

# 2024-2025





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# Message from the director

The Japanese name of this institute has been drastically changed from “Virus-Saisei-Ikagaku Kenkyu-sho (meaning Institute for Virus and Regenerative Medicine)” to “I-Seibutsugaku Kenkyu-sho (meaning Institute for Medical Biology)” since April, 2022. On the other hand, formal English name of this institute has been just slightly changed from “Institute for Frontier Life and Medical Sciences” to “Institute for Life and Medical Sciences”, just deleting “Frontier”. At that time, I was appointed to serve as the Director of the Institute, and will continue for a second two-year term starting from April 2024.

I will explain how the original Japanese name and new one were given, and the thoughts put in the new Japanese name.

## ■ Process of integration of two institutes and renaming

The Institute for Frontier Life and Medical Sciences was established in October 2016 by integrating the Institute for Virus Research (Virus-Kenkyu-sho) and the Institute for Frontier Medical Sciences (Saisei-Ikagaku Kenkyu-sho). At the time of the integration, the names of both institutes were just lined up one after the other, for the time being. Subsequently, discussions continued regarding the new name after the integration, and the name was changed at this occasion, five and a half years after the integration.

## ■ History up to integration

Prior to the integration, each institute had expressed a strong presence in the academic world. The Institute for Virus Research, established in 1956, had led not only virology but also the whole field of molecular biology, and the Institute for Frontier Medical Sciences, originally established in 1941 as Tuberculosis Research Institute, had led a wide range of fields including not only regenerative medicine but also immunology and bioengineering. For example, the Institute of Viruses has produced Dr. Yorio Hinuma, who discovered the causative virus of adult T-cell leukemia, and the Institute for Frontier Medical Sciences has produced Dr. Shinya Yamanaka, who invented iPS cells, and Dr. Shimon Sakaguchi, who discovered regulatory T cells.

## ■ Background that led to the integration and actions made after the integration

In recent years, life science has undergone major changes, and it becomes difficult to be competitive in academic field with the

research activity conducted solely by individual laboratories. In order to develop as a research institute, it is necessary to create a strategy by looking ahead of the times, to accordingly re-build the organization, and to proceed with personnel affairs in line with the strategy. Such strategy requires a certain size of personnel, and the integration has made it easier to pursue such a strategy. Currently, the number of whole workers, that of faculty members, and that of professors, is about 300, 80, and 20, respectively.

In terms of re-organization of structure, for the time of integration in 2016, we have newly established the “Department of Biosystem Sciences”, in addition to the department of the virus research and the regenerative medicine. This “Department of Biosystem Sciences” is the core department that is expected to develop new academic fields. In accordance with this, we have been putting a lot of effort into personnel affairs, such as recruiting young professors majoring in structural biology or theoretical biology, which we think has been very successful up to now.

## ■ Thoughts put in the word “I-Seibutsu-gaku (Medical Biology)”

I think the name of the new research institute more or less sounds old-fashioned with the word “Seibutsu-gaku (Biology)”. Indeed, as it sounds, I think that this name proposes the idea of “emphasizing the viewpoint of biology”.

Recently, there is a tendency for research activities to require a so-called “exit” like the former examples, but the essence of research is to get answer to the intellectual curiosity of human beings, and I think there exists fundamental fun there. There also may exist a point that research that seeks fun is more likely to lead to a big leap than the one that seeks actual profit.


## ■ Launch of a new “Joint Usage/Research Center”

The former two institutes had exerted the functions of research bases for virus research and regenerative medicine, respectively, and the integrated research institute has separately maintained the functions of the two bases. At the same time as this renaming, the two joint centers have been integrated, and a new base called “Virus / Stem Cell System Medical Biology Joint Research Center” has been launched since April, 2022. As a core project of this center, we have established a system to financially support collaborations between the faculty members of this institute and outer researchers by up to 1 million yen per case, and in 2022, we adopted 30 projects as a result of the open call for participants.

## ■ Afterword

The historical integration of research institutes in different fields has allowed a variety of research fields to coexist, making the institute suitable for interdisciplinary research. However, this does not necessarily mean that LiMe is safe in the coming near future. Public organizations are always under pressure from the national government and the Kyoto University headquarters to make organizational changes. If we do not continue to produce solid results, we may be swallowed up by the wave of organizational reform. In order to survive in such situation, the first step is for each field to make remarkable achievements that will make its name known all over the world. The second is to achieve results through interdisciplinary research that is unique to the LiMe. If the LiMe functions organically and efficiently, it is more likely to survive as a stable organization. To this end, it is important for each staff member to have “a sense of belonging” as a member of the institute that has created the history of biology, and to have “a sense of ownership” as a participant in the work, rather than leaving it to others.

While maintaining such a sense of belonging and ownership, all of us at the Institute will work together as one to advance forward with a sense of mission to lead the era.



Hiroshi Kawamoto, MD., Ph.D.  
Director and Professor  
Institute for Life and Medical Sciences



# Organization



As of April 1st, 2024



# History

The predecessor of the Institute, the Institute for Frontier Life and Medical Sciences (inFront), was formed by the merger of the Institute for Virus Research and the Institute for Frontier Life and Medical Science in 2016.

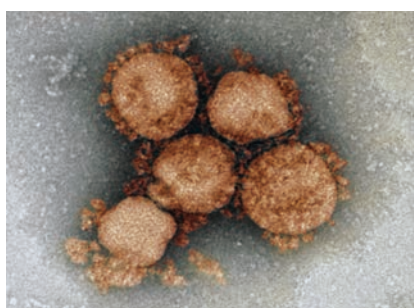
The Institute for Virus Research was known for its brilliant groundbreaking research in medical science, including the discovery of the human leukemia virus, and for pioneering work in molecular biology. The Institute for Frontier Medical Sciences, on the other hand, had built an innovative foundation in regenerative medicine by establishing human embryonic stem cells (ES cells) and discovering induced pluripotent stem cells (iPS cells) and regulatory T cells.

In April 2022, the Institute made a new start under the current name, The Institute for Life and Medical Sciences (LiMe), with the aim of exploring new academic fields in medical science and life science.

**1956**  
Institute for  
Virus Research



Cell processing facility exclusive to human ES cells



Coronavirus image captured by an electron microscope

Joint Usage/Research Center Program for Fusion of Advanced Technologies and Innovative Approaches to Viral Infections and Life Science



Unveiling ceremony for the establishment of the Institute for Frontier Life and Medical Sciences (inFront)

**1980**  
Research Center for  
Medical Polymers  
and Biomaterials

**1990**  
Research Center for  
Biomedical Engineering

**1941**  
Tuberculosis  
Research Institute

**1967**  
Chest Disease  
Research Institute

**1988**  
Chest Disease  
Research Institute  
(structural reorganization)

**1998**  
Institute for Frontier  
Medical Sciences

**2008**  
Joint Usage/Research Center  
Program for Transdisciplinary  
Collaboration on Tissue Engineering  
and Regenerative Medicine

**2016**  
Institute for Frontier Life  
and Medical Sciences

**2022**  
Institute for Life and Medical Sciences

Joint Usage/Research Center Program for  
Transdisciplinary Collaboration on Viral Research,  
Stem Cell Science and System Biology



# LiMe at a Glance



**83**-year History

P.5 ▶

The origin of the Institute for Life and Medical Sciences (LiMe) dates back to 1941.



**Faculty and Staff Members**

**172**

**72 Faculty**  
(17 Professors)

**42 Non-teaching researchers**

**58 Non-teaching staff**

## Faculty and Staff

(As of September 1st, 2024)

Professor	17(3)	Program-Specific Researcher	19
Assoc.Prof.	13(1)	Technical Staff	8
Senior Lecturer	0	Administrative Staff	3
Assist.Prof.	27	Researcher (Part-Time)	23
SUBTOTAL	57(4)	Other	47
Program-Specific Assoc.Prof.	4	TOTAL	100
Program-Specific Senior Lecturer	0		
Program-Specific Assist. Prof.	11		
SUBTOTAL	15		
TOTAL	72(4)		

(\*) Including cocurrent faculty  
Numbers in parenthesis indicate visiting faculty

## Research Fellows and Research Students

(As of September 1st, 2024)

Special research student	1
Research student	3
JSPS*	11
Private Sector Researcher	4
TOTAL	19

\*The Japan Society for the Promotion of Science



**Expenditure in academic year 2023**

**2.3** billion yen

## Financial data in academic year 2023

(Unit: KJPY)

University grants (Cost of equipment and others)	641,160
Grants-in-aid for Scientific Research	348,023
Research funds	1,215,039
Other subsidies	18,824
Donations	81,401
TOTAL	2,304,447

## Graduate Students

**92**



The Institute accepts graduate students from six graduate schools.

(As of May 1st, 2024)

Graduate School of Medicine	13
Graduate School of Science	9
Graduate School of Engineering	29
Graduate School of Human and Environmental Studies	2
Graduate School of Biostudies	20
Graduate School of Pharmaceutical Sciences	19
TOTAL	92



## Organization

P.4 ▶

**3 Departments**  
**3 Attached Research Facilities**

The Institute comprises three departments: the Department of Virus Research, the Department of Regenerative Science and Engineering, and the Department of Biosystems Science, and three attached research facilities: the Research Center for Infectious Diseases, the Center for Animal Experiments, and the Center for Human ES Cell Research.



**27 Laboratories**  
**6 Visiting Laboratories**

P.4 ▶

\* As of April 1st, 2024



**34 Joint Research Projects adopted for Joint Usage/Research Center Program**



## Overseas Partner Institutions

**3 MOUs for academic cooperation and exchange**

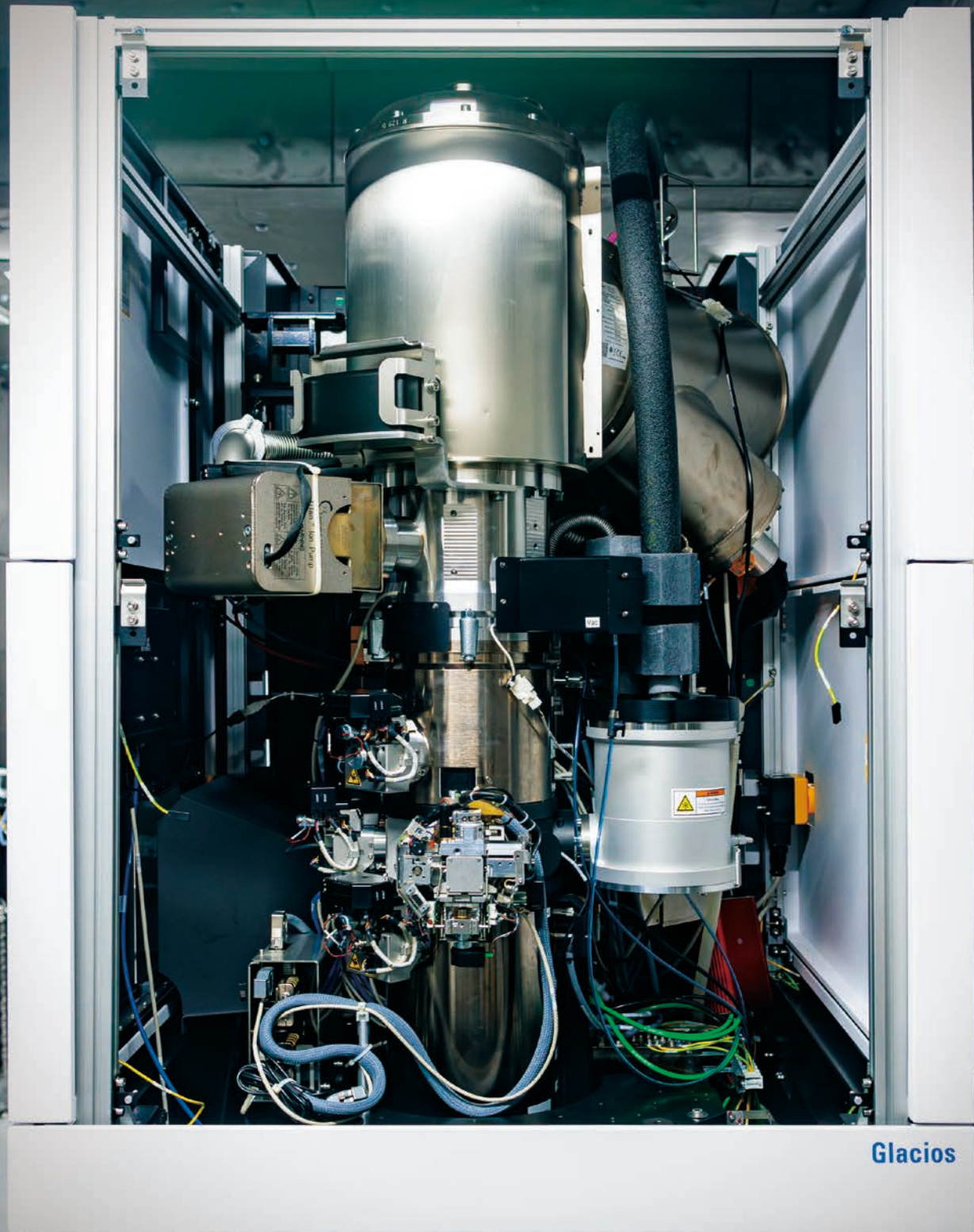
## International exchange

(As of September 1st, 2024)

Departmental-Level Academic Exchange Memoranda	[China] China Medical University China Rehabilitation Research Center [Germany] Bonn Institutes of Immunosciences and Infection, Medical Faculty, University of Bonn
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# Joint Usage/Research Center Initiative



