World Premier International Research Center Initiative (WPI)
FY2024 WPI Project Progress Report

Host Institution	Keio University	Host Institution Head	Kohei Itoh
Research Center	Human Biology-Microbiome-Quantum Research Center (Bio2Q)		
Center Director	Kenya Honda	Administrative Director	Oltea Sampetrean and Haruhiko Siomi

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2025) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

➢ Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

Summary of State of WPI Center Project Progress (write within **2 pages**)

Overview: In our third year, we significantly strengthened cross-team collaboration to accelerate progress across our six scientific goals, while continuing to build the infrastructure and organizational systems needed to evolve into a fully independent, globally recognized research institute.

On the scientific front, we aimed to advance the integration of multiomics, metabolomics, quantum computing, and AI to explore host–microbiome interactions in health and disease. We have made several discoveries, including the identification of gut bacteria and metabolites associated with colonization resistance against pathogens, drug metabolism related to neurodegeneration, and lipid metabolites associated with longevity. These discoveries were enabled by cutting-edge omics, imaging, and computational tools. Studies using organoids, non-human primates, and connectomics further illuminated the liver and microbiota interactions and host–environment dynamics. Operationally, the Open Lab was established to connect people, ideas, and research areas, fostering collaborative research among early career scientists. The newly completed Structural Analysis Core Facility is expected to enhance research and collaboration capacities. Both units represent flagship platforms and potential prototypes for future laboratories in the new Bio2Q building. Planning for new research buildings has also accelerated, guided by the host organization. To support institutional transparency and autonomy, we expanded English-language records, along with the development of new internal regulations.

Research of the Highest Global Level and Fused Disciplines: Research conducted in FY2024 has led to several significant discoveries and substantial progress toward the Center's six scientific goals, as summarized below:

1. Accumulate Multiomics Data and Compile Multidimensional Database

- **Gut Microbiota and Pathogen Resistance:** A key gut bacterial community that limits Enterobacteriaceae pathogen colonization and prevents gut dysbiosis by efficiently competing for gluconate was identified. These findings were published in *Nature* and also contribute to Goal 2.
- **Parkinson's Disease Study**: Continued generation and integration of microbiome datasets from well-phenotyped patient samples in the Parkinson's disease (PD) cohort.
- **Lipidomics Database:** A comprehensive lipidomics dataset spanning multiple tissues and life stages in mice was compiled. This dataset provides insights into aging and microbiota-host interactions, was published in *Nature Aging*, and also contributes to Goal 2.

---

2. Elucidate Structure and Function of Microbiome-Derived Metabolites

- **Cholesterol Metabolism in Longevity**: Phosphoethanolamine-conjugated cholesterol/ steroid hormones enriched in centenarians, with potential roles in cholesterol metabolism and longevity, were identified (these findings also contribute to Goal 1, centenarian cohort).
- **Levodopa Metabolism in PD**: Gut bacterial conversion of levodopa into potentially neurotoxic derivatives in PD was uncovered, revealing implications for therapeutic strategies.
- **D-Amino Acids and Kidney Health:** D-amino acids biosynthesized by gut microbes linked to

kidney function and immune regulation were characterized, with d-asparagine identified as a potential kidney function biomarker.

---

3. Refine Imaging Metabolomics and Structural Biology for In Situ Functional Analysis

- **MS-DIAL 5 Development:** MS-DIAL 5, an advanced integrative analytical platform for untargeted lipidomics and spatial metabolomics, was released, enabling the visualization of bacteria-derived lipids in host tissues. These findings were published in *Nature Communications*.
- **Structural Analysis Infrastructure Set-up**: Cryo-electron microscopy (CryoEM) and tomography (CryoET) platforms were established with the installation of Compact 03 and Arctis, and preparation for KriosG4 deployment at the new Structural Analysis Core Facility.
- **Ultra-high field MRI**: The 11.7T MRI was established to visualize alterations in regional shape changes and to collect MR spectroscopy data to determine the energy metabolism of common marmosets non-invasively.

---

4. Develop Quantum Computing and Multisystem Analysis

- **FMQA Optimization:** Factorization Machine with Quantum Annealing (FMQA) was introduced and enhanced for efficient black-box optimization.
- **Predictive Tools**: Tools such as gutMPT (a transformer-based AI system) and quantum reservoir computing (QRC) algorithms were developed for modeling enzyme–metabolite interactions and biological time-series data (EEG/ECG), thereby enhancing omics data analysis. STRGNN, a deep learning model for predicting drug–disease associations through multimodal omics integration, was created, thereby advancing drug repurposing efforts.
- **Quantum Algorithms and Microbiome**: Quantum Approximate Optimization Algorithm (QAOA) and Quantum Annealing (QA) algorithms were developed for modeling therapeutics against multi-drug resistant Enterobacteriaceae pathogens. This project was submitted to the NEDO 2025-26 Challenge – a premier national competition for the development of quantum technologies.

---

5. Model Environmental-Human Interface via Organoids and Animal Models

- **Hepatocyte and Pancreatic Cancer Organoids:** Long-term culture and differentiation of human adult hepatocyte organoid cultures were optimized, establishing a robust platform for studying liver–gut interactions (*Nature*, in press). Hypoxia was shown to suppress KDM6A activity in pancreatic cancer organoids, driving malignancy via epigenetic reprogramming, findings published in *Nature Cell Biology*.
- **Pioneering Primate Models:** The first natural breeding of germ-free marmosets was achieved, enabling behavioral studies in primates without microbiota. Gene-edited Alzheimer's disease (AD) model marmosets (PSEN1 mutations) were developed, thus facilitating studies on microbiome-neurodegeneration interactions (also contributing to Goal 6).
- **Microbiota and Sugar Preference:** Gut bacteria were found to modulate sugar preference via vagal signaling, highlighting the role of microbiota in metabolic disorders.

---

6. Refine Connectomics and Structural Biology to Understand Gut-Brain Communication

- **Vagus Nerve and Immune Modulation:** Vagus nerve stimulation was shown to modulate gut immunity, and microbial metabolites were shown to influence neural circuit homeostasis.
- **Synaptic Organizers and Sensory Systems:** The roles of synaptic organizers (Cbln1/Cbln2, GluD, GluK) in enteric and sensory systems were described, linking sensory degeneration (e.g., hearing loss) to increased dementia risk.
- **Infant Microbiome–Brain Studies:** Infant studies measuring brain activity were initiated to examine microbiome–brain–behavior relationships, including attachment, interoception, and learning development.

International Research Environment and Organizational Reforms: The newly introduced streamlined onboarding and grant support system enhanced the integration and productivity of international researchers. English committee records and the implementation of an internal portal within the Bio2Q website improved transparency and information sharing, while robust internal systems for biosafety, genetic recombination experiments, and conflict of interest (COI) management advanced the Center's move toward institutional independence. Both Keio University and Bio2Q have put in place internal regulations allowing for the employment of excellent researchers regardless of age, and collaborate in promoting reform, globalization, and diversity.

* Describe clearly and concisely the progress being made by the WPI center project from the following viewpoints.

1. World-Leading Scientific Excellence and Recognition

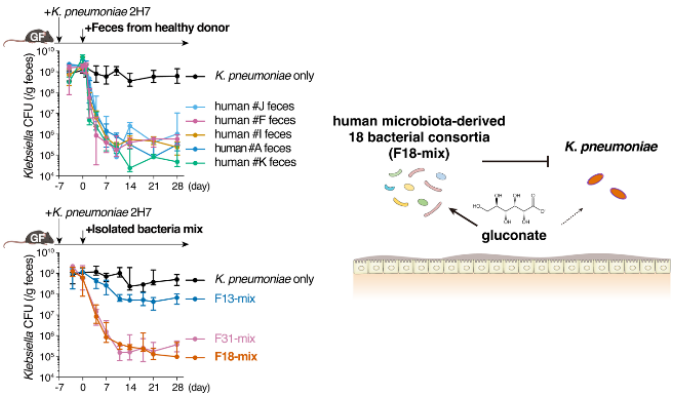
1-1. Advancing Research of the Highest Global Level

* Among the research results achieved by the center, concretely describe those that are at the world's highest level. In Appendix 1, list the center's research papers published in 2024.
* Regarding the criteria used when evaluating the world level of the center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

Bio-1 Multidimensional Data Analysis Core

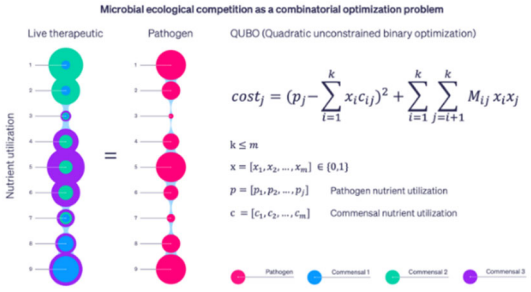
Microbiome Team (Honda, Atarashi, Tuganbaev, Leong, Kanai, Huh, Sampetrean, Sasabe, Pan, V.J. Sahayasheela)

In our latest findings published in ***Nature*** (Furuichi et al., 2024, App.1-19 and right figure), **Honda, Atarashi, and Tuganbaev**, in collaboration with **Arita group**, demonstrated that commensal bacterial consortia could effectively suppress the overgrowth of Enterobacteriaceae pathogens, including antibiotic-resistant *E. coli* and *K. pneumoniae*, through nutrient competition. In this study, key gut bacterial species from healthy volunteers that play a crucial role in limiting pathogen proliferation, colonization, and preventing gut dysbiosis by efficiently utilizing gluconate were identified.



Honda and Atarashi group revealed a direct link between the gut bacteria and cholesterol/steroid hormone metabolism. Notably, the bacterial species within the centenarian gut microbiota produce phosphoethanolamine-conjugated cholesterol/steroid hormones, a newly identified class of bioactive molecules. These metabolites may contribute to the regulation of cholesterol metabolism, support metabolic health, maintain cognitive function, and potentially play a protective role in age-related diseases. These findings provide valuable insights into microbiome-based therapeutic strategies, with significant implications for engineered bacterial consortia and live biotherapeutic products (LBP). Harnessing the beneficial functions of these bacteria could pave the way for novel interventions aimed at improving gut health and promoting healthy longevity.

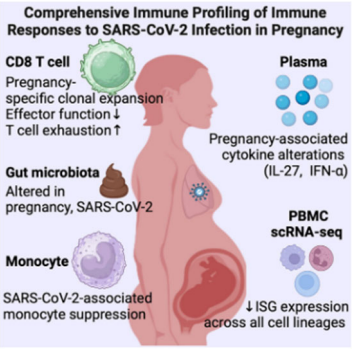
In a cross-core and cross-disciplinary effort, **Tuganbaev** computationally addressed another aspect of the microbiome data in the ***Nature*** study. Identification of bacterial combinations that can positively affect human health is one of the main goals of microbiome research. However, only a small fraction of possible combinations can be explored experimentally. Thus, combinatorial complexity of human microbiome constitutes a barrier preventing empirical identification of optimal bacterial consortia. To overcome this limitation, in the context of the ***Nature*** study, Jr. PI Tuganbaev has developed QAOA and QA hybrid classical-quantum algorithms implemented on IBM quantum (gate-based) and D-wave (quantum annealing) QCs respectively to predict the most effective bacterial combinations against multi-drug-resistant pathogens for experimental validation (figure right). These algorithms have the potential to greatly increase the effectiveness with which limited laboratory resources can be utilized in the exploration of human microbiome. When applied to the urgent medical challenge of multi-drug-resistant infections, the algorithms have the potential to dramatically improve development speed and effectiveness of live therapeutics against multi-drug-resistant pathogens to promote global health in a



post-antibiotic era.

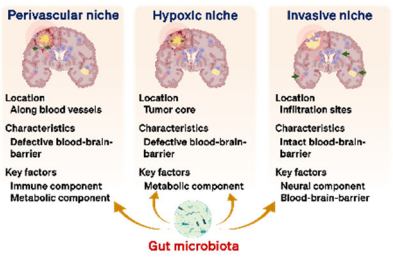
Leong group isolated thousands of bacterial isolates from patients with PD and screened them for levodopa metabolism. Several novel levodopa-metabolizing bacteria have been discovered and their metabolites have been confirmed using LC-MS. These gut microbes produce 3-carboxysalsolinol from levodopa or salsolinol from dopamine in a culture media-dependent manner. Salsolinol production is of significant interest because of its well-studied dopaminergic neuronal toxicity and the hypothesized potential etiological causes of PD. The identification of culture conditions and pathways that are induced to produce salsolinol and 3-carboxysalsolinol is underway. Simultaneously, an AI-guided high-throughput culturomic system was implemented to rapidly isolate diverse species from a broad subset of patients with PD to understand the prevalence of such metabolizers in the PD cohort.

Kanai group employed surgical, bacterial, immunological, and metabolic approaches and uncovered the mechanisms by which the upper small intestinal microbiota controls sugar preference, demonstrating a novel bacteria-metabolite-vagal afferent signaling pathway essential for the preference of glucose over artificial sweeteners. They established potential therapeutic targets for obesity and type 2 diabetes by manipulating gut microbiota-derived metabolites to influence sugar preferences. In addition, the group pioneered the vagus nerve hepatic branch electrical stimulation (VHNS), significantly advancing our understanding of neuroimmune interactions. This innovative method showed enhanced regulatory T cell (Treg) activity in the intestine, effectively reducing the severity of colitis in experimental models. VHNS activated specific brain regions, including the nucleus tractus solitarius and the amygdala, highlighting a novel brain-gut immune axis. These studies demonstrated global leadership in the integration of microbiome research, neuroscience, immune modulation, and related therapeutic applications.

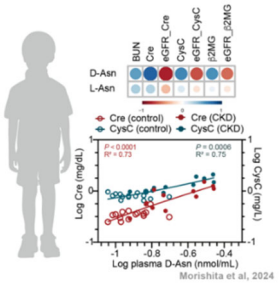


Huh group investigated the effects of SARS-CoV-2 infection, the virus causing the COVID-19 pandemic, on the microbiome and immune changes in pregnant women (Oh et al., 2024, App.1-108 and left figure). By comparing non-pregnant and pregnant women with or without infection, they found that SARS-CoV-2 infection led to pregnancy-associated changes in T cell and monocyte functions. Moreover, they found that SARS-CoV-2 infection led to long-lasting microbiome changes that persisted for more than 6 months by assessing the microbiota community in patients who recovered from COVID-19. Furthermore, they identified the gut bacteria that metabolize glucocorticoids during pregnancy. The above results identify a close interaction between pregnancy, viral infection, and gut microbiome, the dysregulation of which may impact both maternal and offspring's health.

Sampetrean group investigated the role of microbiota in cancer and showed that germ-free or antibiotic-treated mice carrying syngeneic malignant brain tumors had a worse prognosis than their counterparts with intact microbiota (figure right, manuscript under preparation). These results suggest a yet unreported modulation of cancer at a distal site by the microbiota and the possibility of the gut-brain axis shaping brain tumor stem cells niches.



By investigating how the gut microbiome modifies L-amino acids and their impact on host physiology, **Sasabe group** has previously shown that gut commensal bacteria modify various L-amino acids (e.g., L-alanine) into D-enantiomers, which become integral components of bacterial cell walls and modulate host innate defense and immune responses. Microbial D-amino acids accumulate postnatally but are catabolized and excreted via the kidneys, maintaining systemic amino acid homeostasis. In 2024, they discovered that impaired kidney function leads to the accumulation



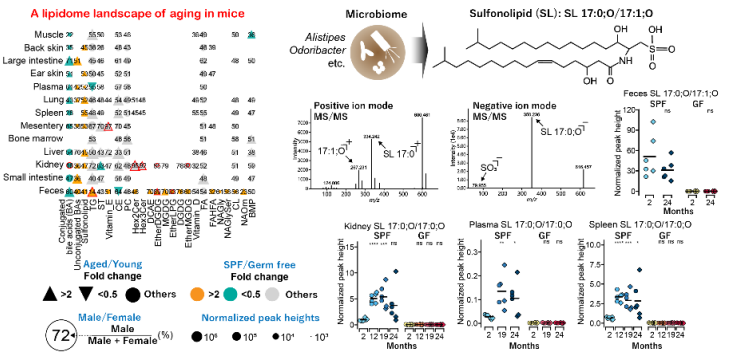
of D-amino acids in the blood, and they proposed D-asparagine as a new kidney biomarker in children (Morishita et al., 2024, App.1-9 and left figure). Moreover, they found that the day-night rhythm of the gut microbiota affects host D-amino acid levels, influencing the hypothalamic-pituitary-adrenal axis in response to microbial metabolites (manuscript under preparation). Currently, their research focuses on understanding D-amino acid metabolism in energy and nitrogen utilization, elucidating the host-microbiome metabolic interplay.

Pan, a Postdoctoral Fellow, investigates the role of gut microbiota in regulating the gut-brain axis, a fundamental pathway governing the host's neurological function, metabolic balance, and immune response. By focusing on the interaction between gut microbiota and the enteric nervous system (ENS), she identified key human bacterial consortia that are essential for maintaining ENS homeostasis. Unraveling these mechanisms provides novel insights into multi-organ crosstalk, advancing the frontiers of microbiome-neuroscience research and paving the way for innovative therapeutic strategies.

Mitochondrial DNA (mtDNA) integrity is vital for cellular functions. Postdoctoral Fellow **V.J. Sahayasheela**, explored the influence of microbiomes and their metabolites, particularly 8-oxo-7,8-dihydroguanine (8-oxoG), on oxidative DNA damage. Using Nanopore sequencing, he successfully detected 8-oxoG, the modifications were distinguished using machine learning. The aim of this study was to further investigate the effects of microbiome-driven oxidative stress on mtDNA using gnotobiotic models and to uncover key microbiome consortia that can reduce oxidative stress-driven 8-oxoG formation. These findings may lead to probiotic-based interventions for reduced DNA damage and healthy aging.

Metabolome Team (Arita, Soga)

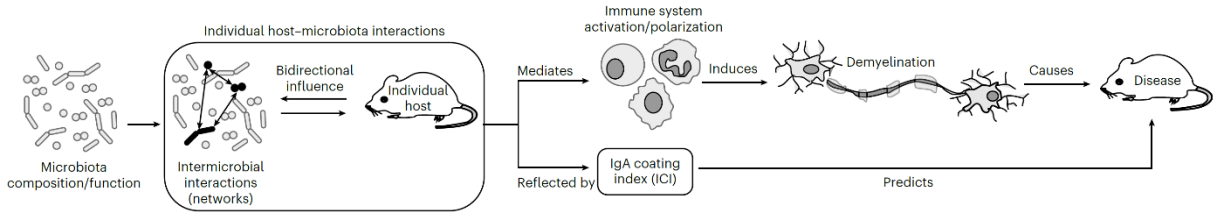
Understanding the molecular mechanisms underlying aging is crucial for enhancing healthy longevity. **Arita group** compiled a comprehensive dataset of non-targeted lipidomics across multiple tissues at various life stages in mice to explore the potential link between aging and lipid metabolism, considering sex (male/female) and microbiome (SPF/germ-free) dependencies. This study provides a valuable resource for illuminating potential links between bacterial lipid metabolism and host tissue homeostasis associated with aging (Tsugawa et al., 2024, App.1-5 and figure right). Indeed, spatial lipidomics using MSI demonstrated that a group of lipids, including sulfonolipids derived from the gut microbiota, were selectively transferred to intestinal lymphoid tissues.



In addition, **Arita group** developed a strategy for isolating genes encoding lipid biosynthetic enzymes from specific lipid-producing bacteria. So far, they have identified four new functional lipids including sulfonolipids, and six types of biosynthetic enzymes that produce them (manuscript under preparation), of which one patent application has been filed. In 2024, the group also developed a new integrative analytical platform, namely **MS-DIAL 5**, for untargeted lipidomics, in-depth lipidome structural elucidation, and their cellular and tissue localization through MALDI-MSI-based spatial lipidomics (Takeda et al., 2024, App.1-110).

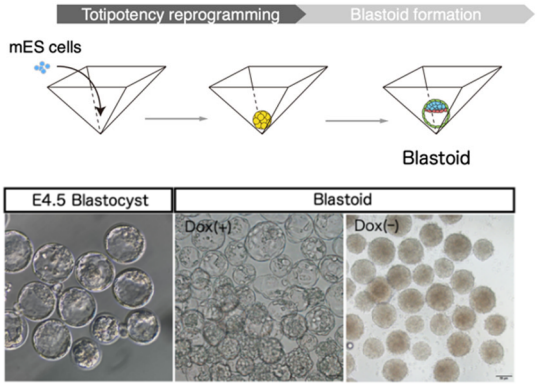
Soga group focused on the fact that gut bacteria are linked to neurodegenerative diseases, but risk factors beyond microbiota composition are limited. Collaborative work with Steimle et al. involved the use of a preclinical model of multiple sclerosis (MS) and experimental autoimmune encephalomyelitis (EAE) to identify microbial risk factors. Mice with different genotypes and complex

microbiota or six combinations of synthetic human microbiota were analyzed, resulting in varying probabilities of severe neuroinflammation. However, the presence or relative abundance of the suspected microbial risk factors failed to predict disease severity. *Akkermansia muciniphila*, often associated with MS, exhibited variable associations with EAE severity, depending on the background microbiota. Significant inter-individual disease course variations were observed among mice harboring the same microbiota. Evaluation of microbial functional characteristics and host immune responses demonstrated that the immunoglobulin A coating index of certain bacteria before disease onset is a robust, individualized predictor of disease development. This study highlights the need to consider microbial community networks and host-specific bidirectional interactions when aiming to predict the severity of neuroinflammation (Steimle et al., 2024, App.1-88 and figure below).



Genome Dynamics Team (Siomi, Ishigaki, Solberg)

During early embryogenesis, a transposable element (TE) burst occurs, accompanied by zygotic genome activation (ZGA), a critical post-fertilization step that promotes totipotency and allows different cell fates to emerge in the developing embryo, cell potency, and normal embryonic development. Recently, **Siomi group** showed that normal embryonic development requires the expression of TE (MERVL). Furthermore, transcriptome and epigenome analyses revealed that MERVL-knockdown (KD) embryos retained an accessible chromatin state and aberrant expression of a subset of two cell-stage-specific genes at the mid-preimplantation stages. These results suggest a model where MERVL plays a critical role in regulating the transition from totipotent to pluripotent state of host cell potency. With this information, the group has developed a cell culture system that induces mESCs into blastocyst-like cells (blastoid) with high efficiency (figure right). Recent studies have shown that the maternal microbiome modulates fetal development and that microbiome stress signaling pathways activate TEs. To elucidate how the maternal microbiome affects TE expression and chromatin processes in embryos, Siomi group has also collaborated with the Affiliated PI **Hase**, a specialist in gut immunity and commensal bacteria.



Ishigaki group is dedicated to elucidating the functions of genetic polymorphisms that influence human immunity, focusing on three major topics. The first is the T cell receptor (TCR). They previously developed a novel analytical pipeline for TCR analysis and reported that human leukocyte antigen (HLA) risk alleles influence thymic selection, leading to an increased frequency of autoreactive TCRs. Using the same pipeline, they identified key TCR features in regulatory T cells. They have since expanded their approach to explore TCR characteristics across different T cell subtypes (Kawajiri et al., 2024, App.1-113) and to investigate T cell plasticity in systemic lupus erythematosus (Nagafuchi et al., 2025). In addition, they are developing a high-throughput experimental system for TCR repertoire analysis, capable of sequencing thousands of samples. The second topic of interest is functional genetics. As part of an international collaboration, the group has contributed to quantitative trait locus (QTL) analysis for splicing (Tian et al., 2024, App.1-112). Furthermore, Ishigaki group established an efficient genome-editing platform to artificially manipulate autoimmunity risk alleles in vitro and experimentally validated the molecular effects of a primary biliary cholangitis risk allele (Hitomi et al., 2024, App.1-71). The third topic was clinical

immunology. In collaboration with clinical researchers, the group investigated immune system abnormalities in patients with autoimmune disease and identified transcriptomic signatures of age-associated helper T (ThA) cells, which undergo clonal expansion and enhance B cell antibody production in multiple autoimmune diseases (Goto et al., 2024, App.1-56). All of these research activities contribute to a deeper understanding of the pathology of human autoimmunity.

During 2024, **Solberg's** research included the identification of the first chromodomain proteins involved in DNA elimination in Paramecium tetraurelia (Solberg et al., 2024, App.1-29), elucidation of the targeting rules of Drosophila Piwi in OSCs, and a review on the role of retrotransposons in preimplantation development in mice. Importantly, Solberg and colleagues identified and reported a class of chromodomain proteins involved in DNA elimination and transposon control in Paramecium tetraurelia, and presented a unified model to explain how Piwi-bound small RNAs target DNA sequences for elimination.

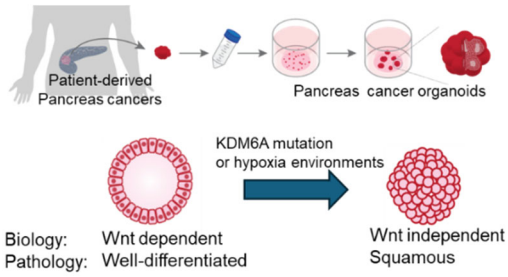
Human Disease Analysis Team (Seki)

Seki group promotes the provision of optimal multidisciplinary team care for patients with PD at Keio University Hospital. Improving the medical care of patients with PD necessitates the optimization of treatment and provision of tailor-made medications based on microbiota assessments. Seki obtained clinical fecal samples from approximately 70 patients with PD at Keio University Hospital with informed consent and provided them to the Microbiome Team for further analysis.

