World Premier International Research Center Initiative (WPI)
FY 2018 WPI Project Progress Report

Host Institution	Kyoto University	Host Institution Head	Juichi Yamagiwa
Research Center	Institute for the Advanced Study of Human Biology	Center Director	Mitinori Saitou

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2019) 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**)

The Institute for the Advanced Study of Human Biology (ASHBi) launched officially on October 30, 2018, with the appointment of Mitinori Saitou as Director (Professor of Kyoto University Institute for Advanced Study). Tadashi Isa and Yasuaki Hiraoka were appointed as Vice Director and Takuya Yamamoto was appointed as Head of the Single-Cell Genome Information Analysis Core on November 1, 2018. Other PIs have been appointed from December 1 onward.

Since the launch of the ASHBi, during FY2018, we held an executive board meeting every week and a domestic PI meeting twice, accelerating the setup of ASHBi (in FY2019, we are holding executive board meetings every two weeks and PI meetings every month). This includes the appointment of overseas PIs; the design and renovation of the main building for ASHBi for housing overseas PIs, young PIs, the Mathematical Science Group, the Bioethics and Philosophy Group, the Single-Cell Genome Information Core, and the administration office (Building B of the Graduate School of Medicine, Kyoto University); the design and organization of the strategic research support section in the administration office; the establishment of the Single-Cell Genome Information Core and the Primate Genome Engineering Core (Shiga University of Medical Science); the creation of ASHBi's website; and the opening of ASHBi's kickoff symposium (see **Realizing an International Research Environment**, **Making Organizational Reforms**, **Efforts to Secure the Center's Future Development**, and **Others**). The renovation of the building for ASHBi will be completed by the autumn of 2019, serving as a critical hub for the activities of ASHBi. The kickoff symposium was broadcast on a TV program (NHK) and featured in some newspapers.

The ASHBi PIs have initiated their projects relevant to ASHBi's activities. The key papers published in 2018, among other papers, include "Generation of human oogonia from induced pluripotent stem cells in vitro" (*Science*, **362**, 356-360, 2018) (**Saitou's group**), "Dual-spindle formation in zygotes keeps parental genomes apart in early mammalian embryos" (*Science*, **361**, 189-193, 2018) (**Hiiragi's Group**), "Strain-triggered mechanical feedback in self-organizing optic-cup morphogenesis" (*Sci. Adv.*, **4** (11), eaau 1354, 2018) (**Eiraku's group**), and "Age-related remodeling of esophageal epithelia by mutated cancer drivers" (*Nature*, **565**, 312-317, 2019 (published online in 2018: doi:10.1038/s41586-018-0811-x)) (**Ogawa's group**) (see **Advancing Research of the Highest Global Level**).

The Mathematical Science Group (PI: **Yasuaki Hiraoka**) and the Bioethics and Philosophy Group (PI: **Misao Fujita**) have initiated interdisciplinary research with scientists in Life Science Groups (see **Generating Fused Disciplines**). To start, the Mathematical Science Group held regular seminar series with the Saitou and Yamamoto group, and discussed themes such as data analysis, dynamics, causality, and graphical probabilistic model, leading to the identification of concrete research ideas. Accordingly, the Hiraoka and Saitou groups have initiated collaborations for topological data analyses (TDA) of the mechanisms of cell-fate specification and their species differences, and causality and gene regulatory network for the specification of human germ-cell fate in vitro based on the Linear non-Gaussian Acyclic Model (LiNGAM). Hiraoka also initiated a discussion

series with several PIs of other Life Science Groups in ASHBi and has introduced mathematical scientists with relevant expertise (including those outside ASHBi) to biological scientists in ASHBi so that interdisciplinary research between mathematics and biology can proceed in a productive fashion. Furthermore, Hiraoka has started developing a research network in mathematical biology inside and outside ASHBi for potential collaborations, resulting in the establishment of cooperative relationships with several relevant mathematical scientists. As a consequence of such activities, Hiraoka will organize a mathematical biology workshop in August 2019.

The Bioethics and Philosophy Group, in collaboration with Life Science Groups, has initiated a project to identify key ethical issues for the advanced study of human biology. The Bioethics and Philosophy Group recognized that it was critical to formulate a rule regarding investigations using samples obtained from aborted human embryos/fetuses, since such investigations are crucial for a better understanding of human development and for the success of regenerative medicine. Such research has frequently been performed in Europe, the US, and China but are very limited in Japan. Thus, the Bioethics and Philosophy Group has initiated a review of the literature, relevant discussions with Life Science Groups, and a questionnaire survey for the general public with the aim of formulating an intra-ASHBi rule, which may serve as a basis for formulating a national rule in the future.

To realize an international research environment, ASHBi has appointed three distinguished overseas PIs (**Ueno**, **Hiiragi**, and **Bourque**), and has provided them with sufficient research space, start-up funding (30 million JPY), and budget support for personnel costs (22.5 million JPY; one associate professor as a co-PI and two postdoctoral fellows). All overseas PIs will frequently come (~6 times/year) or stay long (~3 months) at ASHBi and perform their research at ASHBi. With key contributions by **Hiiragi** as well as two distinguished foreign researchers (James Briscoe, Crick Institute; Barbara Treutlein, ETH Zurich), ASHBi is planning to hold **an ASHBi symposium on "Human development, genetics, and evolution"** in March 2020. The Director (**Saitou**) has been requested by Professor Ian Chamber (University of Edinburgh) to co-organize and hold **the EMBO meetings on the "Molecular mechanisms of developmental and regenerative biology"** in Kyoto in November 2020. Furthermore, Saitou has been appointed as vice chair and chair of the **Gordon Research Conference on Germinal Stem Cell Biology** in Hong Kong in 2021 and 2023, respectively. These activities will substantially help to raise the level of international recognition of ASHBi.

We have initiated careful searches and recruitment of young PIs (up to five PIs by the end of FY2020), who will develop into core investigators of ASHBi in the future. A young PI will receive 10 million JPY for start-up funding, sufficient research space, and a personnel budget to hire one or two postdoctoral fellows. The first such PI (**Cantas Alev**) will join ASHBi on July 1, 2019. We are planning to make opportunities for these young PIs in ASHBi to interact with other young PIs within Kyoto University (PIs in Hakubi and K-CONNEX programs) to construct a network for promoting collaborations/interdisciplinary research among young PIs. We are also creating easy-to-understand administration guidelines to fully support such young PIs and overseas PIs (see **Realizing an International Research Environment** and **Making Organizational Reforms**).

Kyoto University has created a new organizational structure called the Kyoto University Institute for Advanced Study (KUIAS) to accommodate WPI institutes on a permanent basis. KUIAS is designated as a special district with a high degree of autonomy. Under the KUIAS structure, the Institute's director has been given discretion to make decisions on the most important matters concerning ASHBi, and can exercise strong leadership, implementing top-down management. Kyoto University has provided three administrative staffs and one URA for ASHBi, and takes responsibility for the personnel expenses for two research staff positions for Single-Cell Genome Information Analysis Core, with a vision that the Core will function as a key facility not only for ASHBi but also for Kyoto University as a whole for single-cell genome information analysis in the coming years. Also, Kyoto University has provided ASHBi with half of the indirect funds associated with competitive grants acquired by ASHBi's researchers (see **Efforts to Secure the Center's Future Development over the Mid- to Long-term**).