Glacios

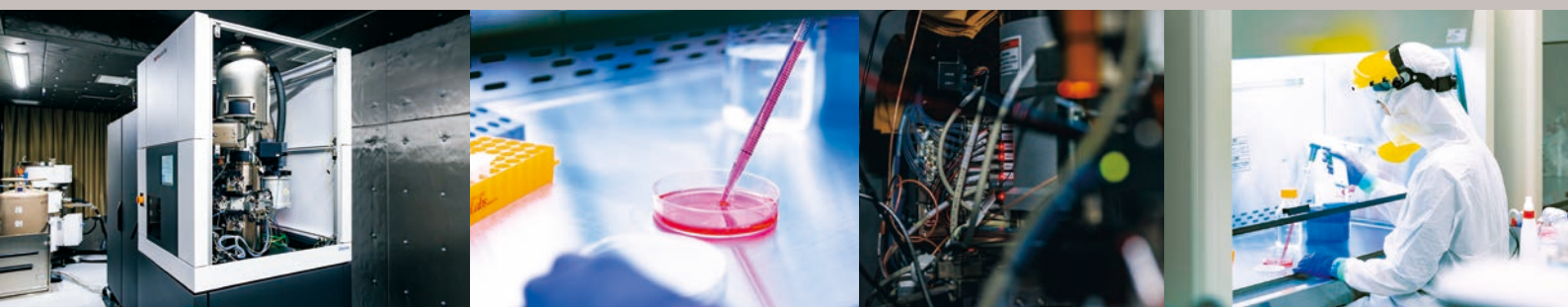
Cryo-TEM Glacios (ThermoFisher Scientific)



# Joint Usage/Research Center

The Institute for Life and Medical Sciences has been accredited by the Minister of Education, Culture, Sports, Science and Technology as a “Joint Usage/Research Center for Transdisciplinary Collaboration on Viral Research, Stem Cell Science and System Biology” since 2022, and provides the international research community with the resources and technologies of the Institute through collaborative research.

Since being formed by the merger of the Institute for Virus Research and the Institute for Frontier Life and Medical Science in 2016, the Institute for Life and Medical Sciences has promoted cutting-edge research in the life sciences in three divisions: the Department of Virus Research, the Department of Regenerative Science and Engineering, and the Department of Biosystems Science. There is collaboration across departments, as well as a system for conducting interdisciplinary research. The activities of the two joint centers, the “Joint Usage/Research Center for Fusion of Advanced Technologies and Innovative Approaches to Viral Infections and Life Science” and the “Joint Usage/Research Center for Transdisciplinary Collaboration on Tissue Engineering and Regenerative Medicine,” which continued at the Institute until FY2021, have been integrated into the new Center, which started activities in FY2022.



## Research conducted at the Center

The Center is involved in activities on three main themes

- (1) Viral Research**
- (2) Stem Cell Science Research**
- (3) Biosystems Science Research**

and the technologies and methodologies developed by the Institute are deployed both domestically and internationally. The Center aims to conduct cutting-edge, interdisciplinary research. Specific initiatives include (1) viral infection experiments and analysis of the microstructure and molecular structure of viruses, (2) the use of human ES cells, stem cell research and the development of tissue regeneration technology through the Human ES Cell Research Center, and (3) activities to explore various life phenomena as systems in collaboration with faculty members from diverse backgrounds in the Biosystems Research Group. In 2024, 34 projects were adopted and implemented.

Total number adopted in 2024	
(1) Viral Research	8
(2) Stem Cell Science Research	8
(3) Biosystems Science Research	18
Total	34

A list of these proposals is available in Japanese on the Institute's website at:



<https://www.infront.kyoto-u.ac.jp/kyoten/00-all/>



# Lab. of Medical Virology

LiMe Bldg. No.2

Lab URL  
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab02/>



Professor

## HASHIGUCHI, Takao

Infectious diseases still have remained a fatal threat to children, worldwide. To solve the problem, we have been studying on pediatric virology. In particular, we focus on the mechanisms of viral entry into cells and the inhibition of entry by compounds, peptides, glycans, and antibodies, using a combination of virological and structural biological approaches. Our major goals are the elucidation of viral pathogenesis and the development of preventive and therapeutic methods for viral diseases. Our laboratory was newly joined in this institute in September 2020, and started to research on paramyxoviruses and coronaviruses.

Measles virus (MeV) and mumps virus (MuV), members of the family Paramyxoviridae, are important human pathogens causing respiratory and neural infections.

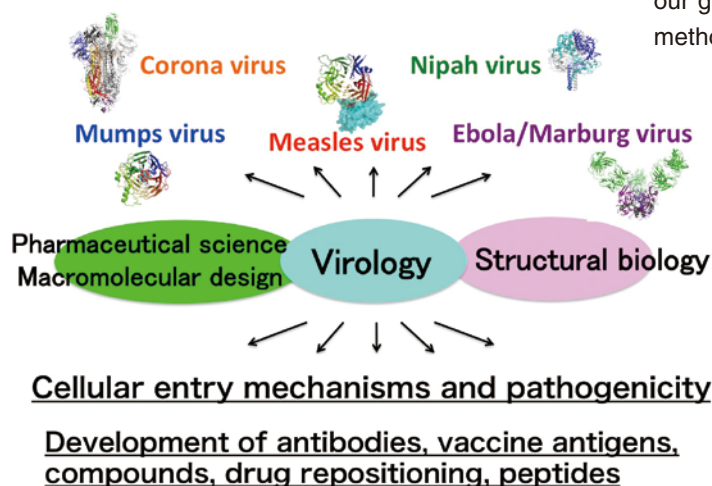


Assistant Professor

Assistant Professor

Assistant Professor

SUZUKI, Tateki  
KIMURA, Kanako  
SATO, Yuma



Globally, MeV has been causing outbreaks recently and over 200,000 deaths were reported in 2019. MeV usually causes acute measles, but in rare instances induces fatal and intractable neurological diseases. MuV causes epidemic parotitis, meningitis, encephalitis and deafness. Large outbreak of mumps occurs once every four to five years in Japan. Currently no licensed therapeutic agents are available for both viruses, and the mechanisms that cause CNS diseases remain unknown. Therefore, we are currently working on research to solve these problems.

Our laboratory has been also studying the development of new drugs for infectious diseases caused by SARS-CoV-2, Ebola and Marburg viruses, and Nipah virus, for which biosafety level 3 or 4 is required. One of our goals is to develop vaccines, therapeutics, and new methods of immunoanalysis using structural information.

Enveloped viruses possess glycoproteins that interact with receptors and other host factors to invade target cells via sequential membrane fusion and exert pathogenicity against humans. On the other hand, viral glycoproteins are also critical antigens in human immune responses and are one of the targets of anti-viral drugs. Therefore, they are important not only in viral pathogenicity but also in the development of vaccines and new drugs. In our laboratory, we aim to elucidate the detailed mechanisms of infection and its inhibition by integrating virology with structural biology and drug discovery science.



# Lab. of RNA Viruses

— LiMe Bldg. No.3

▶ Lab URL  
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab03/>



\*Program-Specific



Professor, Vice Director

**TOMONAGA, Keizo**



Associate Professor

MAKINO, Akiko

Assistant Professor

KITABATAKE, Makoto

Assistant Professor

KANDA, Takehiro

Assistant Professor

MATSUGO, Hiromichi

Assistant Professor (\*)

KOMORIZONO, Ryo

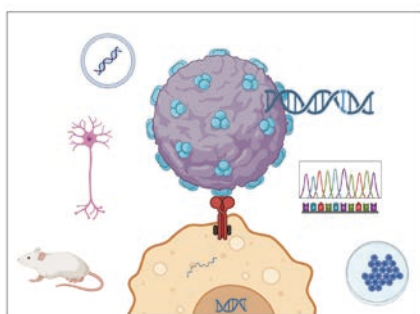
Assistant Professor (\*)

SAKAI, Madoka

All viruses rely on the cellular machinery to complete their replication cycles. Therefore, the study of viruses can provide fundamental knowledge and understanding not only of viral pathogenesis and host responses but also of cellular function. The research carried out in this laboratory are focused on negative strand RNA viruses replicating in the cell nucleus, especially bornaviruses. All our projects aim to understand the fundamental mechanisms of the replication, pathogenesis and evolution of bornaviruses. In current research, we are investigating the replication and persistent mechanism of the

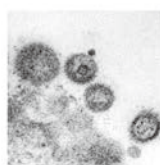
bornaviruses in the nucleus. The understanding the biological and evolutionary significances of the endogenous bornavirus-like elements (EBLs) found in the genomes of many vertebrate species is one of the main focuses of our laboratory. Furthermore, we are analyzing emerging bornaviruses, which include avian bornaviruses as well as a squirrel bornavirus that may be highly pathogenic to humans. We also aim to develop a next-generation RNA viral vector based on bornavirus for applying to gene and cellular therapy using stem cells.

## 朝長研究室 Tomonaga Laboratory



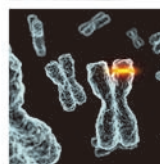
### Replication/pathogenesis

- Persistent infection
- Neuropathogenesis
- Emerging viruses



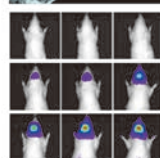
### Endogenous viruses

- Co-evolution
- Endogenization
- Paleovirology



### Viral vectors

- Gene therapy
- Cellular therapy
- Regenerative medicine



# Lab. of Ultrastructural Virology

LiMe Bldg. No.3

Lab URL  
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab04/>



Professor

**NODA, Takeshi**



Associate Professor

Assistant Professor

Assistant Professor

SUGITA, Yukihiro

NAKANO, Masahiro

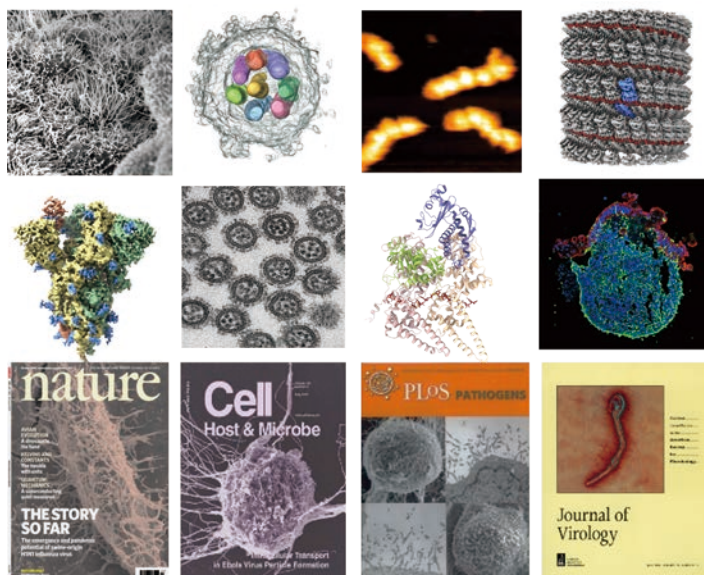
MURAMOTO, Yukiko

In our laboratory, we have been studying pathogenic RNA viruses in human, such as influenza and Ebola viruses. Despite their genome RNA encoding only about 10 kinds of proteins, each of these proteins exhibits multiple functions and properly controls these functions to synthesize genome RNA and viral proteins within infected cells, leading to the formation of progeny virus particles.

Therefore, we focus on the structure, function, and regulation of viral genome RNA and viral proteins that constitute virus particles, aiming to unravel the mystery of why these viruses, with only several kinds of viral proteins,

efficiently replicate within infected cells and cause severe diseases in humans and animals.

In addition, to gain new insights into virus replication mechanisms, we are promoting interdisciplinary research. By integrating new technologies into our virus research, such as structural analysis of viral proteins using cryo-electron microscopy and analysis using human respiratory organoids differentiated from human ES cells/iPS cells through developmental biology techniques, we aim to reveal aspects of the viral world that have never been seen before.



From top left to right: 1. SEM image of human nasal organoids, 2. 3D reconstruction model of influenza virus by electron tomography, 3. AFM image of influenza virus RNP, 4. Structure of helical NP-RNA complex of Ebola virus determined by cryo-electron microscopy. From middle left to right: 5. Structure of S protein of SARS-CoV-2 determined by cryo-electron microscopy, 6. Ultra-thin section image of influenza virus particles, 7. Atomic model of NP-VP24-RNA complex of Ebola virus determined by cryo-electron microscopy, 8. Immunostaining image of human nasal organoids. From bottom left to right: 9. SEM image of cells infected with swine influenza virus, 10. SEM image of cells expressing Ebola virus proteins, 11. TEM and SEM images of Ebola virus-infected cells, 12. Negative staining image of Ebola virus-like particles.



# Lab. of Tumor Viruses

— LiMe Bldg. No.2

▶ Lab URL

<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab05/>



Associate Professor

**SAKAI, Hiroyuki**

Papillomavirus infection and its tumorigenic potential: The infection of papillomavirus induces benign tumors, such as warts and condylomas, and occasionally they are converted into cancers. We are investigating the molecular mechanisms of the virus replication and the virus-related tumor progression.

Analysis of Wnt intracellular signaling pathway: Wnt signaling regulates a variety of adult and developmental processes and mutations in several components of the Wnt pathway are oncogenic. I am analyzing this pathway in vitro and in vivo.



