World Premier International Research Center Initiative (WPI)
FY 2023 WPI Project Progress Report (The center selected in and before FY2020)

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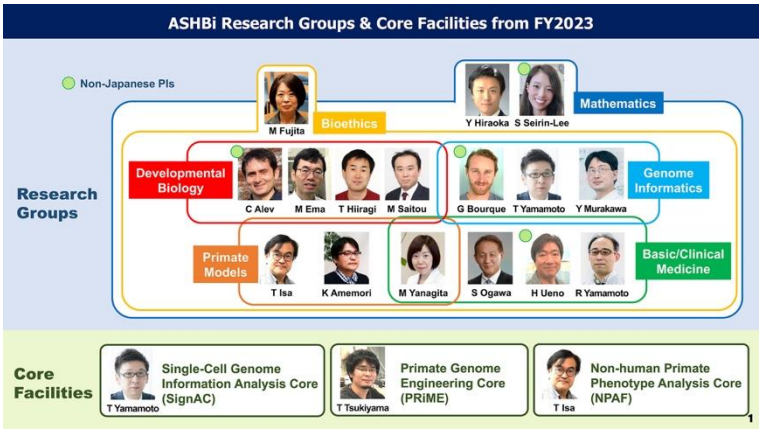
Research Center	Institute for the Advanced Study of Human Biology		
Center Director	SAITOU Mitinori	Administrative Director	OGAWA Tadashi

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2024) 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**)



ASHBi has grown progressively as an institute to investigate the key concepts of human biology. The five focus areas of ASHBi are: **1)** To promote the study of human biology, with a focus on genome regulation; **2)** To clarify the principles defining the species differences and human traits; **3)** To generate primate models for intractable human diseases; **4)** To reconstitute key human cell lineages or tissues *in vitro*, and **5)** To contribute to formalizing an international ethics standard for human biology research. ASHBi consists of 16 PIs and 3 core heads (4 non-Japanese PIs, 3 female PIs, 2 PIs co-appointed as core heads). With his prominent research achievements, **Cantas Alev** was promoted to tenured professor in October 2023. As of April 2024, ASHBi consists of 67 researchers [non-Japanese: 27 (40%); female: 18 (27%)], 91 graduate students [non-Japanese: 27 (30%); female: 28 (31%)], and more than 60 supporting staff. The external funding acquired by ASHBi PIs in FY2023 was more than 1.9 billion yen. The 3 core facilities have run in a productive manner. With its increasing visibility, **Single-Cell Genome Information Analysis Core (SignAC)** has supported more than 100 researchers through collaborative research and analytical services, with the total income in FY2023 of over 130 million yen. To cope with the recent surge in purchase prices of cynomolgus monkeys, **Primate Genome Engineering Core (PRiME)** has begun to breed its own monkeys to ensure a stable supply at a reasonable price (see **1. Advancing Research of the Highest Global Level** and **3. Realizing an International Research Environment**).

During FY2023, ASHBi published 94 papers. The representative papers include: "Embryo-uterine interaction coordinates mouse embryogenesis during implantation: ***EMBO J.***" (**Hiiragi: Focus Areas 2** and **4**), "Induction of fetal meiotic oocytes from embryonic stem cells in cynomolgus monkeys: ***EMBO J.***" (**Saitou, Tsukiyama, T. Yamamoto: Focus Areas 1**, **2**, and **4**), "Transposable elements are associated with the variable response to influenza infection: ***Cell Genom.***" (**Bourque: Focus Area 1**), "Genome graphs detect human polymorphisms in active epigenomic state during influenza infection: ***Cell Genom.***" (**Bourque: Focus Area 1**), "Hypoblast from human pluripotent stem cells regulates epiblast development: ***Nature***" (**T. Yamamoto, Saitou: Focus Areas 1**, **2** and **4**), "Balancing risk-return decisions by manipulating the mesofrontal circuits in primates: ***Science***" (**Isa: Focus Areas 1**, **2**, and **3**), "Spatiotemporal expression patterns

of anxiety disorder-associated genes: ***Transl. Psychiatry***" (**Amemori: Focus Areas 1**, **2**, and **3**), "Deciphering evolutionary histories of breast cancer and related clones: ***Nature***" (**S. Ogawa: Focus Area 1**), "Tertiary lymphoid tissues are microenvironments with intensive interactions between immune cells and proinflammatory parenchymal cells in aged kidneys: ***J. Am. Soc. Nephrol.***" (**Yanagita: Focus Areas 1**), "V-Mapper: topological data analysis for high-dimensional data with velocity: ***NOLTA***" (**Hiraoka: Focus Areas 2**), and "Mathematical-based morphological classification of skin eruptions corresponding to the pathophysiological state of chronic spontaneous urticaria: ***Commun. Med.***" (**Seirin-Lee: Focus Areas 1** and **2**) (see **1. Advancing Research of the Highest Global Level**). In recognitions of their prominent research achievements, **Hiraoka** received **MIMS Mimura Award**, **Yanagita** received **Bywaters Award 2024**, and **S. Ogawa** received the **32nd Tomizo Yoshida Prize**.

In addition to the research activities of individual PIs, ASHBi has continued to perform the 5 Flagship Projects, including fusion studies with mathematics and with bioethics, which represent key research directions of ASHBi. The 5 Flagship Projects are: "**Deconstruction and reconstruction of early primate development**" (**Focus Areas 1**, **2** and **4**), "**Primate-genomics interdisciplinary research for developing new primate models**" (**Focus Areas 1**, **2**, and **3**), "**Age-associated genomic alterations of organ cells and their interplay with the local immune system**" (**Focus Area 1**), "**Establishment of 'data representation theory'**" (**Focus Area 2**), and "**Bioethics at the periphery of birth and death'**" (**Focus Area 5**). The 5 Flagship Projects are conceptually and methodologically interrelated and contribute to addressing our fundamental question of what makes us human in a top-down manner. ASHBi held its 2nd progress meeting on the 5 Flagship Projects with external reviewers in February 2024. The key progress made include the generation of the benchmark datasets for post-implantation development in primates and as described above, a comprehensive analysis of expression profiles of genes associated with anxiety disorders within relevant brain regions (see **2. Generating Fused Disciplines**).

As a bottom-up approach to promote fusion research among young researchers in ASHBi, we have set up the **"ASHBi Fusion Research Grant Program"** since FY 2019. In FY 2023, we have selected three new proposals, "$2^1/_2$D and 3D cellular and molecular mechanisms for self-organization of limb morphogenesis" (mathematics-biology fusion led by **R. Tsutsumi**) and "Spatiotemporal reconstruction of gene expression dynamics during early human development" (mathematics-biology fusion led by **J. Okamoto** in **Hiraoka G**), and "High efficiency generation of in vitro embryo models using totipotent cells" (biology-biology fusion led by **M. Lawrence** in **T. Yamamoto G**). In addition, we have held **ASHBi colloquia** and the **ASHBi Retreat** on a regular basis since FY2019. In FY 2023, we held 8 **ASHBi colloquia** with the 16 PI groups presenting their latest research results, and had 119 ASHBi members join the **ASHBi Retreat**, with more than 50 presentations in total including the poster session and active interactions between researchers and graduate students (see **2. Generating Fused Disciplines**). Furthermore, under the leadership of **Hiiragi**, ASHBi PIs held the 2nd **PI retreat**, in which critical, constructive, and intensive discussions were made on the 1 PI's and 1 early-career researcher's research themes and future directions (see **2. Generating Fused Disciplines**).

To create opportunities for the exchange of scientific ideas with international communities, we have actively held international conferences and seminars. In FY2023, we organized 3 large-scale international meetings: "**ASHBi Workshop: Towards engineering embryonic development**" (July 2023), "**OKO (Oxford-Kyoto-Ohio State) International Symposium: Mathematical biology from genes to cells to humans**" (August 2023), "**Master's Lecture: Visions for development, stem cells and epigenetics**" (November 2023). The ASHBi Administrative Office has provided effective and powerful support for all ASHBi research activities and KU has also provided generous support to ASHBi for its long-term and continued development (see **3. Realizing an International Research Environment**, **4. Making Organizational Reforms** and **5. Efforts to Secure the Center's Future Development over the Mid- to Long-term**).

* Describe clearly and concisely the progress being made by the WPI center project from the viewpoints below.
- In addressing the below-listed 1-6 viewpoints, place emphasis on the following:
  (1) Whether research is being carried out at a top world-level (including whether research advances are being made by fusing disciplines).
  (2) Whether a proactive effort continues to be made to establish itself as a "truly" world premier international research center.
  (3) Whether a steadfast effort is being made to secure the center's future development over the mid- to long-term.

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 2023.
* Regarding the criteria used when evaluating the world level of center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

ASHBi investigates a key concept of human biology with a strong focus on genome regulation and disease modeling, thereby creating a foundation of knowledge for understanding the key biological traits that make us "human" and for developing innovative therapies. Specifically, we perform investigations in line with the following five focus areas:

1. Promote the study of human biology, with a focus on genome regulation
2. Clarify the principles defining the species differences and human traits
3. Generate primate models for intractable human diseases
4. Reconstitute key human cell lineages or tissues *in vitro*
5. Contribute to formalizing an international ethics standard for human biology research

Focus Area 1 is the fundamental theme covering, as a reflection of the PIs' expertise, areas as broad as reproduction, development, growth and aging as well as heredity and evolution.

The **Hiiragi group** published a manuscript entitled "Embryo-uterine interaction coordinates mouse embryogenesis during implantation" (***EMBO J.*** 42, e113280, 2023) (**Focus Areas 2** and **4**).

Embryo implantation into the uterus is a key transition in mammalian development. Implantation is mediated by the trophoblast adhesion to the uterine endometrium and is accompanied by a morphological transformation from the blastocyst to a species-specific form. However, the roles of trophoblast-uterine interactions in embryo morphogenesis during implantation are poorly understood due to in-utero inaccessibility and the remaining challenges in recapitulating it *ex vivo* from the blastocyst. In this study, the group engineered a uterus-like microenvironment to recapitulate mouse peri-implantation development *ex vivo* and revealed essential roles of the physical embryo-uterine interaction. They demonstrated that the trophoblast adhesion to the uterine matrix is required for the in-utero-like transition of the blastocyst to the egg cylinder. Modeling the implanting embryo as a wetting droplet explains embryo shape dynamics and suggests that the adhesion-mediated tension release facilitates egg cylinder formation, as predicted from their earlier findings (***Dev Cell*** 57, 373-386, 2022). Light-sheet live imaging and the experimental control of the engineered uterine geometry and trophoblast velocity uncover the coordination between trophoblast motility and embryo growth, where the trophoblast delineates space for embryo morphogenesis. This study serves as a basis for understanding and reconstituting *in vitro* of peri-implantation development in mammals, including humans.

The **Saitou group** published a manuscript entitled "Induction of fetal meiotic oocytes from embryonic stem cells in cynomolgus monkeys" (***EMBO J.*** 42, e112962, 2023) (**Focus Areas 1**, **2**, and **4**).

Human *in vitro* oogenesis provides a framework for clarifying the mechanism of human oogenesis.

To create its benchmarks, it is vital to promote *in vitro* oogenesis using a model physiologically close to humans. In this study, the group established a foundation for *in vitro* oogenesis in cynomolgus (cy) monkeys. They demonstrated that cy female embryonic stem cells (cyESCs) harboring one active and one inactive X chromosome (Xa and Xi, respectively) differentiate robustly into primordial germ cell-like cells, which in xenogeneic reconstituted ovaries develop efficiently into oogonia and, remarkably, further into meiotic oocytes at the zygotene stage. This differentiation entailed a comprehensive epigenetic reprogramming, including Xi reprogramming, yet Xa and Xi remained epigenetically asymmetric with, as partly observed *in vivo*, incomplete Xi reactivation. In humans and monkeys, the Xi epigenome in pluripotent stem cells functioned as an Xi-reprogramming determinant. The group further showed that developmental pathway over-activation with suboptimal up-regulation of relevant meiotic genes impede *in vitro* meiotic progression. Thus, this study demonstrates that cy *in vitro* oogenesis exhibits critical homology with the human system, including with respect to bottlenecks, providing a salient model for advancing human *in vitro* oogenesis. This work was made possible through close collaborations with **SignAC** and **PRiME**.

The **Bourque group** published manuscripts entitled "Transposable elements are associated with the variable response to influenza infection" (***Cell Genom.*** 3, 100292, 2023) and "Genome graphs detect human polymorphisms in active epigenomic state during influenza infection" (***Cell Genom.*** 3, 100294, 2023) (**Focus Area 1**).

Influenza A virus (IAV) infection causes seasonal epidemics and results in a range of disease severity between individuals. In the first study, given that transposable elements (TEs) contribute to innate immunity, the group used a multi-omics dataset from macrophages from 39 individuals to investigate the transcriptional and epigenetic changes in TEs during IAV infection. They found a significant inter-individual variation in viral load post-infection, detected more than 200 TE subfamilies up-regulated post infection, and the potential involvement of TE transcription in the pre-existing immunity. Using ATAC-seq, the group identified 37 TE subfamilies having enhanced chromatin accessibility post infection; strikingly, fifteen of them displayed high variability between individuals with distinct epigenetic profiles. Motif analysis showed an association with known immune regulators in stably enriched subfamilies and with non-immune regulators in variable subfamilies, including KRAB-ZNFs. The group showed that TEs and host factors were predictive of viral load post-infection. Thus, TEs and KRAB-ZNFs may play in inter-individual variation in immunity. In the second study, given that some TEs involved in regulating influenza infection responses may be polymorphic and not included in the reference genome, the group assembled a set of non-reference mobile element insertions (MEIs) in 35 ancestrally diverse genomes and compiled these into a genome graph representing this population. They mapped histone and chromatin accessibility data from infected and non-infected macrophages to this genome graph, and identified 375 MEIs in active epigenomic states in either condition, including some that change epigenomic state upon infection. The group found an MEI that is an eQTL for TRIM25, a gene known to be involved in the response to influenza. This study demonstrates that structural variation regulates the immune response and can be tackled using genome graphs that represent populations of genomes, in combination with epigenomic and gene profiling techniques.

The **T. Yamamoto group** in collaboration with the Yasuhiro Takashima group in CiRA (co-l corresponding author) published a manuscript entitled "Hypoblast from human pluripotent stem cells regulates epiblast development" (***Nature*** 626, 357–366, 2024; published online 5 December, 2023) (**Focus Areas 1**, **2**, and **4**).

Human pluripotent stem cell (hPSC)-based embryo models that recapitulate human development have attracted much attention as a novel technology for understanding human development. In this study, the group first succeeded in inducing pre-implantation primitive endoderm-like cells from naïve hPSCs (naïve hPSC-derived hypoblast-like cells; nHyC). Next, the group aimed to reconstitute human peri-implantation development by an aggregation culture of hPSCs and nHyC. They found

that the aggregates are self-organized into a bilaminar structure (bilaminoids) with nHyC migrating to the aggregate periphery. Importantly, the bilaminoids exhibited a morphogenesis reminiscent of peri/post-implantation development, forming amnion-like cells, primordial germ cell-like cells, and a primitive streak-like structure. Notably, co-culture with naïve hPSC-derived trophoblast-like cells enhanced the efficiency for the bilaminoids to develop into a post implantation embryo-like structure, and the group demonstrated the role of trophoblast-secreted IL6 in bilaminoid growth and cavitation, and of hypoblast-expressed laminins in epiblast differentiation and morphogenesis. This study serves as a foundation for future in vitro human reconstitution work that provide a more comprehensive understanding of the mechanism of human development and pave the way for new methods of inducing tissues and organs from hPSCs by mimicking a more natural developmental process. This work was the result of close collaborations with the **Saitou group** and **SignAC**.

The **Isa group** published a manuscript entitled "Balancing risk-return decisions by manipulating the mesofrontal circuits in primates" (***Science*** 383, 55-61, 2024; published online, on January 5, 2024) (**Focus Areas 1**, **2**, and **3**).

One of the key factors that makes us "human" is the expansion of the frontal lobe of the brain, which enables us to make flexible decision making. In this study, the group explored the roles of presumed dopaminergic pathway from the ventral tegmental area (VTA) in the midbrain to the frontal cortex while the macaque monkeys were performing decision making task to select either high risk-high return (HH) or low risk-low return (LL) options. They found that among a variety of frontal cortical areas, reversible pharmacological inactivation of the ventrolateral part of area 6 (area 6V) impaired the risk-dependent decision. Using a state-of-the-art optogenetic activation technique, they showed that stimulation of the pathway from VTA to the ventral portion of area 6V (area 6VV) enhanced the HH-preference, while stimulation of the pathway from VTA to more dorsally located area 6VD reduced the HH-preference. Furthermore, as they repeated such stimulation, the effect accumulated in the long term, resulting in persistent high or low level of HH-preference. These results showed how the dopaminergic pathway to the frontal cortex modulates decision making which requires a high level of computation in the short and long term. These results may promote better understanding of the neural mechanism associated with addiction such as gambling disorders. The impact of this work was introduced in the same volume (Stuphorn V, "Dopamine regulates attitude toward risk" (***Science*** 383, 32-33, 2024)).

The **Amemori group** published a manuscript entitled "Spatiotemporal expression patterns of anxiety disorder-associated genes" (***Transl. Psychiatry*** 13, 385, 2023) (**Focus Areas 1**, **2**, and **3**).

Anxiety disorders (ADs) are one of the most prevalent health-related disabilities in the world. ADs have a substantial genetic basis, and genome-wide association studies have revealed relevant mutations. Furthermore, neuroimaging techniques showed how activities in specific neural circuits predict anxious temperament. However, there is still a gap between the genes identified in genetic studies and the neural circuitries identified in physiological studies. In the study, based on the hypothesis that the regions where AD-associated genes are expressed might predict AD neurocircuitry, the group analyzed the spatiotemporal transcriptomic data of over 200 genes linked to four AD subtypes – generalized anxiety disorder, social anxiety disorder, obsessive-compulsive disorder, and panic disorder – in over 200 brain structures of normal human brains available in the Allen Brain Atlas. Their analysis revealed two distinct AD gene clusters with contrasting spatial expression patterns: one expressed in the limbic system and specific cerebral nuclei (limbic-associated spatial cluster 1), and another expressed in the midbrain and different cerebral nuclei (midbrain-associated spatial cluster 2). Notably, certain cerebral nuclei exhibited preferential or exclusive enrichment in spatial cluster 1 (SC1) or spatial cluster 2 (SC2), indicating a dichotomy in AD neurophysiology. State anxiety, a transient and context-dependent worry response to specific events, was associated with regions enriched in genes from SC2, such as the ventral tegmental area,

striatum, and the bed nucleus of the stria terminalis. Conversely, trait anxiety, characterized by a persistent tendency towards anxiety across diverse situations, correlated with regions enriched in genes from SC1, including the hippocampal system and the periaqueductal gray. These distinct gene clusters, enriched in specific brain regions with differing functions and temporal expression patterns, offer promising avenues for further understanding of the underlying mechanisms of ADs. Further investigation into these gene clusters could yield valuable insights into the etiology of ADs and potentially inform more effective therapeutic interventions.

