MISSION for the FUTURE

Creating the future of healthcare through collaborations with the world's leading researchers

Advanced International Collaborative Research Program

ASPIRE

AMED
Japan Agency for Medical Research and Development
ASPIRE

ASPIRE
Adopting Sustainable Partnerships for Innovative Research Ecosystem

To Those with Aspirations

The ASPIRE program aims to accelerate the international mobility of researchers and knowledge within Japan's research community through international collaborative research that partners top Japanese researchers with those in Europe, the United States, and other advanced scientific and technological countries and regions. Of the eight priority research fields designated by the Cabinet Office, AMED is responsible for the healthcare field, providing support and forming networks for international collaborative research.

ASPIRE's mission is to cultivate the next generation of top researchers by providing highly motivated and passionate young Japanese researchers with opportunities to have an impact in the world's premier international research settings, thereby maintaining and enhancing Japan's scientific and technological capabilities.

OUR MISSION

- Build networks among top scientists worldwide
- Participate in leading global research communities
- Foster young researchers for international success

EUROPE

- Austria
- Belgium
- Czech Republic
- Denmark
- EU
- Finland
- France
- Germany
- Italy
- Netherlands
- Norway
- Poland
- Portugal
- Spain
- Sweden
- Switzerland
- United Kingdom

ASIA/ OCEANIA

- Australia
- Japan
- South Korea

NORTH AMERICA

- Canada
- United States

We aim to promote collaboration among leading researchers worldwide and the "global circulation of talent" that generates new knowledge and technologies.

PROGRAM OVERVIEW

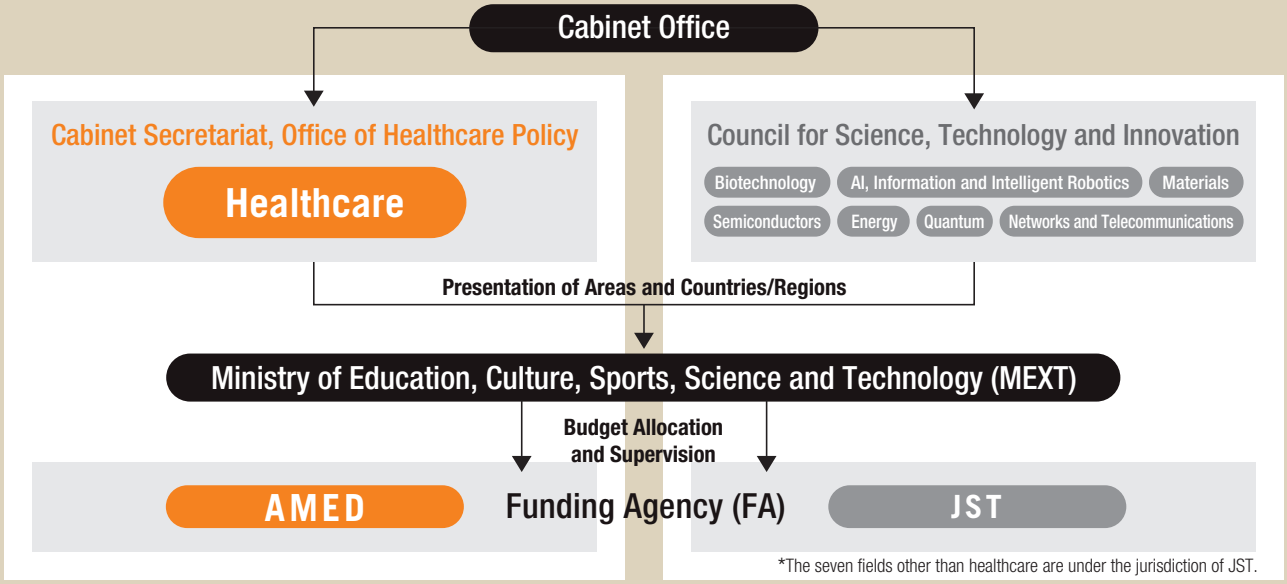
About the ASPIRE Program

Program Overview

ASPIRE aims to maintain and strengthen Japan's scientific and technological capabilities in key policy-defined scientific and technological fields through international joint research that brings together top researchers from Japan and other advanced scientific and technological countries and regions, thereby accelerating the **international mobility of researchers and talent** within Japan's research community.

Support Details	Research Field	Funding Scale	Research Period	Eligibility
	Advanced fields as determined by the Cabinet Office	Type A: Up to approximately 100 million yen annually per project Type B: Up to approximately 30 million yen annually per project	Type A: 5 years Type B: 3-5 years	In principle, Japanese research teams wishing to collaborate with top researchers abroad who have obtained sufficient research funds from their respective countries' major funding agencies.

Program Implementation System



*The seven fields other than healthcare are under the jurisdiction of JST.

Research Areas

After careful deliberations, the Cabinet Office determined the following areas as those to be focused on in the healthcare field.

Cellular Structure and Function

This research area focuses on cellular structure and function. As imaging and analysis technologies have advanced, various phenomena have been observed, such as the dynamic state of organelles in cells and the liquid-liquid phase separation of proteins and nucleic acids. This research area also covers protein structure analysis and prediction using cryo-EM and AI, which can be used in drug design, for example.

Complex Systems of Living Organisms

Our understanding of complex systems, including cell-to-cell and tissue-to-tissue interactions, pathogen-host interactions, and even human-human social relationships, is being enhanced by non-invasive biomedical measurement methods and AI technologies for analyzing large-scale complexity. This research area aims to clarify the mechanisms of maintenance and breakdown of biological functions caused by such interactions. As a result, new medical innovations will be developed for controlling them.

Human Life Stages Research

In this research area, research based on life stages such as human development, maturation, and aging will be studied. It also includes research on phenomena specific to each life stage. Research using age cohorts and birth cohorts, as well as experimental animals and cultured cells that model human life stages, are also actively studied. Within this research area, aging research and healthy longevity research are particularly important issues in a super-aging society and are research themes of global interest.



MISSION for the FUTURE

INTERVIEW with OKABE Shigeo

Envisioning the Future Through ASPIRE

Thoughts from the Program Supervisor

OKABE Shigeo
Director, RIKEN Center for Brain Science

Promoting Research Through Integration of Knowledge

The approach of tackling global challenges that transcend national borders and returning the knowledge gained through research as shared knowledge for humanity, i.e., the concept of global commons, is now attracting attention in the scientific field. It is for this very reason that I believe it is crucial to engage in research with broad-based knowledge and involving interdisciplinary collaborative relationships.

Located in Asia yet actively assimilating Western culture and developing science for over 100 years, Japan has a unique presence that has produced significant economic success. It is true that superb research talent has emerged in India and elsewhere in Asia. However, I believe the capabilities that Japanese researchers exhibit is in large part due to the high-quality natural science education they receive. Therefore, I have high expectations for Japanese researchers' active participation and dissemination of their work in international research forums.

The Importance of Returning to Basic Research

The new cabinet's decision to increase investment in basic research would seem to signal a strengthening of Japan's research environment. However, societal expectations tend to be biased towards tangible results such as the development of therapeutic drugs, diagnostic methods, and medical devices, making it difficult to properly convey the importance of basic research.

Very few studies in actual research yield immediate results; significant developments and applications arise only after the steady accumulation of knowledge through ongoing basic research. There are undoubtedly many basic research projects that contain the seeds of future achievements. While this may run counter to the trend of seeking short-term results, I believe it is crucial to invest heavily in basic research and create an environment where researchers can diligently pursue their work.

Expectations of Results from the ASPIRE Program

Several years ago at a University of Tokyo event, I heard many students speak of their "desire to study abroad in a country with a superior research environment." However, I don't think we can say that Japan's research environment is inferior. Moreover, studying abroad isn't just about going abroad—individuals must take what they learn overseas and bring it back to Japan and apply it in their research after returning. Taking part in joint research settings at major international research institutions conducting exchanges with many countries outside of Japan is highly significant for young researchers, as it can lead to the development of broader research networks. However, maintaining connections abroad after returning to Japan is more difficult than one might expect, and I hope that researchers will utilize ASPIRE's support to that end.

Greater numbers of people have been coming to Japan recently in order to work in Japan's research environment, and various research laboratories are continuing to respond with steps such as adopting English as the lab's official language. Japanese people are generally regarded overseas as having a high standard of education and being diligent workers, but perhaps due to their reserved nature and language barriers, fewer Japanese seem to excel at communication skills in comparison with individuals from other countries. There are, of course, Japanese people living overseas who have established a high reputation abroad, thus we need to develop strategies to increase the number of such individuals.

Current trends in scientific research include "group science," which re-examines the traditional model of individual research laboratories aiming for significant results independently, seeking to advance interdisciplinary research through collaboration among numerous researchers, and the concept of "open science," which not only involves utilizing data and technologies obtained during the research process in one's own papers, but also sharing these results with other researchers. We hope that researchers actively avail themselves of the ASPIRE program, which was designed with these trends in mind, to broaden Japan's core researchers' knowledge through international exchanges and publish research that renews Japan's impact on the world.

ASPIRE Management System

To efficiently utilize competitive research grants and produce outstanding results, AMED has assigned a Program Director (PD) to manage the integrated project, with a Program Supervisor (PS) and Program Officer (PO) being assigned to each of the component projects. Maintaining a grasp of the overall progress of ASPIRE, the Program Supervisor and Program Officers provide necessary guidance and advice to ensure project operations proceed smoothly.

Project for Basic Research for Medical Innovation (PJ6)

Program Director (PD)



KAGEYAMA Ryoichiro

Director
Center for Biosystems Dynamics Research
RIKEN

Program Supervisor (PS)



OKABE Shigeo

Director
Center for Brain Science
RIKEN

Program Officer (PO)



AKUTSU Hidenori

Director
Center for Regenerative Medicine/
Deputy Director
National Center for Child Health
and Development

PO for Alignment Research



SAITOH Noriko

Professor
Medical Institute of Bioregulation
Kyushu University

PO for Alignment Research



NISHIZONO Akira

Professor/Director
Research Center for GLOBAL and
LOCAL Infectious Diseases (RCGLID)
Oita University

PO for Alignment Research



NODE Koichi

President
Saga University

PO for Alignment Research



OKANO Hideyuki

Professor/Director
Regenerative Medicine Research Center
Keio University

PO for Japan-UK
Collaboration Research



SHIBATA Tatsuhiro

Professor
The Institute of Medical Science
The University of Tokyo

PO for Japan-France & Japan-Canada
Collaboration Research



TOYOOKA Shinichi

Professor
Graduate School of Medicine
Dentistry and Pharmaceutical Sciences
Okayama University

PO for Japan-Australia
Collaboration Research



NISHINA Hiroshi

Director General/ Professor
Medical Research Laboratory
Institute of Integrated Research
Institute of Science Tokyo

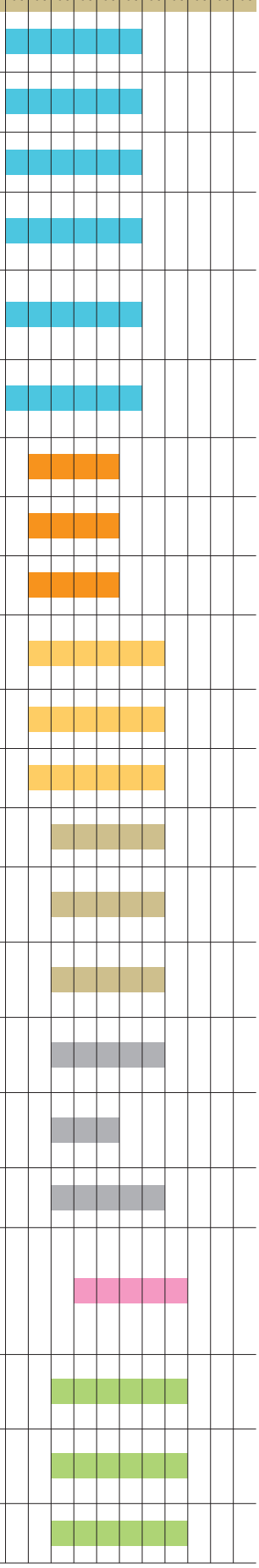
PO for Japan-Switzerland
Collaboration Research

As of October 2026

Awarded Projects

MISSION for the FUTURE

Call Number	Type	Principal Investigator	Affiliation	R&D Project	Partner Country	Year of Implementation
1st Call (Alignment Call)	A	IKAWA Masahito	The University of Osaka	International Collaborative Research Pioneering Next-Generation Assisted Reproductive Medicine	United States	
		SATO Kei	The University of Tokyo	The Pandemic 5W1H Investigation	United States, France	
		SHIRAHIGE Katsuhiko	The University of Tokyo	Chromatin Molecular Pathology for Precision Medicine	Sweden	
		WAKE Hiroaki	National Institute for Physiological Sciences	International Collaboration to Understand Physiological Mechanisms of Glial Cells and Their Pathological Transitions	Canada, Germany, Switzerland, United Kingdom	
	B	FUJIEDA Shigeharu	University of Fukui	Exploration of Personal Medical Strategies and Novel Therapeutic Targets Based on the Pathogenetic Mechanisms of Chronic Rhinosinusitis in Japanese and US Patients	United States	
		YAMAOKA Yoshio	Oita University	Understanding the Immune Responses That Develop Against the Gastric Oncopathogen *Helicobacter pylori* and Its Application to Immunotherapy	Sweden	
2nd Call (Japan-UK Joint Call)	B	ALEV Cantas	Kyoto University	Axioloid-Based Model of Human Kidney Development & Disease	United Kingdom	
		OHKAWA Yasuyuki	Kyushu University	Creating Anti-Senescence Cell Fate by Engineering the Chromatin Landscape	United Kingdom	
		SHIMIZU Yoshihiro	RIKEN	ACROPATH: Artificial Cells for highly sensitive and RObust diagnosis of PATHogen infections	United Kingdom	
3rd Call (Alignment Call)	B	ASAHARA Hiroshi	Institute of Science Tokyo	A Global Study Exploring Lifelong Health through the Maintenance, Promotion, and Restoration of Physical Functionality	United States	
		KOMURO Issei	The University of Tokyo	International Cardiovascular Digital Omics Consortium	United States	
		YOSHIDA Shosei	National Institute for Basic Biology	International and Interdisciplinary Research on Germ Cell Dynamics and Transgenerational Health Risks	United Kingdom, Germany	
4th Call (Japan-France Joint Call)	B	IWAMA Atsushi	The University of Tokyo	Understanding EZH2 Activities in Leukemia, a Potential Therapeutic Strategy	France	
		SETOU Mitsutoshi	Hamamatsu University School of Medicine	Uncovering the Roles of Lipids in the Effects of FLASH Radiotherapy, at the Cellular and Organ Level, to Develop New Lipid-Peptide Treatment	France	
		DAIGAKU Yasukazu	Cancer Institute, Japanese Foundation for Cancer Research	French-Japanese Consortium for Replication Stress-Induced Senescence and Anti-Cancer Immunity	France	
5th Call (Japan-Australia Joint Call)	B	KIKUCHI Kazu	National Cerebral and Cardiovascular Center Research Institute	Mechanisms Blocking the Repair of Mammalian Hearts After Injury: Using AI-Assisted Directed Evolution of Novel Biologics to Empower Regeneration	Australia	
		SUZUKI Yutaka	The University of Tokyo	CELLOGRAMRx: Pan-Cancer Cellular Composition and Signalling Relationship Mapping to Identify Novel Therapeutic Targets	Australia	
		MATANO Tetsuro	National Institute of Infectious Diseases	Control of Endemic HTLV-1 to Prevent Silent Global Spread	Australia	
6th Call (Japan-Canada Joint Call)	A	YACHIDA Shinichi	The University of Osaka	The ELDER Study: Timing Cancer by Tracking How Tissue-Specific Aging Shapes Malignancy	Canada	
7th Call (Japan-Switzerland Joint Call)	B	UEDA R. Hiroki	The University of Tokyo	From Sleep Dynamics to Inflammaging Control: A High-Throughput Systems Biology Initiative for Brain Aging	Switzerland	
		NAKANISHI Makoto	The University of Tokyo	Comprehensive Research on Inflammation and Aging with a Focus on the Role of cGAS-STING in Inflammation-Inducing cells	Switzerland	
		HONDA Kenya	Keio University	Modulating Inflammaging via Microbiome-Regulated Signaling in Hepatocytes and Kupffer Cells	Switzerland	



MISSION 01

Developing Safe Technologies for Pregnancy and Childbirth

JAPAN × USA

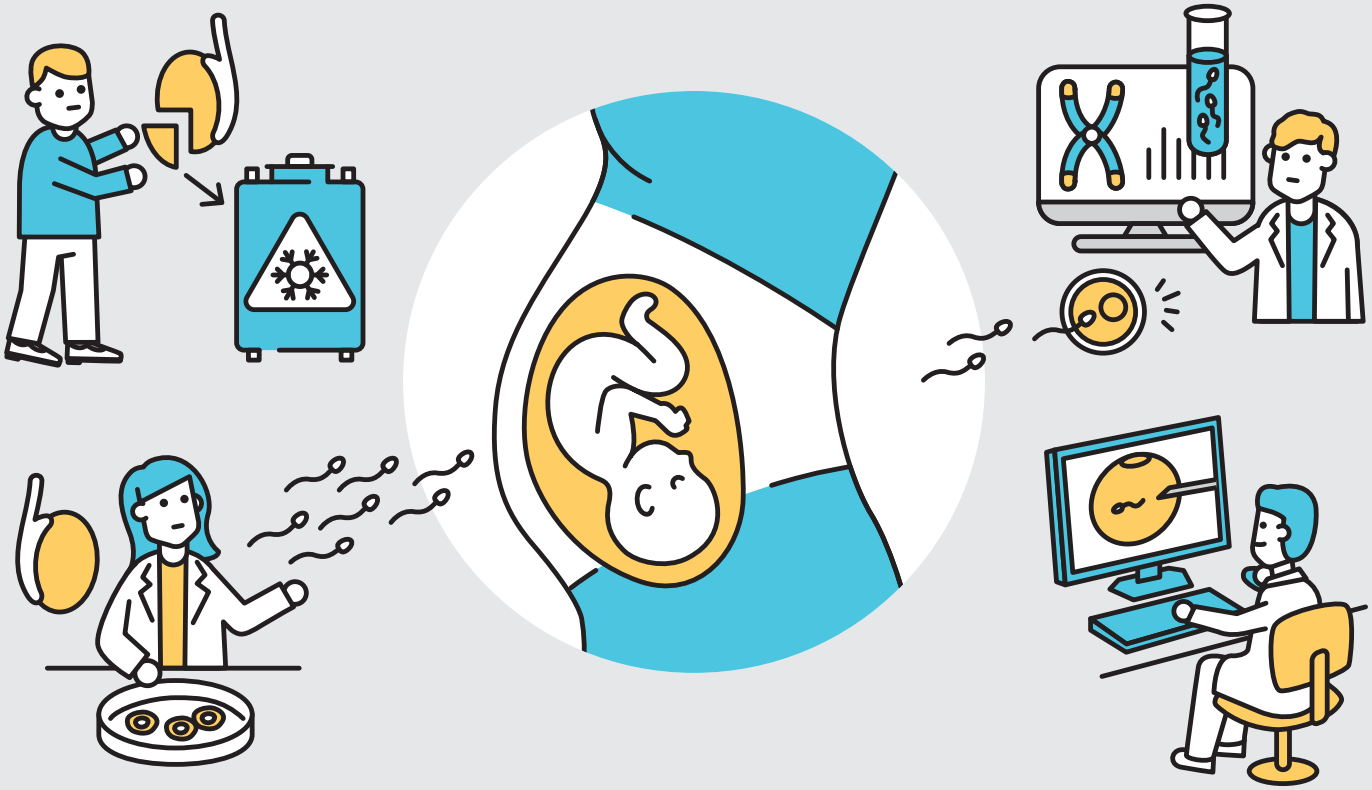
International Collaborative Research Pioneering Next-Generation Assisted Reproductive Medicine

Alignment A IKAWA Masahito

Year Awarded: FY2023	Domestic Research Institutions: Research Institute for Microbial Diseases, The University of Osaka; Graduate School of Medicine, The University of Osaka; Graduate School of Medicine, Kyoto University	Counterpart Research Institutions: (USA) Baylor College of Medicine; University of Pennsylvania	Research Period: FY2023-FY2028

TARGET

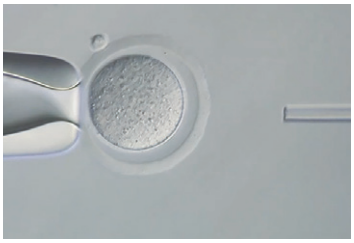
As Japan's trend towards delaying marriage and childbirth continues, it is said that one in five Japanese couples is now dealing with infertility. While aging and lifestyle habits are considered contributing factors, there are many cases where the causes are unknown, and further research is needed to clarify them. Research is underway to elucidate the molecular mechanisms of spermatogenesis and produce sperm from reconstructed testes. This research aims to clarify the impacts on the next generation and to restore the ability to produce sperm more safely.