Bio-2: Homeodynamics Mechanistic Analysis Core

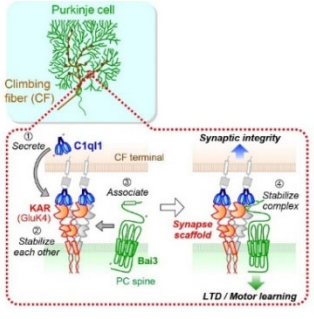
Organoid Team (Sato)

During the research period, **Sato group** advanced organoid culture technologies using human adult hepatocytes to optimize the conditions for both proliferative expansion and functional differentiation. Previously, organoid cultures were successful only in mouse adult or human fetal hepatocytes. This group established a novel culture method that enabled the long-term propagation of human adult hepatocytes. Furthermore, they developed differentiation protocols for hepatocyte organoids, offering a new platform for the study of liver interactions with other organs and the microbiome—key themes of Bio2Q research. This work has been accepted by ***Nature*** and will be published in the next fiscal year.



In parallel, this group conducted pioneering cancer organoid research. Using patient-derived pancreatic cancer organoids, they discovered that low oxygen levels promoted malignant progression by suppressing the activity of the oxygen-sensitive enzyme KDM6A. Loss of KDM6A activity induces epigenetic reprogramming, leading to the adenosquamous transformation of pancreatic cancers. These findings highlight a novel mechanism by which hypoxia drives tumor plasticity and progression. This study was published in *Nature Cell Biology* (Tamagawa et al., 2024, App.1-102, graphical abstract in figure above).

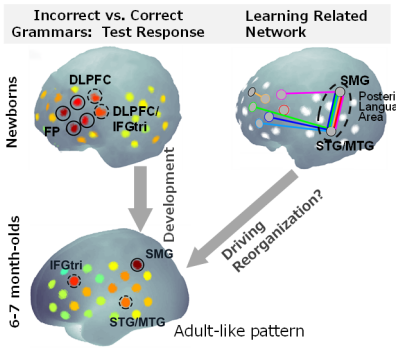
Neuroregulation Team (Yuzaki, Li, Minagawa)



The nervous system, in coordination with the immune, endocrine, and metabolic systems, plays a central role in maintaining homeostasis across the organs. It functions via intricate synaptic connections between neurons and their target organs. The Neuroregulation Team investigated how synapses in the peripheral nervous system, including the autonomic and enteric systems, form and adapt throughout life, focusing on the C1q family synapse organizers (figure right). In FY2024, **Yuzaki group** discovered that Cbln1, a C1q family member, localizes at outer hair cell synapses in the organ of Corti and contributes to noise-induced and age-related hearing loss (Shiozaki et al., under review). Considering that

hearing loss is a major risk factor for dementia, Cbln1 is a promising therapeutic target. In addition, the team explored the role of Cbln1 in activity-dependent neural circuit formation between the dorsal ganglion and spinal cord neurons, which may underlie chronic itch in atopic and contact dermatitis. Although metabolites, nutrients, and bile acids are thought to influence the nervous system through enteroendocrine cells (EECs), their synaptic regulation remains unclear. The team identified Cbln and C1ql subfamilies, as well as GluD and GluK receptors, in enteric and peripheral nerves. Further, they elucidated mechanisms by which GluD and GluK mediate synapse formation in the brain (Itoh et al., 2024, App.1-47; Kakegawa et al., 2024, App.1-86).

Postdoctoral Fellow **Li** is currently investigating synaptic homeodynamics in gut–brain axis regulation. Starting with Cbln2 distribution and molecular mechanisms in the peripheral nervous system, he aims to elucidate its role in enteric synapse organization and neural modulation. In addition, he utilizes CPTX to enhance post-injury corticospinal tract plasticity and explore tissue clearing for gut–brain circuit mapping. Furthermore, by leveraging the Connectoid platform based on brain organoids, he seeks to enhance synaptic integration using CPTX, providing a foundation for future studies on neural regulation in the gut–brain axis.



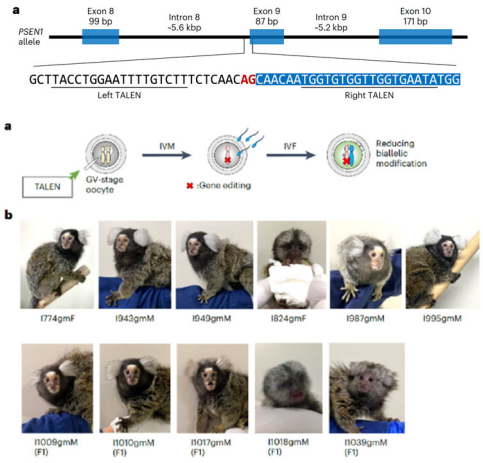
In an international joint research study, **Minagawa group** demonstrated that newborns could learn certain linguistic rules that were previously believed to be unlearnable until approximately their first year. This was demonstrated by measuring the brain activity in response to tone sequences from artificial grammar. However, the brain networks involved differ from those in adults, with newborns exhibiting responses in the left prefrontal cortex. In contrast, six- to seven-month-old infants showed brain responses to correct or incorrect grammar in cortical language areas that corresponded to those of adults. Furthermore, by analyzing brain networks during grammar learning in the left prefrontal cortex of newborns, this study revealed distinct functional connectivity between this region and the language areas of the brain. These connections only became active at six to seven months, illustrating how neural circuits for learning emerge over time (Neural response and learning related network in newborns and 6-7month-olds, figure above). The findings suggest that repeated exposure to stimuli during the first six months of life drives the development of these brain networks. The experimental method used in this study can assess individual differences in infants' learning abilities based on the strength of their brain connectivity. In the future, Minagawa group plans to apply this method to investigate the relationship between the gut microbiome, brain connectivity, and learning abilities in human infants. To conduct a collaborative study with a microbiome research group (Honda Lab), pediatric group, and psychology group (Minagawa Lab), they obtained ethical approval to study young infants and their mothers. They will initiate a neurocognitive experiment using functional near-infrared spectroscopy to examine mother-infant attachment and interoception in relation to the microbiome.

Structural Analysis Team (Aricescu, Suzuki)

Because the Structural Analysis Unit was under construction in FY2024, research progress in the Bio2Q lab was limited. The workflow of the CryoET was developed in MRC-LMB, and the FIB-milling procedure, data collection protocol, and data processing method were further polished and will be applied to Bio2Q research (see Section 5–3 for further details). Regarding the progress in establishing the Structural Analysis Unit, the preparation of the floor plan and the design and construction of an electron microscope (EM) core facility were completed by **Aricescu and Suzuki**. Two world-class instruments, the high-pressure freezer Compact 03 and pFIB/SEM Arctis, were installed for the first time in Japan. Compact 03 was successfully installed and operated with the support of an engineer, Martin Wohlwend, invited from Switzerland. A novel design for the freezing method developed by Martin Wohlwend and MRC-LMB will be applied to Compact 03 in Bio2Q under

collaboration. Arctis (figure right), installed by Thermo Fischer Scientific (TFS), successfully passed a factory-level site acceptance test. Another world-class instrument, the transmission electron microscope (TEM) KriosG4, was ordered and installed in early FY2025. Setting up of all the other lab areas including the wet lab, tissue culture, biophysics room, animal room, bacteria culture room and open/closed office were almost completed, and the Structural Analysis Unit/Core Facility will be able to start the experiments from the beginning of FY2025.

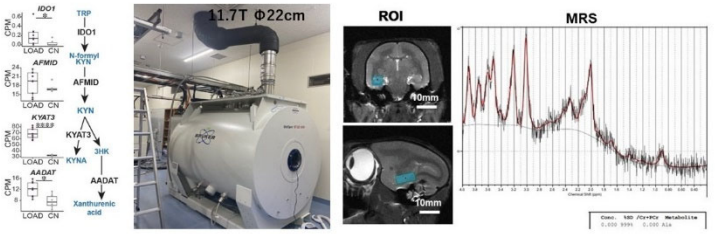
Humanized Animal Model Team (Sasaki)



To investigate the underlying mechanisms of AD onset and its interactions with the microbiome, **Sasaki group** generated presenilin 1 mutant marmosets using gene-editing techniques (Sato et al., 2024, App.1-17 and figure left). In addition, germ-free marmosets were successfully maintained in a sterile state until sexual maturity by the research team during the previous fiscal year. This year, the first successful natural breeding of primates under germ-free conditions in the world was achieved. This accomplishment marks a significant breakthrough, as it demonstrates for the first time that marmosets can deliver and raise offspring without the influence of microbiota. Obtaining germ-free marmosets through natural breeding enables the offspring to be reared by their parents in a natural environment, making them suitable for behavioral analyses. This is particularly important when compared with artificially reared individuals, which often exhibit atypical behaviors. In the future, they will aim to develop germ-free AD model marmosets by transferring fertilized eggs from AD model marmosets into germ-free marmoset recipients. This germ-free AD model facilitates the analysis of the interactions between the microbiome and AD onset. Furthermore, they plan to introduce our touch panel-based motivation/recognition analysis device into a germ-free environment to elucidate the relationship between the gut microbiota and higher cognitive dysfunction in AD.

Imaging Metabolomics Team (Suematsu, Hishiki)

Establishing a mouse model of AD with distinct anatomy and neural system function in humans is challenging. **Suematsu group** chose common marmosets, new-world non-human primates that share comparable networks of communicating fibers in the brain that might determine higher cortical functions. In a conventional mouse model of overexpression of amyloid beta mutants, the group discovered critical roles of increased catabolism of tryptophan metabolism in the Ab-overexpressing model: accelerated tryptophan metabolism in astrocytes causes downstream metabolites, including kynurenine, which downregulates glucose consumption and thereby suppresses the ATP synthesis necessary to maintain neural energy metabolism (Minhas et al., 2024, App.1-16). To examine the brain energy metabolism in the non-human primates, the group established the gene-edited Presenilin-1 (PSEN1) to up-regulate Ab to develop two different types of the mutants (DE9 and P117L) that often occur in Familial AD (Sato et al., 2024, App.1-17). The group has also established ultra-high field MRI (11.7T, figure right) that enables the visualization of alterations in regional shape changes and collection of MR spectroscopy to determine energy metabolism of the common marmosets

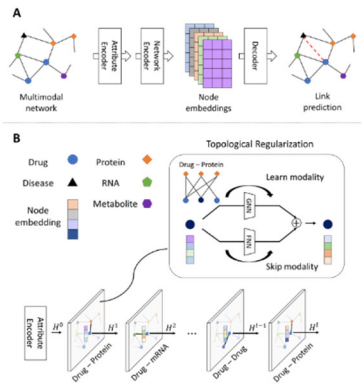


non-invasively. This program allows us to combine metabolic systems biology and mathematical sciences, including MRI calculations, brain physiology, and genetic engineering.

Q-Core (Tanaka, Koyama, Ishikawa, Sakakibara, Yamamoto, and Joshi)

Tanaka group is working on developing new quantum optimization algorithms. Because current quantum computers can only handle small amounts of data, and errors are introduced at a non-negligible rate, the optimization problem to be solved has to be preprocessed. The group investigated the dependence of quantum optimization performance on preprocessing performance using a quantum annealing machine. They also constructed a new method that combines the mathematical optimization method for digital computers, which has been studied for many years, and the quantum optimization method. The proposed method can achieve higher solution accuracy than conventional quantum optimization methods. In addition, the group improved a new black-box optimization method that combines machine learning and quantum computing. This black-box optimization method, called **Factorization Machine with Quantum Annealing (FMQA)**, is applied in the fields of chemistry and materials science, and in these examples, it has been suggested to be more effective than algorithms for digital computers such as Bayesian optimization. The group proposed a method for setting the parameters to further accelerate FMQA.

This year, **Koyama group** advanced multiple frontiers in computational biology and quantum computing, achieving significant milestones in AI and quantum-based approaches to biological data analysis. The team developed **gutMPT**, a transformer-based AI system that predicts metabolites from chemical and enzyme inputs with impressive accuracy rates of 76% for top-1 and 88% for top-5 predictions, aiming to unravel the "dark matter" of metabolites—the vast array of unknown metabolic products from gut microbiome. In parallel, their study on **quantum reservoir computing (QRC)** initially demonstrated improvements over classical methods in analyzing biological time-series data, including ECG and EEG signals; they are now expanding its application to diverse biological data types. The versatility of QRC enables us to tackle complex analytical challenges in single-cell RNA sequencing data and other high-dimensional datasets with limited sample sizes—a common challenge in biomedical research. This broader application of QRC showcases its potential as a powerful tool for biological data analysis. Their exploration of fault-tolerant quantum computing applications in microbiome research and other biological systems shows promising potential for revolutionizing our understanding of complex biological networks and their interactions. They have also reinforced our research through cross-core collaborations, particularly in organoid intelligence, where neuroscience is merged with artificial intelligence and quantum-computing approaches. These interdisciplinary initiatives have positioned us at the frontier of bio-inspired quantum AI, advancing fundamental research in novel directions.



Drug repositioning is the development of new therapies for existing drugs. Although this has resulted in immense research and development costs for companies, the advent of machine learning has presented scientists with new tools to parse data on drug efficacy and potential treatment options. However, as with any type of data analysis, different systems are equipped to handle different types of datasets. In a new research paper published in *Journal of Cheminformatics*, **Sakakibara** proposed their own system, **"STRGNN" (Sequentially Topological Regularization Graph Neural Network)**, a deep learning model that effectively predicts drug-disease associations (figure right). In contrast with numerous methodologies developed to date, STRGNN can analyze large-scale multimodal networks rich in omics data through topological regularization. This means that the system can incorporate relatively complex and holistic datasets, subsequently predicting links between diseases and effective drugs. This approach could ease and speed up the discovery of new treatments for diseases. This initiative also integrates computational science, bioinformatics, and medicinal chemistry and represents a

deep learning approach explicitly designed for the analysis of complex, multimodal omics datasets through advanced topological regularization techniques.

1-2. Generating Fused Disciplines

* Describe the content of measures taken by the center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields. If any, describe the interdisciplinary research/fused discipline that have resulted from your efforts to generate fused disciplines. You may refer to the research results described concretely in "1-1. Advancing Research of the Highest Global Level."

To promote interdisciplinary research, in FY2024 we set up several physical units to act as collaboration hubs and core facilities and enhance the cross-core mentoring system. The specific measures and resulting collaborations are as follows:

Expansion of Science Hubs and Core Facilities

1. The Open Lab: The open laboratory acts as an interaction hub, and as a core facility with advanced analytical equipment, including Orbitrap LC-MS/MS, timsTOF imaging MS, Lightsheet fluorescence microscopy, and plate readers for bacterial phenotype analysis. These resources facilitate collaboration across the Bio-1 and Bio-2 cores, enabling researchers to integrate microbiome science, metabolomics, and imaging technologies for innovative discoveries.
2. The Structural Analysis Unit/Core Facility: The unit has been set up to act as a second-core facility once functional (pp. 8 and 19).
3. The Agora (tentative): A dynamic collaborative space featuring six offices and a shared discussion area designed to foster daily scientific engagement between the PIs and Jr. PIs of three cores.

The Science Meeting Series

WPI-Bio2Q Science Meeting Series is held twice a month in a hybrid onsite/Zoom format to facilitate and promote scientific discussions among Bio2Q members. At each meeting, the PI or Jr. PI gives a 30-min talk on a chosen topic, followed by a 30-min discussion moderated by Jr. PIs and open to all participants. To promote collaboration, in FY2024, the series was opened to participants from the entire Keio University under non-disclosure agreements, and 16 meetings were held to comprehensively discuss intramural research and accelerate interdisciplinary and fusion projects.

Mentoring system

Bio2Q established a co-mentoring system for Postdoctoral Fellows and STaMP graduate students. For example, Postdoctoral Fellow Pan is co-mentored by the Honda Lab (Bio-1 Core) and the Yuzaki Lab (Bio-2 Core); Li is co-mentored by the Yuzaki Lab (Bio-2 Core) and the Koyama Lab (Q-Core); and Caner is co-mentored by the Arita and Miyamoto Labs (Bio-1 Core).

At the Q-Core, Ishikawa and Koyama lead the development of educational programs for members who are not specialists in computer science or quantum physics.

Collaboration between young researchers

Microbiome<->Quantum computing (Tuganbaev, V.J. Sahayasheela, Joshi)

Classical bioinformatics is a subset of quantum bioinformatics, yet most quantum computing biomedical applications currently target problems formulated within the framework of classical bioinformatics. For example, a recent QC application developed by Moderna, a manufacturer of a COVID-19 vaccine, for prediction of mRNA structural stability, while novel in terms of QC utilization, addresses a problem formulated in the 1980s. Thus, there is an important knowledge gap in the discovery and formulation of new biomedical problems uniquely suited to QC. To address this, Tuganbaev has proposed a novel problem formulation grounded in cutting-edge biology (Furuichi et al., 2024, App.1-19). He mapped an urgent medical task of designing anti-MDRO therapeutics onto a quantum circuit and developed QAOA and QA hybrid classical-quantum algorithms implemented on IBM quantum (gate-based) and D-wave (quantum annealing) QCs respectively, thereby expanding the boundaries of quantum bioinformatics into the field of microbiome research.

Sahayasheela integrated Bio-1 Core (microbiome and genomics) and Q-Core research to advance interdisciplinary studies. This cross-core collaboration enables the investigation of the precise role of microbiomes in oxidative DNA modifications in host mitochondria.

Most studies on quantum machine learning (QML) analyzed nonbiological data. Joshi is developing methods specifically tailored to biological applications by fusing QML with biology. He is also collaborating with Tuganbaev to develop an optimization algorithm for bacterial nutrient consumption that can be implemented on a quantum computer, thus fusing optimization methods with microbiome research.

Microbiome<->Neuroregulation (Pan, Li)

These studies investigated the role of enteroendocrine cells in transducing bacterial signals to enteric neurons. Simultaneously, a new collaborative project exploring the contribution of gut bacteria to the development of PD was launched. Furthermore, these collaborations integrate synaptic biology, regenerative medicine, and Bio2Q's Quantum Computing Team, fostering interdisciplinary research at the intersection of molecular neuroscience, artificial synapse engineering, and gut–brain axis regulation.

Cross-institutional and international collaborations

Kanai group actively fosters interdisciplinary research by integrating the fields of microbiology, neuroscience, immunology, and clinical gastroenterology. Initiatives include collaborative research projects both within WPI-Bio2Q and Keio University School of Medicine, and externally with organizations such as Nissin Foods Holdings Co., Ltd., studying molecular nutritional science. These efforts have yielded significant interdisciplinary advancements in gut-brain immune modulation and microbiome-driven dietary behaviors.

To study the interaction between gut bacteria, viral infection, and pregnancy, PI **Huh** collaborated extensively with clinicians and physician-scientists at Massachusetts General Hospital in Boston and Gangnam Yonsei Severance Hospital in South Korea. Furthermore, to identify and study pregnancy-associated bacteria involved in the metabolism of glucocorticoid hormones, he collaborated with another Bio2Q international collaborator, Sloan Devlin, a chemist.

Collaborations to build joint analytical platforms and databases

Metabolome Team (Arita, Soga, Sugiura)

Arita group and **Sato group** collaborated to develop a functional lipidomics platform using SFE-SFC-based lipid fractionation and a human organoid assay system (Postdoctoral Fellow Kuwashima), integrating expertise in analytical chemistry and gut biology. Using supercritical fluid chromatography, they extracted 15 fractions from the mouse intestinal contents enriched in microbe-derived metabolites. This enabled the identification of specific fractions that elicited intestinal hormone production, thereby exemplifying an impactful interdisciplinary research. To verify the structure-activity relationship of functional lipids, **Arita group** collaborated with the affiliated PIs, **Kumagai** and **Miyamoto groups,** to chemically synthesize bacterial lipids, including structural isomers, which will be applied to functional assays (Postdoctoral Fellow Caner).

Soga group has the world's largest polar and charged metabolome analysis platform with over 60 metabolome analysis instruments, including CE-MS, LC-MS, GC/MS, IC-MS, SFC-MS, and NMR. To promote collaboration among researchers in various fields, Soga Lab aids with metabolome analysis free of charge and will measure more than 20,000 samples by 2024.

Utilizing the MALDI Imaging system introduced in the Open Lab, **Sugiura group** began a collaborative study with **Sasabe group** to elucidate the metabolic organs and fate of microbial amino acid metabolites, and with **Sampetrean group** to elucidate microbiota-modulated changes in the normal brain and brain tumors.

A key challenge in metabolomic analysis using organoid cells derived from the intestines or liver as well as mouse fecal samples is obtaining reproducible metabolite data with the smallest possible sample size (cell count). One approach towards addressing this challenge is to establish a semi-targeted metabolomics method for water-soluble metabolites using the latest TFS mass spectrometer (Orbitrap Exploris LC-MS system), introduced this year as part of the shared equipment at the Bio2Q Open Lab. The Orbitrap 120 stands out for its high mass resolution and exceptional ability to identify unknown compounds. Therefore, with a focus on future non-targeted analyses,

Hishiki et al. embarked on the challenge of establishing a measurement system using this equipment. A measurement system was successfully established for the 130 water-soluble metabolites. For 118 of these compounds, the detection rate was confirmed to be either equal to or higher than that achieved using CE-TOFMS. Notably, the Orbitrap Exploris 120 is characterized by its high mass resolution and excels in nontargeted analysis. AI-based methods are required for the analysis of the vast amount of data obtained from nontargeted analyses, and collaboration with quantum computing cores is becoming increasingly important.

Structural Analysis Team (Aricescu, Suzuki)

A Structural Analysis Unit/Core Facility can be used by many researchers from multiple fields to explore, for instance, the structure of molecules in situ. Pre-consultation with internal and external collaborators was conducted for applications in gut microbiota, brain, immune system, and other systems and organs. The Quantum Computing Team was also involved in discussions on data processing and how to apply a high-performance computer cluster. The Structural Analysis Unit also plans joint research with the Okinawa Institute of Science and Technology (OIST), and knowledge and ideas were exchanged at the OIST-Keio Showcase Symposium. The technical staff of the Structural Analysis Unit travelled to MRC-LMB in the UK to gain comprehensive training in the CryoET pipeline and fostered productive partnerships with researchers and students at the MRC-LMB and Cambridge University.

2. Global Research Environment and System Reform

2-1. Realizing an International Research Environment

* Describe what's been accomplished in the efforts to raise the center's recognition as a genuine globally visible research institute, along with innovative efforts proactively being taken in accordance with the development stage of the center, including the following points, for example:
- Efforts being developed based on the analysis of number and state of world-leading, frontline researchers (in Appendix 2); exchanges with overseas entities (in Appendix 4); number and state of visiting researchers (in Appendix 5)
- Proactive efforts to raise the level of the center's international recognition and to obtain diversity within the center.
- Efforts to make the center into one that attracts excellent young researchers from around the world (such as efforts fostering young researchers and contributing to advancing their career paths)

Recruiting and Hiring Researchers and Research Support Personnel

Creating an authentic international environment by recruiting international researchers and English-speaking administrative personnel remains a top organizational priority. In FY2024, we continued to emphasize the WPI missions of globalization and diversity in all open calls, and the international recruitment of researchers was widely published on the Center's website and on social media. Our LinkedIn digital recruiting platform was especially useful for direct conversations with female and international researchers interested in Bio2Q. As a result, four new PIs were recruited, including two foreign PIs residing at the Center. We also welcomed an international collaborator and hired four Postdoctoral Fellows and two research support staff members fluent in English. Moreover, we recruited two female Jr. PIs to join in FY2025.

Efforts to Attract Young Researchers

- **Internationalization of research environment:** In FY2024, Bio2Q continued to make efforts to internationalize the research environment. This includes providing funding information in English and expanding support systems for grant applications in the Japanese academic system. WPI-Bio2Q also promoted the translation of documents, contracts, laboratory safety-related materials, and training courses that are mandatory for researchers. English protocols for equipment use and online reservation systems were also implemented.
- **Relocation and living support:** The Center and host institution collaborated in the provision of relocation and living support services (including visa applications) for international researchers joining WPI-Bio2Q.
- **Research onboarding support:** To assist new international researchers in acclimatizing to new environments, we expanded the Onboarding Handbook for WPI-Bio2Q researchers.
- **STaMP Program:** In FY2024, we expanded our joint interdisciplinary graduate English program, Science and Technology and Medicine, Pharmacy (STaMP) (see Section 3-2 for details).

❖ **Bio2Q Internship Program:** We rolled out a newly established research internship program, under which students interested in Keio University's master's or doctoral programs in a WPI-related field are invited to spend up to eight weeks in one or more laboratories led by WPI-Bio2Q's PIs. The selected applicants were provided with round-trip travel tickets and a daily stipend for conducting the research. Two research internship students (from the USA and the Philippines) completed the program in FY2024. Two additional international students are studying under two supervising PIs in FY2025 (June – August 2025). This internship program aims to encourage talented students from all over the world to enroll in the STaMP program.

2-2. Making Organizational Reforms

* Describe the system reforms made to the center's research operation and administrative organization, along with their background and results.
* Describe the measures taken and results achieved in implementing the center's gender-balance plan.
* If innovated system reforms generated by the center have had a ripple effect on other departments of the host institutions or on other research institutions, clearly describe in what ways.
* Describe the center's operation and the host institution's commitment to the system reforms. (Include measures taken made by the host institution to provide a support system and to work toward improving the environment for achieving gender balance.)

Development of Internal Rules and Research Support System

We established internal regulations for genetic recombination experiments, biosafety, and conflict of interest (COI) management, along with an independent committee for COI management. These initiatives have been put in place to advance the Center's move toward institutional independence.

Reform of the management system

We started bilingual records for Executive Committee Meetings and shared English summaries within the Center to increase transparency and shared information.

We also launched an internal website that centralized key resources and information, including best practices, training materials, onboarding guides, standard operating procedures, policies, and internal regulations. This initiative promotes transparency and accountability across Bio2Q. Subsequently, we plan to integrate progress tracking and performance metrics related to the Center and reform goals. This will help transform the site into a dynamic platform that actively supports cultural and operational reform by making processes more transparent, information more accessible, and collaboration more seamless.

Strategy and Coordination Hub (tentative): The physical space of the former administrative office was reorganized to include three new offices and host PIs and Jr. PIs with substantial organizational and administrative contributions. Together with three science-related hubs and core facilities, these represent flagship platforms and potential operational prototypes for new Bio2Q buildings.