The **Ogawa group** published a manuscript entitled "Deciphering evolutionary histories of breast cancer and related clones" (***Nature*** 620, 607-614, 2023) (**Focus Area 1**).

Recent studies have documented frequent evolution of clones carrying common cancer mutations in apparently normal tissues, which are implicated in cancer development. However, our knowledge is still missing regarding what additional driver events take place in what order, before one or more of these clones in normal tissues ultimately evolve to cancer. In this study, using phylogenetic analyses of multiple micro-dissected samples from both cancer and non-cancer lesions, the group showed unique evolutionary histories of breast cancers harbouring der(1;16), a common driver alteration found in approximately 20% of breast cancers. The approximate timing of early evolutionary events was estimated from the mutation rate measured in normal epithelial cells. In der(1;16)(+) cancers, the derivative chromosome was acquired from early puberty to late adolescence, followed by the emergence of a common ancestor by the patient's early 30s, from which both cancer and non-cancer clones evolved. Replacing the pre-existing mammary epithelium in the following years, these clones occupied a large area within the premenopausal breast tissues by the time of cancer diagnosis. Unexpectedly, evolution of multiple independent cancer founders from the non-cancer ancestors was common, contributing to intratumour heterogeneity. This study provides new insights into the evolution of breast cancer.

The **Yanagita group** published a manuscript entitled "Tertiary lymphoid tissues are microenvironments with intensive interactions between immune cells and proinflammatory parenchymal cells in aged kidneys" (***J. Am. Soc. Nephrol.*** 34, 1687-1708, 2023) (**Focus Area 1**).

Tertiary lymphoid tissues (TLTs) are ectopic lymphoid structures that develop in chronically inflamed organs. The group has reported key roles of TLTs in the development of chronic kidney disease (***JCI Insight*** 1, e87680, 2016; ***Kidney Int.*** 98, 448-463, 2020; ***J. Clin. Invest.*** 132, e146071, 2022). To investigate the roles of renal parenchymal cells and their cell-cell interactions with immune cells within TLTs, the group conducted single-nucleus RNA sequencing of aged injured murine kidneys with TLTs. *Vcam1*+ injured proximal tubular (PT) cells with proinflammatory and profibrotic phenotypes were identified and demonstrated to be localized adjacent to TLTs. Such cells are currently known as "failed repair PTs" in injured kidneys. Lymphocytes within TLTs highly expressed proinflammatory cytokines, TNFa and IFNg, which enhanced expression of *Vcam1* and proinflammatory chemokines, such as *CCL2* and *CXCL10*, in cultured PT cells, suggesting that TLTs may contribute to maladaptive repair of PT cells and promote their proinflammatory phenotypes. The group identified proinflammatory fibroblasts within TLTs and profibrotic fibroblasts surrounding TLTs. The proinflammatory fibroblasts expressed various chemokines and cytokines, such as *Cxcl9*, *Cxcl10*, and *Tnfsf13b* (encoding B cell activating factors), potentially contributing to CXCR3+ T cell migration and B cell survival and proliferation within TLTs. *Cxcr3*+ T cells highly expressed *Ifng*, which enhanced the expression of *Cxcl9*, *Cxcl10*, and *Tnfsf13b* in cultured fibroblasts in a STAT1-dependent manner. These results suggest that cell-cell interactions between the proinflammatory fibroblasts and CXCR3+ T cells promote inflammation and TLT expansion. Understanding these molecular mechanisms may contribute to the development of an effective therapeutic approach for aged injured kidneys with TLTs.

The **Hiraoka group** published a manuscript entitled "V-Mapper: topological data analysis for high-

dimensional data with velocity" (***NOLTA*** 14, 92-105, 2023) (**Focus Area 2**).

Mapper is a well-known topological data analysis method for visualizing high-dimensional data structures as an abstract graph. Mapper has been applied to single-cell RNA-sequencing (scRNA-seq) data and used to clarify structures of cell differentiation hidden in high-dimensional gene expression space. In comparison to tree-based trajectory inference methods (pseudo-time analysis, e.g., Monocle), topology-based methods more precisely capture high-dimensional topological structures like holes and cavities associated with biological features such as plasticity and cyclicity. In contrast, tree-based methods have the superiority of determining the dynamic flow of cell differentiation by providing the source node of the graph. In this study, the group developed V-Mapper (velocity Mapper) as a generalization which simultaneously describes the topological structure and time evolution as a weighted directed graph (V-Mapper graph). Specifically, V-Mapper extracts topological structures using a conventional Mapper algorithm from point cloud data and embeds the velocity field onto the edges of the Mapper graph. In addition, they developed an algorithm based on the graph Hodge theory, which decomposes a weighted directed graph into graphs representing potential and rotational flows. This algorithm enabled the group to simplify complex velocity structures on the V-Mapper graph and characterize the irreversible flow of the cell differentiation dynamics. They applied V-Mapper to scRNA-seq data of pancreatic endocrine cell differentiation, and found more precise and interpretable cell differentiation pathways including plasticity among mature endocrine cell types than those obtained by prior research using only RNA velocity. The Python code of V-Mapper is open to the public on GitHub.

The **S. Seirin-Lee group** published a manuscript entitled "Mathematical-based morphological classification of skin eruptions corresponding to the pathophysiological state of chronic spontaneous urticaria" (***Commun. Med.*** 3, 171, 2023) (relevant to **Focus Areas 1** and **2**).

Chronic spontaneous urticaria (CSU) is one of the most intractable human-specific skin diseases. However, as no experimental animal model exists, the mechanism underlying disease pathogenesis remains unclear, making the establishment of a curative treatment challenging. In this study, using a novel approach combining mathematical modeling, *in vitro* experiments, and clinical data analysis, the group showed that the pathological state of CSU can be inferred by geometric features of the skin eruptions. Based on hierarchical mathematical modelling, the eruptions of CSU were classified into five categories, each with distinct histamine, basophils, mast cells and coagulation factors network signatures. The analysis of 105 CSU patients with this classification by six individual dermatologists achieved 87.6% agreement. Furthermore, the group's network analysis revealed that the coagulation status likely determines boundary/area pattern of wheals, while the state of spontaneous histamine release from mast cells may contribute to the divergence of size and outline of the eruptions. This study not only demonstrates that pathological states of diseases can be defined by geometric features, but will also facilitate more accurate decision-making to manage CSU in the clinical setting.

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. Advancing Research of the Highest Global Level."

ASHBi Flagship Projects (Top-down approach to generating fused disciplines)

ASHBi has been performing fusion research between life sciences and mathematics (the **Hiraoka** and **Seirin groups**), and humanities/social sciences (the **Fujita group**). Furthermore, ASHBi has initiated **the Flagship Projects**, which represent key research directions of ASHBi and involve close collaborations among ASHBi PI groups. Accordingly, we have organized the key fusion research projects between life sciences and mathematics, and humanities/social sciences under the framework of the Flagship Projects. We here describe the progress of the five Flagship Projects.

1. Deconstruction and reconstruction of early primate development

The Developmental Biology subdivision (**Alev**, **Ema**, **Hiiragi**, and **Saitou G**) is performing an investigation into "**Deconstruction and reconstruction of early primate development**" (**Focus Areas 1**, **2** and **4**). This consists of three interrelated initiatives: **a)** To explore the mechanism of post-implantation primate development at a single-cell resolution using methodologies including scRNA-seq combined with novel analysis methods such as RECODE and GMM-OT; **b)** To develop *ex vivo* culture systems for analyzing the pre-/post-implantation development of mouse and monkey embryos using technologies including advanced light-sheet imaging coupled with scRNA-seq analysis; and **c)** To perform *in vitro* reconstitution and analysis of pre-/post-implantation development of human and non-human primates using PSC-based synthetic embryo model systems and high-end 3D/4D imaging and scRNA-seq analysis.

In FY2023, relevant members have met and discussed regularly to foster collaborations and help the members align their efforts towards realizing the project's overall goal of understanding early human and primate embryonic development. The **Alev group** took a leading role in constructing *in vitro* models of human and non-human primate embryonic development. Notably, significant strides have been made in developing both reductionist and integrated models. Meanwhile, the **Saitou group** has advanced their studies of *in vivo* models of primate development and provided valuable benchmarking datasets [scRNA-seq data for cynomolgus monkey embryos at embryonic days (E)15, 17, 19, 20, 21, and 23 (manuscript in preparation)] for comparison with *in vitro* models made by the **Alev group** or others. The **Ema** and **Hiiragi groups** continued to collaborate on studying early peri-implantation development of non-human primates (NHPs) with a focus on trophoblast and placental development. Joint efforts between the **Ema** and **Alev groups** on in vitro/ex vivo modeling for NHP implantation and peri-implantation development are also progressing. Exchanges of samples and data between the **Alev** and **Saitou groups** also continued. The Developmental Biology subdivision has been performing the research on *in vitro* human embryo models in close discussion with the **Bioethics group (Fujita group)**.

2. Primate-genomics interdisciplinary research for developing new primate models

NHPs share genetic, structural, and functional similarities with humans. Accordingly, the Primate Models/Macaque Genome Engineering subdivision and the Genome Informatics subdivision (**Amemori**, **Isa**, and **Murakawa G**) are performing "**Primate-genomics interdisciplinary research for developing new primate models**" (**Focus Areas 1**, **2**, and **3**).

The core of this project consists of two interrelated studies:

a) Generating NHP models of anxiety disorders (ADs) (**Amemori** and **Murakawa G**):

In FY2023, the **Amemori** and **Murakawa groups** performed a comprehensive analysis of expression profiles of genes associated with AD within brain regions. As described above, their analysis (***Transl. Psychiatry*** 13, 385, 2023) revealed compelling correlations between AD-associated gene expression and specific brain regions. Based on these findings, they have set out preliminary tissue samplings from NHP brains for single-nucleus RNA sequencing (snRNA-seq) to elucidate cell-type specific characteristics within the identified AD-associated brain regions, which will serve as a foundation for generating NHP models of ADs.

b) Elucidating the plasticity of corticospinal motor neurons in NHPs (**Isa** and **Murakawa G**):

In FY2023, the **Isa** and **Murakawa groups** established the methodology of tissue sampling from the rat model of recovery from spinal cord injury (SCI). They injected a retrograde viral vector to label the rerouting corticospinal neurons and performed snRNA-seq with labeled corticospinal neurons. Furthermore, they established a better stimulation for the recovery from SCI in NHPs. They introduced a non-invasive transcranial magnetic stimulation to avoid potential damage. These methods will improve the quality of tissues that will be sampled for snRNA-seq in NHP models for elucidating the plasticity of corticospinal motor neurons in NHPs.

The analyses of KO monkeys for *PKD1* (**Ema G**), *NPHP1* (**Yanagita G**) and *DISC1* (**Isa G**) have been performed through this collaborative platform (**Focus Areas 1**, **2**, and **3**).

c) *PKD1* KO (**Ema G**) as a model for autosomal dominant polycystic kidney disease (ADPKD):

The **Ema group** has been continuing to work on elucidating the mechanism of ADPKD by utilizing *PKD1* mutant monkeys (*Nat. Commun*. **10**, 5517, 2019). They have been analyzing 14 monkeys (6 heterozygotes and 8 mosaics, with 2 of the mosaics being nearly completely homozygous; 5–8 years old) and performing echo analysis twice a year and have found that renal cysts are progressively increasing with age in 2 of the mosaics with nearly completely homozygous *PKD1* mutations. Moreover, these 2 monkeys are showing the marked increased total kidney volume with elevated creatinine and cystatin C, that are markers for kidney injury. The group plans to carefully analyze the renal epithelial lining in the cysts to understand the initial mechanism of cyst development. To maintain the monkey line, the group has been training the *PKD1* KO male monkeys for sperm collection.

d) *NPHP1* KO (**Yanagita G**) as a model for Nephronophthisis:

In FY2023, with careful analyses of *NPHP1* KO monkeys, **Yanagita group** found that the *NPHP1* KO kidneys showed characteristic lesions of juvenile nephronophthisis and, notably, abnormal EGFR phosphorylation in the collecting ducts, that suggests the EGFR signaling pathway might be a therapeutic target of juvenile nephronophthisis. Additionally, they performed a comprehensive comparison of kidney diseases/disease models in mice, monkeys, and humans, and identified *LRRC31* as one of the primate-specific disease associated genes, which might protect kidney by regulating apoptosis and DNA repair.

e) *DISC1* KO (**Isa G**) as a model for Psychosis:

The **Isa group** has been analyzing the growth and phenotypes of 6 *DISC1* KO monkeys in comparison to 4 monkey controls. The group generated iPSCs from the *DISC1* KO and wild-type monkeys. They induced neural cells from these iPSCs and conducted the bulk RNA-seq analysis and found changes in the expression of a number of genes, particularly those related to mitochondrial functions. At the age of 2 years, resting state fMRI analysis showed that the functional connectivity between the frontal and parietal, and that between the frontal and temporal association cortices were weaker than the control animals, similarly to the schizophrenia patients. In the behavioral analysis, the human intruder test was conducted and the KO monkeys tended to pay less attention to the human intruders, but pay more attention to the surrounding environment. The results suggested interesting phenotype regarding the sociality of the animals. Abnormal nocturnal sleep has been observed in some monkeys by video and nano-tag based analysis. Thus, the KO monkeys started showing phenotypes of psychosis. **The group** will further deepen the analysis of these animals from various aspects. When **the group** become convinced of such phenotypes, they will explore the effects of deep brain stimulation and other therapeutic strategies to see whether they ameliorate the symptoms.

3. Age-associated genomic alterations of organ cells and their interplay with the local immune system

The Basic/Clinical Medicine subdivision (**Ogawa**, **Ueno** and **Yanagita G**) is investigating "**Age-associated genomic alterations of organ cells and their interplay with the local immune system**" (**Focus Area 1**). Cancer development can be a consequence of immune system deterioration and increased alterations in pre-cancerous cells. However, the interplay between pre-cancerous cells and the immune system in the local microenvironment remains unknown. This project focuses on primary sclerosing cholangitis (PSC), a rare chronic cholestatic liver disease with an increased malignancy risk (400-1,500-fold increase), and aims to define the interplay between aging immune cells and altering tissue cells in PSC liver tissues.

Genome-wide association studies of PSC show multiple risk loci associated with Tfh/Th17 cells, suggesting the contribution of the adaptive immune system to its pathogenesis. The recent

discovery of anti-α-v/β-6 Abs as an autoantibody unique to PSC further supports this hypothesis. In FY2023, the **Ueno group** analyzed, by high-parameter FCM and scRNA-seq, $CD4^+$ T cell subsets present in the perfusate of PSC liver and identified abundant IL-17^+ Th17 cells, a T cell subset absent in the normal liver perfusate, and few regulatory T cells, suggesting the involvement of Th17 cells in PSC pathogenesis. To clarify Th17 cell localization in PSC tissues together with their interactions with neighboring cells, the **Ueno group** is currently comparing the three spatial transcriptomics platforms, including CosMx, Xenium, and Merscope. The **Murakawa group** has developed a novel method to define active enhancers using 5' scRNA-seq data (named Reap TEC; ***Science***, in press, 2024). In collaboration with the **Ueno group**, they have identified 23,890 active enhancers across 30,000 immune cells in human liver perfusate by ReapTEC. By comparing the blood $CD4^+$ T cells dataset, they identified 439 enhancers uniquely activated in liver $CD4^+$ T cells. In FY 2024, the **Ueno** and **Murakawa groups** will establish a comprehensive human liver immune cell scRNA-seq dataset together with their enhancer landscape by analyzing approximately 4 million cells from > 50 liver perfusate samples. The **Ogawa group** also obtained bile and tissue samples from PSC patients. The mutation rate analysis using cholangiocyte organoids suggested that it was not increased in PSC cholangiocytes. Nonetheless, cholangiocytes from extrahepatic (n=4) and intrahepatic bile ducts (n=3) showed clusters of mutations with high variant allele frequency (VAF), suggesting clonal expansion in PSC. Cholangiocytes from one case showed mutations in genes associated with the Th17 pathway, consistent with the observation from the **Ueno group**.

4. Establishment of "data representation theory"

The mathematics groups (**Hiraoka** and **Seirin-Lee G**) in collaboration with the life sciences groups are working on "**Establishment of 'data representation theory'**", with the goal of understanding mathematical structures (static and dynamic) underlying large and complex datasets and to develop informative descriptors tailored to the respective specific analyses (**Focus Area 2**). In FY 2023, the groups realized the following developments:

Hiraoka Group:

RECODE: the publicly available noise reduction method RECODE has attained 221,846 downloads as of March 11, 2023.

Topological node2vec: To capture relevant information from a multi-contact chromatin capture method, Pore-C, the group developed a machine learning network that corrects a major failure in the prevalent data pipeline, i.e., the loss of topological information. The previously proposed MATCHA framework remains one of the only effective methods for handling Pore-C data, but the group found that with very trivial examples, they could demonstrate a loss of topological information during the embedding process — the lost information includes structures like loops, gaps, and densely tangled regions in genomic data (TADs). The group introduced a topological loss function derived from optimal transport research which allows their machine learning network to reconstruct structures from Pore-C data while preserving topological information. They demonstrated the advantages of this construction on synthetic data, from which they are ready to return to the original question of superior treatment of Pore-C data from a topological perspective. Thus, they have achieved a bidirectional fusion of research between mathematics and biology [manuscript accepted in principle in the ***J. Mach. Learn. Res.***].

