World Premier International Research Center Initiative (WPI)
FY 2022 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		
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Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2023) 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 core concepts of human biology. In FY2022, the ASHBi director, **Saitou**, performed an interim evaluation of the activities of ASHBi PIs and made a decision to reorganize the PI board members. Accordingly, from April 2023 onward, ASHBi consists of 16 PIs and 3 core heads (2 PIs are co-appointed as core heads), increasing the ratio of foreign and female PIs and creating open positions to recruit at least 2 new PIs. As of April 2023, ASHBi consists of 67 researchers [non-Japanese: 25 (37%); female: 18 (27%)], 89 graduate students [non-Japanese: 26 (29%); female: 28 (31%)], and 52 supporting staff. The 3 core facilities have run in a productive manner and in particular, SignAC appointed 3 new members, resulting in a group of 10 members in total, and has assisted many key investigations in ASHBi as well as Kyoto University with forefront technologies (see **3. Realizing an International Research Environment** and **4. Making Organizational Reforms**).

During 2022, ASHBi published 90 scientific papers. The representative papers in line with the ASHBi's five key themes include: "Reconstituting human somitogenesis *in vitro*: ***Nature***" (**Alev, T. Yamamoto, Tsujimura: Focus Areas 1**, **2**, and **4**), "An *ex vivo* system to study cellular dynamics underlying mouse peri-implantation development: ***Dev. Cell***" (**Hiiragi: Focus Areas 2** and **4**), "Nucleome programming is required for the foundation of totipotency in mammalian germline development: ***EMBO J.***" (**Saitou, Hiraoka, Murakawa, T. Yamamoto**: **Focus Areas 1**, **2**, and **4**), "*Ex vivo* reconstitution of fetal oocyte development in humans and monkeys: ***EMBO J.***" (**Saitou, Tsukiyama: Focus Areas 1**, **2**, and **4**), "Delamination of trophoblast-like syncytia from the amniotic ectodermal analogue in human primed embryonic stem cell-based differentiation model: ***Cell Rep.***" (**Eiraku: Focus Areas 2** and **4**), "Machine learning dissection of human accelerated regions in primate neurodevelopment: ***Neuron***" (**Inoue: Focus Areas 1**, **2**, and **4**), "Temporal dynamics of the sensorimotor convergence underlying voluntary limb movement: ***PNAS***" (**Isa: Focus Areas 1**, **2**, and **3**), "T Amplified EPOR/JAK2 Genes Define a Unique Subtype of Acute Erythroid Leukemia: ***Blood Cancer Discov.***" (**S. Ogawa: Focus Area 1**), "CD153/CD30 signaling promotes age-dependent tertiary lymphoid tissue expansion and kidney injury: ***J. Clin. Invest.***" (**Yanagita: Focus Areas 1** and **2**), "Lineage tracing analysis defines erythropoietin-producing cells as a distinct subpopulation of resident fibroblasts with unique behaviors: ***Kidney Int.***" (**Yanagita:**

Focus Areas 1 and **2**), "Resolution of the curse of dimensionality in single-cell RNA sequencing data analysis: ***Life Sci. Alliance***" (**Hiraoka, Saitou, T. Yamamoto: Focus Areas 1** and **2**), and "Current status of cell-based interventions in Japan: ***Cell Stem Cell***" (**Fujita: Focus Areas 5**) (see **1. Advancing Research of the Highest Global Level**).

In addition to the research activities of individual PIs, we have ongoing the 5 Flagship Projects, including fusion studies with mathematics and with bioethics, which represent key research directions of ASHBi and involve close collaborations/interactions among various ASHBi PI groups. The 5 Flagship Projects are: "**Deconstruction and reconstruction of early primate development**" (relevant to **Focus Areas 1**, **2** and **4**), "**Primate-genomics interdisciplinary research for developing new primate models**" (relevant to **Focus Areas 1**, **2**, and **3**), "**Age-associated genomic alterations of organ cells and their interplay with the local immune system**" (relevant to **Focus Area 1**), "**Establishment of 'data representation theory'**" (relevant to **Focus Area 2**), and "**Bioethics at the periphery of birth and death'**" (relevant to **Focus Area 5**). The 5 Flagship Projects are topically and methodologically interrelated and contribute to addressing the fundamental question of our Institute, which is "what makes us human?" in a top-down manner. The 5 Flagship Project groups have progress meetings regularly and in January 2023, ASHBi held a meeting to discuss the progress of all the Flagship Projects.

As a bottom-up approach to promote fusion research and interactions among young researchers in ASHBi, we have set up the **"ASHBi Fusion Research Grant Program"** since FY 2019. In FY 2022, we have selected a further two new proposals, "Single-molecule elucidation of higher-order chromatin folding dynamics in individual cells" (mathematics-biology fusion led by **Tsujimura** in **SignAC**) and "Unraveling transcriptional regulatory mechanism of transposable elements across species" (biology-biology fusion led by **Nagano** in **Saitou G**), and currently, 11 projects in total are in progress. Some of the research from this program has served as a basis for key papers, including "Reconstituting human somitogenesis *in vitro*: ***Nature***" (**Alev, T. Yamamoto, Tsujimura: Focus Areas 1**, **2**, and **4**), "Nucleome programming is required for the foundation of totipotency in mammalian germline development: ***EMBO J.***" (**Saitou, Hiraoka, Murakawa, T. Yamamoto**: **Focus Areas 1**, **2**, and **4**), and "Resolution of the curse of dimensionality in single-cell RNA sequencing data analysis: ***Life Sci. Alliance***" (**Hiraoka, Saitou, T. Yamamoto: Focus Areas 1** and **2**). In addition, since FY 2019, we have held **ASHBi colloquium** and **ASHBi Retreat** on a regular basis. In FY 2022, we held **ASHBi colloquium** 9 times with the 18 PI groups presenting their latest research results, and more than 100 ASHBi members joined **ASHBi Retreat** and nearly 50 presentations were made during the poster session, and active interactions between researchers and graduate students took place (see **2. Generating Fused Disciplines**). Furthermore, under the leadership of **Hiiragi**, in FY 2022, ASHBi PIs held the first **PI retreat**, which offered dedicated time for critical, constructive, and intensive discussions of the research themes and future directions from 3 PIs (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 FY2022, we organized 6 large-scale international meetings in an onsite/online format: "**EMBO Workshop: Molecular Mechanisms of Developmental and Regenerative Biology**" (April 2022), international summer school "**JANUBET Symposium**" (September 2022), "**Workshop for Mathematical Human Biology**" (November 2022), "**Ethical, Legal, and Social Issues of Human Brain Organoid Research and Application**" (December 2022), "**Human Development from Embryos to Stem Cell Models**" (March 2023), and "**Deconstructing and Reconstructing embryonic development**" (March 2023) (see **3. Realizing an International Research Environment**).

KU recognizes the Institute's research support/administration system as one of the best practice models for its reforms at the KU-wide level. KU highly evaluates the activity of the **SignAC** and actively expand its service as a KU-wide shared core facility. KU Provost reviewed activities of the **Administrative Office** to implement it into the new system reform plans at KU, showing the KU's intentions to expand the best practices at the Institute to the KU-wide system reform (see **7. Center's Response to Results of Last Year's Follow-up**).

* 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 2022.
* 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 particular 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 **Alev group** published a manuscript entitled "Reconstituting human somitogenesis *in vitro*" (***Nature*** 614, 509–520, 2023; published online 21 December, 2022) (relevant to **Focus Areas 1**, **2**, and **4**).

Key events in early embryonic development, including somitogenesis, have been extensively studied using model organisms such as mice, but remain largely elusive in humans. Extending on their earlier findings (***Nature*** 580, 124–129, 2020), the group used human pluripotent stem cell (hPSC)-based technologies to establish a 3D *in vitro* model of human somitogenesis, which exhibited periodic formation of properly patterned epithelial somites in synchrony with the segmentation clock. The self-organizing "axioloids" shared morphological and molecular features of the human embryo and emerging embryonic axis, including the presence of opposing morphogen gradients. The group demonstrated a critical role of retinoic acid (RA) in the stabilization of segments, suggesting synergy between RA and the extracellular matrix (ECM) in the formation and epithelialization of somites. They applied their *in vitro* system to study the pathogenesis of human congenital diseases of the spine, using patient-like iPSC cells with mutations in *HES7* and *MESP2*, which revealed disease-associated phenotypes including loss of epithelial somite formation and abnormal rostrocaudal patterning. Thus, the axioloid model that the group established is a powerful platform to study and understand the mechanism of human development, disease and evolution.

This work was the result of close collaborations with the **T. Yamamoto group** and **SignAC**.

The **Hiiragi group** published a manuscript entitled "An *ex vivo* system to study cellular dynamics underlying mouse peri-implantation development" (***Dev. Cell*** 57, 373-386, 2022) (relevant to **Focus Areas 2** and **4**).

Upon implantation, mammalian embryos undergo major morphogenesis and key developmental processes such as body axis specification and gastrulation. However, limited accessibility obscures the study of these crucial processes. The group developed an *ex vivo* Matrigel-collagen-based culture to recapitulate mouse development from E4.5 to E6.0. Not only does this system

recapitulate embryonic growth, axis initiation, and overall 3D architecture in 49% of cases, but its compatibility with light-sheet microscopy also enables the study of cellular dynamics through automatic cell segmentation. They find that, upon implantation, release of the increasing tension in the polar trophectoderm is necessary for its constriction and invagination. The resulting extra-embryonic ectoderm plays a key role in growth, morphogenesis, and patterning of the neighboring epiblast, which subsequently gives rise to all embryonic tissues. This 3D *ex vivo* system thus offers unprecedented access to peri-implantation development for *in toto* monitoring, measurement, and spatiotemporally controlled perturbation, revealing a mechano-chemical interplay between extra-embryonic and embryonic tissues. This study serves as a basis for the understanding of human peri-implantation development.

The **Saitou group** published manuscripts entitled "Nucleome programming is required for the foundation of totipotency in mammalian germline development" (***EMBO J.*** 41, e110600) and "*Ex vivo* reconstitution of fetal oocyte development in humans and monkeys" (***EMBO J.*** 41, e110815) (relevant to **Focus Areas 1**, **2**, and **4**).

In the former study, the group performed comprehensive and in-depth nucleome analysis of mouse germ-cell development *in vitro*. They showed that 1) the 3D genome matures unidirectionally over epigenetic reprogramming in primordial germ cells (PGCs) and programming during spermatogonia development; 2) epigenetic reprogramming creates broadly open chromatin with enhanced insulation; 3) spermatogonia show minimal, peripherally positioned, and pericentromeric lamina-associated domains (LADs); and 4) nucleome mis-programming leads to impaired spermatogenic potential. Given that PGCs after epigenetic reprogramming (i.e., oogonia) serve as oogenic progenitors as well, these findings elucidate a principle for the nucleome programming that creates gametogenic progenitors in both sexes, defining a basis for nuclear totipotency. In the latter study, the group demonstrated *ex vivo* reconstitution of fetal oocyte development in both humans and cynomolgus monkeys (*Macaca fascicularis*). With an optimized culture of fetal ovary reaggregates over three months, human and monkey oogonia entered and completed the first meiotic prophase to differentiate into diplotene oocytes that form primordial follicles, the source for oogenesis in adults. The cytological and transcriptomic progressions of fetal oocyte development *in vitro* closely recapitulated those *in vivo*. A comparison of single-cell transcriptomes among humans, monkeys, and mice unraveled primate-specific and conserved programs driving fetal oocyte development, the former including a distinct transcriptomic transformation upon oogonia-to-oocyte transition and the latter including two active X chromosomes with little X-chromosome up-regulation. This study provides a critical step forward for realizing human *in vitro* oogenesis and uncovers salient characteristics of fetal oocyte development in primates.

The former work was the result of close collaborations with the **T. Yamamoto, Murakawa,** and **Hiraoka groups** and **SignAC**, and the latter work was the result of close collaboration with **PRiME**.

The **Eiraku group** published a manuscript entitled "Delamination of trophoblast-like syncytia from the amniotic ectodermal analogue in human primed embryonic stem cell-based differentiation model" (***Cell Rep.*** 39, 110973, 2022) (relevant to **Focus Areas 2** and **4**).

Human embryonic stem cells (hESCs) under a primed condition are known to be differentiated into cells with several trophoblast properties, but it remains controversial whether this phenomenon recapitulates the developmental pathway *in vivo* and represents the inherent differentiation competence of hESCs to trophoblast lineages. The group showed that chemical blockage of ACTIVIN/NODAL and FGF signals is sufficient to steer hESCs into GATA3-expressing cells that give rise to placental hormone-producing syncytia analogous to syncytiotrophoblasts of the post-implantation stage of the human embryo. Despite their cytological similarity to syncytiotrophoblasts, these syncytia arise from the non-trophoblastic differentiation trajectory that recapitulates amniogenesis. These results provide insights into the possible extraembryonic differentiation pathway that is unique in primate embryogenesis.

The co-PI of the **Bourque group**, **Fumitaka Inoue**, published a manuscript entitled "Machine

learning dissection of human accelerated regions in primate neurodevelopment" (***Neuron*** 111, 857-873, 2022) (relevant to **Focus Areas 1**, **2** and **4**).

Human accelerated regions (HARs) are highly conserved sequences that have acquired many nucleotide substitutions in humans since their divergence from chimpanzees and, more recently, from archaic hominins. This accelerated substitution rate suggests that HARs are important and that their functions change during human evolution, perhaps altering traits that distinguish humans from chimpanzees and other animals. Inoue and his colleagues investigated the function of all human-chimpanzee variants in 2,645 HARs using machine learning (ML), and found that 43% of HARs have variants with large opposing effects on the chromatin state and 14% have variants with large opposing effects on neurodevelopmental enhancer activity. Consistent with compensatory evolution, this pattern was confirmed using massively parallel reporter assays in chimpanzee and human neural progenitor cells. The species-specific enhancer activity of HARs was accurately predicted from the presence and absence of transcription factor footprints in each species. Despite these striking cis effects, the activity of a given HAR sequence was nearly identical in human and chimpanzee cells, suggesting that HARs did not evolve to compensate for changes in the trans environment but instead altered their ability to bind factors present in both species. Thus, ML prioritized variants with functional effects on human neurodevelopment and revealed an unexpected reason why HARs may have evolved so rapidly.

The **Isa group** published a manuscript entitled "Temporal dynamics of the sensorimotor convergence underlying voluntary limb movement" (***PNAS*** 119, e2208353119, 2022) (relevant to **Focus Areas 1**, **2**, and **3**).

To delineate the mechanism of sensory- and motor-signal integration for dexterous hand movements, a specific trait in primates, the group simultaneously recorded activity in the motor cortices (MCx), somatosensory afferent neurons, and forelimb muscles in monkeys performing reaching and grasping movements. They constructed a linear model to explain the instantaneous muscle activity using the activity of MCx (descending input) and peripheral afferents (afferent input). Decomposition of the reconstructed muscle activity into each subcomponent indicated that muscle activity before movement onset could first be explained by descending input from the primary motor cortex and that after movement onset by both descending and afferent inputs. Descending input had a facilitative effect on all muscles, whereas afferent input had a facilitative or suppressive effect on each muscle. Such antagonistic effects from afferent input can be explained by reciprocal effects of the spinal reflex. These results suggest that descending input contributes to the initiation of limb movement, and this initial movement subsequently affects muscle activity via the spinal reflex in conjunction with the continuous descending input. Thus, the group clarified how the descending motor commands and the effect of late-coming commands are integrated to form the flexible movements of the hand; the spinal motor neurons are subjected to temporally organized modulation by direct activation through the descending pathway and the lagged action of the spinal reflex during voluntary limb movement.

The **Ogawa group** published a manuscript entitled "Amplified EPOR/JAK2 Genes Define a Unique Subtype of Acute Erythroid Leukemia" (***Blood Cancer Discov.*** 5, 410-427, 2022) (relevant to **Focus Area 1**).

Acute erythroid leukemia (AEL) represents a rare but the most aggressive subtype of acute myeloid leukemia (AML), for which no effective therapy has been developed. The molecular pathogenesis of AEL has been a long-standing issue in hematology. To clarify the mechanism of erythroid predominance in AEL and identify molecular targets for the development of novel therapeutics for AEL, the group enrolled a total of 124 AEL patients and characterized their somatic mutations, copy number alterations (CNAs), structural variations (SVs), and/or gene expression profiles, which were compared with those of 409 cases of non-AEL and 229 high-risk myelodysplastic syndrome (MDS) cases without erythroid hyperplasia. On the basis of common mutations that were mutually exclusive, AEL cases were classified into four distinct categories according to the presence/absence of biallelic TP53 mutations, NPM1, and STAG2 mutations. The group found a high frequency of

amplifications involving EPOR/JAK2 in TP53-mutated AEL cases, particularly those having >80% erythroblasts designated as pure erythroid leukemia (PEL) (10/13). These cases were frequently accompanied by gains/amplifications of ERG/ETS2 and associated with a very poor prognosis, even compared with other TP53-mutated AEL. As expected, these cases uniformly showed an activated JAK/STAT signaling pathway and an increase in cell proliferation and often showed high sensitivity to JAK2 inhibition by ruxolitinib in vitro and in xenograft models, highlighting a potential role of JAK2 inhibition in the therapeutics of AEL. These findings highlight a critical role of erythropoietin signaling in the pathogenesis of AEL and provide the basis for a clinical trial of JAK2 inhibition for this highly dismal hematological malignancy.

