regulatory mechanisms underlying brain development, plasticity, and regeneration.

[Staff] IMAYOSHI, Itaru (Program-Specific Assoc. Prof.)

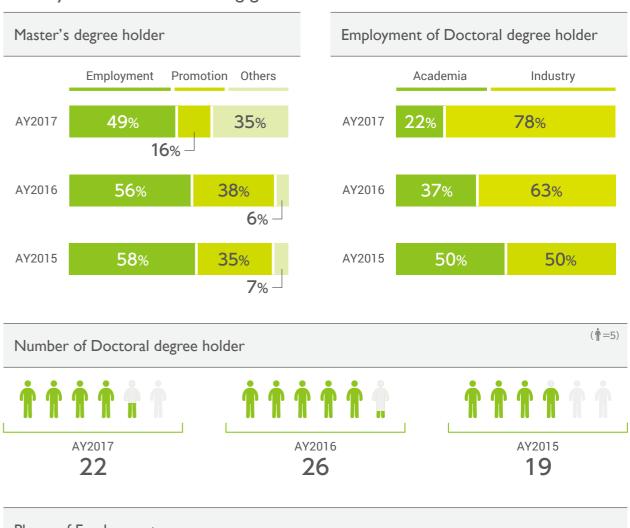


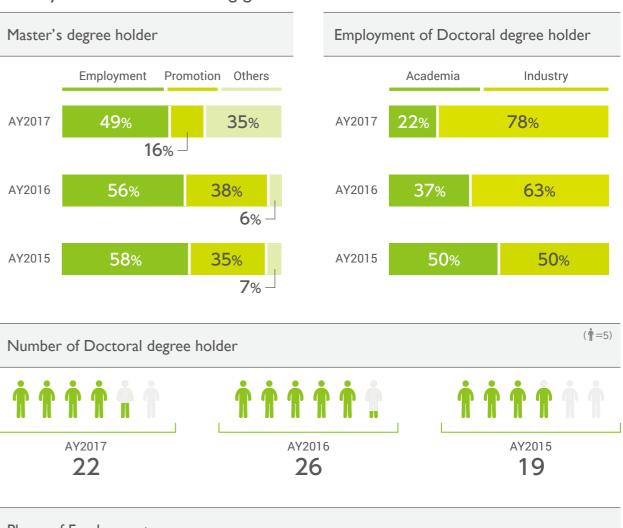
Scheme of projects: Chemotactic mechanism of topographic axonal projection and Identification of intracellular information processing in cell migration.

# Data



### Activity of Students following graduation





Places of Employment

### **Business**

DENKA SEIKEN Co., Ltd. / KAWASUMI LABORATORIES. INC. / KOSÉ Corporation / Shionogi & Co., Ltd. / Astellas Pharma Inc. / Waqoo, Inc / choseido Pharmaceutical Co., Ltd. / TAKII & CO., LTD / Panasonic Corporation / Sumitomo Mitsui Card Co., Ltd. / KYORIN CO., LTD / SEIWA KASEI Co, Ltd. / Kyowa Hakko Kirin Co., Ltd. / JAPAN POST Co., Ltd. / Gakken Holdings Company, Limited / CMIC HOLDINGS Co., Ltd. / Mandom Corporation / DENTSU INC. / Toho Co., Ltd. / OSAKA GAS CO., LTD / Lion Corporation. / Maruho Co., Ltd. / Sysmex Corporation / NICHIREI CORPORATION / NISSIN FOODS HOLDINGS CO., LTD / Mediscience Planning Inc. / Linical.Co., Ltd / NBC Meshtec Inc. / NEXCO EAST Corporate / AIREX INC. / Works Applications Co., Ltd. / Sumitomo Dainippon Pharma Co., Ltd. / CHUGAI PHARMACEUTICAL CO., LTD / FUJIREBIO Inc. / fixpoint, Inc. / Daiichi Sankyo Healthcare Company, Limited / Taiyo Kagaku Co., Ltd. / Shiseido Company, Limited / KYOKUTO PHARMACEUTICAL INDUSTRIAL CO., LTD / SDS Biotech K.K. / AOHATA Corporation / JCR Pharmaceuticals Co., Ltd. / MORINAGA MILK INDUSTRY CO., LTD. / EUGLENA CO, LTD / ASAHI BREWERIES, LTD / ARKRAY, Inc. / SANYO FOODS.Co., Ltd. / Kobayashi Pharmaceutical Co., Ltd. / GLICO NUTRITION CO., LTD. / CHUGOKU ELECTRIC POWER CO., INC. / Sunstar Inc. / NIDEC CORPORATION / Takara Bio Inc. / Toyota Motor Corporation. / Idemitsu Kosan Co., Ltd. / Oriental Yeast Co., Itd. / ROHTO Pharmaceutical Co., Ltd. / MANDA FERMENTATION CO., LTD. / Otsuka Pharmaceutical Co., Ltd. / P&G. / TOYO SHINYAKU Co., Ltd. / Santen Pharmaceutical Co., Ltd. / TSUMURA & CO. / AJINOMOTO CO., INC.

### Others

Kyoto University / RIKEN / JICA / Hokkaido University / Shiga University of Medical Science / Okinawa Institute of Science and Technology Graduate University / University of Tokyo / City of Kobe / Ministry of Agriculture, Forestry and Fisheries