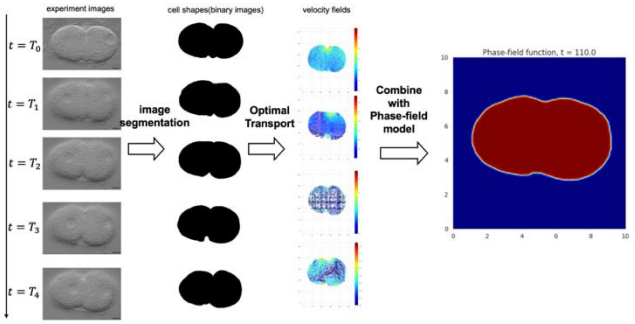
Optimal transport (OT) theory: OT is one of the most active research areas in the advanced mathematics, providing a natural formulation to interpolate multiple data. The group developed several data analysis methods in single-cell biology using OT for interpolations of time, space-time, and species:

Time interpolation: A trajectory inference method scEGOT, which they have developed in the last few years, was improved to be equipped with 6 functions (cell state graph, cell velocity, time interpolation, animation, gene regulatory network, and Waddington's landscape). They applied scEGOT to human primordial germ cell-like cell (hPGCLC) induction, identified the pathways and progenitor cell populations for hPGCLC differentiation, discovered several key genes for hPGCLC differentiation, and verified their functions with the **Saitou group** (Manuscript under submission).

Space-time interpolation: They started a project "spatio-temporal reconstruction of gene expression dynamics during early human development" with the **Alev group**, where OT is used to interpolate single-cell data for both space and time. They developed a prototype of the mathematical method, applied it to the human axioloids, and found many genes whose expression overlaps with the somite rostro-caudal marker *TBX18* or the anterior PSM specific gene *MESP2*. They proposed a concept of "*universal axioloid"* to utilize limited and non-consistent experimental data and to study spatio-temporal dynamics in a unified framework.

Species interpolation: The two OT-based methods described above assume that multiple data exist in the same space (e.g., a gene space of humans), but the Gromov-Wasserstein OT theory allows to interpolate data even in different spaces. This enabled the group to compare multiple gene expression spaces (e.g., in mice, monkeys, and humans), and to set out to elucidate species differences, one of the key research themes in ASHBi. In FY 2023, the group initiated this challenging project with the **Saitou group**.

Seirin Group:



Imaging Data-based Model Description Tool: Capturing the geometrical shapes of cells are important in biology. Despite advances in technology, the time resolution of live imaging is often limited. The group developed mathematical tools to infer intermediate cell shapes from limited live imaging data. Their method combines the data science method OT and the mathematical modeling method Phase-field Model (PM). This successfully reconstituted cell dynamics with smooth and natural cell shapes using live imaging data of C. elegans embryo and a human leukemia cell (HL-60). This can be applied to studies that need to estimate cell tracking with limited imaging data. Furthermore, this method enables a mathematical modeling approach to describe the dynamics of biomolecules on the actual cell shape. The group will apply this method to the study of cell patterning and migration during the post-implantation development in mice and monkeys (with the **Hiiragi** and **Ema groups**).

5. Bioethics at the periphery of birth and death

The bioethics group (**Fujita G**) in collaboration with life sciences groups is working on "**Bioethics at the periphery of birth and death**" (**Focus Area 5**). The procurement and use of human samples, including tissues from aborted fetuses or from early postmortem individuals, are critical for promoting human biology. This project explores philosophical and empirical approaches for making guidelines on the research use of such human tissues:

a) To formulate rules for fetal tissue research:

Together with **Saitou** and Takashima groups in CiRA, the group established an academic team, including philosophers, ethicists, and legal scholars, to discuss ethical considerations for research use of human fetal tissues. They aim to create guidelines for conducting fetal tissue studies, compile reports that form the basis for these studies, and clarify the items that should be written in explanatory documents to donors. In FY2023, they conducted interviews with researchers and administrators at fetal tissue banks or other institutions in Europe (the UK, Switzerland, France) and USA. They visited in person the Human Developmental Biology Resource (HDBR) facilities in London and Newcastle, and identified following guidelines of the HDBR's operations:

1. The HDBR is operated under the supervision of the relevant government agencies.
2. The HDBR is subject to ethics review, while researchers who use samples are not.
3. The HDBR decides whether to distribute tissues for a given project.
4. The HDBR collaborates with local clinics to collect fetal tissues.
5. 60-70% of recruited women consent to tissue donation.

6. Informed consent (IC) for tissue donation is obtained by staff not involved in abortion care (mainly bank staff) who visit the clinic 3-5 days a week.
7. Each bank collects 1-3 tissue samples per day, 400 samples per year.
8. The HDBR effectively maintains a database of fetal tissue information (e.g., number of weeks, types of organs, etc.) requested by researchers.
9. The HDBR collects feedback from researchers who have received fetal tissue and enhances methods for storing and transporting it.

(Left) With Prof. Copp & Dr. Solanky at HDBR (London)

(Right) With Dr. Lisgo at HDBR (Newcastle)

The group confirmed similar guidelines in the Birth Defects Research Laboratory (BDRL) in Washington State, USA (Manuscript in preparation). Additionally, the group translated the "ISSCR Informed Consent Standard for Human Fetal Tissue Donation for Research" into Japanese, which was published on the ISSCR website.

b) To construct a platform for early postmortem tissue research:
A group of junior scientists consisting of 4 Bioethicists and 8 Life Science researchers, aim to produce a guideline for ethical, legal, and social issues (ELSI) and to construct a platform for early postmortem tissue research. Literature review and interviews on the rapid autopsy program (RAP) revealed that IC and stakeholder engagement is crucial for the sustainability of RAP. In FY2023, they prepared a report regarding ELSI, IC, philosophy of death, funeral history, and the discourse of death on SNS. In addition to the six domestic and international institutions interviewed in the previous fiscal year, they conducted another on-site interview at Fukushima Medical University, where RAP is de facto in operation for its biobank. Furthermore, a questionnaire survey was conducted among healthcare professionals at KU Hospital to prepare for the incorporation of RAP. Based on these results, recommendations for ethical guidelines have been formulated.

c) To establish a research ethics consultation system:
Research ethics consultation on advanced human biology research is an activity that has become widespread at universities and research institutes in USA since around 2000. The **Fujita group** provides consultation on various issues, including research design, ethical review applications, ethical considerations in publications, and legal compliance. As an example, since last year, they have been assisting the **Alev group** in acquiring ethical permission to conduct long-term in vitro cultures of human ESC-derived embryo models. With the support by ASHBi administration, the application was finally received/accepted by the MEXT. This milestone marks the first approval in Japan for a long-term culture of human embryo models to a developmental stage equivalent to CS12-14. To broaden their support, they, in collaboration with **Yanagita, Ema, Alev groups** and **Spyros Goulas** (scientific advisor of ASHBi), are developing a website for ASHBi researchers requiring/requesting consultation.

ASHBi Fusion Research Grant Program (Bottom-up approach to generating fused disciplines)

To intensively promote interdisciplinary research based on unconstrained ideas of young researchers, we established the "ASHBi Fusion Research Grant Program" in 2019. To ensure interdisciplinary research, this program requires applicants to form a team consisting of different disciplines (math-biology, ethics-biology, or biology-biology). Applicants are also required to attend meetings held twice a year to evaluate the progress of their research projects. The duration of the program is between 1–3 years and the funding can be up to 3 million yen per year for each project. In FY2023, three additional projects were selected, making a total of 11 funded projects.

Year	Category	Applicant	Project title
FY2021	Math-Bio	R Yamaguchi	*Statistical inference of the causality among brain regions with recovery from spinal cord injury*
	Ethics-Bio	G Okui	*The research use of fresh postmortem tissues: From a regulatory and ethical perspective*
	Bio-Bio	H Saito	*Functional dissection of primate striatal structure using viral vectors with genome informatics*
	Bio-Bio	Y Yamanaka	*Spatial transcriptome analysis of human axial development in vitro*
	Bio-Bio	S Hamidi	*Reconstruction and analysis of peri & post-implantation non-human primate development*
	Bio-Bio	S Bhagat	*Deciphering regulatory heterogeneity of human hematopoietic stem and progenitor cells*
FY2022	Math-Bio	T Tsujimura	*Single-molecule elucidation of higher-order chromatin folding dynamics in individual cells*
	Bio-Bio	M Nagano	*Unraveling transcriptional regulatory mechanism of transposable elements across species*
FY2023	Math-Bio	R Tsutsumi	*2½D and 3D cellular and molecular mechanisms for self-organization of limb morphogenesis*
	Math-Bio	J Okamoto	*Spatiotemporal reconstruction of gene expression dynamics during early human development*
	Bio-Bio	M Lawrence	*High efficiency generation of in vitro embryo models using totipotent cells*

Institution-wide gatherings for generating interdisciplinary research

The ASHBi Retreat FY2023 was held in-person at a hotel on the shores of Lake Biwa on January 26-27, with participated by 119 ASHBi members and 3 invited speakers. The 2-day program consisted of 14 oral and 53 poster presentations. Active interactions took place between researchers and graduate students from different PI groups to enhance curiosity-driven interdisciplinary collaboration opportunities.

The ASHBi PI Retreat, a discussion-oriented event to achieve a deeper mutual understanding among PIs, was held for the second time on November 23, 2023. Hiiragi PI and one early-career researcher from Saitou G, gave two-hour presentations each on their scientific vision and one ongoing project in front of other ASHBi PIs and senior researchers who attended to effectively elicit critical and constructive feedback from their colleagues. The next PI retreat will be held in June 2024.

The ASHBi Colloquium is held monthly to promote collaborative research within the Institute, with two members from PI groups presenting their ongoing research each time. This format allows speakers and participants with different research backgrounds to come together for discussion. In FY2023, 8 colloquia were held by 16 PI groups, leading to a total of 42 colloquia since 2019.

3. 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
- 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)

Core facilities to promote world-class research

To establish an excellent research environment that attracts highly-skilled researchers, ASHBi operates three core facilities as its fundamental infrastructure for human biology research.

SignAC (Single-Cell Genome Information Analysis Core) is a core facility that supports large-scale genomic analysis of samples at single-cell resolution by providing the shared use of state-of-the-art equipment and data analysis services. Importantly, it employs its own researchers that focus on the development of new analytical methods/tools. The overall operation of SignAC is supervised by the Core Head, **Takuya Yamamoto**, while on-site management is carried out by Core Manager **Taro Tsujimura**, two post-doctoral fellows, four technical staff members, and one administrative staff member. SignAC is part of the university's core facility integration platform (iSAL: Innovative Support Alliance for Life Science), and its online service system enables researchers inside and outside ASHBi to access the equipment and analytical services seamlessly. With its increasing visibility, SignAC has supported more than 100 researchers through collaborative research and analytical services, with the total income of over 130 million yen in FY2023. In addition, SignAC has received funding from the Japan Agency for Medical Research and Development (AMED) from FY2022 to promote the nationwide development of analytic methods using long-read sequencers.

PRiME (Primate Genome Engineering Core) is a domestic satellite of ASHBi and is in RCALS, the Shiga University of Medical Science. RCALS has a large primate colony (~700 cages) and state-of-the-art technologies for animal reproduction. **Tomoyuki Tsukiyama** has been appointed as the Core Head and employs two skilled staff for animal reproduction and breeding management. To cope with the recent surge in purchase prices of cynomolgus monkeys, PRiME plans to breed its own monkeys to ensure a stable supply at a reasonable price. PRiME plans to begin in-house breeding at a pace of about once a month and aims to produce 10-20 new macaques per year from FY2025. With this measure, ASHBi researchers can obtain monkeys for their experiments at reasonable prices even after the WPI program funding ends.

NPAF (Non-human Primate Phenotype Analysis Facility) is a facility to analyze phenotypes of genome-edited monkeys located on KU medical school campus, a five-minute walk from the Institute. **Tadashi Isa** supervises the overall operation of the facility, and **Hirotaka Onoe** manages the genome-edited monkey research on site, along with one postdoctoral researcher that conducts behavioral analysis through video recording and eye movement measurements, and two support staff who take care of animal health, feeding, and cage cleaning.

Internationalization of PIs, researchers, and students

ASHBi is actively recruiting and promoting excellent non-Japanese PIs. Of 16 PIs, 4 (25%) are foreign nationality (Alev, Bourque, Seirin-Lee, and Ueno). Alev PI was promoted from non-tenured associated professor to tenured professor in October 2023, filling one of the tenured positions provided by KU to ASHBi. Further, to increase the ratio of female/non-Japanese PIs, the Institute will work closely with the KU's "HAKUBI Project", which recruits 20 promising junior PI-level researchers from around the world each year. Through this collaboration, we plan to establish a system that provides opportunity for outstanding female/non-Japanese HAKUBI researchers to join our institute as junior PIs.

To increase the number of female/non-Japanese researchers, we continue to utilize the **"ASHBi Foreign and Female Researcher Recruitment Support Program"** established in 2019. With this program, PIs can receive personnel cost of up to 5.5 million yen for hiring new non-Japanese or female researchers. Through this support, the number of non-Japanese/female researchers was increased or maintained in FY2023. As of April 2024, the ratio of non-Japanese researchers has increased to 40% and that of female researchers to 27%.

Moreover, to increase the number of international students, we continue to utilize the **"ASHBi Financial Support Program for International Graduate Students"** established in 2020. This program provides 150,000 yen per month to support living expenses for international students enrolled in a master's or doctoral course. In addition, we also make use of the **"McGill-Kyoto International Joint PhD Program in Genomic Medicine"**. As of April 2024, with the support of these two programs, the ratio of international students has reached 30% and that of female students 31%.

Collaboration with world-leading research institutions/organizations

ASHBi signed institutional collaboration agreements with world-class research institutions/organizations such as **EMBO** (the European Molecular Biology Organization), **ISSCR** (the International Society for Stem Cell Research), and the **Max Delbrück Center for Molecular Medicine** (Berlin, Germany). In FY2023, ASHBi signed additionally new institutional collaboration agreements with two research centers, the **Jackson Laboratory** (Bar Harbor, US) and the **Institut Pasteur** (Paris, France). For the latter, the Pasteur International Unit (headed by Alev PI) was established within ASHBi to pursue research collaborations in the fields of stem cell, developmental, and integrative biology.

Research exchanges via international conferences/seminars

In FY2023, ASHBi organized a total of 54 meetings in English, 49 of which were conducted on-site/hybrid (https://ashbi.kyoto-u.ac.jp/events/). We held 3 largescale international meetings ("ASHBi Workshop - Towards engineering embryonic development" in July, "OKO International Symposium" in August and "Master's Lecture" in November 2023), 23 ASHBi seminars (each PI is required to invite overseas researchers to organize at least one seminar per year), 8 ASHBi colloquia, and 3 Research Acceleration Program Seminars. The Institute has hosted more than 250 gathering events since its establishment in October 2018.

Dissemination of international scientific news releases

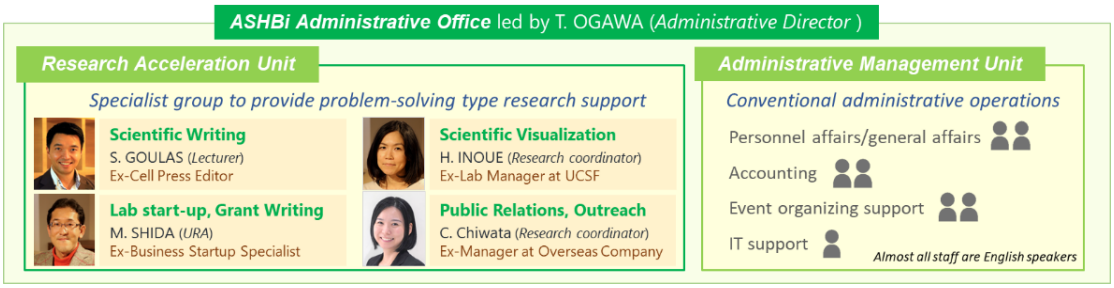
To increase the international visibility of ASHBi, we have been actively disseminating science news releases through EurekAlert!. We strive to deliver press releases with easy-to-understand titles, illustrations and images that capture people's interests, together with clear, jargon-free, research stories. In FY2023, we posted press releases for 9 research papers to EurekAlert! and to the ASHBi website.

4. Making Organizational Reforms

* Describe the system reforms made to the center's research operation and administrative organization, along with their background and results.
* 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.

Flexible and problem-solving support to accelerate the Institute's research

The ASHBi Administrative Office provides effective support for the Institute's researchers. The office consists of the two units and is managed by **Tadashi Ogawa**. The Administrative Management Unit is responsible for regular administrative operations, such as human resources and accounting. Whereas the **"Research Acceleration Unit"** is unique in that it provides flexible and problem-solving type support. To achieve this objective, four specialists have been assigned to the Unit. **Spyros Goulas** is a former editor at Cell Press, **Makoto Shida** is a specialist of business startup, **Hiromi Inoue** has extended experience and skills as a lab manager at UCSF, and **Chieko Chiwata** has a background working as a manager in an overseas company with customer service operations. These specialists have greatly enhanced the Institute's research environment with their experience and highly specialized skills. For example, Goulas provided strategic advice as well as critical comments and suggestions in writing manuscripts/cover letters and responses to editors and reviewers, contributing to the acceptance/provisional acceptance of 8 papers (including 3 *Science*/*Nature* papers) from ASHBi in FY2023.



Seminars aimed at fostering early-career researchers and students

The Research Acceleration Unit continues its efforts to organize seminars to train early-career researchers and graduate students. In FY2023, the Unit held seminars on topics such as how to write research papers/cover letters **"Entering the Minds of Scientific Editors and Understanding Journal Strategies"** by Goulas and how to write effective grant application **"KAKENHI Writing Seminar"** by Shida. These seminars were held online in order to maximize the dissemination of information/knowledge throughout Japan, with participants from more than 100 academic institutions, thereby contributing to the development of young researchers nationwide.

The experts of the **Research Acceleration Unit** were invited for lectures from institutions outside of KU, including in more rural areas of Japan, to share their expertise with young researchers. **Goulas** was invited to give talks at WPI-IIIS, RIKEN Life Sciences Retreat, and other international conferences, sharing his knowledge on scientific writing and his career. **Inoue** shared her knowledge of how to visualize research effectively to the young researchers at Nippon Medical School. **Shida** shared knowledge for effective research support to the URAs and administrators at the seminars hosted by JICA, and Hiroshima University.