Ensuring diversity and implementation of gender balance plan

Enacting the measures proposed in our plan, the Center's leadership continued to advocate for gender balance. Furthermore, regular analysis of applicants' demographic data and sharing of relevant data within and outside the Center led to an increase from 20% to 40% in applications from women scientists for Bio2Q Jr. PIs. As a result, two female Jr. PIs (one international and one from Japan) from Bio2Q-related laboratories joined the Center in FY2025. Importantly, as the Center reached its third year, we started internal promotions and two female Jr. PIs have been promoted to PIs. Flexible work arrangements are in place for both researchers and support staff, and family-friendly policies, such as organizing meetings and seminars almost exclusively within business hours, have been implemented.

3. Values for the Future

3-1. Creating and Disseminating the Societal Value of Basic Research

* Describe the content of measures taken by the center to widely disseminate the results of its basic research to the general public.
* Describe what was accomplished in the center's outreach and other activities last year and how they have contributed to creating the Societal Value of Basic Research. In Appendix 6, describe concretely the contents of these outreach activities. In Appendix 7, describe media reports or coverage, if any, of the activities.

Website Outreach Activities

❖ The website's WPI-Bio2Q news section is updated four times a month to engage the general

public, including scientists, students, and the private sector worldwide, in research, events, and announcements.

- ❖ A donation page for stakeholders and two digital and printable research introduction brochures for young researchers were released on the website.
- ❖ Google Analytics was installed on the website to monitor the website activities and obtain insights for improvement.

Social Media Outreach

Through our WPI-Bio2Q account on LinkedIn (SNS), we actively shared updates on WPI-Bio2Q activities and job openings while directly engaging with scientists in related research fields. Consequently, we built a global network of 1,307 scientists, including students and research professionals. This network played a key role in our digital recruiting efforts, with several members originally from Columbia University (USA), Imperial College London (UK), Kyoto University, and Keio University (Japan), later joining the Center for Jr. PI, Postdoctoral Fellowships, or Research Internship Program.

Symposia and Events

On March 6–13, 2025, several scientific events converged for a Bio2Q Spring Science Week, fostering interdisciplinary collaboration and knowledge exchange. The week started with the 3rd International Symposium, held onsite at the Shinanomachi Campus on March 6–7, 2025, featuring talks from 12 globally renowned scientists from Harvard University, Columbia University, Sloan Kettering Institute, the Icahn School of Medicine at Mount Sinai (USA), Kyoto University, University of Osaka WPI-IFREC, and Keio University (Japan). The diverse audience of the 198 participants included 75 female researchers, 42 international attendees from 14 countries, 45 from the private sector, and 23 from other academic institutions. The invited speakers remained at the Center for up to one week, engaging in in-depth discussions and collaboration with individual researchers. On March 13, Bio2Q welcomed 40 young scientists attending this year's HOPE meeting for an exclusive lab tour and networking session with early career researchers at the Center.

In addition, Bio2Q invited top international scientists from the USA and Korea to hold six open scientific seminars at the Center, facilitating face-to-face knowledge exchanges with a broad audience. Bio2Q exhibited at the Metabolome Symposium 2024 in Yamagata and the WPI Science Symposium 2024 in Kyoto to introduce WPI and Bio2Q to attendees from academia and industry. Finally, outreach to young students included a detailed presentation of the WPI and Bio2Q programs to 20 high school students who visited the Yuzaki laboratory and publishing three new booklets for young readers featuring PIs Arita, Sato, and Tanaka.

3-2. Human Resource Building: Higher Education and Career Development

* Describe the content of measures taken by the center to foster young researchers, including doctoral students, through their participation in a research system that creates new interdisciplinary domains within a rich international environment.
* Describe measures taken for fostering researchers with a view to achieving gender plans, and measures taken for domestic and international promotion activities to attract female researchers to the center.

The STaMP program

The STaMP program, initially launched to cover graduate students from three graduate schools (i.e., Medicine, Pharmaceutical Sciences, and Science and Technology), aims to create a "place of resonance" where faculty, researchers, and students from the three graduate schools can interact directly and where each graduate student works with multiple mentors to receive guidance across graduate school boundaries.

In FY2024, the program was expanded to cover further graduate schools in Keio University, allowing students to be mentored and placed in the laboratories of WPI-Bio2Q and affiliated PIs. The WPI Research Assistant (WPI-RA) system was implemented to allow students to work as part-

time researchers and receive monthly stipends. This system allows students to actively engage in research and participate in activities and exchanges across the three graduate schools. The conditions for completion of the program were revised to include participation in Bio2Q events and activities such as the "Science Meeting Series," open seminars, retreats and international symposia. Fourteen graduate students were enrolled in the STaMP program as WPI-RAs; 5 of them received a STaMP certificate of completion this year. Twenty domestic and international graduate students have been selected as WPI-RAs for the upcoming year.

STaMP also expanded its curriculum with the "AI/Quantum Workshop", which aims to enhance Quantum Computing/AI literacy within Bio2Q, particularly among young researchers and graduate students. We conducted five introductory sessions during FY2024, which covered the history of IT/AI/quantum technologies, the current state of generative AI, examples of the application of AI and Quantum technologies to Bio2Q, and hints and tips on applications for Bio-1 and Bio-2 research activities. Beginning in June 2025, roundtable workshops will be held once a month to discuss the research themes relevant to STaMP students. These round-table sessions are led by "ambassadors," consisting of Jr. PIs, Postdoctoral Fellows, and technical staff of Bio2Q with Quantum Computing/AI skills. A letter of appreciation will be issued to the ambassadors providing evidence for their career development activities.

The Annual Bio2Q retreat

To facilitate active exchange between researchers and students in the STaMP, we held the first scientific retreat in May 2024. This 2-day retreat was joined by 10 PIs, 6 Affiliated PIs, 5 Jr. PIs, 3 Postdoctoral Fellows, 14 WPI-RAs, 13 researchers/students from outside WPI-Bio2Q, and 5 staff members, who participated in scientific presentations, team/group work to establish fusion research proposals, and recreational activities.

3-3. Self-sufficient and Sustainable Center Development

* Describe the state of implementation of the host institution's mid-to-long term measures for supporting the center toward becoming self-sufficient and sustainable after the 10-year funding period ends, such as reforming the host institution's organization, providing personnel with priority allocation of tenured posts to the center, providing fundamental financial support, and material support, including land and buildings.

To support Bio2Q in achieving self-sufficiency and sustainability, the host organization, the Keio University Headquarters, is implementing several strategic measures.

The "Under One Roof" initiative

The university's executive team, including the President and Vice Presidents, successfully secured a large donation of 6 billion yen from a food company at the end of FY2023. However, this donation is made under the condition that the funds cannot be used for an animal experimentation facility. Therefore, the construction and allocation of an additional experimental facility is under consideration. As stated in the application documents, this initiative is positioned within the university-wide campus development plan. A "New Research Building Construction Planning Committee" has been established, bringing together Bio2Q, the School of Medicine, and Keio University Headquarters to discuss the facility's development. Based on these discussions, negotiations for government subsidies from the Ministry of Education, Culture, Sports, Science, and Technology (MEXT) are ongoing.

Institutional Support and Reform

Keio University has established the "Internal regulations regarding the employment of project professors at Keio University's World Premier International Research Center (special zone)" for hiring excellent researchers regardless of age. In addition, at the university-wide level, a special system for "Specially-appointed Advanced Project Professors" that allows employment of outstanding researchers over the age of 70 from both within and outside the university has been established.

Strategic activities toward achieving self-sufficiency

We formed Bio2Q NEXUS (**N**ext-gen, **E**nterprise, **X** (for innovation), **U**pscaling, **S**ustainability), a Working Group (WG) headed by the Administrative Director and consisting of Bio2Q PIs, members from the Bio2Q Administrative Division, and support departments of the host institution such as the Office of Innovation and Entrepreneurship and the Office of Research Development and Sponsored Projects, and external advisors. This WG is developing strategies to strengthen the financial foundation necessary for Bio2Q's financial independence. In FY2024, The WG collaborated with the Keio University Office for Fund Raising to increase the Center’s visibility and refine Bio2Q’s fundraising strategies.

Financial support

Keio University has been selected for “Program for Forming Japan’s Peak Research Universities (J-PEAKS).” The J-PEAKS program is one of its objectives for the further growth and development of existing large-scale research centers such as Bio2Q. Keio University advanced completion of the state-of-the-art Structural Analysis Unit, by adding approximately 1.19 billion yen of J-PEAKS funding to the WPI grant for the purchase of the CryoET KriosG4.

4. Others

* In addition to the above 1-3 points, if there is anything else that deserves mention regarding the center project’s progress, please note it.

5. Center’s Response to Results of Last Year’s Follow-up

* Transcribe the item from the “Actions required and recommendations” section in the site visit report and the Follow-up report, then note how the center has responded to them.
* If you have already provided this information, indicate where in the report.

1) It is recommended that Bio2Q enhance their collaboration with top-level clinical scientists in Japan and internationally. Bio2Q will make extensive use of biosamples (blood, stool, biopsies, etc.) from human patients, and it will be very advantageous if these samples come from very well characterized patients and healthy subjects (e.g., deeply phenotyped*, longitudinally followed cohorts and biobanks). In short, Bio2Q member labs will likely make new, potentially high-level discoveries in human biosamples, but the biological meaning and clinical relevance of these discoveries will be easier to identify, if deep phenotyping is carried out in patients.

Regular meetings with the clinical team have strengthened collaboration in PD studies with an increased number of enrolled patients. This expanded the dataset of stool and blood samples linked to detailed clinical histories and phenotypic data. Moreover, Bio2Q already has access to longitudinal cohorts such as the centenarian cohort. To reinforce this research pipeline, the Bio2Q Affiliated PI and the Director of the Center for Supercentenarian Medical Research, Y. Arai will join as a full PI, and Bio2Q will support a dedicated technical staff member responsible for sample collection and banking.

2) The change in strategy from direct integration with quantum computing to integration with quantum computing by introducing generative AI techniques in the early stages and the hiring of two computational experts as new PIs for Q-Core, is a pragmatic approach. On the other hand, it is essential that the Center develop a strategy for reaching a visionary yet concrete project that develops quantum computing in the two bio cores. In this effort, Bio2Q could seek broader collaboration with emerging biomedical research initiatives in quantum computing across academia and industry. While Bio2Q has already established partnerships with organizations such as RIKEN and IBM, expanding these collaborations could further enhance its impact. For designing and (eventually) executing quantum computing biological analyses that are truly relevant for Bio2Q, it will be crucial to form effectively collaborating pairs of Jr. PIs from both life science and quantum computing who have the freedom to identify and develop such boundary projects. At present, however, manpower on the computational side appears to be too small. Recruitment of Jr. PIs, not PhD students, is recommended for such interdisciplinary activities. A specific example would be to find a dedicated quantum collaborating partner to work with Jr. PI Tuganbaev. It would be important for them to not be incumbered by established PIs so as to maximize the originality and creativity that is urgently needed for the center to overcome hurdles in making quantum computing useful for applications in life science.

First, regarding our integration strategy, we have already demonstrated progress through the development of gutMPT, which successfully leverages generative AI techniques to predict metabolites with high accuracy. This tool is not merely a stepping stone but is ready to be deployed for dark matter exploration in metabolomics.

Second, our quantum-computing integration strategy demonstrates progress through two complementary approaches. Our work on quantum reservoir computing (QRC) has already demonstrated superior performance over classical methods in the analysis of biological time-series data, including ECG and EEG signals, and is now expanding to include single-cell RNA analysis and other high-dimensional datasets with limited samples. More importantly, we have established a clear technical roadmap centered on a quantum phase estimate algorithm, which represents a significant breakthrough for microbiome analysis as it requires only $\log_2 N$ qubits while delivering exponential acceleration in computational speed. The true transformative potential of our quantum approaches will be realized with the advent of Fault-Tolerant Quantum Computing (FTQC), enabling revolutionary analyses of microbiomes at scales that are currently impossible using classical computing. Our approach was designed to scale with advances in quantum computing, enabling increasingly complex analyses from a simple model to a gut world model in the near future. This scalable strategy ensures that our research will remain at the forefront of computational biology as quantum capabilities expand.

Third, we are engaged in discussions with Research Institutes in Singapore through the Riken TRIP initiative, which focuses on AI for scientific applications. In addition, we are exploring collaborative opportunities with Carnegie Mellon University for both AI and quantum AI under the Keio AI (KAI) framework. Our ongoing talks with the CiRA Foundation, which were initially centered on AI applications, present a potential expansion into quantum computing. While we acknowledge the Cleveland Clinic as a potential partner, we also recognize its strong existing relationship with IBM and its substantial internal resources. We anticipate that our forthcoming publications will naturally attract additional collaborative opportunities, creating organic growth in our partnership network. These strategic engagements, combined with our existing relationships with RIKEN and IBM, have positioned Bio2Q to effectively bridge the gap between quantum computing and biological applications.

We appreciate the feedback on Bio2Q's strategic direction and agree that expanding collaboration is crucial for advancing quantum computing applications. We are actively pursuing several promising partnerships that align with our vision. We are currently engaged in discussions with Research Institutes in Singapore through the Riken TRIP Initiative, which focuses on AI for scientific applications. In addition, we are exploring collaborative opportunities with Carnegie Mellon University for both AI and quantum AI under the KAI framework. Our ongoing talks with the CiRA Foundation, which were initially centered on AI applications, present a potential expansion into quantum computing. While we acknowledge the Cleveland Clinic as a potential partner, we also recognize its strong existing relationship with IBM and its substantial internal resources. Notably, we are pursuing opportunities through the NEDO Challenge "Solve Social Issues!" program, where we submitted a proposal focusing on optimization problems for the development of natural bacteria-based therapy. We anticipate that our forthcoming publications will naturally attract additional collaborative opportunities, creating organic growth in our partnership network. These strategic engagements, combined with our existing relationships with RIKEN and IBM, have positioned Bio2Q to effectively bridge the gap between quantum computing and biological applications.

We agree that creating effective collaborations between the life sciences and quantum computing is essential for breakthrough work at this interdisciplinary boundary. The gap in computational expertise is well documented. To address this, we will collaborate with Carnegie Mellon University to rectify the shortage of computational staff at multiple levels, including junior PIs and postdoctoral researchers. We recognize the significant challenges in recruiting specialized quantum computing and AI talent for today's competitive markets. This is particularly concerning, given the limited talent pool available in Japan. In addition, we face constraints regarding available research grants, which affect our ability to fully develop this critical interdisciplinary work. Our strategy includes direct

recruitment and the training of PhDs from related fields, such as mathematics, computer science, and physics, to develop expertise in quantum computing and AI applications for biological research. This approach will help us build our computational capacity while creating meaningful partnerships with Bio-core researchers, such as Jr. PI Tuganbaev.

3) Invest time into careful planning on how to use the CryoEM that will be installed in early 2025. The presentation by Jr. PI Suzuki only mentioned instrumentation and methods but not their use. Likewise, none of the other presentations provided convincing arguments for structural analyses. While we don't doubt the relevance of such methods, we strongly recommend that Bio2Q define more clearly how to exploit these capabilities. The joint research using CryoEM with MRC Lab, which has been announced as a key international collaboration framework of Bio2Q, needs to be implemented.

We are currently discussing the strategic uses of CryoEM and CryoET from three perspectives.

- Technology: A plan to verify the full functionality of the CryoEM and CryoET systems upon installation and establish protocols for instrument operation, specimen preparation, and data acquisition from a technical standpoint.
- Operations: A plan outlining usage schedules and procedures, training program for new users, and support provided by the EM Facility.
- Research: A plan for research projects utilizing CryoEM and CryoET, including the development and sharing of research agendas through collaboration among the Bio-1, 2, Q teams and other laboratories within Keio University.

The CryoEM and CryoET systems installed at Bio2Q are the Arctis and KriosG4, which are expected to begin operations in April and July 2025, respectively. Below is an overview of the current status and plans for these instruments, organized into three key areas:

Arctis:

1. A functional test with a nonbiological sample was conducted, and the basic functionality at the factory level was acceptable. However, as this was the first installation of this equipment in Japan, it was important to confirm that it was fully functional for biological samples. Arctis and a similar plasma-focused beam (pFIB) / scanning electron microscope (SEM) device, Hydra, have been installed in the MRC lab (LMB) in the UK, where collaborative research is being conducted, and the technology and experience to apply the instrument to biological samples have been accumulated. Bio2Q has already sent a researcher to LMB to learn about the technology. Bio2Q will invite collaborators who have experience with biological applications of Arctis from the LMB after April 2025 to confirm the operation of this device on biological samples, and at the same time, to establish a method for sample preparation using an automated protocol in the Bio2Q EM facility.

2. Workshops, training, and basic lectures by TFS, and EM facility will be held and released to users both inside and outside the university. Thus far, one basic piece of knowledge has been shared at the Bio2Q science meeting. The booking/operation system will be arranged based on the status of use and requests from users, referring to a successful system running external institutes (e.g., LMB, RIKEN).

3. We are providing pre-consulting to Bio-1, Bio-2, and Keio University researchers on the research topics they would like to study with CryoET using this device. In addition, together with the Quantum Computing Team, we have started discussions on the IT infrastructure and operations for data analysis and the development of AI-based methods.

KriosG4:

1. This system is widely used in Japan and internationally, and a performance verification test using biological samples has been planned. Standard materials will be provided by the LMB and the University of Cambridge, with whom we have collaborated. Engineers from these institutions, as well as from the TFS, will be invited to conduct tests and confirm that the system’s performance is equal to or exceeds that of other institutions.

2. As with Arctis, workshops, training, and introductory lectures will be provided by the TFS and the

Facility. A new researcher with CryoEM experience, W. Shihoya, will join Bio2Q as a Jr. PI to help establish the operation of the instrument for single-particle analysis. Regarding the use of the instrument for tomography, operational procedures will be developed based on the use and performance of Arctis.

3. We have begun discussing research topics with Shihoya and are currently conducting preliminary consultations for collaborative research with university researchers in the areas of single-particle analysis and tomography. In parallel, we are inviting new researchers from overseas to initiate structural studies of small molecules using microcrystal electron diffraction (MicroED), a technique that can be applied to metabolites produced by the microbiota.

Jr. PIs Suzuki and Shihoya, who will play central roles in the operation and utilization of the Structural Analysis Unit, will be based full-time at Bio2Q and Keio University starting in April 2025. They will continue to develop more detailed and carefully considered plans on the discussions outlined above.

4) This year, the activities of international PIs at Bio2Q were not very visible, e.g., there were no presentations by international PIs. This needs to be improved to demonstrate their involvement in Bio2Q, which is urgently needed for forming an international environment at Bio2Q. Further recruitment of international members is also necessary to enhance the center's international research environment. To start, a students/researchers exchange program with international collaborators would be of some help.

In response to these recommendations and to enhance Bio2Q internationalization and visibility, two new international PIs have already relocated to the Center in FY2024. They have already started research, international collaborative studies, and mentoring of Bio2Q Postdoctoral Fellows and have also signed up to mentor medical students for a Medical School research elective. Another international Jr. PI and a Director of Research Programs are expected to start working at the Center in FY2025 and, through the measures detailed in Section 2-1, we plan to increase international participation. The exchange/training program with the MRC-LMB has already started with technical staff and will be extended to postdoctoral researchers and students in international collaborator laboratories.

5) Increasing the number of both international and domestic female researchers should be prioritized. The percentage of female researchers is still low, especially in the senior positions. While currently most female researchers are recruited from overseas, supporting and promoting domestic female researchers is an important issue as well.

Based on these recommendations, we increased our recruitment efforts both nationally and internationally, resulting in the recruitment of two female Jr. PIs for FY2025 (one international and one from Japan). According to our initial plan, we started promoting women and young scientists within the Center. As a result, Bio2Q expect to reach 6 out of 21 (29%) international PIs and 4 out of 21 (19%) female PIs, and 36% international and 29% female researchers in FY2025.

6) The STaMP graduate school program represents an excellent example of fused disciplines with regard to young researcher education. The presentations by STaMP students were well prepared and impressive. On the other hand, it is unclear what kinds of education and training unique to STaMP, such as lecture courses on microbiome or quantum computing, the graduate students will receive. A more comprehensive plan should be shown. Specifically, efforts aimed at enhancing the informatics background of graduate students should be made to promote the future fusion of biological and computational disciplines.

Building on the framework outlined in Sections 2-1 and 3-2, we launched the AI/Q Workshop in FY2024 based on the recommendations mentioned above. The curriculum will continue to expand to include courses on other key Bio2Q topics, such as the microbiome. To develop and implement a sustainable and comprehensive plan, we will establish a committee in FY2025 called Broadening Research and Interdisciplinary Development in Graduate Education (BRIDGE). This committee will promote interdisciplinary research by reviewing the overall curriculum and program structure and identifying any challenges encountered during implementation. The insights gained will be used to guide ongoing improvements in the STaMP graduate programs.

Appendix 1　FY 2024 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2024. (Note: The list should be for the calendar year, not the fiscal year.)

(1) Divide the papers into two categories, A and B.
   A. WPI papers
      List papers whose author(s) can be identified as affiliated with the WPI program (e.g., that state "WPI" and the name of the WPI center (WPI-center name)). (Not including papers in which the names of persons affiliated with the WPI program are contained only in acknowledgements.)
   B. WPI-related papers
      List papers related to the WPI program but whose authors are not noted in the institutional affiliations as WPI affiliated. (Including papers whose acknowledgements contain the names of researchers affiliated with the WPI program.)

      Note: On 14 December 2011, the Basic Research Promotion Division (the Basic and Generic Research Division at present) in MEXT's Research Promotion Bureau circulated an instruction requiring paper authors to include the name or abbreviation of their WPI center among their institutional affiliations. From 2012, the authors' affiliations must be clearly noted.

(2) Method of listing paper
   - List only refereed papers. Divide them into categories (e.g., original articles, reviews, proceedings).
   - For each, write the author name(s); year of publication; journal name, volume, page(s) (or DOI number), and article title. Any listing order may be used as long as format is consistent. (The names of the center researchers do not need to be underlined.)
   - If a paper has many authors (say, more than 10), all of their names do not need to be listed.
   - Assign a serial number to each paper to be used to identify it throughout the report.
   - If the papers are written in languages other than English, underline their serial numbers.
   - Order of Listing
      A. WPI papers
         1. Original articles
         2. Review articles
         3. Proceedings
         4. Other English articles

      B. WPI-related papers
         1. Original articles
         2. Review articles
         3. Proceedings
         4. Other English articles

(3) Submission of electronic data
   - In addition to the above, provide a .csv file output from the Web of Science (e.g.) or other database giving the paper's raw data including Document ID. (Note: the Document ID is assigned by paper database.)
   - The papers should be divided into A or B categories on separate sheets, not divided by paper categories.

(4) Use in assessments
   - The lists of papers will be used in assessing the state of WPI project's progress.
   - They will be used as reference in analyzing the trends and whole states of research in the said WPI center, not to evaluate individual researcher performance.
   - The special characteristics of each research domain will be considered when conducting assessments.

(5) Additional documents
   - After all documents, including these paper listings, showing the state of research progress have been submitted, additional documents may be requested.

A. WPI papers

1. Original articles

1) Gao Y, Solberg T, Wang R, Yu Y, Al-Rasheid KAS, Gao F. Application of RNA interference and protein localization to investigate housekeeping and developmentally regulated genes in the emerging model protozoan Paramecium caudatum. ***Commun Biol***. 2024 Feb 19;7(1):204. doi: 10.1038/s42003-024-05906-2.

2) Yamamoto T, Hayashida T, Masugi Y, Oshikawa K, Hayakawa N, Itoh M, Nishime C, Suzuki M, Nagayama A, Kawai Y, Hishiki T, Matsuura T, Naito Y, Kubo A, Yamamoto A, Yoshioka Y, Kurahori T, Nagasaka M, Takizawa M, Takano N, Kawakami K, Sakamoto M, Wakui M, Yamamoto T, Kitagawa Y, Kabe Y, Horisawa K, Suzuki A, Matsumoto M, Suematsu M. PRMT1 Sustains De Novo Fatty Acid Synthesis by Methylating PHGDH to Drive Chemoresistance in Triple-Negative Breast Cancer.

Cancer Res. 2024 Apr 1;84(7):1065-1083. doi: 10.1158/0008-5472.CAN-23-2266.

3) Kuwashima Y, Yanagawa M, Maekawa M, Abe M, Sako Y, Arita M. TRPV4-dependent Ca(2+) influx determines cholesterol dynamics at the plasma membrane. ***Biophys J***. 2024 Apr 2;123(7):867-884. doi: 10.1016/j.bpj.2024.02.030. Epub 2024 Mar 2.

4) Liu Y, Niu J, Ye F, Solberg T, Lu B, Wang C, Nowacki M, Gao S. Dynamic DNA N (6)-adenine methylation (6mA) governs the encystment process, showcased in the unicellular eukaryote Pseudocohnilembus persalinus. ***Genome Res***. 2024 Mar 20;34(2):256-271. doi: 10.1101/gr.278796.123.

5) Tsugawa H, Ishihara T, Ogasa K, Iwanami S, Hori A, Takahashi M, Yamada Y, Satoh-Takayama N, Ohno H, Minoda A, Arita M. A lipidome landscape of aging in mice. ***Nat Aging***. 2024 May;4(5):709-726. doi: 10.1038/s43587-024-00610-6. Epub 2024 Apr 12.

6) Tabata S, Endo H, Makinoshima H, Soga T, Inoue M. The γ-glutamyl cycle serves as an amino acids supply system in colorectal cancer organoids under chronic hypoxia. ***Biochem Biophys Res Commun***. 2024 Jun 25;714:149977. doi: 10.1016/j.bbrc.2024.149977. Epub 2024 Apr 22.

7) Wang J, Taki M, Ohba Y, Arita M, Yamaguchi S. Fluorescence Lifetime Imaging of Lipid Heterogeneity in the Inner Mitochondrial Membrane with a Super-photostable Environment-Sensitive Probe. ***Angew Chem Int Ed Engl***. 2024 Jul 8;63(28):e202404328. doi: 10.1002/anie.202404328. Epub 2024 May 28.