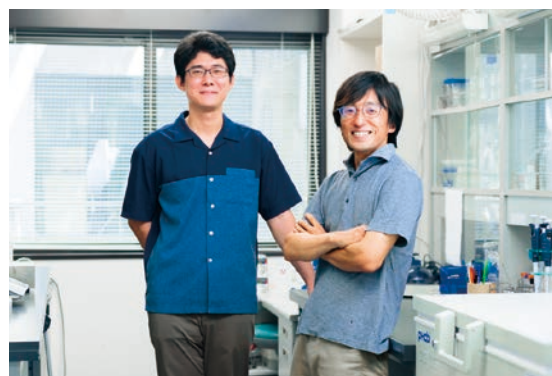
Horn-shaped warts induced by Shope papillomavirus infection

# Lab. of Cell Regulation

— South Research Bldg. No.1 / LiMe Bldg. No.1

▶ Lab URL

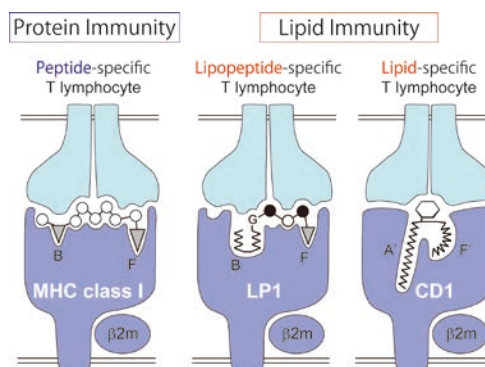
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab06/>



Assistant Professor

**MORITA, Daisuke**

The universe of antigens recognized by the immune system has recently been expanded to include not only protein antigens but also lipid and lipopeptide antigens. By orchestrating immunological, cell biological, structural, and lipid-biochemical approaches and by developing valuable animal systems, our laboratory aims to establish the molecular and cellular basis underlying “lipid immunity” and develop a new types of lipid-based vaccines.



Whereas MHC molecules bind peptide antigens and present them to T lymphocytes, LP1 and CD1 molecules bind lipopeptide and lipid antigens, respectively, and activate specific T lymphocytes. Our frontier research focuses on these lipid-specific immune responses, that we call “lipid immunity”.

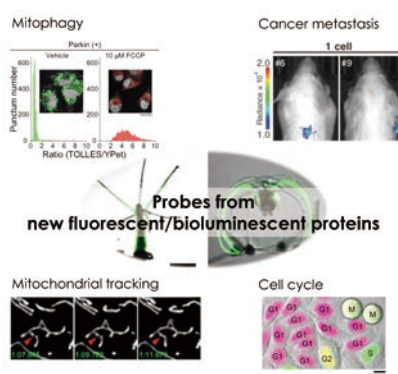
# Lab. of Bioresponse Analysis (Visiting)

► Lab URL  
<https://cfds.riken.jp/>



Visiting Professor  
**MIYAWAKI, Atsushi**

Lab. of Bioresponse Analysis is developing fluorescent and bioluminescent probes to study various biological processes, such as mitophagy and cancer metastasis.



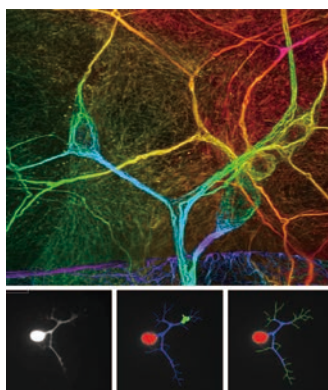
generated principally using fluorescent or bioluminescent proteins and are used to investigate the function of specific signaling mechanisms in a variety of biological systems. We believe that these approaches will continue to improve due to the various features of fluorescent/bioluminescent proteins that serve as the interface between light and life.



Visiting Associate Professor  
**Adrian Walton Moore**

Drosophila sensory neurons.  
Top: A super-resolution image of neuronal microtubules.  
Bottom: AI-based feature extraction from in vivo imaging of dendrite arbor differentiation

As neurons differentiate and assemble into circuits, they form among the most complex and diverse structures of any cell type. They construct complex dendrite arbors that connect them to their partners, and which must be patterned to support the precise connectivity and computational requirements of each neuron. The differentiation programs that create this pattern and connectivity are genetically programmed, and when they fail this leads to neurodevelopmental disorders. To reveal the molecular control processes of neuron differentiation, my lab is using multidisciplinary approaches in *Drosophila*, mouse and human experimental systems. Our work connects from transcriptional and genomic level controls, through cell biological cytoskeleton effector interaction networks, to in vivo mapping of neuron structural differentiation, and arbor pattern formation over time.



► Lab URL  
<https://cbs.riken.jp/en/faculty/a.moore/>





# Lab. of Viral Immunology (Visiting)

▶ Lab URL

<https://www.ims.u-tokyo.ac.jp/Kawaguchi-lab/KawaguchiLabTop.html>

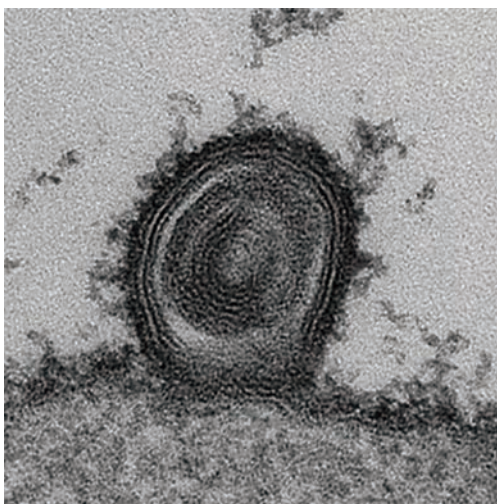


Visiting Professor

## KAWAGUCHI, Yasushi

Using herpes simplex viruses (HSVs) as models, we are promoting strategic fundamental research aimed at developing novel methods to control viral infections by elucidating the mechanisms underlying viral proliferation and pathogenesis. By utilizing viruses as biological probes to precisely analyze interactions with host cells,

we are advancing research that uncovers unknown cellular and physiological mechanisms that are often overlooked in general biological studies. Moreover, we are challenging next-generation virology to reconsider the viruses as homeostasis factors and exploring their significance on the host.



An electron micrograph image of HSV invading a host cell. We discovered a new receptor necessary for HSV cell entry and demonstrated that its regulatory mechanism could be a target for antiviral drug development. The identified receptor was later found to be a receptor not only for herpesviruses but also for other RNA and DNA viruses, influencing various virology studies.



\*Program-Specific



Professor, Director

**KAWAMOTO, Hiroshi**



Associate Professor

MIYAZAKI, Masaki

Assistant Professor

NAGANO, Seiji

Assistant Professor (\*)

KOBAYASHI, Yuka

Assistant Professor (\*)

UEHORI, Junji

Inter-Organ Communication Research Team

Associate Professor (\*)

KAWAOKA, Shimpei

Assistant Professor (\*)

KONISHI, Riyo

The major aim of our laboratory is to elucidate the molecular mechanisms that regulate cell fate decisions in the process of lineage restriction from multipotent hematopoietic stem cells to unipotent progenitors. We are recently studying how various blood lineages have been created during evolution (Figure 1).

As another project, we have been developing an approach aiming to apply our culture method in clinical settings. Whereas cytotoxic T lymphocytes (CTLs) represent the most promising therapeutic avenue in cancer immunotherapy, adaptive transfer of antigen-specific CTLs has faced difficulty in efficient expansion of CTLs from patients in ex vivo culture.

To solve this issue, we have proposed a strategy to use iPSC technology for cloning and expansion of tumor antigen specific CTLs; iPSCs produced from T cells (T-iPSCs) should inherit rearranged TCR genes, and thus all regenerated T cells from T-iPSCs should express the same TCR. Based on this idea, we have succeeded in regenerating MART1-specific CTLs from a melanoma patient (Vizcardo et al, Cell Stem Cell, 2013). Recently we have developed a method by which CTLs are regenerated from iPS cells transduced with exogenous TLR gene (TCR-iPSCs). This new method provides a convincing rationale for application of this strategy in clinical settings targeting cancer or viral infection (Figure 2).

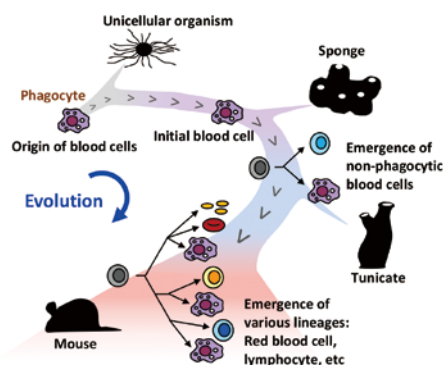


Figure 1 Evolutionary history of blood cells

In order to trace the evolutionary history of blood cells, gene expression profiles of blood cells in mouse, tunicate, and sponge were compared. Those of phagocytes/macrophages in the 3 animal species were similar to each other, and to a eukaryotic unicellular organisms. CEBPa and its homologs were found to determine this similarity. Collectively, we revealed that the initial blood cells emerged by inheriting a phagocytic program from ancestral unicellular organisms, and various lineage blood cells have stepwisely evolved from the prototypic phagocytes (Nagahata et al, Blood 140: 2611, 2022).

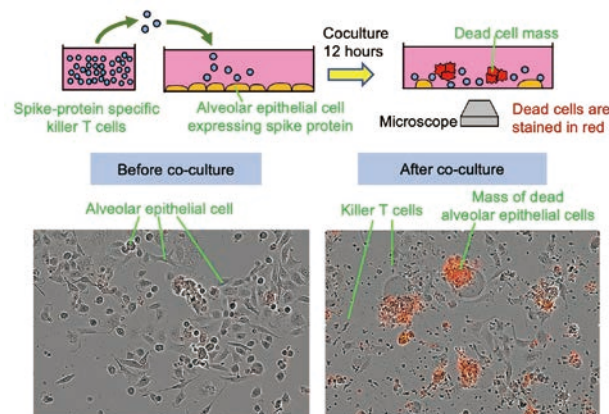


Figure 2 Killing of alveolar epithelial cells expressing viral protein by the killer T cell medicine

Alveolar epithelial cells were used as target cells that were enforced to express spike protein of SARS-CoV-2 to mimic infected cells. Killer T cells produced from HLA-deleted ES cell expressing T cell receptors specific for the spike protein were added and co-cultured for 12 hours. Most of epithelial cells were found to be killed.



## Lab. of Biomaterials

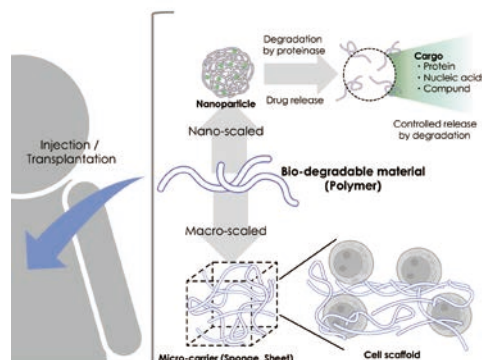
— South Research Bldg. No.1 / LiMe Bldg. No.1 <https://www.infront.kyoto-u.ac.jp/en/laboratory/lab12/>

► Lab URL



Assistant Professor  
**ANDO, Mitsuru**

Scaffold materials in regenerative therapy (tissue engineering) and cell transplantation, Drug carriers in drug delivery system to enhance therapeutic efficacy, Biomaterials are essential to support aforementioned therapy. In our laboratory, we research on the development of biodegradable biomaterials. In addition, we are also working on the reconstitution of artificial systems that mimetic cellular systems.



Technologies developed in this Laboratory  
As DDS carriers, cell scaffolds, and matrices for regenerative medicine, nano-sized and micro-sized carriers are constructed using biodegradable polymers.

## Lab. of Developmental Epigenome

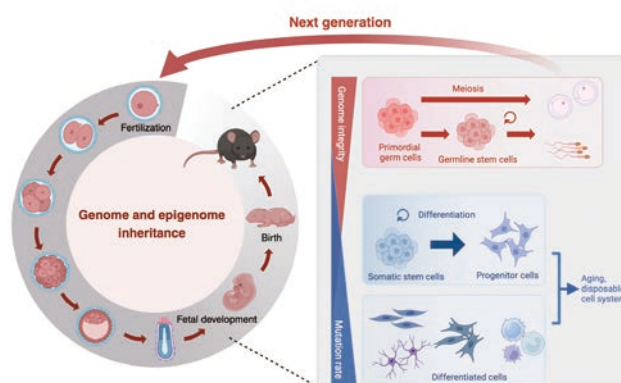
— South Research Bldg. No.1 / LiMe Bldg. No.1 <https://www.infront.kyoto-u.ac.jp/en/laboratory/lab17/>

► Lab URL

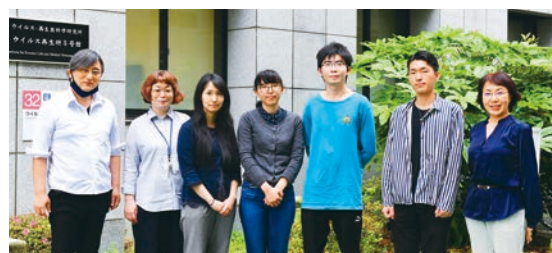


Associate Professor  
**CHUMA, Shinichiro**

During development of multicellular organisms, genetic stability is differentially regulated depending on developmental stages, cellular lineages and physiological conditions etc. We are currently investigating (1) how pluripotent stem cells and germline cells maintain their genome and epigenome integrity, and (2) how the genome and epigenome stability is coordinated with developmental programs of the germline-stem cell cycle. We also aim to identify genes and pathways with which the genetic stability of stem cell resources can be improved.