KEY POINT

Reproductive Technologies for a Brighter Future

As assisted reproductive technology becomes more commonplace, assuring safety is a particularly important issue. In Japan, we are developing assisted reproductive technologies using germline stem cells and iPS derived somatic cells using mouse/rat and primate models. Efforts by our collaborating research partners in the United States include using genomic DNA modifications as markers in analyzing conditions in the regulation of gene expression and using DNA-encoding technology to develop pharmaceuticals. The two countries are working together to elucidate the mechanisms of sperm formation, maturation, and fertilization. This research is expected to assist not only men already struggling with infertility, but also those who, due to side effects from pediatric cancer treatments, are experiencing fertility problems. The findings are also expected to have applications for livestock and endangered wild animals. This research will help pave the way for safer assisted reproductive technologies in the future.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



IKAWA Masahito
Professor,
Research Institute for Microbial Diseases,
The University of Osaka



Marisa Bartolomei
Professor,
Perelman School of Medicine,
University of Pennsylvania



Martin Matzuk
Professor,
Center for Drug Discovery,
Baylor College of Medicine

TARGET

IN VITRO SPERMATOGENESIS

Understanding of and applications for spermatogenesis

METHODS

RECONSTRUCTION

- Inducing differentiation of testicular somatic cells
- Culturing sperm stem cells
- Culturing eminiferous tubules
- Performing epigenomic analysis
- Screening for small molecules

OUTPUT

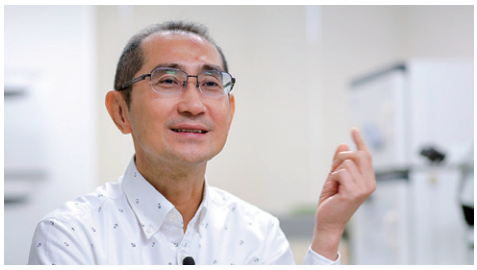
FERTILITY

- Developing safe next-generation assisted reproductive technologies
- Establishing testicular banking
- Preserving fertility for pediatric cancer survivors

INTERVIEW with IKAWA Masahito

Research Supported by Give-and-Take Relationships

I believe the appeal of collaborative research lies in leveraging each other's strengths and compensating for each other's weaknesses. Here in Japan, our team of three, including myself, work together in realizing each step in the production of sperm, starting with germ cells in a test tube. My laboratory has a strong advantage in technological development, particularly excelling at techniques such as in-vitro culturing of testicular tissue and restoring spermatogenesis through mRNA replacement therapy. Meanwhile, the researchers in U.S. excel in analyzing the effects of assisted reproductive technology on germ cells and developing molecules that function as drugs to treat those effects. We hope this collaboration results in treatments for infertility.





Meeting with Professor Matzuk during Osaka visit



Meeting with joint research partners from the U.S. Leveraging each other's strengths has a synergistic effect in helping overcoming male infertility.

Working to Establish Treatments for Male Infertility

Japan has subsidized public programs to help maintain fertility providing cryopreservation of ovaries, ova, and sperm. However, testis freezing is not yet eligible for subsidies, thus we cannot claim that adequate care is being provided to men with infertility. We are aiming at a future in which, for example, we can offer pediatric and AYA (adolescent and young adult) cancer patients various treatment options, cryopreserving testicular tissue and transplanting it back after cancer treatment, producing cultured sperm, and performing in vitro fertilization. Furthermore, while there were no existing treatments in cases where sperm cannot be produced due to genetically caused infertility, we demonstrated the efficacy of mRNA replacement therapy using mouse models. With our advanced assisted reproductive technology, Japan will lead the way in promoting research aimed at overcoming male infertility.

IKAWA Masahito
PROFILE

Prof. Ikawa graduated from The University of Osaka's Faculty of Pharmaceutical Sciences in 1992 and received his PhD in Pharmaceutical Sciences in 1997. He worked as a Japan Society for the Promotion of Science (JSPS) Research Fellow (DC1, PD) and in 1998 became a Research Associate at the Genome Information Research Center at The University of Osaka. He was appointed Associate Professor at The University of Osaka's Research Institute for Microbial Diseases (RIMD) in 2004, and has been a full Professor there since 2012. Born and raised in Osaka (only leaving Osaka for two years to study at the Salk Institute in the U.S.), he is extremely fond of "nikuman" pork buns and "takoyaki" octopus snacks. Specializing in approaches using genetically engineered mice, his research traces processes from fertilization to sperm maturation and spermatogenesis.

RESEARCH APPROACH

START 2023

The aim is to perfect a complete system for producing sperm from pluripotent stem cells in mice and to replicate this in primates (if possible, in humans). This also includes development of analytical and control technologies to ensure safety. Further aims include communicating with society, discussing the social and bioethical aspects to gain a deeper understanding of these issues, and establishing a testicular bank to preserve fertility for pediatric cancer survivors.

+ 5 YEARS

FUTURE

Pediatric cancer survivors who have completed treatment may not wish to have children for 10 or 20 years. To prepare for that day, the project aims to fully develop techniques for the cryopreservation and transplantation of testicular tissue, preparation and propagation of spermatogonial stem cells derived from testicular tissue as well as in vitro spermatogenesis techniques. Furthermore, the more profound understanding of spermatogenesis gained through this research is expected to contribute to the development of treatments for male infertility caused by other factors. We look forward to the next generation now being fostered through ASPIRE playing an active role in this endeavor.

MISSION 02

Uncovering Pandemic Characteristics and Preparing for Emergencies

JAPAN × FRANCE × USA

The Pandemic 5W1H Investigation

Alignment A SATO Kei

Year Awarded: FY2023	Domestic Research Institutions: The Institute of Medical Science, The University of Tokyo; Institute for Life and Medical Sciences, Kyoto University; Medical Research Laboratory, Institute of Integrated Research, Institute of Science Tokyo; National Research Center for the Control and Prevention of Infectious Diseases (CCPID), Nagasaki University; Hokkaido University International Institute for Zoonosis Control	Counterpart Research Institutions: (France) Institut Pasteur; (USA) Rocky Mountain Laboratories (RML)	Research Period: FY2023-FY2028

TARGET

Focusing on highly pathogenic viruses that infect humans via wild animals, this research is aimed at elucidating the “5W1H” (When, Where, Who, What, Why, How) of pandemics that may lead to drug development. We are collaborating with world-leading scientists and fostering young researchers in the aim of preparing for a pandemic that could occur at any time. Based on the foundation established by “G2P-Japan,” an organization of young Japanese researchers, we have established a research system on par with those in Europe and the United States.



KEY POINT

Preparing for the Next Pandemic by Thoroughly Investigating the “5W1H” of Pandemics in Collaboration with Researchers from Diverse Fields

The “When/Where” team is conducting fieldwork to identify highly pathogenic viruses carried by bats, ticks, and other organisms. The “Who/What/Why” team investigates the pathogenicity of these viruses and the efficacy of drugs and antibodies, while the “How” team is tasked with creating the actual drugs and antibodies. Under this arrangement, collaborators from different countries are working together to elucidate the 5W1H of pandemics. During the then-expanding COVID-19 pandemic, Japan experienced periods when labor shortages caused research to lag, making it difficult to conduct experiments as intended. This is precisely why collaborations with a wide range of researchers towards a common goal is so important.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



SATO Kei
Professor,
The Institute of Medical Science,
The University of Tokyo



Anavaj Sakuntabhai
Professor, Institut Pasteur



Andrea Marzi
Senior Investigator,
National Institutes of Health, Rocky Mountain Laboratories (RML)

TARGET

VIRUS

Focusing on viruses with presumed high pandemic potential that are transmitted from the environment (e.g., wild animals) to human society.

METHODS

EXPLORATION

- Conducting virus discovery and selection through fieldwork
- Elucidating pathogenicity, drug resistance, and immune resistance
- Conducting antibody-based drug discovery research based on structural biology

OUTPUT

PREDICTION

- Conducting drug discovery and constructing pandemic prediction models
- Developing novel therapies, primarily based on antibodies
- Understanding the time, locations, factors, and mechanisms (When/Where/Who/What/Why/How) of pandemics

INTERVIEW with SATO Kei

Interdisciplinary Collaboration in Facing an Unprecedented Crisis

I originally specialized in HIV (AIDS virus) research, but after witnessing the course of the COVID-19 pandemic, I wanted to contribute using a virologist's perspective. The first thing to do is to investigate the risk of the pathogen. In this field, where the differentiation of target viruses is relatively clear, I'd say that being able to apply my own research methods while working in collaboration with various researchers was highly significant.





A scene from the lab: wet team conducting experiments using actual animals and cells



International conference on Awaji Island

Sustainable Research Environment and Experience Overseas Key to Human Resource Development

Using COVID-19 as an example shows that suspending research just because the pandemic has subsided does not do anything for human resource development. ASPIRE has enabled us to address the problem start to finish, working on everything from virus discovery to drug development, which is possible only in an environment where research can be sustained. ASPIRE is also useful in helping young researchers gain international experience. There are many international students in my lab, and conversations in English are a daily occurrence. I definitely want them to become accustomed to English in this environment and then go abroad to practice their skills.

SATO Kei
PROFILE

Born in Yamagata Prefecture in 1982, Prof. Sato received his Ph.D. in Medicine in 2010 (graduating early) at the Graduate School of Medicine, Kyoto University. After serving as an Assistant Professor at the Institute for Virus Research, Kyoto University, in 2018 he was appointed Associate Professor (Principal Investigator) at the International Research Center for Infectious Diseases in The University of Tokyo's Institute of Medical Science. He become a Professor in the Division of Systems Virology at The University of Tokyo's Institute of Medical Science in April of 2022. He is a recipient of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) Young Scientists' Award (2020), the Japan Society for the Promotion of Science (JSPS) Prize (2023), and other awards. He is the Director of G2P-Japan.

START 2023 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

In preparation for the next pandemic, the lab will collaborate with other international organizations, conducting the full range of research, from fieldwork to laboratory analysis. Tasks include collecting samples from animals, identifying unknown viruses through isolation, culture, and metagenomic analysis, and sharing identified high-risk candidates. Organoids (mini-organs) and animal models will be used in evaluating the infectivity and pathogenicity of bat-derived viruses and hemorrhagic fever viruses as the team concurrently verifies optimal therapeutic agents, takes part in international conferences, and continues with human resource development.

The aim is to establish a comprehensive, integrated system ranging from researcher training to drug development, and to be fully prepared to respond to the next pandemic.

MISSION 03

Unraveling Folded DNA Information with the Aim of Developing Precise Treatments Tailored to Each Individual Patient

JAPAN × SWEDEN

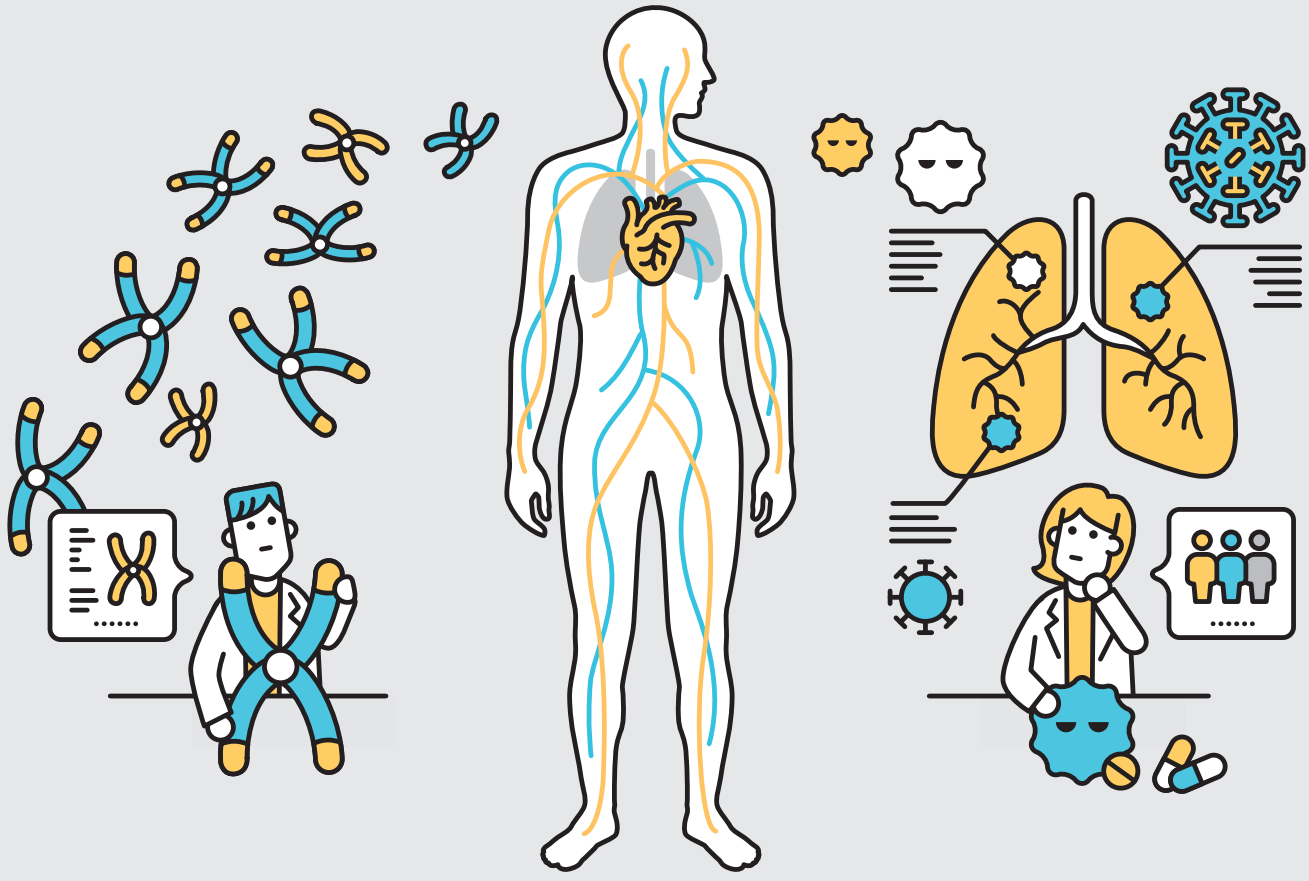
Chromatin Molecular Pathology for Precision Medicine

Alignment A SHIRAHIGE Katsuhiko

Year Awarded: FY2023	Domestic Research Institutions: Institute for Quantitative Biosciences (IQB), The University of Tokyo; Graduate School of Medicine, The University of Tokyo; Graduate School of Frontier Sciences, The University of Tokyo	Counterpart Research Institution: (Sweden) Karolinska Institutet	Research Period: FY2023-FY2028

TARGET

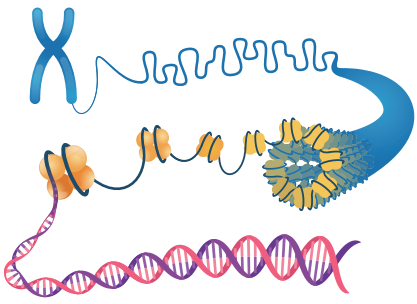
DNA exists within cells in the form of chromatin, but to activate the genes necessary for treating diseases, the DNA must be unwound and put in a readable form. “Enhancers”—genetic switches located within the chromatin—facilitate this unwinding process. This research investigates in detail how chromatin is produced by folding DNA and how genetic switches are activated.



KEY POINT

Developing Therapies Targeting Chromatin, Which Governs How Genes Function

This research focuses on the structure of chromatin, which is formed from DNA wrapped around proteins. The concept here is that concentrating on chromatin—a fundamental unit of genetic organization—will lead to the development of treatments for diseases linked to abnormalities in chromosomes (packages of coiled chromatin), such as cancer, heart disease, and blood disorders. Since gene activity is determined by genetic switches (enhancers) within chromatin toggling on and off, this research aims to elucidate how the mechanisms of these switches induce disease. The aim is to control these switches artificially with the goal of realizing precision medicine tailored to each individual to prevent or cure diseases.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



SHIRAHIGE Katsuhiko
Professor, Advanced Quantitative Life Sciences Division,
Institute for Quantitative Biosciences (IQB),
The University of Tokyo/ Visiting Professor, Karolinska Institutet



Camilla Björkegren
Professor, Department of Cell and Molecular Biology Karolinska Institutet/
Visiting Professor, Institute for Quantitative Biosciences (IQB),
The University of Tokyo

TARGET

CHROMATIN

Analyzing the mechanisms of enhancers and chromatin compaction

METHODS

ENGINEERING

- Predicting and designing enhancers with enhancer generators
- Artificially inducing chromatin compaction at targeted loci
- Enhancing single-cell and spatial analysis techniques
- Integrating AI, information science, and experimental science

OUTPUT

PRECISION

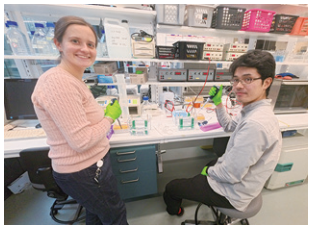
Seeking to develop technologies for precision medicine through disease stratification and the establishment of "chromatin molecular pathology"

INTERVIEW with SHIRAHIGE Katsuhiko

Tailored Medical Care Using Clues from Individuals' Genome Sequences

This research is informed by my curiosity as to how DNA is copied and passed on to the next generation. Now adding AI to the genome analysis technologies we have developed this far, our aim is to assess disease risks and symptoms based on an individual's genome sequence, and then be able to provide individually personalized medical care.





At Karolinska Institutet



The lab hosts many international researchers, including a number who have transferred from Karolinska Institutet.

Urging Young Researchers to Gain Experience Abroad

Our collaborating partner, Karolinska Institutet, has highly versatile technologies that produce data of superior quality and quantity compared to what we could generate in Japan alone, which benefits us tremendously. In contrast to Japan, where research concepts are emphasized, our partners have a clear focus on technological development, with the widespread mindset that technological capability is what reveals the next stage of science. Their take on research itself and uptake in society differ significantly from Japan's approach, creating a stimulating and motivating environment where there is always someone at the next desk writing cutting-edge research papers. This is the kind of environment that I hope young Japanese researchers will dive right into.

SHIRAHIGE Katsuhiko
PROFILE

Professor and Director of the Institute for Quantitative Biosciences at The University of Tokyo, Dr. Shirahige is also a Visiting Professor at Karolinska Institutet. After earning his Ph.D. in Medical Science from Osaka University, he held positions at Nara Institute of Science and Technology (NAIST), RIKEN, Tokyo Institute of Technology, and the Institute of Molecular and Cellular Biosciences before assuming his current role. He has also served as President of the Molecular Biology Society of Japan (2021–2022). Dedicated to grasping the "big picture" of biological phenomena through genome analysis, he discovered the function of cohesin and the roles of cohesin in chromosome and chromatin architecture. Dr. Shirahige now aims to develop an AI environment for use in this research.