* Describe clearly and concisely the progress being made by the WPI center project from the viewpoints below.
- In addressing the below-listed 1-6 viewpoints, place emphasis on the following:
  (1) Whether research is being carried out at a top world-level (including whether research advances are being made by fusing fields).
  (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 2018.
* 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 officially launched on October 30, 2018, with the appointment of Mitinori Saitou as Director (Professor of Kyoto University Institute for Advanced Study). Tadashi Isa and Yasuaki Hiraoka were appointed as Vice Directors, and Takuya Yamamoto was appointed as Chief of the Single-Cell Genome Information Analysis Core on November 1, 2018. Other PIs have been appointed since December 1 (see **Appendix 2**). This section describes key research achievements of the ASHBi PIs in 2018, irrespective of their appointment dates.

Saitou's group published the article "Generation of human oogonia from induced pluripotent stem cells in vitro" (*Science*, **362**, 356-360, 2018). Germ cells differentiate into sperm or eggs, which unite to form new individuals and transmit our genetic information. The aim of Saitou's research has been to understand the mechanism of and the in vitro reconstitution of germ cell development in mice, monkeys, and humans. This work demonstrated the induction of human-induced pluripotent stem cells (iPSCs) first into primordial germ-cell–like cells (PGCLCs), and in turn, into oogonia, the immediate precursors of oocytes, in a xenogeneic reconstituted ovary culture. The hPGCLC-derived oogonia display hallmarks of epigenetic reprogramming—genome-wide DNA demethylation, imprint erasure, and extinguishment of aberrant DNA methylation in hPSCs—and acquire an immediate precursory state for meiotic recombination. This work will serve as a critical basis for understanding the mechanism of human oogonia development and its diseased states, including infertility.

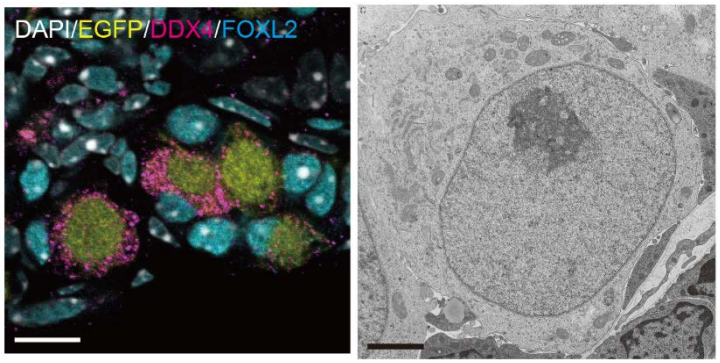

Figure 1. Immunufluorescence (left) and electron microscopic (right) images of oogonia induced from human iPS cells (Yamashiro et al, Science, 2018). DDX4- and EGFP (TFAP2C)-positive human iPS cell-derived oogonia are delineated by FOXL2-positive mouse granulosa cells (left).

Hiiragi's group, as a joint project with the lab of Jan Ellenberg and Lars Hufnagel at EMBL, published "Dual-spindle formation in zygotes keeps parental genomes apart in early mammalian embryos" (*Science*, **361**, 189-193, 2018). Hiiragi's research has been aimed at understanding fundamental principles governing the morphogenesis of early mammalian development through live imaging analysis. Using a custom-made light-sheet microscope, this work showed that two bipolar spindles form in mouse zygotes and then independently congress the maternal and paternal genomes. These two spindles align their poles before anaphase and keep the paternal genomes apart during the first cleavage, demonstrating a way to separate the parental genome in mammalian embryos. A similar mechanism of dual zygotic spindle assembly may also occur in humans, which may have important implications in failures in human early development.

Eiraku's group published "Strain-triggered mechanical feedback in self-organizing optic-cup morphogenesis" (*Sci. Adv.*, **4** (11), eaau 1354, 2018). Eiraku's laboratory has been pioneering the work for inducing neural tissues, such as optic cup structures with well-stratified retina, from mouse and human pluripotent stem cells (PSCs). Based on both computer simulations and experimental measurements, this work has uncovered mechanical forces that shape the morphogenesis of the optic cup that is induced from mouse embryonic stem cells (ESCs). This work demonstrates that individual cells modulate the spherical shape of the optic cup by sensing the deformation rate of the entire tissue during the process of shaping its structure. These findings clarify a role of mechanical forces in shaping tissue structures, providing a useful model for generating complicated tissues and organs in vitro, which may promote regenerative medicine in the future.

Bourque's group published "Human copy number variants are enriched in regions of low mappability" (*Nucleic Acids Res.*, **46** (14), 7236-7249, 2018). Bourque's laboratory has been investigating the impact of repetitive elements on the acquisition of specific regulatory circuitry and on genome evolution. Copy number variants (CNVs) are known to affect a large portion of the human genome and have been implicated in many diseases. Although whole-genome sequencing (WGS) can help identify CNVs, most analytical methods suffer from limited sensitivity and specificity, especially in regions of low mappability. This work developed PopSV, a CNV caller that relies on multiple samples to control for technical variation. Applying PopSV to 640 human genomes, it has been shown that low-mappability regions are approximately 5 times more likely to harbor germline CNVs, in stark contrast to the nearly uniform distribution observed for somatic CNVs in 95 cancer genomes. In addition to known enrichments in segmental duplication and near centromeres and telomeres, CNVs are enriched in specific types of satellite and in some of the most recent families of transposable elements. This work also identifies 3455 regions with recurrent CNVs that were missing from existing catalogs; in particular, 347 genes with a novel exonic CNV in low-mappability regions, including 29 genes previously associated with disease.

Yamamoto's group published "In vivo reprogramming drives Kras-induced cancer development" (*Nat. Commun.*, **9**, 2081, 2018). Yamamoto's research has been aimed at understanding the mechanism of epigenetic reprogramming associated with induced pluripotency and its implication in relevant diseases. This work explores the impact of the expression of reprogramming factors in pancreatic cancer formation, demonstrating that reprogramming-related epigenetic regulation has a profound impact on Kras-induced pancreatic cancer formation, leading to a proposal that epigenetic fluctuations provoked by environmental factors may cause a transient dedifferentiation state, which is sufficient for cancerous growth of quiescent pancreatic cells with Kras mutation.

Ogawa's group published "Age-related remodeling of esophageal epithelia by mutated cancer drivers" (*Nature*, **565**, 312-317, 2019 (published online in 2018: doi:10.1038/s41586-018-0811-x)). Ogawa's research has been aimed at clarifying pathways through which successive aging-associated mutations lead to tumorigenesis. Cancer is thought to comprise a heterogeneous population of neoplastic cells showing a complex hierarchical structure in terms of gene mutations. With an intensive genome sequence of 682 micro-scale esophageal samples, this work has demonstrated that clones carrying mutations in driver genes (predominantly NOTCH1 mutation) progressively expand according to age in physiologically normal esophageal epithelia and such mutations are substantially accelerated by alcohol consumption and smoking. Driver-mutated clones emerge multifocally from early childhood, increase their number and size with aging, and ultimately replace almost the entire esophageal epithelium in very elderly people. Thus, the remodeling of the esophageal epithelium by driver-mutated clones is an inevitable consequence of normal aging, which—depending on lifestyle risks—may affect cancer development. This work serves as a basis for delineating a comprehensive picture of clonal selection and evolution as a nascent step of tumorigenesis.