Our research aims to understand the genome and epigenome dynamics of the germline cycle and apply the findings to stem cell resources



# Lab. of Integrative Biological Science

— LiMe Bldg. No.5

https://www.infront.kyoto-u.ac.jp/en/laboratory/lab19/

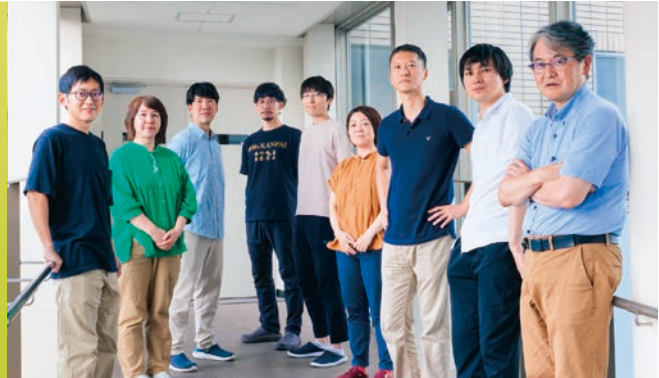
► Lab URL



Professor

**KONDOH, Gen**

Mammalian sperm undergo multiple maturation steps after leaving testis to be competent for fertilization. Serial important changes occur in the female reproductive tract on sperm, although the molecular mechanisms underlying these processes remain unclear. In our early study, we found that angiotensin-converting enzyme (ACE) releases GPI-anchored proteins (GPI-AP) from the cell membrane and plays a critical role in mammalian fertilization. We also found that sperm undergoing GPI-AP release associated with reorganization of lipid raft and acrosome reaction acquire fertilization potential. In terms of identifying factors triggering these processes in vivo, we found Lipocaline2 as a sperm maturation factor of female. Recently, we started new research projects elucidating character and function of new helper T cell, Th17 cell, to clarify the mechanism of inflammation.

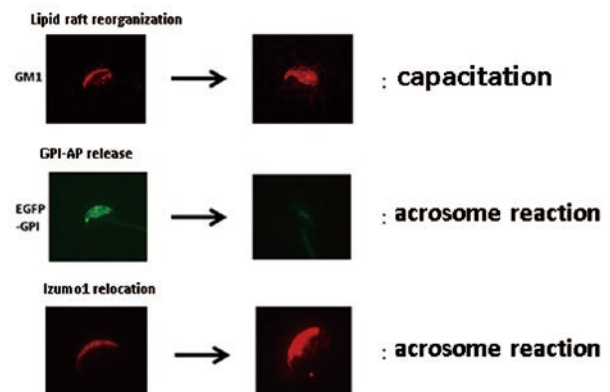


Associate Professor

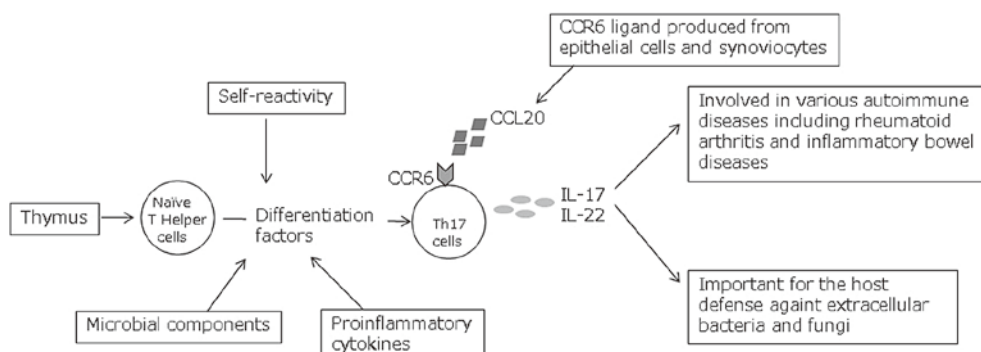
Assistant Professor (concurrent)

HIROTA, Keiji

WATANABE, Hitomi



H. Watanabe & G. Kondoh *J. Cell Sci.*, 2011.





# Lab. of Immunopathogenesis

— South Research Bldg. No.1 / LiMe Bldg. No.1

► Lab URL  
<https://ito-lab-en.labby.jp/>



Assistant Professor

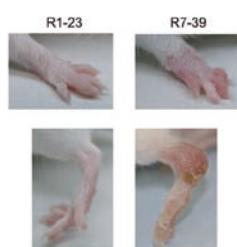
OSAKI, Motonao

Professor

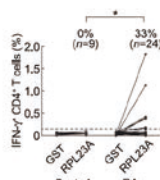
## ITO, Yoshinaga

We study an interplay between immune system and self-organs/tissues, with particular focus on its physiological roles and the mechanisms of disease development when the interaction becomes aberrant. We place autoimmunity and cancer immunology from an integrated perspective: both of them are 'destruction of

self-derived components by immune system'. We strive to discover key molecular pathways shared by both autoimmune diseases and cancer immunotherapy in order to develop innovative treatment arms for these devastating diseases.

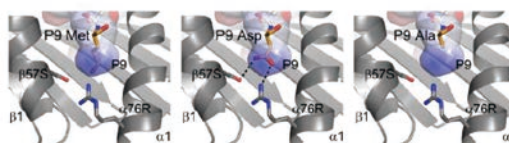


自己免疫疾患新規モデルマウス  
 A novel autoimmune disease model

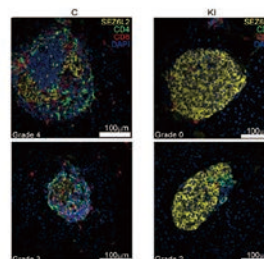


ヒト関節リウマチの標的自己抗原の同定  
 Identification of an autoantigen in rheumatoid arthritis

Ito Y et. al. *Science*. 2014



生化学的特性に基づく遺伝子改変モデルマウス設計  
 An animal model with a single amino acid substitution



自己免疫炎症の抑制  
 Control of autoimmune inflammation

Ito Y et. al. *J Exp Med*. 2018

By employing our own new technology, we will elucidate the whole repertoire of autoantigens critical for disease development in autoimmune diseases in order to establish antigen-specific therapeutics.

# Lab. of Experimental Immunology (Visiting)

— South Research Bldg. No.1 / LiMe Bldg. No.1

► Lab URL  
<http://exp.immunol.ifrec.osaka-u.ac.jp/?lang=en>



\*Program-Specific



Assistant Professor (\*) | KAWAKAMI, Ryoji

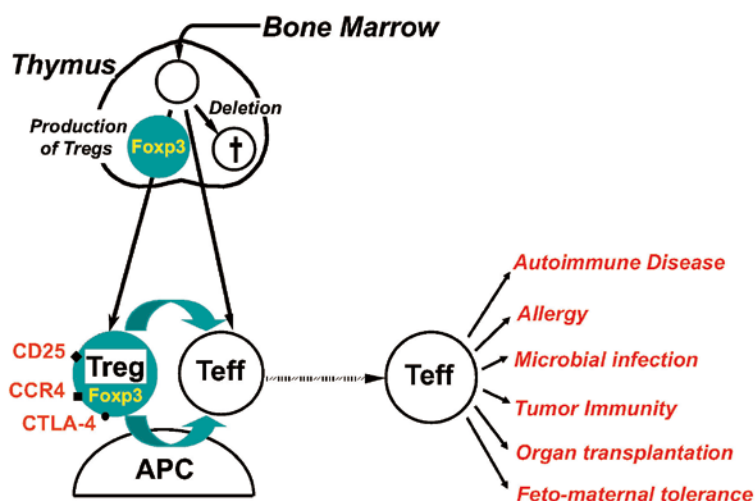
Visiting Professor

## SAKAGUCHI, Shimon

Our laboratory studies the mechanisms of immunological tolerance. We discovered naturally occurring regulatory T (Treg) cells as a T-cell subpopulation that is specialized for immune suppression and engaged in the maintenance of immunological self-tolerance and homeostasis. We have been studying the molecular and cellular basis of Treg cells development and maintenance, in mice and humans by using immunological, genetic and bioinformatics approaches. Since Treg cells are involved in various physiological as well as pathological immune responses, we are developing various ways to manipulate Treg cells for clinical application, which is

a novel immuno-therapy for autoimmune diseases, allergy, infection, organ transplantation and cancer. We are also studying the pathogenetic mechanism of rheumatoid arthritis by analyzing our newly developed model (SKG mouse). SKG mice have a mutation in the ZAP70 gene, which plays a critical role in T cell receptor signaling. Because of this mutation, SKG mice show altered thymic selection and allow a leakage of self-reactive T-cell from the thymus. We are investigating how such impaired signal transduction causes autoimmune diseases.

### Control of immune responses by Foxp3<sup>+</sup>CD25<sup>+</sup>CD4<sup>+</sup> Tregs



CD25<sup>+</sup>CD4<sup>+</sup> regulatory T (Treg) cells are produced by the normal thymus as a functionally mature T-cell subpopulation. They specifically express the transcription factor FoxP3. Reduction of Treg cells or attenuation of their suppressive activity may enhance tumor immunity and microbial immunity. In contrast, increase of the number of Treg cells or augmentation of their suppressive activity can treat autoimmunity and induce transplantation tolerance.



# Lab. of Biomechanics

— South Research Bldg. No.1 / LiMe Bldg. No.1

▶ Lab URL  
<http://www2.infront.kyoto-u.ac.jp/bf05/index-e.html>



Professor, Vice Director

**ADACHI, Taiji**



\*Program-Specific

Assistant Professor  
 Assistant Professor  
 Assistant Professor  
 Assistant Professor (\*)

MAKI, Koichiro  
 KIM, Youngkwan  
 TAKEDA, Hironori  
 SUMITA, Hiromi

The Laboratory of Biomechanics aims to clarify the self-organized regulatory mechanisms of diverse biological phenomena through interdisciplinary approaches encompassing mechanics, life science, and medical science. Our research topics cover developmental processes (cell differentiation, morphogenesis, and growth) as well as tissue/organ remodeling and regeneration which underlie functional adaptation to the envi-

ronment. A major focus of our research is to understand how well-organized dynamics of living systems emerges from complex molecular and cellular interactions. To this end, we are integrating biomechanics and mechanobiology approaches to highlight the roles of “adaptation to mechanical environment” and “hierarchy of structure and function” in the living organisms using mathematical modeling, simulation and experiments.

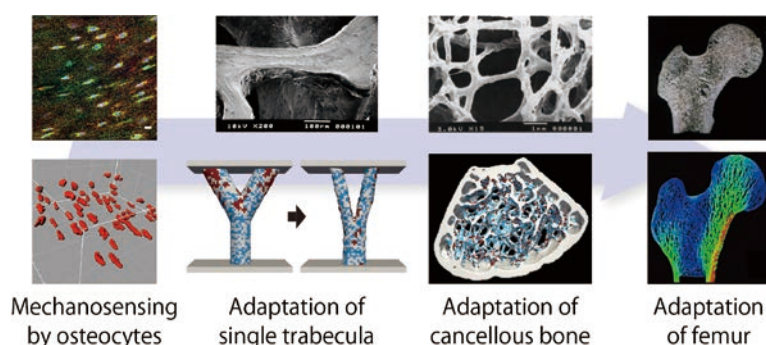


Figure 1 Bone can remodel its outer shape and inner structure to adapt to the surrounding mechanical environment. This study aims to clarify the mechanism of bone functional adaptation achieved through cooperative cellular activities.

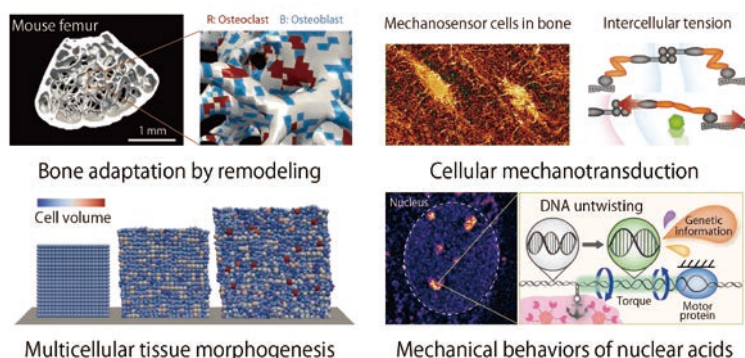


Figure 2 We combine experiments and modeling at multiscale to provide mechanical insights into biological systems, such as morphogenesis of multicellular tissues and cell fate determination under mechano-bio-chemical environment.