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

* Address the following items, which are essential to mid- to long-term center development:
- Future prospects with regard to the research plan, research organization and PI composition; prospects for fostering and securing of next-generation researchers.
- Prospects for securing resources such as permanent positions and revenues; plan and/or implementation for defining the center's role and/or positioning the center within the host institution's institutional structure
- Measures to sustain the center as a world premier international research center after program funding ends
- Host institution's organizational reforms carried out for the center's autonomous administration simultaneously with the creation of the center.

To maintain the ASHBi's research activities after the end of the WPI program funding, KU will provide various support as described below.

KU's personnel support

- KU has provided 7 tenure professorship positions to ASHBi as of April 2024, two at the establishment of ASHBi (Saitou and Hiraoka) and five after its establishment (three of which are

assigned by Alev, Murakawa, and Seirin). KU is actively seeking the possibility to provide additional posts.

KU's financial support

- Normally, half of the indirect fundings acquired by researchers in KU centers and departments are allocated to the University headquarters. To financially support ASHBi, special measures have been taken by KU to allocate this part of the funding to ASHBi.

- Financial support for hiring at least one post-doctoral fellow for each ASHBi PI in KU will be provided from KU after the end of the WPI program.

- To ensure sustainability and further development of SignAC after the end of the WPI program funding, KU will make SignAC a university-wide shared facility and take responsibility of its personnel, operating costs, and further developments.

- To maintain the ASHBi's administrative functions (including Research Acceleration Unit) after the end of the WPI program funding, KU will provide a special budget to cover the personnel and operating costs of the ASHBi Administrative Office.

KU's system reforms for the ASHBi's autonomous administration

- KU recognizes the importance of giving a high degree of autonomy to the ASHBi Director and the Institute by placing ASHBi within the special framework of the Kyoto University Institute for Advanced Study (KUIAS).

- To secure the employment of outstanding researchers regardless of age, ASHBi/KUIAS has been allowed to hire researchers who have passed the university's mandatory retirement age (65 years old) as faculty members. This systemic reform was extended to some other departments beginning in FY2022.

- To provide flexibility in the salary of tenured faculty members, whose amount is currently uniformly determined by university regulations, special allowance that can be added at the discretion of the Institute has been introduced at ASHBi which has been effective. This allowance system has been extended to the entire university in FY2023 as part of the university reforms.

- KU allows ASHBi to carry a portion of its budget over to the following fiscal year, allowing for more flexible multi-year budget management.

- To increase the ratio of female/non-Japanese PIs, ASHBi will work closely with the KU's "HAKUBI Project", which recruits 15-20 promising researchers from around the world annually. Through this collaboration, ASHBi plans to establish a system that provides opportunity for outstanding female/non-Japanese HAKUBI researchers to join ASHBi as junior PIs.

6. Others

* Describe what was accomplished in the center's outreach activities last year and how the activities have contributed to enhancing the center's "globally visibility." In Appendix 6, describe concretely the contents of these outreach activities. In Appendix 7, describe media reports or coverage, if any, of the activities.
* In addition to the above 1-5 viewpoints, if there is anything else that deserves mention regarding the center project's progress, note it.

The ASHBi's website: To publicize the Institute's research activities to society, we make effective use of websites and social networking services. The Institute's website was launched in FY2018. Although the number of page views has settled between 20,000 and 30,000 since FY2021, the number of active users (who view the webpage for more than 10 seconds or who clicks or scrolls) has steadily increased from 4,000 at the beginning of FY2021 to 8,000 at the end of FY2023.

Outreach to industry: The Institute has the so-called **'First Contact Program'** which provide opportunity for early-career researchers to present their research to the company researchers. This program aims to create interaction opportunities between industry and academia to foster potential future collaborations. In collaboration with the Kyoto Research Park, a industrial hub hosting over 500 companies, 3 seminars were held in FY 2023 acuumulating to a total of 9 seminars since FY2021. In December, the seminar was held for the first time in ASHBi, enabling researchers from industries to visit SignAC to see the analytical equipment and services with their own eyes and to engage in more casual interactions with researchers in ASHBi.

7. 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) **Monkey Project**: There is opportunity for the Center's non-human primate research to be very impactful in tackling human diseases. To address the issue of insufficient supply and high cost of macaque monkeys, ASHBi is considering having its satellite at Shiga University of Medical Science breed the macaque monkeys. The size of the satellite's facility and its current monkey count will need to be assessed toward obtaining a consistent research supply. On the other hand, sufficient ethical reflection should be shown in their work on genetically modified non-human primates.*

Response 1. From FY2024 onwards, in parallel to the development of genetically modified monkeys, we are performing in-house breeding once a month. This will allow us to produce 10 to 20 monkeys annually from FY2025 onwards. To this end, we require approximately 15 oocyte donors and 25 recipients annually. Among approximately 80 monkeys affiliated to ASHBi, about 50 are capable of oocyte retrieval, and thus we assume that we have enough monkeys to achieve our goals. To address the ethical issues, we are conducting appropriate animal experiments based on the principles of the 3Rs (Replacement, Reduction, Refinement). This includes, but are not limited to, efforts to minimize the number of animals used by sharing and utilizing wild-type monkeys as controls for the genetically modified monkeys.

*2) **Mathematics**: ASHBi has created advanced analysis systems like RECODE and V-Mapper. The goal should now be to set these systems as global benchmarks in biological data analysis.*

Response 2. The noise reduction method RECODE is available through ASHBi's website (https://github.com/yusuke-imoto-lab) and has attained 221,846 downloads as of March 11, 2023. Furthermore, several collaborations are currently ongoing within ASHBi using latest data analysis methods developed by the **Hiraoka group**, and we will disseminate these methodologies worldwide by showing their biological impact through high-tier publications.

*3) **Ethics**: ASHBi appears able to become a leader in creating ethical guidelines for research, particular in the domain of stem and germ cells. Eventually, it should share this knowledge internationally.*

Response 3. We have played a leading role in ethics and guideline developments in forefront research areas (e.g., see ***Stem Cell Reports*** S2213-6711(21)00263-0, 2021). Furthermore, in FY2023/2024, we contributed not only to the approval of a long-term culture of PSC-based human embryo models at ASHBi (up to CS12-14) for the first time in Japan, but also to a Cabinet Office task force discussing the regulation of human embryo models, in addition to an expert discussion panel at the Cabinet Office on whether human embryos can be created from stem cell-derived gametes. We will continue to disseminate the findings from these efforts internationally through publications and lectures.

*4) **Clinical Science**: ASHBi should develop "Better Cures for Disease". It is expected that ASHBi will advance research plans aimed at developing new therapies for diseases based on human biology. They should not be satisfied with just developing genetically modified monkey models of human diseases but should proactively investigate ways to develop innovative therapeutic strategies using the monkey models they develop.*

Response 4. Multiple ASHBi PIs collaborate closely with clinicians at KU Hospital, actively collecting clinical samples (including blood, tissue, and fluids) from various departments such as surgery, nephrology, gastroenterology, gynecology, and orthopedic surgery. Their primary goal is to unravel the mechanisms underlying human diseases. For instance, in the Flagship Project of the Medical/Clinical Medicine Group, three ASHBi PIs —each specializing in immunology, functional genomics, and cancer genomics— jointly investigate the immune-evasion process occurring during the transition from primary sclerosing cholangitis to cholangiocarcinoma. This emphasis on understanding disease pathogenesis and identifying novel therapeutic targets underscores the pivotal role of ASHBi PIs in cutting-edge research.

We agree with the comments that the findings in genetically modified monkey models should be used to develop therapeutic strategies. Our finding that abnormal EGFR signaling in collecting ducts potentially contributing to the development of pathological changes in the kidneys of NPH patients suggests that EGFR inhibitors, currently widely used for the treatment of lung cancers, may also be used for the treatment of NPH. We have also identified signaling molecules other than EGFR that are up- or down-regulated in *NPHP1* KO kidneys by snRNA-seq, and therefore currently looking at the potential contribution of these signaling pathways in the progression of NPH using 3D cultures as described above. If the role of these signaling molecules can be determined, they could be additional candidates as therapeutic targets.

Conversely, development of therapeutic strategies against the psychiatric disorders is more complex and difficult. First, we need to clarify the biomarkers based on the pathophysiology and phenotypes of psychosis in our NHP models, which has been extremely difficult in rodent models that have limited frontal lobe functional capacity. The difficulty in human psychosis patients, on the other hand, lies in variability of symptoms which might reflect a variety of genetic and environmental backgrounds. Now, we are getting some behavioral and physiological (reflected in the resting state connectivity revealed by fMRI) phenotypes in the monkey model with identified genetic background, which is the advantage of this system. We need to start by pinning down the pathophysiology and phenotypes of this particular group of model animals. Recently, Prof. Akira Sawa (our collaborator in this project) and his colleagues in Johns Hopkins University showed that deep brain stimulation of the substantia nigra pars reticulata is effective in ameliorating delusion in some of the schizophrenia patients. In the future, we are planning to test the effect of neuromodulation therapies including deep brain stimulation for the treatment of these animals.

*5) **Diversity**: The Center's female and non-Japanese ratios are reasonably good. However, considering the fields related to the Center's research, ASHBi could aim at a higher percentage of female researchers. While ASHBi stated that they are going to recruit more females, they did not tell us much about their plan to increase female researchers in the Center. ASHBi needs to take an even more concerted and strategic approach to encouraging gender diversity, especially at the PI level.*

Response 5. To increase the number of non-Japanese researchers, we established the "ASHBi Foreign Researcher Recruitment Support Program" in 2019. In addition, we have modified this program in 2020 to support the recruitment of female researchers as well to improve the gender balance in the Institute. Through this program, the percentage of female researchers at ASHBi increased from 13% in 2020 to 23% in 2022, and 27% in 2024, showing a steady increase yearly. We will continue this program to further increase the female ratio in ASHBi, while maintaining the

budgetary limit of the Institute for its sustainability. Furthermore, to increase the number of female/non-Japanese PIs at ASHBi, we plan to recruit promising young female/non-Japanese researchers as junior PIs in collaboration with the "HAKUBI Project."

*6) **Support from Kyoto University**: Kyoto University considers ASHBi and SignAC as exemplary models of research organizations and plans to expand them to university-wide system reforms and promises continuing financial support for that.*

Response 6. ASHBi has grown into one of KU's unrivaled high-performing research centers. This has been accomplished by strategically organizing PI members that are well suited to ASHBi's goals of human biology research and by innovatively establishing core facility/administrative functions to effectively support PI groups' research (such as SignAC and ASHBi Administrative Office). These systemic reforms have been highly appreciated by the university headquarters, and KU will support the operating costs of SignAC and the Administrative Office after the WPI program ends, with the intention of developing them into university-wide systemic reforms.

Appendix 1 FY 2023 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2023. (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.

NOTE: The articles published after Jan 2024 in blue for reference.

A WPI Papers

1. Original Articles

1) Aoki, K., Hyuga, M., Tarumoto, Y., Nishibuchi, G., Ueda, A., Ochi, Y., Sugino, S., Mikami, T., Kobushi, H., Kato, I., Akahane, K., Inukai, T., Takaori-Kondo, A., Takita, J., **Ogawa, S.**, & Yusa, K. (2024). Canonical BAF complex regulates the oncogenic program in human T-cell acute lymphoblastic leukemia. ***Blood***, *143*(7), 604-618. doi:10.1182/blood.2023020857

2) Aoki, T., Shiba, N., Tsujimoto, S., Yamato, G., Hara, Y., Kato, S., Yoshida, K., **Ogawa, S.**, Hayashi, Y., Iwamoto, S., Taki, T., Shimada, A., Iijima-Yamashita, Y., Horibe, K., Tawa, A., Taga, T., Adachi, S., & Tomizawa, D. (2024). High IL2RA/CD25 expression is a prognostic stem cell biomarker for pediatric acute myeloid leukemia without a core-binding factor. ***Pediatric Blood & Cancer***, *71*(2). doi:10.1002/pbc.30803

3) Asao, Y., **Hiraoka, Y.**, & Kanazawa, S. (2024). Girth, magnitude homology and phase transition of diagonality. ***Proceedings of the Royal Society of Edinburgh Section a-Mathematics***, *154*(1), 221-247. doi:10.1017/prm.2023.7

4) Boddu, P. C., Gupta, A. K., Roy, R., De La Peña Avalos, B., Olazabal-Herrero, A., Neuenkirchen, N., Zimmer, J. T., Chandhok, N. S., King, D., Nannya, Y., **Ogawa, S.**, Lin, H., Simon, M. D., Dray, E., Kupfer, G. M., Verma, A., Neugebauer, K. M., & Pillai, M. M. (2024). Transcription elongation defects link oncogenic SF3B1 mutations to targetable alterations in chromatin landscape. ***Mol Cell***. doi:10.1016/j.molcel.2024.02.032

5) Kanazawa, S., **Hiraoka, Y.**, Miyanaga, J., & Tsunoda, K. (2024). Large deviation principle for persistence diagrams of random cubical filtrations. ***Journal of Applied and Computational Topology***. doi:10.1007/s41468-023-00161-6

6) Elbadry, M. I., Tawfeek, A., Hirano, T., El-Mokhtar, M. A., Kenawey, M., Helmy, A. M., **Ogawa, S.**, Mughal, M. Z., & Nannya, Y. (2024). A rare homozygous variant in TERT gene causing variable bone marrow failure, fragility fractures, rib anomalies and extremely short telomere lengths with high serum IgE. ***British Journal of Haematology***, *204*(3), 1086-1095. doi:10.1111/bjh.19176

7) Hayashi, A., Mizuno, K., Shinkawa, K., Sakoda, K., Yoshida, S., Takeuchi, M., **Yanagita, M.**, & Kawakami, K. (2024). Effect of multidisciplinary care on diabetic kidney disease: a retrospective cohort study. ***Bmc Nephrology***, *25*(1), 12. doi:10.1186/s12882-024-03550-w

8) **Hiraoka, Y.**, & Shirai, T. (2024). Torsion-weighted spanning acycle entropy in cubical lattices and Mahler measures. ***Journal of Applied and Computational Topology***. doi:10.1007/s41468-024-00163-y

9) Katagiri, T., Iwasaki, H., Fujieda, A., Kasashima, S., Ozaki, S., Uemori, M., **Ogawa, S.**, & Nakao, S. (2024). A case of hepatitis-associated aplastic anaemia following living-donor liver transplantation for fulminant hepatitis showing loss of heterozygosity in the 6p chromosome in the affected liver. ***British Journal of Haematology***, *204*(2), 623-627. doi:10.1111/bjh.19219

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11) Masuda, T., Funakoshi, T., Horimatsu, T., Yamamoto, S., Matsubara, T., Masui, S., Nakagawa, S., Ikemi, Y., **Yanagita, M.**, Muto, M., Terada, T., & Yonezawa, A. (2024). Low serum concentrations of bevacizumab and nivolumab owing to excessive urinary loss in patients with proteinuria: a case series. ***Cancer Chemother. Pharmacol.***, 8. doi:10.1007/s00280-024-04659-3

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14) Nishikawa, A., Ito, I., Yonezawa, A., Itohara, K., Matsubara, T., Sato, Y., Matsumura, K., Hamada, S., Tanabe, N., Kai, S., Imoto, E., Yoshikawa, K., Ohtsuru, S., **Yanagita, M.**, Hirai, T., & Terada, T. (2024). Pharmacokinetics of GS-441524, the active metabolite of remdesivir, in patients receiving continuous renal replacement therapy: A case series. ***J Infect Chemother***, *30*(4), 348-351. doi:10.1016/j.jiac.2023.10.015

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Kaneko, Y., Hasegawa, N., Ueda, S., Sasaki, M., Izumo, T., Inomata, M., Miyazawa, N., Kimura, Y., Suzuki, Y., Harada, N., Ichikawa, M., Takata, T., Ishikura, H., Yoshiyama, T., Kokuto, H., Murakami, K., Sano, H., Ueda, T., Kuwahara, N., Fujiwara, A., Ogura, T., Inoue, T., Asami, T., Mutoh, Y., Nakachi, I., Baba, R., Nishi, K., Tani, M., Kagyo, J., Hashiguchi, M., Oguma, T., Asano, K., Nishikawa, M., Watanabe, H., Okada, Y., Koike, R., Kitagawa, Y., Kimura, A., Imoto, S., Miyano, S., **Ogawa, S.**, Kanai, T., & Fukunaga, K. (2023). Propensity-Score Matched Analysis of the Effectiveness of Baricitinib in Patients With Coronavirus Disease 2019 (COVID-19) Using Nationwide Real-World Data: An Observational Matched Cohort Study From the Japan COVID-19 Task Force. ***Open Forum Infect. Dis.***, *10*(7), 10. doi:10.1093/ofid/ofad311

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2. Review Articles

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

- List up to 10 main presentations during FY 2023 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
2023/12/6	Cantas Alev	Towards reconstituting axial development in vitro	2023 Vienna International ISSCR Symposium - Elucidating the principles of development with stem cells. Vienna, Austria
2023/11/28	Hideki Ueno	Human liver-resident immune cells and their alterations by age	Human Cell Atlas in Asia, Kolkata, India
2023/10/28	Seishi Ogawa	Life history of breast cancer and clonal evolution in breast tissues	127th International Titisee Conference, The Boehringer Ingelheim Fonds, Lake Titisee, Germany
2023/9/7	Tadashi Isa	Large-scale adult brain plasticity for recovery after spinal cord injury in primates.	Benzon symposium no. 67, Copenhagen, Denmark
2023/8/22	Yasuaki Hiraoka	Persistent Homology from Viewpoints of Representation, Probability, and Application	10th International Congress on Industrial and Applied Mathematics (ICIAM) 2023, Tokyo, Japan (every 4 years)
2023/6/14	Sungrim Seirin-Lee	Mathematical Dermatology linking eruption morphology and skin disease	The 8th CIJK Conference on Mathematical and Theoretical Biology, Jeju Island, Republic of Korea
2023/6/2	Takashi Hiiragi	Optimality for developmental robustness	Physics of Biology seminar series, University of Geneva, Switzerland
2023/6/1	Mitinori Saitou	Mechanism and In Vitro Reconstitution of Mammalian Germ-Cell Development	Cold Spring Harbor Laboratory Meeting: on Quantitative Biology - Stem Cells, CSHL, USA
2023/5/23	Guillaume Bourque	Graph genomes reveal missing signal in epigenomic data.	Gordon Research Conference: Cancer Genetics and Epigenetics. Tuscany, Italy
2023/5/8	Misao Fujita	An initiative towards establishing guidelines for fetal tissue research in Japan	Germinal Stem Cell Biology Gordon Research Conference "Induction and Programming of the Germ Cell Lineage", Barcelona, Spain
2023/4/11	Yasuhiro Murakawa	Uncovering new transcripts and RNA regulation in humans using full-length RNA sequencing	FANTOM6 SPRING MEETING Human Technopole, Milan, Italy
2023/4/2	Motoko Yanagita	“Immuno-aging of the Kidney”	ISN World Congress of Nephrology 2023 (WCN’23), Bangkok, Thailand