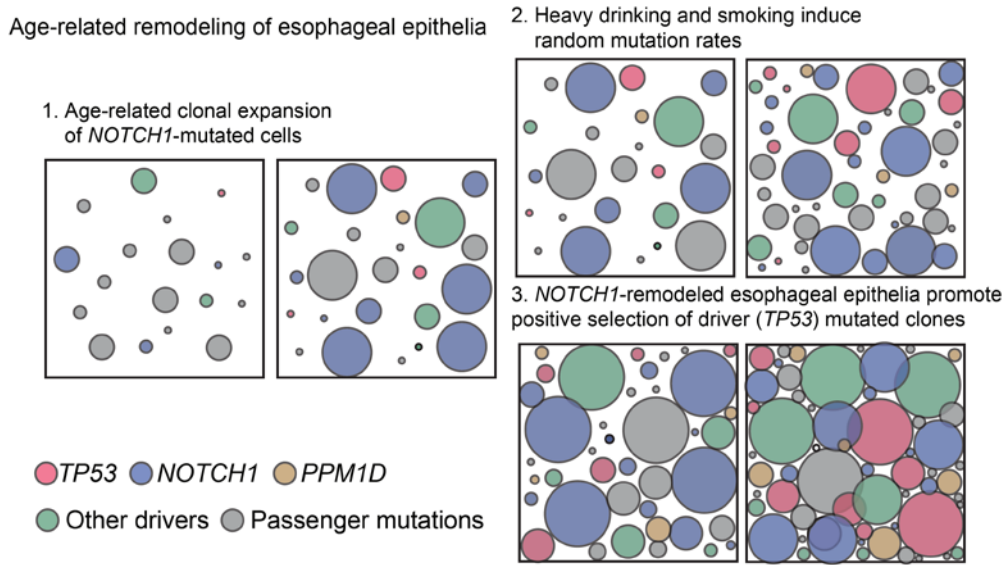

Figure 2. Age-related remodeling of esophageal epithelia (Yokoyama et al, Nature, 2019).

Ueno's group published "Anti-α4β7 therapy targets lymphoid aggregates in the gastrointestinal tract of HIV-1-infected individuals" (*Sci. Transl. Med.*, **10** (461). eaau4711, 2018). Ueno's research has been aimed at promoting human immunology focusing on an investigation into human T follicular helper cells (Tfh). Gut homing CD4+ T cells expressing the integrin α4β7 are early viral targets and contribute to HIV-1 pathogenesis. By sampling the immune inductive and effector sites of the gastrointestinal tract, this work has shown that anti-α4β7 therapy led to a significant and unexpected attenuation of lymphoid aggregates, most notably in the terminal ileum. Given that lymphoid aggregates serve as important sanctuaries for maintaining HIV reservoirs, their attrition by anti-α4β7 therapy has important implications for HIV-1 therapeutics and eradication efforts and defines a rational basis for the use of anti-α4β7 therapy in HIV-1 infection.

Isa's group published "Dynamic reorganization of motor networks during recovery from partial spinal cord injury in monkeys" (*Cerebral Cortex*, 2018, doi: 10.1093/cercor/bhy172). Isa's laboratory has been exploring the mechanism of behavioral recovery after spinal cord injury (SCI) using a non-human primate model (macaque monkeys). The results of this work indicated the possibility of a cortical compensatory mechanism after SCI, where two interdependent motor networks—grasping-related intrahemispheric interactions from the contralesional premotor cortex (PM) to the contralesional primary motor cortex (M1) in the high-γ band (>70 Hz) and motor-preparation–related interhemispheric interactions from the contralesional to ipsilesional PM in the α and low-β bands (10–15 Hz)—redirect activity from the contralesional hemisphere to the other hemisphere to facilitate functional recovery.

Yanagita's group published "Myofibroblasts acquire retinoic acid-producing ability during fibroblast-to-myofibroblast transition in kidney disease" (*Kidney Int.*, **95**, 526-539, 2019: accepted for publication in 2018: doi: 10.1016/j.kint.2018.10.017). Yanagita's laboratory has made key contributions to understanding the pathogenesis of many kidney diseases. Tubular injury and interstitial fibrosis are the hallmarks of various types of kidney disease, but the impact of fibrosis on tubular injury remains poorly understood. With the use of a mouse model that specifically provides injuries in renal fibroblasts, the results of this work indicate a possible role of retinoic acid signaling during tubular injury and regeneration, and suggests a potentially beneficial aspect of fibrosis at least in the early stage of kidney disease.

Hiraoka's group published "Kernel method for persistence diagrams via kernel embedding and weight factor" (*J. Mach. Learn. Res.*, **18**, 1-41, 2018). Hiraoka's laboratory has been developing mathematical methodologies based on topological data analysis (TDA) and machine learning for effective analysis of large-scale datasets. This work reported a novel machine-learning method

(persistence-weighted kernel) for persistence diagrams based on the kernel method. The persistence-weighted kernel is based on the kernel embedding technique. Namely, for a given kernel function, input data are embedded as a vector in the reproduced kernel Hilbert space specified by that kernel function. One of the significant advantages of the persistence-weighted kernel is the ability to respect the topological persistence in this vectorization. As a result, statistical methods based on the persistence-weighted kernel allow the reflection of topological persistence in the machine learning process. This method can be applied to digital image analysis obtained by experiments in general. Furthermore, anomality detection in time series analysis of complex data (e.g., gene expression profiles, time series digital images, etc.) and pattern recognition in spatiotemporal dynamics analysis may also be in the scope of this method.

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."