# Lab. of Developmental Systems

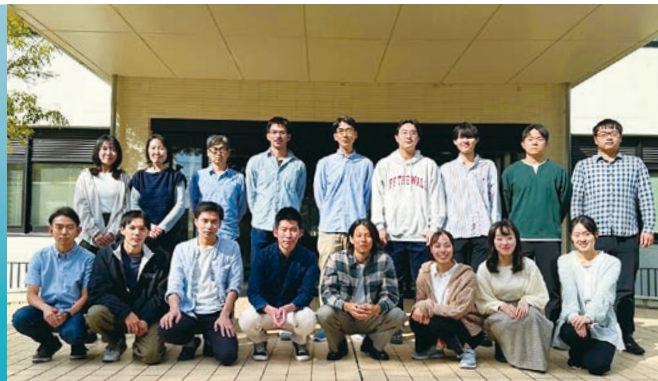
— South Research Bldg. No.1 / LiMe Bldg. No.1

▶ Lab URL  
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab26/>



Professor

**EIRAKU, Mototsugu**



Associate Professor

Assistant Professor

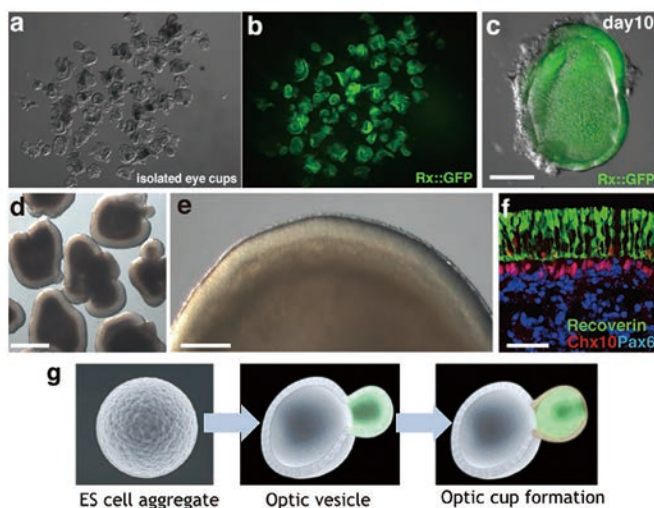
**OHGUSHI, Masatoshi**

**MII, Yusuke**

Organogenesis is a highly dynamic process in which multicellular behaviors are regulated by mechanisms in multiple scales from molecules and cells to tissues. In vitro generation of functional organ with complex structure is a major challenge of cell biology. Toward this goal, it is a reasonable strategy to recapitulate the ontogeny that is the most efficient and robust process for organogenesis acquired through evolution. Our laboratory aims to clarify molecular and cellular mechanisms underlying organogenesis, and to develop new technologies for in vitro recapitulation, that is, three-dimensional functional organ generation from stem cells. We have previously established efficient three-dimensional cultures for generation of mouse and human ES/iPS cell-derived brain and retinal tissue as well as other

ectoderm-derived tissues. Based on our past achievements in 3D tissue formations from pluripotent stem cells, we have been attempting to extend our limit of understanding for self-organization phenomena in neural development and advance the culture technology for generation of more complex tissues from ES/iPS cells in a more robust manner. To do that, we mainly focus on following points.

- 1) Elucidation of self-organization phenomena in neural development and morphogenesis
- 2) Development of novel technologies for in vitro formation of functional organ
- 3) Molecular analysis of species-specific regulation for developmental timing and tissue size determination.



in vitro formation of optic cup and layered retina from ES cells

a-c, Isolated optic cup structure generated from mouse ES cells. d-f, ES cell-derived optic cup differentiate into layered retinal structure. g, Scheme of in vitro optic cup formation in ES cell culture.



# Lab. of Biological Membrane System

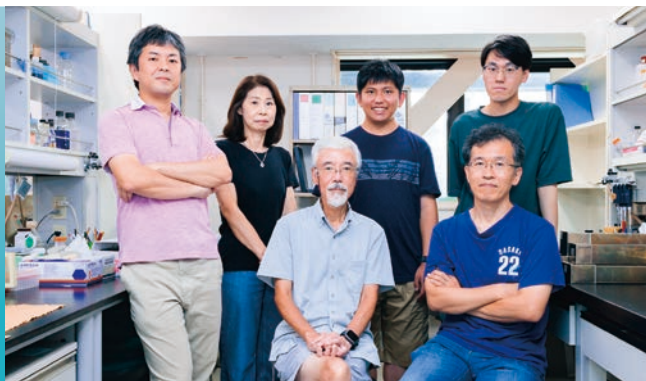
— LiMe Bldg. No.2

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<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab31/>



Professor

**AKIYAMA, Yoshinori**



Associate Professor

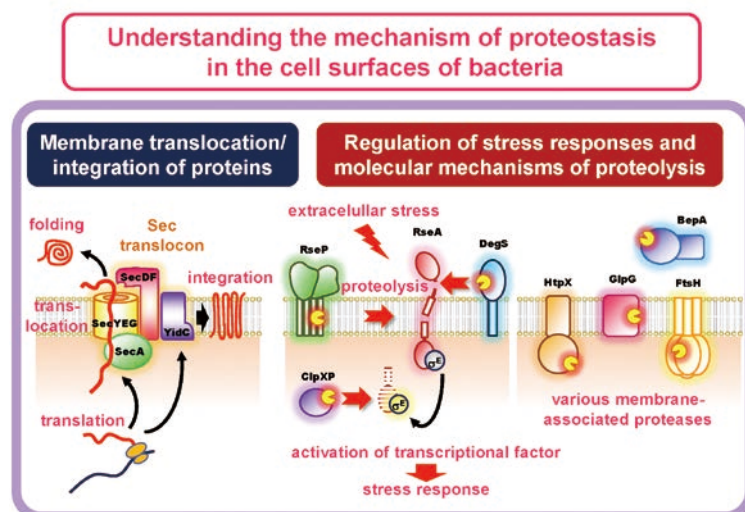
Assistant Professor

MORI, Hiroyuki

HIZUKURI, Yohei

The research projects carried out in this group are concerned with dynamic aspects of cell surface proteins in bacteria including *Escherichia coli* and *Vibrio alginolyticus*. Specifically, processes of protein folding, protein translocation across and integration into the membrane, membrane protein proteolysis and extracytoplasmic stress responses are studied by combined molecular genetic, biochemical biophysical and structural approaches. We are mainly focusing on the following two topics. (1) Function and regulation of protein translocation machinery: Protein export across the bacterial cytoplasmic membrane is promoted by cooperation of

the evolutionary conserved SecYEG translocon associated with auxiliary factors (such as SecDF) and the SecA ATPase motor. We are investigating the structure and molecular function of these and related cellular factors and regulation of their expression. (2) Membrane protein degradation and extracytoplasmic stress response: Membrane proteins play central roles in the functions of biological membranes. We are investigating the mechanism and physiological roles of membrane protein degradation by envelope proteases. We are also interested in the cellular system to sense and cope with abnormality of cell surface proteins.



The research projects carried out in the laboratory of Biological membrane system.

# Lab. of Tissue Homeostasis

— LiMe Bldg. No.2

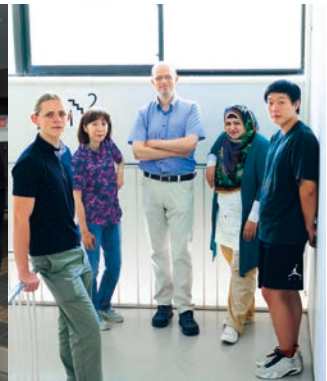
<https://www2.infront.kyoto-u.ac.jp/Toyoshima-HP/index-En.html>

▶ Lab URL



▶ Lab URL

<https://genomics.virus.kyoto-u.ac.jp/alexisvdb/index.html>



Associate Professor  
Assistant Professor

VANDENBON, Alexis  
ICHIJO, Ryo

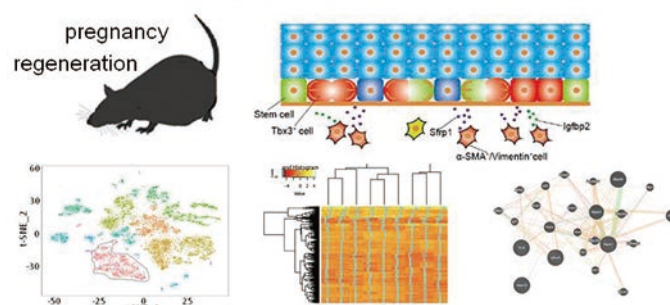
Professor

## TOYOSHIMA, Fumiko

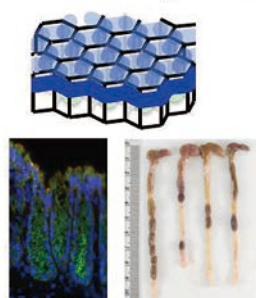
Each organ in the adult body responds to tissue damage or physiological changes of the body through regulating the multicellular network by which organ size and functions are determined. Our laboratory studies the mechanisms of tissue remodeling especially focusing on a regenerating organ from acute and chronic damage, as well as maternal remodeling organ during pregnancy. How the tissue mechanics and secretory

molecules affect the transcriptional network in the multi-cellular systems is one topic in the projects. These endogenous tissue remodeling mechanisms would be applied for regenerative medicine. We also interested in how the maternal tissue remodeling contributes to fetal growth or developmental origin of health and disease (DOHaD).

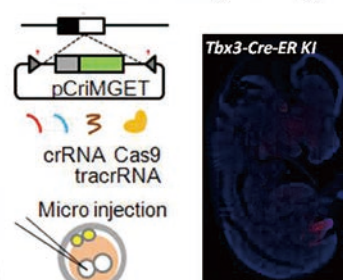
### Tissue remodeling in physiological condition and regeneration



### Epithelial barrier regeneration



### Genome editing strategy





# Lab. of Mathematical Biology

— LiMe Bldg. No.3

▶ Lab URL  
<https://mathbio.infront.kyoto-u.ac.jp/en/>



\*Program-Specific



Professor

**MOCHIZUKI, Atsushi**



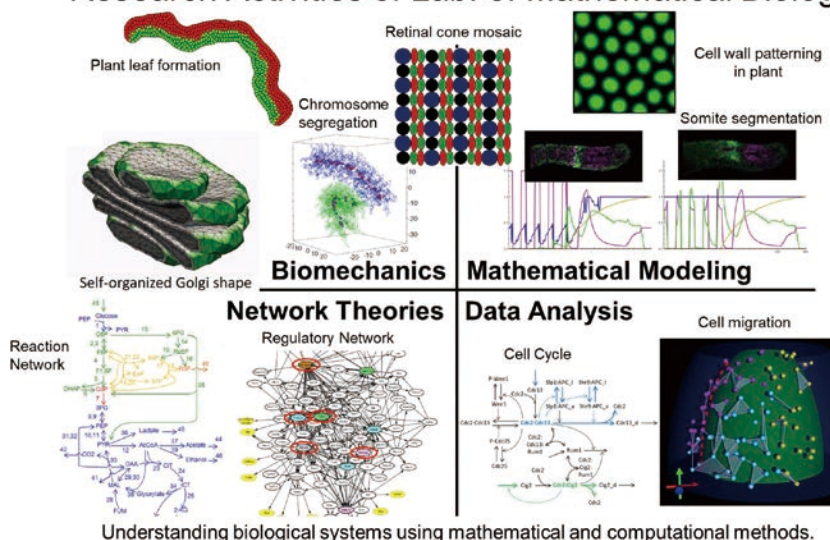
Associate Professor  
 Assistant Professor  
 Assistant Professor (\*)

OKADA, Takashi  
 ISHIKAWA, Masato  
 YAMAUCHI, Yuhei

The progress of modern biology revealed that biological phenomena are governed by complex network systems including many molecules, cells or organs. For the aim of understanding the functions of complex systems, we adopt mathematical and computational methods. By theoretical approaches we decipher huge amounts of experimental information, and to give integrative understanding for the biological systems. Our final goal is to open a new bioscience which will progress by the repeats of the theoretical predictions and the experi-

mental verifications. We are promoting multiple projects of collaborations with experimental biologists. One of our recent projects is studying dynamics of complex network systems in biology. We developed some theoretical frameworks to extract the important aspects of dynamics from network structure alone, without assuming other quantitative details. By combining our theory with experimental measuring and controlling, we will determine mechanism of dynamical behaviours and understand the principles for the biological functions.

## Research Activities of Lab. of Mathematical Biology



Research topics in lab. of Mathematical Biology

# Lab. of Stem Cell Genetics

— South Research Bldg. No.1 / LiMe Bldg. No.1

▶ Lab URL <https://www.infront.kyoto-u.ac.jp/en/laboratory/lab40/>



Professor

**YUSA, Kosuke**



Assistant Professor

Assistant Professor

Assistant Professor

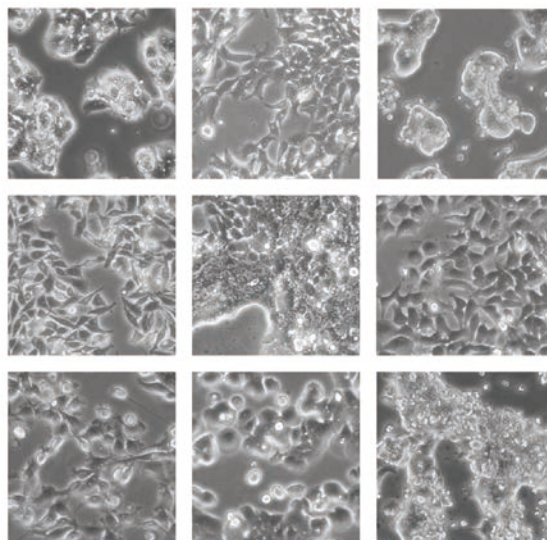
TARUMOTO, Yusuke

NISHIBUCHI, Gohei

AOKI, Kazunari

Forward genetic approach can comprehensively reveal genes involved in a phenotype of interest. This approach was frequently applied in lower model organisms such as yeast, *Caenorhabditis elegans* and fruit fly to identify genes involved in fundamental biological processes. In contrast, forward genetic approach had been hampered in mammalian cultured cells as there was no efficient way to inactivate all copies of every gene. Our research has been focusing on developing novel genetic tools that enable us to apply powerful forward genetics in mammalian cells. As one solution, we developed a functional genetic screening method using the CRIS-

PR-Cas9 system, which is highly efficient to genetically dissect a wide range of mammalian biology. Our current work focuses on molecular function studies of genes identified through CRISPR-based genetic screening in the following two research area: 1. Molecular mechanisms of pluripotency maintenance and differentiation of human pluripotent stem cells and 2. Genetic vulnerabilities in cancer cells and drug development. In the oncology area, we also focus on tackling drug resistance. Additionally, we also aim to develop novel genetic methodology by combining CRISPR methods with emerging technologies.