3. Major Awards

- List up to 10 main awards received during FY 2023 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
2023/12/23	Yasuaki Hiraoka	MIMS Mimura Award, Meiji Institute for Advanced Study of Mathematical Sciences, Meiji University
2023/12/12	Motoko Yanagita	Bywaters Award 2024、International Society of Nephrology (ISN)
2023/09/23	Seishi Ogawa	The 32nd Tomizo Yoshida Prize

Appendix 2　FY 2023 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 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 FY2023> **Principal Investigators Total: 16**

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 SAITOU Mitinori	53	Professor, Kyoto University Institute for Advanced Study, Kyoto University	Cell Biology, Developmental Biology	90%	Oct.30, 2018	Usually stays at the center and participates in the center's activities as Center Director and Executive Board member	
Cantas ALEV	49	Professor Institute for the Advanced Study of Human Biology (WPI-ASHBi) Kyoto University	Developmental Biology	100%	Jul.1, 2019	Usually stays at the center and participates in the center's activities	
AMEMORI Ken-ichi	50	Associate Professor Institute for the Advanced Study of Human Biology (WPI-ASHBi) Kyoto University	Neuroscience	100%	Sep. 1, 2020	Usually stays at the center and participates in the center's activities	
Guillaume BOURQUE	47	Professor, Human Genetics, McGill University	Bioinformatics, Genomics, Epigenomics	25%	Oct.30, 2018	Stays at Kyoto University 3 times per year for 3-4 weeks	Student Exchange utilizing McGill-Kyoto International Joint Program in Genomic Medicine
EMA Masatsugu	55	Professor, Department of Stem Cells and Human Disease Models, Research Center for Animal Life Science, Shiga University of Medical Science	Developmental Biology, Developmental Engineering	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
FUJITA Misao	54	Professor, Center for iPS Cell Research and Application, Kyoto University	Bioethics	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
HIIRAGI Takashi	56	Group Leader/ Professor Hubrecht Institute, Professor, Graduate School of Medicine, Kyoto University	Developmental Biology	23%	Oct.30, 2018	Stays at the center every 2-3 months and participates in the center's activities	
Vice director HIRAOKA Yasuaki	46	Professor, Kyoto University Institute for Advanced Study, Kyoto University	Applied Mathematics	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities as Vice Director and Executive Board member	

ISA Tadashi	63	Professor/Dean, Graduate School of Medicine, Kyoto University	Neuroscience	80%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
MURAKAWA Yasuhiro	41	Professor Kyoto University Institute for Advanced Study, Kyoto University	HumanGenomics, Medical Science, Systems Biology	100%	Sep. 1, 2020	Usually stays at the center and participates in the center's activities	
OGAWA Seishi	62	Professor, Department of Pathology and Tumor Biology, Graduate School of Medicine, Kyoto University	Molecular Oncology	90%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
Sungrim SEIRIN-LEE	46	Professor Institute for the Advanced Study of Human Biology (WPI-ASHBi) Kyoto University	Mathematical Biology&Medicine , Mathematical modeling, Applied Mathematics	100%	Oct.1, 2021	Usually stays at the center and participates in the center's activities	
Vice director Hideki UENO	56	Professor, Graduate School of Medicine, Kyoto University	Immunology	95%	Oct.30, 2018	Usually stays at the center and participates in the center's activities as Vice Director and Executive Board member	
YAMAMOTO Ryo	48	Associate Professor Institute for the Advanced Study of Human Biology (WPI-ASHBi) Kyoto University	Hematology	100%	Apr. 1, 2020	Usually stays at the center and participates in the center's activities	
Core Head (SignAC) YAMAMOTO Takuya	46	Associate Professor, Department of Life Science Frontiers, Center for iPS Cell Research and Application, Kyoto University	Molecular Biology, Bioinformatics	80%	Oct.30, 2018	Usually stays at the center and participates in the center's activities as Executive Board member	
YANAGITA Motoko	54	Professor, Graduate School of Medicine, Kyoto University	Nephrology	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	

*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 2023

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)

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

Academic degree and specialty

Effort **%**

* 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

Achievements and highlights of past research activities

Achievements

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

a) Recipient of international awards

b) Member of a scholarly academy in a major country

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

d) Editor of an international academic journal

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

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

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

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

Appendix 3-1 FY 2023 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.

- KU has provided 7 professorship tenure positions to ASHBi by April 2024, at the establishment of ASHBi (Saitou and Hiraoka) and five after its establishment (three of which are assigned to Alev, Murakawa, and Seirin). KU is actively seeking the possibilities of providing additional posts.
- To increase the number of female/non-Japanese researchers, we continue to utilize the "ASHBi Foreign and Female Researcher Recruitment Support Program" established in 2019. With this program, PIs can receive personnel cost of up to 5.5 million yen for hiring new non-Japanese or female researchers. Through this support, the number of non-Japanese/female researchers was increased or maintained in FY2023. As of April 2024, the ratio of non-Japanese researchers has increased to 40% and that of female researchers to 27%.

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
Shiga University of Medical Science	Masatsugu Ema	Primate Genome Editing Core (PRiME) is located in the Satellite (Core Head: Tomoyuki Tsukiyama)

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes

2. Holding international research meetings

- Indicate the number of international research conferences or symposiums held in FY2023 and give up to three examples of the most representative ones using the table below.

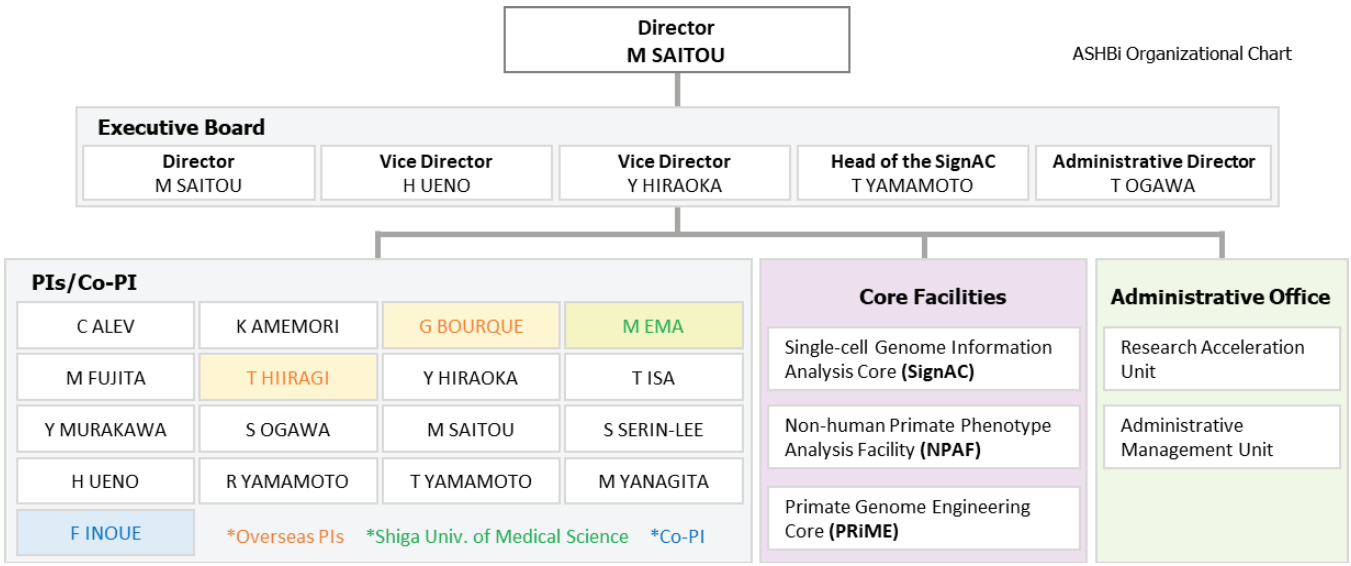
FY 2023: 3 meetings

Major examples (meeting titles and places held)	Number of participants
ASHBi Workshop – Towards engineering embryonic development – July 20, 2023 Faculty of Medicine Memorial Auditorium, Kyoto University	**Total:** From domestic institutions: 71 From overseas institutions: 7 **Speakers:** From domestic institutions: 5 From overseas institutions: 3

OKO International Symposium 2023 – Mathematical Biology from Genes to Cells to Humans – *Join symposium with University of **O**xford, **K**yoto University and **O**hio State University* August 28 – 31, 2023 Shirankaikan, Kyoto University	**Total:** From domestic institutions: 64 From overseas institutions: 43 **Speakers:** From domestic institutions: 10 From overseas institutions: 21
Master's Lecture – Visions for development, stem cells and epigenetics – November 21, 2023 Shirankaikan, Kyoto University	**Total:** From domestic institutions: 182 From overseas institutions: 9 **Speakers:** From domestic institutions: 0 From overseas institutions: 3

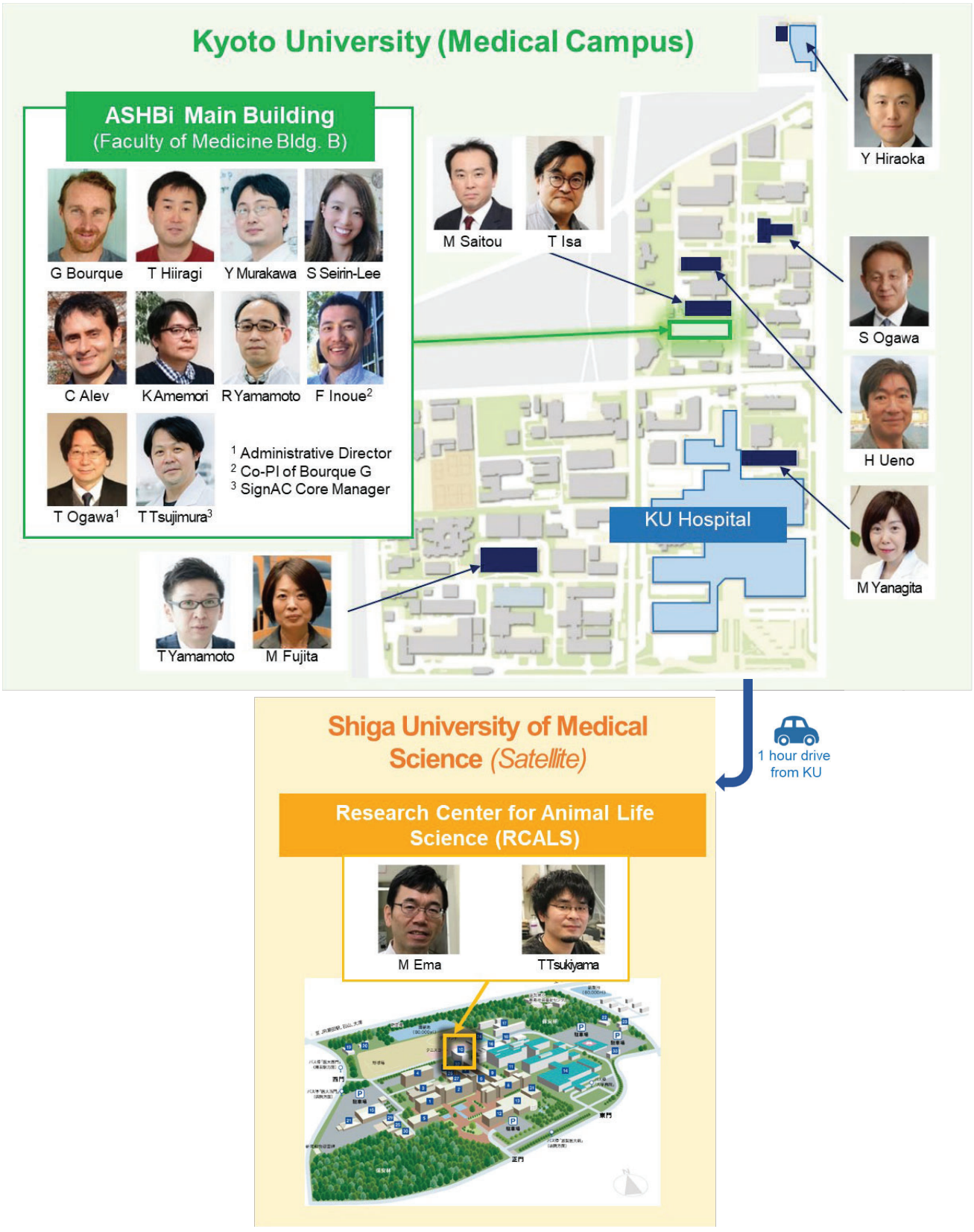
3. Diagram of management system

- 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 FY2023

Total: 1,932,742,590 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.

[Breakdown according to type of funding]

Type of Funding	Funding Amount
Grants-in-Aid for Scientific Research (KAKENHI)	300,193,736 yen
Commissioned Research Projects	1,149,975,057 yen
Joint Research Projects	201,375,245 yen
Others (Donation funds, etc)	281,198,552 yen
Total* (total for above mentioned)	**1,932,742,590 yen**

[Acquired large-scale research grants (30,000,000+ yen)]

Organization	Fund name	PI	Funding amount
AMED	Japan Initiative for World-leading Vaccine Research and Development Centers (Support institutions)	Hideki Ueno	254,003,205 yen
AMED	Biobank-Construction and Utilization biobank for genomic medicine Realization (Genome Research Biobank)	Seishi Ogawa	228,000,000 yen
Open Philanthropy	Open Philanthropy Fund	Mitinori Saitou	176,266,875 yen
AMED	Moonshot Research and Development Program	Seishi Ogawa	116,458,661 yen
AMED	Advanced Research & Development Programs for Medical Innovation (AMED-CREST)	Seishi Ogawa	74,850,000 yen
KAKENHI	Grant-in-Aid for Specially Promoted Research	Mitinori Saitou	58,600,000 yen
Company	Collaborative research	Ryo Yamamoto	56,705,602 yen
Company	Collaborative research	Motoko Yanagita	37,409,309 yen
JST	Strategic Basic Research Programs (CREST)	Takuya Yamamoto	36,500,000 yen
AMED	Basis for Supporting Innovative Drug Discovery and Life Science Research (BINDS program)	Taro Tsujimura	35,446,201 yen

Company	Collaborative research	Seishi Ogawa	31,639,734 yen
AMED	Moonshot Research and Development Program	Motoko Yanagita	31,000,000 yen

Appendix 3-1a FY 2023 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 2023	Final goal (Date: March, 2025)
Researchers from within the host institution	8	13	13
Researchers invited from overseas	4	2	2
Researchers invited from other Japanese institutions	1	1	1
Total principal investigators	13	16	16

b) Total members

	At the beginning of project		At the end of FY 2023		Final goal (Date: March, 2025)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	13		68		70	
Overseas researchers	4	31	27	40	26	37
Female researchers	3	23	19	28	21	30
Principal investigators	13		16		16	
Overseas PIs	4	31	4	25	4	25
Female PIs	3	23	3	19	3	19
Other researchers	0		24		27	
Overseas researchers	0	0	5	21	8	30
Female researchers	0	0	5	21	9	33
Postdocs	0		28		27	
Overseas postdocs	0	0	18	64	14	52
Female postdocs	0	0	11	39	9	33
Research support staffs	2		33		22	
Administrative staffs	3		33		30	
Total number of people who form the "core" of the research center	18		134		122	

	At the beginning of project		At the end of FY 2023		Final goal (Date: March, 2025)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	-		81		90	
Employed	-	0.0	14	17.3	20	22.2

※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" culumn 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	Center director and administrative director	30	4
	Principal investigators (no. of persons):14	160	42
	Other researchers (no. of persons):44	259	228
	Research support staff (no. of persons):56	132	117
	Administrative staff (no. of persons):37	113	61
	Subtotal	694	452
Project activities	Research startup costs	25	0
	Fusion Research startup cost	100	86
	Cost of satellite organizations, etc.	165	78
	Cost of international symposiums	26	6
	Rental fees for facilities	24	2
	Cost of utilities	12	0
	Cost of maintenance of Core Facility	55	21
	Cost of Young Researcher Foster programs	2	1
	Cost of outreach	4	0
	Cost of maintenance contracts	30	13
	Cost of consumables, etc.	25	7
	Other costs	0	0
	Subtotal	468	214
Travel	Domestic travel costs	2	0
	Overseas travel costs	4	3
	Travel and accommodations cost for invited scientists	1	0
	Travel cost for scientists on transfer	0	0
	Subtotal	7	3
Equipment	Cost of laboratory maintenance (repair work, etc.)	31	31
	Cost of open laboratory equipments maintenance, etc.	25	0
	Subtotal	56	31
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	16	0
	KAKENHI	300	0
	Commissioned research projects, etc.	1,150	0
	Joint research projects	202	0
	Ohers (donations, etc.)	281	0
	Subtotal	1,949	0
Total		3,174	700

Costs (Million yens)

WPI grant in FY 2023	700
Costs of establishing and maintaining facilities	25
Repairing facilities	25
(Number of facilities:2, 2,043 m²)	
Costs of equipment procured	6
Telemetry implant system	5
(Number of units:1)	
Monkey Brain Matrix	1
(Number of units:1)	

*1. Management Expenses Grants (including Management Enhancements Promotion Expenses (機能強化経費)), subsidies including National university reform reinforcement promotion subsidy (国立大学改革強化推進補助金) 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"

*1 運営費交付金（機能強化経費を含む）、国立大学改革強化推進補助金等の補助金、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):1		
	Other researchers (no. of persons):3		
	Research support staff (no. of persons):1		
	Administrative staff (no. of persons):0		
	Subtotal	29	20
Project activities	Subtotal	36	36
Travel	Subtotal	0	0
Equipment	Subtotal	22	22
Research projects	Subtotal	45	0
Total		132	78

Appendix 4 FY 2023 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2023 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. 2024 and not described in Appendix 1.