START 2023 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

Work includes detailed analyses of the mechanisms of the switches regulating gene function (enhancers) as well as the arrangement of and differences between cells within cancerous tissues. It is hoped that spatially visualizing gene activity in each cell will reveal the reasons behind individual differences in cancer and other diseases. These insights will be the basis for exploring technologies to artificially regulate gene function and investigate potential pathways to new therapies. A foundation for sustainable research will be established through international collaboration and development of young researchers.

The aim is to be able to examine individuals' personal genome sequences and provide customized medical care based on treatment strategies tailored to each person.

MISSION 04

Targeting Brain Immune Cells Toward New Therapies for Neurological and Psychiatric Disorders

JAPAN × CANADA × GERMANY × SWITZERLAND × USA × UK

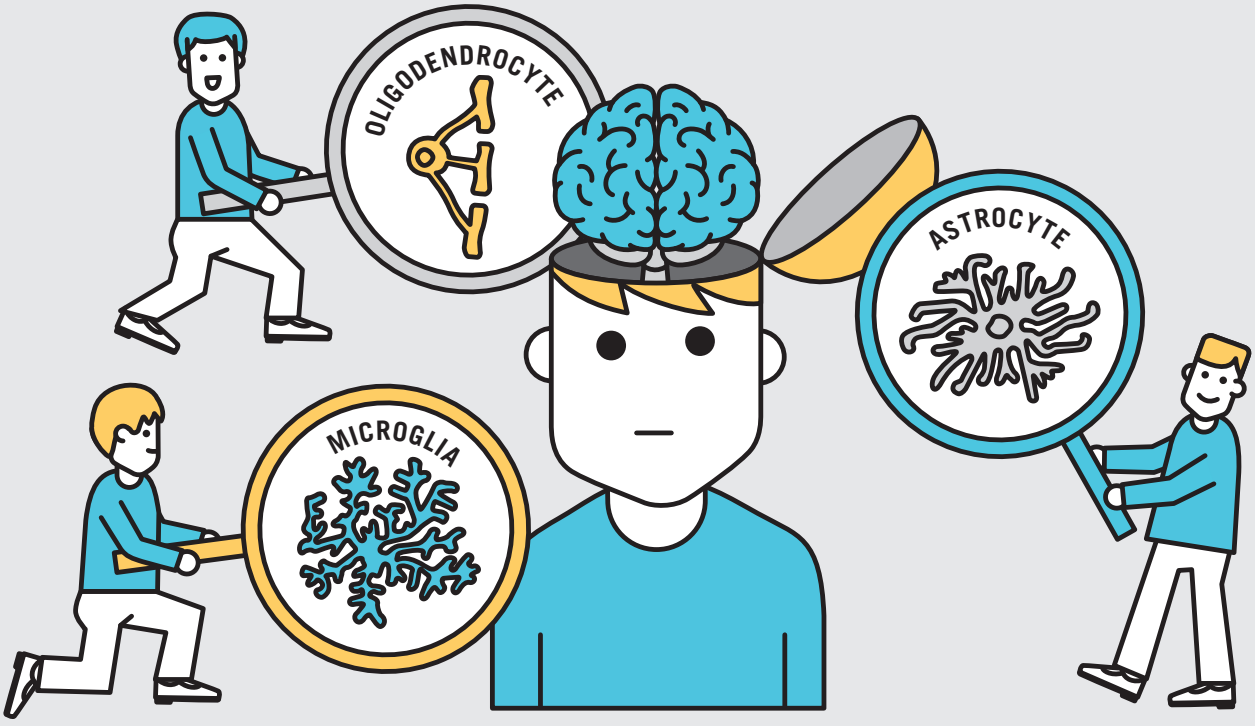
International Collaboration to Understand Physiological Mechanisms of Glial Cells and Their Pathological Transitions

Alignment A WAKE Hiroaki

Year Awarded: FY2023	Domestic Research Institutions: National Institute for Physiological Sciences; Center for High-Depth Omics Science, Medical Institute of Bioregulation, Kyushu University; National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP); Graduate School of Medicine, The University of Tokyo; Graduate School of Medicine, Nagoya University; Graduate School of Medicine, University of Yamanashi; RIKEN Center for Brain Science (CBS)	Counterpart Research Institutions: (Canada) Victoria University; Research Institute of the McGill University Health Centre; (Germany) Max Planck Institute for Biology of Ageing; Medical Center - University of Freiburg; (Switzerland) University of Lausanne; (UK) UK Dementia Research Institute at Cardiff University; (USA) Icahn School of Medicine at Mount Sinai	Research Period: FY2023-FY2028

TARGET

The biological brain is composed of neurons and glial cells, which support neuronal function. While glial cells were previously considered to play only a support role, recent research has revealed that they actively influence neural circuits. Elucidating these functions through various approaches is expected to contribute to the treatment of conditions such as dementia, developmental disorders, and psychiatric diseases.



KEY POINT

Making Full Use of in Vivo Imaging in Understanding the Characteristics of Microglia

Glial cells are classified into three types: oligodendrocytes, which assist in neuronal signal transmission; astrocytes, which support networks of neural circuits; and microglia, which reside in the central nervous system and are responsible for immune functions. Using state-of-the-art microscopy employing lasers to observe living organisms (in vivo imaging), researchers have discovered that microglia play a crucial role in the formation of connections (synapses) between neurons and are involved in the remodeling of neural circuits and the removal of synapses with abnormal activity. Research is currently underway to explore how maintaining microglial health may help preserve overall brain health.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



WAKE Hiroaki
Professor, Division of Basic NeuroscienceNational Institute for Physiological Sciences

Keith Murai
Professor, McGill University

Marie-Ève Tremblay
Professor, Victoria University

Rosa Chiara Paolicelli
Assistant Professor, University of Lausanne

Anne Schaefer
Director, Max Planck Institute for Biology of Ageing, Icahn School of Medicine at Mount Sinai

Marco Prinz
Professor, University of Freiburg

Baljit S Khakh
Professor, UK Dementia Research Institute at Cardiff University

TARGET
GLIA
Comprehensive targeting of microglia, astroglia, and glia in disease models

METHODS
IMAGING
Conducting in vivo imaging, super-resolution microscopy, visualization and manipulation of cellular activity, and integrated profiling

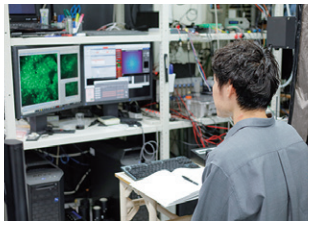
OUTPUT
MECHANISM
Aiming to elucidate metabolic mechanisms and their relationships to synapses and the underlying mechanisms of brain function and disease

INTERVIEW with WAKE Hiroaki

From a Single Channel to an International Network: Fostering Organic Relationships Based in Japan

It all began with a joint seminar with Germany in 2013. Since 2018, our exchanges have expanded to include Canada, the United States, and Denmark. The program involves young researchers discussing proposals for international collaborative research and receiving evaluations at progress report meetings. Many research projects prompted by this initiative have led to published papers. Furthermore, given the stimulation of these young researchers' international activities, this ASPIRE program is a bold step in reenergizing participants. Having grown personally through such person-to-person interactions, I hope to pass the torch on to the next generation.





Analyzing images obtained with microscopy. Cell images are colored and analyzed on a monitor screen.



Dinner gathering with researchers from abroad

A Future Where Diseases Can Be Treated Through Manipulation of Glial Cells

The rising number of people unable to work due to mental illness poses a major societal problem. The complex interplay of genetics, lifestyle, and other factors underlying these conditions makes them difficult to cure using a single approach. Therefore, we aim to develop a new approach to therapy that targets neurological disorders such as Alzheimer's and Parkinson's diseases through the regulation of the glial cells that support brain function.

WAKE Hiroaki
PROFILE

2001: Graduated from Graduate School of Medical Sciences and Medical School, Nagoya City University; 2007: Completed doctoral program at Nagoya City University Graduate School of Medical Sciences (Ph.D. in Medicine); 2007: CREST Researcher, National Institute for Physiological Sciences (NIPS); 2009: Visiting Fellow, National Institutes of Health (NIH), USA; 2012: Assistant Professor, National Institute for Basic Biology (NIBB), National Institutes of Natural Sciences (NINS); 2013: Researcher, PRESTO Sakigake (concurrent); 2014: Associate Professor, NIPS, NINS; 2016: Professor, Division of System Physiology, Kobe University Graduate School of Medicine; 11/2019: Professor, Department of Molecular and Cellular Biology, Nagoya University Graduate School of Medicine; Specially Appointed Professor, Organization for Advanced and Integrated Research, Kobe University (concurrent/cross-appointment); 9/2021: Professor, Department of Molecular and Cellular Biology (Functional Morphology), Nagoya University Graduate School of Medicine; Professor, Division of Multicellular Circuit Dynamics, National Institute for Physiological Sciences (NIPS), NINS (concurrent/cross-appointment); Specially Appointed Professor, Organization for Advanced and Integrated Research (OAIR), Kobe University (concurrent/cross-appointment); 9/2022: Professor, Department of Molecular and Cellular Biology, Nagoya University Graduate School of Medicine; Professor, Division of Multicellular Circuit Dynamics, National Institute for Physiological Sciences (NIPS), NINS (concurrent/cross-appointment); Specially Appointed Professor, Center of Optical Scattering Image Science, Kobe University (concurrent/cross-appointment)

START 2023

+ 5 YEARS

FUTURE

RESEARCH APPROACH

Partnering with international researchers, this program will combine high-performance microscopy, gene function analysis techniques, and animal studies to investigate brain mechanisms and the causes of disease. Studies will involve a comprehensive examination of how brain cells change according to the stage of development and sensory differences, clarify their relationship with developmental disorders and mental illnesses. Insights gained are expected to lead to new therapeutic approaches and medical treatments in the future.

This research aims to increase the prospects for treatments for Alzheimer's and Parkinson's diseases and other neurological disorders, and further establish methods to treat psychiatric disorders merely by manipulating glial cells.

05 MISSION

Leveraging a Variety of Analysis Technologies to Resolve Patients' Nasal Problems

JAPAN × USA

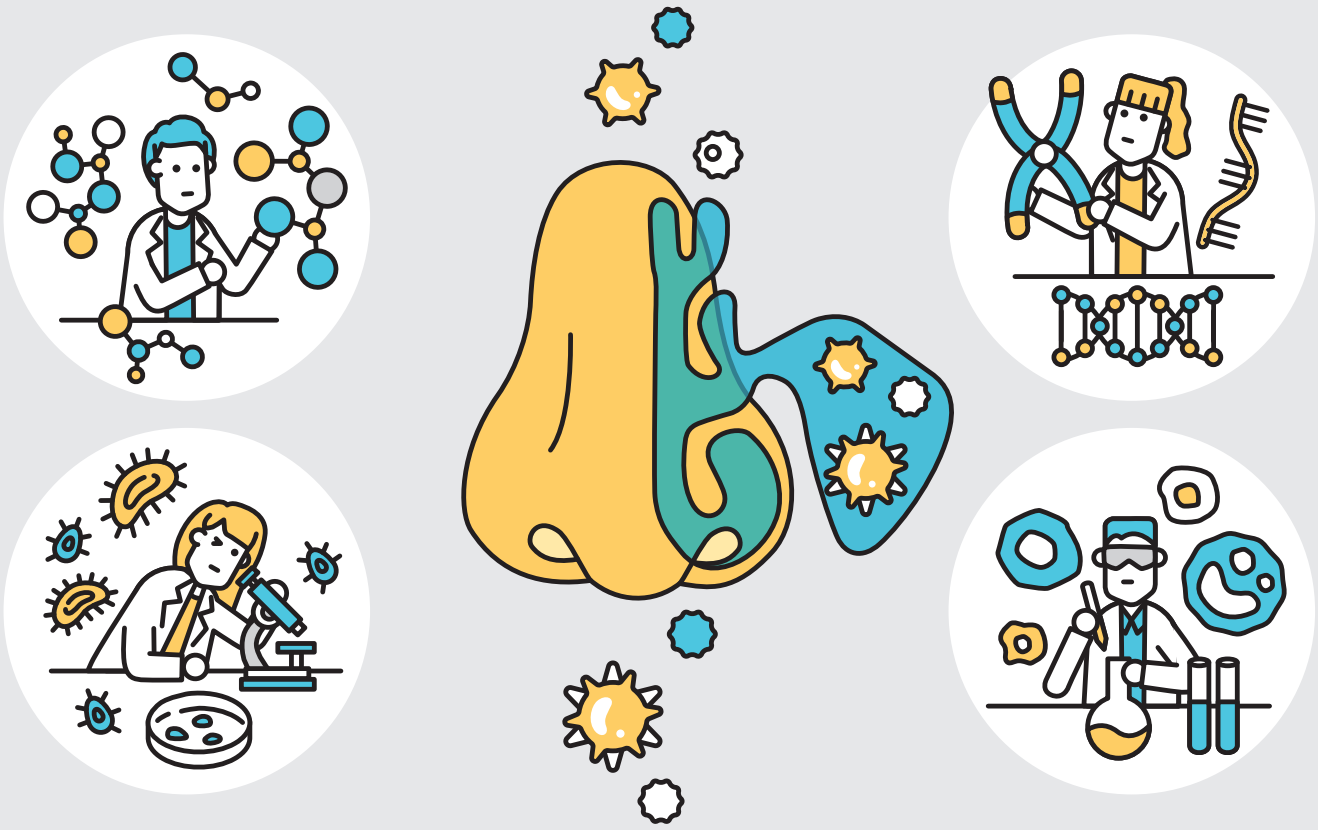
Exploration of Personal Medical Strategies and Novel Therapeutic Targets Based on the Pathogenetic Mechanisms of Chronic Rhinosinusitis in Japanese and US Patients

Alignment B FUJIEDA Shigeharu

Year Awarded: FY2023	Domestic Research Institutions: Faculty of Medical Sciences, University of Fukui; School of Medicine, International University of Health and Welfare	Counterpart Research Institution: (USA) Northwestern University	Research Period: FY2023-FY2028

TARGET

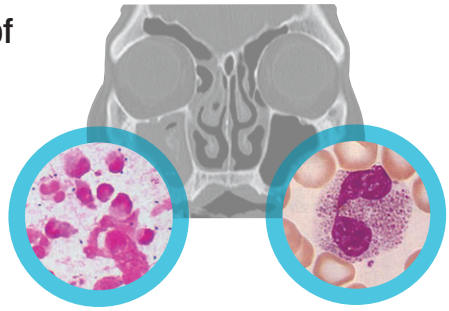
Rhinosinusitis (empyema) is a condition wherein pus accumulates in the nasal cavities, causing symptoms such as olfactory dysfunction, runny nose, and nasal congestion. This has traditionally been treated with antibiotics or surgery, but recent years have seen an increase in patients with a new type of rhinosinusitis that rapidly recurs, even after surgery. A type of white blood cell known as eosinophil plays a major role in this condition. Research into treatments for this new eosinophilic rhinosinusitis is currently underway, utilizing various methods to study the nasal microbiome.



KEY POINT

Developing New Treatments Through Analysis of Genetic-Level Inflammatory Mechanisms

In patients with rhinosinusitis, the nasal mucosa becomes inflamed, sometimes leading to the formation of sticky, jelly-like polyps. Researchers are conducting detailed analyses of the bacteria and fungi present in mucosal tissue and polyps collected from patients, examining their types, balance, functions, and surrounding environments as they elucidate the causes of rhinosinusitis that recurs even after surgery (eosinophilic rhinosinusitis). Methods for diagnosing and assessing the severity of eosinophilic rhinosinusitis have already been established, and analyses using this data are currently underway. Furthermore, the program is developing "personalized medicine" with treatments tailored to each patient's specific type of inflammation and genetic profile with the aim of releasing patients from nasal ailments and enabling them to lead comfortable daily lives.



Ordinary rhinosinusitis

Rhinosinusitis with nasal polyps

Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



FUJIEDA Shigeharu
Director, University of Fukui Hospital/
Professor, Division of Otorhinolaryngology Head & Neck Surgery, University of Fukui



KATO Atsushi
Associate Professor, Division of Allergy and Immunology, Northwestern University Feinberg School of Medicine

TARGET
SINUSITIS
Chronic Rhinosinusitis

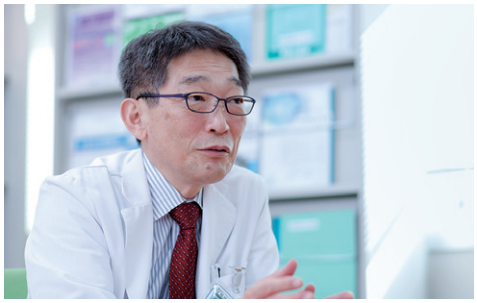
METHODS
MULTI-OMICS
Utilizing techniques including bulk RNA analysis, DNA analysis, microbiome analysis, single-cell RNA analysis, and spatial transcriptomics

OUTPUT
SUBTYPE
Using endotype and genotype analysis in classifying diseases, with applications in personalized medicine

INTERVIEW with FUJIEDA Shigeharu

Answering Unsolved Mysteries to Achieve a Fundamental Cure for Rhinosinusitis

We still do not know what causes intractable (eosinophilic) rhinosinusitis. While symptoms can be suppressed with continued injections of antibody drugs, the high costs of these drugs are a major burden for patients. Our goal is not merely to introduce "good germs" and kill "bad germs," but to actually cure rhinosinusitis by cultivating an environment within the nasal cavity that fosters healthy bacterial flora.





Analysis of clinical samples; the analyzed data is used in joint research abroad.



At an international conference

Discovering New Perspectives and Approaches Through Comparative Analysis with the U.S.

The nature of rhinosinusitis found in Japanese patients has changed recently, making it particularly difficult to treat. We are now seeing an increase in types that were previously rare among the Japanese population but common among patients in Europe and the U.S. This fact is also highly significant to our joint research with the U.S., and we are proceeding with studies involving genetic analysis of RNA extracted from Japanese samples, bringing the data to the U.S., and comparing the results with analyses of clinical samples obtained locally. Beyond the differences in the nature of the disease itself, the contrasting approaches to research also offer fascinating insights for joint research. It is interesting how each partner has different priorities and areas where they are more flexible, revealing new perspectives and providing inspiration I wouldn't have found in a community made up solely of Japanese researchers.

FUJIEDA Shigeharu
PROFILE

Prof. Fujieda is leading researcher in the field of rhinosinusitis disorders, including intractable eosinophilic chronic rhinosinusitis and Japanese cedar pollinosis, a condition that is considered a "national affliction" in Japan. In aiming to overcome these disorders, he applies various methods that include genetic analysis, microbiome and omics analysis, and novel antibody drugs. Prof. Fujieda graduated from Fukui University of Medical Science (now University of Fukui) in 1986. In 1994, he began a two-year period studying molecular biology at UCLA in the United States. In 2002, he became a Professor of Otorhinolaryngology at the University of Fukui Faculty of Medical Sciences. He was appointed Dean of the Graduate School of Medical Sciences in 2021 and became Director of the University of Fukui Hospital (and University Vice President) in 2025.

START 2023 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

The research will include multi-omics analysis (comprehensive analysis of diverse biological data) to examine the genetic backgrounds of patients with eosinophilic chronic rhinosinusitis, gene expression in various cell types, and the status of bacterial and fungal communities. The resulting data will be applied in developing new therapeutic methods designed to restore a healthy, comfortable nasal environment. Researchers will also evaluate and verify new drug candidates with the aim of establishing promising treatments for intractable forms of the disease. Efforts to deepen international collaborations will continue throughout the project period, along with initiatives to foster the next generation of young researchers.