The **Yanagita group** published manuscripts entitled "CD153/CD30 signaling promotes age-dependent tertiary lymphoid tissue expansion and kidney injury" (***J. Clin. Invest.*** 132, e146071, 2022) and "Lineage tracing analysis defines erythropoietin-producing cells as a distinct subpopulation of resident fibroblasts with unique behaviors" (***Kidney Int.*** 102, 280-292, 2022) (relevant to **Focus Areas 1** and **2**).

In the former study, the group identified TNF superfamily CD153/CD30 signaling between two unique age-dependent lymphocyte subpopulations, $CD153^{+}PD\text{-}1^{+}CD4^{+}$ senescence-associated T (SAT) cells and $CD30^{+}T\text{-}bet^{+}$ age-associated B cells (ABCs), as a driver for TLT expansion. In kidney injury models, CD153 or CD30 deficiency impaired functional SAT cell induction, resulting in reduced ABC numbers and attenuated TLT formation with improved inflammation, fibrosis, and renal function. Clonal analysis showed that SAT cells and ABCs in the kidneys arise from both local differentiation and recruitment from the spleen. Furthermore, this work showed a possible contribution of this signaling pathway to human TLT formation. These results reveal a previously unappreciated function of CD153/CD30 signaling in TLT formation and suggest that the CD153/CD30 signaling pathway could be a therapeutic target for slowing kidney disease progression. In the latter study, the group generated EpoCreERT2/+ mice, a strain that enables labeling of Epo-producing cells and examined the behaviors of Epo-producing cells under pathophysiological conditions. Lineage-labeled cells were found to be a small subpopulation of fibroblasts located in the interstitium of the kidney, and their number increased during phlebotomy-induced anemia. Around half of lineage-labeled cells expressed Epo mRNA, and this percentage was maintained even 16 weeks after recombination, supporting the idea that a distinct subpopulation of cells with Epo-producing ability make Epo repeatedly. During fibrosis caused by ureteral obstruction, EpoCreERT2/+-labeled cells were found to transdifferentiate into myofibroblasts with concomitant loss of Epo-producing ability, and their numbers and the proportion among resident fibroblasts increased during fibrosis, indicating their high proliferative capacity. The group confirmed that EpoCreERT2/+-labeled cells that lost their Epo-producing ability during fibrosis regained their ability after kidney repair due to relief of the ureteral obstruction. These findings uncover previously unappreciated behaviors of Epo-producing cells.

The **Hiraoka group** published a manuscript entitled "Resolution of the curse of dimensionality in single-cell RNA sequencing data analysis" (***Life Sci. Alliance*** 5, e202201591, 2022) (relevant to **Focus Areas 1** and **2**).

Single-cell RNA sequencing (scRNA-seq) determines gene expression in numerous individual cells. However, scRNA-seq data are high-dimensional with substantial technical noise. Upon analysis, such noise engenders statistical problems known as the curse of dimensionality (COD). Based on high-dimensional statistics, the group formulated a noise reduction method, RECODE (resolution of the curse of dimensionality), for high-dimensional data with random sampling noise. RECODE eliminates COD in scRNA-seq data with unique molecular identifiers. RECODE recovers expression values for all genes, including lowly expressed genes, realizing precise delineation of cell-fate transitions/identification of rare cells with all gene information. RECODE exhibits superior performance in cell-clustering and single-cell analysis over imputation methods. RECODE is parameter-free, data-driven, deterministic, and high speed, and its applicability is predictable based on the variance normalization performance. The software of RECODE is open to the public and

available at: https://ashbi.kyoto-u.ac.jp/topgene/recorde/

The **Fujita group** published manuscripts entitled "Financial risks posed by unproven stem cell interventions: Estimation of refunds from medical expense deductions in Japan" (***Stem Cell Rep.*** 17, 1016-1018, 2022) and "Current status of cell-based interventions in Japan" (***Cell Stem Cell*** 29, 1294-1297, 2022) (relevant to **Focus Areas 5**).

In recent years, under the "Act on the Safety of Regenerative Medicine (ASRM)," a major problem has arisen with respect to "treatments" that have not been proven safe or effective being offered in private clinics. In the former study, the group hypothesized that there may be a "financial risk" associated with these treatments that the public bears through the tax system in the form of refunds based on medical expense deductions, and estimated the total amount of refunds paid by the government in 2017 or 2018, which was between 100 million and 238.2 billion yen per year. Since regenerative medicine offered as treatments is a society-wide issue affecting the national budget, the group recommended that the government take responsibility for guaranteeing the safety and efficacy of the treatment and also consider amending the law. In the latter study, the group analyzed the explanatory documents for each treatment published by the Ministry of Health, Labor, and Welfare. They found that 3,467 regenerative medicine treatments by 2,377 medical institutions are available, including some scientifically unproven treatments that foreign medical societies have condemned. Also, about 40% of the explanatory documents did not contain basic safety-related information. The group argued that there are structural issues in the ASRM which impede clarification of three basic concepts that are key to the process from research to treatment: (1) the manner in which medical treatments that have been proven safe and effective in research become treatments; (2) the definition and distinction between research and treatment; and (3) the distinction between "medical innovations" and "unproven interventions". These papers were reported in several media outlets as research results of social significance.

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 has been performing fusion research between mathematics (the **Hiraoka** and **Seirin groups**) and life sciences, and between humanities/social sciences (the **Fujita group**) and life sciences, and such research has been progressively expanding and maturing. Furthermore, in response to the recommendation by the WPI WG, we have initiated a series of **Flagship Projects**, which represent key research directions of ASHBi and involve close collaborations/interactions among ASHBi PI groups. Accordingly, we have organized the key fusion research projects between mathematics and life sciences and between humanities/social sciences and life sciences under the rubric 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 currently performing an investigation into "**Deconstruction and reconstruction of early primate development**" (relevant to **Focus Areas 1**, **2** and **4**). This project 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:

The **Saitou group** has been acquiring single-cell transcriptome data associated with post-implantation development in cynomolgus monkeys [embryonic days (E)15, 17, 19, 20, 21, and 23] and, by using RECODE and other methodologies, performing an integrated analysis of such data with publicly available data with complementary significance, creating a comprehensive transcriptomic atlas for primate peri-/early post-implantation development. Preliminary analyses have uncovered a number of so far unidentified developmental pathways and rare cell populations, demonstrating that these datasets are an invaluable resource and serve as a robust benchmark for

the *in vitro* and *ex vivo* models of primate and human development.

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:
As described in the **1. Advancing Research of the Highest Global Level** section, the **Hiiragi group** developed an *ex vivo* Matrigel-collagen-based culture to recapitulate mouse development from E4.5 to E6.0 (***Dev. Cell*** 57, 373-386, 2022). This 3D *ex vivo* system offers unprecedented access to peri-implantation development for *in toto* monitoring, measurement, and spatiotemporally controlled perturbation, creating a basis for understanding human and primate peri-implantation development. The **Ema group** has been exploring the origin of the placenta in primates and found that, unlike in mice, polar trophectoderm (TE) cells are derived continuously from inner cell mass (ICM) cells, and most parts of the placenta are derived from the polar TE and/or ICM. Through collaboration with the **Hiiragi group**, they performed live-imaging analyses of monkey blastocysts and obtained preliminary data indicating the migration of ICM cells toward polar TEs.

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:
As described in the **1. Advancing Research of the Highest Global Level** section, the **Alev group** published a PSC-based model of human post-gastrulation 3D development reconstituting the formation of the metameric axis and segmented body plan in humans ("axioloids") (***Nature*** 614, 509–520, 2023). The **Alev group** is continuing to develop and utilize even more advanced models of human and non-human primate embryonic development, including axioloids with somites and neural tubes or integrated multi-germ layer models of complex development and organogenesis.

The Developmental Biology subdivision has been holding regular in-person meetings for the Flagship Project. All groups are enhancing their interactions and strengthening their joint efforts towards realization of the shared research goal of establishing and analyzing advanced *ex vivo* and *in vitro* models of early primate embryonic development. 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
Non-human primates (NHPs) share many genetic, structural, and functional similarities with humans, making them a valuable model for neuroscience and pathological investigations. Accordingly, the Primate Models/Macaque Genome Engineering subdivision and the Genome Informatics subdivision (**Amemori**, **Isa**, and **Murakawa G**) are currently performing an investigation into "**Primate-genomics interdisciplinary research for developing new primate models**" (relevant to **Focus Areas 1**, **2**, and **3**).

The core of this project consists of two interrelated studies:
a) A study of anxiety disorders (ADs) (**Amemori** and **Murakawa G**):
The **Amemori** and **Murakawa groups** will systematically study the brain regions associated with AD in NHPs. In FY 2022, the groups examined the spatial expression pattern of genes identified by genome-wide association studies (GWAS) of ADs. Specifically, the groups used the whole-brain microarray of the Allen Brain Institute to examine the expression of these genes in the whole human brain. They found two distinct groups of AD-associated genes that were differentially expressed in specific neural circuits. Specifically, one group of AD genes was significantly enriched in the basal ganglia (e.g., striatum) and midbrain (e.g., ventral tegmental area), regions that have previously been implicated in state anxiety in physiological studies. The other group of AD genes was enriched in the hippocampus and midbrain circuitry (e.g., raphe nucleus), which have been associated with trait anxiety. This study is the first report of a preferential bias in the expression patterns of AD-associated genes and listed the specific brain structures enriched with AD-associated genes (currently under review for publication). Guided by these results, the group plans to perform sampling for single-nucleus RNA sequencing (snRNA-seq) to identify AD-associated cis-regulatory

elements. For this purpose, in FY 2022, the group established a protocol for efficient sampling from the deep brain structures in cynomolgus monkeys. The study of ADs will provide insights into the neurobiological implications of AD-associated genes and will bridge the gap between these genes and the specific neural circuitry involved in AD-associated behavior.

b) A study of the plasticity of corticospinal motor neurons (**Isa** and **Murakawa G**):
The **Isa** and **Murakawa groups** aim to investigate the recovery process from spinal cord injury in NHPs, specifically focusing on the plasticity of corticospinal neurons. Recent studies have shown that corticospinal neurons in primates exhibit greater plasticity than those in rodents, and the **Isa group** discovered a massive re-routing of corticospinal axons in NHPs after recovery, whereby axons from the contralesional motor cortex change their route and re-connect to the motoneurons of the hand. To examine the gene regulatory networks underlying the re-routing, the groups plan to use snRNA-seq analysis. In FY 2022, the group established a spinal cord injury model in both rats and macaques by training the animals to perform a reach-and-grasp task. They have also established protocols for efficient sampling of corticospinal neurons from the deep brain structures in both species to perform snRNA-seq analysis. The results of this study could shed light on the molecular processes involved in the recovery of spinal cord injury and inform future development of treatments for patients.

The phenotypes of knockout monkeys for *PKD1* (**Ema G**), *NPHP1* (**Yanagita G**) and *DISC1* (**Isa G**) have been analyzed through this collaborative platform (relevant to **Focus Areas 1**, **2**, and **3**). Advancements in the KO monkey projects are as follows:

c) Autosomal dominant polycystic kidney disease (ADPKD) model: *PKD1* KO (**Ema G**):
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 15 monkeys (6 heterozygotes and 9 mosaics, with 2 of the mosaics being nearly completely homozygous; 4–5 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 elevated creatinine and cystatin C, 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 preserve the genotypes, the group has started training the *PKD1* KO male monkeys for sperm collection.

d) Nephronophthisis model: *NPHP1* KO (**Yanagita G**):
The **Yanagita group** has been analyzing the phenotypes of 3 *NPHP1* KO monkeys in comparison to 3 wild-type controls. The *NPHP1* KO monkey kidneys exhibited tubular diverticula, tubular florets, and disturbed cellular polarity in the collecting ducts and fibrosis. In addition, they showed extrarenal lesions, such as cerebellar atrophy and retinal atrophy lesions. These findings faithfully recapitulate the pathological findings of familial nephronophthisis in humans. In addition, snRNA-seq analysis of the WT and KO kidneys suggested a decreased EGF network in KO kidneys. To corroborate these findings, the **Yanagita group** created *NPHP1* KO MDCK cells (a renal collecting duct cell line of a dog), which showed disturbed cellular polarity and reduced AKT phosphorylation in 3D culture. In addition, *NPHP1* KO MDCK cells showed reduced responsiveness to EGF. The **Yanagita group** is currently trying to generate collecting duct organoids by differentiating human iPSCs derived from familial nephronophthisis patients and *NPHP1* KO iPSCs. Their findings reveal the early phenotypes and pathogenesis of familial nephronophthisis.

e) Psychosis model: *DISC1* KO (**Isa G**):
The **Isa group** has been analyzing the growth and phenotypes of 5 *DISC1* KO monkeys in comparison to 5 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 including those related to psychosis, and mitochondrial functions as has been reported in the mouse model. At the age of 2 years, MRI showed that the brains of monkeys with large *DISC1* deletions were smaller when compared to age-matched control monkeys. The group are currently performing resting-state fMRI measurements to analyze the neural network in the brain of *DISC1* KO monkeys. In addition, they have established a system to measure eye movements noninvasively and will examine whether the monkeys exhibit

a psychopathic phenotype, which has been revealed in human patients, using free viewing and various cognitive tasks. Since abnormal nocturnal sleep has been observed in some monkeys by video and nano-tag based analysis, the group are preparing to introduce a telemetry system to examine detailed sleep EEG. In the next step, the group will apply social stress and cannabinoid which are known to enhance psychosis. When **the group** observes 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**, **R. Yamamoto**, and **Yanagita G**) is currently performing an investigation into "**Age-associated genomic alterations of organ cells and their interplay with the local immune system**" (relevant to **Focus Area 1**).

Aging induces progressive alterations in the genome and epigenome of various cells, and a fraction of pre-cancerous cells eventually become malignant. This process simultaneously generates neo-antigens which can be targeted by the immune system. Therefore, cancer development can be regarded as a consequence of the deterioration of the immune system and increased alterations of the pre-cancerous cells. However, how such dynamic interplay between pre-cancerous cells and the immune system operates in the local microenvironment remains unknown. Primary sclerosing cholangitis (PSC) is a rare chronic cholestatic liver disease with an increased malignancy risk (400–1,500-fold increase). This project aims to define the dynamic interplay between the aging immune system and the changing tissue cells in human organs, focusing on PSC as an exemplary model.

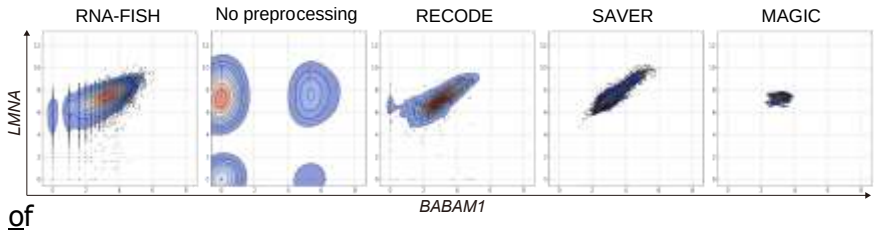
In FY 2022, the **Ueno group** collected more than 80 healthy liver perfusate and tissue samples and more than 50 diseased liver perfusate and tissue samples. An analysis with super-multicolor flow cytometry revealed that the liver perfusate contained a much broader range of liver-resident immune cells than anticipated, and even hepatocytes and non-parenchymal cells including hepatic stellate cells were included. Accordingly, the **Ueno group** has established multi-pronged approaches to analyze these diverse types of immune cells and non-parenchymal cells. The **Ueno group** has also successfully generated cholangiocyte organoids from frozen/thawed human liver tissues. They will develop a novel immune-organoid system which permits the assessment of interactions between the liver-resident immune cells and cholangiocytes. The **Ogawa group** also independently obtained bile and tissue samples from PSC patients. The preliminary data on the mutation rate analysis determined by analyzing the gene mutations of single-cell cholangiocyte organoids revealed that the number of mutations in PSC increased with age at an annual rate of 28.4 mutations per genome, versus 38.2 mutations per genome in non-PSC cholangiocytes, raising a possibility that the mutation rate is not substantially increased in PSC cholangiocytes. Nonetheless, cholangiocytes obtained from extrahepatic (n=4 patients) and intrahepatic bile ducts (n=1 patient) showed *ARID2* and *PIK3CA* gene mutations and evidence of their clonal expansions. Cholangiocytes from one case showed mutations in genes associated with the Th17 pathway, which is similar to the findings in cases of ulcerative colitis, which often co-develops with PSC. In FY 2023, the group anticipates to gain more insights into the alterations of the immune system and of gene mutations of the cholangiocytes in the PSC liver.