8) Katsuumi G, Shimizu I, Suda M, Yoshida Y, Furihata T, Joki Y, Hsiao CL, Jiaqi L, Fujiki S, Abe M, Sugimoto M, Soga T, Minamino T. SGLT2 inhibition eliminates senescent cells and alleviates pathological aging. ***Nat Aging***. 2024 Jul;4(7):926-938. doi: 10.1038/s43587-024-00642-y. Epub 2024 May 30.

9) Morishita T, Nishizaki N, Taniguchi S, Sakai S, Kimura T, Mita M, Nakagawa M, Endo A, Ohtomo Y, Yasui M, Shimizu T, Sasabe J. Plasma D-asparagine and the D/L-serine ratio reflect chronic kidney diseases in children regardless of physique. ***Amino Acids***. 2024 Jun 6;56(1):38. doi: 10.1007/s00726-024-03400-x.

10) Guo Y, Kitano T, Inoue K, Murano K, Hirose M, Li TD, Sakashita A, Ishizu H, Ogonuki N, Matoba S, Sato M, Ogura A, Siomi H. Obox4 promotes zygotic genome activation upon loss of Dux. ***Elife***. 2024 Jun 24;13:e95856. doi: 10.7554/eLife.95856.

11) Endo K, Matsuda Y, Tanaka S, Muramatsu M. Novel real number representations in Ising machines and performance evaluation: Combinatorial random number sum and constant division. ***PLoS One***. 2024 Jun 13;19(6):e0304594. doi: 10.1371/journal.pone.0304594. eCollection 2024.

12) Honda R, Endo K, Kaji T, Suzuki Y, Matsuda Y, Tanaka S, Muramatsu M. Development of optimization method for truss structure by quantum annealing. ***Sci Rep***. 2024 Jun 16;14(1):13872. doi: 10.1038/s41598-024-64588-2.

13) Sasaki H, Miyata J, Kawashima Y, Konno R, Ishikawa M, Hasegawa Y, Onozato R, Otsu Y, Matsuyama E, Sunata K, Masaki K, Kabata H, Kimizuka Y, Ueki S, Asano K, Kawana A, Arita M, Fukunaga K.

Distinct roles of types 1 and 2 interferons in human eosinophil regulation: A multi-omics analysis. ***Allergy***. 2024 Nov;79(11):3141-3145. doi: 10.1111/all.16215. Epub 2024 Jul 3.

14) Sunata K, Miyata J, Kawashima Y, Konno R, Ishikawa M, Hasegawa Y, Onozato R, Otsu Y, Matsuyama E, Sasaki H, Okuzumi S, Mochimaru T, Masaki K, Kabata H, Kawana A, Arita M, Fukunaga K. Multiomics analysis identified IL-4-induced IL1RL1(high) eosinophils characterized by prominent cysteinyl leukotriene metabolism. ***J Allergy Clin Immunol***. 2024 Nov;154(5):1277-1288. doi: 10.1016/j.jaci.2024.07.012. Epub 2024 Jul 25.

15) Mi-Ichi F, Tsugawa H, Vo TK, Kurizaki Y, Yoshida H, Arita M. Characterization of Entamoeba fatty acid elongases; validation as targets and provision of promising leads for new drugs against amebiasis. ***PLoS Pathog***. 2024 Aug 22;20(8):e1012435. doi: 10.1371/journal.ppat.1012435. eCollection 2024 Aug.

16) Minhas PS, Jones JR, Latif-Hernandez A, Sugiura Y, Durairaj AS, Wang Q, Mhatre SD, Uenaka T, Crapser J, Conley T, Ennerfelt H, Jung YJ, Liu L, Prasad P, Jenkins BC, Ay YA, Matrongolo M, Goodman R, Newmeyer T, Heard K, Kang A, Wilson EN, Yang T, Ullian EM, Serrano GE, Beach TG, Wernig M, Rabinowitz JD, Suematsu M, Longo FM, McReynolds MR, Gage FH, Andreasson KI. Restoring hippocampal glucose metabolism rescues cognition across Alzheimer's disease pathologies. ***Science***. 2024 Aug 23;385(6711):eabm6131. doi: 10.1126/science.abm6131. Epub 2024 Aug 23.

17) Sato K, Sasaguri H, Kumita W, Sakuma T, Morioka T, Nagata K, Inoue T, Kurotaki Y, Mihira N, Tagami M, Manabe RI, Ozaki K, Okazaki Y, Yamamoto T, Suematsu M, Saido TC, Sasaki E. Production of a heterozygous exon skipping model of common marmosets using gene-editing technology. ***Lab Anim (NY)***. 2024 Sep;53(9):244-251. doi: 10.1038/s41684-024-01424-0. Epub 2024 Aug 30.

18) Ezaki T, Kishima K, Shibao S, Matsunaga T, Pareira ES, Kitamura Y, Nakayama Y, Tsuda N, Takahara K, Iwama T, Sampetrean O, Toda M, Ohnishi K, Shimono T, Sasaki H. Development of microsurgical forceps equipped with haptic technology for in situ differentiation of brain tumors during microsurgery. ***Sci Rep***. 2024 Sep 13;14(1):21430. doi: 10.1038/s41598-024-72326-x.

19) Furuichi M, Kawaguchi T, Pust MM, Yasuma-Mitobe K, Plichta DR, Hasegawa N, Ohya T, Bhattarai SK, Sasajima S, Aoto Y, Tuganbaev T, Yaginuma M, Ueda M, Okahashi N, Amafuji K, Kiridoshi Y, Sugita K, Stražar M, Avila-Pacheco J, Pierce K, Clish CB, Skelly AN, Hattori M, Nakamoto N, Caballero S, Norman JM, Olle B, Tanoue T, Suda W, Arita M, Bucci V, Atarashi K, Xavier RJ, Honda K. Commensal consortia decolonize Enterobacteriaceae via ecological control. ***Nature***. 2024 Sep;633(8031):878-886. doi: 10.1038/s41586-024-07960-6. Epub 2024 Sep 18.

20) Sato H, Taketomi Y, Murase R, Park J, Hosomi K, Sanada TJ, Mizuguchi K, Arita M, Kunisawa J, Murakami M. Group X phospholipase A(2) links colonic lipid homeostasis to systemic metabolism via host-microbiota interaction. ***Cell Rep***. 2024 Oct 22;43(10):114752. doi: 10.1016/j.celrep.2024.114752. Epub 2024 Sep 17.

21) Sone M, Mitsuhashi N, Sugiura Y, Matsuoka Y, Maeda R, Yamauchi A, Okahashi R, Yamashita J, Sone K, Enju S, Anegawa D, Yamaguchi Y. Identification of genes supporting cold resistance of

mammalian cells: lessons from a hibernator. ***Cell Death Dis***. 2024 Sep 19;15(9):685. doi: 10.1038/s41419-024-07059-w.

22) Pan Y, Hatano A, Ohno S, Morita K, Kokaji T, Bai Y, Sugimoto H, Egami R, Terakawa A, Li D, Uematsu S, Maehara H, Fujita S, Inoue H, Inaba Y, Nagano AJ, Hirayama A, Soga T, Kuroda S. Time and dose selective glucose metabolism for glucose homeostasis and energy conversion in the liver. ***NPJ Syst Biol Appl***. 2024 Sep 30;10(1):107. doi: 10.1038/s41540-024-00437-2.

23) Cai L, Arimitsu T, Shinohara N, Takahashi T, Hakuno Y, Hata M, Hoshino EI, Watson SK, Townsend SW, Mueller JL, Minagawa Y. Functional reorganization of brain regions supporting artificial grammar learning across the first half year of life. ***PLoS Biol***. 2024 Oct 22;22(10):e3002610. doi: 10.1371/journal.pbio.3002610. eCollection 2024 Oct.

24) Sunata K, Miyata J, Kawashima Y, Konno R, Ishikawa M, Hasegawa Y, Onozato R, Otsu Y, Matsuyama E, Sasaki H, Okuzumi S, Mochimaru T, Masaki K, Kabata H, Chubachi S, Arita M, Fukunaga K. Inflammatory profile of eosinophils in asthma-COPD overlap and eosinophilic COPD: a multi-omics study. ***Front Immunol***. 2024 Oct 8;15:1445769. doi: 10.3389/fimmu.2024.1445769. eCollection 2024.

25) Wang C, Lyv L, Solberg T, Zhang H, Wen Z, Gao F. GTSF1 is required for transposon silencing in the unicellular eukaryote Paramecium tetraurelia. ***Nucleic Acids Res***. 2024 Nov 27;52(21):13206-13223. doi: 10.1093/nar/gkae925.

26) Arai K, Ono Y, Hirai N, Sugiura Y, Kaneko K, Matsuda S, Iio K, Kajino K, Saitoh T, Wei FY, Katagiri H, Inoue A. Chemogenetic activation of hepatic G(12) signaling ameliorates hepatic steatosis and obesity. ***Biochim Biophys Acta Mol Basis Dis***. 2025 Feb;1871(2):167566. doi: 10.1016/j.bbadis.2024.167566. Epub 2024 Nov 12.

27) Soma Y, Tohyama S, Kubo A, Yamasaki T, Kabasawa N, Haga K, Tani H, Morita-Umei Y, Umei TC, Sekine O, Nakamura M, Moriwaki T, Tanosaki S, Someya S, Kawai Y, Ohno M, Kishino Y, Kanazawa H, Fujita J, Zhang MR, Suematsu M, Fukuda K, Ieda M. Metabolic changes of human induced pluripotent stem cell-derived cardiomyocytes and teratomas after transplantation. ***iScience***. 2024 Oct 23;27(11):111234. doi: 10.1016/j.isci.2024.111234. eCollection 2024 Nov 15.

28) Sakamoto N, Oka T, Matsuzawa Y, Nishida K, Jayaprakash J, Hori A, Arita M, Tsugawa H. MS2Lipid: A Lipid Subclass Prediction Program Using Machine Learning and Curated Tandem Mass Spectral Data. ***Metabolites***. 2024 Nov 7;14(11):602. doi: 10.3390/metabo14110602.

29) Solberg T, Wang C, Matsubara R, Wen Z, Nowacki M. Heterochromatin-dependent transcription links the PRC2 complex to small RNA-mediated DNA elimination. ***EMBO Rep***. 2025 Jan;26(1):273-296. doi: 10.1038/s44319-024-00332-1. Epub 2024 Nov 29.

30) Ariura M, Solberg T, Ishizu H, Takahashi H, Carninci P, Siomi H, Iwasaki YW. Drosophila Piwi distinguishes transposons from mRNAs by piRNA complementarity and abundance. ***Cell Rep***. 2024 Dec 24;43(12):115020. doi: 10.1016/j.celrep.2024.115020. Epub 2024 Dec 4.

31) Saito Y, Sugiura Y, Sakaguchi A, Sada T, Nishiyama C, Maeda R, Kaneko M, Kiyonari H, Kimura W.

Redox-dependent purine degradation triggers postnatal loss of cardiac regeneration potential. ***Redox Biol***. 2025 Feb;79:103442. doi: 10.1016/j.redox.2024.103442. Epub 2024 Nov 25.

32) Yanagibashi T, Ikutani M, Nagai T, Arita M, Watanabe Y, Nagai Y, Takatsu K. IL-5-producing group 2 innate lymphoid cells promote T cell-independent IgA production in cooperation with eosinophils. ***Int Immunol***. 2024 Dec 4:dxae070. doi: 10.1093/intimm/dxae070. Online ahead of print.

33) Lee KH, Kim YO, Dho SH, Yong JJH, Oh HS, Lee JH, Yang SJ, Cha I, Chun J, Lee EH, Jeong SJ, Woo W, Choi JP, Han SH, Choi GB, Huh JR, Kim LK, Song YG. Altered gut microbiome in convalescent patients with coronavirus disease 2019. ***Front Cell Infect Microbiol***. 2024 Nov 28;14:1455295. doi: 10.3389/fcimb.2024.1455295. eCollection 2024.

2. Review articles

34) Tsumagari K, Isobe Y, Imami K, Arita M. Exploring protein lipidation by mass spectrometry-based proteomics. ***J Biochem***. 2024 Mar 4;175(3):225-233. doi: 10.1093/jb/mvad109.

35) Solberg T, Kobayashi-Ishihara M, Siomi H. The impact of retrotransposons on zygotic genome activation and the chromatin landscape of early embryos. ***Ann N Y Acad Sci***. 2024 Dec;1542(1):11-24. doi: 10.1111/nyas.15260. Epub 2024 Nov 22.

3. Proceedings None

4. Other English articles None

B. WPI-related papers

1. Original articles

36) Takabayashi K, Sugimoto S, Nanki K, Yoshimatsu Y, Kiyohara H, Mikami Y, Sujino T, Kato M, Hosoe N, Shimoda M, Yahagi N, Ogata H, Iwao Y, Kanai T. Characteristics of flat-type ulcerative colitis-associated neoplasia on chromoendoscopic imaging with indigo carmine dye spraying. ***Dig Endosc***. 2024 Apr;36(4):446-454. doi: 10.1111/den.14628. Epub 2023 Jul 26.

37) Takabayashi K, Kobayashi T, Matsuoka K, Levesque BG, Kawamura T, Tanaka K, Kadota T, Bise R, Uchida S, Kanai T, Ogata H. Artificial intelligence quantifying endoscopic severity of ulcerative colitis in gradation scale. ***Dig Endosc***. 2024 May;36(5):582-590. doi: 10.1111/den.14677. Epub 2023 Oct 11.

38) Tabata S, Umemura S, Narita M, Udagawa H, Ishikawa T, Tsuboi M, Goto K, Ishii G, Tsuchihara K, Ochiai A, Kobayashi SS, Soga T, Makinoshima H. Metabolic Hallmarks for Purine Nucleotide Biosynthesis in Small ***Cell*** Lung Carcinoma. ***Mol Cancer Res***. 2024 Jan 2;22(1):82-93. doi: 10.1158/1541-7786.MCR-23-0386.

39) Shiraishi K, Takahashi A, Momozawa Y, Daigo Y, Kaneko S, Kawaguchi T, Kunitoh H, Matsumoto S, Horinouchi H, Goto A, Honda T, Shimizu K, Torasawa M, Takayanagi D, Saito M, Saito A, Ohe Y, Watanabe SI, Goto K, Tsuboi M, Tsuchihara K, Takata S, Aoi T, Takano A, Kobayashi M, Miyagi Y, Tanaka K, Suzuki H, Maeda D, Yamaura T, Matsuda M, Shimada Y, Mizuno T, Sakamoto H, Yoshida T, Goto Y, Yoshida T, Yamaji T, Sonobe M, Toyooka S, Yoneda K, Masago K, Tanaka F, Hara M, Fuse N, Nishizuka SS, Motoi N, Sawada N, Nishida Y, Kumada K, Takeuchi K, Tanno K, Yatabe Y,

Sunami K, Hishida T, Miyazaki Y, Ito H, Amemiya M, Totsuka H, Nakayama H, Yokose T, Ishigaki K, Nagashima T, Ohtaki Y, Imai K, Takasawa K, Minamiya Y, Kobayashi K, Okubo K, Wakai K, Shimizu A, Yamamoto M, Iwasaki M, Matsuda K, Inazawa J, Shiraishi Y, Nishikawa H, Murakami Y, Kubo M, Matsuda F, Kamatani Y, Hamamoto R, Matsuo K, Kohno T. Identification of telomere maintenance gene variations related to lung adenocarcinoma risk by genome-wide association and whole genome sequencing analyses. ***Cancer Commun (Lond)***. 2024 Feb;44(2):287-293. doi: 10.1002/cac2.12498. Epub 2023 Oct 26.

40) Harada S, Ohmomo H, Matsumoto M, Sata M, Iida M, Hirata A, Miyagawa N, Kuwabara K, Kato S, Toki R, Edagawa S, Sugiyama D, Sato A, Hirayama A, Sugimoto M, Soga T, Tomita M, Shimizu A, Okamura T, Takebayashi T. Metabolomics Profiles Alterations in Cigarette Smokers and Heated Tobacco Product Users. ***J Epidemiol***. 2024 Sep 5;34(9):403-410. doi: 10.2188/jea.JE20230170. Epub 2024 Jun 30.

41) Okubo T, Rivron N, Kabata M, Masaki H, Kishimoto K, Semi K, Nakajima-Koyama M, Kunitomi H, Kaswandy B, Sato H, Nakauchi H, Woltjen K, Saitou M, Sasaki E, Yamamoto T, Takashima Y. Hypoblast from human pluripotent stem cells regulates epiblast development. ***Nature***. 2024 Feb;626(7998):357-366. doi: 10.1038/s41586-023-06871-2. Epub 2023 Dec 5.

42) Nakatsutsumi K, Morishita K, Costantini TW, Adachi T, Suekane A, Suzuki K, Kojima M, Arita M, Otomo Y. Analysis of lipid metabolites derived from gut microbiota in ischemia-reperfusion model. ***J Trauma Acute Care Surg***. 2024 Apr 1;96(4):542-547. doi: 10.1097/TA.0000000000004230. Epub 2023 Dec 8.

43) Shinohara H, Meguro-Horike M, Inoue T, Shimazu M, Hattori M, Hibino H, Fukasawa K, Sasaki E, Horike SI. Early parental deprivation during primate infancy has a lifelong impact on gene expression in the male marmoset brain. ***Sci Rep***. 2024 Jan 3;14(1):330. doi: 10.1038/s41598-023-51025-z.

44) Harada S, Iida M, Miyagawa N, Hirata A, Kuwabara K, Matsumoto M, Okamura T, Edagawa S, Kawada Y, Miyake A, Toki R, Akiyama M, Kawai A, Sugiyama D, Sato Y, Takemura R, Fukai K, Ishibashi Y, Kato S, Kurihara A, Sata M, Shibuki T, Takeuchi A, Kohsaka S, Sawano M, Shoji S, Izawa Y, Katsumata M, Oki K, Takahashi S, Takizawa T, Maruya H, Nishiwaki Y, Kawasaki R, Hirayama A, Ishikawa T, Saito R, Sato A, Soga T, Sugimoto M, Tomita M, Komaki S, Ohmomo H, Ono K, Otsuka-Yamasaki Y, Shimizu A, Sutoh Y, Hozawa A, Kinoshita K, Koshiba S, Kumada K, Ogishima S, Sakurai-Yageta M, Tamiya G, Takebayashi T. Study Profile of the Tsuruoka Metabolomics Cohort Study (TMCS). ***J Epidemiol***. 2024 Aug 5;34(8):393-401. doi: 10.2188/jea.JE20230192. Epub 2024 Jun 30.

45) Tsukimi T, Obana N, Shigemori S, Arakawa K, Miyauchi E, Yang J, Song I, Ashino Y, Wakayama M, Soga T, Tomita M, Ohno H, Mori H, Fukuda S. Genetic mutation in Escherichia coli genome during adaptation to the murine intestine is optimized for the host diet. ***mSystems***. 2024 Feb 20;9(2):e0112323. doi: 10.1128/msystems.01123-23. Epub 2024 Jan 11.

46) Hatano T, Sengoku R, Nagayama H, Yanagisawa N, Yoritaka A, Suzuki K, Nishikawa N, Mukai Y, Nomura K, Yoshida N, Seki M, Matsukawa MK, Terashi H, Kimura K, Tashiro J, Hirano S, Murakami

H, Joki H, Uchiyama T, Shimura H, Ogaki K, Fukae J, Tsuboi Y, Takahashi K, Yamamoto T, Kaida K, Ihara R, Kanemaru K, Kano O. Impact of Istradefylline on Levodopa Dose Escalation in Parkinson's Disease: ISTRA ADJUST PD Study, a Multicenter, Open-Label, Randomized, Parallel-Group Controlled Study. ***Neurol Ther***. 2024 Apr;13(2):323-338. doi: 10.1007/s40120-023-00574-6. Epub 2024 Jan 16.

47) Itoh M, Yuzaki M. The hidden face of GluD1 at inhibitory synapses. ***Cell Res***. 2024 Jun;34(6):405-406. doi: 10.1038/s41422-024-00931-6.

48) Matsubara Y, Kiyohara H, Mikami Y, Nanki K, Namkoong H, Chubachi S, Tanaka H, Azekawa S, Sugimoto S, Yoshimatsu Y, Sujino T, Takabayashi K, Hosoe N, Sato T, Ishii M, Hasegawa N, Okada Y, Koike R, Kitagawa Y, Kimura A, Imoto S, Miyano S, Ogawa S, Fukunaga K, Kanai T; Japan COVID-19 Task Force. Gastrointestinal symptoms in COVID-19 and disease severity: a Japanese registry-based retrospective cohort study. ***J Gastroenterol***. 2024 Mar;59(3):195-208. doi: 10.1007/s00535-023-02071-x. Epub 2024 Jan 25.

49) Miyake A, Harada S, Sugiyama D, Matsumoto M, Hirata A, Miyagawa N, Toki R, Edagawa S, Kuwabara K, Okamura T, Sato A, Amano K, Hirayama A, Sugimoto M, Soga T, Tomita M, Arakawa K, Takebayashi T, Iida M. Reliability of Time-Series Plasma Metabolome Data over 6 Years in a Large-Scale Cohort Study. ***Metabolites***. 2024 Jan 22;14(1):77. doi: 10.3390/metabo14010077.

50) Kurihara K, Fujioka S, Mizutani Y, Watanabe H, Iwaoka K, Maeda T, Seki M, Tezuka T, Nakahara J, Konno T, Ishiguro T, Onodera O, Asano Y, Takahashi K, Rizos A, Chaudhuri KR, Tsuboi Y. Validation study of the Japanese version of the King's Parkinson's Disease Pain Scale and the King's Parkinson's Disease Pain Questionnaire. ***Parkinsonism Relat Disord***. 2024 Mar;120:106012. doi: 10.1016/j.parkreldis.2024.106012. Epub 2024 Jan 28.

51) Nonaka H, Sakamoto S, Shiraiwa K, Ishikawa M, Tamura T, Okuno K, Kondo T, Kiyonaka S, Susaki EA, Shimizu C, Ueda HR, Kakegawa W, Arai I, Yuzaki M, Hamachi I. Bioorthogonal chemical labeling of endogenous neurotransmitter receptors in living mouse brains. ***Proc Natl Acad Sci U S A***. 2024 Feb 6;121(6):e2313887121. doi: 10.1073/pnas.2313887121. Epub 2024 Jan 31.

52) Dewa KI, Arimura N, Kakegawa W, Itoh M, Adachi T, Miyashita S, Inoue YU, Hizawa K, Hori K, Honjoya N, Yagishita H, Taya S, Miyazaki T, Usui C, Tatsumoto S, Tsuzuki A, Uetake H, Sakai K, Yamakawa K, Sasaki T, Nagai J, Kawaguchi Y, Sone M, Inoue T, Go Y, Ichinohe N, Kaibuchi K, Watanabe M, Koizumi S, Yuzaki M, Hoshino M. Neuronal DSCAM regulates the peri-synaptic localization of GLAST in Bergmann glia for functional synapse formation. ***Nat Commun***. 2024 Feb 1;15(1):458. doi: 10.1038/s41467-023-44579-z.

53) Hirata A, Harada S, Iida M, Kurihara A, Fukai K, Kuwabara K, Kato S, Matsumoto M, Sata M, Miyagawa N, Toki R, Edagawa S, Sugiyama D, Sato A, Hirayama A, Sugimoto M, Soga T, Tomita M, Okamura T, Takebayashi T. Association of Nonalcoholic Fatty Liver Disease with Arterial Stiffness and its Metabolomic Profiling in Japanese Community-Dwellers. ***J Atheroscler Thromb***. 2024 Jul 1;31(7):1031-1047. doi: 10.5551/jat.64616. Epub 2024 Feb 2.

54) Okusa S, Nakahara J, Seki M. The Early Onset of Levodopa-induced Dyskinesia in a Patient with

Multiple System Atrophy. ***Intern Med***. 2024 Sep 1;63(17):2451-2453. doi: 10.2169/internalmedicine.3058-23. Epub 2024 Feb 5.

55) Mizumoto Y, Hirakawa A, Sugiura Y, Nishikawa T, Nishimoto K, Mano Y, Higashi T. Determination of three C18-oxygenated steroids in adrenal lesion segments in primary aldosteronism by super-selective adrenal venous sampling and LC/ESI-MS/MS. ***Biomed Chromatogr***. 2024 May;38(5):e5841. doi: 10.1002/bmc.5841. Epub 2024 Feb 7.

56) Goto M, Takahashi H, Yoshida R, Itamiya T, Nakano M, Nagafuchi Y, Harada H, Shimizu T, Maeda M, Kubota A, Toda T, Hatano H, Sugimori Y, Kawahata K, Yamamoto K, Shoda H, Ishigaki K, Ota M, Okamura T, Fujio K. Age-associated CD4(+) T cells with B cell-promoting functions are regulated by ZEB2 in autoimmunity. ***Sci Immunol***. 2024 Mar 29;9(93):eadk1643. doi: 10.1126/sciimmunol.adk1643. Epub 2024 Mar 29.

57) Saijo Y, Nagoshi N, Kawai M, Kitagawa T, Suematsu Y, Ozaki M, Shinozaki M, Kohyama J, Shibata S, Takeuchi K, Nakamura M, Yuzaki M, Okano H. Human-induced pluripotent stem cell-derived neural stem/progenitor cell ex vivo gene therapy with synaptic organizer CPTX for spinal cord injury. ***Stem Cell Reports***. 2024 Mar 12;19(3):383-398. doi: 10.1016/j.stemcr.2024.01.007. Epub 2024 Feb 15.

58) Nagao M, Oshima M, Suto H, Sugimoto M, Enomoto A, Murakami T, Shimomura A, Wada Y, Matsukawa H, Ando Y, Kishino T, Kumamoto K, Kobara H, Kamada H, Masaki T, Soga T, Okano K. Serum Carbohydrate Antigen 19-9 and Metabolite Hypotaurine Are Predictive Markers for Early Recurrence of Pancreatic Ductal Adenocarcinoma. ***Pancreas***. 2024 Apr 1;53(4):e301-e309. doi: 10.1097/MPA.0000000000002304. Epub 2024 Feb 20.