The aim is to treat intractable chronic rhinosinusitis by artificially recreating within the nasal cavity the kind of environment that exists when bacteria and other microorganisms function in a well-balanced state.

06 MISSION

Preventing *H. pylori* Infection Through Vaccine Development

JAPAN × SWEDEN

Understanding the Immune Responses That Develop Against the Gastric Oncopathogen *Helicobacter pylori* and Its Application to Immunotherapy

Alignment B YAMAOKA Yoshio

Year Awarded: FY2023	Domestic Research Institutions: Faculty of Medicine, Oita University; Research Center for GLOBAL and LOCAL Infectious Diseases (RCGLID), Oita University	Counterpart Research Institution: (Sweden) Umeå University	Research Period: FY2023-FY2028

TARGET

Helicobacter pylori is a pathogenic bacterium that infects nearly half of the world's population. Infection causes inflammation and atrophy of the gastric mucosa and can lead to cancer and other diseases. This research focuses on the more than 60 types of outer membrane proteins expressed by *H. pylori*. Using the combined outer membrane proteins discovered by the Japanese and Swedish teams, the project aims to develop a vaccine that prevents the bacterium from adhering to the gastric mucosa.



KEY POINT

Combating Drug-Resistant *Helicobacter pylori*, Supporting Prevention and Treatment of Gastric Diseases Worldwide

Antibiotic-based eradication therapy has long been the standard treatment for *H. pylori* infection. However, the increasing prevalence of antimicrobial-resistant strains has created an urgent global need for new treatment strategies. Because the pathogenicity, genetics, and protein structures of *H. pylori* vary by region, collecting samples from multiple locations is highly effective. The joint research being conducted in Japan and Sweden leverages each team's respective strengths in areas such as genomic analysis and the functional and structural analysis of outer membrane proteins. Research into development of a vaccine continues to advance, with the ultimate goal being to reduce the incidence of *H. pylori* infection, improve the efficacy of eradication therapies, and decrease mortality rates associated with gastric cancer and other *H. pylori*-related diseases.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



YAMAOKA Yoshio
Professor, Department of Environmental and Preventive Medicine, Faculty of Medicine, Oita University



Thomas Borén
Professor, Department of Medical Biochemistry and Biophysics, Umeå University

TARGET

H. PYLORI

- *Helicobacter pylori*: cause of gastric cancer and gastric/duodenal diseases
- Utilizing Japan's collection of clinical *H. pylori* isolates, the world's largest
- OipA and BabA: proteins discovered by the Japanese and Swedish teams

METHODS

ADHESION

- Analyzing the adhesion mechanism between *H. pylori* outer membrane proteins and host cell surface glycans
- Aiming to prevent *H. pylori* from adhering to the gastric mucosa
- Conducting basic experiments for outer membrane protein vaccines

OUTPUT

VACCINE

- Developing novel vaccines and antibody drugs to prevent *H. pylori* infection
- Establishing treatment and prevention strategies to combat antimicrobial-resistant strains

INTERVIEW with YAMAOKA Yoshio

Collaboration Between Developed Countries Results in a New Approach

Our previous joint research focused primarily on human resource development in developing countries. In partnering with a developed nation, as we are with this project, we are not only teaching but also learning a great deal from our counterparts, which provides us with a different sort of intellectual stimulus. Our strengths lie in our world's largest *H. pylori* strain collection and our extensive expertise in genomic analysis and genomic epidemiology. Meanwhile, the Swedish team has established an experimental system using mice, enabling them to make precise evaluations in conditions close to those in a human environment. Combining bacterial diversity with an experimental model that closely resembles humans has produced a research approach unlike any before it.





The laboratory has a distinctively international character. Lively discussions take place during regular meetings, with Professor Yamaoka actively participating.



At Professor Borén's laboratory

Identifying Cancer-Causing Genes and Linking Them to Vaccine Development

One of our primary goals is to identify genes within *H. pylori* that are likely to cause cancer. Through years of research, the Japanese team discovered the protein OipA, while the Swedish team discovered BabA. These discoveries have helped establish both teams as leaders in the field. We are fully leveraging an interdisciplinary research approach spanning molecular biology, genomic science, and immunology with the aim of progressing toward vaccine development. We envision a future where affordable vaccines are widely available and routinely administered, even in developing nations.

YAMAOKA Yoshio
PROFILE

Prof. Yamaoka is Vice President of Oita University (International Strategy) and heads the university's Crisis Management Organization. A Professor in the Department of Environmental and Preventive Medicine at Oita University, he also holds the position of Professor in the Department of Gastroenterology at the Baylor College of Medicine (USA). Specializing in *Helicobacter pylori* virulence, drug resistance, and genomic epidemiology, he promotes international collaborative endoscopy-based research in Asia and Africa. He maintains the world's largest collection of *H. pylori* strains, comprising more than 10,000 isolates. Building upon his research into OipA and other outer membrane proteins, Dr. Yamaoka leads a joint Japan-Sweden initiative to develop a practical vaccine, aiming to prevent stomach cancer and other gastric diseases.

START 2023

+ 5 YEARS

FUTURE

RESEARCH APPROACH

The project will continue to evaluate the efficacy of OipA and BabA as vaccine antigens and verify the inhibitory effect of their combination on *H. pylori* adhesion using mouse models. Following in vivo adhesion inhibition testing with antibodies against these outer membrane proteins, the results will be compared with those from the joint research partners. The project is also committed to fostering young researchers and facilitating personnel exchanges through seminars and collaboration with the National Institutes of Health (*H. pylori* Genomics Group) in the United States.

The aim is to contribute to public health by providing the world with new countermeasures against *H. pylori*, including strategies to combat drug-resistant strains.

07 MISSION

Developing Axioloid Models of Human Kidney Development and Disease

JAPAN × UK

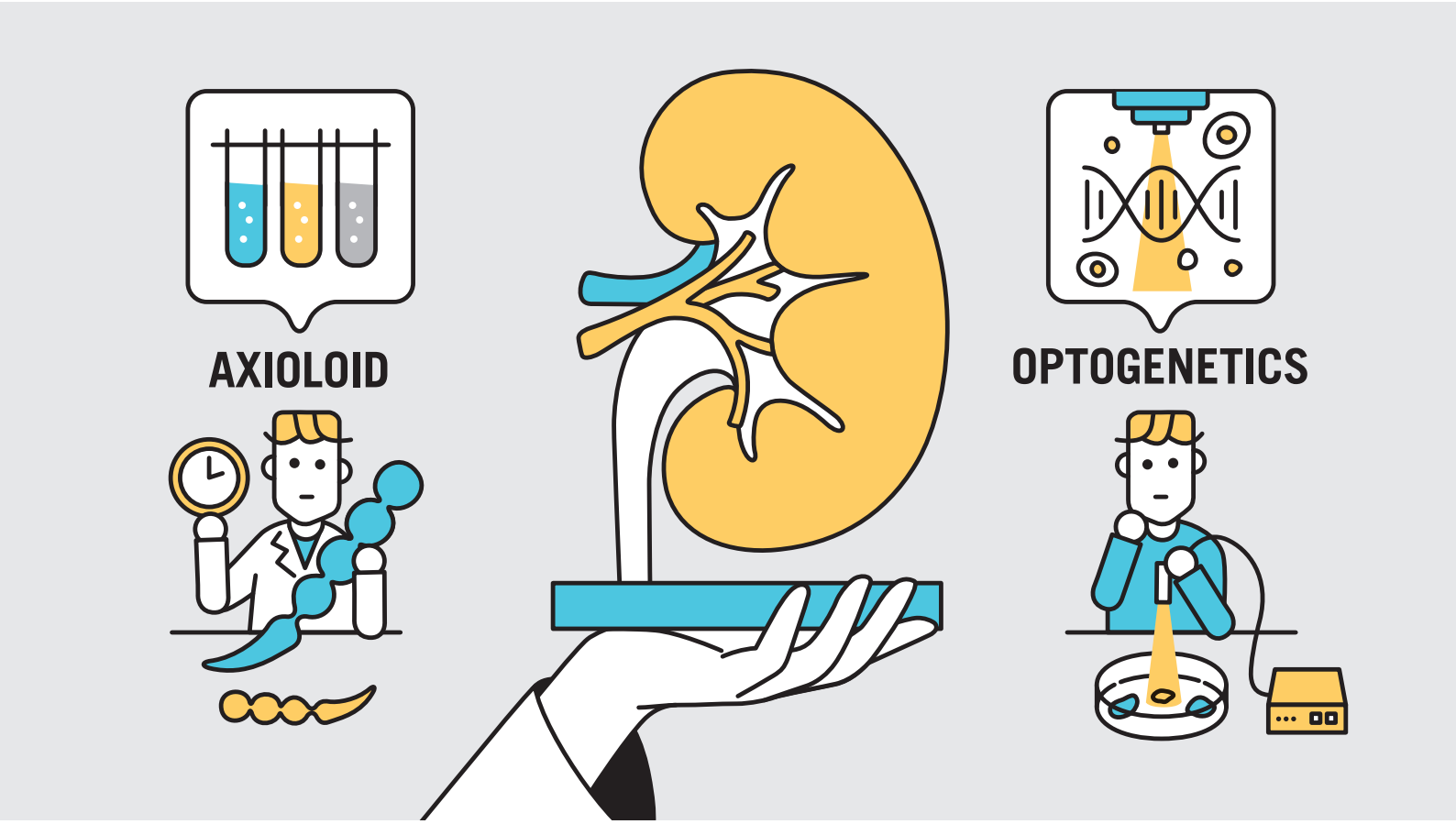
Axioloid-Based Model of Human Kidney Development & Disease

Japan-UK Joint Research ALEV Cantas

Year Awarded: FY2024	Domestic Research Institutions: Institute for Advanced Study (KUIAS), Institute for the Advanced Study of Human Biology (WPI-ASHBi), Kyoto University; Graduate School of Biostudies, Kyoto University	Counterpart Research Institution: Centre for Discovery Brain Sciences (CDBS), The University of Edinburgh	Research Period: FY2024-FY2027

TARGET

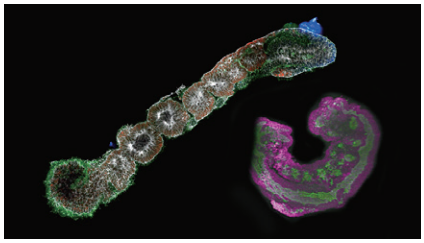
Human pluripotent stem cells, including induced pluripotent stem (iPS) cells, can be differentiated into kidney cell types to study aspects of kidney development and disease in vitro. In this Japan–UK project, the Alev Lab at ASHBi, Kyoto University, and the Davies Lab at the University of Edinburgh aim to extend axioloid-based developmental models to generate kidney progenitors and early kidney tissues. Building on the axioloid model, the researchers will investigate how kidney tissues form and work towards establishing models that capture key features of kidney development and disease, with the long-term goal of supporting the development and evaluation of new therapeutic approaches.



KEY POINT

Studying Kidney Development and Disease Using Human Pluripotent Stem Cells

iPS cells are generated by reprogramming somatic cells, such as skin or blood cells, into a pluripotent state. They can then be directed to form a wide range of cell types, including kidney cells. Axioloids are three-dimensional pluripotent stem cell-derived in vitro models that reproduce aspects of early body-axis development, particularly somite formation. Somites are embryonic structures that contribute to the vertebrae and skeletal muscles; kidneys arise from a distinct mesodermal population, the intermediate mesoderm. This project aims to extend the axioloid approach to include intermediate mesoderm and kidney progenitors by controlling developmental signals in space and time. Patient-derived iPS cells could subsequently be used to study disease-associated changes in these processes.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



Alev Cantas
Professor, Institute for the Advanced Study of Human Biology (WPI-ASHBi), Kyoto University



Jamie Davies
Professor, Centre for Discovery Brain Sciences (CDBS), The University of Edinburgh

TARGET
AXIOLOID
Human intermediate mesoderm and early kidney development in stem cell-derived models

METHODS
OPTOGENETICS
- Extending axioloid-based models to generate kidney progenitors
- Using optogenetics to control developmental signaling in space and time

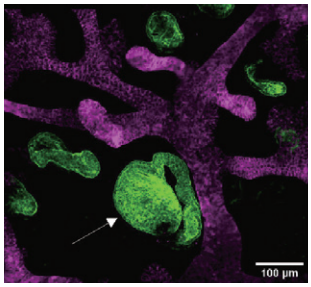
OUTPUT
DISEASE MODEL
- Models of early kidney tissue formation
- A basis for studying kidney diseases, including polycystic kidney disease (PKD)

INTERVIEW with ALEV Cantas

Extending Axioloids to Study Kidney Development and Disease

My background is in developmental biology, and our approach is to understand how cells self-organize and form tissues by reconstructing selected developmental processes in vitro. Our lab established axioloids as models of human somite formation and axial development. In this project, we are extending these models to include the intermediate mesoderm, which gives rise to kidney progenitors. Existing kidney organoids reproduce important aspects of renal differentiation and tissue organization. We aim to complement these approaches by investigating how kidney progenitors emerge and organize into tissues within a model of early body-axis development. This could help clarify how developmental signals and interactions between neighboring tissues influence kidney formation, and how disruptions in these processes may contribute to kidney disease.





Comparison of cultured mouse embryonic kidney rudiments with and without cyst formation in a model of polycystic kidney disease



Welcome lunch party in Kyoto

Combining Expertise in Developmental and Synthetic Biology

This collaboration combines the Alev Lab's expertise in developing human pluripotent stem cell-based models of embryonic development and organogenesis with the Davies Lab's expertise in kidney development, tissue engineering, and synthetic biology. Together, we aim to use optogenetic tools to control developmental signaling and investigate how its timing and spatial distribution influence kidney progenitor formation and tissue organization. Establishing reproducible models could provide a basis for investigating kidney disease mechanisms, including those underlying polycystic kidney disease. The methods developed through this collaboration may also inform future efforts to model other tissues and organs.

ALEV Cantas PROFILE

Dr. Alev serves as Professor at the Institute for the Advanced Study of Human Biology (ASHBi) at Kyoto University. After completing his studies in medicine and biochemistry in Germany, he has worked in developmental biology and stem cell research in Japan for more than two decades. He conducted postdoctoral research on early embryonic development at the RIKEN Center for Developmental Biology (CDB; now the Center for Biosystems Dynamics Research, BDR) and subsequently served on the faculty at the Center for iPS Cell Research and Application (CiRA), Kyoto University, before establishing his own lab at ASHBi. He leads an international team developing stem cell-based models of human and non-human primate embryonic development and organogenesis, aiming to deepen our understanding of human biology and disease and develop applications for regenerative medicine and novel therapies.

START 2024

+ 3 YEARS

FUTURE

RESEARCH APPROACH

The Alev and Davies labs aim to use light-responsive molecular tools to control developmental signaling in human iPS cell-derived axioloid models. They will identify conditions that promote the formation of intermediate mesoderm and kidney progenitors, and characterize the cell types and tissue organization that emerge. Cellular and molecular analyses will assess how closely these models reproduce key features of kidney development and how consistently they can be generated. The longer-term aim is to establish models for investigating congenital and genetic kidney diseases, including models derived from patient-specific iPS cells. This work focuses on developing research models; generating functional kidneys suitable for transplantation remains a distinct, longer-term challenge.

The Japan–UK partnership also supports training and exchange opportunities for early-career researchers, combining complementary expertise in developmental biology, kidney research and synthetic biology.

08 MISSION

Analyzing DNA Structure to Help Prevent Aging

JAPAN × UK

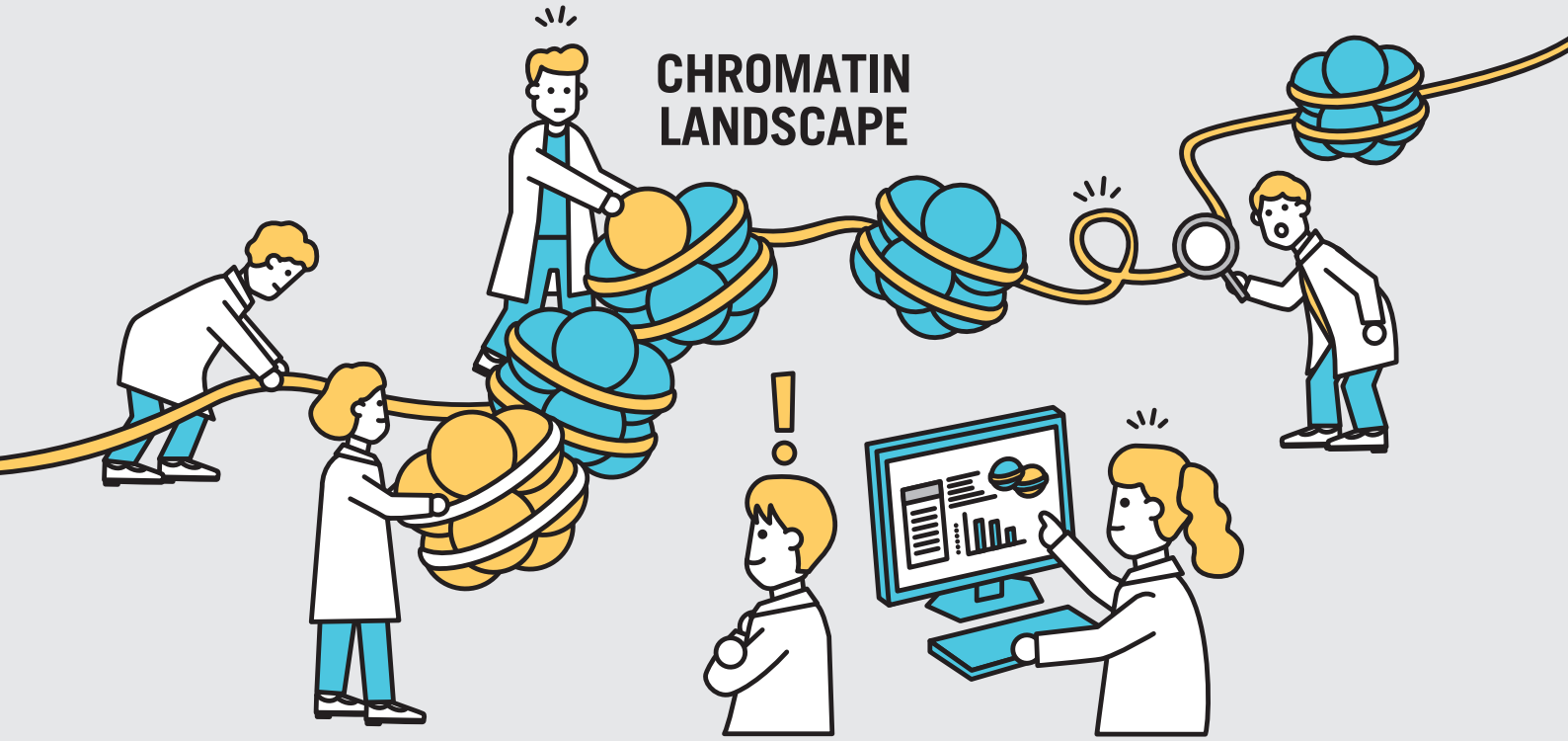
Creating Anti-Senescence Cell Fate by Engineering the Chromatin Landscape

Japan-UK Joint Research OHKAWA Yasuyuki

Year Awarded: FY2024	Domestic Research Institutions: Medical Institute of Bioregulation, Kyushu University; Cell Biology Center, Institute of Integrated Research, Institute of Science Tokyo	Counterpart Research Institution: Cancer Research UK Cambridge Institute, University of Cambridge	Research Period: FY2024-FY2027

TARGET

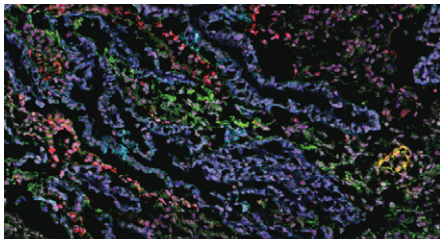
Expression of particular genes in a cell is determined by the state of chromatin formed by DNA cohesion and by higher-order folding. There are hopes that using antibodies to modify chromatin states or altering DNA loop structures via genome editing technologies may suppress the activity of genes associated with aging and thereby prevent the aging process.