To initiate interdisciplinary research within ASHBi in a prompt and effective fashion, the **Mathematical Science Group** and the **Bioethics and Philosophy Group** (**Misao Fujita** was appointed PI of the Bioethics and Philosophy Group on February 1, 2019), in collaboration with **Life Science Groups**, have performed the following activities:

Mathematical Science Group (PI: Yasuaki Hiraoka)
Organizations:

1. Regular seminar series: The Mathematical Science Group organized regular seminars with Life Science Groups every two weeks. This year, the seminars focused on the mathematical analysis of the mechanism of early development of cynomolgus monkeys and of germ cell specification in vitro. The members of the Mathematical Science Group and key members of Saitou and Yamamoto's groups have had active discussions about such themes from various viewpoints such as data analysis, dynamics, causality, and the graphical probabilistic model. Through this seminar series, mathematical and biological scientists have progressively been recognizing salient issues for the creation of effective interdisciplinary sciences between mathematics and biology, and identifying concrete research ideas.
2. Discussions with PIs of Life Science Groups: Yasuaki Hiraoka has initiated a discussion series with several PIs of Life Science Groups within ASHBi to identify key research themes in mathematical biology. Based on these discussions, Hiraoka has been introducing mathematical scientists with relevant expertise (including those outside ASHBi) to biological scientists in ASHBi so that interdisciplinary research involving mathematics and biology proceed in a productive fashion in ASHBi. These interactions are expected to lead to a regular seminar series between the relevant mathematical and biological scientists, as described above, to create concrete research ideas.
3. Developing a research network in mathematical biology: Hiraoka has started developing a research network in mathematical biology inside and outside of ASHBi, Kyoto University, for potential collaborations, resulting in cooperative relationships with the following scientists: Shohei Shimizu (Shiga University: Causality and Machine Learnings), Shingo Iwami (Kyushu University: Mathematics in Immunology), Hiroshi Kokubu (Kyoto University: Dynamical System), Konstantin Mischaikow (Rutgers University: Dynamical Systems and Mathematical Biology), and Kathryn Hess (EPFL: Mathematics in Brain Science).

Collaborations:
To establish a key framework for interdisciplinary research in ASHBi, the Mathematical Science Group has initiated collaborations with Saitou's group as follows:

1. Topological data analysis (TDA) for cell-fate specification/species differences: To begin to establish a novel mathematical framework to analyze the mechanism of cell-fate specification and principles for their species differences, we have analyzed single-cell RNA seq data for embryonic cells during cynomolgus monkey development (Nakamura et al., Nature, 2016) with a topological clustering method called Mapper. This year, we have mainly focused on developing

appropriate software modules on Mapper to accommodate input-output data structures and facilitate data visualization. With the preliminary results, we have identified several characteristic topological features of the dataset (Figure 3) and will investigate its biological significance in the coming years. We have also applied Mapper to the RNA-seq data for in vitro germ-cell specification in humans, monkeys and mice to uncover key species differences in germ cell specification, and will continue this investigation in the coming years.

2. Causality and gene regulatory network: We have initiated a project to determine a gene regulatory network for the specification of human germ-cell fate in vitro using a mathematical method calculating potential causality from large-scale datasets. For this purpose, we have selected the Linear non-Gaussian Acyclic Model (LiNGAM). LiNGAM is one of the most powerful methods for causality detection, which, compared to conventional methods, requires only milder assumptions for network construction. In collaboration with Prof. Shohei Shimizu (Shiga University), who developed LiNGAM, we have applied the transcriptome data for hPGCLC specification to LiNGAM, which resulted in a network model of four transcription factors consistent with that obtained from extensive biological experiments. We will continue this investigation further to describe a more complete regulatory network structure for hPGCLC specification in coming years.

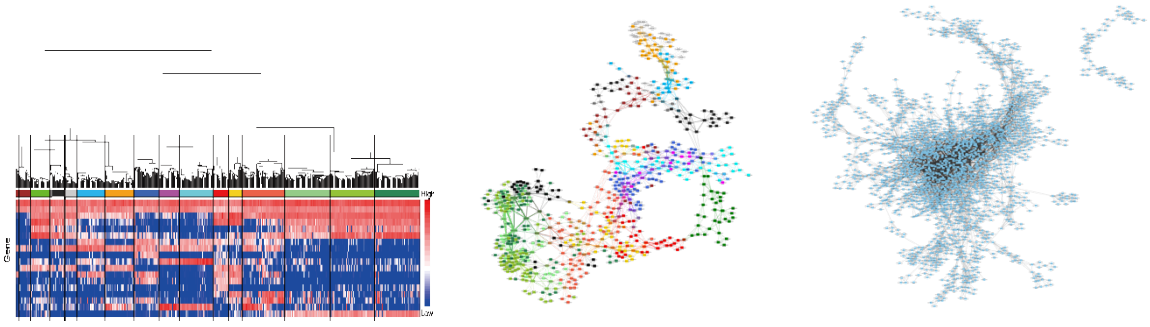

Figure 3. Unsupervised hierarchical clustering of single-cell RNA seq data in (Nakamura et al, Nature, 2016) (left). Cell-wise (middle) and gene-wise topological clustering (right) of the same dataset.

Bioethics and Philosophy Group (PI: Misao Fujita)

With the aim of taking a proactive approach, the Bioethics and Philosophy Group, in collaboration with Life Science Groups, has initiated a project to identify key ethical issues for the advanced study of human biology. There has been recognition that to promote research for regenerative medicine, such as in vitro generation of medically relevant cell types/tissues (organoids) from human PSCs, it is critical for us to have a better understanding of human development, which is substantially different from that of model organisms such as mice. For this purpose, in Europe and the US as well as in China, investigations using samples obtained from aborted human embryos/fetuses have frequently been performed. In contrast, we know of only a few such research projects in Japan. It is also of note that currently, Japan has no laws or guidelines for using such tissues for research purposes. Formulating proper regulations would be important to move this type of research forward while gaining the trust of the society.

Thus, as one of the first projects of the Bioethics and Philosophy Group, an intra-ASHBi rule regarding the use of samples obtained from aborted human embryos/fetuses is being formulated. This could serve as a basis for formulating national regulations in the future. The Bioethics and Philosophy Group has initiated a review of the literature and relevant discussions with Life Science Groups. It is important to gauge the extent to which such research is accepted by the general public and to understand the expectations and concerns of the society. Accordingly, the Bioethics and Philosophy Group has implemented a questionnaire survey for the general public and provided feedback to researchers in Life Science Groups based on some of the survey results.

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)

Setting up ASHBi's main building

We started setting up ASHBi's main building (total space is 1,700 m^2) in December 2018 by renovating Building B on the Faculty of Medicine campus. This building is close to most research spaces related to ASHBi and is convenient for researcher interactions. The main building will be used for overseas/young PIs (up to 8 PIs), the core for Single-cell Genome Information Analyses, the lounge for researcher interaction, seminar/meeting rooms, and the administrative office.