59) Yurimoto T, Kumita W, Sato K, Kikuchi R, Oka G, Shibuki Y, Hashimoto R, Kamioka M, Hayasegawa Y, Yamazaki E, Kurotaki Y, Goda N, Kitakami J, Fujita T, Inoue T, Sasaki E. Development of a 3D tracking system for multiple marmosets under free-moving conditions. ***Commun Biol***. 2024 Feb 21;7(1):216. doi: 10.1038/s42003-024-05864-9.

60) Ohtsuka Y, Suehiro S, Inoue A, Ohnishi T, Nishikawa M, Yamashita D, Yano H, Choudhury ME, Ozaki S, Sampetrean O, Saya H, Watanabe H, Tanaka J, Kunieda T. Berberine as a potential enhancer for 5-ALA-mediated fluorescence in glioblastoma: increasing detectability of infiltrating glioma stem cells to optimize 5-ALA-guided surgery. ***J Neurosurg***. 2024 Mar 8;141(3):653-663. doi: 10.3171/2023.12.JNS231506. Print 2024 Sep 1.

61) Shimada F, Yoshimatsu Y, Sujino T, Fukuda T, Aoki Y, Hayashi Y, Tojo A, Kawaguchi T, Kiyohara H, Sugimoto S, Nanki K, Mikami Y, Miyamoto K, Takabayashi K, Hosoe N, Kato M, Ogata H, Naganuma M, Kanai T. Clinical outcomes of patients with remitting ulcerative colitis after discontinuation of indigo naturalis. ***Sci Rep***. 2024 Mar 9;14(1):5778. doi: 10.1038/s41598-024-56543-y.

62) Longfield SF, Gormal RS, Feller M, Parutto P, Reingruber J, Wallis TP, Joensuu M, Augustine GJ, Martínez-Mármol R, Holcman D, Meunier FA. Synapsin 2a tetramerisation selectively controls the presynaptic nanoscale organisation of reserve synaptic vesicles. ***Nat Commun***. 2024 Mar 12;15(1):2217. doi: 10.1038/s41467-024-46256-1.

63) Mochizuki T, Manita S, Shimura H, Kira S, Sawada N, Bito H, Sakimura K, Augustine GJ, Mitsui T, Takeda M, Kitamura K. Optogenetic stimulation of neurons in the anterior cingulate cortex induces changes in intravesical bladder pressure and the micturition reflex. ***Sci Rep***. 2024 Mar 16;14(1):6367. doi: 10.1038/s41598-024-56806-8.

64) Bai Y, Morita K, Kokaji T, Hatano A, Ohno S, Egami R, Pan Y, Li D, Yugi K, Uematsu S, Inoue H, Inaba Y, Suzuki Y, Matsumoto M, Takahashi M, Izumi Y, Bamba T, Hirayama A, Soga T, Kuroda S. Trans-omic analysis reveals opposite metabolic dysregulation between feeding and fasting in liver associated with obesity. ***iScience***. 2024 Feb 26;27(3):109121. doi: 10.1016/j.isci.2024.109121. eCollection 2024 Mar 15.

65) Fukuda H, Arai K, Mizuno H, Nishito Y, Motoi N, Arai Y, Hiraoka N, Shibata T, Sonobe Y, Kayukawa Y, Hashimoto E, Takahashi M, Fujii E, Maruyama T, Kuwabara K, Nishizawa T, Mizoguchi Y, Yoshida Y, Watanabe SI, Yamashita M, Kitano S, Sakamoto H, Nagata Y, Mitsumori R, Ozaki K, Niida S, Kanai Y, Hirayama A, Soga T, Tsukada K, Yabuki N, Shimada M, Kitazawa T, Natori O, Sawada N, Kato A, Yoshida T, Yasuda K, Ochiai A, Tsunoda H, Aoki K. Molecular subtypes of lung adenocarcinoma present distinct immune tumor microenvironments. ***Cancer Sci***. 2024 Jun;115(6):1763-1777. doi: 10.1111/cas.16154. Epub 2024 Mar 25.

66) Ishibashi Y, Harada S, Eitaki Y, Kurihara A, Kato S, Kuwabara K, Iida M, Hirata A, Sata M, Matsumoto M, Shibuki T, Okamura T, Sugiyama D, Sato A, Amano K, Hirayama A, Sugimoto M, Soga T, Tomita M, Takebayashi T. A population-based urinary and plasma metabolomics study of environmental exposure to cadmium. ***Environ Health Prev Med***. 2024;29:22. doi: 10.1265/ehpm.23-00218.

67) Uehara M, Inoue T, Hase S, Sasaki E, Toyoda A, Sakakibara Y. Decoding host-microbiome interactions through co-expression network analysis within the non-human primate intestine. ***mSystems***. 2024 May 16;9(5):e0140523. doi: 10.1128/msystems.01405-23. Epub 2024 Apr 1.

68) Momota Y, Bun S, Hirano J, Kamiya K, Ueda R, Iwabuchi Y, Takahata K, Yamamoto Y, Tezuka T, Kubota M, Seki M, Shikimoto R, Mimura Y, Kishimoto T, Tabuchi H, Jinzaki M, Ito D, Mimura M. Amyloid-β prediction machine learning model using source-based morphometry across neurocognitive disorders. ***Sci Rep***. 2024 Apr 1;14(1):7633. doi: 10.1038/s41598-024-58223-3.

69) Watanuki S, Kobayashi H, Sugiura Y, Yamamoto M, Karigane D, Shiroshita K, Sorimachi Y, Fujita S, Morikawa T, Koide S, Oshima M, Nishiyama A, Murakami K, Haraguchi M, Tamaki S, Yamamoto T, Yabushita T, Tanaka Y, Nagamatsu G, Honda H, Okamoto S, Goda N, Tamura T, Nakamura-Ishizu A, Suematsu M, Iwama A, Suda T, Takubo K. Context-dependent modification of PFKFB3 in hematopoietic stem cells promotes anaerobic glycolysis and ensures stress hematopoiesis. ***Elife***. 2024 Apr 4;12:RP87674. doi: 10.7554/eLife.87674.

70) Wiriyasermkul P, Moriyama S, Suzuki M, Kongpracha P, Nakamae N, Takeshita S, Tanaka Y, Matsuda A, Miyasaka M, Hamase K, Kimura T, Mita M, Sasabe J, Nagamori S. <sc>A</sc> multi-hierarchical approach reveals <sc>d</sc>-serine as a hidden substrate of sodium-coupled monocarboxylate transporters. ***Elife***. 2024 Apr 23;12:RP92615. doi: 10.7554/eLife.92615.

71) Hitomi Y, Ueno K, Aiba Y, Nishida N, Kono M, Sugihara M, Kawai Y, Kawashima M, Khor SS, Sugi K,

Kouno H, Kohno H, Naganuma A, Iwamoto S, Katsushima S, Furuta K, Nikami T, Mannami T, Yamashita T, Ario K, Komatsu T, Makita F, Shimada M, Hirashima N, Yokohama S, Nishimura H, Sugimoto R, Komura T, Ota H, Kojima M, Nakamuta M, Fujimori N, Yoshizawa K, Mano Y, Takahashi H, Hirooka K, Tsuruta S, Sato T, Yamasaki K, Kugiyama Y, Motoyoshi Y, Suehiro T, Saeki A, Matsumoto K, Nagaoka S, Abiru S, Yatsuhashi H, Ito M, Kawata K, Takaki A, Arai K, Arinaga-Hino T, Abe M, Harada M, Taniai M, Zeniya M, Ohira H, Shimoda S, Komori A, Tanaka A, Ishigaki K, Nagasaki M, Tokunaga K, Nakamura M. A genome-wide association study identified PTPN2 as a population-specific susceptibility gene locus for primary biliary cholangitis. ***Hepatology***. 2024 Oct 1;80(4):776-790. doi: 10.1097/HEP.0000000000000894. Epub 2024 Apr 23.

72) Fukuda T, Aoki Y, Kiyohara H, Yokoyama A, Nakazawa A, Yoshimatsu Y, Sugimoto S, Nanki K, Mikami Y, Fukuhara K, Mizuno S, Sujino T, Mutaguchi M, Takabayashi K, Morohoshi Y, Hosoda Y, Ogata H, Iwao Y, Naganuma M, Kanai T. Efficacy of Dose Escalation of Oral 5-Aminosalicylic Acid for Ulcerative Colitis With a Mayo Endoscopic Subscore of 1: An Open Label Randomized Controlled Trial. ***Inflamm Bowel Dis***. 2024 Apr 24:izae088. doi: 10.1093/ibd/izae088. Online ahead of print.

73) Miyamoto Y, Kikuta J, Matsui T, Hasegawa T, Fujii K, Okuzaki D, Liu YC, Yoshioka T, Seno S, Motooka D, Uchida Y, Yamashita E, Kobayashi S, Eguchi H, Morii E, Tryggvason K, Shichita T, Kayama H, Atarashi K, Kunisawa J, Honda K, Takeda K, Ishii M. Periportal macrophages protect against commensal-driven liver inflammation. ***Nature***. 2024 May;629(8013):901-909. doi: 10.1038/s41586-024-07372-6. Epub 2024 Apr 24.

74) Cuhadar U, Calzado-Reyes L, Pascual-Caro C, Aberra AS, Ritzau-Jost A, Aggarwal A, Ibata K, Podgorski K, Yuzaki M, Geis C, Hallerman S, Hoppa MB, de Juan-Sanz J. Activity-driven synaptic translocation of LGI1 controls excitatory neurotransmission. ***Cell Rep***. 2024 May 28;43(5):114186. doi: 10.1016/j.celrep.2024.114186. Epub 2024 May 2.

75) Sakakibara R, Sugimoto S, Takabayashi K, Kiyohara H, Wakisaka Y, Kaieda Y, Kawaida M, Yoshimatsu Y, Sujino T, Hosoe N, Kato M, Shimoda M, Mikami Y, Iwao Y, Kanai T. Ulcerative colitis-associated neoplasms often harbor poor prognostic histologic components with low detection by biopsy. ***Intest Res***. 2024 Oct;22(4):428-438. doi: 10.5217/ir.2024.00006. Epub 2024 May 7.

76) Watanuki S, Kobayashi H, Sugiura Y, Yamamoto M, Karigane D, Shiroshita K, Sorimachi Y, Morikawa T, Fujita S, Shide K, Haraguchi M, Tamaki S, Mikawa T, Kondoh H, Nakano H, Sumiyama K, Nagamatsu G, Goda N, Okamoto S, Nakamura-Ishizu A, Shimoda K, Suematsu M, Suda T, Takubo K. SDHAF1 confers metabolic resilience to aging hematopoietic stem cells by promoting mitochondrial ATP production. ***Cell Stem Cell***. 2024 Aug 1;31(8):1145-1161.e15. doi: 10.1016/j.stem.2024.04.023. Epub 2024 May 20.

77) Kayashima A, Sujino T, Fukuhara S, Miyamoto K, Kubosawa Y, Ichikawa M, Kawasaki S, Takabayashi K, Iwasaki E, Kato M, Honda A, Kanai T, Nakamoto N. Unique bile acid profiles in the bile ducts of patients with primary sclerosing cholangitis. ***Hepatol Commun***. 2024 May 22;8(6):e0452. doi: 10.1097/HC9.0000000000000452. eCollection 2024 Jun 1.

78) McCurry MD, D'Agostino GD, Walsh JT, Bisanz JE, Zalosnik I, Dong X, Morris DJ, Korzenik JR, Edlow

AG, Balskus EP, Turnbaugh PJ, Huh JR, Devlin AS. Gut bacteria convert glucocorticoids into progestins in the presence of hydrogen gas. ***Cell***. 2024 Jun 6;187(12):2952-2968.e13. doi: 10.1016/j.cell.2024.05.005. Epub 2024 May 24.

79) Inamo J, Suzuki A, Ueda MT, Yamaguchi K, Nishida H, Suzuki K, Kaneko Y, Takeuchi T, Hatano H, Ishigaki K, Ishihama Y, Yamamoto K, Kochi Y. Long-read sequencing for 29 immune cell subsets reveals disease-linked isoforms. ***Nat Commun***. 2024 May 28;15(1):4285. doi: 10.1038/s41467-024-48615-4.

80) Yamamoto E, Hirokawa M, Nunez E, Hakuno Y, Sekine K, Miyahara S, Suzuki K, Minagawa Y. Neural and Physiological Correlates of Prosocial Behavior: Temporoparietal Junction Activity in 3-year-old Children. ***J Cogn Neurosci***. 2024 Sep 1;36(9):1977-1994. doi: 10.1162/jocn_a_02199.

81) Ham GX, Ong JZ, Augustine GJ, Leong V. Protocol to study dam-pup social transmission using a modified paradigm for transmission of food preference. ***STAR Protoc***. 2024 Jun 21;5(2):103077. doi: 10.1016/j.xpro.2024.103077. Epub 2024 Jun 6.

82) Tsuzuki A, Yamasaki M, Konno K, Miyazaki T, Takei N, Tomita S, Yuzaki M, Watanabe M. Abundant extrasynaptic expression of α3β4-containing nicotinic acetylcholine receptors in the medial habenula-interpeduncular nucleus pathway in mice. ***Sci Rep***. 2024 Jun 20;14(1):14193. doi: 10.1038/s41598-024-65076-3.

83) Tezuka T, Nukariya T, Kizuka Y, Okusa S, Okochi R, Sakai Y, Nihei Y, Nakahara J, Seki M. Potential Psychosis Induced by a Sustained High Plasma Levodopa Concentration Due to Continuous Subcutaneous Foslevodopa/Foscarbidopa Infusion in a Patient With Parkinson's Disease: A Case Report. ***J Mov Disord***. 2024 Oct;17(4):453-455. doi: 10.14802/jmd.24114. Epub 2024 Jun 28.

84) Mimura Y, Komatsu K, Yasushi Y, Seki M, Nakajima S, Uchida H, Mimura M. A case of painful legs and moving toes syndrome mimicking somatic symptom disorder. ***Psychogeriatrics***. 2024 Jul;24(4):1023-1029. doi: 10.1111/psyg.13155. Epub 2024 Jun 21.

85) Song SH, Augustine GJ. A role for synapsin tetramerization in synaptic vesicle clustering. ***J Physiol***. 2024 Jul 9. doi: 10.1113/JP286177. Online ahead of print.

86) Kakegawa W, Paternain AV, Matsuda K, Aller MI, Iida I, Miura E, Nozawa K, Yamasaki T, Sakimura K, Yuzaki M, Lerma J. Kainate receptors regulate synaptic integrity and plasticity by forming a complex with synaptic organizers in the cerebellum. ***Cell Rep***. 2024 Jul 23;43(7):114427. doi: 10.1016/j.celrep.2024.114427. Epub 2024 Jul 9.

87) Salim F, Mizutani S, Shiba S, Takamaru H, Yamada M, Nakajima T, Yachida T, Soga T, Saito Y, Fukuda S, Yachida S, Yamada T. Fusobacterium species are distinctly associated with patients with Lynch syndrome colorectal cancer. ***iScience***. 2024 Jun 4;27(7):110181. doi: 10.1016/j.isci.2024.110181. eCollection 2024 Jul 19.

88) Steimle A, Neumann M, Grant ET, Willieme S, De Sciscio A, Parrish A, Ollert M, Miyauchi E, Soga T, Fukuda S, Ohno H, Desai MS. Gut microbial factors predict disease severity in a mouse model of multiple sclerosis. ***Nat Microbiol***. 2024 Sep;9(9):2244-2261. doi: 10.1038/s41564-024-01761-3.

Epub 2024 Jul 15.

89) Maciag G, Hansen SL, Krizic K, Kellermann L, Inventor Zøylner MJ, Ulyanchenko S, Maimets M, Baattrup AM, Riis LB, Khodosevich K, Sato T, Bressan RB, Nielsen OH, Jensen KB. JAK/STAT signaling promotes the emergence of unique cell states in ulcerative colitis. ***Stem Cell Reports***. 2024 Aug 13;19(8):1172-1188. doi: 10.1016/j.stemcr.2024.06.006. Epub 2024 Jul 18.

90) Nakasuka F, Hirayama A, Makinoshima H, Yano S, Soga T, Tabata S. The role of cytidine 5'-triphosphate synthetase 1 in metabolic rewiring during epithelial-to-mesenchymal transition in non-small-cell lung cancer. ***FEBS Open Bio***. 2024 Sep;14(9):1570-1583. doi: 10.1002/2211-5463.13860. Epub 2024 Jul 19.

91) Itoh M, Piot L, Mony L, Paoletti P, Yuzaki M. Lack of evidence for direct ligand-gated ion channel activity of GluD receptors. ***Proc Natl Acad Sci U S A***. 2024 Jul 30;121(31):e2406655121. doi: 10.1073/pnas.2406655121. Epub 2024 Jul 25.

92) Shimomura A, Oshima M, Suto H, Matsukawa H, Kondo A, Ando Y, Kishino T, Kumamoto K, Sato K, Sugimoto M, Nagao M, Miyatake N, Norikane T, Soga T, Okano K. Prognostic Significance of (18)F-FDG PET/CT and Tumor Metabolic Changes in Patients With Pancreatic Ductal Adenocarcinoma. ***Anticancer Res***. 2024 Aug;44(8):3321-3330. doi: 10.21873/anticanres.17151.

93) Ooga M, Sahayasheela VJ, Hirose Y, Sasaki D, Hashiya K, Bando T, Sugiyama H. A dual DNA-binding conjugate that selectively recognizes G-quadruplex structures. ***Chem Commun (Camb)***. 2024 Aug 13;60(66):8744-8747. doi: 10.1039/d4cc01572j.

94) Yurimoto T, Seki F, Yamada A, Okajima J, Yambe T, Takewa Y, Kamioka M, Inoue T, Inoue Y, Sasaki E. Development of a noninvasive olfactory stimulation fMRI system in marmosets. ***Sci Rep***. 2024 Aug 1;14(1):17830. doi: 10.1038/s41598-024-68508-2.

95) Sato Y, Hishiki T, Masugi Y, Florence L, Yu YM. Vitamin D administration increases serum alanine concentrations in thermally injured mice. ***Biochem Biophys Res Commun***. 2024 Dec 3;736:150505. doi: 10.1016/j.bbrc.2024.150505. Epub 2024 Aug 6.

96) Kubosawa Y, Sujino T, Miyamoto K, Kayashima A, Minezaki D, Morioka K, Iwata K, Miyazaki K, Masunaga T, Mizutani M, Akimoto T, Takatori Y, Matsuura N, Nakayama A, Takabayashi K, Nakamoto N, Honda A, Kato M, Yahagi N, Kanai T. Distinctive duodenal microbiomes and bile acid profiles in duodenal tumor patients revealed by prospective observational study. ***Sci Rep***. 2024 Aug 12;14(1):18705. doi: 10.1038/s41598-024-69820-7.

97) Miyahara S, Ohuchi M, Nomura M, Hashimoto E, Soga T, Saito R, Hayashi K, Sato T, Saito M, Yamashita Y, Shimada M, Yaegashi N, Yamada H, Tanuma N. FDX2, an iron-sulfur cluster assembly factor, is essential to prevent cellular senescence, apoptosis or ferroptosis of ovarian cancer cells. ***J Biol Chem***. 2024 Sep;300(9):107678. doi: 10.1016/j.jbc.2024.107678. Epub 2024 Aug 14.

98) Ohnuki Y, Akiyama M, Sakakibara Y. Deep learning of multimodal networks with topological regularization for drug repositioning. ***J Cheminform***. 2024 Aug 23;16(1):103. doi: 10.1186/s13321-024-00897-y.

99) Ueno M, Sugiyama H, Li F, Nishimura T, Arakawa H, Chen X, Cheng X, Takeuchi S, Takeshita Y, Takamura T, Miyagi S, Toyama T, Soga T, Masuo Y, Kato Y, Nakamura H, Tsujiguchi H, Hara A, Tajima A, Noguchi-Shinohara M, Ono K, Kurayoshi K, Kobayashi M, Tadokoro Y, Kasahara A, Shoulkamy MI, Maeda K, Ogoshi T, Hirao A. A Supramolecular Biosensor for Rapid and High-Throughput Quantification of a Disease-Associated Niacin Metabolite. ***Anal Chem***. 2024 Sep 10;96(36):14499-14507. doi: 10.1021/acs.analchem.4c02653. Epub 2024 Aug 25.

100) Sato K, Sasaguri H, Kumita W, Sakuma T, Morioka T, Nagata K, Inoue T, Kurotaki Y, Mihira N, Tagami M, Manabe RI, Ozaki K, Okazaki Y, Yamamoto T, Suematsu M, Saido TC, Sasaki E. Production of a heterozygous exon skipping model of common marmosets using gene-editing technology. ***Lab Anim (NY)***. 2024 Sep;53(9):244-251. doi: 10.1038/s41684-024-01424-0. Epub 2024 Aug 30.

101) Kanai M, Nishino T, Daassi D, Kimura A, Liao CW, Javanfekr Shahri Z, Wakimoto A, Gogoleva N, Usui T, Morito N, Arita M, Takahashi S, Hamada M. MAFB in Macrophages Regulates Prostaglandin E2-Mediated Lipid Mediator Class Switch through ALOX15 in Ischemic Acute Kidney Injury. ***J Immunol***. 2024 Oct 15;213(8):1212-1224. doi: 10.4049/jimmunol.2300844.

102) Tamagawa H, Fujii M, Togasaki K, Seino T, Kawasaki S, Takano A, Toshimitsu K, Takahashi S, Ohta Y, Matano M, Kawasaki K, Machida Y, Sekine S, Machinaga A, Sasai K, Kodama Y, Kakiuchi N, Ogawa S, Hirano T, Seno H, Kitago M, Kitagawa Y, Iwasaki E, Kanai T, Sato T. Wnt-deficient and hypoxic environment orchestrates squamous reprogramming of human pancreatic ductal adenocarcinoma. ***Nat Cell Biol***. 2024 Oct;26(10):1759-1772. doi: 10.1038/s41556-024-01498-5. Epub 2024 Sep 4.

103) Uemura S, Kabe Y, Kitago M, Matsuda S, Abe Y, Hasegawa Y, Hori S, Tanaka M, Nakano Y, Sato Y, Itonaga M, Ono M, Kawakami T, Suematsu M, Kitagawa Y. Prognosis prediction of PDAC via detection of O-glycan altered extracellular vesicles in perioperative sera. ***Cancer Sci***. 2024 Nov;115(11):3718-3728. doi: 10.1111/cas.16341. Epub 2024 Sep 16.

104) Wang QS, Hasegawa T, Namkoong H, Saiki R, Edahiro R, Sonehara K, Tanaka H, Azekawa S, Chubachi S, Takahashi Y, Sakaue S, Namba S, Yamamoto K, Shiraishi Y, Chiba K, Tanaka H, Makishima H, Nannya Y, Zhang Z, Tsujikawa R, Koike R, Takano T, Ishii M, Kimura A, Inoue F, Kanai T, Fukunaga K, Ogawa S, Imoto S, Miyano S, Okada Y; Japan COVID-19 Task Force. Statistically and functionally fine-mapped blood eQTLs and pQTLs from 1,405 humans reveal distinct regulation patterns and disease relevance. ***Nat Genet***. 2024 Oct;56(10):2054-2067. doi: 10.1038/s41588-024-01896-3. Epub 2024 Sep 24.

105) Siriwardena D, Munger C, Penfold C, Kohler TN, Weberling A, Linneberg-Agerholm M, Slatery E, Ellermann AL, Bergmann S, Clark SJ, Rawlings TM, Brickman JM, Reik W, Brosens JJ, Zernicka-Goetz M, Sasaki E, Behr R, Hollfelder F, Boroviak TE. Marmoset and human trophoblast stem cells differ in signaling requirements and recapitulate divergent modes of trophoblast invasion. ***Cell Stem Cell***. 2024 Oct 3;31(10):1427-1446.e8. doi: 10.1016/j.stem.2024.09.004. Epub 2024 Sep 24.

106) Aikawa S, Matsuo M, Akaeda S, Sugimoto Y, Arita M, Isobe Y, Sugiura Y, Taira S, Maeda R, Shimizu-Hirota R, Takeda N, Hiratsuka D, He X, Ishizawa C, Iida R, Fukui Y, Hiraoka T, Harada M, Wada-

Hiraike O, Osuga Y, Hirota Y. Spatiotemporally distinct roles of cyclooxygenase-1 and cyclooxygenase-2 at fetomaternal interface in mice. ***JCI Insight***. 2024 Aug 27;9(19):e181865. doi: 10.1172/jci.insight.181865.

107) Shiraishi M, Mikami K, Kamo H, Okuma Y, Tsunemi T, Fujimoto K, Kamo T, Yokota Y, Nogawa S, Osada T, Seki M, Nagayama H, Hatano T, Nakajima H, Suzuki K, Yamamoto T, Yamano Y, Hattori N, Iijima M. The effect of subjective postural vertical on forward flexed posture in Parkinson's disease. ***Parkinsonism Relat Disord***. 2024 Dec;129:107102. doi: 10.1016/j.parkreldis.2024.107102. Epub 2024 Aug 13.

108) Oh DS, Kim E, Normand R, Lu G, Shook LL, Lyall A, Jasset O, Demidkin S, Gilbert E, Kim J, Akinwunmi B, Tantivit J, Tirard A, Arnold BY, Slowikowski K; MGH COVID-19 Collection & Processing Team; Goldberg MB, Filbin MR, Hacohen N, Nguyen LH, Chan AT, Yu XG, Li JZ, Yonker L, Fasano A, Perlis RH, Pasternak O, Gray KJ, Choi GB, Drew DA, Sen P, Villani AC, Edlow AG, Huh JR. SARS-CoV-2 infection elucidates features of pregnancy-specific immunity. ***Cell Rep***. 2024 Nov 26;43(11):114933. doi: 10.1016/j.celrep.2024.114933. Epub 2024 Nov 5.