KEY POINT

Redrawing the Chromatin Landscape to Restore Normalcy and Develop Bodies Resistant to Aging

The latest analysis technologies now make it possible to measure the regulated state and degree of expression of genes at the single-cell level, enabling research focused on the mechanisms by which chromatin controls gene expression. Chromatin structures are known to loosen or disintegrate with age. The core objective of this research is to correct these disruptions, restore chromatin to its normal state, and suppress age-related changes. Leveraging each team's measurement technologies will lead to the creation of a "chromatin landscape" enabling visualization of active regions and identification of mechanisms to counter aging.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



OHKAWA Yasuyuki
Professor, Medical Institute of Bioregulation, Kyushu University



NARITA Masashi
Professor, Cancer Research UK Cambridge Institute, University of Cambridge

TARGET
CHROMATIN
Fusion of chromatin modification-specific antibodies with various modifying enzymes

METHODS
ENGINEERING
Researching cells responsive to anti-aging interventions using epigenome analysis and other techniques

OUTPUT
ANTI-AGING
Selectively suppressing senescent cells to prevent and treat age-related diseases

INTERVIEW with OHKAWA Yasuyuki

Decoding the Mechanisms of Aging and the Challenge of Prevention

My research is based on the dream of “ageless” bodies that do not decline, even with age. So closely linked to a range of diseases, aging touches upon life’s essential nature, making it the ultimate subject for research. The research group led by my collaborator, Dr. Masashi Narita, discovered that aging induces structural changes in chromatin, which regulates gene expression. By improving the world-leading technologies possessed our teams both in Japan and the UK, we aim to intervene in the aging process, suppress aging, and ultimately come to understand the nature of aging itself. I believe that the existence of this ambitious ASPIRE program is what makes it possible for us to tackle such a challenging research topic.





A variety of equipment is used in analysis, and research constantly advances in the quest for a future free of the burdens of aging.



Meeting between Japanese and UK researchers

An Opportunity for Young Researchers to Experience Research That Truly Affects Society

Imagine a society free from aging, and you realize there are a number of issues to consider. For example, how would our society change if aging ceased and generations were no longer succeeded? Researchers need to communicate these issues and involve society in the discussion. A key benefit of the ASPIRE program is that it allows the next generation of researchers to join in these discussions.

OHKAWA Yasuyuki
PROFILE

Dr. Ohkawa received his Ph.D. from the Graduate School of Medicine at The University of Osaka. After conducting research at the University of Massachusetts Medical School, he joined Kyushu University. He currently serves as Professor at the university’s Medical Institute of Bioregulation, where he directs research in the field of transcriptomics, and as Director of the Institute since 2024. Specializing in the study of chromatin and the fields of epigenomics and transcriptomics, he conducts research with the aim of explaining a diversity of biological phenomena, with activities ranging from the development of measurement technologies and instrumentation to their practical applications in research.

START 2024

+ 3 YEARS

FUTURE

RESEARCH APPROACH

Japan and the UK are establishing a collaborative research framework aimed at developing new treatments to address aging. Sharing data and research tools, the two nations will then expand their joint research network. In addition, by hosting international symposia, they will broaden the exchange of research findings and personnel, sharing verification systems and databases related to the study of aging while deepening their joint research.

This research involves manipulating factors associated with aging and utilizing senescence-resistant cells in realizing precision medicine, with the aim of preventing age-related diseases and enhancing quality of life.

09 MISSION

Developing Artificial Cell-Based Sensors for Highly Sensitive and Rapid Diagnostics

JAPAN × UK

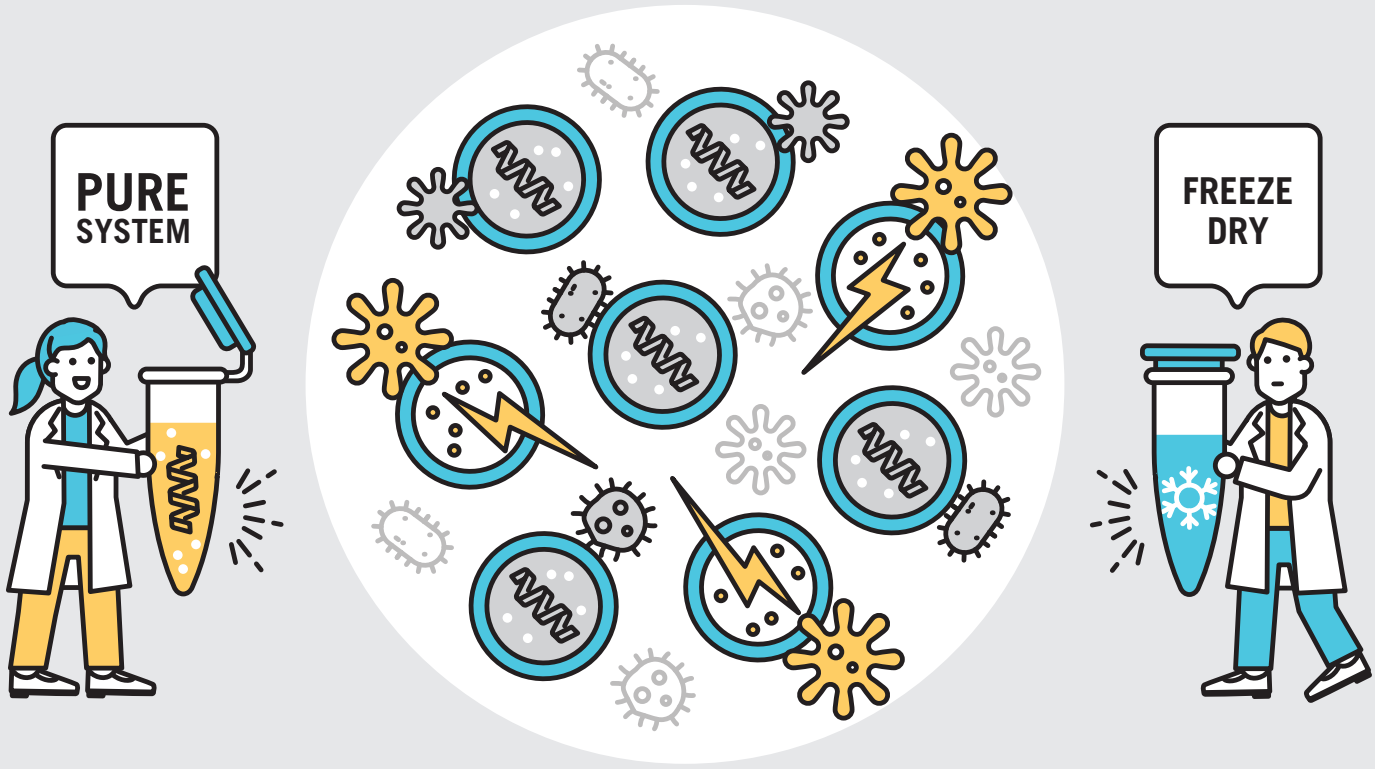
ACROPATH: Artificial Cells for highly sensitive and RObust diagnosis of PATHogen infections

Japan-UK Joint Research SHIMIZU Yoshihiro

Year Awarded: FY2024	Domestic Research Institutions: RIKEN Center for Biosystems Dynamics Research; Institute for Extra-cutting-edge Science and Technology Avant-garde Research (X-Star), Japan Agency for Marine-Earth Science and Technology (JAMSTEC); RIKEN Pioneering Research Institute (PRI)	Counterpart Research Institution: (UK) University of Leeds	Research Period: FY2024-FY2027

TARGET

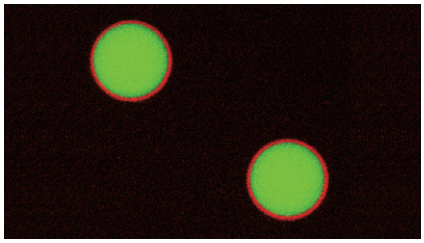
This research aims to develop highly sensitive artificial cell-based sensors for specific pathogens by combining only the cellular components required for sensing, rather than using whole living cells. By precisely controlling their internal composition, the artificial cells can be engineered to produce a fluorescent or luminescent signal in response to a target pathogen. These sensors could be employed in diagnosing blood-borne infections as well as in a variety of other medical applications.



KEY POINT

Developing Innovative Artificial Cell Sensors with Communication Systems Linking Internal and External Environments

Rapid identification of pathogens in patient samples can provide significant benefits not only to patients but also to healthcare professionals. This project aims to construct an artificial cell system capable of transmitting extracellular signals into the cell and to design a sensor that is activated upon pathogen detection. Reporters such as fluorescent or luminescent proteins can be incorporated so that the artificial cells generate detectable optical signals when a target pathogen is detected. By applying this mechanism for transmitting information across the membrane, we anticipate that this technology could ultimately be extended well beyond the medical field.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



SHIMIZU Yoshihiro
Team Director, Laboratory for Cell-Free Protein Synthesis, RIKEN Center for Biosystems Dynamics Research



Paul Beales
Professor, School of Chemistry, University of Leeds

TARGET

artCell

Development of a platform for producing artificial cells with synthetic transmembrane modules

METHODS

INTEGRATION

- Forming transmembrane sensors
- Assembling proteins
- Controlling transcription and translation
- Devising an oligonucleotide-based strategy
- Encapsulating and optimizing the PURE system

OUTPUT

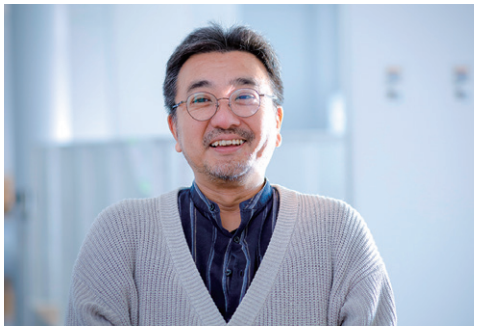
PROTOTYPE

Improving the fidelity of signal integration, expanding potential for other applications, and developing the system for clinical use

INTERVIEW with SHIMIZU Yoshihiro

Starting with the Development of Artificial Cell-Based Sensors for Two Bacterial Species

This research uses proteins displayed on the outer surface of artificial cells as sensors for detecting viruses and bacteria. A key feature of artificial cells is that they can be flexibly designed for specific applications. We expect the platform to be adaptable to the detection of a wide range of pathogens by changing the proteins displayed on the artificial cell surface. Within the ASPIRE program, we are focusing on Staphylococcus aureus and Vibrio cholerae. Our joint research partners in the UK possess technology to create “pseudo-antibodies” that function similarly to natural antibodies to these bacteria. We believe that by incorporating this technology into artificial cells, we can advance the research more effectively.





Laboratory testing in progress. The team actively engages with society while advancing their research.

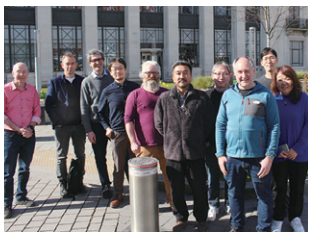


Photo with joint research partners overseas

Addressing Ethical Considerations for Societal Implementation of Artificial Cells

The greatest advantage of the sensors we are developing is that they enable rapid testing anywhere, without the need for the specialized equipment or labor-intensive amplification processes used in PCR-based diagnostics. At the same time, while this technology offers considerable versatility, it is essential that its development and use be carefully managed from an ethical perspective. This international collaboration provides a valuable opportunity for us to learn from European approaches, which place greater emphasis on ethical considerations than those in Japan. We are committed to maintaining an ongoing dialogue with the public as we work toward the societal implementation of these technologies.

SHIMIZU Yoshihiro PROFILE

Dr. Shimizu is Team Director of the Laboratory for Cell-Free Protein Synthesis at RIKEN Center for Biosystems Dynamics Research. After receiving his degree from the Graduate School of Engineering at The University of Tokyo in 2003, he joined the startup Post Genome Institute Co., Ltd., where he contributed to the commercialization of the cell-free protein synthesis system (the PURE system) he had developed. In 2004, he moved to the Graduate School of Frontier Sciences at The University of Tokyo, where he served as an Assistant Professor. He became a principal investigator at RIKEN in 2010, and has since focused on developing technologies and applications based on the PURE system.

RESEARCH APPROACH

START 2024

+ 3 YEARS

Researchers will continue to investigate the regulatory mechanisms of sensor proteins that form the basis of the cell-free systems. They will integrate these findings with the diagnostic hybrid artificial cells developed by the team to create artificial cells that function as pathogen-detecting sensors. The team will also continue to develop highly efficient detection systems using gene analysis technologies. The research will be accelerated through the mutual transfer and adoption of technologies with the research partners in the UK.

FUTURE

The aim is to expand the sensors to a broader range of pathogens and to promote their implementation in a wide range of settings beyond medical facilities.

MISSION 10

Mapping Genes to Overcome Musculoskeletal Diseases

JAPAN × USA

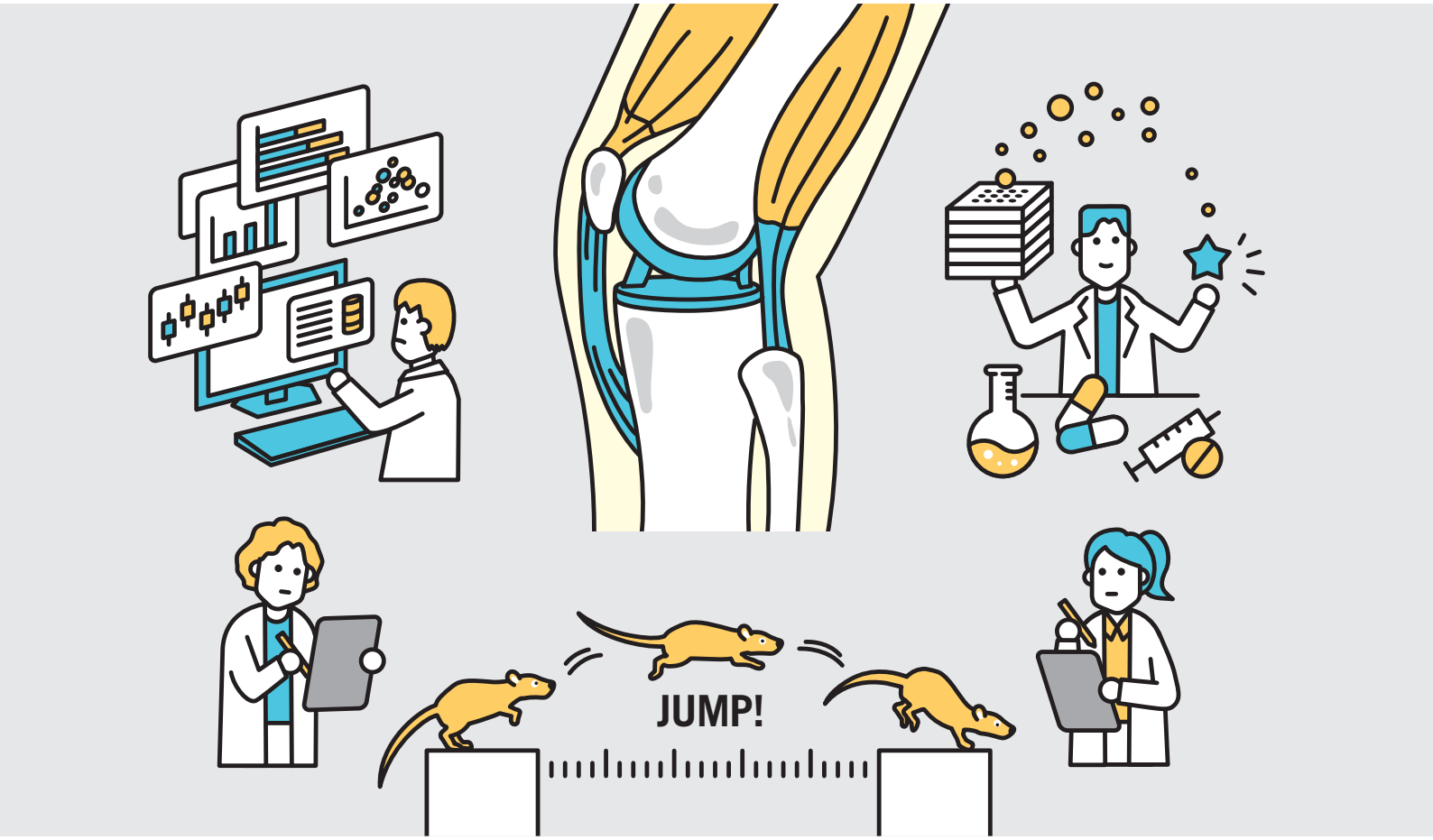
A Global Study Exploring Lifelong Health through the Maintenance, Promotion, and Restoration of Physical Functionality

Alignment B ASAHARA Hiroshi

Year Awarded: FY2024	Domestic Research Institutions: Graduate School of Medical and Dental Sciences, Institute of Science Tokyo; Medical Research Laboratory, Institute of Integrated Research, Institute of Science Tokyo	Counterpart Research Institution: (USA) Scripps Research	Research Period: FY2024-FY2029

TARGET

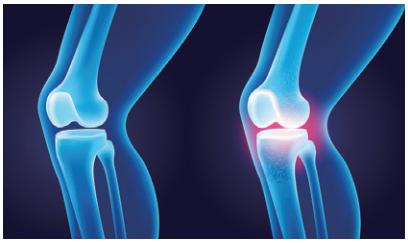
This project involves analyzing samples of tendon, cartilage, and other musculoskeletal tissue from various parts of the body to create “gene maps” showing how genes in each cell type function. Combining general data derived from these maps with individuals’ genetic data indicating susceptibility to disease, researchers aim to understand the mechanisms underlying the onset of disease. The findings will then be used to further regenerative medicine and drug development, helping to bring about a society where people can remain active and healthy even as they age.



KEY POINT

A Collaboration Capitalizing on the U.S.’s Extensive Sample Library and Japan’s Superior Analysis Technologies

Utilizing the diverse library of samples varying by race and gender maintained by Scripps Research in the U.S. and combining that with Japan’s expertise in computer-based analysis technologies, researchers aim to identify which genes influence the functioning of the musculoskeletal system. In this tremendously synergistic collaboration, the teams continuously update their databases as research progresses, aiming to build the world’s first detailed human genetic database to serve as a foundation for future research and development. With the focus switching from the disease’s effects, such as worn cartilage, to the underlying genetic causes, research will lead to development of fundamental therapeutic drugs.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



ASAHARA Hiroshi
Professor, Department of Systems Biomedicine, Institute of Science Tokyo



Martin Lotz
Professor, Department of Molecular and Cellular Biology, Scripps Research

TARGET

MUSCULOSKELETAL SYSTEMS

- Collecting human musculoskeletal tissue samples and analyzing them at the genetic level
- Utilizing the human musculoskeletal tissue bank

METHODS

GENOME AND QTL ANALYSIS

- Comprehensively analyzing samples
- Utilizing cellular RNA and e/sQTL analysis

OUTPUT

HOMEOSTASIS AND REGENERATION

- Developing technologies for tissue regeneration and reconstructive medicine
- Selecting compounds for therapeutic drugs
- Establishing a musculoskeletal system database

INTERVIEW with ASAHARA Hiroshi

International Joint Research Takes Long-Term View in Contemplating Medicine's Next Stages

Our research partner, Dr. Martin Lotz at Scripps Research, possesses one of the world's best sample libraries, but the relatively low awareness about medical research in Japanese society makes it difficult to obtain such samples. However, advances in medicine depend on actual experimentation, so I see this collaboration as a highly meaningful endeavor in the long term. We hold regular online discussions and share the data we obtain in real time.