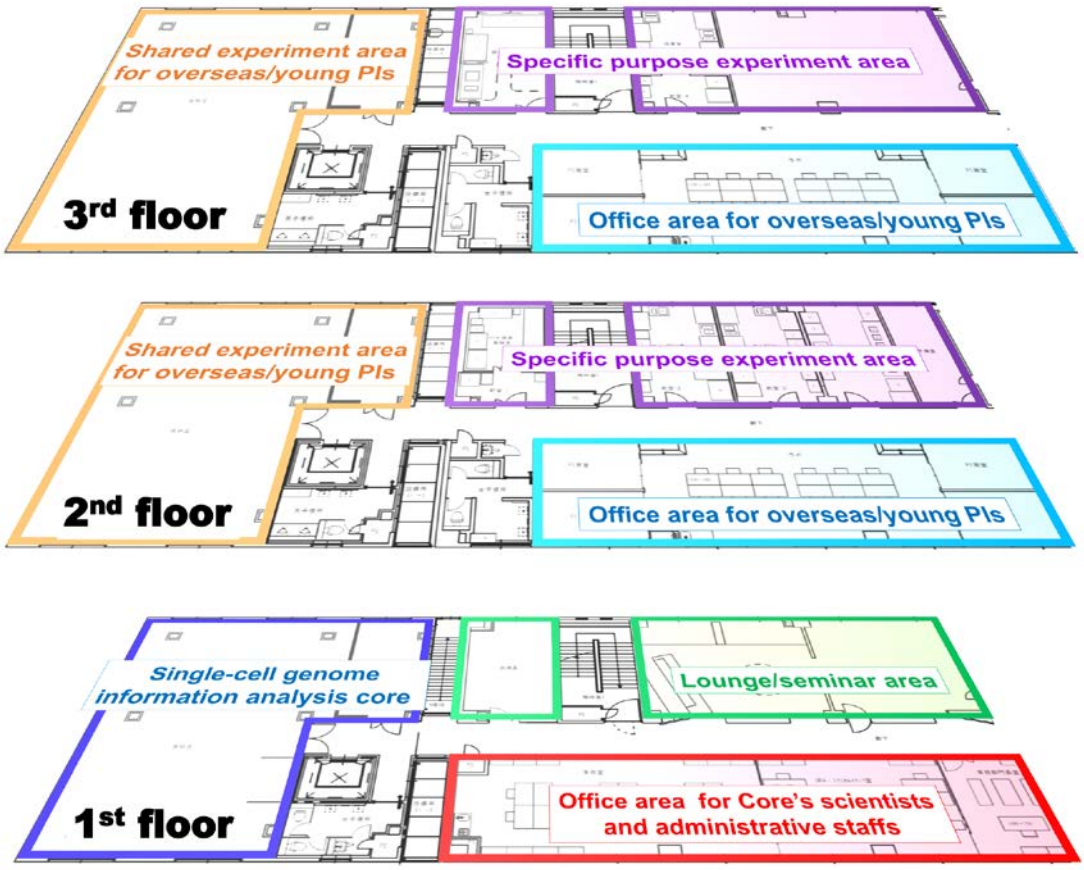

Figure 4. Layout design of ASHBi's main building.

By the end of FY2018, we established the Core for Single-cell Genome Information Analysis on the ground floor (see below) and the commonly used laboratory rooms on the 2nd and 3rd floors of this building. By October 2019, we will finish constructing the administrative office rooms, the lounge for interactions, seminar rooms (1st floor), and the research spaces for the overseas/young PIs (2nd and 3rd floors).

Setting up the Facility for Genome-edited Macaques in the Kyoto University Campus

ASHBi implemented a facility to maintain the genome-edited macaque monkeys generated in the Core for Primate Genome Editing Shiga Medical University. Scientists in ASHBi can observe their behavior and conduct physiological experiments in the Med-Pharm Collaboration Building in the

Kyoto University Campus. We are building the facility with maximized consideration of well-beings for the experimental animals with the global standard.

Figure 5. Facility at Med-Pharm Collaboration Building

Formation of worldwide researcher networking

To enhance the research activities and expand international networking of the Institute, we have proactively hired three distinguished overseas PIs (**Ueno**, **Hiiragi**, and **Bourque**). For a smooth startup of their research at ASHBi, we provide sufficient research space, start-up funding (10–30 million JPY), and budget support for personnel costs (22.5 million JPY; one associate professor as a co-PI and two postdoctoral fellows) for each individual overseas PI. All overseas PIs will frequently come (~6 times/year) or stay long (~3 months) at ASHBi and have close discussions with the Director and other PIs. All the overseas PIs are distinguished researchers and their close cooperation with ASHBi substantially helps to raise the level of the Institution's international recognition. With the faithful contribution from one of the overseas PIs (**Hiiragi**), the ASHBi's director plans to hold **an ASHBi symposium on "Human development, genetics, and evolution"** on the 19th and 20th of March 2020, co-organizing with Hiiragi and two distinguished foreign researchers (James Briscoe, Crick Institute; Barbara Treutlein, ETH Zurich). This symposium will invite ~20 world-class researchers and is highly expected to enhance the visibility of the Institute.

The Director (**Saitou**) himself has networks with distinguished researchers worldwide. He has been requested by Professor Ian Chamber (University of Edinburgh) to join the Organising Committee of **the EMBO meetings on the "Molecular mechanisms of developmental and regenerative biology"** and hold a future EMBO meeting on a similar topic in Japan around November 2020. Furthermore, **Saitou** will serve as Vice Chair and Chair of **the Gordon research conference on "Germinal stem cell biology"** in 2021 and 2023, respectively, which will contribute to enhancing the institute's visibility.

ASHBi Searches for and Hires Excellent Young PIs from around the World

We have made great efforts to search and hire early-career foreign researchers with a great ability as independent associate professors (young PIs). To attract excellent early-career researchers from around the world, we provide plenty of support and opportunities so that young PIs can devote themselves to research activities. A young PI will receive 10 million JPY start-up funding, sufficient research space, and a personnel budget to hire one or two postdoctoral fellows. In addition, we have introduced a special allowance based on the competence of the hired researchers. We plan to hire three to five young PIs by the end of FY2020. The first foreign young PI will join ASHBi on July 1st, 2019.

Administrative Supports for Foreign Researchers

To efficiently support foreign researchers, the administrative staffing comprises bilingual employees. Paperwork, e-mail exchanges, and other internal communications are performed in both English and Japanese. Importantly, we have Japanese-English translations, and make efforts to make the

administrative procedures easy to understand. For example, it is difficult for foreign PIs to understand the University's recruitment procedures for hiring research staff to make their own research groups, even if those procedures are written in English. To substantially resolve this issue, we have made a graphical guidebook for the University's recruitment procedures. Thus, to truly establish an international research environment in ASHBi, we pay plenty of attention to providing administrative information in an easy-to-understand way for foreign PIs/researchers.

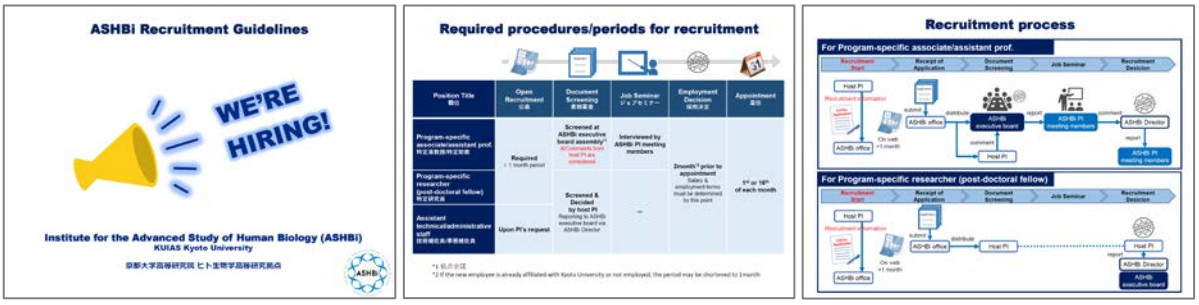

Figure 6. Illustrative guide for recruitment procedures.

4. Making Organizational Reforms

* 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.