109) Daté Y, Bun S, Takahata K, Kubota M, Momota Y, Iwabuchi Y, Tezuka T, Tabuchi H, Seki M, Yamamoto Y, Shikimoto R, Mimura Y, Hoshino T, Kurose S, Shimohama S, Suzuki N, Morimoto A, Oosumi A, Hoshino Y, Jinzaki M, Mimura M, Ito D. Can the clinical sign "head-turning sign" and simple questions in "Neucop-Q" predict amyloid β pathology?. ***Alzheimers Res Ther***. 2024 Nov 21;16(1):250. doi: 10.1186/s13195-024-01605-6.

110) Takeda H, Matsuzawa Y, Takeuchi M, Takahashi M, Nishida K, Harayama T, Todoroki Y, Shimizu K, Sakamoto N, Oka T, Maekawa M, Chung MH, Kurizaki Y, Kiuchi S, Tokiyoshi K, Buyantogtokh B, Kurata M, Kvasnička A, Takeda U, Uchino H, Hasegawa M, Miyamoto J, Tanabe K, Takeda S, Mori T, Kumakubo R, Tanaka T, Yoshino T, Okamoto M, Takahashi H, Arita M, Tsugawa H. MS-DIAL 5 multimodal mass spectrometry data mining unveils lipidome complexities. ***Nat Commun***. 2024 Nov 28;15(1):9903. doi: 10.1038/s41467-024-54137-w.

111) Luo Y, Huang CC, Howard NC, Wang X, Liu Q, Li X, Zhu J, Amariuta T, Asgari S, Ishigaki K, Calderon R, Raman S, Ramnarine AK, Mayfield JA, Moody DB, Lecca L, Fortune SM, Murray MB, Raychaudhuri S. Paired analysis of host and pathogen genomes identifies determinants of human tuberculosis. ***Nat Commun***. 2024 Nov 29;15(1):10393. doi: 10.1038/s41467-024-54741-w.

112) Tian C, Zhang Y, Tong Y, Kock KH, Sim DY, Liu F, Dong J, Jing Z, Wang W, Gao J, Tan LM, Han KY, Tomofuji Y, Nakano M, Buyamin EV, Sonthalia R, Ando Y, Hatano H, Sonehara K; Asian Immune Diversity Atlas Network; Jin X, Loh M, Chambers J, Hon CC, Choi M, Park JE, Ishigaki K, Okamura T, Fujio K, Okada Y, Park WY, Shin JW, Roca X, Prabhakar S, Liu B. Single-cell RNA sequencing of peripheral blood links cell-type-specific regulation of splicing to autoimmune and inflammatory diseases. ***Nat Genet***. 2024 Dec;56(12):2739-2752. doi: 10.1038/s41588-024-02019-8. Epub 2024 Dec 3.

113) Kawajiri A, Li J, Koinuma K, Yang Z, Yoon HJ, Yi J, Nagashima H, Ishii M, Gao F, Sato K, Tayama S, Harigae H, Iwakura Y, Ishii N, Sher A, Ishigaki K, Zhu J, Kim KS, Kawabe T. Naturally arising

memory-phenotype CD4(+) T lymphocytes contain an undifferentiated population that can generate T(H)1, T(H)17, and T(reg) cells. ***Sci Adv***. 2024 Dec 6;10(49):eadq6618. doi: 10.1126/sciadv.adq6618. Epub 2024 Dec 4.

114) Honda K, Tanoue T, Nagayama M, Roochana A, Zimmerman S, Ashenberg O, Jain T, Sasajima S, Takeshita K, Hetherington N, Okahashi N, Ueda M, Konishi M, Nakayama Y, Minoda A, Skelly A, Minokoshi Y, Pucci N, Mende D, Arita M, Yamamoto H, Watanabe S, Miura K, Suda W, Atarashi K, Matsushita M, Kajimura S, Plichta D, Saito M, Xavier R. Identification of specific microbiota members that induce beige fat biogenesis in response to dietary cues. ***Res Sq*** [Preprint]. 2024 Dec 3:rs.3.rs-5454144. doi: 10.21203/rs.3.rs-5454144/v1.

115) Wong KLL, Graf M, Augustine GJ. Serotonin Inhibition of Claustrum Projection Neurons: Ionic Mechanism, Receptor Subtypes and Consequences for Claustrum Computation. ***Cells***. 2024 Nov 29;13(23):1980. doi: 10.3390/cells13231980.

116) Flanagan J, Liu X, Ortega-Reyes D, Tomizuka K, Matoba N, Akiyama M, Koido M, Ishigaki K, Ashikawa K, Takata S, Shi M, Aoi T, Momozawa Y, Ito K, Murakami Y, Matsuda K; Biobank Japan Project; Kamatani Y, Morris AP, Horikoshi M, Terao C. Population-specific reference panel improves imputation quality for genome-wide association studies conducted on the Japanese population. ***Commun Biol***. 2024 Dec 19;7(1):1665. doi: 10.1038/s42003-024-07338-4.

2. Review articles

117) Sahayasheela VJ, Sugiyama H. RNA G-quadruplex in functional regulation of noncoding RNA: Challenges and emerging opportunities. ***Cell Chem Biol***. 2024 Jan 18;31(1):53-70. doi: 10.1016/j.chembiol.2023.08.010. Epub 2023 Oct 30.

118) Ichikawa M, Okada H, Nakamoto N, Taniki N, Chu PS, Kanai T. The gut-liver axis in hepatobiliary diseases. ***Inflamm Regen***. 2024 Jan 8;44(1):2. doi: 10.1186/s41232-023-00315-0.

119) Kim E, Huh JR, Choi GB. Prenatal and postnatal neuroimmune interactions in neurodevelopmental disorders. ***Nat Immunol***. 2024 Apr;25(4):598-606. doi: 10.1038/s41590-024-01797-x. Epub 2024 Apr 2.

120) Miyamoto K, Sujino T, Kanai T. The tryptophan metabolic pathway of the microbiome and host cells in health and disease. ***Int Immunol***. 2024 Nov 14;36(12):601-616. doi: 10.1093/intimm/dxae035.

121) Hammerhøj A, Chakravarti D, Sato T, Jensen KB, Nielsen OH. Organoids as regenerative medicine for inflammatory bowel disease. ***iScience***. 2024 May 27;27(6):110118. doi: 10.1016/j.isci.2024.110118. eCollection 2024 Jun 21.

122) Wada M, Watanabe K, Sugimoto S, Sato T, Kobayashi E. A Novel Organoid-Based Strategy Using Hybrid Colon Interposition for Short Bowel Syndrome: A Mini Review of In Vivo Models and Possible Human Candidates. ***Gastroenterol Clin North Am***. 2024 Sep;53(3):481-491. doi: 10.1016/j.gtc.2024.01.005. Epub 2024 Feb 13.

3. Proceedings None

4. Other English articles None

2. Invited Lectures, Plenary Addresses (etc.) at International Conferences and International Research Meetings

- List up to 10 main presentations during FY 2024 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
2025/03/07	*Kenya Honda Makoto Arita Jumpei Sasabe Kaoru Hida Leong	*Lipidome signatures associated with aging and host-microbiome interactions, etc.	The 3rd Keio University WPI-Bio2Q International Symposium, Japan
2024/11/19	Kenya Honda	Development of live biotherapeutic products based on understanding of the gut microbiota	Nature Café: Restoration of a Healthy Gut Microbiome to Treat Disease, UK
2024/11/09	Kazuyoshi Ishigaki	Polygenic risk of rheumatoid arthritis regulates the abundance of circulating regulatory T cells	American Society of Human Genetics Annual Meeting 2024. Denver, U.S.
2024/11/06	Therese Solberg	The role of histone methylations on DNA elimination in the ciliate *Paramecium*	APCOP-V, Brisbane, Australia
2024/10/04	Makoto Suematsu	Imaging metabolomics to decipher cancer metabolism	Vilnius University Medical Research Center Opening Symposium, Lithuania
2024/08/21	Makoto Arita	Lipidome signatures associated with aging and the host-microbiome interaction (Keynote Lecture)	25th International Mass Spectrometry Conference (IMSC2024), Australia
2024/7/14-19	Michisuke Yuzaki	Molecular Basis of Fast Neurotransmitter-Independent Synaptic Signaling in the Mammalian CNS.	Gordon Research Conference on Synaptic Transmission, Italy
2024/07/12	Michisuke Yuzaki	Regulation of Synapses in the CNS and PNS by C1q Family Molecules.	Seminaires de Biologie, IBENS, France
2024/07/08	Kenya Honda	Developing Live Biotherapeutic Products Through Understanding the Gut Microbiota	ICMI13（The 16th International Congress of Mucosal Immunology）, Denmark
2024/06/28	Kenya Honda	Development of live biotherapeutic products based on understanding of the gut microbiota	The 51st Naito Conference, Japan

3. Major Awards

- List up to 10 main awards received during FY 2024 in order from the most recent.
- For each, write the date issued, the recipient's name, and the name of award.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
2025/03/11	Michisuke Yuzaki	Uehara Award
2024/12/19	Kenya Honda	Takamine Memorial Daiichi Sankyo Award, Japan
2024/11/19	Kenya Honda Toshiro Sato Takanori Kanai Koji Atarashi	Clarivate's Highly Cited Researchers 2024
2024	Jun Huh	Fairbairn Lyme Initiative Lyme Disease Initiative Project Award, USA
2024	Jun Huh	The Marcus Foundation Award, USA

Appendix 2　FY 2024 List of Principal Investigators

NOTE:

*Underline names of principal investigators who belong to an overseas research institution.

*In the case of researcher(s) not listed in the in the latest report, attach a "Biographical Sketch of a New Principal Investigator"(Appendix 2a).

*Enter the host institution name and the center name in the footer.

<Results at the end of FY2024> **Principal Investigators Total: 21**

Name	Age	Affiliation (Position title, department, organization)	Academic degree, specialty	Effort (%)*	Starting date of project participation	Status of project participation (Describe in concrete terms)	Contributions by PIs from overseas research institutions
Center director Kenya Honda	56	Professor, Keio University School of Medicine	M.D., Ph.D. Microbiome, Immunology	90	November 11, 2022	Usually stays at the center	
Toshiro Sato	52	Professor, Keio University School of Medicine	M.D., Ph.D. Gastroenterology	90	November 11, 2022	Usually stays at the center	
Makoto Arita	55	Professor, Keio University Faculty of Pharmacy	Ph.D. Lipid biology, Lipidomics	80	November 11, 2022	Usually stays at the center	
Shu Tanaka	44	Associate Professor, Keio University Faculty of Science and Technology	Ph.D. Quantum annealing, Statistical mechanics, Computational physics	80	November 11, 2022	Usually stays at the center	
Haruhiko Siomi	65	Professor, Keio University School of Medicine	Ph.D. Epigenetics	90	November 11, 2022	Usually stays at the center	
Michisuke Yuzaki	65	Professor, Keio University School of Medicine	M.D., Ph.D. Neuroscience, Synaptopathy	90	November 11, 2022	Usually stays at the center	
Jun Huh	51	Associate Professor, Department of Immunology, Harvard Medical School, Harvard University	Ph.D. Microbiome and Neuroimmunology	10	November 11, 2022	Usually stays at home institution and attends meetings online	Attended the Bio2Q meeting at the center
Erika Sasaki	58	Director, Department of Marmoset Biology and Medicine, Central Institute for Experimental Medicine and Life Science	Ph.D. Laboratory animal science, Reproductive biology	80	November 11, 2022	Usually stays at the center	
Yasuyo Minagawa	54	Professor, Keio University Faculty of Letters	Ph.D. Developmental cognitive neuroscience, Developmental psychology, Psycholinguistics	80	November 11, 2022	Usually stays at the center	
Radu Aricescu	52	Programme Leader, Neurobiology Division, MRC Laboratory of Molecular Biology	Ph.D. Neuroscience & Structural Biology	30	November 11, 2022	Usually stays at home institution and attends meetings online or onsite	Attended meetings for laboratory setup
Tomoyoshi Soga	65	Professor, Keio University Faculty of Environment and Information Studies	Ph.D. Analytical chemistry, Metabolomics, Cancer metabolism	80	November 11, 2022	Usually stays at the center	
Naoki Yamamoto	48	Professor, Keio University Faculty of Science and Technology	Ph.D. Quantum computation, Quantum control	80	November 11, 2022	Usually stays at the center	

Yasubumi Sakakibara	64	Professor, Keio University Faculty of Science and Technology	Ph.D. Bioinformatics	80	November 11, 2022	Usually stays at the center	
Makoto Suematsu	67	Director, Live Imaging Center, Central Institute for Experimental Medicine and Life Science	M.D., Ph.D. Biochemistry	80	November 11, 2022	Usually stays at the center	
George Augustine	69	Professor, Temasek Life Sciences Laboratory, National University of Singapore	Ph.D. Neurobiology	30	November 11, 2022	Usually stays at home institution and attends meetings online or onsite	Attended the Bio2Q retreat and conducted presentation skills seminar and provided tutoring at the center
Takahiko Koyama	53	Project Professor, Keio University Bio2Q	Ph.D. Physics	100	January 1, 2024	Usually stays at the center	
Shigeki Ishikawa	64	Project Professor, Keio University Bio2Q	Ph.D. Quantum Computing, Artificial Intelligence for Healthcare & Medicine, Strategy Development	100	April 1, 2024	Usually stays at the center	
Takanori Kanai	63	Professor, Keio University School of Medicine	M.D., Ph.D. Gastroenterology and Hepatology	80	April 1, 2024	Usually stays at the center	
Kazuyoshi Ishigaki	44	Professor, Keio University School of Medicine	M.D., Ph.D. Genetics, Immunology	80	April 1, 2024	Usually stays at the center	
Daniel Richard Mende	40	Project Professor, Keio University Bio2Q	Ph.D. Microbiome, Metagenomics, Computational Biology	100	January 1, 2025	Usually stays at the center	
Nadinath Navaratne Mudiyanselage Bandara Nillegoda	46	Project Professor, Keio University Bio2Q	Ph.D. Proteostasis, Cell Repair, Protein Quality Control, Protein Disaggregation, Molecular Chaperones	100	January 1, 2025	Usually stays at the center	

*Percentage of time that the principal investigator devotes to working for the center vis-à-vis his/her total working hours.

Principal investigators unable to participate in project in FY 2024

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) Shigeki Ishikawa (64)

Affiliation and position (Position title, department, organization, etc.)
Project Professor, Keio University WPI-Bio2Q

Academic degree and specialty Ph.D. (Electrical Engineering) / Quantum Computing, Artificial Intelligence for Healthcare & Medicine, Strategy Development

Effort **100 %**
* Percentage of time that the principal investigator devote to working for the center vis-à-vis his/her total working hours.

Research and education history

- 3/31/1983 Graduated from Keio University, Faculty of Engineering, Department of Electrical Engineering, bachelor's degree
- 3/31/1985 Completed Master's degree of Electrical Engineering, Graduate School of Engineering, Keio University
- 9/30/1993 Obtained Ph.D. degree from Keio University Graduate School of Engineering

Achievements and highlights of past research activities

Summary @ IBM:

- Involved in planning and developing IT solutions that support business operations at companies.
- 1993-96: Planning and development of electronic information sharing and collaborative work support solutions using IT to smoothly carry out engineering, ordering, production management, production preparation, and production processes in the manufacturing industry (CAD/CAE), PDM, ERP, MES and Web Technology fusion). Planning and development of tools to smoothly perform CAE in design work (Meshing Technology, Filleting Technology)
- 1998 Participated in VCALS: Lead part of the concept design of Digital Engineering Collaboration. Lead some commercialization plans
- 2001 Proposed participation in a government demonstration project in the public sector. Appointed as a Solution Specialist. 20M$ level Business Contribution (2001)
- 2002 – 2006 Pervasive Computing Business Development. Focused on mobile solutions. Lead the planning, drafting, and construction of the OWDS function of the previous generation Hakozaki mobile phone system (lead the collaboration with KDDI).
- 2006 – 2009 Participated in business development at Yamato Research Institute. Lead the establishment and operation of Gold Client Program, Japan Business Solution Center Through these programs, contributed to business development of technology solutions.
- 2010 –2020 I achieved great results in the field of research and development, including research and development of production technology, software development and planning, launching e-Japan solutions, launching and operating customer centers at research laboratories, and AI education. I was involved in program planning and management, promotion of collaborative programs with universities, and support for launching quantum computing. In addition, we provided support for the launch of a healthcare business in Japan (support for the launch of Watson Health), promoted data science and AI business in this area, and furthermore, in 2019, established the Keio University KGRI IoT Health and Life Research Consortium. I also contributed to the increase. In addition, I collaborated with the Department of Surgery, Keio University School of Medicine, and provided support for cancer genome information infrastructure. I retired from IBM Japan on December 31, 2020

Summary @ KEIO:

- From 2012 to 2020, while working at IBM Japan, I worked for KEIO Leading Graduate School Program (all-round type) as a project professor and visiting professor. I provided educational guidance by

conducting interactive research with students on issues in various fields and summarizing their solutions as the form of policy recommendations.

- In January 2021, I started working for the AI Consortium (AIC), and in April of the same year, I became the director of the AIC Coordinator Office as project professor. I was responsible for managing AIC's operations, and an education course of "Introduction to AI Healthcare and Medical Care." I established a course and held 10 classes every half term. Among these activities, it is also active as a medical science and engineering collaborative course. Additionally, AIC will also be holding a seminar on quantum computing.
- I am also continuing the collaboration between the School of Medicine's Department of Surgery and IBM Japan that began in 2019, supporting ontology research regarding the side effects of medication.

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards

- 12/12/1995 Robotics Society of Japan Technical Paper Award

b) Member of a scholarly academy in a major country

IEEE, IEICE, IPSJ, RSJ

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field

None

d) Editor of an international academic journal

- 1992 IEEE International Conf. Reviewer, Session Chair, etc.
- 1992-94 Robotics Society of Japan: Councilor, Editorial Committee member
- 07-12/1996 IROFA FA Open Promotion Council member (FA Open Vision, etc.)

e) Peer reviewer for an overseas competitive research program (etc.)

- 1994-1999 Consortium Open System Environment for Controller

(2) Receipt of major large-scale competitive funds (over the past 5 years)

None (over the past 5 years)

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

<<Academic papers>>

- "Target object position estimation method using shape information for video tracking system," Information Processing Society of Japan Transactions, Vol. 26, No. 3, pp. 399-406, 05/1985
- "A visual system for automatic guided vehicles using white line recognition," Transactions of the Institute of Electronics and Communication Engineers, Vol.J68-D, No.4, pp.580-590, 04/1985
- "An Obstacle Detection Method for Visual Guidance for Automated Guided Vehicles," Journal of the Institute of Electronics and Communication Engineers, Vol.J68-D, No.10, pp.1789-1791, 10/1985
- "Visual Navigation for Autonomous Vehicle Using White Line Recognition," IEEE Trans. on Pattern Analysis & Machine Intelligence, Vol.10, No.5, pp.743-749, 09/1988
- "A method for monitoring the driving environment and avoiding obstacles in automatic guided vehicles using white line recognition," Journal of the Information Processing Society of Japan, Vol.30, No.9, pp.1248-1257, 9/1989
- "Study of guidance method for autonomous mobile robot using fuzzy control," Robotics Society Original Papers, Vol.9, No.2, pp149-161, 04/1991
- "A Method of Autonomous Mobile Robot by Using Fuzzy Control," Advanced Robotics, Vol.9, No.1, pp.29-52, 04/1992
- "Travel guidance method for an autonomous mobile robot in a dynamically changing driving environment including moving obstacles," academic paper in the Journal of the Robotics Society
- "Behavior control of autonomous mobile robots in dynamic environments," Robotics Society

Technical Papers, June 1986

<< International Conference >>
- "A Method of Estimating the Target Position for an Image Tracking System of Moving Targets," Proc. of IEEE 7th International Conference on Pattern Recognition, Montreal, Canada, pp. 9-12
- "A Method of Image Guided Vehicle Using White Line Recognition," Proc. IEEE Computer Society Conf. on Computer Vision and Pattern Recognition, pp.47-52, Miami Beach, Florida, USA, Nov 1991
- "A Method of Indoor Mobile Robot Navigation by Using Fuzzy Control," Proc. of IEEE International Workshop on Intelligent Robots and Systems, pp.1013-1018, Osaka, Japan, Dec 1986

<< Technical report meeting >>
- "Report on Computer Vision & Pattern Recognition (CVPR) '85," IEICE Technical Research Report, Vol. PRU86-80, No.288, pp.75-86, Sep 1988
- "Object processing method in the interactive compound document processing system MOE," IEICE technical research report, Data Engineering, Vol.88, No.170, pp.9-15, Oct 1986

<< Presentation at the national conference of the academic society >>
- "A study on visual guidance of automatic guided vehicles using white line recognition," Information Processing Society of Japan 33rd National Conference, pp.2059-2060, Mar 1987
- "Traveling distance detection method in visual guidance using white circular grid points for automatic guided vehicles," IEICE 70th Anniversary National Conference Vol. 6, pp. 240, Sep 1987
- "Image halftone representation using pyramid error diffusion method," Information Processing Society of Japan 35th National Conference, pp1979-1980, Sep 1987
- "A method of obstacle avoidance in visual guidance of automatic guided vehicles using white line recognition," Information Processing Society of Japan 35th National Conference, pp2059-2060, Sep 1988
- "Automated guided vehicle for driving in factories," Information Processing Society of Japan 37th National Conference, pp1623-1624, Sep 1988
- "Handling of compound documents in the compound document processing system MOE", Information Processing Society of Japan 37th National Conference, pp1859-1860, Nov 1990
- "Study of guidance method for autonomous mobile robot using fuzzy control," 8th Annual Conference of the Robotics Society of Japan, Nov 1991
- "Study of guidance method for autonomous mobile robot using fuzzy control - No.2 -," 9th Academic Conference of the Robotics Society of Japan pp.925-926, Nov 1991
- "Software configuration for state transition type programming of autonomous mobile robots," 9th Annual Conference of the Robotics Society, pp.923-924, Nov 1991
- "Integration of different types of sensors based on hypothesis and verification for obstacle avoidance in mobile robots," 9th Robotics Society Academic Conference, pp.545-546, May 1992
- "Study of autonomous mobile robot travel guidance in dynamic travel environments, Robotics Society of Japan, 6th Intelligent Mobile Robot Symposium, pp.135-140, Nov 1992
- "Study on evaluation of moving obstacle avoidance performance of autonomous mobile robots," 10th Academic Conference of the Robotics Society, pp.101-102, Nov 1992
- "Traveling route information guidance method for autonomous mobile robots," 10th Robotics Society Academic Conference pp.931-932, Nov 1992

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

- 04/01/2008-03/31/2009 Part-time lecturer at Graduate School, Sangyo-Noritsu University

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) Takanori Kanai (63)

Affiliation and position (Position title, department, organization, etc.)

Dean, Keio University School of Medicine

Professor and Chairman, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine

Academic degree and specialty M.D., Ph.D. Gastroenterology and Hepatology

Effort **80 %**

* Percentage of time that the principal investigator devote to working for the center vis-à-vis his/her total working hours.

Research and education history

EMPLOYMENT:

1989-1998 Instructor of Medicine, Keio University School of Medicine

1998-2000 Instructor of Medicine, Keio Cancer Center

2000- Instructor of Medicine, Tokyo Medical and Dental University

2003- Assistant Professor of Medicine, Tokyo Medical and Dental University

2005- Committee of Hovard Medical Institute Educational Program, TMDU

2006- Inflammatory Bowel Diseases. Section Editor

2007- Associate Professor of Medicine, Keio University School of Medicine

2008- Clinical Professor of Medicine (Visiting), Tokyo Medical and Dental University

2009- J Gastroenterology, Associate Editor

2011- Am J Physiol Gastrointest & Liver Physiol, Editorial Board member

2013- Professor of Medicine, Keio University School of Medicine

2017- Vice Dean, Keio University School of Medicine

2021- Dean, Keio University School of Medicine

2022- Director, Japan Medical Specialist Organization, General Incorporated Association

2023- Chair, Keio University Graduate School of Medicine

2023- 26th Affiliated member of Science Council of Japan

EDUCATION:

1982-1988 BSc, Keio University School of Medicine

1988-1992 Admitted to Keio University Graduate School of Medicine

1994 Ph.D in Medicine. Keio University School of Medicine

Achievements and highlights of past research activities

Summary: I have focused on elucidating the pathophysiology of inflammatory bowel disease (IBD), gut microbiota, and immune system interactions. My research has provided new insights into how gut microbiota influence immune regulation and disease mechanisms. In addition, I have advanced studies in neuroimmunology and gut immunity. At Keio University Hospital, I am dedicated to advancing both the clinical care and research in IBD and related diseases.

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards

2001 10th International Congress of Mucosal Immunology; Young Investigator Award
2004 The American Physiology Society Symposium; Travel Awards
2008 Kitasato-Kitajima Memorial Science Award
2009 Keio Science Promotion Award
2015 Yakult BioScience Research Foundation Research Grant Award
2020 Japanese Society of Immunology Human Immunology Research Award
2021 Japanese Society of Gastroenterology Academic Award
2023 Clarivate Highly Cited Researcher 2023
2024 Clarivate Highly Cited Researcher 2024

b) Member of a scholarly academy in a major country

The Science Council of Japan, Associate Member

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field

Asian Society of Inflammatory Bowel Disease, Director and Ex-President
Japanese Society of Gastrointestinal Immunology, President
Japanese Society of Internal Medicine, Japanese Society of Gastroenterology, Vice-chairman
Japanese Society of Inflammatory Bowel Disease, Director
Japanese Society of Coloproctology, Director
Japanese Society of Colon Testing, Director
Japanese Society of Sterile Materials Note Biology, Director

d) Editor of an international academic journal

The Keio Journal of Medicine, Honorary Editor
JMA journal, Editor

e) Peer reviewer for an overseas competitive research program (etc.)