Colorectal cancer cell lines showing various cell morphologies. This cancer type can be classified into a few sub-groups based on gene mutations and gene expression profiles. Drug targets that show specificity in certain groups are most valuable as these targets are associated with biomarkers that can be used for patient stratification, and prioritised in follow-up analysis and subsequent drug development process.



# Lab. of Cell Fate Dynamics and Therapeutics

— LiMe Bldg. No.3

▶ Lab URL  
<https://cellfate.infront.kyoto-u.ac.jp/>



Professor

**ITO, Takahiro**



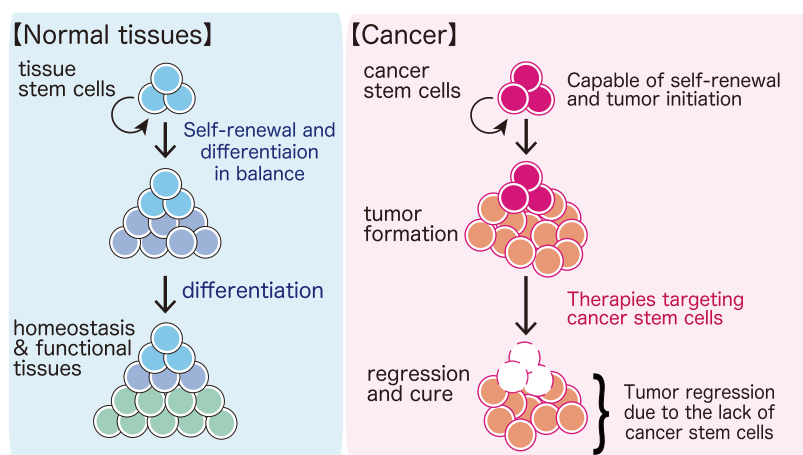
Associate Professor  
 Assistant Professor  
 Assistant Professor

HATTORI, Ayuna  
 MATSUURA, Kenkyo  
 OKIGAWA, Sayumi

My laboratory studies the molecular basis of cell fate regulation in normal and malignant stem cells. We are currently investigating several pathways of hematopoiesis and skeletal muscle systems in mice and human. Stem cells have a remarkable ability to propagate themselves, self-renewal. It allows tissue regeneration and repair damaged tissue after injury. But this ability is a double-edged sword; the same mechanism of self-renewal can be a target of malignant transformation and lead to cancer development. In the past decades, we have learned a great deal about the mechanisms of cancer-causing transformation, and yet finding effective ways to eradicate cancer cells has remained an elusive goal in many types of cancers. This is partly because tumors are often complex and heterogeneous mixtures

of neoplastic cells with different self-renewal and differentiation capacities. Unlike many differentiated cells within a tumor, some cancer cells have the ability to self-renew. These self-renewing cancer cells, or cancer stem cells, are therapy-resistant and can drive tumor relapse and metastasis following treatment cessation. Recent studies, including our own work, suggest that the normal and malignant stem cells operate on cell fate regulatory signals that are common or specific to each population. Our research program seeks to improve our understanding of stem cell and cancer biology, and to apply this knowledge to the development of novel and effective approaches to treat human disease and cancer.

## Stem cells in tissues and cancer



Stem cells in tissues and cancer. Stem cells maintain both normal and malignant tissues, and we seek to uncover the molecular basis of cell fate regulation essential for the stem cell functions.

# Lab. of Deconstruction of Stem Cells

— LiMe Bldg. No.2

▶ Lab URL  
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab43/>

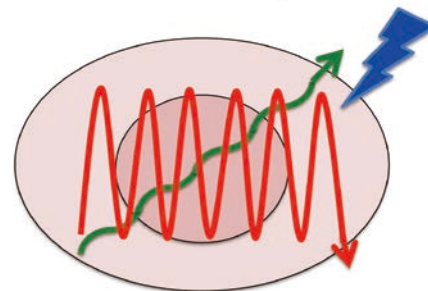
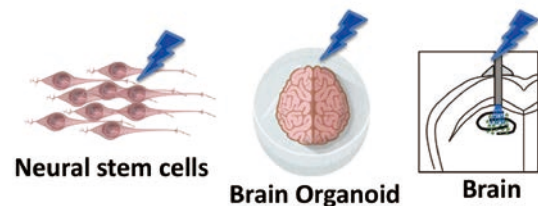


Professor

**IMAYOSHI, Itaru**

The recent discovery of neural stem cells in the adult central nervous system has raised the possibility of repairing the damaged tissue by recruitment of their latent, endogenous regenerative potentials. Development of innovative methods that can noninvasively manipulate neural stem cells in the brain has been expected for regenerative medicine of the nervous system. We have recently demonstrated the first success of such an approach in artificial manipulation of proliferation and neuronal differentiation of neural stem cells by light. We are currently extending this regenerative approach to various types of neural disease models in mice and primates, such as traumatic injury, neurodegeneration or psychiatric disorder. In our laboratory, by applying the novel light-inducible gene expression system, we will try developing novel methods to selectively and efficiently induce various neural cell types from neural stem cells.

More specifically, we will focus on the dynamic expression changes of transcription factors in neural stem cells and manipulate them by the optogenetic approach. We will improve the specificity and efficiency of differentiation of neural stem cells and direct reprogramming processes. We will apply these light-mediated control methods to neural stem cells in the brain and iPS cells-derived brain organoids, as well as to cultured neural stem cells.



***Optical control of gene expression  
dynamics in stem cells***

Development of novel optical methods to regulate differentiation of neural stem cells in neural stem cell cultures, brain organoids, and living brains.



# Lab. of Nano Bioengineering

— LiMe Bldg. No.2

▶ Lab URL  
<https://www.hshintaku.com/>



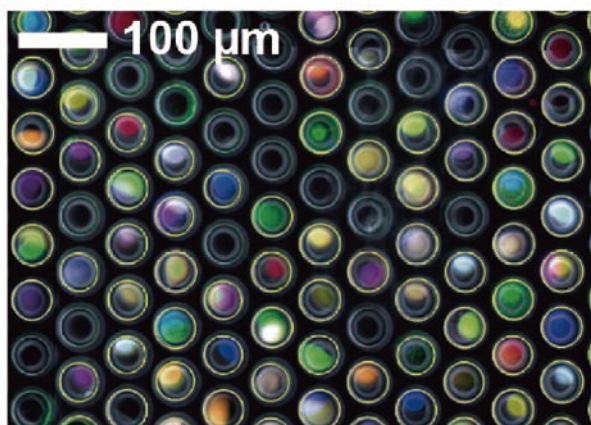
\*Program-Specific



Professor

**SHINTAKU, Hirofumi**

Established in April 2023, the Nano Bioengineering Lab delves into the intricate organization of multicellular systems. Our research endeavors focus on elucidating the cross-scale system from single cells to complex organisms and understanding the mechanisms underlying diseases that arise from organizational disruptions. We pioneer innovative omics methodologies, leveraging advancements in micro/nanofluidics and electrokinetics, to unravel these fundamental questions. Our interdisciplinary approach unites experts from diverse fields including basic biology, cancer biology, biophysics, and mechanical engineering. As a recent achievement, we developed ELASTomics (electroporation-based lipid-bilayer assay for cell surface tension and transcriptomics), which measures cell surface tension and gene expression with single-cell resolution. Additionally, we created an optical-indexing method that integrates microscopic



Assistant Professor  
Assistant Professor (\*)

KANEKO, Taikopaul  
MINEGISHI, Misa

images and gene expression by combining fluorescent color codes and DNA barcodes. At the heart of our work lies the collaborative environment of LiMe, serving as a dynamic hub for interdisciplinary exchange. Together, we strive to push the boundaries of knowledge and contribute to breakthroughs in biomedical science and engineering.

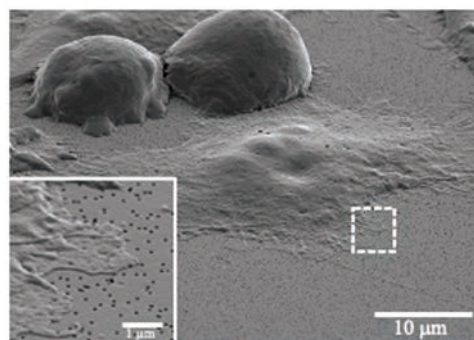


Figure 1 The mechanical properties of cells are known to be associated with physiological states in various biological contexts, such as cell differentiation, cancer, and aging. To elucidate the intricate molecular mechanisms governing mechanical properties of cells, we have developed a novel method capable of integrating cell mechanics profiling with unbiased transcriptomics for thousands of single cells (Shiomi et al., Nat Commun., 2024).

Figure 2 Genetically identical cells can show diverse responses to drugs, leading to different cell fates, such as drug resistance in cancer. To study the molecular cascade of how the variation in gene expression gives rise to different phenotypic responses, we introduced a method combining optical indices from cells and hydrogel beads with single-cell RNA sequencing, linking cellular drug responses to gene expression variations (Tsuchida et al., LabChip, 2024).

# Lab. of Aging and Infection Control

— LiMe Bldg. No.2

▶ Lab URL  
<https://www.kagenakadailab.com/English.html>



Professor

**NAKADAI, Eriko**

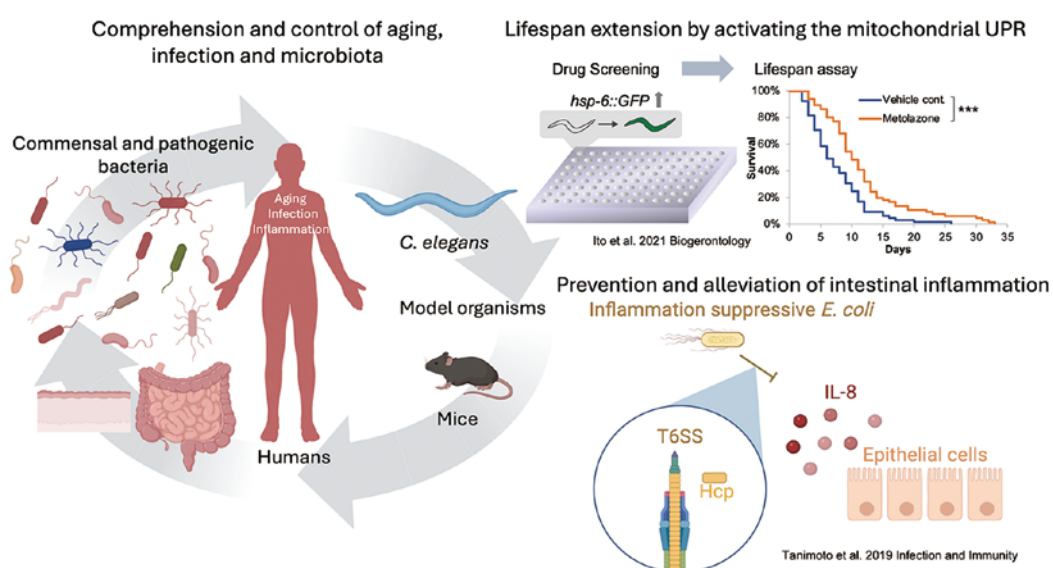


Assistant Professor

TANIMOTO, Yoshihiko

We aim to elucidate the mechanisms of interaction between the indigenous microflora and host aging, infection, and inflammation. Based on those mechanisms, we hope to construct methods to control aging and infection through food and indigenous microbiota. We are also developing methods to extend healthy life span by targeting life phenomena such as mitochondrial

quality control and epigenetics, which are closely related to aging. In recent years, it has become clear that inflammation is closely related not only to infection but also to various chronic diseases, and we are focusing on the possibility of using intestinal bacteria to suppress inflammation. We invite you to join us in our research.



We aim to understand the mechanisms of aging, infection and inflammation, and to construct methods to control them via food and indigenous microorganisms. We are mainly using the nematode *C. elegans* as a model organism, but we also incorporate cultured cells and mouse models of pathological conditions, depending on the topic.