System Reformation for the Institution's Autonomous Administration

Kyoto University has created a new organizational structure called the "**K**yoto **U**niversity **I**nstitute for **A**dvanced **S**tudy (KUIAS)" to house a WPI center on a permanent basis. The KUIAS is designated as a special district with a high degree of autonomy. Under the KUIAS umbrella, the Institute's director has been given discretion for making decisions on the most important matters concerning the Institute, and can exercise strong leadership, implementing top-down management.

The Strategic Research Support Section in the Administrative Office

The Administrative Office of the Institute will consist of the administrative director, **the strategic research support section**, and the management section. We have secured one URA and two dedicated staffs in the strategic research support section, and they are expected to play a key role in planning and implementing programs to foster younger researchers and academic–industry cooperation, as well as provide research support, international training courses, and other programs. To effectively fulfill such missions, the administrative director and the section staff operate as a hub, maintaining close cooperation with the University's projects for fostering early-career researchers (HAKUBI/K-CONNEX projects) and the University URA Office (KURA).

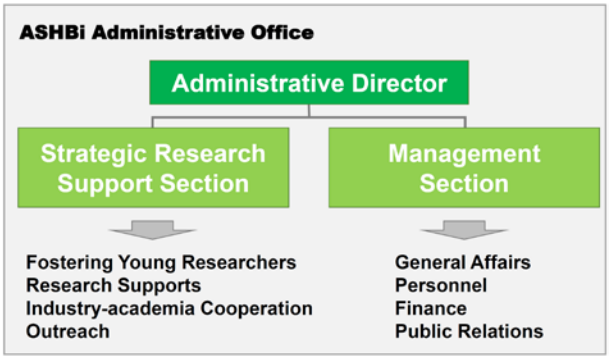

Figure 7. ASHBi administrative office.

Workshops/Seminars & Interdisciplinary Exchange for Young Researchers

The Strategic Research Support Section of the Institute designs and provides various workshops/seminars to learn knowledge/skills for promoting the research activity of young researchers. In May 2019, for example, we plan to have a workshop on "Scientific illustration", jointly sponsored with the University's international PR section (the Office of Global Communications), to learn how to visualize scientific achievements in an illustration. Three designers, who have made

many scientific illustrations (e.g. cover illustrations of high-impact journals), will give lectures about the critical points in making scientific illustrations.

The Institute also provides opportunities for interdisciplinary exchange for young researchers. For example, we plan to have a retreat camp in June 2019, collaborating with the University's projects for fostering young researchers (Hakubi, K-CONNEX). Such a joint retreat could be an ideal meeting for ASHBi's young researchers to initiate interdisciplinary exchange with promising researchers from the same generation.

Figure 8. Young researcher development program. Workshops/seminars and meetings for interdisciplinary exchange.

Furthermore, the Institute provides special programs for foreign PIs/researchers. When they apply for Japanese research grants, the members of the Strategic Research Support Section support the foreign PIs'/researchers' cooperation with the University URA office (KURA: Kyoto University Research Administrator Office). Thus, the ASHBi's efforts described above would provide considerable opportunities for cultivating the ability of young researchers.

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 the 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.

Fostering Next-generation Researchers

We have made great efforts to search for excellent early-career researchers and hire them as young PIs (independent associate professors) of the Institute. Three to five young PIs would be hired by the end of FY2020. This strategic recruitment of young PIs would contribute to securing next-generation PIs who are expected to be the core investigators of ASHBi and lead the future development of the Institute. In addition, for fostering young researchers including postdoctoral fellows in ASHBi, the Strategic Research Support Section provides a series of workshops/seminars and meetings for interdisciplinary exchange as mentioned before. Thus, we make an effort to successfully foster next-generation researchers in ASHBi, not only by hiring young researchers but also by providing effective researcher development programs.

Exceptional Core Facilities Will Enhance the Competitiveness of the Institution

ASHBi has implemented two core facilities to increase its capacity for research development. We have established **the Core for Single-cell Genome Information Analysis** within the ASHBi main building (Building B in the Faculty of Medicine campus) by the end of FY2018. To greatly strengthen the international competitiveness of the Institute, we have strategically established a core facility consisting of ultra-high–throughput sequencing systems that enable large-scale genomics analysis (e.g. Illumina NovaSeq 6000 system, NextSeq 550system, HiSeq 2500 system, etc). This core facility for basic research will be provided open access to researchers. We plan to improve facility

performance and the accumulation of technical know-how by hiring researchers who are able to develop new methods in genome data analyses. This effort will enhance the visibility and competitiveness of the institute and allow us to acquire major external funding and maintain/renew the core facilities after the end of the WPI support period.

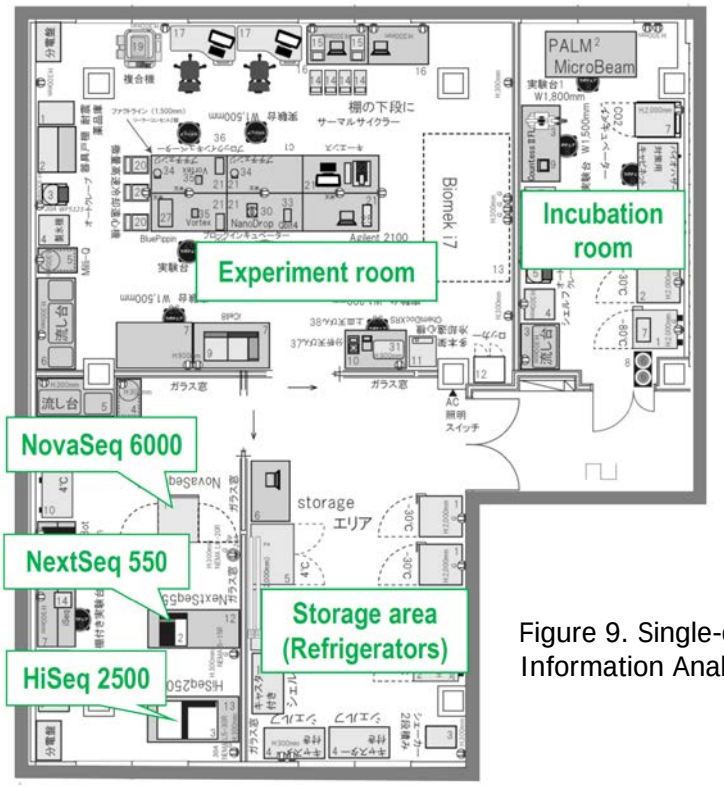

Figure 9. Single-cell Genome Information Analysis Core

We also implemented **the Core for Primate Genome Editing** as a domestic satellite facility at the Research Center for Animal Life Science, Shiga University of Medical Science, which maintains one of the largest primate colonies and most advanced reproductive technologies, both in Japan and worldwide (currently ~700 cages, isolation of ~40 oocytes per week). By providing budget support for increasing the number of monkey cages and oocyte isolation, we greatly enhance the researcher's accessibility to non-human primates.