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

1)
2)
3)
4)

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

1)
2)
3)
4)

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2023. 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
FY2023					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023					

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
FY2023					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023					

Appendix 5 FY 2023 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: 81

	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	ROBERT DE MASSY, Bernard Jean Paul	65	Research Director, Institute of Human Genetics	France	PhD Molecular Biology	Research Director and Head of Meiosis and recombination research team, Institut de Genetique Humaine, CNRS 2016 Coups d'Élan Awards for French Research, Bettencourt Schueller Foundation 2012 médaille d'argent du CNRS	2023/3/5-4/21	short-term stay as an invited researcher for joint research
2	GROZA, Cristian	28	PhD student, Quantitative Life Sciences, McGill University	Canada	JSPS Postdoctoral Fellowships, short-term	Mr. Cristian Groza is a PhD student at Bourque lab in McGill University, Canada and joins Inoue lab at ASHBi as a JSPS short-term international fellow.	2023/4/4-6/3	joined the lab as part of a short term research, Speaker at the ASHBi Seminar
3	Barry Richmond		Chief, Section on Neural Coding and Computation (SNCC), NIH	USA	PhD	He is board certified in Pediatrics and Neurology with Special Competence in Child Neurology. He joined the Laboratory of Neurobiology in 1976 to study the neurophysiology of the visual system in awake, behaving monkeys. In 1980 he joined the Laboratory of Neuropsychology to set up a program to study how information about visual stimuli is encoded and processed by single neurons and ensembles of neurons. This work led to formation of the Section on Neural Coding and Computation in 1996.	2023/4/7	Speaker at ASHBi Seminar
4	Mark Eldridge		Postdoctoral Fellow, NIH	USA	PhD Neuroscience	His research focuses on understanding how the perceptual and reward value systems interact in the formation of visual memory in non-human primates. He uses traditional techniques (e.g. aspiration lesions & pharmacology), combined with the application of modern molecular tools (e.g. chemogenetics) to explore the neural substrates of recognition, categorization and stimulus value assignment in the inferior temporal lobe and inter-connected regions.	2023/4/7	Speaker at ASHBi Seminar
5	Niklas Kolbe		Postdoc, RWTH Aachen University	Germany	PhD, applied mathematics	Postdoc in the group of Michael Herty at the Institute for Geometry and Applied Mathematics (IGPM) of RWTH Aachen University working on numerical methods for hyperbolic and parabolic differential equations and on mathematical modeling.	2023/4/13 - 26	short-term stay for joint research
6	Henry Evrard		Senior Investigator, International Center for Primate Brain Research, Chinese Academy of Sciences	China	PhD	In 2021, he joined the ICPBR and CEBSIT/ION at the Chinese Academy of Sciences as a Senior Investigator. Dr. Evrard further holds faculty positions at the Nathan Kline Institute for Psychiatric Research (NKI, USA) and the Center for Integrative Neuroscience (CIN, Germany). He is also a guest scientist at the University of Leuven (Belgium) and at the Yale School of Medicine (USA). Together with Drs. George Paxinos and Michael Petrides, he co-authored the novel edition of the Rhesus Monkey Brain in Stereotaxic Coordinates, an influential brain atlas that guides non-human primate neuroscience research in numerous laboratories worldwide.	2023/4/19	Speaker at ASHBi Seminar

	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				
7	Steve I. Perlmutter		Research Associate Professor, Department of Physiology & Biophysics /Research Affiliate, Washington National Primate Research Center, University of Washington	USA	PhD Neuroscience and Physiology	Dr Perlmutter is a professor at the University of Washington specialized in Computational neuroscience and Systems neuroscience. His lab is interested in interdisciplinary, collaborative approaches to facilitate neural regeneration in corticospinal pathways after spinal cord injury.	2023/4/24	Speaker at ASHBi Seminar
8	Sébastien Mace		The École Normale Supérieure de Rennes (ENS Rennes)	France	bachelor		2023/5/15 - 7/15	short-term stay for internship
9	Seong-min KIM	27	Graduate Student, Seoul National University College of Pharmacy	Korea	Graduate Student	Joined the lab as part of a collaboration with the Hyuk-Jin Cha lab at SNU; will rejoin our lab in 2024 as a post-poc	2023/6/5-8/29	Joined the lab as part of a collaboration with the Hyuk-Jin Cha lab at SNU
10	Eikan Mishima		Senior scientist, Helmholtz Zentrum München Adjunct Instructor, Tohoku University School of Medicine	Germany	MD, PhD	Dr. Eikan Mishima conducted various studies at the Department of Nephrology, Rheumatology and Endocrinology, Tohoku University before coming to Helmholtz Zentrum München, where he elucidated the regulatory mechanism of ferroptosis and published his findings in Nature last year. Oshima Award JSN 2023, Helmholtz Munich Best Paper Award 2022, etc.	2023/6/7	Speaker at ASHBi Seminar
11	Xaq Pitkow		Associate Professor, Neuroscience Institute, Carnegie Mellon University	USA	PhD	Dr Pitkow's lab aims to understand how the brain works using mathematical principles. In August 2023, Dr. Pitkow became the Associate Professor at the Carnegie Mellon University, in the Neuroscience Institute and with affiliation to the Department of Machine Learning in the School of Computer Science.	2023/6/15	Speaker at ASHBi Seminar
12	Jerome N. Sanes		Professor, Department of Neuroscience, Rober J. and Nancy D. Carney Institute for Brain Science, Brown University	USA	PhD	Professor Sanes studies brain mechanisms of voluntary movement, motor learning and non-image forming vision using neuroimaging, neurophysiology, and behavioral methods in healthy adults and individuals with brain disorders. He has published approximately 90 scientific articles, with work appearing in Science, the Proceedings of the National Academy of Science, the Journal of Neuroscience, the Journal of Neurophysiology, Cerebral Cortex, and other leading neuroscience journals.	2023/7/17-18	Speaker at ASHBi Seminar
13	Mo Ebrahimkhani		Associate Professor Department of Pathology, Experimental Pathology Unit Pittsburgh Liver Research Center The McGowan Institute for Regenerative Medicine University of Pittsburgh	USA	MD	Dr. Ebrahimkhani leads the Laboratory for Synthetic Biology and Regenerative Medicine which combines synthetic biology, systems biology and stem cell engineering to advance regenerative medicine. Mayo Clinic accelerated regenerative medicine award New Investigator Award from Arizona Biomedical Research Council Charles E Kaufman Foundation initiative award	2023/7/20	Speaker at ASHBi workshop ASHBi Workshop "Towards engineering embryonic development"

	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				
14	Vincent Pasque		Group leader Laboratory of Epigenetic Reprogramming, KU Leuven	Netherlands	PhD Developmental Biology	UCLA Molecular Biology Institute Research Excellence Award for Excellent Postdoctoral Research in Molecular Biology, Chemistry and Biochemistry. 2015 UCLA Chancellor's Award for postdoctoral research with honorable mention. 2015 Journal of Cell Science Prize for Young Scientist for best paper published in 2012, shared with Dr. Aliaksandra Radzisheuskaya. 2013 Wellcome Trust 2012 Image Award. 2012 Gurdon Institute Annual Report Cover Competition. 2011 Woods Hole Marine Biological Laboratory Photomicrography Prize. 2009	2023/7/20	Speaker at ASHBi workshop ASHBi Workshop "Towards engineering embryonic development"
15	Nika Shakiba		Allen Distinguished Investigator, Assistant Professor, School of Biomedical engineering, University of British Columbia	Canada	PhD	Dr. Shakiba's research program seeks to apply a combined systems and synthetic biology approach to reverse- and forward-engineer the role of cell competition in developmental and stem cell systems. 2022 Allen Distinguished Investigator 2021 Michael Smith Foundation of Health Research Scholar Award 2018 NSERC Postdoctoral Fellowship 2017 Gordon Cressy Leadership Award 2015 Jennifer Dorrington Graduate Research Award	2023/7/20	Speaker at ASHBi workshop ASHBi Workshop "Towards engineering embryonic development"
16	Elli Papaemmanuil	42	Memorial Sloan Kettering Cancer Center (MSK)	USA	Ph.D. Molecular genetics	Awards Josie Robertson Investigator Award; Giuseppe Sciaccia International Award; Top Women Hellenic Awards Woman Scientist of the Year; Tito Bastianello Young Investigators Award; Damon Runyon-Rachleff Innovation Award	2023/7/24	short-term stay for giving a seminar "Precision midicine for pediatric cancer"
17	Philip K. Maini		University of Oxford	UK	PhD, Mathematics	Since 1998, he has been the Professor of Mathematical Biology at the University of Oxford and is the director of the Wolfson Centre for Mathematical Biology in the Mathematical Institute. 1982 Prosser Prize, Balliol College, Oxford 1997 Bellman Prize for best paper published in Mathematical Biosciences 1994-96 (paper [44]) 2006-11 Royal Society-Wolfson Research Merit Award 2009 LMS Naylor Prize 2013 MPLS Teaching Award: Individual Award (Oxford) 2014 ISI Web of Knowledge High Cited Researcher (top 1% of researchers 2002-14) 2014 Listed in "The World's Most InFluential Scentific Minds 2014" (Thomson Reuters) 2015 Elected Fellow of the Royal Society (FRS) 2017 SMB Arthur T. Winfree Prize 2017 Inaugural Fellow of the Society of Mathematical Biology	2023/7/24 - 31	short-term stay for joint research ASHBi Summer Camp

	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				
18	Jun Wu		Associate Professor, University of Texas Southwestern Medical Center	USA	PhD Cell and Molecular Biology, Genetics, Development and Disease	In 2018, Dr. Wu joined UT Southwestern as an assistant professor in the Department of Molecular Biology. 2018 Virginia Murchison Linthicum Scholar in Medical Research 2017 CPRIT Scholar: First-Time, Tenure-Track Faculty Members Program	2023/7/26	Speaker at ASHBi Seminar
19	Adriana Dawes		Professor,The Ohio State University	USA	PhD, Applied Mathematics	Prof. Dawes' research tightly weaves experimental and theoretical approaches to better understand how biochemical, mechanical and geometric cellular features interact and regulate each other during development to give rise to a functional organism. Prof. Dawes is the recipient of an NSF CAREER award, and has also been funded by NIH and private foundations including the Gordon and Betty Moore Foundation.	2023/7/28 - 9/28	joint research OKO symposium Speaker at ASHBi Seminar
20	Pamela Guruciaga	34	Postdoctoral fellow, European Molecular Biology Laboratory (EMBL)	Germany	PhD	Since April 2021 she is a postdoc at the European Molecular Biology Laboratory, Germany, where she now uses the tools of statistical physics to study biological problems. She is particularly interested in symmetry-breaking processes in morphogenesis and the role of the environment in tissue patterning. She is a Marie Curie Fellow (EIPOD4) and a member of the Joachim Herz Foundation.	2023/8/1-4	Presentation in ASHBi Seminar (1st Aug.) and discussion about collaborative research
21	Tianyi Mao		Associate Professor, Vollum Institute Oregon Health and Science University Portland, Oregon	USA	PhD Neuroscience	Mao was appointed as an assistant scientist at the Vollum Institute in September 2010 and was promoted to scientist in 2017.	2023/8/10	Speaker at ASHBi Seminar
22	Eamonn Gaffney		Professor of Applied Mathematics, Mathematical Institute, University of Oxford	UK	PhD	His research objectives are typically to extract the macroscale consequences of mechanisms operating at much smaller scales, usually the microbiological level, for instance how cells interact and signal, together with the associated biophysics of reaction, diffusion, deformation and flow.	2023/8/12 - 31	OKO symposium
23	Won Seok LEE	29	Graduate Student, Seoul National University College of Medicine	Korea	Graduate Student	Joined experiments in the lab as part of a research internship	2023/8/20-9/17	Joined experiments in the lab as part of a research internship
24	Keita Tamura		Assistant Professor, PI, Department of Physiology, Development and Neuroscience, University of Cambridge	UK	PhD	Dr. Tamura is a physiologist studying cognitive functions. In 2022, he joined PDN as an Assistant Professor to study neuronal circuits for cognition and memory by opto-physiological approaches in animal models.	2023/8/21	Speaker at ASHBi Seminar
25	Adam Maclean		Assistant Professor of Quantitative and Computational Biology, University of Southern California	USA	PhD, Systems Biology	His group focuses on developing mathematical and computational methods to study stem cell fate. Ultimately, his group seeks to derive a mechanistic theory for stem cell function in health and disease.	2023/8/28 - 31	OKO symposium

	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				
26	Alex Mogilner		Professor, Courant Institute and Department of Biology, New York University	USA	PhD, Appl. Math	Alex Mogilner is an American professor at the Courant Institute of Mathematical Sciences and the Department of Biology at New York University. His major contribution to science are in the areas of cell motility and division and innovations in cell imaging. His key papers on the subject have been cited hundreds of times; the most cited one, in Biophysical Journal has been cited 614 times by October 2014.	2023/8/28 - 31	OKO symposium
27	Andrew Krause		Assistant Professor in Applied Mathematics, Department of Mathematical Sciences, Durham University	UK	PhD, Mathematics	Dr. Krause is primarily involved in teaching and research within mathematical biology and nonlinear dynamical systems. 2020 Mathematical Institute Award for Excellence, University of Oxford	2023/8/28 - 31	OKO symposium
28	Anita Layton		Professor, University of Waterloo	Canada	PhD, Computer Science	Anita Layton is the Canada 150 Research Chair in Mathematical Biology and Medicine, and Professor of Applied Mathematics, Computer Science, Pharmacy and Biology at the University of Waterloo. She leads a diverse and interdisciplinary team of researchers who use computational modeling tools to better understand aspects of health and disease. 2021 Krieger-Nelson Prize 2021 Canada's Most Powerful Women: Top 100 Award 2023 John L. Synge Award, Royal Society of Canada.	2023/8/28 - 31	OKO symposium
29	Barbara Keyfitz		Professor of Mathematics, Ohio State University	USA	PhD	Barbara Lee Keyfitz is the Dr. Charles Saltzer Professor of Mathematics at Ohio State University. In her research, she studies nonlinear partial differential equations and associated conservation laws. 2005 Krieger–Nelson Prize, Canadian Mathematical Society 2011 Noether Lecturer, Association for Women in Mathematics 2012 SIAM Prize for Distinguished Service to the Profession 2012 AWM-SIAM Sonia Kovalevsky Lecturer	2023/8/28 - 31	OKO symposium
30	Benjamin Walker		Research Fellow, University College London	UK	PhD	Dr. Wlker's research interests are in Solid mechanics and biological growth, Filament mechanics, Microscale swimming, Flagellar analysis, and Slender-body theory.	2023/8/28 - 31	OKO symposium
31	Calina Copos		Assistant Professor of Mathematics, College of Science, Northeastern University	USA	PhD, Applied Mathematics	Calina Copos is a mathematical biologist with applications to cell locomotion and cell cytoskeleton dynamics.	2023/8/28 - 31	OKO symposium
32	Carsten Conradi		Professor, Life Science Engineering, Hochschule für Technik und Wirtschaft Berlin	Germany	PhD	Carsten Conradi is a professor focusing on Bioprocess control and simulation at the Berlin University of Technology and Economics.	2023/8/28 - 31	OKO symposium
33	Elebeoba (Chi-Chi) May		Associate Professor, University of Wisconsin	USA	PhD, Computer Engineering	As Director of the Multi-scale Immunobiology Design, Algorithms, and Simulation (MIDAS) Lab, Dr. May's research focuses on the design of integrated quantitative and empirical platforms for the development of multi-scale, predictive models of biological systems.	2023/8/28 - 31	OKO symposium

	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				
34	Jessica Crawshaw		Postdoc, Mathematical Institute, University of Oxford	UK	PhD	2020: SMB Presentation award 2020: The Cheryl E. Praeger travel grant 2020: ANZIAM travel grant 2019: ANZIAM travel grant 2018: SBM travel grant	2023/8/28 - 31	OKO symposium
35	Leah Edelstein-Keshet		Professor, The University of British Columbia	Canada	PhD, Applied Mathematics	Dr. Edelstein-Keshet is known for her contributions to the field of mathematical biology and biophysics. Her research spans many topics including sub-cellular biology, ecology, and biomedical research, with particular focus on cell motility and the cytoskeleton, modeling of physiology and diseases, such as autoimmune diabetes, and swarming and aggregation behavior in social organisms. 2003 Krieger–Nelson Prize of the Canadian Mathematical Society	2023/8/28 - 31	OKO symposium
36	Marcus Tindall		Professor, Head of the Department of Mathematics and Statistics, University of Reading	UK	PhD	Mathematical biologist whose primary interest is in the mathematical modelling of biological and biomedical systems. He works with international leading life scientists in academic institutions and industry to formulate and solve mathematical models which are used to understand the system of interest, test hypotheses and direct future experimental/practical work.	2023/8/28 - 31	OKO symposium
37	Mariia (Masha) Dvoriashyna		Chancellor's Fellow (equivalent to a Lecturer), School of Mathematics, University of Edinburgh	UK	PhD, Fluid Dynamics and Environmental Engineering	Dr Dvoriashyna's research interests lie in applying mathematics to problems in biology and physiology. The general scope of her research is to develop continuum models aimed at understanding and explaining experimentally and/or clinically observed phenomena and predicting physical quantities of interest.	2023/8/28 - 31	OKO symposium
38	Mark Coles		Professor, Immunology, Kennedy Institute of Rheumatology, University of Oxford	UK	PhD Molecular Cell Biology	Dr. Coles is a Professor of Immunolgy at the Kennedy Institute of Rheumatology and also is a Kennedy Trust Senior Research Fellow, Director of Graduate Studies, Official Fellow at Reuben College, Theme Lead for Cellular Life Parks College and Affiliate Faculty Mathematics Institute.	2023/8/28 - 31	OKO symposium
39	Marty Golubitsky	79	Distinguished Professor,The Ohio State University	USA	PhD, Mathematics	Martin Golubitsky is Distinguished Professor of Natural and Mathematical Sciences at the Ohio State University. He received his PhD in Mathematics from M.I.T. in 1970 and has been Professor of Mathematics at Arizona State University, Cullen Distinguished Professor of Mathematics at the University of Houston. At Ohio State, he served as Director of the Mathematical Biosciences Institute (2008-16). 1997 University of Houston Esther Farfel Award 2001 Ferran Sunyer i Balaguer Prize 2009 Moser Lecture Prize of the SIAM Dynamical Systems Activity Group. 2005-2006 President, Society for Industrial and Applied Mathematics (SIAM)	2023/8/28 - 31	OKO symposium