In addition, the Basic/Clinical Medicine subdivision continues to explore age-associated systems alterations in diverse organs, creating a solid basis for success in the Flagship Project.

4. Establishment of "data representation theory"

The mathematics groups (**Hiraoka** and **Seirin-Lee G**) in collaboration with the life sciences groups in ASHBi have embarked on "**Establishment of 'data representation theory'**" as a Flagship Project. The goal of this project is to comprehensively understand mathematical structures (both static and dynamic) underlying large and complex datasets and to develop precise and informative descriptors tailored to the respective specific analyses (relevant to **Focus Area 2**). In FY 2022, the groups realized the following developments:

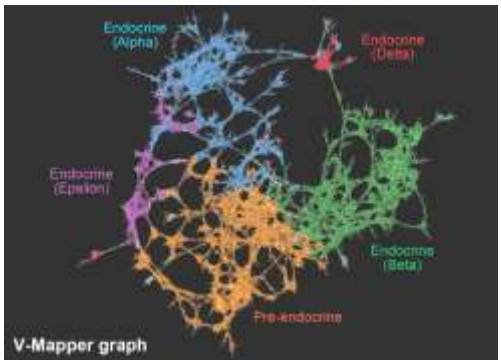
a) RECODE (resolution of curse of dimensionality):



The **Hiraoka group** has been investigating the noise reduction in single-cell RNA-sequence (scRNA-seq) data and have developed a method called RECODE (resolution of curse of dimensionality). In FY 2022, by conducting comprehensive performance comparisons with other existing methods, including Seurat, MAGIC, ENHANCE, and SAVER, the **Hiraoka group** verified that RECODE realizes the best single-cell resolution analysis among the methods; these results were published as described earlier (***Life Sci. Alliance*** 5, e202201591, 2022) (Figure: Performance comparison of RECODE, SAVER, and MAGC with RNA-FISH (ground truth)). Further, the **Hiraoka group** has made several improvements in RECODE to make it a standard preprocessing method for single-cell data analysis: (i) accuracy improvement using the latest high-dimensional statistics theory; (ii) comprehensive noise reduction (data integration) for technical noise and batch effects; and (iii) extension to epigenomic data such as scATAC-seq and scHi-C data. RECODE is currently being applied to many projects in ASHBi (**Saitou G**, **Ueno G**, **Alev G**, **T. Yamamoto G**, and others).

b) scEGOT (single-cell entropic Gaussian optimal transport):
The **Hiraoka group** has been developing a novel trajectory inference method called GMM-OT (Gaussian Mixture Model-Optimal Transport) for characterizing cell differentiations from scRNA-seq time-series data. In FY 2022, the **Hiraoka group** proved a series of mathematical theorems which provide mathematical justifications for the relevant algorithms. In particular, the main theorem about the convergence of the entropic Gaussian mixture model provides both a novel result in mathematics and a novel biological data analysis method, achieving true bidirectional fusion between mathematics and biology research. Moreover, based on this mathematically rigorous formulation, the **Hiraoka group** found that their method can also be applied to other types of problems, such as the spatio-temporal reconstruction of gene expression (with **Alev G**) and the identification of species differences, by embedding the gene expressions of multiple species into the same gene expression space using optimal transport theory (with **Saitou G**). Regarding the computational code, all the programs used were reconstructed and refactored in order to make render them robust and reusable, and now their codes are available to the public. In view of the significant mathematical improvements of this fiscal year, the **Hiraoka group** renamed the method scEGOT (single-cell entropic Gaussian optimal transport).

c) V-Mapper:
Mapper is a well-known topological data analysis method for extracting high-dimensional topological structures as a graph. The **Hiraoka group** has already applied Mapper to several biological problems of identifying cell differentiation pathways in immunological cells (with **Ueno G**) and germ cells (with **Saitou G**). They recognized that visualizing a velocity field (like RNA-velocity) of differentiation is important for obtaining the time information of the biological processes. To meet this biological demand, the **Hiraoka group** developed V-Mapper (velocity Mapper), which simultaneously describes a topological structure and time evolution as a weighted directed graph (V-Mapper graph) (Figure: V-Mapper for single-cell gene expression data of endocrine cells). They applied V-Mapper to single-cell gene expression data of pancreatic endocrine cell differentiation and found finer cell differentiation pathways than those obtained in prior research using RNA velocity. This result was published (***NOLTA IEICE*** 14, 92-105, 2023), and the code is open to the public (https://github.com/yusuke-imoto-lab/V-Mapper).



5. Bioethics at the periphery of birth and death
The bioethics group (**Fujita G**) in collaboration with life sciences groups in ASHBi has embarked on

"**Bioethics at the periphery of birth and death**'" as a Flagship Project (relevant to **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. However, it is difficult to access such tissues, and critically, there are no clear rules/regulations for such research in Japan. This project explores philosophical and empirical approaches for making rules/guidelines on the research use of such human tissues and consists of three interrelated initiatives:

a) To formulate rules for fetal tissue research:
Together with the **Saitou group** at ASHBi and **Takashima group** at CiRA, the **Fujita group** established an academic group that included philosophers, ethicists, and legal scholars, and discussed the ethical considerations of using fetal tissues in research, with goals for creating guidelines for conducting fetal tissue studies, compiling reports that form the academic basis for these studies, and clarifying the items that should be written in explanatory documents to donors. In FY 2022, to understand international trends, the group 1) reviewed the Vatican reports on fetal tissue research, and confirmed that while Catholics oppose abortion itself, they do not explicitly oppose life-saving measures such as vaccine development using aborted fetuses; and 2) translated the guidelines for fetal tissue research published by the International Society of Stem Cell Research into Japanese. However, since it is difficult to apply the international guidelines directly to the Japanese situation, the group 3) analyzed the relevant laws and regulations in Japan and clarified the need to consider several unresolved issues as follows. First, under Japanese law it is not clear whether a dead fetus less than 12 weeks old is a cadaver or waste, and therefore it is not clear who can make the decision to donate. In addition, because local ordinances regulating companies and facilities that collect and process placentae, umbilical cords, and omenta vary from region to region, researchers and abortion clinics must ensure to check and comply with their local regulations. Finally, when handling genomic information of fetal tissue that constitutes "personal information" of the parents, Japanese research guidelines require that consent be obtained from both the genetical father and mother, regardless of whether the information is anonymized or not. The group completed draft guidelines that reflect these considerations.

b) To construct a platform for early postmortem tissue research:
For studies on human aging, such as those of the Flagship Project of Basic/Clinical Medicine subdivision, it is desirable to procure early postmortem tissues from healthy elderly individuals. However, in addition to the difficulty in accessing such tissues, there are no clear rules governing their procurement in Japan. Young investigators led by **Dr. Okui** in **Fujita G** (4 junior researchers from the **Fujita group** and 8 from the life sciences group) aim to create institutional guidelines to address ethical, legal and social issues and construct a platform for early postmortem tissue research.

With Dr. Hewitt
in front of the NIH Clinical Center

As an early step in this process, the group performed a literature review on the Rapid Autopsy Program (RAP), which revealed that the sustainability of RAP requires substantive (not merely formal) informed consent that truly respects the donor's voluntariness and that stakeholder engagement is important for this purpose. Hence, the group conducted interview research on 6 institutions that practice some form of RAP, out of which the 4 institutions listed below were visited onsite, to gain first-hand insight into actual practice. Interviews with staff of the City of Hope National Medical Center and the Department of Molecular Diagnostic Pathology, Iwate Medical University were conducted online.

1. Weill Cornell Medicine:
   Juan Miguel Mosquera, M.D., M.Sc.; David Pisapia, M.D.
2. Memorial Sloan Kettering Cancer Center
   Michael H. A. Roehrl, MD, PhD, MBA
3. Alzheimer's Disease Research Center, Duke University
   Jerry Wang, MD, PhD; John Ervin, Lab Research Analyst
4. National Institute of Health
   Stephen Hewitt, M.D., Ph.D.; Daniel Chertow, MD; Ann Berger, MSN, MD; Nitin Roper, M.D., M.Sc.; Udayan Guha, M.D., Ph.D.

The result of the interview research confirmed the critical nature of the first-person patient consent that was suggested by our literature review. It further revealed that institutions are making efforts, in which various stakeholders are engaged, to ensure the integrity of the process by which individual patients and family members cope with the possibility or eventuality of death. It also revealed that such a process is not only an antemortem but a perimortem one, which continues even after the death of the patient.

c) To establish a research ethics consultation system:
In recent years, research on *in vitro* gametogenesis and culturing of human embryo models has developed rapidly. However, the existing laws and regulations were not written with such dramatic developments in mind, and thus there are currently no clear rules to govern such research either in Japan or abroad. To avoid ethical issues that may arise with the progress of such research as well as to promote such research in a timely manner, it is essential to have a system that can immediately address questions and concerns that scientists in ASHBi may have about the ethical aspects of their research. Accordingly, the **Fujita group** aims to establish a research ethics consultation system. Research ethics consultation is an advisory activity on research ethics that has become widespread at universities and research institutes in the United States since around 2000. Specifically, it advises scientists on protocol development, application for ethical review, writing on ethical considerations in papers, and knowledge of existing regulations. The **Fujita group** initiated these activities on a pilot basis with the **Alev group**, which plans to culture human embryo models in the long-term. Although culturing of human embryos beyond 14 days after fertilization is currently not permitted, there are no clear rules regarding human embryo models. So far this year, the group has prepared and submitted a research protocol, while exchanging information with the KU Headquarters, the institutional ethics committee, and the Ministry of Education, Culture, Sports, Science and Technology. Also, the group started similar discussions with the **Alev group** on culturing organoids derived from human–chimpanzee tetraploid hybrid iPSC lines.

Bottom-up approach to generate fused disciplines

Year	Category	Applicant	Project title
FY2020	Math-Bio	Y Imoto	Identification of multi-resolution cell differentiation dynamics from scRNA-seq data
	Math-Bio	T Yachimura	Characterization of gene regulatory networks in human and non-human in vitro segmentation clocks
	Math-Bio	T Tsujimura	Topological approaches for integrative 3D epigenomics
	Math-Bio	Y Yabuta	Inference of genome-wide DNA demethylation kinetics by dynamic model fitting research
	Ethics-Bio	T Sawai	Examining ethics and governance in developmental biology
	Bio-Bio	X Chen	Deciphering evolutionary differences of germline transposable element dynamics
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 guided by 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

To intensively promote bottom-up fusion research based on unconstrained ideas of young researchers, we established the **"ASHBi Fusion Research Grant Program"** in 2019. Ensuring fusion 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 progress report 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 is up to 3 million yen per year for each project. Two additional projects were selected in FY2022, making a total of 11 currently funded projects.

Generating fused disciplines through regular discussions
The ASHBi Colloquium is held once a month to promote collaborative research and to create opportunities for interaction between researchers of different disciplines. Each colloquium consists of presentations from two PI groups, in order to create an environment where participants with backgrounds in different research fields can come together for discussion. The Colloquium has been

held continuously since 2019 and has been held a total of 34 times. In FY2022, the Colloquium was held 9 times, with the 18 PI groups reporting their latest research results.

Generating fused disciplines through institution-wide gatherings

The ASHBi PI Retreat# was held for the first time on April 2-3, 2023, to achieve a deeper mutual understanding between PIs. This event was initiated to follow the good practices of other leading overseas institutes, such as EMBL, where the discussion-oriented seminars in which speakers and participants are limited to senior researchers (PI level) are held. The three PIs, **Alev**, **Murakawa**, and **Amemori**, each gave a two-hour presentation of their vision and one specific ongoing work to effectively elicit critical and constructive feedbacks from their colleagues.

The ASHBi Retreat# was held in-person for the first time in three years as an overnight event on April 3-4, 2023 at Arima in Hyogo Prefecture. During the COVID-19 pandemic, the ASHBi Retreat was conducted online in FY2020 and FY2021. More than 100 participants attended for this onsite event, including an external invited speaker. Nearly 50 presentations were made during the poster session, and active interaction between researchers and graduate students from different PI groups took place.

 # These PI and ASHBi Retreat were originally intended to take place in FY2022, but were postponed to April 2023 due to the COVID-19 pandemic.

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 researchers, we operate three core facilities as fundamental infrastructure, equipped with state-of-the-art technologies, to promote human biology research.

- **SignAC (Single-Cell Genome Information Analysis Core)** is a core facility that supports large-scale genomic analysis, including single-cell resolution analysis. In addition to the management of equipment, SignAC also offers data analysis services to researchers who are outside their field of expertise. Three new members have joined SignAC since FY2022, bringing the total number of members to ten: the Core Head (**Takuya Yamamoto**,), the Core Manager (**Taro Tsujimura**), two postdocs, four technical staff, one admin staff, and one office assistant. Under the supervision of the Core Head, the team is actively engaged in the facility operation and development of new analytical methods.

  As part of the KU's "**Innovative Support Alliance for Life Science (iSAL)**", an unified platform of core facilities related to life science studies, SignAC provides researchers in and out of ASHBi with smooth access to its facilities. Last year, SignAC launched analysis services using new long-read sequencers from PacBio and ONT, which can be accessed by both university researchers and external researchers through iSAL. Moreover, SignAC received an external grant from the Japan Agency for Medical Research and Development (AMED) in April 2022 to further expand the use of analysis expertise with long-read sequencers throughout Japan. With an increasing number of researchers using the SignAC facility, the total revenue exceeded 70 million yen in FY2022 while supporting more than 150 projects as collaboration or for analysis services.

- **PRiME (Primate Genome Engineering Core)** is a domestic satellite of ASHBi and is located in RCALS of the Shiga University of Medical Science. RCALS maintains a large primate colony

(~700 cages) and has some of the most advanced technologies for animal reproduction. In order to specifically generate genome-edited monkeys and retrieve oocytes/embryos for the research of ASHBi, we have been expanding the space of PRiME to maintain cynomolgus monkeys (126 m_2, 84 cages). We have appointed **Tomoyuki Tsukiyama** as the Core Head, and have hired two trained staff with advanced skills and knowledge of animal reproduction and breeding management.

- **NPAF (Non-human Primate Phenotype Analysis Facility)** is located in the Med-Pharm Building at the Faculty of Medicine Campus. In this facility, we analyze the phenotypic aspects of genome-edited macaque monkeys, including social interaction behavior, cognitive function, and emotional expressions. In FY 2022, we increased the cages and the total number of animals kept in the facility increased to 50 (by 12 since FY2021). In addition to the laboratory space for conducting physiological experiments (56.4 m^2), we constructed another experimental booth of 56.4 m^2. **Tadashi Isa** supervises the operation of this facility, and **Hirotaka Onoe** is responsible for studies using genome-edited monkeys. In addition to the two staff members who have been employed for the health care of the animals, animal feeding, cage cleaning, etc., we employed one additional technician who observes the animal behavior continuously and conducts eye movement measuring experiments in the monkey chair with head fixed, which we initiated in FY2022.

Internationalization of researchers and students

As of April 2023, 4 out of 16 PIs are of foreign nationality (**Alev**, **Bourque**, **Seirin-Lee**, and **Ueno**), bringing the ratio of non-Japanese PIs to 25%, exceeding the WPI standard of 20%. In order to further increase the ratio of non-Japanese PIs, the Institute will work closely with the KU's **"HAKUBI Project"**, which recruits 20 or more promising young researchers from around the world per year, with the aim of fostering world-class researchers at the University. Through the collaboration with the HAKUBI project, we will establish a system that allows some non-Japanese HAKUBI researchers to be invited to join the Institute as young PIs.

To increase the ratio of non-Japanese researchers at the Institute, we continue to utilize the **"ASHBi Foreign and Female Researcher Recruitment Support Program"**, which was originally established in 2019. Under this program, PIs can receive up to 5.5 million yen in support for hiring new non-Japanese or female researchers. Through this support, 4 new non-Japanese/female researchers were hired in FY2022. As of April 2023, the ratio of non-Japanese researchers in the Institute has increased to 37% and that of female researchers to 27%. We will continue to actively promote the recruitment of non-Japanese researchers, especially female non-Japanese researchers.

In order 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 supports the living expenses of international students studying at the Institute. Graduate students selected for this program can receive a monthly stipend of 150,000 yen for the duration of their enrollment in the doctoral (or master) degree program. Through this support, 11 new international students were recruited in FY2022. In addition, we also utilize the aforementioned **"McGill-Kyoto International Joint Program in Genomic Medicine (Joint PhD Program)"** to recruit international students, that has resulted in an additional 1 more international student who were recruited in FY2022. Due in part to the effectiveness of these two programs, as of April 2023,

of the 89 students hosted and supervised by the Institute's PIs, 26 are international students (29%) and 28 are female students (31%).