# Lab. of Mechanosensory Physiology

— LiMe Bldg. No.2

▶ Lab URL  
<https://www.infront.kyoto-u.ac.jp/laboratory/lab49/>

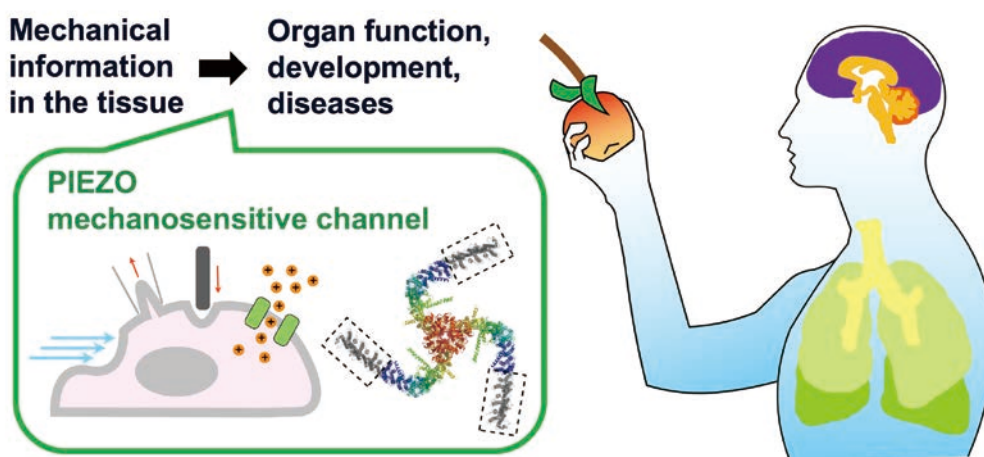


Professor

## NONOMURA, Keiko

We are studying physiological roles of mechanosensation mediated by PIEZO mechanically activated channel (awarded Nobel prize 2021) in tissues/cells including sensory neurons, brain tissue and lymphatic vessels. <Main themes> 1. Elucidating physiological roles of PIEZO expressing mechanosensory neurons innervating lung and/or other organs. We have been specifically investigating their contribution to breathing pattern of newborns, as starting breathing immediately after birth

is critical for survival of mammalian newborns and its underlying mechanism is still mostly elusive. 2. Studying the contribution of PIEZO mediated mechanosensation in the brain, focusing on both developmental process and brain function. 3. Studying the mechanism in which PIEZO1 mediated mechanosensation contributes to venous/lymphatic valve formation, utilizing KO or reporter mouse lines and cultured endothelial cells.



PIEZO mechanically activated channel senses positive/negative stretch of cell membrane or fluid flow around the cell. We are investigating the physiological roles of the mechanosensory system involving PIEZO channel and also types of mechanical stress activating PIEZO.

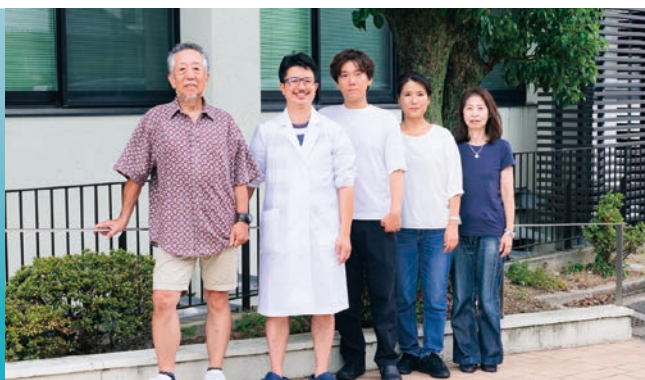
# Lab. of Regulatory Information (Visiting)

South Research Bldg. No.1 / LiMe Bldg. No.1

Lab URL  
<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab50/>



\*Program-Specific



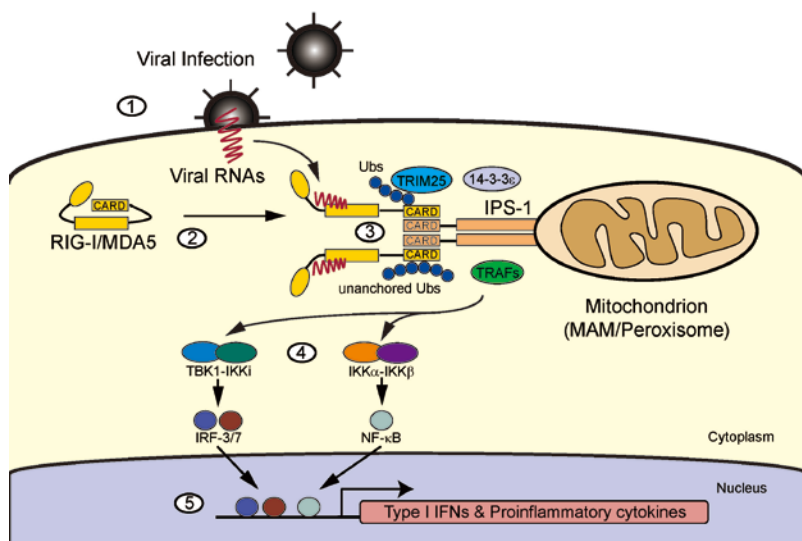
Assistant Professor (\*) | TAKEUCHI, Fumihiko

Cooperative Professor

## FUJITA, Takashi

Virus infections, such as influenza A epidemic and Chronic Hepatitis C virus infection are still 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. RIG-I, MDA5 and LGP2, collectively termed as RIG-I-Like Receptors (RLRs)

function as sensor for viral dsRNA to initiate production of interferon (IFN) and proinflammatory cytokines (Figure), which block viral replication and promote acquired immunity against viruses. Recently we discovered that persistent activation of MDA5 leads to lupus-like autoimmune disorder in mice. The purpose of our project is to clarify the molecular mechanism underlying the antiviral innate immunity and autoimmunity regulated by RLR, and to develop new diagnostic and therapeutic tools for these diseases.



### Sensing viral dsRNA and activation of RLR

When cells were infected with virus (1), viral dsRNA is sensed by RIG-I or MDA5 (2). CARD of RIG-I and MDA5 interacts with another CARD-containing protein expressed on mitochondria, termed Interferon Promoter Stimulator-1 (IPS-1) (3). As a result of these molecular interactions, transcription factors, IRF-3, IRF-7 and NF-κB are activated (4). These transcription factors cooperatively activate several antiviral genes, including those of type I and type III interferon are activated (5).



# Research Center for Infectious Diseases

## Lab. of Primate Model

— LiMe Bldg. No.2

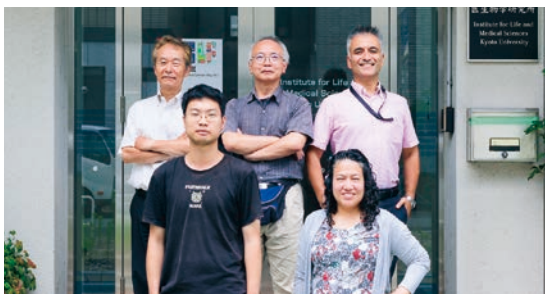
► Lab URL

<https://www.infront.kyoto-u.ac.jp/en/laboratory/lab35/>



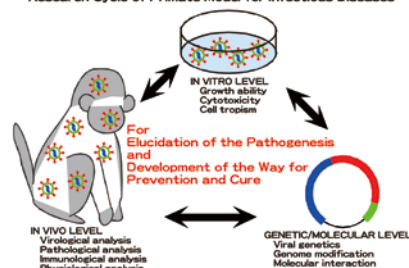
Associate Professor

**MIURA, Tomoyuki**



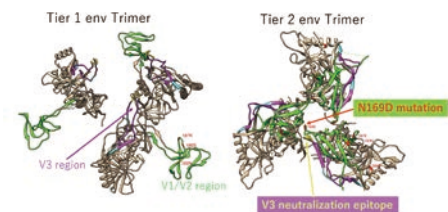
Since the nonhuman primate is the closest experimental animal to human, it is expected to establish the most useful model for human infectious disease in many aspects. Some pathogenic viruses (HIV-1, for example) can only infect primates. We have a large scale facility for infection experiments using nonhuman primates at P3 level. We establish infection and disease development models using macaque monkeys, and carry out the basic research for clarifying the in vivo pathogenesis and developing prevention and cure of infectious diseases.

Research Cycle of Primate Model for Infectious Diseases



We will elucidate the pathogenicity and develop preventive and therapeutic methods of infectious diseases by comprehensive analysis at the level of molecules, cultured cells, and infected individuals.

The virus mutated in monkeys acquired neutralization resistance by structural shield of the target site.



• N169D is a key substitution for gaining neutralization resistance.

## Animal Experiment Facility for Viral Infection

— Molecular Biology Research Bldg.

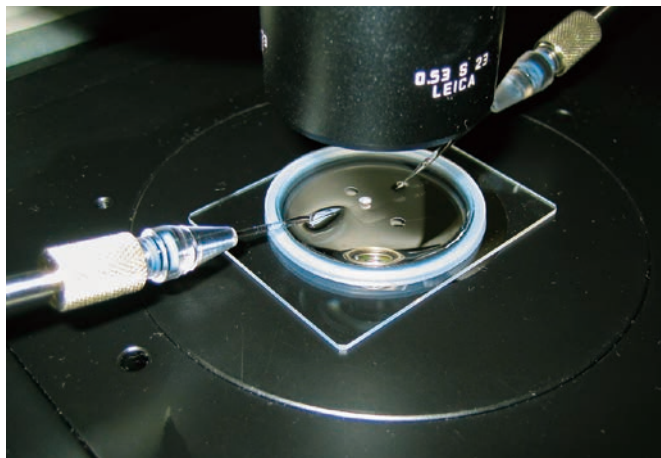


We have a laboratory facility for investigation of biological reactions with virus infection. The purpose of this facility is to analyze pathogenicity of human pathogenic viruses and develop useful vaccines. BSL2 and BSL3 rooms are in operation at each pathogen level. Small

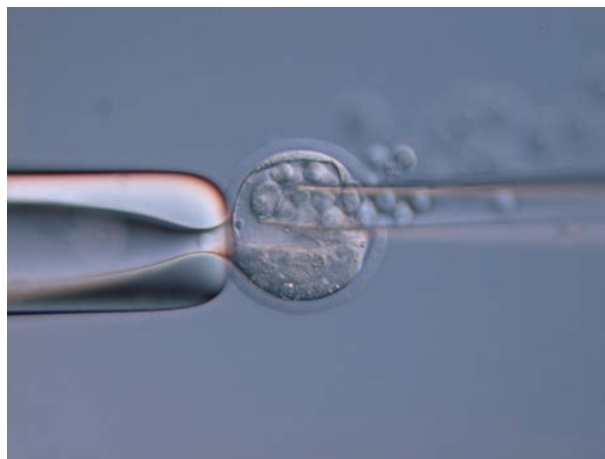
animals such as mice and medium animals such as monkeys can be used as experimental animals. After permission from the committee of faculty and technical staff (veterinarians), viral infection experiments are conducted under strict control.

# Reproductive Engineering Team

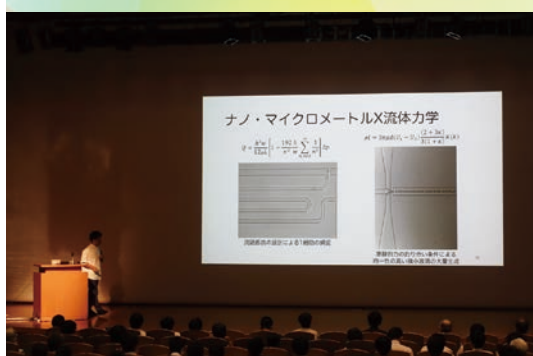
— LiMe Bldg. No.3



Reproductive engineering team is a support unit for generating transgenic mouse (Tg) and knockout mouse (KO). We also perform cryopreservation of mouse-fertilized eggs.

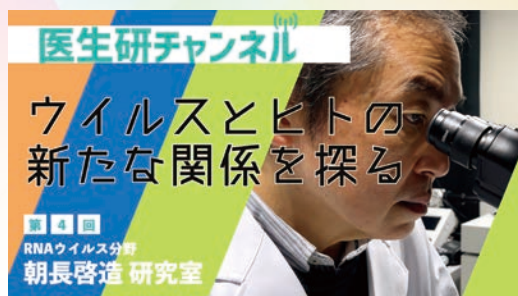


## Announcement from LiMe



The Institute for Life and Medical Sciences (LiMe) holds various events open to the public and to people inside and outside the university, including an open seminar every July.

We also have an official YouTube channel "Iseiken Channel" that provides the latest information about research at the Institute and interviews with faculty members. Our newsletters give a broad overview of the Institute's activities, from research to events. Please take a look.





# Center for Animal Experiments

LiMe Bldg. No.3 / No.4

<https://anif4.infront.kyoto-u.ac.jp/> [Internal Access Only]

▶ Lab URL



Associate Professor (concurrent)

HIROTA, Keiji

Assistant Professor

WATANABE, Hitomi

Professor (concurrent)

**KONDOH, Gen**

Experimental animals, such as mouse, rat and others, are housed in our Center under strict regulation of animal experimental committee and institutional guidelines for animal welfare. Moreover, we have been considered for long time: how to make gene-manipulated mice more rapidly and conveniently. Recently,

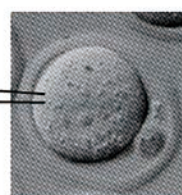
genome engineering methods have been established using TALEN or CRISPR-Cas9 systems. We have searched for many methods and finally developed our own protocol making such mice more easily and reproducibly.

Select unique sequence by:

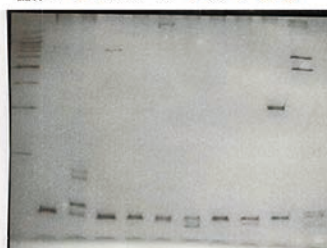


Cas9  
+  
guide RNA

Embryo microinjection



MW 1 2 WT 3 4 5 6 7 8 9



Detecting genome-edited mice by urea-denaturing gel electrophoresis

Our strategy for developing genome-edited mice using CRISPR-Cas9 system.