	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				
40	Michael Shelley		Lilian and George Lyttle Professor of Applied Mathematics Professor of Mathematics, Neural Science, and Mechanical Engineering, Co-Director, Applied Mathematics Laboratory,New York University	USA	PhD, Applied Mathematics	Besides to his position as a professor, Dr. Shelleyy is also a Director at the Center for Computational Biology and a Group Leader at the Biophysical Modeling of The Flatiron Institute, Simons Foundation	2023/8/28 - 31	OKO symposium
41	Mike Murrell		Associate Professor of Biomedical Engineering, Yale School of Engineering & Applied Science, Yale University	USA	PhD, Biological Engineering	Dr Murrell's research interests are in understanding the mechanical principles that drive major cellular life processes through the design and engineering of novel biomimetic systems.	2023/8/28 - 31	OKO symposium
42	Pablo A. Iglesias		Interim Department Head and Edward J. Schaefer Professor, Johns Hopkins Whiting School of Engineering, Johns Hopkins University	USA	PhD, Information Engineering	Dr Iglesias uses computational techniques grounded in control and information theory to study biological signal transduction pathways. In addition to his primary appointment in the Department of Electrical and Computer Engineering, he holds secondary appointments in the Department of Applied Mathematics and Statistics and the departments of Cell Biology and Biomedical Engineering at the School of Medicine.	2023/8/28 - 31	OKO symposium
43	Tetsuya Hiraiwa		Associate Research Fellow, PI, Institute of Physics, Academia Sinica	Taiwan	PhD, 理学	Formaerly a MBI fellow at National University of Singapore, his research subject continues to be theoretical physical biology based on physics of softmatter, far-from-equilibrium systems and complex systems, and a major aim is to seek the possible mechanisms and roles of dynamic self-organization processes in living organisms.	2023/8/28 - 31	OKO symposium
44	Sara Merino-Aceituno		Associate Professor, Faculty of Mathematics, University of Vienna	Austria	PhD Mathematics	Dr Merino works in kinetic theory applied to the study of emergent phenomena in biology, medicine and social sciences using partial differential equations, probability, numerical simulations and modelling.	2023/8/28 - 9/8	short-term stay for joint research OKO symposium
45	Herbert Edelsbrunner	64	Professor, IST Austria	Austria	PhD	Herbert Edelsbrunner is a computer scientist working in the field of computational geometry, the Arts & Science Professor of Computer Science and Mathematics at Duke University, Professor at the Institute of Science and Technology Austria (ISTA), and the co-founder of Geomagic, Inc. He was the first of only three computer scientists to win the National Science Foundation's Alan T. Waterman Award.	2023/9-2024/8	stay for joint research
46	Nobuhiro Morone	56	Head of Electron Microscopy & Ultrastructural Pathology Facility, MRC Toxicology Unit, University of Cambridge	UK	PhD.	2015-Present Senior Investigator Scientist at MRC Toxicology Unit and visiting Professor at Kyoto University, Kyoto, Japan. 2010-2015 Senior Lecturer at iCeMS Kyoto University, Kyoto, Japan.	2023/9/4-5	Guidance and advice on collaborative research

	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				
47	Maria Anisimova		Professor, Computational Genomics, Zürich University of Applied Sciences Group leader, Swiss Institute of Bioinformatics	Switzerland	PhD statistical genomics	Maria Anisimova leads the Applied Computational Genomics Team at the Institute of Applied Simulations (ZHAW – Zurich University of Applied Sciences) and at the SIB – Swiss Institute of Bioinformatics.Her areas of expertise and research interests include stochastic modeling and simulations that can be used on genomic data, algorithm development for genomic sequence analysis; methods for evolution, and semantic web technologies with applications for various problems in pharmacology, forensic medicine, ecology, and agriculture.	2023/10/10	Speaker at ASHBi Seminar
48	Ilse Ariadna Valtierra Gutierrez		Senior Editor, Cancer Team, Nature Communications	UK	PhD	Ilse joined Nature Communications in June 2020. She did her PhD at the Ludwig Maximilian University of Munich, where she studied clonal heterogeneity and evolution in acute myeloid leukaemia using genomic and single-cell transcriptomic data.	2023/10/11	Speaker at ASHBi Seminar
49	Maria Anisimova		Professor, Computational Genomics Zürich University of Applied Sciences Group leader, Swiss Institute of Bioinformatics	Swiss	PhD Computational Genomics	2021- Professor in Computational Genomics 2015- Research Group leader, Swiss Institute of Bioinformatics (SIB), Switzerland 2014- Research Group leader, ZHAW Wädenswil, Switzerland	2023/10/23	ASHBi Seminar
50	Ian Chambers		Head of Institute, Institute for Stem Cell Research, School of Biological Sciences, The University of Edinburgh	UK	PhD Embryonic stem cell biology	Hooke Medal 2020	2023/11/15	Joint Meeting
51	Elisa Barbieri		Marie-Curie Postdoc, The University of Edinburgh	UK	PhD Embryonic stem cell biology	Postdoc in the Chambers lab, University of Edinburgh	2023/11/15	Joint Meeting
52	Ella Thomson		Post Doctoral Research Assistant, The University of Edinburgh	UK	PhD Embryonic stem cell biology	Post Doctoral Research Assistant in the Chambers lab, University of Edinburgh	2023/11/15	Joint Meeting
53	Sara Brito Gonzalez		PhD Student, The University of Edinburgh	UK	-	PhD student in the Chambers lab, University of Edinburgh	2023/11/15	Joint Meeting
54	Hiroshi Hamada	73	Visiting Professor, National Center for Biological Sciences, Distinguished Visiting Professor, Ashoka University	India	MD, PhD	former Team leader at RIKEN BDR 2022 Foreign Member of the Royal Society 2016 Associate Member of the European Molecular Biology Organization 2023 Orders of the Sacred Treasure, Japan 2017 Toray Science and Technology Prize 2014 Medal with Purple Ribbon, Medal of Honour 2014 Keio Medical Science Prize	2023/11/21	Speaker at Master's Lecture

	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				
55	Austin Smith	64	Director, Living Systems Institute, University of Exeter	UK	PhD Developmental Genetics	He is notable for his pioneering work on the biology of embryonic stem cells. 2016 McEwen Award for Innovation, ISSCR 2010 Member of Academia Europaea 2010 Prix Louis-Jeantet de médicine 2006 Fellow of the Royal Society of London 20014, Member, EMBO 2003 Medical Research Council Professor 2003 Fellow of the Royal Society of Edinburgh 2002 Ellison-Cliffe Medal, Royal Society of Medicine 2000 Pfizer Academic Award	2023/11/21	Speaker at Master's Lecture
56	Azim Surani	79	Director of germline and epigenetics research, Gurdon Institute, University of Cambridge	UK		2022 Mendel Medal, Genetics Society 2018 Canada Gairdner International Award 2014 McEwen Award for Innovation, International Society for Stem Cell Research 2014 Jawaharlal Nehru Fellowship, Government of India 2010 Galton Lecture, The Galton Institute 2010 Royal Medal, Royal Society 2010 Mendel Lecture (Brno, Czech Republic) 2007 Commander of the British Empire for services to biology 2007 Lewis S Rosenstiel Award for Distinguished Work in Basic Medical Science 2001 Fellow of the Academy of Medical Sciences 1999 Wellcome-Burroughs Research Pioneer Award, National Institute of Child Health and Human Development (USA) 1994 Member of Academia Europaea 1993 Member of EMBO 1992 Associate Fellow of the Third World Academy of Sciences 1986 & 1992 BBSRC Individual Merit Award 1991 William Bate Hardy Prize, Cambridge Philosophical Society 1990 Fellow of the Royal Society	2023/11/21	Speaker at Master's Lecture
57	Shinichiro Imai	60	Professor, Washington University School of Medicine	USA	MD, PhD	International Okamoto Award 2020, 2016 The Most Influential 100 People for JAPAN 2017, Nikkei Business, etc.	2023/12/1	invited Lecturer of seminar, "for PRODUCTIVE AGING CONSORTIUM"
58	Louis-Pierre Chaintron		PhD student, École Normale Supérieure, Université PSL	France	Master of Applied Mathematics	PhD student under the supervision of Julien Reygner (CERMICS, École Nationale des Ponts et Chaussées) and Philippe Moireau (Inria M3DISIM, LMS, École Polytechnique)	2023/12/4 - 12/8	short-term stay for joint research
59	Michèle Romanos		CNRS Researcher, Institut Camille Jordan, Lyon, France	France	PhD, applied Mathematics	Michèle Romanos currently works at the Camille Jordan Institute (Lyon 1, France). Michèle's research is in the field of Mathematical modeling for biological phenomena.	2023/12/4 - 12/8	short-term stay for joint research

	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				
60	Eric Theveneau		Group Leader, Centre for Integrative Biology, Université Paul Sabatier, Toulouse	France	PhD, cell and developmental biology	Theveneau lab focuses on mechanisms of cell dynamics: epithelial-mesenchymal transition, directional cell migration, cell polarity and tissue mechanics. We aim at understanding basic principles that rule cell movements in complex environments during embryogenesis and cancer.	2023/12/4 - 12/8	short-term stay for joint research
61	Takuya Azami		Research Associate, MRC Human Genetics Unit, Institute of Genetics and Cancer, The University of Edinburgh	UK	PhD	Research associate at the MRC HGU, he is a developmental biologist and interested in the mechanisms of mammalian gastrulation and lineage differentiation.	2023/12/4	Speaker at ASHBi Seminar
62	Jennifer Nichols		Professor, MRC Human Genetics Unit, Institute of Genetics and Cancer, The University of Edinburgh	UK	PhD	Professor of MRC HGU at The University of Edinburgh, is a leading mammalian developmental and stem cell biologist. Her research focuses on lineage specification and regulation, devising genetic systems to investigate processes of mammalian development, initially focussing on preimplantation stages.	2023/12/4	Speaker at ASHBi Seminar
63	Lon Cardon		President and CEO, The Jackson Laboratory	USA	PhD	Responsible for the Laboratory's global vision, strategic direction, research and operations and internationally recognized human geneticist and demonstrated leader in academic, pharma and biotech research.	2023/12/14	Exchange of opinions on potential future collaborations/exchanges
64	Martin Pera		Professor, The Jackson Laboratory	USA	PhD Pharmacology	Martin F. Pera, Ph.D., is a leading stem cell researcher with interests in neuroscience and regenerative medicine. 1979 National Institutes of Health (U.S.) National Research Service Award 2007 Distinguished Alumni Award, George Washington University 2009 Honorary Appointment, Conjoint Professor, School of Psychiatry, The University of New South Wales, Sydney, Australia 2010 Honorary Professorship, University of Queensland 2017 Honorary Professorship, University of Melbourne	2023/12/14	Exchange of opinions on potential future collaborations/exchanges
65	Paul Robson		Professor, The Jackson Laboratory	USA	PhD	Paul Robson is a molecular cell biologist utilizing advanced technologies to understand the cellular composition of tissues, their development, and progression to disease and is leading a JAX team as part of the Human BioMolecular Atlas Program.	2023/12/14	Exchange of opinions on potential future collaborations/exchanges
66	Yui Sato	45	Assistant Professor, Department of Medicine/Immunology, Mayo Clinic	USA	MD, PhD	The 3rd Japan Kidney Council Award 2019, JSN Best Englich Presentation Award 2018, etc.	2023/12/18	invited Lecturer of our seminar, "Immune mediated mechanisms of maladaptive tissue responses: Tertairy lymphoid structures in aging and autoimmunity""
67	Shota Nakanoh		Postdoctral fellow, Babraham Institute, UK	UK	PhD	Dr. Nakanoh earned his bachelor's, master's and PhD degrees from Kyoto University under supervision of Professor Kiyokazu Agata for the studies of embryonic pluripotency in birds and reptiles. He has further developed expertise in human pluripotent stem cells with Professor Ludvic Vallier at University of Cambridge and with Dr. Teresa Rayon at Babraham Institute.	2023/12/18	Speaker at ASHBi Seminar
68	Tomokazu Sumida	44	Assistant professor of Neurology, Yale School of Medicine	USA	MD, PhD	Harry Weaver Scholar Awards 2023, Race to Erase MS Young Investigator Award 2020, etc.	2024/1/5	Speaker at ASHBi Seminar

	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				
69	Tobias B. Huber	52	Professor, Department of Internal Medicine and Nephrology, University Medical Center Hamburg-Eppendorf (UKE)	Germany	MD, PhD	Young Investigator Award of the American Society of Nephrology and the American Heart Association in 2012	2024/1/22	participation as an invited Lecturer, NEPHROLOGY EXPERT SEMINAR organized by Astellas Pharma Inc.
70	Peter Boor	44	Professor, Institute of Pathology, RWTH Aachen University	Germany	MD. PhD	Franz Volhard Prize 2020, Bernd Tersteegen-Award 2019	2024/2/9	RWTH Aachen Dleegation visit
71	Sari Lindblom	63	Rector/Professor, Department of Education, University of Helsinki	Finland	PhD psychology	She is the first female rector in the university's history. Her new five-year term of office began on 1 August 2023. A particular focus during her term is wellbeing and a thriving community. She is a psychologist (Doctor of Philosophy) and Professor of Higher Education. She previously served as Vice-Rector (2017-2020) of the University of Helsinki and as the director of the Centre for University Teaching and Learning HYPE (2004-2017).	2024/3/1	Exchange of opinions on expanding academic exchange
72	Anne Portaankorva		Vice-Rector/Professor of Neurology , University of Helsinki	Finland	MD	She is responsible for research, doctoral education and sustainable development. She is Professor of Neurology, MD and served as the Dean of the Faculty of Medicine, University of Helsinki (2022-2023). She is also Board member of the Executive of the Joint Authority for Helsinki and Uusimaa of the Helsinki University Hospital (HUS). Previously, she was the Dean of the Faculty of Medicine at the University of Oulu (2017-2021).	2024/3/1	Exchange of opinions on expanding academic exchange
73	Hanna Snellman		Vice-Rector/Professor of European Ethnology, University of Helsinki	Finland	PhD	She is responsible for international affairs and public engagement, as well as equality, diversity and inclusion. She is a Doctor of Philosophy and has worked as Professor of European Ethnology at the University of Helsinki since 2012. She served as the Dean of the Faculty of Arts at the University of Helsinki (2017–2018). She is the Immediate Past Chair of Una Europa's Board of Directors.	2024/3/1	Exchange of opinions on expanding academic exchange
74	Esa Hämäläinen		Director of Administration, University of Helsinki	Finland	MD, PhD	He is managing the general administration of the University in support of the rector. He leads the University Services of the University of Helsinki and serves as the Secretary General of the Board of the University. For six years, he also served as President and Chairman of HUMANE Aibsl, European Network for Heads of University Management as well as Vice-President for OECD IMHE Programme.	2024/3/1	Exchange of opinions on expanding academic exchange
75	Anna-Maria Salmi		Head of Services, University of Helsinki	Finland	PhD	Dr Anna-Maria Salmi works as Head of Services, leading the University of Helsinki's International Affairs Unit.	2024/3/1	Exchange of opinions on expanding academic exchange
76	ROBERT DE MASSY, Bernard Jean Paul	65	Research Director, Institute of Human Genetics	France	PhD Molecular Biology	Research Director and Head of Meiosis and recombination research team, Institut de Genetique Humaine, CNRS 2016 Coups d'Élan Awards for French Research, Bettencourt Schueller Foundation 2012 médaille d'argent du CNRS	2024/3/4-4/19	short-term stay as an invited researcher for joint research

	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				
77	Greg Neely		Professor, The University of Sydney	Australia	PhD	Based in the Charles Perkins Center at the University of Sydney. His lab utilizes functional genomics, leveraging the power of multiple model organisms/systems, to identify the genes and underlying mechanisms that control human biology and health, with a strong focus on chronic pain.	2024/3/4	Speaker at ASHBi Seminar
78	Aydan Bulut-Karslioglu		Group Leader, Max Plank Institute for Molecular Genetics	Germany	PhD	Stem cell researcher and developmental biologist based at the Max Planck Institute for Molecular Genetics in Berlin, Germany. Her research at the MPIMG in Berlin focuses on how the environment actively shapes the timing and trajectories of embryonic development including mechanisms that control diapause and embryonic dormancy.	2024/3/7	Speaker at ASHBi Seminar
79	Katalin Susztak	52	Professor of Medicine, University of Pennsylvania	USA	MD, PhD	Alfred Newton Richards Award from the International Society of Nephrology 2021, Young Investigator Award 2011 of the American Society of Nephrology and American Heart Association	2024/3/11	ITMAT Kyoto University International Symposium
80	Ehsan Shamsi Gooshki		Lecturer, Monash Bioethics Center, Monash University Associate Professor, Tehran University of Medical Sciences	Australia	MD PhD Medical Ethics	Physician and internationally renowned bioethicist who spearheaded numerous bioethical initiatives, including the development of Iran's Medical Council Code of Ethics and the establishment of national research ethics accreditation systems. Member and Vice-Chair, The World Health Organization (WHO) Ethics Review Committee Member and Vice-Chair, UNESCO International Bioethics Committee (IBC)	2024/3/27	Speaker at ASHBi Seminar
81	Miria Ricchetti		Research Director Laboratory for Molecular Mechanisms of Pathological and Physiological Ageing, Institut Pasteur	France	Ph.D.	Renowned scientist investigating the role of mitochondria and oxidative stress in pathophysiology and ageing. Her research at the Insitut Pasteur focuses currently on mitochondrial defects, epigenomic and transcriptional changes, and rescue strategies, in Cockayne syndrome and normal ageing.	2024/3/28	Speaker at ASHBi Seminar

Appendix 6 FY2023 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2023 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2023 (number of activities, times held)
PR brochure, pamphlet	3; Brochure for WPI Science Symposium, Illustration Booklet "Visualize Your Science", Pamphlet "Learning at ASHBi, Working at ASHBi" for increasing female junior-high/high school students
Lectures, seminars for general public	0
Teaching, experiments, training for elementary, secondary and high school students	0
Science café	3; First Contact Program
Open houses	0
Participating, exhibiting in events	1; WPI Science Symposium
Press releases	20 releases
Publications of the popular science books	0
Others（ Seminars ）	3; Writing Seminar, Kakenhi Seminar, Editor's Seminar

*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.