Scene from the laboratory. Continuous basic research leads to future clinical applications.

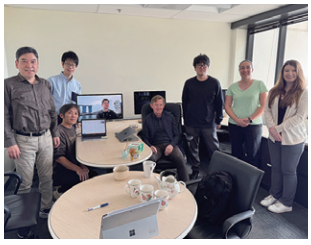


Photo with Professor Lotz and team members

Fostering Independent Researchers to Bridge Basic and Clinical Science

The ASPIRE program offers young researchers the opportunity to take on challenging international projects alongside overseas researchers from diverse backgrounds. I look forward to the new ideas that will emerge from this process, and I hope that having researchers participate in an internationally competitive environment will produce scientists capable of conducting research independently with a clear long-term vision. I see young Japanese researchers acting as bridges between basic and clinical research and believe the day will come when research originating in Japan leads the way in global medicine.

ASAHARA Hiroshi
PROFILE

After conducting clinical and basic research in orthopedics and rheumatology, Prof. Asahara went to the United States, where he studied gene expression control mechanisms at Harvard University and the Salk Institute. In 2002, he began a term directing an independent laboratory at The Scripps Research Institute (now Scripps Research), and from 2004 he served as a Division Chief at the National Center for Child Health and Development. He became a Professor at Tokyo Medical and Dental University (now the Institute of Science Tokyo/Science Tokyo) in 2011, and is working on elucidating the molecular mechanisms of chronic inflammation and tissue homeostasis, focusing particularly on the musculoskeletal system and arthritis, and developing medical applications.

RESEARCH APPROACH

START 2024

+ 5 YEARS

The project is progressing with international joint research to elucidate the causes of diseases of the joints and translate findings into treatments and regenerative medicine. The initial focus will be on collaborating with U.S. partners to analyze human joint tissue and identify the genes involved in these diseases. Functions and positioning of individual cells will then be analyzed to systematically map out the processes occurring within the joint. The resulting database of findings will be shared globally to support researcher development and drive medical applications.

FUTURE

The project's aim is to realize a society where surgery and medications will enable people to maintain a flexible body and recover from injuries to live healthy, active lives.

MISSION

Comprehensive Analysis of Heart Diseases to Enhance Treatment Precision

JAPAN × USA

International Cardiovascular Digital Omics Consortium

Alignment B KOMURO Issei

Year Awarded: FY2024	Domestic Research Institutions: The University of Tokyo Hospital; Graduate School of Medicine, Chiba University; Institute for Quantitative Biosciences (IQB), The University of Tokyo	Counterpart Research Institution: (USA) Stanford University	Research Period: FY2024-FY2029

TARGET

With the surging incidence of heart failure worldwide due to aging populations, understanding the molecular mechanisms underlying the disease is now an urgent matter. Since cardiovascular diseases involve both genetic and environmental factors, comprehensive data collection and analysis factoring in racial differences and changes over time are crucial. In this joint Japan-U.S. project, researchers analyze patients' daily activities, genetic information, and other data with the aim of developing treatments for a wide variety of cardiovascular diseases.



KEY POINT

Linking Global Cardiovascular Research to Discover Optimal Individualized Approaches for Treatment of Heart Disease

Heart disease symptoms and characteristics vary widely. For example, in contrast to Western countries, where the patient's obesity is often a factor in heart failure, patients in Japan tend to be lean, elderly individuals. To gain a detailed understanding of such diverse cardiovascular systems and systematically resolve causal elements ranging from molecular-level mechanisms to social and environmental factors, efforts are underway to foster collaboration among Japanese cardiovascular research institutions and promote their international development. Through integrated analyses of data collected via digital devices in both Japan and the U.S., along with genetic information, which remains constant throughout life, this research is expected to provide further advancements in precision medicine for heart disease.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



KOMURO Issei
Professor, Department of Frontier Cardiovascular Science, The University of Tokyo



Michael Snyder
Professor, Department of Genetics, Stanford University

TARGET
GENOMICS
Aiming to elucidate the mechanisms underlying homeostatic regulation of the cardiovascular system from integrated analyses by the international consortium

METHODS
INTEGRATION
Constructing a foundation from single-cell omics and multimodal AI analysis, integrating data from digital devices, and verifying with animal models and iPS cells

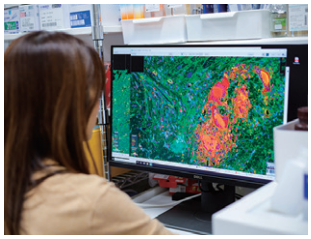
OUTPUT
BIOMARKER
Identifying and verifying novel biomarkers with the aim of contributing to the implementation of precision medicine

INTERVIEW with KOMURO Issei

Fully Utilizing Equipment and Technology for Research Standards Comparable to the West's

Because we collaborate with hospitals in our research, we possess numerous tissue samples obtained from patients. We examine these samples using single-cell analysis, a technique that allows us to observe every gene expressed within an individual cell. However, adopting the latest analytical equipment, let alone mastering its use, at a pace on par with Western institutions is no easy task. That is precisely why collaborative research is so significant.





Data analysis



Members of Professor Snyder's laboratory

Realizing Personalized Medicine to Provide the Necessary Treatment to the Right Person

Following the Western model, we sought to establish a Japanese consortium of research groups handling tasks such as managing samples from heart disease patients. We created a system whereby individuals in charge of specific areas are appointed in each research organization, and the results of genomic and omics analysis are shared across the entire consortium. We aim to expand this framework globally through ASPIRE. The more data is collected, the easier it is to detect genetic mutations and investigate the respective pathways leading to disease, which is why international joint research is so exceedingly important. In the future, I hope to realize a society where, to a certain extent, cardiovascular diseases can be diagnosed at home, ensuring that those who truly need to visit a hospital or require treatment receive care promptly.

KOMURO Issei PROFILE

Prof. Komuro graduated from The University of Tokyo's School of Medicine in 1982. After serving as a postdoctoral research fellow at Harvard Medical School and as an assistant professor in the Department of Internal Medicine III and lecturer in Cardiology at The University of Tokyo, beginning in 2001 he held professorships in Cardiology at Chiba University, The University of Osaka, and The University of Tokyo. Since 2023, he has served as Vice President of the International University of Health and Welfare, as well as a Project Professor and Professor Emeritus at The University of Tokyo. His research focuses on understanding the pathology of heart failure. His numerous awards and honors include the Erwin von Bälz Prize, the American College of Cardiology Award, the Japanese Circulation Society Award, the Academic Award of the Mochida Memorial Foundation, the Medical Award of the Japan Medical Association, the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology, and the European Society of Cardiology Gold Medal.

START 2024 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

The project will continue to foster collaboration between research institutions in Japan and the United States, including exchanges of personnel and collection of samples and data, combining genome and single-cell analysis with AI-based analysis to clarify the mechanisms of heart and cardiovascular diseases at the cellular level. Findings gained from animal models and iPS cells will be verified with the aim of bringing about precision medicine that incorporates global diversity. This project will set the foundation for development of the next generation of researchers and sustainable international research.

The aim is to achieve "digital omics analysis," with factors scaling from the cell to the individual's lifestyle, enabling a highly detailed understanding of the mechanisms underlying various cardiovascular diseases and paving the way for precision medicine in the future.

MISSION 12

Revealing the Hidden Biology of Germ Cells Through Their Lifelong Dynamics

JAPAN × UK × GERMANY

International and Interdisciplinary Research on Germ Cell Dynamics and Transgenerational Health Risks

Alignment B YOSHIDA Shosei

Year Awarded: FY2024	Domestic Research Institution: National Institute for Basic Biology (NIBB), National Institutes of Natural Sciences (NINS)	Counterpart Research Institutions: (UK) University of Cambridge; (Germany) German Cancer Research Center (DKFZ)	Research Period: FY2024-FY2029

TARGET

The aim of this project is to gain a deeper understanding of the nature of sperm-producing stem cells, or spermatogonial stem cells (SSCs), from their intracellular molecular mechanisms to their behavior and function within the testis. Recent advances in ultra-accurate sequencing technologies have made it possible to detect the extremely rare mutations that arise *de novo* in germ cells. Studying these mutations, which also fuel evolution, may help uncover the genetic causes of male infertility and assess the risk of hereditary diseases.



KEY POINT

Revealing the Characteristics of Stem Cells That Survive and Produce Offspring; Understanding the Benefits and Risks of Germ Cell Mutations

Sperm must be produced both in huge numbers and with high accuracy, and a decline in either aspect can lead to infertility or an increased risk of hereditary disease, making this an issue of growing concern in ageing societies. The key to achieving both high productivity and fidelity lies in sperm stem cells. Real-time *in vivo* observation of sperm stem cell dynamics has been driving research at the cellular scale. We will extend this to an integrated understanding across molecular, cellular, tissue, and organ scales. For example, we combine the observed fate of individual germ cells with their spatial localization. We will also reveal which germ-cell lineages disappear and which ultimately contribute to the next generation. This research helps clarify the impact of germ cell mutations on the next and subsequent generations.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



YOSHIDA Shosei
Professor, National Institute for Basic Biology (NIBB), National Institutes of Natural Sciences (NINS)



Benjamin Simons
Director, Gurdon Institute, University of Cambridge



Thomas Höfer
Professor, Division of Theoretical Systems Biology, German Cancer Research Center (DKFZ)

TARGET
GERMLINE
- Understanding the characteristics of sperm stem cells
- Tracing the germline lineage from primordial germ cells to the next generation

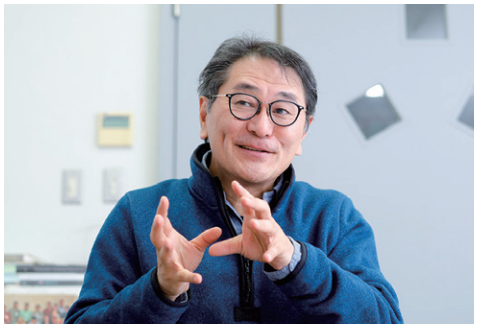
METHODS
LINEAGE TRACING
- Cell lineage analysis using DNA barcoding
- Multiscale analyses of gene expression and genome regulation

OUTPUT
INHERITANCE
- Detecting new mutations and elucidating mechanisms of transmission to the next generation
- Potential applications to diagnosing male infertility and assessing the risk of genetic disorders

INTERVIEW with YOSHIDA Shosei

Driven by a Desire to Explore the Fundamental Nature of Life

How do stem cells manage to produce such vast numbers of sperm with nearly zero mutations? What causes the rare errors that do occur? What impact can even such rare errors have on the next generation? My research is motivated by a pure desire to answer these fundamental questions. Our partner laboratories are based in different countries, each with its own unique strengths.





Our in-person meeting: Researchers from different countries exchange ideas.



Frank discussions take place over a meal.

This research can only be accomplished by working together with these laboratories. For example, this collaborative framework allows us to analyze mutations in sperm stem cells with a level of precision that can detect roughly one mutation among 100 million base pairs. Underpinning these collaborations are the experimental technologies we have developed and the knowledge of germ cells we have accumulated in our own laboratory.

Contributing to Science is Our Ultimate Goal in Collaborative Research

Discussions with world-leading researchers are incredibly stimulating. This is especially important for young researchers and students. I believe the most important aspect of collaborative research is the rapport we build as people, regardless of nationality or research field. Building on this mutual trust, we communicate closely about each experiment and analysis as the research progresses. Ultimately, what matters is what we achieve through these efforts and how much we contribute to science.

YOSHIDA Shosei
PROFILE

Dr. Yoshida is a Professor in the Division of Germ Cell Biology at the National Institute for Basic Biology (NIBB), National Institutes of Natural Sciences (NINS). After graduating from The University of Tokyo Faculty of Medicine in 1991, he received his Ph.D. in Medicine in 1995. He held positions at the National Center of Neurology and Psychiatry, The University of Osaka, and Kyoto University before assuming his current role in 2008. He has investigated the dynamics and fate of mouse sperm stem cells, combining techniques such as real-time *in vivo* imaging, cell lineage analysis, and mathematical modelling to elucidate the mechanisms underpinning the robustness of spermatogenesis. Dr. Yoshida has been collaborating with Benjamin Simons (University of Cambridge, UK), the UK Principal Investigator of this ASPIRE program, for approximately 20 years.

START 2024 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

First, by combining genetic data and mathematical modelling, we investigate how stem cells, the precursors of sperm, proliferate, differentiate, and are selected. In addition, using DNA barcoding and spatial information, we elucidate what determines which stem cells survive, and which are eliminated. We also investigate the mechanisms by which mutations arise and are transmitted to the next generation. Senior and young researchers from Japan, the UK, and Germany form an international team to advance this interdisciplinary research.

By expanding this international and interdisciplinary research network, we aim to pioneer a new field of biology that investigates the mechanisms of heredity and genetic variation, while informing future approaches to male infertility and genetic disorders.

MISSION 13

Treating Leukemia by Rescuing Cells That Fail to Become Mature Blood Cells

JAPAN × FRANCE

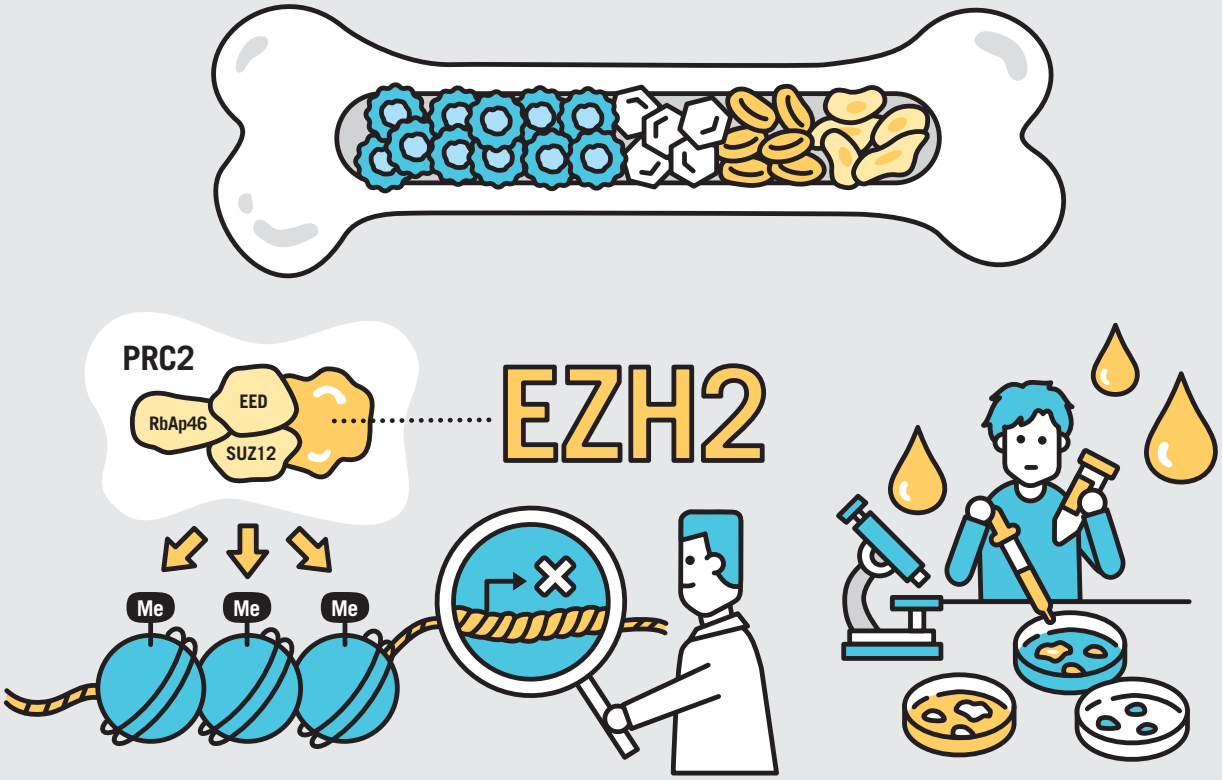
Understanding EZH2 Activities in Leukemia, a Potential Therapeutic Strategy

Japan-France Joint Research IWAMA Atsushi

Year Awarded: FY2025	Domestic Research Institutions: The Institute of Medical Science, The University of Tokyo; International Research Center for Medical Sciences (IRCMS), Kumamoto University	Counterpart Research Institutions: (France) National Centre for Scientific Research (CNRS); National Institute of Health and Medical Research (INSERM)	Research Period: FY2025-FY2029

TARGET

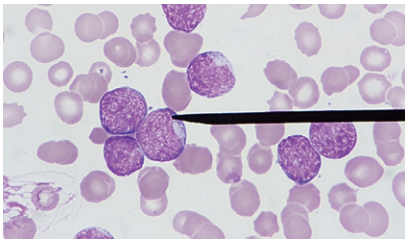
The onset of leukemia was previously considered to involve the histone methyltransferase activity of EZH2, a protein that regulates gene expression. However, recent research suggests that EZH2 may bind to new partners, causing leukemia through a process other than its enzymatic activity. Detailed investigations and targeting of this mechanism are underway with the aim of finding new treatments for leukemia, a disease for which conventional drugs have been ineffective.



KEY POINT

Discovering a Novel Mechanisms Inducing Leukemia in a New Approach to Drug-Resistant Cases

Leukemia is a disease that arises when hematopoietic stem cells, the precursors of all blood cell lineages, fail to differentiate normally due to genetic abnormalities or abnormal gene expression. EZH2, a Polycomb protein, typically binds with other Polycomb proteins to suppress gene expression. However, researchers have discovered novel binding partners of EZH2 that enable it to activate gene expression, making it suspect as a major factor in many cases of leukemia. This research aims to identify and develop therapies inhibiting these novel EZH2-containing complexes with the goal of realizing more diverse and effective leukemia treatments tailored to individual patients.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



IWAMA Atsushi
Professor, The Institute of Medical Science, The University of Tokyo



Estelle Duprez
DR1 Researcher, National Centre for Scientific Research (CNRS)

TARGET
EZH2
Elucidating the influence of EZH2 on gene expression

METHODS
MECHANISM
- Analyzing how EZH2 functions at the molecular level
- Analyzing the processes in leukemia's emergence and verifying their role in treatment resistance and recurrence

OUTPUT
STRATEGY
Developing new therapeutic strategies targeting EZH2

INTERVIEW with IWAMA Atsushi

Long-Standing Relationship Predating ASPIRE Led to New Discoveries

I have been conducting joint research with Dr. Duprez, the Principal Investigator for the French team, for about ten years. In researching leukemia that does not respond to the therapeutic drug retinoic acid, we discovered an overexpression of EZH2 in these non-responsive cells. We found that EZH2, which normally suppresses gene expression, was binding with a new molecule whereby it activated rather than suppressed gene expression.





Scene from the laboratory



A meal with overseas researchers; researchers' interactions are stimulating and lead to new ideas.

A Network of Researchers That is Also Valuable to Young Scientists

Thanks to the French researchers' approach in developing therapies, our own data and research methods are getting closer to clinical application. It's clear to me that bringing researchers together and leveraging their respective areas of expertise has expanded the scope of our research and helped it advance to the next stage. Such interactions should be stimulating for young researchers as well. Science is not something confined to a narrow scope, it is an endeavor that progresses simultaneously throughout the world, and we intend to continue focusing on the importance of building international networks.