Cooperation with world-leading research institutions/organizations

The Institute has actively participated in research exchanges with some of the world's leading research communities. One example being the relationship with **EMBO** (the **European Molecular Biology Organization**). The Institute and EMBO has and will continue to co-organize "EMBO-Japan Virtual Lectures", with particular emphasis on exchanges between senior researchers and young researchers and students. To date, two lectures have already been held. We will continue to co-host these lectures in 2023 and beyond. In addition, the Institute has been involved in activities with the **ISSCR** (the **International Society for Stem Cell Research**). In Aug 2020, ASHBi joined the "International Circle of Stem Cell Research Institutes and Centers", consisting of 25 leading institutes/centers. Two of the Institute's PIs are currently participating as working group members of ISSCR Guidelines Update Task Force for Stem Cell Research and Clinical Translation. Furthermore, the Institute, together with KU School of Medicine, has signed an agreement with the **Max Delbrück Center for Molecular Medicine** (Berlin, Germany) to initiate an organized research collaboration from 2022. This collaboration will promote the following activities: 1) exchange of scientific materials, publications, and information; 2) exchange of faculty and researchers; 3) exchange of students; and 4) joint research and meetings for research.

Research exchanges via international conferences/seminars

In order to create opportunities for exchanges with overseas researchers, we have held about 200 symposia, workshops, and seminars of both large and small scale (https://ashbi.kyoto-u.ac.jp/events/) since the Institute was established in October 2018. In FY2022, we continued to make effort to hold international meetings and organized a total of 51 meetings, including 6 large-scale international meetings in an onsite/online format: "**EMBO Workshop: Molecular Mechanisms of Developmental and Regenerative Biology**" (April 2022), international summer school "**JANUBET Symposium**" (September 2022), "**Workshop for Mathematical Human Biology**" (November 2022), "**Ethical, Legal, and Social Issues of Human Brain Organoid Research and Application**" (December 2022), "**Human Development from Embryos to Stem Cell Models**" (March 2023), and "**Deconstructing and Reconstructing embryonic development**" (March 2023).

Additionally, to increase the opportunities for exchange with overseas researchers, each PI is required to organize one seminar per year inviting researchers from abroad (**ASHBi Seminars**). In FY2022, 18 seminars were organized and the Institute covered the travel expenses of speakers to Japan if they were held at the Institute.

Participation in the graduate student education

As ASHBi/KUIAS is not a graduate school, it does not have its own graduate/undergraduate students or program. Hence, only those who are tenured professors at the ASHBi/KUIAS can be a collaborative faculty member of KU's graduate school and have their own students. Currently, the Institute's tenured professors **Murakawa** and **Seirin PIs,** are collaborative faculty members of the KU Graduate school of Medicine.

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.

Interim evaluation of the Institute's PIs

Before the start of the second half of the WPI program in April 2023, an interim evaluation was conducted for the Institute's PIs at the end of FY2022. The Evaluation was held for the 11 PIs who joined the Institute since its establishment (excluding the Institute's Director). Since the employment period of other young PIs who were hired after the Institute's establishment was still short, their performance was not evaluated. Each PI was asked to write a self-evaluate report on their own performance based on research achievements over the first five years of the WPI program, research plans for the next five years, and by providing a numerical self-evaluation score of their own research activities. On the basis of this assessment, the Institute's research organizational structure was optimized from 18 PIs to 16 PIs. The two PI posts that were opened will be used to recruit new promising young PIs in the future.

Creating an environment that accelerates research

The Institute's administrative organization (Administrative Office) is led by **Tadashi Ogawa** and composed of the "Research Acceleration Unit" and the "Administrative Management Unit". The former consists of four experts (**Spyros Goulas**, **Tomoki Shimizu**, **Makoto Shida**, and **Hiromi Inoue**) that provide unique problem-solving type support associated with conducting research (e.g. creating programs to implement an institute-wide issue, supporting non-Japanese researcher activities).

In addition to direct support to the Institute's researchers, this Unit also organized seminars with the aim of fostering young researchers and graduate students. In FY2022, the Unit held two seminars for scientific writing, one for international news release, and two for grant/fellowship writing. To improve the likelihood of papers being accepted in high impact journals, the Unit also held seminars inviting editors of top-tier journals (e.g. *Nature*, *Cell*, and *EMBO Journal*), to present details behind article review policies and editorial processes. The majority of these seminars were held as a hybrid format and were open to academic researchers outside the Institute, thereby helping to foster early-career researchers throughout Japan.

Comprehensive support for holding research meetings

Since the Institute's establishment in Oct 2018, a total of 200 international symposia and seminars have been held to date. In FY2022 alone, the Institute has hosted 51 meetings, including 6 large-scale international conferences. Our ability to hold numerous meetings is largely due to the fact that the Institute has two staff members dedicated to organizing research meetings. They handle most of the preparations for holding meetings (including creating posters, disseminating meeting information, registering participants, and arranging airline tickets and lodging for overseas speakers), that greatly reduce the burden on the Institute's researchers when organizing such meetings.

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.

In order to carry out the Institute's operations and research activities after the WPI program, KU will provide various support as described below.

KU's personnel support
KU will provide 5 professorship tenure positions to the Institute. Two of these tenure positions have already been given to the Institute at the end of 2021. KU will provide three more tenure positions by April 2024 and actively seek possibilities to assign additional posts when necessary. In order to increase the number of foreign PIs at the Institute in the long-term, KU will establish a system to assign researchers from the HAKUBI Project as young PIs to the Institute. With the aim of fostering world-leading researchers, the HAKUBI project recruits 20 or more promising young researchers around the world each year. Through close collaborations with the HAKUBI Project, we will effectively promote the further internationalization of the Institute's PIs.

KU's financial support
For indirect funding acquired by the Institute's researchers, the portion that is regularly allocated to the university headquarters' will be allocated to the Institute as a special budget for KU's WPI centers[#1]. Under this special KU budget, KU provides three types of cost assistance as follows.
[#1] A special budget for WPI centers secured by the university headquarters.

- The Institute's PIs will continue to receive allowance and post-doctoral employment expenses (at least one) to keep the integrity of the Institute's PIs even after the end of WPI funding.
- The Institute's main building will be maintained by covering its rental costs / utility expenses with the financial support from KU.
- The Administrative Office's functions will be maintained by covering its personnel/operating costs with the financial support from KU.

KU's support for the core facility maintenance
SignAC serves as the foundation for single-cell genomics research at the Institute. To enhance visibility and convenience of this facility, KU has invited SignAC to join the "Innovative Support Alliance for Life Science (iSAL) in December 2020. This alliance is a university-wide platform of core facilities from various departments related to life science studies and provides open access to KU's internal and external researchers. To ensure the sustainability and further development of SignAC after the WPI program, KU will make SignAC a university-wide shared facility and take responsibility of its personnel, operating costs and further developments.

System reform for supporting the Institute's development
Kyoto University Institute for Advanced Study (KUIAS), to which the Institute belongs, is an organization that receives special incentives from the University in order to serve as a vanguard for KU's system reform. The Institute has received the following four incentives from KU.

- KU allows high-degree of independence for the Institute Director with the special structure of the KUIAS.
- KU allows the Institute to incorporate a flexible multiple-year budget for its funds. This enables the Institute to carry over a portion of its budget over to the next fiscal year to ensure flexibility in its budget operations.
- KU allows the Institute to retain its excellent researchers to be employed even after the retirement age of 65.
- KU allows the Institute to introduce a flexible allowance payment system so that the annual salary of tenured researchers, which is determined by the academic regulations, can be increased in accordance with their research achievements.

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 Institute's Outreach Activities (see Appendix 6 for details of each activity)

- **Open house:** Activities such as site visit by students from Takamatsu Dai-ichi High School (Kagawa Prefecture) during their school excursion and an open campus event for KU undergraduate and graduate students contributed in raising visibility of the Institute to younger generations.

- **The Institute's website:** In addition to the ASHBi website (20,000-30,000 PV per month), we hired KU graduate students to create website homepages focusing on research activities of the graduate students at the Institute.

- **Outreach to industry:** The Institute's **'First Contact Program'** enabled 3 early-career researchers to present his/her research in an easy and understandable way, to the company researchers, creating interaction opportunities between industry and academia to foster potential future collaborations.

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.

Advice/recommendations
(Including opinions on the host institution's plan toward a sustainable Center)

1) Accelerating the synthesis and coherence of research that is strategically aligned with ASHBi's founding vision should be the Center's top priority. Utmost effort needs to be made to execute the Flagship Projects from this point of view. The five flagship projects should be more cohesively correlated so that they do not appear to be a collection of research from different fields. Clear goals and milestones need to be set for the successful completion of the project in order to effectively address ASHBi's fundamental question of what makes us "human."

Response 1. Please see **2. Generating Fused Disciplines** for details and progresses of the 5 Flagship Projects. We believe that the 5 projects, including those for fusions with mathematics and bioethics, are topically and methodologically interrelated and contribute to addressing our fundamental questions of what makes us human in a bottom-up manner. The 5 Flagship Projects groups have progress meetings in a regular manner and all groups report their progress in the annual ASHBi Flagship meeting.

In addition, as stated in the Self-Evaluation Report for Interim Evaluation, in line with the recommendation of WPI WG ("*one of ASHBi's goals is to identify the genomic sequences (or regions) that make us human*"), we have been performing a number of relevant investigations each at PI level. Please see **Response 5** in **10. Center's Response to Results of FY 2021 Follow-up** in the Self-Evaluation Report for Interim Evaluation.

2) For ASHBi to become a true international hub for human biology, it would be advisable for it to increase the number of its foreign and female PIs and also its junior researchers including postdocs.

Response 2. We have been continuing our efforts to increase the number of foreign and female PIs/researchers in ASHBi. First, the ASHBi director performed interim evaluation of the activities of ASHBi PIs and their contributions to ASHBi and decided to reorganize the PI board. Accordingly, from April 2023 onward, ASHBi consists of 16 PIs (a change from 18 PIs to 16 PIs) and 3 core heads (2 of them are co-appointed with PI), increasing the ratio of foreign and female PIs and creating at least 2 more positions to recruit new PIs. In collaboration with the HAKUBI project and other KU departments, ASHBi is currently searching for excellent young foreign and/or female PI candidates. Second, to increase the ratio of foreign and female researchers and students, we are continuing to implement the "Foreign and Female Researcher Recruitment Support Program" and "International

Graduate Student Financial Support Program." As of April 2023, the ratios of foreign and female researchers in ASHBi are 37% and 27%, respectively, and the ratios of foreign and female graduate students are 30% and 32%, respectively (see "**Internationalization of researchers and students**" in pages 15-16). We will continue to strongly pursue the internationalization of ASHBi in the second half through these efforts.

3) Kyoto University should clarify the following points in its support plan; (i) Transferring senior PI positions to ASHBi so that its core researchers can be sustainably maintained after the WPI funding ends, (ii) Maintaining the center's administration, including its Research Acceleration Unit, after the WPI funding ends, and (iii) Effort to be made to change the system and culture of the host institution, rather than just maintaining ASHBi after the WPI funding ends.

Response 3. (i) To maintain the long-term research excellence of ASHBi, we, at ASHBi, consider it important to establish a system for flexible updating of the PI-member formation so that excellent and relevant PIs in KU can join the ASHBi activities in a timely manner, while maintaining the core PI positions at ASHBi (currently, we have 7 core PI posts in ASHBi: **Saitou**, **Hiraoka**, **Murakawa**, **Seirin-Lee**, and 3 additional posts allocated by KU currently under recruitment). We believe that this affiliation format is a more sustainable and flexible system compared to the format to transfer all PIs to one affiliation, which might result in the reduction of its flexibility. To establish a true "Center for Excellence", through tight co-operation with the KU headquarters, we will continue to work to maintain and develop excellent research environments and support systems including providing PI allowances and postdoc positions, which will be crucial for attracting excellent PIs.

(ii) A special budget for ASHBi will be secured by the KU headquarters (see "**KU's financial support**" in page 18), which will be used to ensure that the Administrative Office's functions, including its Research Acceleration Unit, will be maintained after the end of the WPI funding program.

(iii) KU is currently planning to reform its research support/administration system at the KU-wide level. In its plan, KU recognizes the research support activities and functions of ASHBi as one of the best practice models for its reforms. For the core facility function, KU has evaluated SignAC highly as a good practice model of a KU-wide shared facility and will support its operational costs to more actively expand its service throughout KU. For the research administrative/support function, the KU Provost made an on-site visit to review the activities of the Administrative Office and the Research Acceleration Unit to find what can be implemented into the system reform at the KU-wide level. These plans and activities clearly show the KU's intentions to extend the system reforms made at ASHBi into the KU-wide systems reform.

Appendix 1 FY 2022 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2022. (Note: The list should be for the calendar year, not the fiscal year.)

(1) Divide the papers into two categories, A and B.

A. WPI papers
List papers whose author(s) can be identified as affiliated with the WPI program (e.g., that state "WPI" and the name of the WPI center (WPI-center name)). (Not including papers in which the names of persons affiliated with the WPI program are contained only in acknowledgements.)

B. WPI-related papers
List papers related to the WPI program but whose authors are not noted in the institutional affiliations as WPI affiliated. (Including papers whose acknowledgements contain the names of researchers affiliated with the WPI program.)

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

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

A. WPI papers
1. Original articles
2. Review articles
3. Proceedings
4. Other English articles

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

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

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

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

A. WPI Papers

1. Original Articles

1) Asao, Y., **Hiraoka, Y.**, & Kanazawa, S. (2023). Girth, magnitude homology and phase transition of diagonality. ***Proceedings of the Royal Society of Edinburgh Section a-Mathematics***. doi:10.1017/prm.2023.7

2) Gyobu-Motani, S., Yabuta, Y., Mizuta, K., Katou, Y., Okamoto, I., Kawasaki, M., Kitamura, A., **Tsukiyama, T.**, Iwatani, C., Tsuchiya, H., Tsujimura, T., **Yamamoto, T.**, Nakamura, T., & **Saitou, M.** (2023). Induction of fetal meiotic oocytes from embryonic stem cells in cynomolgus monkeys. ***Embo Journal***. doi:10.15252/embj.2022112962

3) Imoto, Y., & **Hiraoka, Y.** (2023). V-Mapper: topological data analysis for high-dimensional data with velocity. ***Nonlinear Theory and Its Applications, IEICE***, *14*(2), 92-105. doi:10.1587/nolta.14.92

4) Miyazaki, T., Kanatsu-Shinohara, M., **Ema, M.**, & Shinohara, T. (2023). Signal regulatory protein alpha is a conserved marker for mouse and rat spermatogonial stem cells(dagger). ***Biology of Reproduction***. doi:10.1093/biolre/ioad006

5) Mori, T., Okamoto, Y., Mu, A. F., Ide, Y., Yoshimura, A., Senda, N., Inagaki-Kawata, Y., Kawashima, M., Kitao, H., Tokunaga, E., Miyoshi, Y., Ohsumi, S., Tsugawa, K., Ohta, T., Katagiri, T., Ohtsuru, S., Koike, K.,

Ogawa, S., Toi, M., Iwata, H., Nakamura, S., Matsuo, K., & Takata, M. (2023). Lack of impact of the ALDH2 rs671 variant on breast cancer development in Japanese BRCA1/2-mutation carriers. ***Cancer Medicine***, *12*(6), 6594-6602. doi:10.1002/cam4.5430

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7) Sugawara, Y., Hirakawa, Y., Nagasu, H., Narita, A., Katayama, A., Wada, J., Shimizu, M., Wada, T., Kitamura, H., Nakano, T., Yokoi, H., **Yanagita, M.**, Goto, S., Narita, I., Koshiba, S., Tamiya, G., Nangaku, M., Yamamoto, M., & Kashihara, N. (2023). Genome-wide association study of the risk of chronic kidney disease and kidney-related traits in the Japanese population: J-Kidney-Biobank. ***Journal of Human Genetics***, *68*(2), 55-64. doi:10.1038/s10038-022-01094-1

8) Takeuchi, M., Shinkawa, K., **Yanagita, M.**, & Kawakami, K. (2023). Hypothetical intervention of targeted systolic blood pressure control of < 120 mmHg on renal prognosis for persons with stage 3-4 chronic kidney disease: an application of parametric g-formula using health checkup data in Japan. ***Clinical and Experimental Nephrology***. doi:10.1007/s10157-023-02341-1

9) Utagawa, K., Shin, T., Yamada, H., Ochi, H., Sunamura, S., Unno, A., Akazawa, C., **Ema, M.**, Takeda, S., Okawa, A., & Sato, S. (2023). Three-dimensional visualization of neural networks inside bone by Osteo-DISCO protocol and alteration of bone remodeling by surgical nerve ablation. ***Sci Rep***, *13*(1), 4674. doi:10.1038/s41598-023-30492-4