Nature Communications, Intestinal Research, Journal of Gastroenterology, Clinical Journal of Gastroenterology, Digestion, JMA Journal

(2) Receipt of major large-scale competitive funds (over the past 5 years)

Japan Agency for Medical Research and Development (AMED)-CREST 16gm1010003h0001
Japan Agency for Medical Research and Development (AMED)-CREST JP21gm1510002
Japan Society for the Promotion of Science (JSPS) KAKENHI Grant-in-Aid (A) 20H00536
Japan Society for the Promotion of Science (JSPS) KAKENHI Grant-in-Aid (A) 23H00425
Takeda Science Foundation

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

1. Ichikawa M, Nakamoto N, Kredo-Russo S, Weinstock E, Weiner IN, Khabra E, Ben-Ishai N, Inbar D, Kowalsman N, Mordoch R, Nicenboim J, Golembo M, Zak N, Jablonska J, Sberro-Livnat H, Navok S, Buchshtab N, Suzuki T, Miyamoto K, Teratani T, Fujimori S, Aoto Y, Konda M, Hayashi N, Chu PS, Taniki N, Morikawa R, Kasuga R, Tabuchi T, Sugimoto S, Mikami Y, Shiota A, Bassan M, Kanai T. Bacteriophage therapy against pathological Klebsiella pneumoniae ameliorates the course of primary sclerosing cholangitis ***Nat Commun.*** 2023 Jun 5;14(1):3261. doi: 10.1038/s41467-023-39029-9. [52 citations]
2. Namkoong H, et al. (co-author) DOCK2 is involved in the host genetics and biology of severe COVID-19. ***Nature*** 2022; 609(7928): 754–760.Published online 2022 Aug 8. doi: 10.1038/s41586-022-05163-5 [76 citations]
3. Sugimoto S, Kobayashi E, Fujii M, Ohta Y, Arai K, Matano M, Ishikawa K, Miyamoto K, Toshimitsu K, Takahashi S, Nanki K, Hakamata Y, Kanai T, Sato T. An organoid-based organ-repurposing approach to treat short bowel syndrome. ***Nature***. 2021 Apr;592(7852):99-104. doi: 10.1038/s41586-021-03247-2. Epub 2021 Feb 24. PMID: 33627870 [168 citations]
4. Koda Y, Teratani T, Chu PS, Hagihara Y, Mikami Y, Harada Y, Tsujikawa H, Miyamoto K, Suzuki T, Taniki N, Sujino T, Sakamoto M, Kanai T, Nakamoto N. CD8+ tissue-resident memory T cells promote liver fibrosis resolution by inducing apoptosis of hepatic stellate cells. ***Nature Communications*** 2021 Jul 22;12(1):4474. doi: 10.1038/s41467-021-24734-0.PMID: 34294714 [158 citations]
5. Teratani T, Mikami Y, Nakamoto N, Suzuki S ,Harada, Okabayashi K, Hagihara Y, Taniki N, Kohno K, Sibata S, Miyamoto K, Ishigame H, Chu P, Sujino S, Suda W, Hattori M, Matsui M, Okada T, Okano H, Inoue M, Yada T, Kitagawa Y, Yoshimura A, Tanida M, Tsuda M, Iwasaki Y, Kanai T. The liver-brain-gut neural arc maintains the regulatory T cell niche in the gut. ***Nature*** 585; 891-6, 2020a. doi: 10.1038/s41586-020-2425-3. Epub 2020 Jun 11. PMID: 32526765 [197 citations]

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

None

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) Kazuyoshi Ishigaki (44)

Affiliation and position (Position title, department, organization, etc.)

- Professor, Keio University Bio2Q
- Professor, Department of Microbiology and Immunology, Keio University School of Medicine
- Team Leader, Laboratory for Human Immunogenetics, RIKEN Center for Integrative Medical Sciences

Academic degree and specialty M.D., Ph.D. Genetics, Immunology

Effort **80 %**

* Percentage of time that the principal investigator devote to working for the center vis-à-vis his/her total working hours.

Research and education history

RESEARCH EXPERIENCE

2024-present Professor, Department of Microbiology and Immunology, Keio University School of Medicine

2021-present Team Leader, Laboratory for Human Immunogenetics
RIKEN Center for Integrative Medical Sciences, Yokohama, Japan

2018-2021 Postdoctoral Researcher, The Raychaudhuri Lab
Harvard Medical School, Brigham And Women's Hospital, Department of Medicine, Division of Genetics, Boston, USA.
Broad Institute, Cambridge, USA

2016-2018 Postdoctoral Researcher, Laboratory for Statistical Analysis,
RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
Principal Investigator: Yoichiro Kamatani, M.D., Ph.D.

2014-2016 Postdoctoral Researcher, Laboratory for Autoimmune Diseases,
RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
Principal Investigator: Kazuhiko Yamamoto, M.D., Ph.D.

EDUCATION

2014 Ph.D., Allergy and Rheumatology, The University of Tokyo, Tokyo, Japan
Principal Investigator: Keishi Fujio, M.D., Ph.D.

2005 M.D., The University of Tokyo, Tokyo, Japan

2004 Clinical Externship, Ohio State University Hospital, Columbus, Ohio

Achievements and highlights of past research activities

While traditional immunology has advanced through animal models, understanding the fundamental causes and individual variability of human autoimmune diseases requires integrating human immunology and genetics. To address this, I am conducting multifaceted research to elucidate the immunological mechanisms of risk polymorphisms in autoimmune diseases leveraging multi-omics data and genome-editing technology.

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards: None
b) Member of a scholarly academy in a major country: American Society of Human Genetics
c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field: None
d) Editor of an international academic journal: None
e) Peer reviewer for an overseas competitive research program (etc.): None

(2) Receipt of major large-scale competitive funds (over the past 5 years)

[Grant received as a PI]

- Technological development for evaluating the impact of polygenic risk scores on the human body (AMED; total budget = 123.5 million yen)
- Elucidation of the Pathogenesis of Rheumatoid Arthritis Using Risk Polymorphism Functional Analysis in Combination with Genome Editing Technology (AMED; total budget = 62.4 million yen)
- Exploration of novel diagnostic markers for autoimmune diseases based on T-cell receptor analysis (AMED; total budget = 91 million yen)
- Establishment of personalized anti-cytokine therapy through functional analysis of risk polymorphisms in autoimmune diseases (JSPS Grant in Aid for Scientific Research B; total budget = 16.2 million yen)
- Identification of master regulatory factors related to disease onset and development of experimental screening methods for inhibitors of their recruitment (Takeda Pharmaceutical Company Limited, COCKPI-T Funding; 8 million yen)
- Development of an algorithm for predicting the severity of a disease using genomic information (The Uehara Memorial Foundation; total budget = 5 million yen)

[Grant received as a co-PI]

- Elucidation of Immune System Mechanisms Underlying Centenarian Dynamic Resilience (Wellcome Leap Solicitation for Dynamic Resilience; total budget = $420,000)
- Support organization for establishing and supporting human immune evaluation methods centered on multi-omics related to genetic diversity and function (AMED; total budget = 75 million yen)

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

[Publication as a first author]

- Multi-ancestry genome-wide association analyses identify novel genetic mechanisms in rheumatoid arthritis (2022, *Nature Genetics*, 226 citations)
- HLA autoimmune risk alleles restrict the hypervariable region of T cell receptors (2022, *Nature Genetics*, 78 citations)
- Improving the trans-ancestry portability of polygenic risk scores by prioritizing variants in predicted cell-type-specific regulatory elements (2020, *Nature Genetics*, 176 citations)
- Large-scale genome-wide association study in a Japanese population identifies novel susceptibility loci across different diseases (2020, *Nature Genetics*, 469 citations).
- Polygenic burdens on cell-specific pathways underlie the risk of rheumatoid arthritis (2017, *Nature Genetics*, 155 citations)

[Publication as a corresponding author]

- Repertoire analyses reveal TCR sequence features that influence T cell fate (2022, *Nature Immunology*, 60 citations).
- Distinct transcriptome architectures underlying lupus establishment and exacerbation (2022, *Cell*, 72 citations)

[Publication as a co-author]

- Single-cell eQTL models reveal dynamic T cell state dependence of disease loci. (2022, *Nature*, 137 citations)
- Multimodally profiling memory T cells from a tuberculosis cohort identifies cell state associations with demographics, environment and disease (2021, *Nature Immunology*, 76 citations)
- Chromosomal alterations among age-related haematopoietic clones in Japan (2020, *Nature*, 144 citations)
- Dynamic landscape of immune cell-specific gene regulation in immune-mediated diseases (2021, *Cell*, 236 citations).
- Mobile element variation contributes to population-specific genome diversification, gene regulation and disease risk (2023, *Nature Genetics,* 27 citations).

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

None

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) Daniel Richard Mende (40)

Affiliation and position (Position title, department, organization, etc.)

Project Professor, Keio University Bio2Q

Academic degree and specialty Ph.D. Microbiome, Metagenomics, Computational Biology

Effort **100 %**

* Percentage of time that the principal investigator devote to working for the center vis-à-vis his/her total working hours.

Research and education history

RESEARCH

Keio University Center Tokyo, Japan
Bio2Q Project Professor 2024 - present

Amsterdam University Medical Center Amsterdam, The Netherlands
Assistant Professor 2019 - 2024

University of Hawai'i at Mānoa Honolulu, USA
Postdoctoral Scholar, Advisor: Edward F. DeLong 2014 - 2019

European Molecular Biology Laboratory (EMBL) Heidelberg, Germany
Postdoctoral Fellow, Advisor: Peer Bork 2013 - 2014

EDUCATION

European Molecular Biology Laboratory (EMBL) Heidelberg, Germany
Ph.D., *summa cum laude*, Biological Sciences 2009-2013
Joint Degree with the University of Heidelberg (Germany)

Achievements and highlights of past research activities

The main focus of my scientific career has been the advancement of our understanding of the human microbiome and microbial communities in general through innovative computational and metagenomic approaches. During my doctoral studies, I developed novel methods to characterize microbial ecosystems, particularly the human gut microbiome and co-authored multiple highly influential publications establishing a framework for understanding the structure and function of the human microbiome. Most recently, my research group published on the microbial dynamics in the infant gut microbiome, showing how nutrition and milk glycan-metabolic potential drive bacterial subspecies development using deep functional annotation of metagenome assembled genomes. Further, I am a core developer for both the mOTUs tool for taxonomically profiling microbial communities and the proGenomes database which provides nearly one million consistently annotated prokaryotic genomes with detailed and rich functional annotations. My

international research impact is reflected in my Clarivate Highly Cited Researcher status (2022-24).

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards: None

b) Member of a scholarly academy in a major country: None

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field: None

d) Editor of an international academic journal: None

e) Peer reviewer for an overseas competitive research program (etc.):

Peer reviewer for ERC and SNF

(2) Receipt of major large-scale competitive funds (over the past 5 years)

NWA-ORC METAHEALTH (Netherlands) – 9M Euro overall	2022
HealthHolland Track-AMR (Netherlands) – 186k Euro	2023
NWO-XL PhyVir – 3M Euro overall (rejected due to move to Japan)	2024

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

(Shared first authorship denoted by *, corresponding authorships by **#**)

proGenomes3: approaching one million accurately and consistently annotated high-quality prokaryotic genomes
Fullam A, et al. **Nucleic Acids Research**, 2023 **#**. 36 Citations

Microbial abundance, activity and population genomic profiling with mOTUs2
Milanese A*, **Mende DR***, et al. **Nature Communications**, 2019. 446 Citations

Metagenomic DNA sequencing for semi-quantitative pathogen detection from urine: a prospective clinical laboratory-based proof-of-concept study
Janes VA, et al. **The Lancet Microbe**, 2022 **#.** 18 citations

Accurate and universal delineation of prokaryotic species
Mende DR, et al. **Nature Methods**, 2013. 339 Citations

Enterotypes of the human gut microbiome
Arumugam M, Raes J, et al. **Nature**, 2011. 8823 citations

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

Clarivate Highly Cited Researcher 2022-2024

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) Nadinath Navaratne Mudiyanselage Bandara Nillegoda (46)

Affiliation and position (Position title, department, organization, etc.)

Professor, Keio University Bio2Q

Academic degree and specialty Ph.D. Proteostasis, Cell/tissue Repair, Protein Quality Control, Protein Disaggregation, Molecular Chaperones

Effort **100 %**

* Percentage of time that the principal investigator devote to working for the center vis-à-vis his/her total working hours.

Research and education history

Ph.D. in Biomedical Sciences, Mount Sinai School of Medicine of New York University, New York, USA (2005-2010)
B.A. in Zoology (Major: Genetics; Minors: Chemistry and Microbiology), Ohio Wesleyan University, Ohio, USA (2000-2004)

Academic & Professional Positions

Principal Investigator/ Project Professor, Human Biology Microbiome Quantum Research Center (Bio2Q), Keio University, Tokyo, Japan (2025-present)
Senior Research Fellow, National Health and Medical Research Council (NHMRC), Australia (2021-2024)
Group Leader/ Senior Research Fellow, Australian Regenerative Medicine Institute and Center for Dementia and Brain Repair, Monash University, Clayton, Australia (2018-2024)
Honorary Senior Research Fellow, The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia (2019-2023)
Project Leader, German Cancer Research Center (DKFZ) and Center for Molecular Biology (ZMBH) Alliance, Heidelberg University, Heidelberg, Germany (2015-2018)
Alexander von Humboldt Postdoctoral Fellowship, The Alexander von Humboldt Foundation, Bonn and Heidelberg University, Heidelberg, Germany (2012-2014)
Postdoctoral Fellowship, Center for Molecular Biology (ZMBH), Heidelberg University, Heidelberg, Germany (2011-2015)
Adjunct Lecturer. Dept. of Microbiology, City University of New York, New York, USA (2009)

Achievements and highlights of past research activities

In brief, since 2011, I have led pioneering research into how multicellular animals disassemble toxic protein aggregates, a key aspect of cellular protein quality control. Conducted at institutions including Heidelberg University, the German Cancer Research Center, and Monash University, this work has significantly advanced our understanding of protein disaggregation mechanisms that are not only essential for cellular recovery following protein damage but are also increasingly recognized as critical modulators in diseases linked to protein aggregation, such as neurodegenerative disorders, metabolic conditions, and cancer.

My team (including collaborators) employ a multidisciplinary approach which includes methods in biochemistry, cell and molecular biology, evolutionary biology, mouse modeling, to machine learning solve fundamental questions in proteostasis. A few highlights are as follows: Using biochemical and biophysical approaches, we have identified a new class of chaperone-based disaggregases comprising of metazoan Hsp70, its nucleotide exchange factor Hsp110, and two classes of J-domain proteins (JDPs) that complex to scaffold the formation of protein disaggregases on aggregates after protein damage [Nillegoda et al., Nature, 2015; Nillegoda et al., eLIFE 2017; Kirstein et al., Aging Cell, 2017]. This disaggregase system not only disaggregates amorphous protein aggregates but also targets disease-associated amyloid fibrils, including α-synuclein aggregates implicated in neurodegenerative diseases [Gao et al., Mol Cell, 2015; Wentink et al., Nature, 2020; Faust et al., Nature, 2020]. This work has also provided the first in vivo

evidence of Hsp70 disaggregase activity, showing its crucial role in thermotolerance, reproductive success, and lifespan recovery in C. elegans [Kirstein et al., Aging Cell, 2017]. Another key research direction in my lab focuses on the JDP chaperone family, the largest and most functionally diverse class of molecular chaperones in mammals. These proteins are increasingly implicated in a wide range of human diseases. Our work has uncovered several regulatory mechanisms that JDPs employ to modulate their activity and integrate into the broader proteostasis network [Malinverni, PNAS, 2023; Kalidindi et al., In Review @ Nat Comm; Zhang et al., Trends in Cell Biol, 2023]. These findings are shedding light on how individual JDPs contribute to cellular protein quality control and how their dysregulation may lead to disease. My authority in these fields is demonstrated through several key invited reviews published in leading journals, including Nature Reviews Molecular Cell Biology [Rosenzweig, Nillegoda et al., 2019, equal contribution], Trends in Biochemical Sciences [Nillegoda et al., 2018], and Trends in Cell Biology [Zhang et al., 2023]. I have delivered 46+ invited or selected talks at major universities and international conferences, underscoring my international reputation and recognized expertise in the metazoan protein disaggregation field and the J-domain chaperone family. My leadership is further reflected through competitive grant success and by organizing a major proteostasis-focused scientific conference.

Building on this foundation, my recent research focuses on the evolutionary adaptations of proteostasis in primates. My team has uncovered a novel, largely primate-specific mechanism for disaggregase formation, termed the stress-induced disaggregase assembly pathway (siDAP). This acetylation-driven pathway dramatically enhances aggregate clearance and cellular recovery following proteotoxic stress, compared to less effective systems in non-primates. This marks the first identification of (a) a dedicated cellular pathway for disaggregase assembly, and (b) a largely primate-specific adaptation within proteostasis networks. At Bio2Q, I have initiated a new research direction aimed at exploring how these evolutionary adaptations in protein disaggregation protect gut barrier integrity following proteotoxic stress caused by dysbiosis. This work has the potential to transform our understanding of gut health and may pave the way for novel therapeutic approaches to treat gut-related diseases.

Achievements

(1) International influence * Describe the kind of attributes listed below.

a) Recipient of international awards None

b) Member of a scholarly academy in a major country

The Alexander von Humboldt Foundation, Bonn, Germany
The Australian Society for Medical Research, Sydney, Australia

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field

- Invited Conference Speaker, 98th Annual meeting of the Japanese Biochemical Society (JBS), Kyoto, Japan (pending Nov, 2025)
- Invited Conference Speaker, 2nd International workshop on J-domain proteins of the Cell Stress Society International (CSSI), Gdansk, Poland (2023)
- Invited Conference Speaker, Protein Aggregation and Proteostasis Symposium at ComBio2020, Melbourne Convention and Exhibition Centre, Melbourne, Australia (2022)
- Invited Conference Speaker, 2nd Virtual International Congress on Cellular and Organismal Stress Responses of the Cell Stress Society International (CSSI), USA (2022)
- Invited Conference Speaker, 16th Federation of Asian and Oceanian Biochemists and Molecular Biologists Congress, Christchurch, New Zealand (2021)
- Conference Speaker, 46th Lorne Conference on Protein Structure and Function. Lorne, Australia (2021)
- Invited Conference Speaker, 4th Proteostasis and Disease Symposium, Wollongong, Australia (2020)
- Invited Conference Speaker, International workshop on J-domain proteins of the Cell Stress Society International (CSSI). Gdansk, Poland (2018)
- Conference Speaker, Gordon Conference on Stress Proteins in Growth, Development & Disease. ME, USA (2017)
- Plenary Speaker, 9th International Research Conference. General Sir John Kotelawala Defense University,

Ratmalana, Sri Lanka (2017)
- Keynote Speaker, The Annual Dutch Huntington Disease Meeting. University of Groningen, Groningen, The Netherlands (2015)
- Opening Ceremony Featured Speaker, 60th Annual Meeting of the Alexander von Humboldt Foundation, Berlin, Germany (2013)
- Conference Speaker, The 5th Cold Spring Harbor Meeting on the Ubiquitin Family. Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA (2009)
- Conference Speaker, The 4th International Conference on the Hsp90 Chaperone Machine. Seeon, Germany (2008)

d) Editor of an international academic journal None

e) Peer reviewer for an overseas competitive research program (etc.)

Biotechnology and Biological Sciences Research Council (BBSRC), UK (2022)
National Science Center Poland (NCN), Poland (2021); The Israel Science Foundation (ISF), Israel (2021); Australian Research Council, Australia (2021)

(2) Receipt of major large-scale competitive funds (over the past 5 years)

FAMOUS Grant, Characterization of posttranslational modifications regulating protein disaggregases, FAPESP-Monash Seed Program, Brazil-Australia 2022-2024
NHMRC Equipment Grants (Automatic quantitative locomotion and behavior phenotyping setup for small animals, Synergy H1M Microplate reader) Australia 2021
Investigator Fellowship for Emerging Leadership, Counteracting age-associated neurodegenerative diseases using chaperone-based amyloid disaggregases, NHMRC, Australia 2021-2025
The Yulgilbar Foundation Grant for Alzheimer's disease research, The Yulgilbar Foundation, Australia 2019-2020

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)

Data-driven large-scale genomic analysis reveals an intricate phylogenetic and functional landscape in J-domain proteins. 2023. Proc Natl Acad Sci U S A. [Citations 19]
J-domain protein chaperone circuits in proteostasis and disease. 2023. Trends Cell Biol. [44]
Hidden information on protein function in censuses of proteome foldedness. 2022. Nat Commun. [13]
Molecular dissection of amyloid disaggregation by human HSP70. 2020. Nature. [210]
HSP40 proteins use class-specific regulation to drive HSP70 functional diversity. 2020. Nature. [187].
The Hsp70 chaperone network. 2019. Nat Rev Mol Cell Biol. [1131]
Protein disaggregation in multicellular organisms. 2018. Trends Biochem Sci. [132]
In vivo properties of the disaggregase function of J-proteins and Hsc70 in Caenorhabditis elegans stress and aging. 2017. Aging Cell. [73]
Evolution of an intricate J-protein network driving protein disaggregation in eukaryotes. 2017. eLife. [81]
Hsp70 displaces small heat shock proteins from aggregates to initiate protein refolding. 2017. EMBO J. [176]
Human Hsp70 Disaggregase Reverses Parkinson's-Linked α-Synuclein Amyloid Fibrils. 2015. Mol Cell. [433]
Crucial HSP70 co-chaperone complex unlocks metazoan protein disaggregation. 2015. Nature. [381]
Metazoan Hsp70-based protein disaggregases: emergence and mechanisms. 2015. Front Mol Biosci. [134]
Metazoan Hsp70 machines use Hsp110 to power protein disaggregation. 2012. EMBO J. [351]
A network of ubiquitin ligases is important for the dynamics of misfolded protein aggregates in yeast. 2012. J Biol Chem. [83]
Ubr1 and Ubr2 function in a quality control pathway for degradation of unfolded cytosolic proteins. 2010. Mol Biol Cell. [175]

(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)

Conference Organizer, Cellular and Protein Homeostasis Webinars (Virtual International Conference Series) (2020-2022); Interviewed in mass media: News and Features. SBS (Special Broadcasting Service) Australia (January 28th, 2016); News First, Sirasa TV, MTV Channel Sri Lanka (January 06th, 2016)

Appendix 3-1 FY 2024 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

1-1. Number of researchers in the "core" established within the host institution

- Regarding the number of researchers at the Center, fill in the table in Appendix 3-1a.

Special mention

- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing main researchers, particularly principal investigators.
- As background to how the Center is working on the global circulation of world's best brains, give good examples, if any, of how career paths are being established for the Center's researchers; that is, from which top-world research institutions do researchers come to the Center and to which research institutions do the Center's researchers go, and how long are their stays at those institutions.

One international Postdoctoral Fellow and a Director of Research Programs are expected to start working at the Center in FY2025.
Career paths for young researchers from satellite institutions: A researcher from Columbia University, former postdoctoral researcher in the lab of International Collaborator Ivaylo Ivanov, was appointed as a new international Jr PI and is expected to start activities in the Shinanomachi Campus in the first quarter of FY2025.
Training programs: The exchange/training program with MRC-LMB has already started with technical staff. Training programs will be extended to postdoctoral researchers and students in International Collaborator laboratories.

1-2. Satellites and partner institutions

- List the satellite and partner institutions in the table below.
- Indicate newly added and deleted institutions in the "Notes" column.
- If satellite institutions have been established overseas, describe by satellite the Center's achievements in coauthored papers and researcher exchanges in Appendix 4.

<Satellite institutions>

Institution name	Principal Investigator(s), if any	Notes
N/A		

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
The Medical Research Council Laboratory of Molecular Biology (MRC-LMB)	Radu Aricescu	
Harvard Medical School	Jun Huh	
National University of Singapore	George Augustine	
The Central Institute for Experimental Medicine and Life Science	Erika Sasaki Makoto Suematsu	

1-3. Postdoctoral Positions through Open International Solicitations

- In the columns "number of applications" and "number of selections," put the total number (upper) and the number and percentage of overseas researchers in the < > brackets (lower).

Fiscal year	Number of applications	Number of selections
FY 2024	10	5
	〈 9, 90%〉	〈 4, 80%〉

2. Holding international research meetings

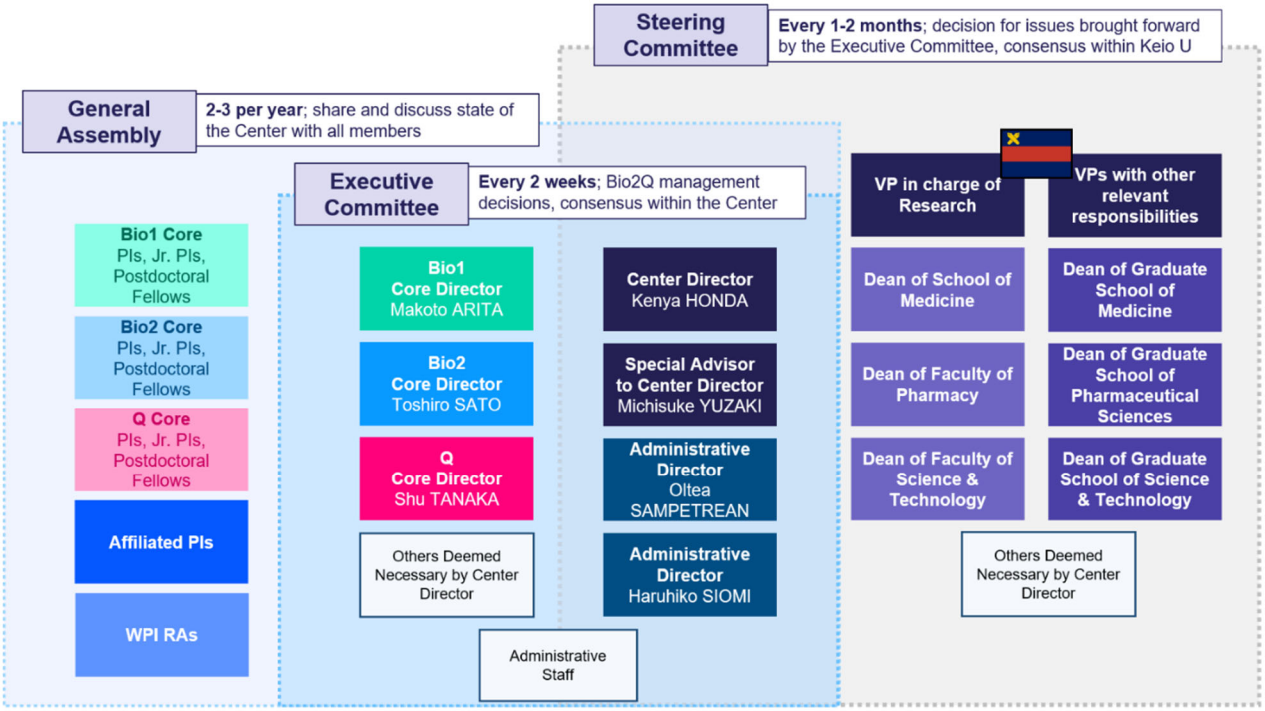
- Indicate the number of international research conferences or symposiums held in FY2024 and give up to three examples of the most representative ones using the table below.