IWAMA Atsushi
PROFILE

Dr. Iwama graduated from Niigata University School of Medicine in 1987. After completing his internship at Niigata University Hospital, he underwent residency training at Jichi Medical University Hospital. Following clinical work in hematology, he began basic research on hematopoietic stem cells. He obtained his Ph.D. in Medicine from Kumamoto University in 1996. In 2005, he was appointed Professor at the Graduate School of Medicine, Chiba University, where he has been advancing research on the epigenetics of hematopoietic stem cell biology and hematological malignancies. Since 2018 he has served as a Professor at the Institute of Medical Science, The University of Tokyo, where he also conducts research on hematopoietic stem cell aging.

START 2025 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

Research will focus on elucidating the novel functions of EZH2, a protein that regulates gene expression and is deeply implicated in leukemia, and translating the findings into therapeutic applications through international joint research. Tasks include identifying the sites where EZH2 is activated and investigating the impact of these changes on cells. With a fuller understanding of EZH2's role in leukemia and other diseases, researchers will evaluate the possibilities for new therapeutic methods. Interchanges between researchers in Japan and France and development of young researchers will continue throughout the project, with the results leading to next-generation medical treatment.

Development of new therapeutic drugs will enable treatments for cases of leukemia for which current drugs are ineffective.

MISSION 14

Unraveling How “FLASH” Targets Only Cancer Cells

JAPAN × FRANCE

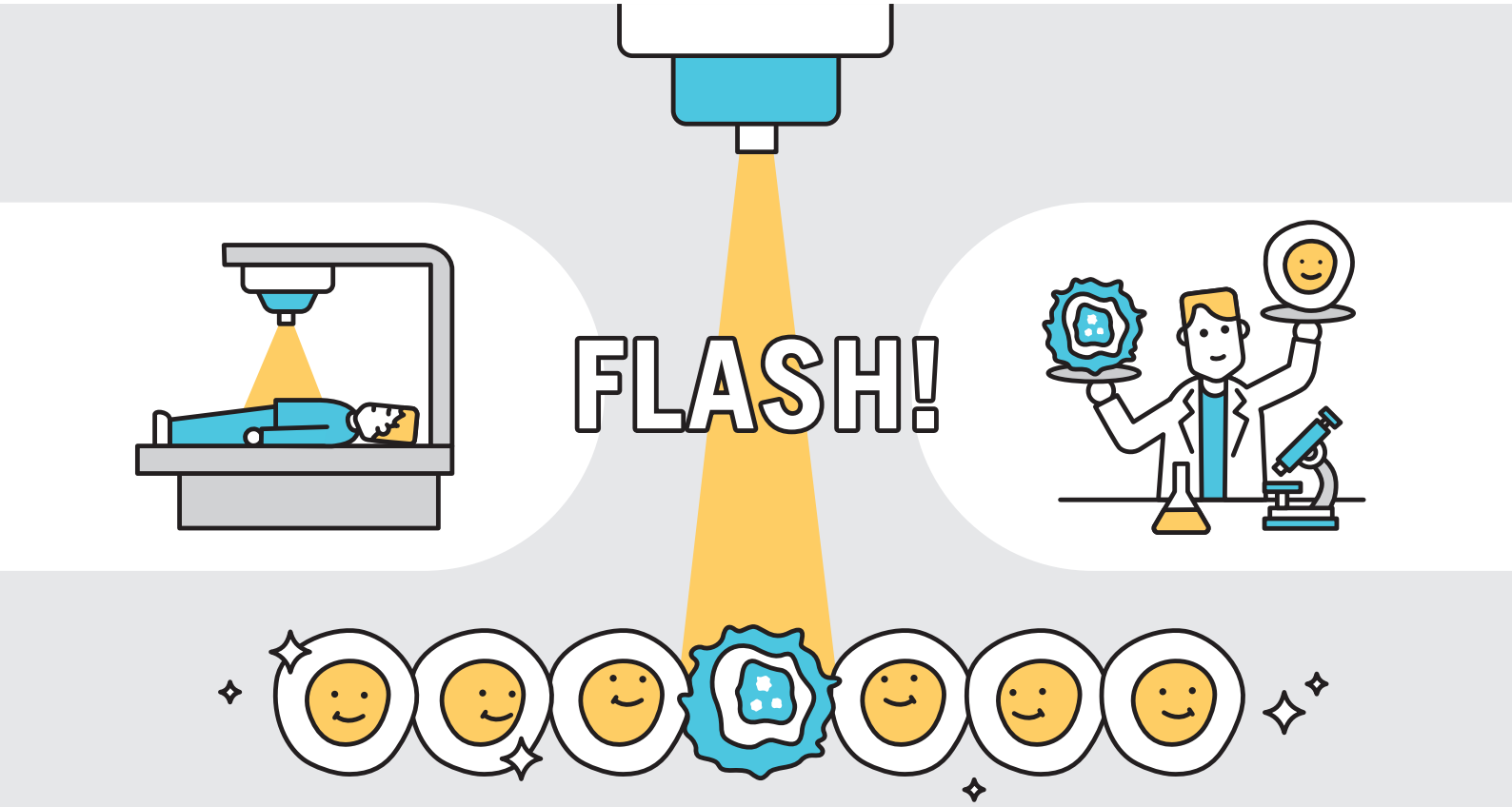
Uncovering the Roles of Lipids in the Effects of FLASH Radiotherapy, at the Cellular and Organ Level, to Develop New Lipid-Peptide Treatment

Japan-France Joint Research SETOU Mitsutoshi

Year Awarded: FY2025	Domestic Research Institutions: Faculty of Medicine, Hamamatsu University School of Medicine; Graduate School of Engineering, The University of Tokyo	Counterpart Research Institution: (France) Institut Curie	Research Period: FY2025-FY2029

TARGET

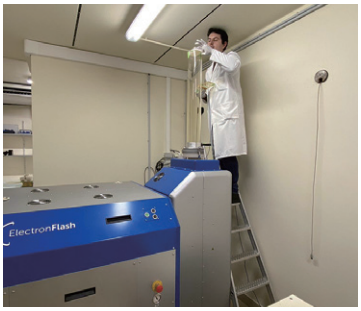
Radiotherapy, a type of cancer treatment, destroys cancer cells but can also damage normal tissue. However, it has been discovered that treatment without side effects may be possible with “FLASH radiation,” which is delivered instantaneously at a dose rate hundreds of times higher than that of conventional radiotherapy. Research thus far suggests that changes in lipid metabolism after FLASH irradiation facilitate protection of tissues, and studies focusing on lipid metabolism are now underway.



KEY POINT

Detailed Study of Lipids’ Functions in the Quest for Cancer Treatments Without Side Effects

The development of mass spectrometry imaging, a technology that measures not only the abundance of molecules but also their spatial distribution, has made it possible to observe molecular distributions within extremely small samples of biological tissue. Researchers have been attempting to elucidate the mechanism by which normal tissue remains protected even with the instantaneous, ultra-high-dose-rate irradiation of FLASH radiotherapy. Analyzing the changes in lipid metabolism following irradiation with mass spectrometry imaging and other techniques is thought to be the key in explaining this mechanism. Development of even more effective treatments utilizing lipid-peptide complexes is also expected.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



SETOU Mitsutoshi
Professor, Department of Cellular and Molecular Anatomy, Hamamatsu University School of Medicine/Deputy Director, Institute of Photonics Medicine/Director, International Mass Imaging Center



Charles Fouillade
Senior Scientist, FLASH Radiotherapy Research Program, Institut Curie

TARGET
FLASH
Collecting samples for analysis and FLASH irradiation at Institut Curie

METHODS
METABOLOMICS
Understanding metabolome and peptide data through transcriptomics analysis, lipid metabolism analysis, and mass spectrometry

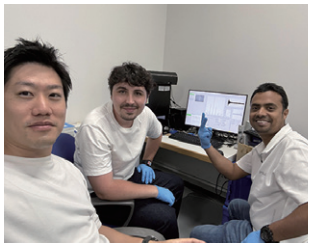
OUTPUT
THERAPY
Developing new treatments using lipid-peptide complexes (LIPID-PEPTIDE) and reducing side effects

INTERVIEW with SETOU Mitsutoshi

Collaboration with FLASH Began Serendipitously

Although mass spectrometry imaging systems were originally developed for use in analyzing proteins and genes, visualizing lipids was an unexpected side benefit. However, Dr. Fouillade, a researcher specializing in FLASH, took an interest in this and contacted me. Looking into this further, we discovered differences between the state of lipids in cancer cells that were exposed to FLASH and in those that were not. Another unique aspect of this approach is that of taking the discovery that “lipids are the key” and commercializing it in the form of the “lipid-peptide complex,” something that had never existed before. I believe researchers have a responsibility not only to pursue the truth but also to consider how to use those findings to benefit society.





Japanese and French researchers of the same generation inspire each other’s research through mutual challenge and encouragement.



Group photo with international joint researchers

Developing Talent with the Aim of Creating a Society of People Living Long, Happy Lives

My own research specialty is aging, and my hope through this research is to overcome, as soon as possible, the diseases that cut people’s lives short before they reach their average life expectancy. I would be happy for the young researchers in my lab to accomplish this, but as this is for the sake of humanity as a whole, I wouldn’t mind at all if this were achieved by other researchers. I aim to create an environment where junior researchers can learn by observing their seniors and personnel are in turn capable of mentoring younger researchers, in an expanding and sustainable community of researchers.

SETOU Mitsutoshi PROFILE

Following coursework that included participation in an exchange program at Harvard Medical School, Prof. Setou graduated from the School of Medicine, The University of Tokyo, in 1994 (M.D.), and received his Ph.D. from the same university in 2001. After serving in positions including Associate Professor at the National Institute for Physiological Sciences (NIPS), he became a Professor in the Department of Cellular and Molecular Anatomy at Hamamatsu University School of Medicine in 2008. Awards and honors he has received include the Amersham Biosciences & Science Prize for Young Scientists in 2002, the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (Young Scientist Category) in 2008, and the Nakatani Prize Grand Prize in 2025. He currently serves as Director of the International Mass Imaging Center and Deputy Director of the Institute of Photonics Medicine, Hamamatsu University School of Medicine.

START 2025 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

Researchers will compare differences between FLASH and conventional irradiation and investigate the mechanisms that protect normal tissue. Through verification of new therapeutic candidates and analyses of changes in lipids and gene activity, the team will seek to identify sensitizers that enhance the effects of radiation on cancer while protecting normal tissue. These candidates will be evaluated as researchers continue to examine the role of lipid metabolism and novel irradiation techniques with the aim of finding clinical applications. The project will maintain a simultaneous focus on international cooperation, sharing findings, and development of young researchers through collaboration between Japan and France.

We aim to overcome cancer by establishing an innovative approach that expands the therapeutic window of radiotherapy.

MISSION 15

Turning Replication Stress into a Therapeutic Opportunity

JAPAN × FRANCE

French-Japanese Consortium for Replication Stress-Induced Senescence and Anti-Cancer Immunity

Japan-France Joint Research　DAIGAKU Yasukazu

Year Awarded: FY2025	Domestic Research Institutions: Cancer Institute, Japanese Foundation for Cancer Research (JFCR); National Institute of Genetics	Counterpart Research Institutions: (France) French National Centre for Scientific Research (CNRS), University of Montpellier; Institut Curie; Institut Pasteur	Research Period: FY2025-FY2029

TARGET

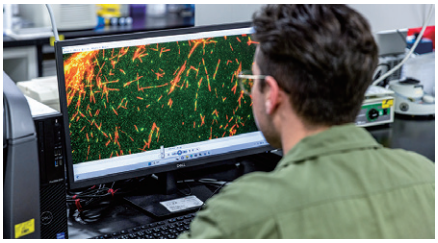
DNA stores genetic information and serves as the blueprint for cells to synthesize proteins. Enzymes called DNA polymerases replicate DNA with high accuracy, but occasional errors can occur. Disruptions to DNA replication, collectively referred to as “replication stress,” can compromise genome stability and contribute to cancer development. This project aims to clarify the relationship between DNA replication fidelity and replication stress and to uncover how disruptions to replication trigger inflammation and cellular senescence. These insights could help guide the development of new cancer therapies.



KEY POINT

“One-Two Punch” Cancer Treatment: Inducing Senescence, Then Eliminating Senescent Cells

When DNA replication is disrupted, cells can enter senescence, a state in which they stop dividing. This response can prevent abnormal cells from becoming cancerous. However, substances released by senescent cells can also sustain immune responses and inflammation, sometimes promoting cancer cell growth. Researchers are therefore exploring a two-step treatment strategy known as the “one-two punch”: first inducing senescence in cancer cells, then eliminating those senescent cells.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



DAIGAKU Yasukazu
Project Leader, Cancer Institute, Japanese Foundation for Cancer Research (JFCR)



Philippe Pasero
Director, Institute of Human Genetics, French National Centre for Scientific Research (CNRS), University of Montpellier

TARGET

REPLICATION STRESS

Elucidating oncogene-induced replication stress, immune responses to nucleic acids, and cellular senescence

METHODS

SENESCENCE CONTROL

- Inducing/suppressing senescence by controlling the amount of DNA that leaks out of the nucleus
- Selectively eliminating senescent cells through senolysis

OUTPUT

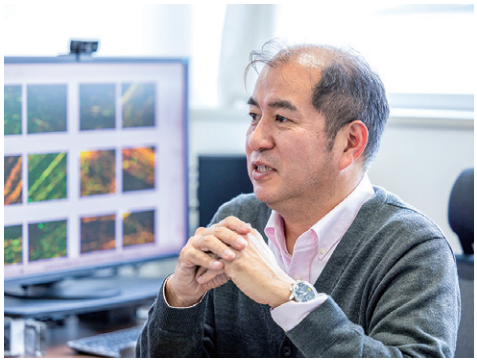
THERAPEUTIC STRATEGY

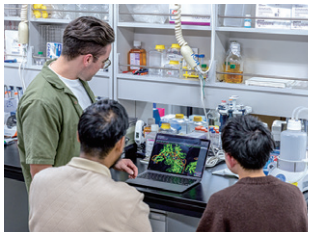
- New strategies for cancer treatment
- Approaches to regulating innate immune responses
- Strategies to enhance antitumor immunity

INTERVIEW with DAIGAKU Yasukazu

Understanding Replication Stress to Address the Underlying Mechanisms of Cancer

My research has focused on understanding how DNA is replicated. In cancer cells, this process can become disrupted, causing what we call “replication stress.” Yet important questions remain about the mechanisms linking replication stress to inflammation and cellular senescence. In this project, we aim to understand this sequence of events in detail, from disrupted DNA replication to inflammation and senescence. By exploiting features unique to cancer cells, we hope to selectively induce senescence in these cells and develop treatments that address the underlying mechanisms of the disease.





Researchers from different countries working together in the laboratory.



After a meeting in Montpellier

Anticipating the Synergies That Only Arise in Cross-Disciplinary Projects

The idea for this consortium began with an invitation from Dr. Pasero, a leading researcher in the field who discovered that DNA replication can trigger inflammation. The opportunity to collaborate with him was one I had hoped for. As the project brings together expertise spanning DNA replication and cellular senescence, more researchers have joined, allowing the consortium to grow to its current size. Our laboratory has developed techniques to track and analyse how DNA polymerases copy DNA. I look forward to advancing this research together, drawing on the strengths of each team.

DAIGAKU Yasukazu
PROFILE

Dr. Daigaku graduated from the Faculty of Science at Tohoku University and completed his Ph.D. studies at the university’s Graduate School of Life Sciences. He held research positions at Cancer Research UK and the Genome Damage and Stability Centre at the University of Sussex, followed by an appointment as Assistant Professor of Frontier Research Institute for Interdisciplinary Sciences at Tohoku University. In April 2022, he became a Project Leader at the Cancer Institute of Japanese Foundation for Cancer Research. His research spans DNA replication, repair, and related molecular processes, with the aim of understanding how mutations arise.

START 2025

+ 5 YEARS

FUTURE

RESEARCH APPROACH

This project investigates how oncogene-induced replication stress and the resulting leakage of DNA into the cytoplasm contribute to inflammation, cellular senescence, and cancer progression. Using human cells, cancer models and tumors transplanted into mice, we will combine advanced genomic analyses with microscopy to characterise these changes and test the mechanisms involved. By sharing findings between teams in Japan and France and training early-career researchers, we aim to lay the groundwork for new therapeutic strategies.

We aim to develop a new cancer treatment strategy by selectively inducing senescence in cancer cells and then eliminating those senescent cells.

MISSION 16

Understanding the Mechanism of Heart Muscle Regeneration: Application in the Prevention and Treatment of Heart Disease

JAPAN × AUSTRALIA

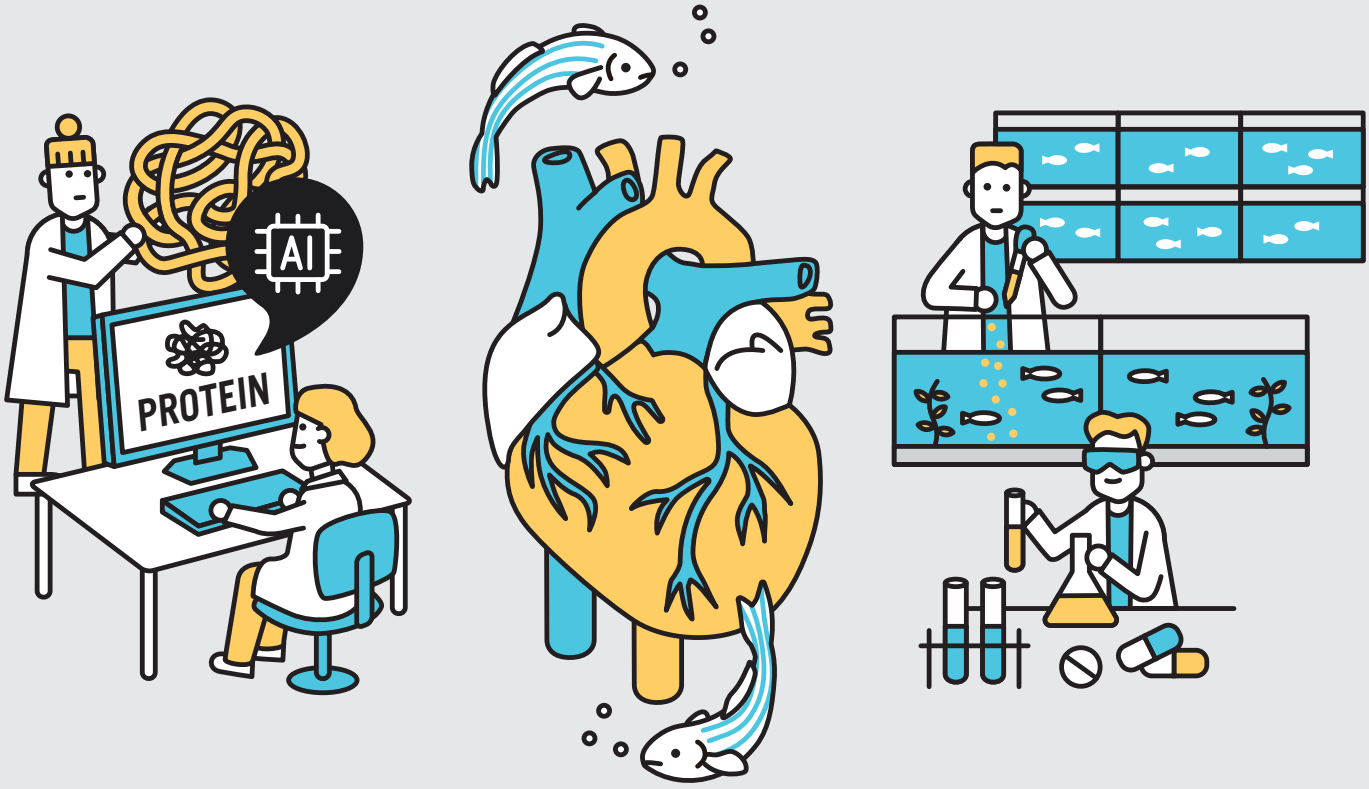
Mechanisms Blocking the Repair of Mammalian Hearts After Injury: Using AI-Assisted Directed Evolution of Novel Biologics to Empower Regeneration

Japan-Australia Joint Research KIKUCHI Kazu

Year Awarded: FY2025	Domestic Research Institution: Research Institute, National Cerebral and Cardiovascular Center (NCVC)	Counterpart Research Institutions: (Australia) Victor Chang Cardiac Research Institute, The University of New South Wales; The Australian National University; Centenary Institute	Research Period: FY2025-FY2029

TARGET

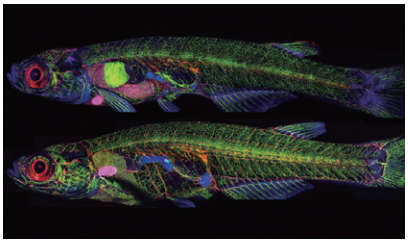
Zebrafish, a favorite aquarium fish, possess a special capability: their hearts regenerate rapidly even after they've sustained an injury. Danionella is a highly transparent minnow that shares the zebrafish's remarkable ability to regenerate heart tissue. Research is currently underway using Danionella to identify the factors responsible for this ability and to observe biological responses in real time. This project is utilizing AI and other technologies with the aim of developing therapeutic drugs that alleviate symptoms following a myocardial infarction.