10) Watase, M., Masaki, K., Chubachi, S., Namkoong, H., Tanaka, H., Lee, H., Fukushima, T., Otake, S., Nakagawara, K., Kusumoto, T., Asakura, T., Kamata, H., Ishii, M., Hasegawa, N., Oyamada, Y., Harada, N., Ueda, T., Ueda, S., Ishiguro, T., Arimura, K., Saito, F., Yoshiyama, T., Nakano, Y., Mutoh, Y., Suzuki, Y., Edahiro, R., Sano, H., Sato, Y., Okada, Y., Koike, R., Kitagawa, Y., Tokunaga, K., Kimura, A., Imoto, S., Miyano, S., **Ogawa, S.**, Kanai, T., Fukunaga, K., & Japan, C.-T. F. (2023). Impact of accumulative smoking exposure and chronic obstructive pulmonary disease on COVID-19 outcomes: report based on findings from the Japan COVID-19 task force. ***International Journal of Infectious Diseases***, *128*, 121-127. doi:10.1016/j.ijid.2022.12.019

11) Ariyasu, Y., Sato, Y., Isobe, Y., Taniguchi, K., **Yanagita, M.**, & Arita, M. (2022). Sterol O-Acyltransferase Inhibition Ameliorates High-Fat Diet-Induced Renal Fibrosis and Tertiary Lymphoid Tissue Maturation after Ischemic Reperfusion Injury. ***International Journal of Molecular Sciences***, *23*(24). doi:10.3390/ijms232415465

12) Ashida, S., Kondo, T., Fujii, C., Hamatani, M., Mizuno, T., & Ochi, H. (2022). Association of cerebrospinal inflammatory profile with radiological features in newly diagnosed treatment-naive patients with multiple sclerosis. ***Frontiers in Neurology***, *13*. doi:10.3389/fneur.2022.1012857

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14) Bloem, B., Huda, R., **Amemori, K.**, Abate, A. S., Krishna, G., Wilson, A. L., Carter, C. W., Sur, M., & Graybiel, A. M. (2022). Multiplexed action-outcome representation by striatal striosome-matrix compartments detected with a mouse cost-benefit foraging task. ***Nature Communications***, *13*(1). doi:10.1038/s41467-022-28983-5

15) Butler-Laporte, G., Povysil, G., Kosmicki, J. A., Cirulli, E. T., Drivas, T., Furini, S., Saad, C., Schmidt, A., Olszewski, P., Korotko, U., Quinodoz, M., Celik, E., Kundu, K., Walter, K., Jung, J., Stockwell, A. D., Sloofman, L. G., Jordan, D. M., Thompson, R. C., Del Valle, D., Simons, N., Cheng, E., Sebra, R., Schadt, E. E., Kim-Schulze, S., Gnjatic, S., Merad, M., Buxbaum, J. D., Beckmann, N. D., Charney, A. W., Przychodzen, B., Chang, T., Pottinger, T. D., Shang, N., Brand, F., Fava, F., Mari, F., Chwialkowska, K., Niemira, M., Pula, S., Baillie, J. K., Stuckey, A., Salas, A., Bello, X., Pardo-Seco, J., Gomez-Carballa, A., Rivero-Calle, I., Martinon-Torres, F., Ganna, A., Karczewski, K. J., Veerapen, K., Bourgey, M., **Bourque, G.**, Eveleigh, R. J., Forgetta, V., Morrison, D., Langlais, D., Lathrop, M., Mooser, V., Nakanishi, T., Frithiof, R., Hultstrom, M., Lipcsey, M., Marincevic-Zuniga, Y., Nordlund, J., Barrett, K. M. S., Lee, W., Bolze, A., White, S., Riffle, S., Tanudjaja, F., Sandoval, E., Neveux, I., Dabe, S., Casadei, N., Motameny, S., Alaamery, M., Massadeh, S., Aljawini, N., Almutairi, M. S., Arabi, Y. M., Alqahtani, S. A., Al Harthi, F. S., Almutairi, A., Alqubaishi, F., Alotaibi, S., Binowayn, A., Alsolm, E. A., El Bardisy, H., Fawzy, M., Cai, F., Soranzo, N., Butterworth, A., Geschwind, D. H., Arteaga, S., Stephens, A., Butte, M. J., Boutros, P. C., Yamaguchi, T. N., Tao, S., Eng, S., Sanders, T., Tung, P. J., Broudy, M. E., Pan, Y., Gonzalez, A., Chavan, N., Johnson, R.,

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2. Review articles

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B. WPI-related Papers

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2. Review articles

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Neuroimaging at 7 Tesla: a pictorial narrative review. ***Quantitative Imaging in Medicine and Surgery**, 12*(6), 3406-3435. doi:10.21037/qims-21-969

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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 2022 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
2023/3/31	Yasuhiro Murakawa	Mapping novel functional genetic elements in mammals	36th International Mammalian Genome Conference (IMGC2023), Tsukuba, Japan
2023/3/17	Yasuaki Hiraoka	Persistent Homology: Theory and Application	Mathematical Society of Japan Spring Meeting 2023, Chuo University, Japan
2023/2/22	Ken-ichi Amemori	Exploring the neural pathway of anxiety and depression in non-human primates	Mental Health Challenge Area (MHCA) at Wellcome Trust
2022/10/15	Motoko Yanagita	Role of tertiary lymphoid tissues in kidney inflammation	International Society of Hypertension 2022, Kyoto, Japan
2022/9/19	Takashi Hiiragi	Self-organization in mammalian development	Janelia Conference "Imaging Mouse Development", Janelia, USA
2022/9/14	Hideki Ueno	B cell response in the tumor microenvironment of human endometrial cancer	The International Symposium "Cancer Immunology, Genomics and Metabolism", Nagoya University, Japan
2022/9/10	Tadashi Isa	Sensorimotor and cognitive functions of blindsight macaques	"Comparative Neurobiology of higher cognitive functions", Erice, Italy
2022/6/29	Takuya Yamamoto	Spatial transcriptomics to elucidate subcellular RNA localization	The 74th Annual Meeting of the Japan Society for Cell Biology, Tokyo, Japan
2022/6/22	Guillaume Bourque	Transposable elements are a source of innovation and variability in our response to infection	Journées Ouvertes en Biologie, Informatique et Mathématiques (JOBIM 2022), Rennes, France
2022/6/17	Seishi Ogawa	Clonal evolution in normal tissues	2nd International Congress of Asian Oncology Society (AOS 2022), Seoul, Korea
2022/6/15	Cantas Alev	Modeling the human segmentation clock with pluripotent stem cells	20th Annual Meeting of the International Society for Stem Cell Research (ISSCR), San Francisco, USA
2022/6/2	Mitinori Saitou	Mechanism and In Vitro Reconstitution of Mammalian Germ-Cell Development	CSHL 2022 Symposium/Genome Stability & Integrity, Cold Spring Harbor, USA
2022/5/9	Mototsugu Eiraku	Mechanical forces in morphogenesis	24th Biennial Meeting of the International Society for Developmental Neuroscience, Vancouver, Canada
2022/4/27	Misao Fujita	Ethical and regulatory issues in developmental biology	EMBO/The Company of Biologists Workshop "Molecular mechanisms of developmental and regenerative biology", Online

3. Major Awards

- List up to 10 main awards received during FY 2022 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
2023/2/17	Motoko Yanagita	Academic Award, The Kidney Foundation, Japan

Appendix 2　FY 2022 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 FY2022> **Principal Investigators Total: 18**

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 Mitinori SAITOU	52	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	48	Associate Professor Institute for the Advanced Study of Human Biology (ASHBi) Kyoto University	Developmental Biology	100%	Jul.1, 2019	Usually stays at the center and participates in the center's activities	
Ken-ichi AMEMORI	49	Associate Professor Institute for the Advanced Study of Human Biology (ASHBi) Kyoto University	Neuroscience	100%	Sep. 1, 2020	Usually stays at the center and participates in the center's activities	
Guillaume BOURQUE	46	Professor, Human Genetics, McGill University	Bioinformatics, Genomics, Epigenomics	25%	Oct.30, 2018	Stays at Kyoto University 3 times per year for 3-4 weeks (total ~11 weeks)	Student Exchange utilizing McGill-Kyoto International Joint Program in Genomic Medicine
Mototsugu EIRAKU	48	Professor Laboratory of Developmental System, Institite for Frontier Life and Medical Sciences, Kyoto University	PhD Developmental Biology	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
Masatsugu EMA	54	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	

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
Misao FUJITA	53	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	
Takashi HIIRAGI	55	Hubrecht Institute Group Leader/ Professor, Graduate School of Medicine, Kyoto University	Developmental Biology	20%	Oct.30, 2018	Stays at the center every 2-3 months and participates in the center's activities	
Vice director Yasuaki HIRAOKA	45	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	
Vice director* Tadashi ISA	62	Professor, Graduate School of Medicine, Kyoto University	Neuroscience	80%	Oct.30, 2018	Usually stays at the center and participates in the center's activities as Vice Director and Executive Board member (*Vice Director until Sep. 30, 2022)	
Yasuhiro MURAKAWA	40	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	
Seishi OGAWA	61	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	

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
Sungrim SEIRIN-LEE	45	Professor Institute for the Advanced Study of Human Biology (ASHBi) Kyoto University	Mathematical Biology and Medicine, Mathematical modeling, Applied Mathematics	100%	Oct.1, 2021	Usually stays at the center and participates in the center's activities	
Tomoyuki TSUKIYAMA	39	Associate Professor, Research Center for Animal Life Science, Shiga University of Medical Science	PhD Developmental Engineering, Reproductive and Stem Cell Biology	100%	Jan.1, 2020	Usually stays at the center and participates in the center's activities	
Ryo YAMAMOTO	47	Associate Professor Institute for the Advanced Study of Human Biology (ASHBi) Kyoto University	Hematology	100%	Apr. 1, 2020	Usually stays at the center and participates in the center's activities	
Core Head (SignAC) Takuya YAMAMOTO	45	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	
Hideki UENO	55	Professor, Graduate School of Medicine, Kyoto University	Immunology	95%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
Motoko YANAGITA	53	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 2022

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 2022 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 will provide 5 professorship tenure positions to the Institute. Two of these tenure positions have already been given to the Institute at the end of 2021. KU will provide three more tenure positions by April 2024 and actively seek possibilities to assign additional posts when necessary.

In order to increase the number of foreign PIs at the Institute in the long-term, the Institute and KU will collaborate to establish a system to assign researchers from the HAKUBI Project as young PIs to the Institute. With the aim of fostering world-leading researchers, the HAKUBI project recruits 20 or more promising young researchers around the world each year. Through close collaborations with the HAKUBI Project, we will effectively promote the further internationalization of the Institute's PIs.

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 FY2022 and give up to three examples of the most representative ones using the table below.

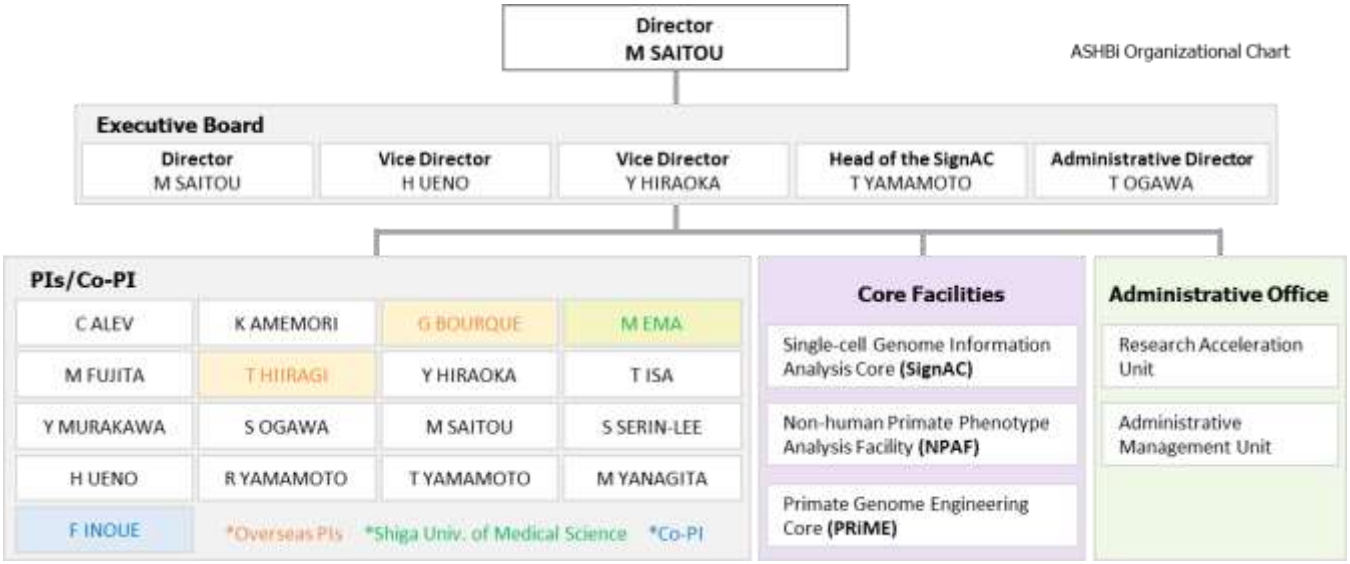
FY 2022: 5 meetings	
Major examples (meeting titles and places held)	Number of participants
EMBO Workshop: Molecular Mechanisms of Developmental and Regenerative Biology *(ONLINE)* *with EMBO & Company of Biologists* Apr 26-29, 2022 *Originally planned at Kyoto but changed to Online*	**Total:** From domestic institutions: 196 From overseas institutions: 307 **Speakers/Chairs:** From domestic institutions: 8 From overseas institutions: 18
JANUBET Symposium *(HYBRID)* *With Norwegian University of Science and Technology (NTNU) and Tohoku University* Sep 20-22, 2022 Clock Tower Centennial Hall, Kyoto University	**Total:** From domestic institutions: 64 From overseas institutions: 30 **Speakers/Chairs:** From domestic institutions: 6 From overseas institutions: 15

Human Development - from Embryos to Stem Cell Models *(ONSITE)* *with Cold Spring Harbor Asia (CSHA)* Mar 5-10, 2023 Awaji Yumebutai International Conference Center	**Total:** From domestic institutions: 17 From overseas institutions: 78 **Speakers/Chairs:** From domestic institutions: 6 From overseas institutions: 49

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).

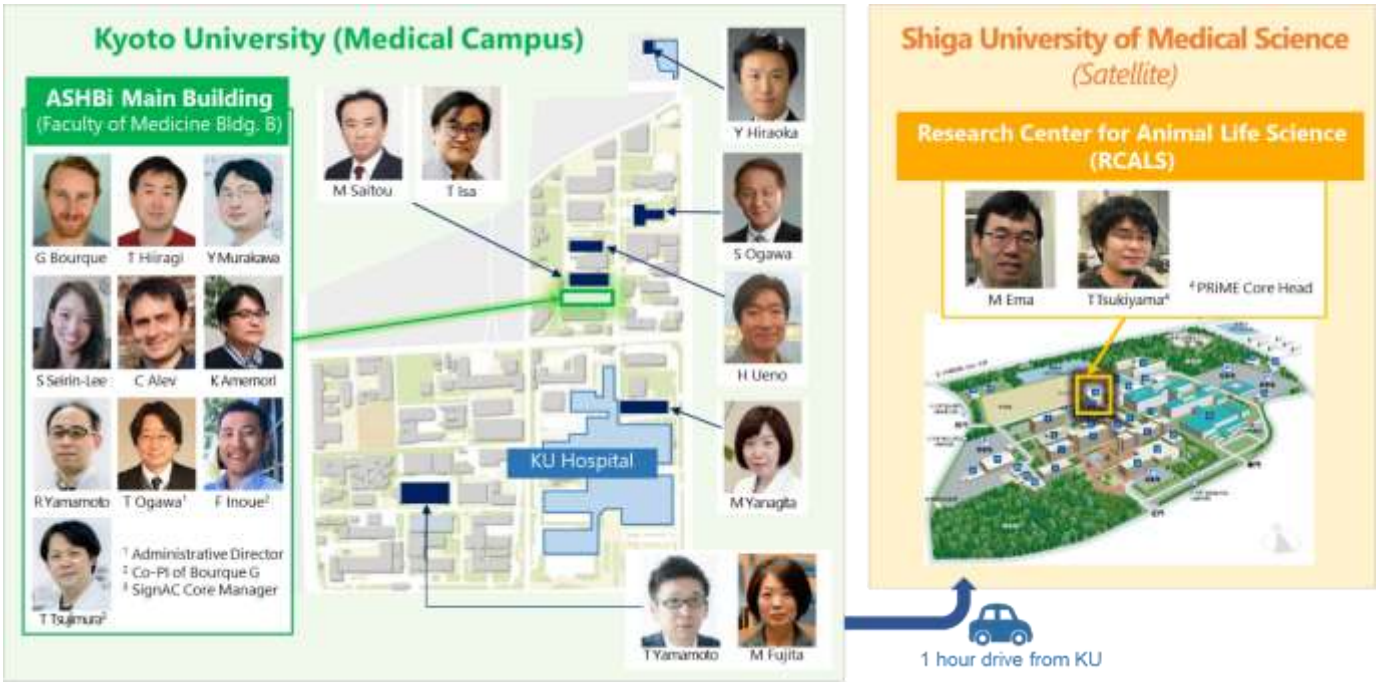
Organizational Diagram as of Apr. 2023



4. Campus Map

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

Campus Map as of Apr. 2023



5. Securing external research funding*

External research funding secured in FY2022

Total: 1,372,837,560 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 (Proportionally distributed)
Grants-in-Aid for Scientific Research (KAKENHI)	284,760,545 yen
Commissioned Research Projects	701,200,725 yen
Joint Research Projects	136,833,253 yen
Others (Donation funds, etc)	250,043,037 yen
Total* (total for above mentioned)	**1,372,837,560 yen**