# Center for Human ES Cell Research

LiMe Bldg. No.5

▶ Lab URL  
<http://chesr.infront.kyoto-u.ac.jp/>



## Our mission

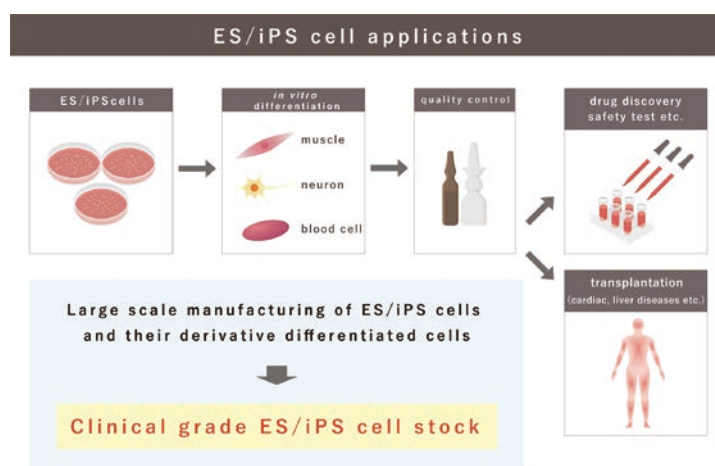
The Center for Human ES Cell Research was newly established in April 2020 with the mission of promoting the establishment and distribution of human embryonic stem (ES) cell lines and the advancement of applied studies on them. ES cells, like induced pluripotent stem (iPS) cells, are a type of pluripotent stem cell, and human ES cells precede human iPS cells in the history of their first establishment. Two institutes in Japan are approved for the generation of human ES cell lines: the National Center for Child Health and Development and our institute. Currently, we are manufacturing human ES cell lines for clinical use in our

MHLW-approved cell processing facility.

Regarding the importance of human ES cells in academic research and their potential benefits in clinical applications, a robust and stable supply of high-quality human ES cells is essential for the advancement of regenerative medicine as well as basic research. To realize the clinical application of human ES cells, we strengthen our current facility of ES cell production and, through further cooperation with other research organizations and hospitals inside and outside of Japan, we accelerate the progression of stem cell research and regenerative medicine.

## History

Institute for Life and Medical Sciences first succeeded in establishing human ES cell lines in 2002, and since 2017, directed by the former laboratory of Embryonic Stem Cell Research, has been serving as the supplier of clinical-grade human ES cell lines in Japan (as of April 2020). To enhance our capability and performance in the research and development of human ES cells for clinical use, the facility underwent a reorganization in 2020, and the Center for Human ES Cell Research was newly founded.





The Center for Human ES Cell Research comprises two divisions, namely, the division of clinical basis for ES cell research and the division of basic technology development for ES cell research. The division of Clinical Basis for ES Cell Research consists of two groups: the Laboratory of Embryonic Stem Cell Research, which is responsible for the establishment and distribution of human ES cell lines, and the Laboratory of Embryonic Stem Cell Application, which takes charge of quality control of and comparative genome/ epigenome analyses of human ES cell lines. The Division of Basic Tech-

nology Development for ES Cell Research consists of three groups, which aim for research and development, with mid-to long-term vision, intended for clinical applications of human ES cells: the Laboratory of Organoids Technology, the Laboratory of Regenerative Immune Cell Therapy and the laboratory of ES cell differentiation. Together, our center works toward the establishment of an international and stable research facility for human ES cell distribution, as well as the development of basic technologies required for its clinical application, such as quality control and cell/organoid culturing methods.

### Center for Human ES Cell Research

#### Division of Clinical Basis for ES Cell Research

##### Lab. of Embryonic Stem Cell Research

Associate professor Kawase (full time)  
Program-Specific Assist. Prof. Takada (full time)

- Establishment and distribution of hES cell lines
- Library construction of hES cell lines

##### Lab. of Embryonic Stem Cell Application

Associate professor Chuma (concurrent)

- Quality control of hES cell lines
- Comparative analyses of genome/epigenome regulation

#### Division of Basic Technology Development for ES Cell Research

##### Lab. of Organoids Technology

Professor Eiraku (Center Director/concurrent)  
Associate professor Ohgushi (concurrent)

- Generation of organoids from hES cells
- Regenerative medicine & drug discovery by organoids

##### Lab. of Regenerative Immune Cell Therapy

Professor Kawamoto (concurrent)  
Program-Specific Assist. Prof. Konishi (concurrent)

- Regeneration of T cells from hES cells
- Cancer immunotherapy by regenerative T cells

##### Lab. of ES Cell Differentiation

Professor Yusa (concurrent)

- Analyses of hES cell differentiation and lineage commitment
- Development of hES cell differentiation methods

## Division of Clinical Basis for ES Cell Research Lab. of Embryonic Stem Cell Research

LiMe Bldg. No.5

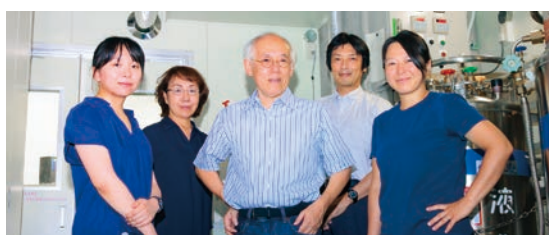
► Lab URL

<https://www2.infront.kyoto-u.ac.jp/es01/englishtop.htm>



Associate Professor

**KAWASE, Eihachiro**

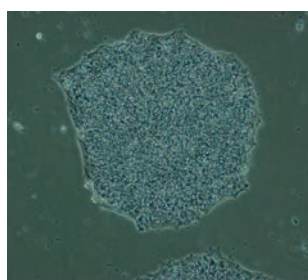


Assistant Professor (\*)

TAKADA, Kei

\*Program-Specific

Human embryonic stem (ES) cell lines are expected to have great potential in medical research and applications such as cell transplantation therapy and drug discovery. We have established human ES cell lines with high efficiency and analyzed their characteristics in detail. The established human ES cells have been distributed to more than 50 research projects in Japan and have produced many research results. We are also researching the molecular mechanisms of self-renewal and differentiation of human ES cells and developing technologies for the genetic manipulation of human ES cells. We have constructed a cell processing facility (CPF) and have successfully generated human ES cell lines for clinical use.

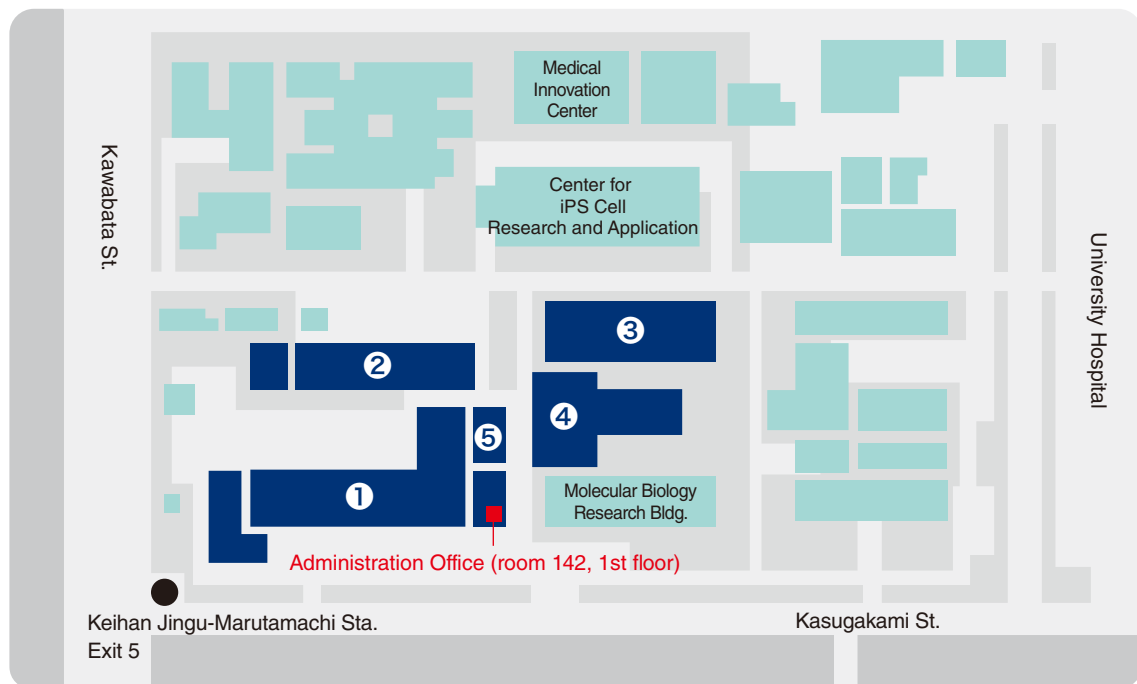


Human Embryonic Stem Cells

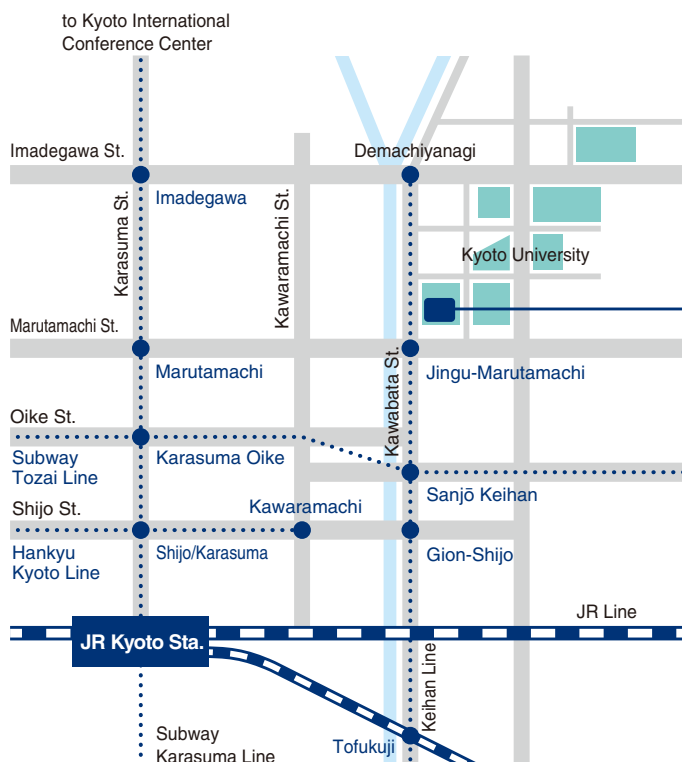


Clinical-grade hESC Processing Facility

# Map & Access



- ① South Research Bldg. No.1 /  
Institute for Life and Medical Sciences (LiMe) Bldg. No.1
- ② Institute for Life and Medical Sciences (LiMe) Bldg. No.2
- ③ Institute for Life and Medical Sciences (LiMe) Bldg. No.3
- ④ Institute for Life and Medical Sciences (LiMe) Bldg. No.4
- ⑤ Institute for Life and Medical Sciences (LiMe) Bldg. No.5



## [ Access to LiMe ]

- From Kansai International Airport (KIX) by Train  
Take JR Kansai-Airport Express "HARUKA" to Kyoto Station.  
It takes about 80 minutes.
- From Kyoto Station by Taxi It takes 20 minutes and costs 2,000 yen, approximately.
- From Kyoto Station by City Bus Take a No. 206 bus bound for "Higashiya-ma St. and Kitaoji Bus Terminal", and get off at "Kumano Jinja-mae". Walk two blocks to the west. It takes 5 minutes.
- From Kyoto Station by Subway Take Subway Karasuma Line and get off at "Marutamachi". Walk east for about 20 minutes.

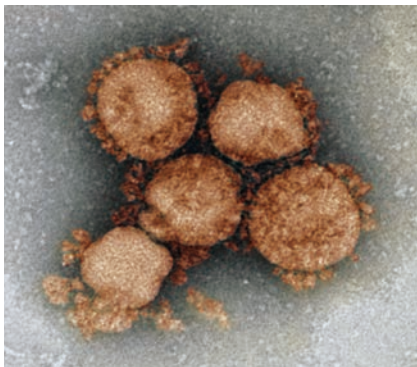


## 【 Life and Medical Sciences Research Fund 】

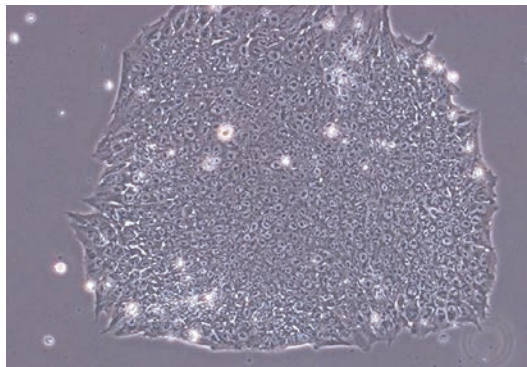
### Uncovering the secrets of vital activity to shape the future of medical sciences

The Institute for Life and Medical Sciences (LiMe) aims to explore new academic fields. The institute is known for previous brilliant research findings in medical sciences, including discovering the human leukemia virus and regulatory T cells.

By promoting integrated research activities that combine virology, immunology, genetics, the study of stem cells, structural science, and mathematical science, we intend to develop researchers and entrepreneurs with broad perspectives and the ability to get things done. This fund will help us take the lead in medical sciences and biostudies in Japan and the world. We aim to eradicate viral diseases and put regenerative medicine to practical use.



SARS-CoV-2 (EM was taken by Prof. Noda's group).



Human ES cell produced for clinical purposes for the first time in Japan (KthES11).  
It has been already distributed to various research institutions.

You can make a donation through credit card or other means.

For more details, please visit the Kyoto University Fund website.

<https://www.kikin.kyoto-u.ac.jp/en/contribution/infront/>





**LiMe**  
Institute for Life and Medical Sciences  
Kyoto University

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