KEY POINT

Modeling the Zebrafish's Capabilities in Developing Treatments for Human Heart Disease Patients

Heart disease is a common illness and the second leading cause of death among the Japanese. Although patients may recover from a myocardial infarction, at this point there are no effective treatments for any heart disease that subsequently tends to occur more easily. In this project, researchers seek to identify the factors underlying cardiac muscle regeneration in zebrafish and Danionella. They will then apply AI to that data in an effort to artificially design proteins capable of inducing similar effects in mammalian hearts. Validation will initially use mice, with the hope this technology will lead to a novel therapy for human cardiac patients that generates new heart muscle directly from existing tissue, thereby aiding in the treatment and prevention of ischemic heart disease.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



KIKUCHI Kazu
Director, Department of Cardiac Regeneration Biology, Research Institute, National Cerebral and Cardiovascular Center (NCVC)



Robert Graham
Professor, Molecular Cardiology Laboratory, Victor Chang Cardiac Research Institute, The University of New South Wales

TARGET
REGENERATION
- Using zebrafish and mice in researching mechanisms of the heart muscle regeneration "switch"
- Analyzing live-imaging of heart regeneration using Danionella

METHODS
DESIGN
- Using AI to estimate ancestral forms of targeted factors
- Using directed molecular evolution to enhancing regenerative capacity

OUTPUT
INNOVATION
- Elucidating cardioregenerative mechanisms
- Designing variants that promote heart regeneration
- Establishing a foundation for future cardioregenerative medicine

INTERVIEW with KIKUCHI Kazu

Regenerating Cardiac Muscle Cells, an Ability We Actually Once Had

We know that mammals, like zebrafish, possess the ability to regenerate heart muscle shortly after birth. With the body's growth, however, this regenerative capacity is gradually lost, apparently as development of other functions is prioritized. Our goal is to identify factors that can reprogram human cardiomyocytes—heart muscle cells—into a state wherein they possess that regenerative capacity. This approach acts directly on the patient's own cardiomyocytes, eliminating concerns about tissue rejection, as can occur with heart transplants.





Raising vast numbers of Danionella in one of the largest breeding operations in the world



With visitors inspecting the Center

From Identification to Functional Enhancement, Enabling Regenerative Capacity in the Human Heart Through Collaborative Efforts

Cardiovascular disease is also a leading cause of death in Australia. The Japanese team is tasked with research to discover the mechanisms of heart regeneration using zebrafish and Danionella. Meanwhile, the Australian team's research employs machine learning to retrace the evolutionary lineage, returning targeted factors to their state prior to losing their regenerative capacity, and even enhance their regenerative function. With therapeutic effects already having been confirmed in mouse and rat experiments, the goal going forward is to provide the human heart this cardiac muscle regenerating capacity via catheter-administered treatments.

KIKUCHI Kazu
PROFILE

After graduating from the Tohoku University School of Medicine, Dr. Kikuchi earned his Ph.D. from the university's Graduate School of Medicine. His doctoral studies involved research into the mechanisms regulating lymphocyte development in mice. He conducted research on immunology and zebrafish heart development and regeneration at Duke University in the United States, and subsequently headed the Cardiac Regeneration Laboratory at the Victor Chang Cardiac Research Institute in Australia. Now at the National Cerebral and Cardiovascular Center, he is working to elucidate the mechanisms regulating cardiac muscle regeneration using fish and mouse models.

START 2025 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

Using zebrafish and Danionella, the team will find the genes and molecules involved in regenerating cardiac muscle and investigate their functions in detail. AI will then be applied to the findings to design factors that enhance regenerative capacity, followed by validation of their effects on cardiac muscle derived from mouse cells and human iPS cells, evaluation of their safety and efficacy, and assessment of their potential for therapeutic applications. This research is advancing in stages through a Japanese-Australia international collaboration, aiming to pave the way for next-generation cardiac regenerative medicine.

Research will aim to develop a novel treatment for heart disease, developing gene therapies that generate new cardiac muscle from the patient's own existing heart muscle.

MISSION 17

Mapping Active Genes to Enable Precision Cancer Care

JAPAN × AUSTRALIA

CELLOGRAMRx: Pan-Cancer Cellular Composition and Signalling Relationship Mapping to Identify Novel Therapeutic Targets

Japan-Australia Joint Research

SUZUKI Yutaka

Year Awarded: FY2025	Domestic Research Institutions: Graduate School of Frontier Sciences, The University of Tokyo; RIKEN Center for Integrative Medical Sciences	Counterpart Research Institutions: (Australia) Garvan Institute of Medical Research; The University of Sydney; St Vincent's Hospital Sydney	Research Period: FY2025-FY2027

TARGET

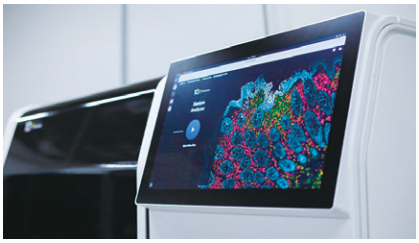
This project focuses on utilizing "spatial transcriptomics," a technology that, like a map, delineates the locations of cells within tissues and identifies active genes, and combining this data with pathology imaging and patient treatment histories to enable a deeper analysis of cancer cell characteristics and their relationships with the surrounding microenvironment. A key element of this research is the ability to analyze data that includes the precise spatial location of cancer cells. The Japanese team is collaborating with the research team in Australia to collect over 2,000 cancer tissue samples and create a "spatial cell map" for each type of cancer.



KEY POINT

Spatial Information Advances Cancer Tissue Research, Helps in Identify Key Molecules for Therapy

Research using spatial transcriptomics has revealed the presence of "onco-fetal" cells amid non-cancerous cells. These cells exhibit characteristics resembling the cellular environment found during fetal development. This environment is believed to promote the growth of cancer cells and help them evade the immune system. Investigating these "fetal-like" cells may also shed light on why certain cancer cells resist immunotherapy. Further research using a combination of spatial transcriptomics and machine learning is expected to lead to personalized medicine tailored to the unique characteristics of each patient's cancer.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



SUZUKI Yutaka
Professor, Life Science Data Research Center, Graduate School of Frontier Sciences, The University of Tokyo



Ankur Sharma
Laboratory Head, Translational Genomics Program, Garvan Institute of Medical Research

TARGET

STAMP2K

Spatial Transcriptomics Atlas for Multi-cancer Profiling:
Building a comprehensive atlas encompassing 2,000 tissue samples from Japan and Australia

METHODS

ONCO-FETAL

- Identifying cells that undergo fetal-like reprogramming
- Analyzing immune interactions
- Conducting spatial analysis with machine learning models and integrating pathology imaging

OUTPUT

BIOMARKER

- Discovering novel therapy targets
- Rationally selecting targets for precision therapy
- Developing new therapeutic interventions to supplement ICIs

INTERVIEW with SUZUKI Yutaka

Fundamental Cancer Therapies with the Optimal Treatment for Each Individual Cell

The conventional approach to treating cancer has been based on the concept of observing and eliminating abnormalities in DNA. However, cancer cells possess various mechanisms that cannot be understood solely by observing DNA, and achieving more precise treatments requires tailoring the right treatment for each individual cell. Spatial transcriptomics has recently enabled simultaneous analysis of millions of cells within a tissue, along with their positional data. The better we understand the characteristics of cell clusters, the greater the possibilities are for selecting the optimal anti-cancer drugs.





At a conference in Australia. Demonstrating leadership in Japan-Australia cooperation, the project aims to foster collaboration with other Asian nations.



Developing closer ties over a meal

Spatial Transcriptomics Data Also Stimulates Joint Research with Organizations Abroad

Cellular data obtained through spatial transcriptomics can be released publicly, so it holds immense potential as data that can involve and be utilized by researchers overseas. In particular, our collaboration with Australia, which leads the world with its vast collection of samples, is serving to advance our joint research. Just as Japan once led the world in DNA sequencing analysis, this represents a significant opportunity for Japan to play a leading global role again.

SUZUKI Yutaka
PROFILE

Prof. Suzuki runs one of Japan's largest facilities for generating large-scale, multi-layered omics data at The University of Tokyo's Kashiwa II campus. Adopting the most advanced large-scale measurement technologies, such as next-generation sequencing and more recently single-cell analysis and spatial analysis, he collaborates with researchers nationwide on over 100 joint projects annually, while investigating how these technologies can be applied in researching human disease.

RESEARCH APPROACH

START 2025

+ 3 YEARS

The project will proceed in stages, utilizing spatial information from cancer tissues to build a "spatial map of cells." Through the Japan-Australia collaboration, researchers will conduct spatial transcriptomic analysis of cancer cases, start collecting data and building out the database, and search for cellular clues linked to malignant progression. Once the spatial database is complete, it will be combined with image data for integrated analysis, with the aim of developing technologies for predicting optimal treatment strategies.

FUTURE

The project further aims to expand research networks and establish Japan as a leader in Asia in the field of spatial analysis for cancer treatment.

MISSION 18

Preventing the Silent Spread of Infectious Diseases

JAPAN × AUSTRALIA

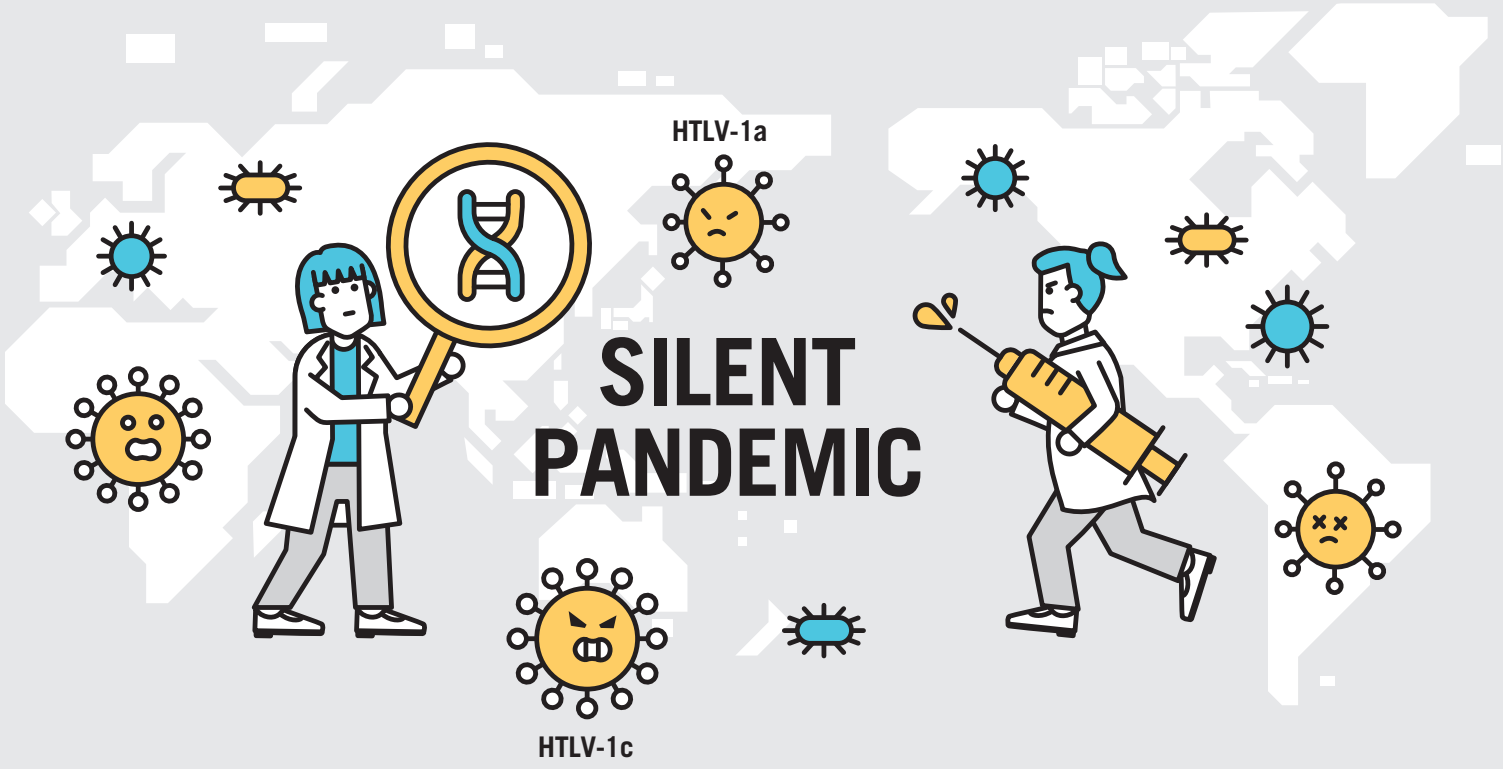
Control of Endemic HTLV-1 to Prevent Silent Global Spread

Japan-Australia Joint Research MATANO Tetsuro

Year Awarded: FY2025	Domestic Research Institutions: National Institute of Infectious Diseases (NIID), Japan Institute for Health Security (JIHS); Joint Research Center for Human Retrovirus Infection, Kumamoto University; Graduate School of Frontier Sciences, The University of Tokyo	Counterpart Research Institutions: (Australia) The Peter Doherty Institute for Infection and Immunity, The University of Melbourne; The University of New South Wales; Queensland University of Technology (QUT); Walter and Eliza Hall Institute of Medical Research	Research Period: FY2025-FY2029

TARGET

HTLV-1 (human T-cell leukemia virus type 1) induces a chronic life-long latent infection in humans. Control of silent HTLV-1 transmission from asymptomatic carriers is a global public health priority. This international joint project led by advanced research teams in Japan and Australia aims to elucidate the mechanisms of HTLV-1 transmission and disease onset towards the development of vaccines and therapeutics against HTLV-1 infection.



KEY POINT

Aiming at the Establishment of a Novel Strategy to Control HTLV-1 Infection by Leveraging the Respective Strengths of Japanese and Australian Teams

HTLV-1 can infect T cells and develop into severe diseases—including leukemia—after long-term asymptomatic latent infection. It is estimated that over 10 million people worldwide are infected with HTLV-1. In this project, the Japanese teams, who have advanced research systems utilizing clinical samples and animal models, share samples, technologies, and information with the Australian teams, who have cutting-edge technologies, including mRNA engineering, to conduct joint research, analyzing potential differences in the phenotype and pathogenesis between HTLV-1a and HTLV-1c subtypes prevailing in Japan and Australia, respectively. This project focuses on elucidating the molecular mechanisms of HTLV-1 transmission/infection and disease progression to determine the targets for prophylaxis and therapy, leading to the development of vaccines and therapeutics against HTLV-1 infection. Additionally, this research may contribute to the establishment of a global database.



Principal Investigators

RESEARCH COLLABORATION FRAMEWORK



MATANO Tetsuro
Director-General, National Institute of Infectious Diseases (NIID), Japan Institute for Health Security (JIHS)



Damian Purcell
Professor, The Peter Doherty Institute for Infection and Immunity, The University of Melbourne

TARGET

HTLV-1 INFECTION

- Elucidation of the mechanisms of transmission/infection & disease onset
- Comparison of HTLV-1a & HTLV-1c strains
- International collaboration & human resource development towards the next generation

METHODS

ADVANCED TECHNOLOGY

- Development of mRNA vaccines inducing antibodies with evaluation in animal models
- Epidemiological & omics analyses to determine the onset factors & pathogenesis
- Exchange of human resources and sharing of samples, technologies & information

OUTPUT

PREVENTION

- Acquisition of non-clinical POC for newly developed mRNA vaccines inducing anti-HTLV-1 antibodies
- Development of diagnostic methods & measures for disease prevention utilizing cutting-edge technologies
- Establishment of a global HTLV-1 vaccine research consortium

INTERVIEW with MATANO Tetsuro

Research Collaboration Leveraging the Respective Strengths of Partners to Prevent HTLV-1 Transmission & Disease Progression

Our partnership is based on the long-term reliable relationship between Professor Purcell and me since both were working as visiting fellows at NIH, USA. Given that the Australian government has recently focused on HTLV-1 control, we have launched this joint research project. The Japanese teams conduct virological, immunological, epidemiological, and omics analyses using clinical samples & non-human primate (NHP) models to develop prophylactic HTLV-1 vaccines and therapeutics for disease prevention in collaboration with the Australian teams having advanced RNA technologies. Our research focuses on two key concepts, “transmission prevention” and “disease prevention,” for HTLV-1 control.



Professors Purcell and Matano, joint project partners. They share a long history of collaborative research.





“Kickoff” gathering at Melbourne in 2025

Global Initiative Towards Eradication of the “Silent Spread of Infection”

Japan has been leading research on HTLV-1 infection. In this project, we are collaborating with the Australian teams towards the control of chronic infectious diseases including HTLV-1 infection. We promote not only basic and clinical research but also social initiatives to encourage HTLV-1 spread awareness and testing, potentially communicating with Aboriginal communities in Australia. The Japanese and Australian teams are leading the establishment of a global consortium with researchers all over the world for the control of “silent spread of infection”.

MATANO Tetsuro
PROFILE

Dr. Matano worked as an orthopaedic surgeon for five years after graduating from Faculty of Medicine, University of Tokyo. He then started basic research and obtained Doctor of Medical Sciences at Graduate School of Medicine, University of Tokyo. He has been a Professor at Institute of Medical Science, University of Tokyo since 2006. He was appointed as the Director of the AIDS Research Center at NIID in 2010 and is now working as the Director-General of NIID and Executive Director in JIHS. He also serves as the President of the Japanese Society for AIDS Research and a Governing Council member of the International AIDS Society. Dr. Matano is working on viral immunology, NHP models, and vaccine development against HIV-1, HTLV-1, and respiratory virus infection towards the control of chronic infection. Guided by the keywords “reliable”, “diversified”, and “advanced,” he is promoting international collaboration and human resource development towards the next generation.

START 2025 | **+ 5 YEARS** | **FUTURE**

RESEARCH APPROACH

The project focuses on elucidating the mechanisms of HTLV-1 transmission and developing a vaccine to prevent its spread with verification of vaccine efficacy in NHP models, leading to the establishment of a strategy for clinical trials. The project also performs epidemiological and omics analyses of clinical samples to elucidate the onset factors and pathogenesis in HTLV-1 infection and utilize cutting-edge technologies to develop diagnostic agents and therapeutics. The Japanese and Australian teams lead the establishment of a global joint research consortium, encouraging human resource development.

Establishment of a global consortium for HTLV-1 research will lead to the control of chronic infectious diseases towards the next generation.



ASPIRE

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