The Host Institution's Supports for the Institution's Independence

<PERSONNEL SUPPORT>

Kyoto University takes responsibility for the personnel expenses for eight PIs designated to the University (including the director and the vice directors). The University also takes responsibility for the personnel expenses for the administrative director, two URAs (one secured) at the Strategic Research Support Section of the Administrative Office, and two research staffs at the Single-cell Genome Information Analysis Core. We are planning to hire three to five young PIs, and the University will take responsibility for the personnel expenses for the researchers with excellent achievements during their recruitment term (up to three researchers from FY2023).

The positions at the Single-cell Genome Information Analysis Core are very important, because the Core's activity is crucially determined by the performance of staff at those positions. We therefore request the University to provide us permanent positions for research staff at the Single-cell Genome Information Analysis Core.

<FINANCIAL SUPPORT>

The Institute is allowed to take half of the indirect funds associated with competitive grants acquired by the Institute's researchers.

6. Others

* Describe what was accomplished in the center's outreach activities in FY 2018 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.

ASHBi's Website

To enhance the visibility of the Institute, we recently created ASHBi's website, which started from February 2019, in both English (http://ashbi.kyoto-u.ac.jp/en/) and Japanese (http://ashbi.kyoto-u.ac.jp/) using a professional website builder. Our website has announced symposiums, retreats, seminars, workshops, and job openings. In addition, to advertising ASHBi's research activities to the scientific community and the public, our website also announces detailed information about the vision and research purpose of the Institution, the research contents of the individual PIs of our institute.

ASHBi Held the Kick-off Symposium in March 2019

ASHBi held the kick-off symposium on March 11, 2019 in Kyoto. At the symposium, the Director (**Saitou**) gave the opening address to announce the Institute's research focus and approach. His speech was followed by 12 presentations from individual PIs to introduce their aim and outline their own research. This message was the first public announcement of the inauguration of ASHBi with the aim of enhancing our research activities in the public eye. Details about this ASHBi symposium were featured on TV (NHK) and some newspapers. This symposium became a good opportunity to advertise the establishment of ASHBi to the scientific community throughout Japan.

Figure 10. ASHBi Kick-off Symposium

Cooperation with the University's International PR Section for Enhancing the Institution's Visibility across the World

ASHBi Director Saitou, for over a decade a regular contributor to the University's output of scientific achievements in news media, has a close working relationship with the University's Office of Global Communications.

In addition, several senior members of ASHBi have now also begun increasing their news exposure, delivering a strong message of the leading-edge science being pursued in Kyoto and under the WPI program. By making full use of the University's press club (for domestic media) together with international science media distribution (EurekAlert!), a number of important global media outlets have already covered ASHBi's science (see Appendix 7).

Notable among these was an extensive profile of Director Saitou that appeared in the online news magazine *Medium* in January 2019, which was influential in attracting the attention of noted bioscience author Jamie Metzl, prompting Metzl to travel to meet Saitou in March 2019, prior to attending the inaugural meeting of a WHO expert advisory committee on human genome editing.

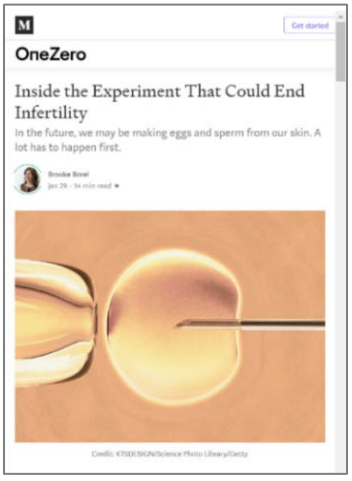

Figure 11. Outreach activities.

Saitou's science media outreach is therefore already connecting directly with key opinion leaders and policy makers in the fields of human biology and ethics: the core areas of ASHBi's mission.

Kyoto University Global Communications, which has extensive experience working with iCeMS, will

continue seeking new ways of sharing ASHBi's message to the press and to the public. Two examples of this cooperation are a video interview of Saitou that will soon appear in the University's English-language profile series *KURNe*, and a jointly sponsored workshop on "Scientific illustration" to be held in late May 2019 (described before).

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 "Actions required and recommendations" in the Follow-up report, then note how the center has responded to them.
* For the center launched in FY 2018, describe the status of response to the pointed items in "Major points that need to be improved" of "The screening result for WPI centers launched in FY 2018."
* However, if you have already provided this information, indicate where in the report.

ASHBi has launched officially on the 30th of October, 2018, and we have described our responses to the pointed items in "Major points that need to be improved" of "The screening result for WPI centers launched in FY 2018" in the revised version of Research Center Project that we submitted upon the selection of our proposal in October, 2018.

1. *A very important issue to be considered is the Center name. The Program Committee members considered the word "synthesis" in the title, "Institute for Advanced Synthesis of Human Biology," to be misleading. Although "synthesis" is defined in the application documents as "comprehensive understanding of target processes," the approaches described in the proposal are mostly analytical. Also, how the approaches for human biology and primate studies are to be "synthesized" is not clearly laid out. The members suggested that a better title might be needed to avoid possible misunderstanding and misleading. The Program Committee suggests that the center carefully consider this issue.*

Response to 1. In response to the suggestion made by the WPI committee, we have formally decided on the following name: **Institute for the Advanced Study of Human Biology (ASHBi)**.

2. *Knowledge from model organisms is often difficult to translate into human biology. Monkeys are much closer to humans than rodents but large gaps still exist. Furthermore, links between different approaches is an issue that needs to be resolved. The director is requested to establish theoretical and practical strategies for overcoming these gaps and links.*

3. *As excellent researchers are gathered in the proposed WPI center, one can naturally expect outstanding scientific outcomes to be accumulated in the list of publications by its PIs on their own enthusiasm. However, the WPI mission entails more than excellent publications. To be a WPI center, new disciplines and breakthroughs or even paradigm shifts need to be made through the integration of various approaches under a clear mission identity, which in this case is human biology.*

Responses to 2 and 3. All PIs are committed to creating a new chapter in the study of human biology, on the basis of their research focusing on key targets in human biology.

To date, there have been no studies making a careful comparison of human disease phenotypes with those of non-human primate models. As a major and unique initiative of ASHBi, we will conduct such studies using cynomolgus monkeys with a major focus on brain and kidney diseases. **Ema's Group** has generated monkeys deficient in *PKD1*, a gene responsible for autosomal dominant polycystic kidney disease in humans, and demonstrated that monkey models recapitulate the phenotypes in humans, including those uncaptured in mouse models (submitted). At the outset, **Yanagita's** and **Isa's Group** have initiated the generation of monkeys deficient in *NPHP1* and *DISC1*, respectively, which will lead to the generation of monkey models for nephronophthisis type 1 and a type of schizophrenia, respectively.

Under the leadership of the director, **Life Science Groups** will acquire multi-hierarchical omics data for gene expression, genome sequences and structures, and epigenetic profiles of relevant "homologous" cell types and their differentiation processes among mice, monkeys, and humans, which they will then use to **actively contribute to the clarification of the principles**

explaining the emergence of species differences. These two approaches will define a strategy to create an original benchmark for exploring human gene functions.