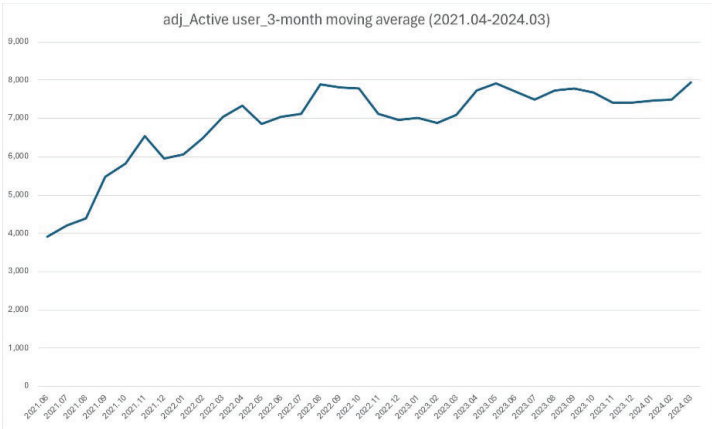
Outreach Activities and Their Results

List up to three of the Center's outreach activities carried out in FY 2023 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.

The Institute's Website

To publicize the Institute's research activities to society, we make effective use of websites and social networking services. The Institute's website was launched in FY2018. Although the number of monthly visitors has settled between 20,000 and 30,000 PV since FY2021, the number of active users (who view the webpage for more than 10 seconds or who clicks or scrolls) has steadily increased from 4,000 at the beginning of FY2021 to 8,000 at the end of FY2023.



A gradually increase of the active users can be observed, suggesting the growing interest towards activities at ASHBi.

Through the ASHBi website, we have disseminated 48 news pages and 55 event pages in English, contributing to the global visibility of the Institution.

In addition, the SignAC core facility website has been modified in a more "user-friendly format" by providing a user guide for the equipment and analytical services provided at SignAC. Here, the users can quickly understand how to use SignAC by simply following the steps shown in the flow chart. Other important information such as price, payment procedures, regulations, publication acknowledgement, etc., are also provided in an easy-to-find manner. These modifications will allow first time and non-ASHBi users to access the SignAC core and its services more easily, which is an important factor upon expanding its services to serve as a university-wide core facility.

A simple flow chart allows the users to easily grasp what they need to do when using SignAC.

A booklet to introduce ASHBi to female junior-high/high school students.

Furthermore, as part of the outreach to the younger generation, the student office assistants at the Research Acceleration Unit utilizes the "ASHBi for Student" website to disseminate the student and research life at ASHBi from the student's perspective. As part of this activity, the office assistants obtained a KU internal grant in their challenge to publish a booklet to introduce ASHBi to female junior-high/high school students. In the booklet, interviews to graduate students about their research are introduced in comic-style, and the interviews to the female PIs about their research career provides a guide for the young students who wish to explore their career as researchers. All of the contents including the website and the booklet are planned, designed and produced by the student office assistants, which serves as an effective on-the-job training for students who are interested in exploring career options in scientific writing and illustrations.

As seen above, information dissemination through the website has been gradually strengthened over the years.

Seminars aimed at fostering early-career researchers and students

The **Research Acceleration Unit** continues its efforts to organize seminars to train early-career researchers and graduate students. In FY2023, the Unit held seminars on topics how to write research papers/cover letters "Entering the Minds of Scientific Editors and Understanding Journal Strategies" by Goulas and how to write effective grant application "KAKENHI Writing Seminar" by Shida. A unique feature of these seminars was that they were held in a Zoom online format and made with reaching out to participants from more than 100 widely available to academic institutions throughout Japan, contributing to the development of young researchers nationwide.

The seminars by the Research Acceleration Unit are open to researchers and students throughout Japan.

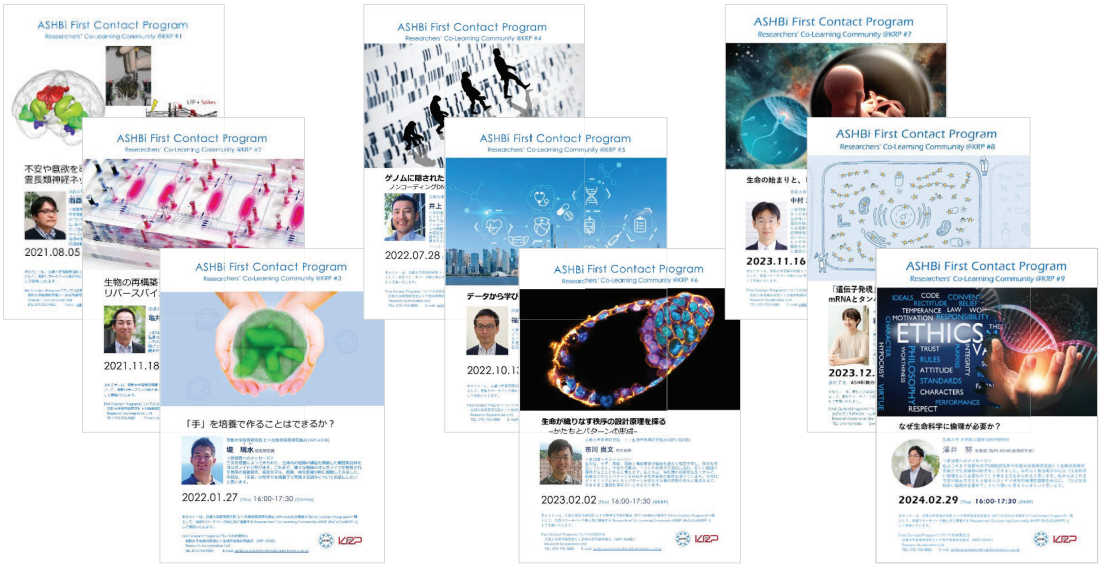
The experts of the **Research Acceleration Unit** have also been invited individually to give lectures to share their expertise to young researchers at institutions outside of KU. **Goulas** was invited to give talks at WPI-IIIS, RIKEN Retreat, and other international conferences, sharing his knowledge on scientific writing and his career. **Inoue** shared her knowledge of how to visualize research effectively to the young researchers at Nippon Medical School. **Shida** shared knowledge for effective research support to the URAs and administrators at the seminars hosted by JICA and Hiroshima University.

Date	Name	Presentation Title	Seminar/ Conference Name
2023/5/16	Makoto Shida	Strategic Research Support Foreign and Early-Stage researchers at WPI-ASHBi	Research Skill Enhancement Seminar, Hiroshima University
2023/6/1	Spyros Goulas	The Art of Publishing Scientific Papers	181st WPI-IIIS Seminar, WPI-IIIS, University of Tsukuba
2023/6/26	Spyros Goulas	Telling your Story in a Scientific Paper	Oita University Graduate School Lecture
2023/8/14	Makoto Shida	Problem solving utilizing mapping strategies	KEMRI RMA Process Mapping Project, KEMRI-JICA TCP in-Country Training, Kenya Medical Research Institute
2023/11/7	Makoto Shida	'-First Contact Program- Creating opportunities for industry-academia collaboration from the perspective of fostering young talent	7th Annual Symposium of Research University Consortium (RUC)
2024/1/29	Spyros Goulas	The Art of Publishing Scientific Papers	RIKEN Symposia: The 9th RIKEN Life Science Retreat
2024/2/8	Hiromi Inoue	Visualizing your research	2024 Science Illustration Seminar, Nippon Medical School
2024/2/21	Makoto Shida	Let's observe your work from a different perspective!	CoPURA vol.10, The University of Electro-Communications
2024/2/28	Spyros Goulas	Telling a story in a scientific paper	The 3rd Asia Pacific Drosophila Neurobiology Conference (APDNC3), Tokyo

Outreach to industry

The Institute initiates **'First Contact Program'** which provide opportunity for early-career researchers to present their research to the company researchers. This program aims to create interaction opportunities between industry and academia to foster potential future collaborations. In collaboration with the Kyoto Research Park, an industrial hub hosting over 500 companies, 3 seminars were held in FY 2023 to interact with the researchers of the resident companies accumulating to a total of 9 seminars from FY2021. In December, the seminar was held for the first time in ASHBi, enabling researchers from industries to visit SignAC to see the analytical equipment and services with their eyes and to engage in casual interaction with researchers in ASHBi.

First Contact Program has been held 3 times a year from FY2021 to enhance interactive research discussions in a casual atmosphere.



The researchers from the industry visited ASHBi for the first time in December's First Contact Program to engage in interactions with academic researchers.

Appendix 7 FY 2023 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2023.

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	April 3, 2023	News Website (Japanese)	[読売新聞オンライン] Introduction about the recent research result by Saitou Group regarding inducing primate oocytes successfully (Saitou Group)
2	April 17, 2023	News Website (English)	[The New Yorker] Introduction about the recent research result by Saitou Group regarding inducing primate oocytes successfully (Saitou Group)
3	May 12, 2023	News Website (English)	[Daily Advent.com] [Phys Org] Introduction about the recent research result of the role of transposable elements on the severity of illness after influenza by Bourque Group (Bourque Group)
4	May 22, 2023	News Website (English)	[Technology Networks] [Mirage News] Introduction about the recent research result of the role of transposable elements on the severity of illness after influenza by Bourque Group (Bourque Group)
5	July 2, 2023	News Website (English)	[KCRW] Introduction about the recent research result by Saitou Group regarding inducing primate oocytes successfully (Saitou Group)
6	July 27, 2023	News Website (Japanese, English), Newspaper (Japanese)	[NHK] [京都新聞][日本経済新聞][genomeweb][産経新聞][日刊工業新聞] Introduction about the recent research result by Ogawa Group (Ogawa Group)
7	July 31, 2023	Website (Japanese, English, Chinese)	[Medical meets Technology][CN-Healthcare][Opera News] Introduction about the recent research result by Ogawa Group (Ogawa Group)
8	August 2, 2023	Website (English, French)	[The Medical News][Nouvelles du monde] Introduction about the recent research result by Ogawa Group (Ogawa Group)
9	August 10, 2023	Website (Chinese)	[Yahoo News] Introduction about the recent research result by Ogawa Group (Ogawa Group)
10	August 16, 2023	Website (Korean)	[Nature Asia] Introduction about the recent research result by Ogawa Group (Ogawa Group)
11	August 23, 2023	Website (Japanese)	[がんプラス] Introduction about the recent research result by Ogawa Group (Ogawa Group)
12	August 30, 2023	Website (English)	[Psychreg] Introduction about the recent research result by Ogawa Group (Ogawa Group)
13	August 31, 2023	Website (English)	[ScienMag][Bioengineer] Introduction about the recent research result by Ogawa Group (Ogawa Group)
14	August 31, 2023	News Website (English)	[MedicalXpress] Introduction about the recent research result of chronic kidney disease by Yanagita Group (Yanagita Group)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
15	September 2, 2023	Website (English)	[Today Headline][Germanic News] Introduction about the recent research result by Ogawa Group (Ogawa Group)
16	September 3, 2023	Website (English)	[Swift Telecast] Introduction about the recent research result by Ogawa Group (Ogawa Group)
17	September 4, 2023	News Website (Japanese)	[QlifePro] Introduction about the recent research result of chronic kidney disease by Yanagita Group (Yanagita Group)
18	September 5, 2023	Website (English)	[healthcare-in-europe.com] Introduction about the recent research result by Ogawa Group (Ogawa Group)
19	September 6, 2023	Website (English)	[Technology Networks] Introduction about the recent research result by Ogawa Group (Ogawa Group)
20	September 26, 2023	News Website (Chinese)	[Yahoo! News] Introduction about the recent research result of chronic kidney disease by Yanagita Group (Yanagita Group)
21	September 27, 2023	Newspaper	[朝日新聞] Introduction about the recent research result by Ogawa Group (Ogawa Group)
22	September 28, 2023	News Website (English)	[mint] Interview/ introduction about the recent research result to/by Saitou Group regarding inducing primate oocytes successfully (Saitou Group)
23	October 4, 2023	News Website (English)	[BioEdge] Introduction about the recent research result by Saitou Group regarding inducing primate oocytes successfully (Saitou Group)
24	October 11, 2023	News Website (English)	[mint] Introduction about the recent research result by Saitou Group regarding inducing primate oocytes successfully (Saitou Group)
25	October 20, 2023	Website (Chinese)	[sina.com.cn] Introduction about the recent research result by Ogawa Group (Ogawa Group)
26	November 3, 2023	News Website (Czech)	[21 Stoleti.cz] Prof. Saitou's comment was introduced about recent study (Saitou Group)
27	November 20, 2023	Website (Japanese)	[医療NEWS] Introduction about the recent research result by Ogawa Group (Ogawa Group)
28	December 4, 2023	News Website (English)	[ScienMag][MedicalXpress] Introduction about the recent research result of eruption morphology in mathematical dermatology by Seirin Group (Seirin Group)
29	December 6, 2023	News Website (English, French)	[The Medical News][Nouvelles du monde] Introduction about the recent research result of eruption morphology in mathematical dermatology by Seirin Group (Seirin Group)
30	December 18, 2023	News Website (Japanese)	[日経Gooday] Interview to Prof. Ueno regarding COVID after effects (Ueno Group)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
31	December 19, 2023	News Website (English, French)	[Psychreg][Bioengineer.org][ScienMag][MedicalXpress][Nouvelles du monde][The Medical News][Neuroscience News] Introduction about the recent research result of anxiety disorders by Amemori Group (Amemori Group)
32	December 20, 2023	News Website (English)	[Technology Networks] Introduction about the recent research result of anxiety disorders by Amemori Group (Amemori Group)
33	December 21, 2023	News Website (Japanese)	[Mycom][マイナビニュース] Introduction about the recent research result of anxiety disorders by Amemori Group (Amemori Group)
34	December 28, 2023	News Website (Japanese)	[Qlife Pro] Introduction about the recent research result of anxiety disorders by Amemori Group (Amemori Group)
35	January 1, 2024	Scientific Magazine (Japanese)	[日経サイエンス] Interview to Prof. Hiraoka about Topological Data (Hiraoka Group)
36	January 4, 2024	News Website (English)	[Science][MedicalXpress][Mirage News][Daily Mail] Introduction about the recent research result by Isa Group (Isa Group)
37	January 5, 2024	News Website (English, Japanese) Newspaper (Japanese)	[朝日新聞デジタル][読売新聞オンライン][読売新聞][日本経済新聞][京都新聞][Tech Explorist][NewsBeezer] Introduction about the recent research result by Isa Group (Isa Group)
38	January 8, 2024	News Website (English, German)	[ナゾロジー][@niftyニュース][Hannoversche Allgemeine][Goettinger Tageblatt][Redaktionsnetzwerk Deutschland][Luebecker Nachrichten][Solinger Tageblatt][Kieler Nachrichten][Dresdner Neueste Nachrichten][Landeszeitung.de][Elbe-jeetzel-Zeitung][Peiner Allgemeine Zeitung] Introduction about the recent research result by Isa Group (Isa Group)
39	January 10, 2024	News Website (Japanese)	[Ascii.jp] Introduction about the recent research result by Isa Group (Isa Group)
40	January 12, 2024	News Website (Portuguese)	[Estadao.com] Introduction about the recent research result by Isa Group (Isa Group)
41	January 19, 2024	News Website (Japanese)	[Yahoo!ニュース] Introduction about the recent research result by Isa Group (Isa Group)
42	January 19, 2024	News Website (German)	[Die Welt] Introduction about the recent research result by Isa Group (Isa Group)
43	January 23, 2024	Internet TV (Japanese)	[ABEMAニュース] Introduction about the recent research result by Isa Group (Isa Group)
44	January 27, 2024	News Website (Japanese)	[朝日新聞デジタル] Interview to Prof. Saitou regarding his research (Saitou Group)
45	February 5, 2024	News Website (Japanese)	[Yahoo!ニュース] Interview to Associate Investigator Sawai
46	February 13, 2024	Website (Japanese)	[がんナビ] Introduction about the lecture which Prof. Ogawa gave at an event which the Japanese Society of Hematology hosted. (Ogawa Group)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
47	February 16, 2024	Information Website of Health and Medicine (Japanese)	[日経Gooday] Interview to Prof. Ueno regarding Cancer Immunotherapy (Ueno Group)
48	February 26, 2024	Scientific Magazine (Japanese)	[日経サイエンス] Interview to Prof. Hiraoka about Topological Data (Hiraoka Group)
49	February 28, 2024	News Website (Japanese)	[JIJI.COM] Introduction about the recent research result by Isa Group (Isa Group)
50	March 14, 2024	News Website (Japanese)	[日経メディカル] Introduction about Prof. Ogawa's lecture at The 85th Annual Meeting of the Japanese Society of Hematology (Ogawa Group)
51	March 31, 2024	News Website (Japanese)	[News Picks] Interview to Prof. Saitou regarding his research (Saitou Group)
52	February 11, 2024	News Website (Japanese)	[National Geographic] Interview to Associate Investigator Sawai
53	February 5, 2024	News Website (Japanese)	[朝日新聞デジタル] Introduction about the recent research result by Isa Group (Isa Group)

January 9, 2025

Erratum: FY2023 WPI Project Progress Report

The original version of this report contained an error on page 2. This error has now been corrected.

Page	Paragraph	Line	Original text	Corrected text
2	2	10	The 5 Flagship Projects are conceptually and methodologically interrelated and contribute to addressing our fundamental question of what makes us human in a bottom-up manner.	The 5 Flagship Projects are conceptually and methodologically interrelated and contribute to addressing our fundamental question of what makes us human in a top-down manner.