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

Organization	Fund name	PI	Funding amount (Secured amount)
Open Philanthropy	Open Philanthropy Fund	Mitinori Saitou	153,660,121 yen
AMED	Japan Initiative for World-leading Vaccine Research and Development Centers (Support institutions)	Hideki Ueno	88,486,803 yen
AMED	Advanced Research & Development Programs for Medical Innovation (AMED-CREST)	Seishi Ogawa	69,970,400 yen
KAKENHI	Grant-in-Aid for Specially Promoted Research	Mitinori Saitou	66,000,000 yen
AMED	Research Program on Emerging and Re-emerging Infectious Diseases	Hideki Ueno	45,328,770 yen
AMED	Moonshot Research and Development Program	Seishi Ogawa	38,541,339 yen
Collaboration Research (Chordia Therapeutics Inc.)	Next-generation Oncology Discovery	Seishi Ogawa	35,049,805 yen
Collaboration Research (Nanpuh Hospital)	Next-generation Clinical Genomic Medicine	Seishi Ogawa	31,875,991 yen
AMED	Moonshot Research and Development Program	Motoko Yanagita	31,000,000 yen

Appendix 3-1a FY 2022 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 2022	Final goal (Date: Mar, 2025)
Researchers from within the host institution	8	14	13
Researchers invited from overseas	4	2	2
Researchers invited from other Japanese institutions	1	2	1
Total principal investigators	13	18	16

b) Total members

	At the beginning of project		At the end of FY 2022		Final goal (Date: Mar, 2025)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	13		66		70	
Overseas researchers	4	31	23	35	26	37
Female researchers	3	23	16	24	21	30
Principal investigators	13		18		16	
Overseas PIs	4	31	4	22	4	25
Female PIs	3	23	3	17	3	19
Other researchers	0		21		27	
Overseas researchers	0	0	5	24	8	30
Female researchers	0	0	4	19	9	33
Postdocs	0		27		27	
Overseas postdocs	0	0	14	52	14	52
Female postdocs	0	0	9	33	9	33
Research support staffs	2		22		22	
Administrative staffs	3		30		30	
Total number of people who form the "core" of the research center	18		118		122	

	At the beginning of project		At the end of FY 2022		Final goal (Date: Mar, 2025)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	-		83		90	
Employed	-	0.0	12	14.5	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):15	159	46
	Other researchers (no. of persons):46	230	213
	Research support staff (no. of persons):45	102	102
	Administrative staff (no. of persons):36	101	52
	Subtotal	622	417
Project activities	Research startup costs	15	6
	Fusion Research startup cost	114	102
	Cost of satellite organizations (no. of satellite organizations):1	78	78
	Cost of international symposiums	9	5
	Rental fees for facilities	24	2
	Cost of utilities	13	0
	Cost of maintenance of Core Facility	53	23
	Cost of Young Researcher Foster programs	5	3
	Cost of outreach	5	3
	Cost of maintenance contracts	17	13
	Cost of consumables	32	8
	Other costs	0	0
	Subtotal	365	243
Travel	Domestic travel costs	0	0
	Overseas travel costs	1	0
	Travel and accommodations cost for invited scientists	0	0
	(no. of domestic scientists):0	0	0
	(no. of overseas scientists):0	0	0
	Travel cost for scientists on transfer	0	0
	(no. of domestic scientists):0	0	0
	(no. of overseas scientists):0	0	0
	Subtotal	1	0
Equipment	Cost of laboratory maintenance (repair work, etc.)	45	39
	Cost of open laboratory equipments maintenance, etc.	38	0
	Subtotal	83	39
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	12	0
	KAKENHI	285	0
	Commissioned research projects, etc.	701	0
	Joint research projects	137	0
	Ohers (donations, etc.)	250	0
	Subtotal	1385	0
Total		2456	699

Costs (Million yens)

WPI grant in FY 2022	700
Costs of establishing and maintaining facilities	26
Repairing facilities	26
(Number of facilities: 1, 2,010 m²)	
Costs of equipment procured	13
Macaca pair cage	10
(Number of units:1)	
Pre-fabricated soundproof room,white LED Light Unita and aluminum slope	1
(Number of units:1)	
Others	2

*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" block.

*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):2		
	Other researchers (no. of persons):2		
	Research support staff (no. of persons):1		
	Administrative staff (no. of persons):0		
	Subtotal	36	26
Project activities	Subtotal	43	43
Travel	Subtotal	0	0
Equipment	Subtotal	8	8
Research projects	Subtotal	52	0
Total		139	77

Appendix 4 FY 2022 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2022 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. 2023 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 2022. 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
FY2022					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2022					

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
FY2022					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2022					

Appendix 5 FY 2022 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: 93

	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	Bernard de Massy	64	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	Oct 17, 2021 -May 15, 2022	JSPS Invitational Fellowships for Research in Japan (Long-term)
2	Rahul Sinha	46	Instructor, Stanford School Medicine	US	PhD, stem cell	Dr. Rahul Sinha was trained as a molecular biologist and a biochemist with specialization in mammalian pre-mRNA splicing during PhD training at Cold Spring Harbor Laboratory, NY, USA. Later joined Irv Weissman' s lab as a post-doc where received training in cancer immunology and stem cell biology with specialization in hematopoietic stem cell and later neural stem cell biology. His long-term goal and research interests is Aberrant neuropoiesis and hematopoiesis.	Apr 15-12, 2022	Short-term stay for joint-HSC research Participation as an invited Lecturer, ASHBi Seminar
3	Ruth Baker		Professor of Applied Mathematics, University of Oxford	UK	PhD, Applied Mathematics	She focuses on developing and applying novel mathematical, computational and statistical methodologies and modelling frameworks for investigating developmental biology systems at the cell and tissue level. 2017-2022 Royal Society Wolfson Research Merit Award 2021 Fellow of the Institute of Mathematics and Its Applications (FIMA) 2020 Fellow of the Royal Society of Biology (FRSB) 2017-2019 Leverhulme Research Fellowship 2014 London Mathematical Society Whitehead Prize	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
4	Anne Ferguson-Smith		Professor, Pro-Vice-Chancellor for Research and International Partnerships, University of Cambridge	UK	PhD	She is an authority on genomic imprinting and the epigenetic control of genome function in health and disease, and is recognised for her work on parental-origin effects and epigenetic mechanisms. Her work has uncovered epigenetically regulated processes in development and over the life course, and identified key in vivo mechanisms involved in the maintenance of epigenetic states. 2021 Buchanan Medal of the Royal Society 2017 Fellow of the Royal Society 2014 Suffrage Science award 2006 Member, EMBO 2002 Fellow, Academy of Medical Sciences (FMedSci)	Apr 26-29, 2022 Nov 16,2022	1) Participation as invited lecturer, EMBO-Japan Virtual Lecture (ONLINE) 2) Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
5	Jianping Fu		Professor, University of Michigan	USA	PhD	2022 Friedrich Wilhelm Bessel Research Award, Alexander von Humboldt Foundation 2020 Fellow, American Society of Mechanical Engineers (ASME), 2020 Analytical Chemistry Young Innovator Award, American Chemical Society (ACS) 2020 Senior Member, Institute of Electrical and Electronics Engineers (IEEE) 2020 Fellow, Royal Society of Chemistry (RSC) 2020 Robert M. Caddell Memorial Award for Research, University of Michigan 2019-2021 Member, International Society for Stem Cell Research (ISSCR) Guidelines Working Group	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"

	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				
6	Anna-Katerina Hadjantonakis		Chair, Developmental Biology Program, Sloan Kettering Institute	USA	PhD	Her research focus is on the endoderm, the progenitor tissue that gives rise to respiratory and digestive tracts, and associated organs such as the lung, liver and pancreas. Her overarching goal is to understand how endodermal organs form - in time and space - from populations of uncommitted progenitor cells in the embryo.	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
7	Carl-Philipp Heisenberg		Professor, Institute of Science and Technology	Austria	PhD, developmental biology	2019 Carus Medal, German Academy of Sciences Leopoldina 2017 ERC Advanced Grant 2017 Lower Austrian Science Award 2015 Member, EMBO 2015 Member, German Academy of Sciences Leopoldina 2000 Emmy Noether Junior Professorship	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
8	Ng Huck Hui		Professor, Genome Institute of Singapore Assistant Chief Executive Biomedical Research Council (BMRC) A*STAR	Singapore	PhD	He is renowned in the field of gene regulation and genomics. His laboratory is developing diagnostic and therapeutics modalities for brain and liver diseases. 2019 The Public Administration Medal (Silver), National Day Awards 2018 President's Science Award (Team Award) 2016 Associate Member, EMBO 2011 President's Science Award (Team Award) 2010 Singapore Youth Award (Commendation Medal)	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
9	Jeannie T. Lee		Professor of Genetics, Harvard Medical School	USA	M.D., Ph.D.	She is known for her work on X-chromosome inactivation and for discovering the functions of a new class of epigenetic regulators known as long noncoding RNAs (lncRNAs), including Xist and Tsix. 2018 Harrington Rare Genetic Disease Scholar 2016 Lurie Prize in Biomedical Sciences, NIH 2016 Centennial Award from GENETICS 2015 member, National Academy of Sciences 2014 Distinguished Graduate Award, U Penn 2011 NIH MERIT Award 2010 Molecular Biology Award, National Academy of Sciences	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
10	Jochen Rink		Director,Department of Tissue Dynamics and Regeneration, Max Planck Institute for Multidisciplinary Science	Germany	PhD	2020 Deutsche Forschungsgemeinschaft award 2020 Behrens-Weise foundation award 2018 VolkswagenStiftung award 2015 EMBO Young Investigator award	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
11	Hans Scholer		Emeritus Professor, Max Planck Institute for Molecular Biomedicine	Germany	PhD	2011 Max Delbrück Medal 2011 Emil von Behring Lecture 2011 Kazemi Prize 2008 Robert Koch Prize	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
12	Marta Shahbazi		Group Leader, MRC LMB, University of Cambridge	UK	PhD	Marta is a group leader at the MRC Laboratory of Molecular Biology. She established a system that allows human embryo development beyond implantation in vitro, and used it to explore the basic cellular and molecular mechanisms that regulate embryo remodelling.	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
13	Amy Shyer		Assistant Professor, Rockefellor University	USA	PhD, cell and developmental biology	She leads the Laboratory of Morphogenesis at the Rockefellor University 2020 Searle Scholar 2017 Burroughs Wellcome Career Award at the Scientific Interface 2017 UC Berkeley MCB Outstanding Postdoctoral Fellow Award 2013 Miller Research Fellowship	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"

	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	Austin Smith		Professor, Director, Living Systems Institute, University of Exeter	UK	PhD, developmental biology	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	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
15	Patrick Tam		Deputy Director of CMRI and Head of the Embryology Research Unit, Children's Medical Research Institute	Australia	PhD	He is a Senior Principal Research Fellow of the National Health and Medical Research Council of Australia and holds a conjoint appointment as Professor in the Discipline of Anatomy and Histology, School of Medical Sciences, Sydney Medical School of the University of Sydney and Mok Hing-Yiu Distinguished Visiting Professor at the University of Hong Kong. 2017 Distinguished Professorial Acheivement Award of the Sydney Medical School 2016 Fellow, Australian Academy of Medical and Health Science 2011 Fellow, Royal Society of London 2009 Fellow, Royal Society of Biology 2008 Fellow Australian Academy of Science 2007 President's Medal of the Australia and New Zealand Society of Cell and Developmental Biology	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
16	Elly Tanaka		Senior Scientist, Institute of Molecular Pathology	Austria	PhD	Biochemist and senior scientist at the Research Institute of Molecular Pathology (IMP) in Vienna, Austria. Tanaka studies the molecular cell biology of limb and spinal cord regeneration as well as the evolution of regeneration. 2021 Member, Austrian Academy of Sciences 2020 FEBS | EMBO Women in Science Award 2018 Erwin Schrödinger Prize 2017 Ernst Schering Prize 2017 Member, EMBO 2015 Member, Academia Europaea	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
17	Xavier Trepat		Group Leader / ICREA Research Professor, Institute for Bioengineering of Catalonia	Spain	PhD	He has been an ICREA Research Professor from 2011. His research at IBEC focuses on integrative tissue dynamics and cytoskeletal mechanics.	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
18	Barbara Treutlein		Professor, Quantitative Developmental Biology, ETH Zürich D-BSSE, Switzerland	Switzerland	PhD Quantitative Developmental Biology	2020 Young Investigator Award, GSCN 2019 EMBO Young Investigator 2019 Dr. Susan Lim Award, ISSCR 2018 NYSCF Investigator Award 2016 Friedmund Neumann Prize, Schering Foundation	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"
19	Maximina Yun		Group Leader, CRTD and MPI-CBG	Germany		She has been a Group Leader at CRTD and MPI-CBG from 2017 focusing on Regeneration of Complex Structures in Adult Vertebrates. 2021 TUD Young Investigator 2017 MPI-CBG Fellow 2016-2018UCL-IHA Associate Fellow 2009-2011UCL-Wellcome Trust VIP Fellowship 2008 Max Perutz Prize for outstanding PhD studies, MRC-LMB Cambridge	Apr 26-29, 2022	Participation as invited lecturer, EMBO Workshop (ONLINE) "Molecular mechanisms of developmental and regenerative biology"

	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				
20	Luis Barreiro		Associate Professor, University of Chicago	USA	PhD, Human Population Genetics	He focuses on a better understanding how natural selection has contributed to the evolution of our species and the extent to which past selection events impact present-day susceptibility to disease	Jun 16, 2022	Participation as invited lecturer, ASHBi Seminar (ONLINE)
21	Samantha A Morris		Associate Professor, Developmental Biology and Genetics, Washington University in St. Louis	USA	PhD, Developmental Biology	A leading scientist in stem cell engineering on how to use single-cell technologies to deconstruct cell identity to improve the efficiency and fidelity of reprogramming	Jun 29, 2022	Participation as invited lecturer, ASHBi Seminar (ONLINE)
22	Matthias Lutolf		Director, Roche Institute for Translational Bioengineering Professor EPFL Lausanne	Switzerland	PhD, Developmental Biology	One of the leading scientists in the world working on organoids and stem cell-based in vitro model systems.	Jul 11, 2022	Participation as invited lecturer, ASHBi Distinguished Seminar (ONLINE)
23	Shigeki Nakagome		Assistant Professor, School of Medicine, Trinity College Dublin	Ireland	PhD	studying modern and ancient human population genomics to understand the history of human demography	Aug 1, 2022	Participation as invited lecturer, ASHBi Seminar
24	Makoto Saito		Postdoctoral fellow, Broad Institute of MIT and Harvard	USA	PhD	Postdoctoral fellow under Dr. Feng Zhang at Broad Institute of MIT and Harvard aiming to develop bioengineering tools with novel modalities through exploring the biological diversity, and apply them for therapeutics	Aug 2, 2022	Participation as invited lecturer, ASHBi Seminar (ONLINE)
25	Demitri Fabrèges		Postdoctoral fellow, Hubrecht Institute	Netherlands	PhD	Postdoctoral fellow under Dr. Takashi hiiragi at the Hubrecht Institute, Netherlands.	Sep 1, 2022	Participation as invited lecturer, ASHBi Seminar (ONLINE)
26	Andreas Linkermann	45	Deputy Director of NephrologyDivision of Nephrology, University Hospital Carl Gustav Carus at the Technische Universität Dresden Deputy director of Nephrology and Heisenbergprofessor, Specialist in Internal Medicine, Nephrology and Transplantation	Germany	MD, PhD	A leading scientist for the mechanism of cell death, and demonstrated that necroptosis and ferroptosis are independent signaling pathways that contribute to the overall picture organ damage.	Sep 9, 2022	Participation as an invited Lecturer, ASHBi Seminar
27	Jacob H. Hanna		Associate Professor, Department of Molecular Genetics, Weizmann Institute of Science, Israel	Israel	MD, PhD	leading scientist in the field of induced pluripotency, artificial embryo models and reprogramming of adult cells.	Sep 15, 2022	Participation as invited lecturer, ASHBi Seminar (ONLINE)
28	Eiman Azim		Associate Professor, Molecular Neurobiology Laboratory, Salk Institute for Biological Studies	USA	PhD (neuroscience)	2019 Presidential Early Career Award for Scientists and Engineers (PECASE) 2018 McKnight Scholar Award 2017 NIH Director's New Innovator Award (DP2) 2017 Kathryn W. Davis Aging Brain Scholar 2017 Pew Scholar in the Biomedical Sciences 2017 Searle Scholar Award 2014 Eppendorf And Science Prize for Neurobiology	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
29	Flavio Donato		Assistant Professor, Biozentrum, University of Basel	Switzerland	PhD (neuroscience)	A neurobiology expert aiming is to reveal the principles driving the structural and functional maturation of neuronal circuits supporting spatial navigation and memory, to understand how cognitive functions emerge in the mammalian brain during development.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)