FY 2024: 2 meetings

Major examples (meeting titles and places held)	Number of participants
-The 3rd Keio University WPI-Bio2Q International Symposium, Tokyo, Japan, Mar. 2025 (https://bio2q.keio.ac.jp/news/wpi-bio2q-third-symposium-report/)	From domestic institutions: 156 From overseas institutions: 42
-Welcomed 40 young scientists attending this year's HOPE meeting, Tokyo, Japan, Mar. 2025	From domestic institutions: 3 From overseas institutions: 40

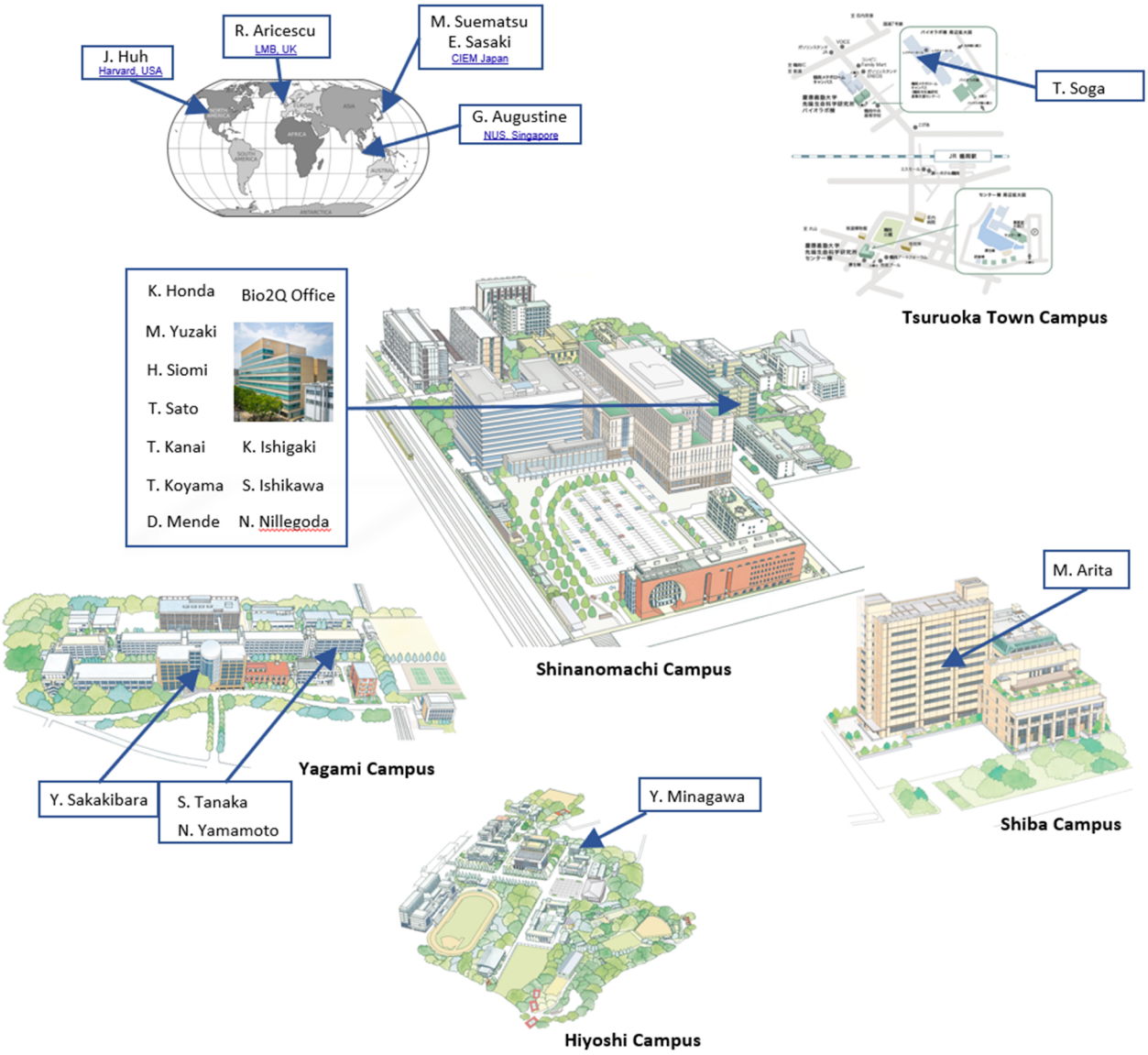
3. Diagram of management system

- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such as the center director, administrative director, head of host institution, and officer(s) in charge at the host institution (e.g., executive vice president for research).



4. Campus Map

- Draw a simple map of the campus showing where the main office and principal investigator(s) are located.



5. Securing external research funding*

External research funding secured in FY2024
Total: 2,013,314,454 yen

- Describe external funding warranting special mention. Include the name and total amount of each grant.
* External research funding includes "KAKENHI," funding for "commissioned research projects," "joint research projects," and for others (donations, etc.) as listed under "Research projects" in Appendix 3-2, Project Expenditures.

Organization	Fund name	Name	Period	Funding amount (Allowable amount)	Funding amount (FY2024)
AMED	Moonshot Research and Development Program	Kenya Honda Atsushi Shiota Makoto Arita Michisuke Yuzaki Makoto Suematsu Erika Sasaki Oltea Sampetrean Kaoru Leong Hida Koji Atarashi Timur Tuganbaev Yuki Sugiura Takako Hishiki Vinodh J Sahayasheela Huizhuo Pan Haowei Li Jun-Ren Dong Satoshi Morozumi Kota Ogasa Mari Shiozaki So Takasugi Mitsuhiro Oishi	2022-2027	Total 1,233,030,500 yen	181,265,500 yen
AMED	Project Focused on Developing Key Technology for Discovering and Manufacturing Drugs for Next-Generation Treatment and Diagnosis	Kenya Honda Atsushi Shiota Koji Atarashi Oltea Sampetrean Timur Tuganbaev Kaoru Leong Hida Huizhuo Pan Vinodh J Sahayasheela	2021-2026	Total 1,498,771,400 yen	440,000,000 yen
JST	ERATO	Toshiro Sato Takako Hishiki	2023-2028	Total 1,707,460,000 yen	440,990,000 yen
KAKENHI	Specially Promoted Research	Kenya Honda	2020-2025	Total 650,000,000 yen	104,000,000 yen
JST	ERATO	Makoto Arita	2021-2026	Total 547,730,000 yen	52,330,000 yen
JST	Moonshot Research and Development Program	Toshiro Sato	2020-2025	Total 308,652,500 yen	83,423,600 yen
NEDO	Development of Quantum/ AI Hybrid Use-Case Technologies in Cyber-Physical Space	Shu Tanaka	2023-2024	Total 68,599,000 yen	28,600,000 yen

Appendix 3-1a FY 2024 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

* Fill in the number of researchers and other center staff in the table blow.
* Describe the final goals for achieving these numbers and dates when they will be achieved described in the last "center project."

a) Principal Investigators

(full professors, associate professors or other researchers of comparable standing)

(number of persons)

	At the beginning of project	At the end of FY 2024	Final goal (Date: March, 2025)
Researchers from within the host institution	10	14	11
Researchers invited from overseas	3	5	3
Researchers invited from other Japanese institutions	2	2	2
Total principal investigators	15	21	16

b) Total members

	At the beginning of project		At the end of FY 2024		Final goal (Date: March, 2025)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	33		64		90	
Overseas researchers	13	39	28	44	28	31
Female researchers	8	24	16	25	45	50
Principal investigators	15		21		16	
Overseas PIs	3	20	5	24	3	19
Female PIs	2	13	2	10	2	13
Other researchers	18		37		62	
Overseas researchers	10	56	17	46	19	31
Female researchers	6	33	12	32	36	58
Postdocs	0		6		12	
Overseas postdocs	0	0	6	100	6	50
Female postdocs	0	0	2	33	7	58
Research support staffs	1		6		15	
Administrative staffs	6		14		11	
Total number of people who form the "core" of the research center	40		84		116	

	At the beginning of project		At the end of FY 2024		Final goal (Date: March, 2025)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	0		14		40	
Employed	0	-	13	92.9	40	100.0

※b) The number of doctoral students in the lower table can be duplicated in the upper table of overall composition.

Appendix 3-2 Project Expenditures

1) Overall project funding

* In the "Total costs" column, enter the total amount of funding required to implement the project, without dividing it into funding sources.
* In the "Amount covered by WPI funding" column, enter the amount covered by WPI within the total amount.
* In the "Personnel," "Project activities," "Travel," and "Equipment" blocks, the items of the "Details" column may be changed to coincide with the project's actual content.

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):17	213	53
	Other researchers (no. of persons):12	114	86
	Research support staff (no. of persons):6	30	30
	Administrative staff (no. of persons):9	54	53
	Subtotal	411	222
Project activities	Cost of outreach activity	4	4
	Cost of international symposiums (no. of symposiums):1	3	3
	Cost of Website・SNS	4	4
	Cost of Retreat	2	2
	Research startup cost (no. of persons):3	11	11
	Gratuities and honoraria (no. of persons):18	2	2
	Cost of consumables(Open lab)	36	36
	Other costs	8	6
	Rental fees for facilities	61	0
	Utilities costs	13	0
	Subtotal	144	68
Travel	Domestic travel costs	0	0
	Overseas travel costs	2	2
	Travel and accommodations cost for invited scientists		
	(no. of domestic scientists):11	1	1
	(no. of overseas scientists):17	16	16
	Travel cost for scientists on transfer		
	(no. of domestic scientists):3	0	0
	(no. of overseas scientists):2	1	1
	Subtotal	20	20
Equipment	Facility renovation and improvement	198	198
	Costs of research equipments	516	516
	Research equipment maintenance and repair costs	1	1
	Subtotal	715	715
Research projects (Detail items must be fixed)	KAKENHI	364	
	Commissioned research projects, etc.	1,608	
	Joint research projects	4	
	Ohers (donations, etc.)	37	
	Subtotal	2,013	0
Total		3,303	1,025

Costs (Million yens)

WPI grant in FY 2024	715
Costs of establishing and maintaining facilities	198
Repairing facilities	198
(Number of facilities:4, 1084.6m²)	
Others	0
Costs of equipment procured	516
FIB-SEM microscope	400
Freezers(Number of units:5)	62
Mass Spectrometer(1 set)	13
Others	41
Costs of equipment maintenance and repai	1

*Of the 700 million yen in WPI Grant in FY2023, 400 million yen was carried over to FY2024.

*Of the 700 million yen in WPI Grant in FY2024, 75 million yen is carried over to FY2025.

*1. Management Expenses Grants (including Management Enhancements Promotion Expenses (機能強化経費)), subsidies etc., indirect funding, and allocations from the university's own resources.
*2 When personnel, travel, equipment (etc.) expenses are covered by KAKENHI or under commissioned research projects or joint research projects, the amounts should be entered in the "Research projects" block.

*1 運営費交付金（機能強化経費を含む）、各種補助金、間接経費、その他大学独自の取組による学内リソースの配分等による財源
*2 科研費、受託研究費、共同研究費等によって人件費、旅費、設備備品等費を支出している場合も、その額は「研究プロジェクト費」として計上すること

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):OO		
	Other researchers (no. of persons):OO		
	Research support staff (no. of persons):OO		
	Administrative staff (no. of persons):OO		
	Subtotal	0	0
Project activities	Subtotal		
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal		
Total		0	0

Appendix 4 FY 2024 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2024 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2025 and not described in Appendix 1.

Overseas Satellite 1 **Name** (Total: OO papers)

N/A

Overseas Satellite 2 **Name** (Total: OO papers)

N/A

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2024. Enter by institution and length of exchange.
- Write the number of principal investigator visits in the top of each space and the number of other researchers in the bottom.

Overseas Satellite 1:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024					

Overseas Satellite 2:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024					

Appendix 5 FY 2024 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.
* Enter the host institution name and the center name in the footer.

Total: 21

	Name	Age	Affiliation		Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
			Position title, department, organization	Country				
1	Daniel R. Mende	40	Assistant Professor, Amsterdam University Medical Centers	Netherlands	PhD	Bioinformatics - Understand the microbial communities constituting the human microbiome	4/19-5/9 21 days	Scientific talk at the open seminar Joint research
2	George Augustine	69	Senior Investigator, Temasek Life Sciences, National University of Singapore, Bio2Q PI	Singapore	PhD	Neurobiology	6/4-6/9 6 days	Scientific talk at the open seminar Joint research
3	Harvey Lodish	83	Professor of Biology, MIT	USA	PhD	Lead author, "Molecular Cell Biology" Founder/scientific board member: Genzyme, Millennium Pharmaceuticals, Rubius Therapeutics, Tevard	6/12 1 day	Scientific talk at the open seminar Joint research
4	Nadinath Nillegoda	46	Monash University, and National Health and Medical Research Council (NHMRC)	Australia	PhD	Protein homeostasis and promote cell repair after protein damage. A recipient of the prestigious Alexander von Humboldt Fellowship	6/13-6/22 10 days	Scientific talk at the open seminar Joint research
5	Ramnik Xavier	62	Professor, Department of Molecular Biology, Harvard Medical School, Bio2Q International Collaborator	USA	PhD	Mucosal immunity from microbes	6/25-6/26 2 days	Scientific talk at the open seminar Joint research
6	Cody Cole	29	Committee on Microbiology, University of Chicago	USA	PhD	Microbiology	6/27-7/3 7 days	Scientific talk at the open seminar Joint research
7	Shingo Kajimura	48	Professor of Medicine, Harvard Medical School, Bio2Q International Collaborator	USA	PhD	Host metabolism and microbiota	7/10-7/31 22 days	Scientific talk at the open seminar Joint research
8	Sungwhan Oh		Assistant Professor, Harvard Medical School	USA	PhD	Bioactive metabolites from symbiotic microbiota, Crohn's and Colitis Foundation Research Fellowship Award (2013–2016)	7/19 1 day	Scientific talk at the open seminar Joint research
9	Robert R Jenq	47	Associate Professor, MD Anderson Cancer Center The University of Texas	USA	MD	Intestinal Mucus and Immunity	7/26 1 day	Scientific talk at the open seminar Joint research
10	Kunimichi Suzuki	39	Neuroscience & Structural Biology, MRC Laboratory of Molecular Biology, Bio2Q Jr.PI	UK	PhD	Neuroscience & Structural Biology Seal of Excellence, European Commission Horizon (2020)	7/23-8/29 38 Days	Scientific talk at the open seminar Joint research
11	Scott Behie	45	Senior Scientific Editor, Cell Press	USA	PhD	Scientific Communication, molecular biology, microbiology, and biotechnology	9/1-9/6 6 days	Scientific talk at the open seminar Joint research
12	Gabriel Núñez	70	Professor of Academic Pathology, University of Michigan Medical School	USA	PhD	Immunology, A member of the National Academy of Medicine of the United States.	9/11 1 day	Scientific talk at the open seminar Joint research
13	Sin-Hyeog Im	61	Professor, Life Sciences Pohang University of Science and Technology	Korea	PhD	Microbiome Therapeutics for Inflammatory Disorders and Cancer	10/11 1 day	Scientific talk at the open seminar Joint research

14	Valentin Naegerl		Professor of Neuroscience and Bioimaging, University of Bordeaux	France	PhD	Imaging of brain microanatomy	10/30 1 day	Scientific talk at the open seminar Joint research
15	Jun Huh	51	Associate Professor of Immunology, Harvard Medical School, Bio2Q PI	USA	PhD	Immunology, the NIH Pathway to Independence (PI) Award (2011), and the Smith Family Awards Program for Excellence in Biomedical Research (2013)	11/24-11/25 2 days	Joint research
16	Leonie Brockmann	38	Research Scientist, Systems Biology, Columbia University Medical Center	USA	PhD	Systems Biology, DFG Forschungsstipendium, Issued by DFG, Jan 2019	12/23-1/6 15 days	Scientific talk at the open seminar Joint research
17	Marco Jost	38	Assistant Professor, Microbiology, Harvard Medical School, Bio2Q International Collaborator	USA	PhD	Define the molecular mechanisms of host-microbiome communication using a combination of systematic CRISPR technologies	2/27-3/9 11 days	Participation in the 3rd WPI-Bio2Q International Symposium
18	Ivaylo Ivanov	51	Associate Professor, Microbiology & Immunology Columbia University, Bio2Q International Collaborator	USA	PhD	Immunomodulatory effects of gut microbiota, Crohn's and Colitis Foundation of America Senior Research Award (2013), NIH Pathway to Independence Award (2010)	3/3-3/14 12 days	Participation in the 3rd WPI-Bio2Q International Symposium
19	Alexander Rudensky		Chair, Immunology, Sloan Kettering Institute	USA	PhD	Regulatory T cells in Cancer, Member of the National Academy of Sciences (2012) and American Academy of Arts and Sciences (2015)	3/1-3/10 10 days	Participation in the 3rd WPI-Bio2Q International Symposium
20	Shruti Naik	39	Immunology, Icahn School of Medicine at Mount Sinai, Bio2Q International Collaborator	USA	PhD	Tissue Immunity and Regeneration, NIH Women's Scholars Award, the International Takeda Innovators in Science Award, NIH Director's New Innovator Award	3/5-3/11 7 days	Participation in the 3rd WPI-Bio2Q International Symposium
21	Dan Littman	72	Professor, Molecular Immunology, New York University School of Medicine, Bio2Q International Collaborator	USA	MD, PhD	T-lymphocyte development, William B. Coley Award, Invitrogen Meritorious Career Award of the American Association of Immunologists	3/5-3/11 7 days	Participation in the 3rd WPI-Bio2Q International Symposium

Appendix 6 FY2024 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2024 by each activity.
* Describe the outreach activities in the "3-1. Societal Value of Basic Research" of Progress Report, including those stated below that warrant special mention.

Activities	FY2024 (number of activities, times held)
PR brochure, pamphlet	3 -Bio2Q Makoto Arita, SEP. 2024 (https://bio2q.keio.ac.jp/#digital-downloads) -Bio2Q Toshiro Sato, SEP. 2024 (https://bio2q.keio.ac.jp/#digital-downloads) -Bio2Q Shu Tanaka, APR. 2025 (https://bio2q.keio.ac.jp/#digital-downloads)
Lectures, open scientific seminars and events for the general public	20 -Bio2Q Open Seminar, Daniel Mende, Amsterdam University Medical Center, Netherlands, Apr. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240425-mende-report/) -Bio2Q Open Seminar, Nadinath Nillegoda, Monash University, Australia, Apr. 2024 -Bio2Q Open Seminar, Harvey F. Lodish, Massachusetts Institute of Technology, USA, Jun. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240612-lodish-report/) -Bio2Q Open Seminar, Ramnik Xavier, Harvard Medical School, USA, Jun. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240624-xavier-report/) -Bio2Q Open Seminar, Ashish Joshi, Kyoto University, Japan, Jun. 2024 -Bio2Q Open Seminar, Haowei Li, The University of Tokyo, Japan, Jun. 2024 -Bio2Q Open Seminar, Shingo Kajimura, Harvard Medical School, USA, Jul. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240716-kajimura-report/) -Bio2Q Open Seminar, Sungwhan Oh, Harvard Medical School, USA, Jul. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240719-oh-report/) -Bio2Q Open Seminar, Cody Cole, The University of Chicago, USA, Jun. 2024 -Bio2Q Open Seminar, Robert R Jenq, The University of Texas, MD Anderson Cancer Center, USA, Jul. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240726-jenq-report/) -Bio2Q Open Seminar, Tsutomu Suzuki, Professor, University of Tokyo, Japan, Sep. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240910-suzuki-report/) -Bio2Q Open Seminar, Gabriel Núñez, University of Michigan Medical School, USA, Sep. 2024 (https://bio2q.keio.ac.jp/news/seminar-20240911-nunez-report/) -Bio2Q Open Seminar, Joaquim Caner, Kyoto University, Japan, Sep. 2024 -Bio2Q Open Seminar, Scott Behie, Cell Press, USA, Sep. 2024 -Bio2Q Open Seminar, Sin-Hyeog Im, Pohang University of Science and Technology, Korea, Oct. 2024 (https://bio2q.keio.ac.jp/news/seminar-20241011-im-report/) -Bio2Q Open Seminar, Valentin Nägerl, University of Bordeaux, France, Oct. 2024 (https://bio2q.keio.ac.jp/news/165th-brain-club-seminar-20241030-nagerl-report/) -Bio2Q Open Seminar, Leonie Brockmann, Columbia University, USA, Dec. 2024 -Bio2Q Open Seminar, Wataru Shihoya, The University of Tokyo, Jan. 2025 (https://bio2q.keio.ac.jp/news/seminar-20250130-shihoya/) -The 3rd Keio University WPI-Bio2Q International Symposium, Tokyo, Japan, Mar. 2025 (https://bio2q.keio.ac.jp/news/wpi-bio2q-third-symposium-report/) -Welcomed 40 young scientists attending this year's HOPE meeting, Tokyo, Japan, Mar. 2025
Teaching, experiments, training for elementary, secondary and high school students	1 -13th WPI Science Symposium, Kyoto University, Japan, Nov. 2024 (https://bio2q.keio.ac.jp/news/13th-wpi-science-symposium-report/)
Participating, exhibiting in events	1 -The 18th Metabolome Symposium, Yamagata, Japan, Oct. 2024 (https://bio2q.keio.ac.jp/news/metabolome-symposium-2024/)

SNS	2 -Expand awareness of Bio2Q and ongoing recruiting activities using LinkedIn and X -Launched Bio2Q account page on YouTube, Dec. 2024 (Five posts per month)

*If there are any rows on activities the center didn't implement, delete that (those) row(s). If you have any activities other than the items stated above, fill in the space between parentheses after "Others" on the bottom with the name of those activities and state the numbers of activities and times held in the space on the right. A row of "Others" can be added, if needed.

Outreach Activities and Their Results

List up to three of the Center's outreach activities carried out in FY 2024 that have contributed to enhancing the brand or recognition of your Center and/or the brand of the overall WPI program, and describe its concrete contents and effect in narrative style. (Where possible, indicate the results in concrete numbers.)

Examples:
- As a result of using a new OO press-release method, a OO% increase in media coverage was obtained over the previous year.
- By holding seminars for the public that include people from industry, requests for joint research were received from companies.
- We changed our public relations media. As a resulting of using OO to disseminate information, a OO% increase in inquiries from researchers was obtained over the previous year.
- As a result of vigorously carrying out OO outreach activity, ¥OO in external funding was acquired.

❶The 3rd Keio University WPI-Bio2Q International Symposium, Tokyo, Japan, Mar. 2025
(https://bio2q.keio.ac.jp/news/wpi-bio2q-third-symposium-report/)
The symposium was held exclusively onsite only at the Shinanomachi Campus in Tokyo, on March 6-7, 2025. The symposium featured talks from twelve globally renowned scientists from Harvard University, Columbia University, Sloan Kettering Institute, Icahn School of Medicine at Mount Sinai (USA), Kyoto University, Osaka University WPI- IFREC, and Keio University (Japan). A diverse audience of 198 participants including 75 female researchers and 42 international attendees from 14 countries. The event attracted 78 participants from outside Keio University, 45 from the private sector, and 23 from other academic institutions. Further strengthening connections, the invited speakers remained at the center for up to one week engaging in in-depth discussions and collaborations with individual researchers.

❷Social Media Outreach:
Through our WPI-Bio2Q account on LinkedIn (SNS), we actively shared updates on WPI-Bio2Q activities and job openings while directly engaging with scientists in related research fields. As a result, we built a global network of 1,307 scientists, including students and research professionals. This network played a key role in our digital recruiting efforts, with several members—originally based in Columbia University (USA), Imperial College London (UK), Kyoto University, and Keio University (Japan) —later joining the center through the WPI-Bio2Q Jr. PI, Postdoctoral, Fellowships, and Research Internship Program.

❸In addition, WPI-Bio2Q invited top international scientists from Massachusetts Institute of Technology, Harvard Medical School, University of Texas, University of Michigan Medical School (USA), University of Tokyo (Japan), and Pohang University of Science and Technology (Korea) to hold six open scientific seminars at the Center, facilitating face-to-face knowledge exchange with a broad audience.

Appendix 7 FY 2024 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2024.

* Enter the host institution name and the center name in the footer.

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	27-Sep-24	Keio University Press release	Novel Treatment of Drug-Resistant Bacteria and Inflammatory Bowel Disease Using Intestinal Indigenous Microflora - Suppression of Enterobacteriaceae by Controlling the Intestinal Environment -. (https://www.keio.ac.jp/ja/press-releases/2024/9/27/28-161929/)
2	19-Nov-24	Clarivate's Highly Cited Researchers 2024	Five of our researchers were selected as Clarivate's Highly Cited Researchers 2024, published on November 19, 2024
3			
4			
5			
6			
7			
8			
9			
10			