	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				
30	Viviana Gradinaru		Professor, Division of Biology and Biological Engineering California Institute of Technology	USA	PhD (neuroscience)	Expert in nieroscience focusing on developing technologies for neuroscience and using them to probe circuits underlying locomotion, reward, and sleep. She has received the NIH Director's New Innovator Award and a Presidential Early Career Award for Scientists and Engineers and has been honored as a World Economic Forum Young Scientist and as one of Cell's 40 under 40. Gradinaru is also a Sloan Fellow, Pew Scholar, Moore Inventor, Vallee Scholar, and Allen Brain Institute NGL Council Member, and received the inaugural Peter Gruss Young Investigator Award by the Max Planck Florida Institute for Neuroscience.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, online)
31	Okihide Hikosaka		NIH Distinguished Investigator, Laboratory of Sensorimotor Research, National Eye Institute, NIH	USA	MD & PhD (neuroscience)	He is an expert in the neural mechanisms of voluntary behavior and studies the mechanisms of motivation, learning, skill, decision-making, attention, and oculomotor control. From 2002, he has been a NEI as a Senior Investigator and Chief of the Section of Neuronal Networks and was elected to the American Academy of Arts & Sciences in 2011.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
32	Kei M Igarashi		Associate Professor, Department of Anatomy and Neurobiology, University of California, Irvine	USA	PhD (neuroscience)	He is Investigating brain circuits for memory in Health and Disease. 2022 Robert & Sylvia Mapel Research Endowment, UC Irvine 2022 Outstanding Early-Career Faculty Research Award, UC Irvine 2019 Alzheimer's Disease Research Award, BrightFocus Foundation 2019 New Vision Award for Alzheimer's Disease Research, Donors Cure Foundation 2018 Ando Momofuku Award, Ando Foundation 2017 Mishima Kaiun Prize, Mishima Kaiun Memorial Foundation	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
33	Boaz P. Levi		Associate Investigator, Human Cell Types, Allen Institute for Brain Science	USA	PhD (neuroscience)	He is working to develop prospective and retrospective techniques to characterize adult human neocortical cell types. He joined the Allen Institute for Brain Science in 2011 as a Scientist in the in vitro human cell types group where he implemented single cell transcriptomic techniques to characterize neural cell types produced from human embryonic stem cells (hESCs), and to compare them to primary human neocortical cells.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
34	Lynette Lim		Assistant Professor, Depart of Neurosciences, VIB-KU Leuven Center for Brain & Disease Research	Belgium	PhD (neuroscience)	She is the head of the Laboratory of Interneuron Developmental Dynamics at VIB-KU Leuven which is interested in defining at single-cell resolution the metabolic and transcriptomic programmes that shape neuronal diversity and circuit assembly in the developing mammalian cortex.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
35	Guillermina López-Bendito		Principal Investigator, Instituto de Neurociencias, CSIC-UMH	Spain	PhD (neuroscience)	She is an expert in studying the cellular and molecular mechanisms involved in the development of axonal connections in the brain. In particular, to uncover the principles underlying thalamocortical axonal wiring, maintenance and ultimately the rewiring of connections, through an integrated experimental programme.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, online)
36	Loreta Medina		Professor Serra i Hunter, Department of Experimental Medicine, University of Lleida	Spain	PhD (neuroscience)	Her research focuses on the study of the amygdala, a very complex brain structure involved in the control of emotions, social behavior and cognition, which is altered in all psychiatric disorders.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)

	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				
37	Wolfram Schultz		Professor, Department of Physiology Development and Neuroscience, University of Cambridge	UK	PhD (neuroscience)	2023 Honorary Member, Swedish Basal Ganglia Society 2019 Lashley Award (Am Philosophical Soc) 2018 Gruber Prize 2017 Brain Prize 2014 Fellow EMBO 2013 Zülch Prize 2010 EJN FENS Award 2009 Fellow Royal Society 2005 Ipsen Prize 2002 Golden Brain Award 1997 Theodore-Ott-Prize 1984 Ellermann Prize	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
38	Aya Takeoka		Assistant Professor, VIB-Neuroelectronics Research Flanders	Belgium	PhD (neuroscience)	Her research aim is to understand how animals learn to generate and control motor behavior in health and disease. In my lab, we study mechanisms of circuit assembly, function and plasticity that lead to motor learning and recovery after neurotrauma. 2019 Japanese Society for Neuroscience Young Investigator Award	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
39	Jonathan Whitlock		Associate Professor, Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	PhD (neuroscience)	He is head of the Whitlock research group at the Kavli Institute for Systems Neuroscience with a research focus on unraveling how higher motor systems in cortex coordinate natural behavior and permit social learning.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
40	Maryam Ziaei		Associate professor, Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	PhD (neuroscience)	She is an associate professor and group leader, and the primary focus of her group is to understand neurocognitive mechanisms underlying social and emotional processing in aging.	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
41	Clifford Kentros		Professor, Kavli Institute of Systems Neuroscience, Norwegian University of Science and Technology	Norway	PhD (neuroscience)	Professor of Medicine and leader of the Kentros research group at the Kavli Institute of Systems Neuroscience, NTNU	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
42	Menno P. Witter		Professor, Kavli Institute for Systems Neuroscience Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology	Norway	PhD (neuroscience)	Also - Director of the Norwegian Research School in Neuroscienc Has received - Member, the Royal Norwegian Society of Sciences and Letters - 2016 Olav Thon Foundation International Research Award	Sep 20-24, 2022	Giving a lecture in the JANUBET International Symposium 2022 (Kyoto Univ, online)
43	Rodolfo da Silva Mazzarini Baldnotti		Department of Biomedicine, University of Bergen	Norway	PhD student (neuroscience)	PhD student at the University of Bergen	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
44	Christiana Bjørkli		Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	PhD student (neuroscience)	PhD student at the Norwegian University of Science and Technology	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
45	Stefan Blankvoort		Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	postdoctoral fellow (neuroscience)	Postdoc at the Norwegian University of Science and Technology	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
46	Miguel Chuapoco		Division of Biology and Biological Engineering California Institute of Technology	USA	PhD student (neuroscience)	PhD student at the California Institute of Technology	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
47	Dohan Jean Joseph Gruau		Department of Biomedicine, University of Bergen	Norway	PhD student (neuroscience)	PhD student at the University of Bergen	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)

	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				
48	Jens E.T. Gundersen		Department of Biomedicine, University of Bergen	Norway	PhD student (neuroscience)	PhD student at the University of Bergen	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
49	Katrine Sjaastad Hanssen		Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	PhD student (neuroscience)	PhD student at the Norwegian University of Science and Technology	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
50	Asgeir Kobro-Flatmoen		Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	postdoctoral fellow (neuroscience)	Postdoc at the Norwegian University of Science and Technology	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
51	Tadiwos-Feyissa Mergiya		Department of Biomedicine, University of Bergen	Norway	PhD student (neuroscience)	PhD student at the University of Bergen	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
52	Maria Letizia Potenza		Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology	Norway	PhD student (neuroscience)	PhD student at the Norwegian University of Science and Technology	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
53	Elisha Sanders		Molecular Neurobiology Laboratory, Salk Institute for Biological Studies	USA	PhD student (neuroscience)	PhD student at the Salk Institute for Biological Studies	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
54	Tatsuki Nakagawa		Department of Anatomy and Neurobiology, University of California, Irvine	USA	PhD student (neuroscience)	PhD student at the UC Irvine	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
55	Andre Alvestad		Department of Biomedicine, University of Bergen	Norway	PhD student (neuroscience)	PhD student at the University of Bergen	Sep 20-24, 2022	Presenting a poster in the JANUBET International Symposium 2022 (Kyoto Univ, on site)
56	Luiza Handschuh		Deputy Director for Scientific Affairs at Institute of Bioorganic Chemistry, Polish Academy of Science, Poznan	Poland	PhD, Bioorganic Chemistry	She is one of the principal investigators in the project devoted to gene expression profiling in a human acute myeloid leukemia. Her main interest is functional genomics, DNA microarray technology and its application in medical science.	Sep 21-Dec 20, 2022	short-term stay for joint research
57	Tetsuya Hiraiwa		MBI Fellow, Mechanobiology Institute, National University of Singapore	Singapore	Ph.D Science	He is a MBI Fellow, at the Mechanobiology Insitite, where he is heading a new research group on theoretical physical biology. He applies concepts from soft matter and out-of-equilibrium physics to understand mechanistic aspects of various biology-related phenomena.	Oct 11, 2022	Seminar on SeirinG-Seminar, Discussion
58	Alberto Bardelli		Scientific Director of IFOM– The AIRC Institute of Molecular Oncology	Italy	PhD	Molecular geneticist and expert in the field of personalized therapies 2020 Guido Venosta Award, FIRC AIRC, Presidenza della Repubblica Italiana 2019 Elected Member of the Johns Hopkins Society of Scholars 2017 ESMO Translational Research Award 2017 Fellow of European Molecular Biology Organization (EMBO) 2015 Fellow of the European Academy of Cancer Sciences 2015 Fellow of the Turin Academy of Sciences	Nov 9, 2022	Lecture at seminar, meetings
59	Stefano Casola		A group leader at IFOM– The AIRC Institute of Molecular Oncology	Italy	PhD	Molecular oncologist and expert in the study of B-lymphocytes and lymphomas 2006 the Armenise Harvard Career Development Award	2022/11/9-10	Lecture at seminar, meetings
60	Theo Lacombe	30	Associate Professor, Gustave Eiffel University	France	Ph. D, mathematics	He is a young talented researcher in topological data analysis. His theory bridging persistent homology and optimal transport is applied for reconstructing 3D structures of DNA from Hi-C data.	Nov 26-Dec 23, 2022	Collaboration in ASHBi and participation in a workshop

	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				
61	Momoko Watanabe		Assistant Professor, University of California, Irvine	USA	Ph.D.	She was recruited to UC Irvine as a part of Faculty Hiring for Leveraged Research Excellence (FHLRE) “Stem Cells in Tissue Engineering”.Her research focus is centralized around 1) creating powerful organ-on-a-chip systems to improve established brain organoids, 2) developing a brain organoid model for neurodevelopmental disorders, and 3) defining the microcircuit properties of brain organoids as a model system for human brain activities.	Dec 2, 2022	Participation as invited lecturer, Ethical, Legal, and Social Issues of Human Brain Organoid
62	Alexander Erler		Associate Professor, National Yang Ming Chiao Tung University	Taiwan		Philosopher studying the ethical implications of new technologies with the potential to significantly transform society and the human condition (e.g. human enhancement technologies, artificial intelligence, or genome editing).	Dec 2, 2022	Participation as invited lecturer, Ethical, Legal, and Social Issues of Human Brain Organoid
63	Elizabeth Thomas		Medical Student, UNC School of Medicine	USA		Thomas's research interests are in the ethics of biomedical technologies, particularly in the areas of reproductive medicine and neuroscience.	Dec 2, 2022	Participation as invited lecturer, Ethical, Legal, and Social Issues of Human Brain Organoid
64	Tsung-Ling Lee		Assistant Professor, Taipei Medical University	Taiwan	Ph.D., Juridical Science	Tsung-Ling Lee is an Assistant Professor of Law at Taipei Medical University. Her research interests lie at the intersection of law, medicine and ethics. She holds a Doctorate in Judicial Science and a Master of Laws in Global Health Law from Georgetown University Law Center; a law degree from the National Taiwan University and a Bachelor in Medical Science from the University of Sydney.	Dec 2, 2022	Participation as invited lecturer, Ethical, Legal, and Social Issues of Human Brain Organoid
65	Megan Munsie		Professor, Melbourne Medical School, University of Melbourne Group leader, Murdoch Children’s Research Institute	Australia	PhD	Professor at the University of Melbourne’s Medical School, group leader at MCRI and leading scholar in the interdisciplinary research of stem cell ethics and regulation and currently a member and past chair of the ISSCR Ethics Committee.	Dec 5, 2022	Participation as invited lecturer, ASHBi Distinguished Seminar (ONLINE)
66	Christopher Gyngell		Senior Lecturer, The University of Melbourne Team Leader, Murdoch Children’s Research Institute	Australia	Ph.D., Bioethics	He is a Research Fellow in Biomedical Ethics. His research interests lie primarily in the ethical implications of biotechnologies and the philosophy of health and disease. 2015 MCF - Marie Curie Fellowship	Dec 8, 2022	Speaker at ASHBi Seminar
67	Julian Savulescu		Chen Su Lan Centennial Professor in Medical Ethics, National University of Singapore	Singapore	PhD	Philosopher who researches the ethics of various new or emerging technologies, including new methods of reproduction and enhancement of physical and cognitive performance through drugs or genetic manipulation. He has been the founding director of the Oxford Uehiro Centre for Practical Ethics, and is or has been a co-director on many large research projects, looking at topics from geoengineering to vaccines. 2019 Research Australia Public Advocacy Award 2018 International Society for Stem Cell Research Public Service Award 2018 The Australian Sociological Association Stephen Crook Memorial Prize	Dec 2 & 8, 2022	Participation as invited lecturer, Ethical, Legal, and Social Issues of Human Brain Organoid Participation as invited lecturer, ASHBi Seminar
68	Katalin Susztak		Professor of Medicine (Renal Electrolyte and Hypertension Division) and Genetics, University of Pennsylvania	U.S.A	MD, PhD	A world authority on renal fibrosis. In January 2021, Dr. Kramann published a paper in Nature on the origin of myofibroblast that causes renal fibrosis using single cell analysis of human kidney.	Dec 10, 2022	Participation as an invited Lecturer, NEPHROLOGY EXPERT 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	Vincent Pasque		University of Leuven	Belgium	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	Dec 14, 2022	Participation as a speaker at PDB Seminar (Web)
70	Wingho Yung		Professor, The Chinese University of Hongkong	Hongkong	PhD, Neuroscience	He has broad research interests in understanding the functions and mechanisms of the nervous system in health and in disease, emphasizing the underlying neural circuits and the roles of neuroplasticity by employing a multitude of cutting-edge neuroscience and computational techniques. He was the founding director of the Gerald Choa Neuroscience Centre and has been serving in international neuroscience bodies including the governing councils of the International Brain Research Organization and the Federation of Asian-Oceanian Neuroscience Societies.	Dec 17-18, 2022	Discussion about the organization of Asia-Oceanisn Neuroscience Societies (FAONS)
71	Sung-jin-Jeong		Principal Researcher, Korean Brain Research Institue	Korea	Ph.D., Molecular Biology	Dr. Sung-Jin Jeong is a developmental neuroscientist and a principal Researcher at the Korea Brain Research Institute, who has been involved in the Korean Brain Initiative which is centered on deciphering the brain functions and mechanisms that underlie decision-making, and the major goal is to map a functional connectome of the brain. She actively works for the 2019 world congress of International Brain Research Organization and International Brain Initiative and serves co-chair of Global Neuroethics Summit which has been held In Korea from 2017.	Dec 17-18, 2022	Discussion about the organization of Asia-Oceanisn Neuroscience Societies (FAONS)
72	Elina Shibata	21	Third-year student, Biochemistry and Molecular Biology, UC Berkeley	USA		Active member of the Foresight Pre-Optometry Club, a student-run organization that seeks to unite UC Berkeley students and individuals around the area who are interested in pursuing a career in the field of optometry.	Dec 27, 2022	Discussion about a potential project for the future
73	Nozomu Yachie		Associate Professor, Director of Research, Associate Director, School of Biomedical Engineering(SBME), The University of British Columbia Specially Appointed Professor, WPI-PRIMe, Osaka University	Canada	PhD	Leading scientist in development of the Base Editor and computing system combining technologies in cell engineering, genome editing, and computational biology. 2022- Allen Distinguished Investigator, Allen Institute 2020- Canada Research Chair in Synthetic Biology, CIHR 2020 文部科学大臣賞若手科学者賞	Jan 11, 2023	Participation as invited lecturer, ASHBi Seminar (ONLINE)
74	Ivano Legnini		Group leader, Human Technopole	Italy	PhD	Young and talented researcher who has integrated various fields such as functional genomics, organoids, spatial transcriptomics, and genome editing to elucidate the genomic mechanism of human development	Jan 20, 2023	Participation as invited lecturer, ASHBi Seminar (ONLINE)
75	Jody E. Hooper		Associate Professor of Pathology, Stanford University School of Medicine Director of Autopsy, Stanford University School of Medicine	USA	MD	Associate Professor of Pathology at Stanford University and the Director of Research Autopsy Collaboration at Stanford (RACS). As a leading scholar on rapid autopsy, she co-edited the recently published book titled Autopsy in the 21st Century	Jan 25, 2023	Participation as invited lecturer, ASHBi Seminar (ONLINE)
76	Woong Sun		Professor, Department of Anatomy, Korea University College of Medicine	Korea	PhD, Developmental Biology	Woong is a leading developmental biologist who is interested in understanding the mechanisms of neuron production and circuit integration during embryonic development	Feb 8, 2023	Participation as invited lecturer, 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				
77	Kyomi J. Igarashi		Ph.D.Student, Stanford University School of Medicine	USA	stem cell, genetics	A Genetics Ph.D. student at Stanford University, co-advised by Dr. Hiro Nakauchi and Dr. Julie Baker. She primarily uses genomic techniques to not only interrogate the mechanism, but also to improve new technology and systems developed in the fields of hematology and developmental biology	Feb 17, 2023	Participation as invited lecturer, ASHBi Seminar
78	Brett Kagan		Chief Scientific Officer, Cortical Labs	Australia	Ph.D., Neuroscience	Brett is a CSO of Cortical Labs, a biological computing startup that combines lab-grown human brain cells with computer chips. He is leading the development of the DishBrain project, in which human cells in a petri dish learnt to play Pong.	Feb 24, 2023	Speaker at CiRA-ASHBi Bioethics Lecture
79	Olivier Pourquie		Frank Burr Mallory Professor of Pathology and Professor in the Department of Genetics at Harvard Medical School and Professor of Pathology at the Brigham and Women's Hospital	USA	PhD, Developmental Biology	Pourquié authored more than 100 peer-reviewed publications. He is an elected member of the European Molecular Biology Organization and of the Academia Europea. His work on the segmentation clock that controls the periodicity of vertebrae was recognized as one of the milestones in developmental biology of the 20th century by Nature Magazine. In 2020, he was elected as President of the Society for Developmental Biology, and as a member of the National Academy of Sciences.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
80	Eric Siggia		Professor, Rockefeller University	USA	PhD, Developmental Biology	VIOLA WARD BRINNING AND ELBERT CALHOUN BRINNING PROFESSOR at the Rockefeller University. Siggia's lab studies embryonic stem cells from mice and humans using methods derived from biophysics that permit the self-organization potential of stem cells to manifest itself. 2009 member, National Academy of Sciences.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
81	Aryeh Warmflash		Associate Professor of BioSciences CPRIT Scholar in Cancer Research, Rice University	USA	PhD, Developmental Biology	Aryeh Warmflash has developed systems to mimic embryonic development in vitro using human embryonic stem cells and is developing dynamical system models of cell fate patterning and morphogenesis that can be rigorously compared with quantitative data on in vitro development.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
82	Alfonso Martinez-Arias		ICREA research Professor, Universitat Pompeu Fabra	Spain	PhD, Developmental Biology	Since 2003 until 2021, he has been Professor of Developmental Mechanics in the Department of Genetics of the University of Cambridge, Cambridge (UK) working on developmental biology with the fruit fly (Drosophila) and more recently Embryonic Stem Cells. His interests cover the interface of cell and developmental biology with Physics and Engineering. He is a member of EMBO, has been awarded two ERC Advanced Investigator grants and in 2012 received the Waddington medal of the BSDB for his contributions to british developmental biology.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
83	Shahragim Tajbakhsh		Professor, Institute Pasteur	France	PhD, Developmental Biology	2014 French Academy of Sciences Prize / Fondation Generale de Sant é, for Stem Cell research 2013 EMBO Member 2013-2018 ERC Advanced Grant 2011-2019 LabEx REVIVE Laboratory of Excellence Consortium; co-coordinator 2010 Vallery-Radot Prize, Institut Pasteur 2000 Prix Georges Zermati; Fondation de France	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
84	Sophie Petropoulus		Assistant Professor, Université de Montréal	Canada	PhD, Developmental Biology	Canada Research Chair in Functional Genomics of Reproduction and Development She has merged her expertise in the fields of physiology, developmental biology, epigenetics and single-cell genomics to gain an understanding of early preimplantation development.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing 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				
85	Jacob Hanna		Associate Professor, Weizmann Institute of Science	Israel	PhD, Developmental Biology	2021 Selected as top thinker for the year 2021 by Prospect magazine (UK) 2021 Top scientific breakthroughs of the year 2021, Science 2018 EMBO member 2016 The Segal Family Award, U Michigan 2014 The Kimmel Prize, Weizmann Institute of Science 2013 Robertson Innovator Award, NYSCF	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
86	Nicolas Rivron		Principal investigator, The Institute of Molecular Biotechnology	Austria	PhD, Developmental Biology	Group Leader of Laboratory for Blastoid Development at the Institute of Molecular Biotechnology, Austrian Academy of Science. His lab explores how self-organization complements hierarchical intrinsic (e.g., HOX genes collinearity) and extrinsic (e.g., positional information) processes that shape the mammalian organism.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
87	Naomi Moris		Principal investigator, The Francis Crick Institute	UK	PhD, Developmental Biology	Naomi is a group leader at the Francis Crick institute from 2021, where her group uses human gastruloids to study the fundamental principles of embryonic cell fate coordination during development.	Mar 10-13, 2023	Participation as invited lecturer, ASHBi Workshop "Deconstructing and reconstructing embryonic development"
88	Norihiro Takakuwa		Postdoc, Max Planck Institute for Brain Research, Germany	Germany	PhD	2019- Postdoc, Memory and navigation circuits group, Max Planck Institute for Brain Research 2018 Assistant Professor, Department of Neuroscience, Kyoto University 2018 Toshihiko Tokizane Memorial Award for Excellent Graduate Study in Neuroscience	Mar 13, 2023	Participation as invited lecturer, ASHBi Seminar
89	David Gokhman		Assistant Professor (PI), Weizmann Institute of Science	Israel	PhD, Evolutionary genetics	Dr. Gokhman is a pioneer in a new field called “paleo-epigenetics”—using bioinformatic analyses to research the recent history of mankind. Particularly interested in the gene regulatory changes that underlie human-specific traits and diseases.	Mar 20-23, 2023	Participated in the joint lab meeting for the collaborative research project. Presentation, and all-day discussions.
90	Simon Fishilevich		Senior bioinformatician, Weizmann Institute of Science	Israel	PhD, Evolutionary genetics	Bioinformatician and Data Scientist at Weizmann Institute of Science.	Mar 20-23, 2023	Participated in the joint lab meeting for the collaborative research project. Presentation, and all-day discussions.
91	Katharina Lange		MSc student, Weizmann Institute of Science	Israel	Evolutionary genetics	MSc student at Gokhman Lab.	Mar 20-23, 2023	Participated in the joint lab meeting for the collaborative research project. Presentation, and all-day discussions.
92	Juha Kere		Professor of Molecular Genetics, Department of Biosciences and Nutrition, Karolinska Institutet	Sweden	MD, PhD	He pioneered the work on chromosome 7 deletions and mutations in myeloid disorders. In recent years, Dr. Kere has used a multidisciplinary approach to study the gene regulation in early human development 2005 Medix Prize (Finland) 2007- Member, EMBO 2010- Member, The Finnish Society of Sciences and Letters, 2011 Matti Äyräpää Prize(Finland) 2012- Member, Finnish Academy of Science and Letters 2016 The RoyalSociety Wolfson Research Merit Award (UK)	Mar 24, 2023	Lecture at seminar, meetings
93	Jose Mordoh		Director, Center of Oncological Research of the Cancer Foundation (CIO-FUCA). Professor, Molecular Medicine and Molecular Oncology at the University of Buenos Aires.	Argentina	M.D., Ph.D.	For the last 30 years his research has focused on cancer immunotherapy, and more specifically on the development of vaccines in cutaneous melanoma. He is an Emeritus member of the American Association for Cancer Research.	Mar 31, 2023	Seminar, Working lunch, Discussions

Appendix 6 FY2022 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2022 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2022 (number of activities, times held)
PR brochure, pamphlet	3 brochure updates (ASHBi, KUIAS, WPI)
Lectures, seminars for general public	
Teaching, experiments, training for elementary, secondary and high school students	1 School visit from Takamatsu
Science café	1 Science Café Itami (Fujita PI) 3 First Contact Program Seminars (Dr. Ichikawa, Dr. Fukuma, Dr. Inoue)
Open houses	2 (Takamatsu Dai-ichi High School visit, ASHBi Open Campus)
Participating, exhibiting in events	3 (100th Anniversary Annual Meeting of The Physiological Society of Japan, WPI Science Symposium, 8th Annual RMAN-J Conference)
Press releases	15 Releases
Publications of the popular science books	
Others（ Site Visits ）	Overseas: 6 visits JICA-KEMRI (Kenya), University of Turin (Italy), CNRS (France), JST- Sakura Science Exchange Program (Paraguay), Italian Ambassador (Italy) Domestic: 6 visits WPI-QUP, WPI-SKCM2, WPI-Mio2Q, Osaka University URAs, Hiroshima University URAs, MEXT State-Minister

*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 2022 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.

- **Open house:** A delegate of 30 students and a teacher from Takamatsu Dai-ichi High School (Kagawa Prefecture) visited the Institute in August 2 as part of their school excursion program. They were given lectures by the Institute's young researchers and had a hands-on experience with biological research. In addition, the Institute held an open campus for KU undergraduate and graduate students on June 27, 2022 where the Institute's young PIs introduced the activities of their research groups.

- **The Institute's website:** The ASHBi website averaged 20,000-30,000 PV per month in FY2022, contributing to its global visibility. In addition, to introduce not only researchers but also graduate students on the website, we hired KU graduate students as administrative assistants to create website homepages focusing on introducing the research activities of the graduate students. The student website, launched in November 2022, is an initiative to provide opportunities to the KU graduate students interested in public relations to take a more active role.

- **Outreach to industry:** The Institute has been active in creating interaction opportunities between industry and academia to foster potential future collaborations and has developed the **'First Contact Program'**. In this program, early-career researchers visit the Kyoto Research Park (an industrial cluster located at the central Kyoto city with over 500 tenant companies) to present his/her research, for 2-3 hours in an easy and understandable way, to the company researchers. During the presentations, company researchers can interrupt to ask questions at any point, in order to stimulate more active discussions, enabling a deeper understanding among all participants. In FY2022, three young researchers presented their research via this program, contributing to an interactive exchange of knowledge between industry-academia researchers.

- **Visitors from overseas institutes/organizations:** In response to the improved visibility of the Institute, there were onsite visits to the Institute from distinguished overseas institutes and organizations in FY2022. The Italian Ambassador and scientific advisor visited in May 2022, the Director of Biological Sciences (INSB) of CNRS in France visited in October, and the Vice President of the University of Turin in Italy visited in February 2023. They toured the Institute's main building and had discussions with the Institute's Director and Board Members.

Appendix 7 FY 2022 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2022.

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	Apr 29. 2022	Television (Japanese)	[テレビ朝日] - Interview to Prof. Ueno on research regarding COVID after effects (Ueno Group)
2	May 17&20, 2022	Television (Japanese)	[テレビ朝日、日本テレビ、日本海テレビ、中京テレビ、etc.] - Interview to Prof. Ueno on research regarding COVID after effects (Ueno Group)
3	May 19, 2022	News website (Japanese)	[日経バイオテク] - Interview to Prof. Ogawa regarding diversity of cancer (Ogawa Group)
4	Jun 7, 2022	Television (Japanese)	[NHKクローズアップ現代] - Interview to Prof. Ueno on research regarding regarding COVID after effects (Ueno Group)
5	Jun 14, 2022	News website (Japanese)	[QLifePro] - Introduction of the recent research result by Yanagita Group regarding EPO producing kidney cells (Yanagita Group)
6	Jun 15-30, 2022	News website (English)	[Medical Xpress, News-Medcial.Net] - Introduction of the recent research result by Yanagita Group regarding EPO producing kidney cells (Yanagita Group)
7	Jul 12, 2022	Newspaper/News website (Japanese)	[毎日新聞] - Introduction of the recent research result by Ueno Group regarding COVID after effects (Ueno Group)
8	Jul 22, 2022	Newspaper/News website (Japanese)	[毎日新聞] - Introduction of the recent research result by Fujita Group regarding Ethics on Regenerative Medicine (Fujita Group)
9	Jul 24, 2022	News website (English)	[The Mainichi] - Introduction of the recent research result by Ueno Group regarding COVID after effects (Ueno Group)
10	Aug 1-4, 2022	Newspaper/News website (Japanese)	[日本経済新聞、朝日新聞、QLifePro] - Introduction of the recent research result by Saitou Group regarding human fetal germ cells (Saitou Group)
11	Aug 4, 2022	News website (Japanese)	[TECH+] - Introduction of the recent research result by Ueno Group regarding tertiary lymphoid structuress in ovarian cancer (Ueno Group)
12	Aug 5, 2022	Television (Japanese)	[NHK] - Introduction of the recent research result by Saitou Group regarding human fetal germ cells (Saitou Group)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
13	Aug 10, 2022	News website (Japanese)	[マイナビニュース] - Introduction of the recent research result by Ogawa Group regarding acute leukemia (Ogawa Group)
14	Aug 14, 2022	News website (English)	[The Excelsior] - Introduction of the recent research result by Hiraoka Group regarding RECODE (Hiraoka Group)
15	Aug 22, 2022	News website (English)	[Phys.org] - Introduction of the recent research result by Saitou Group regarding mammalian germline development (Saitou Group)
16	Aug 22-23, 2022	News website (English)	[Phys.org, MIT Technology Review] - Introduction of the recent research result by Saitou Group regarding human fetal germ cells (Saitou Group)
17	Sep 2, 2022	Television (Japanese)	[NHK] - Introduction of the recent research result by Fujita Group regarding Ethics on Regenerative Medicine (Fujita Group)
18	Sep 5-13, 2022	News website (Japanese)	[Medical meets Technology, 大学ジャーナルオンライン, Medical Tribune, 糖尿病リソースガイド] - Introduction of the recent research result by Fujita Group regarding Ethics on Regenerative Medicine (Fujita Group)
19	Oct 16, 2022	Newspaper/News website (Japanese)	[共同通信、山陽新聞、高知新聞、東奥日報社、愛媛新聞、福島民報、etc] - Introduction of the recent research result by Fujita Group regarding Ethics on Regenerative Medicine (Fujita Group)
20	Dec 12, 2022	News website (Japanese)	[MIT Technology Review] - Feature of the recent research result by Saitou Group regarding human fetal germ cells (Saitou Group)
21	Dec 15, 2022	News website (Japanese)	[日刊工業新聞] - Feature of the recent resrearch collaboration by the Ogawa Group for new cancer drug discovery (Ogawa Group)
22	Dec 22, 2022	Television (Japanese)	[NHK] - Introduction of the recent research result by Alev Group regarding in vitro somitogenesis (Alev Group)
23	Dec 21-28, 2022	News website (English, etc.)	[Phys.org, News-Medical.Net, Mirage News, GEN, Ma Clinique, Drug Target Review] - Introduction of the recent research result by Alev Group regarding in vitro somitogenesis (Alev Group)
24	Dec 22-26, 2022	Newspaper/News website (Japanese)	[京都新聞、日本経済新聞、産経新聞、読売新聞、毎日新聞、共同通信、佐賀新聞、東京新聞、東奥日報社、秋田魁新報、日刊工業新聞、etc.] - Introduction of the recent research result by Alev Group regarding in vitro somitogenesis (Alev Group)
25	Jan 13, 2023	News website (Japanese)	[LabBRAINS] - Introduction of the recent research result by Alev Group regarding in vitro somitogenesis (Alev Group)
26	Jan 18, 2023	News website (Japanese)	[Natureダイジェスト] - Introduction of the recent research result by Ogawa Group regarding COVID task force (Ogawa Group)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
27	Feb 3, 2023	News website (English)	[SciTech Daily, Today Headline, list23] - Introduction of the recent research result by Alev Group regarding in vitro somitogenesis (Alev Group)
28	Mar 1, 2023	Newspaper/News website (Japanese)	[オンコロ] - Introduction of the recent research result by Fujita Group regarding Ethics on Regenerative Medicine (Fujita Group)
29	Mar 7, 2023	Newspaper/News website (Japanese)	[日本経済新聞] - Interview to Prof. Fujita on research regarding regarding Ethics on Regenerative Medicine (Fujita Group)
30	Mar 2, 2023	News website (Japanese)	[国際幹細胞普及機構] - Introduction of the recent research result by Alev Group regarding in vitro somitogenesis (Alev Group)
31	Mar 9-14, 2023	News website (English etc.)	[Nature, Sky News, Net.hr, F5HAber, Gigazine, Science&Vie] - Introduction of the recent research result by Saitou Group regarding oocyte generation from male germ cells (Saitou Group)
32	Mar 10, 2023	News website (Japanese)	[Gigazine] - Introduction of the recent research result by Saitou Group regarding oocyte generation from male germ cells (Saitou Group)