Moreover, note that all the PIs are tightly linked with the theme of how the human genome is regulated and how it has diverged from that of model organisms, creating ample opportunities for mutual discussion and synergistic research development toward **the single theme of addressing "how it is to be human as a biological entity."** We envision that this initiative will lead to the elucidation of the design principle of human beings, a key goal of ASHBi with direct relevance to medical innovation.

Please also see Pages 9 and 10 in the revised version of the Research Center Project that we submitted upon the selection of our proposal in October 2018.

4. *For fused studies, mathematics and ethics are proposed. These aspects are certainly important but their strategy is not clearly defined in the proposal. Their goals as well as strategic approaches should be discussed by the PIs under the leadership of the center director.*

Response to 4. Please see **2. Generating Fused Disciplines** for concrete research activities that we have initiated this year for generating fused disciplines.

Please also see Page 15 and 16 in the revised version of the Research Center Project that we submitted upon the selection of our proposal in October, 2018.

5. *For internationalization, the percentage of effort by the overseas PIs should be increased so that they will be actively involved in the research on site. While the co-PI system is useful, it cannot replace the actual presence of PIs.*

Response to 5. During the course of the development of ASHBi's research, the director will discuss the ways in which to increase opportunities to be present on site with each overseas PI, so that these PIs' work onsite will have a strong presence within ASHBi. Please also note that we have initiated the recruitment of young PIs, and one strong foreign PI will join ASHBi starting at July 1st, 2019.

We are currently in the process of renovating the building for overseas PIs, young PIs, the Mathematical Science Group, the Bioethics and Philosophy Group, the Single-Cell Genome Information Analysis Core, and the administration office, which will be in operation from autumn (~October) of 2019. We will aim to achieve an appropriate international research environment with the inauguration of the building for ASHBi.

Please also see Page 17 in the revised version of the Research Center Project that we submitted upon the selection of our proposal in October 2018.

Appendix 1 FY 2018 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2018. (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.)

Newly selected centers in FY2018 are to list papers under category C below (in addition to categories A and B above).

C. Previously published important WPI-related papers
List previously published papers that provided the basis for the center's research project plan. (Around 30 papers as a yardstick.)

Note: On 14 December 2011, the Basic Research Promotion Division 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. As some WPI-affiliated authors of papers published up to 2011 may not be aware of this requirement, their papers are treated as "WPI-related papers." 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), 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 20), 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
  - C. Previously published important WPI-related papers

(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.)
- These files do not need to be divided into 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

B. WPI-related papers

[Original articles]

1. Asashiba H, Escolar EG, Hiraoka Y, Takeuchi H. Matrix method for persistence modules on commutative ladders of finite type. *Jpn J Ind Appl Math*. 2019;36(1):97-130. doi:10.1007/s13160-018-0331-y

2. Caielli S, Veiga DT, Balasubramanian P, et al. A CD4+ T cell population expanded in lupus blood provides B cell help through interleukin-10 and succinate. *Nat Med*. 2019;25(1):75-81. doi:10.1038/s41591-018-0254-9
3. Kobayashi K, Tsukiyama T, Nakaya M, et al. Generation of an OCT3/4 reporter cynomolgus monkey ES cell line using CRISPR/Cas9. *Stem Cell Res*. 2019;37:101439. doi:10.1016/J.SCR.2019.101439
4. Nakamura J, Sato Y, Kitai Y, et al. Myofibroblasts acquire retinoic acid-producing ability during fibroblast-to-myofibroblast transition following kidney injury. *Kidney Int*. 2019;95(3):526-539. doi:10.1016/j.kint.2018.10.017
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15. Hiraoka Y, Shirai T, Trinh KD. Limit theorems for persistence diagrams. *Ann Appl Probab*. 2018;28(5):2740-2780. doi:10.1214/17-AAP1371
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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 2018 in order from most recent.
- For each, write the lecturer/presenter's name, presentation title, conference name and date(s)

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
Apr.11, 2018	Mitinori Saitou	Epigenetic Reprogramming, Female Sex Determination and Meiotic Entry of Mouse Germ Cells In Vitro	117th International Titisee Conference: From oocyte to embryo – illuminating the origins of life, lake Titisee, Germany
Apr.15, 2018	Mitinori Saitou	Epigenetic Reprogramming, Female Sex Determination and Meiotic Entry of Mouse Germ Cells In Vitro	BSDB Annual Spring Meeting 2018, Warwick, UK
Apr.17, 2018	Misao Fujita	Empirical research on human animal chimeric embryo (HACE) research	Stem Cell Futures: Exploring the Role of Digital and Social Media Engagement Workshop, University of Edinburgh, UK
May.17, 2018	Mitinori Saitou	Mechanism and Reconstitution In Vitro of Germ Cell Development in Mice, Monkeys, and Humans	Weinstein Cardiovascular Development & Regeneration Meeting 2018, Nara, Japan
Jun. 1, 2018	Takuya Yamamoto	Higher-order chromatin features in human pluripotent stem cells	16th Stem Cell Research Symposium, Kyushu University
Jun.20, 2018	Mitinori Saitou	Mechanism and Reconstitution In Vitro of Germ Cell Development in Mice, Monkeys, and Humans	The ISSCR annual meeting 2018, Melbourne, Australia
Jun.29, 2018	Misao Fujita	The ethics of stem cell research: bringing attitude survey into policy formation	The Aga Khan University Ethics Advisory Group Meeting, London, UK
Aug.17, 2018	Yasuaki Hiraoka	Topological data analysis on materials science and several problems in random topology	XXI BRAZILIAN TOPOLOGY MEETING, Satellite conference of ICM 2018
Aug.27, 2018	Mitinori Saitou	Mechanism and In Vitro Reconstitution of Human Germ Cell Development	Yanagimachi 90th Birthday Symposium, Hawaii University, USA
Sep.24, 2018	Mitinori Saitou	Mechanism and In Vitro Reconstitution of Human germ cell development	From Stem Cells to Human Development 2018, Surrey, UK
Oct.19, 2018	Motoko Yanagita	The Mechanism of AKI to CKD	Renal Research Conference, Vanderbilt University, USA
Oct.29, 2018	Takashi Hiiragi	Self-organisation in mouse development	19th International Conference for Systems Biology, Lyon (ICSB 2018 LYON)
Nov.12, 2018	Mototsugu Eiraku	Self-organization of patterned tissues from mouse and human stem cells	EMBO Workshop: Molecular mechanisms of developmental and regenerative biology, Singapore
Dec.13, 2018	Tadashi Isa	Double vector infection technology (DIT) for the pathway-selective manipulation in non-human primates	NIH Symposium on "Genetic technologies for systems neuroscience in non-human primates"
Jan.11, 2019	Guillaume Bourque	The impact of transposable elements (and other genetic changes) on the epigenome	Barbados Workshop on Transposable Elements, Holetown, Barbados

Feb.14, 2019	Tadashi Isa	Large-scaled network reorganization for recovery of hand dexterity after partial spinal cord injury	invited seminar in Johns Hopkins University Medical School, USA
Mar.19, 2019	Guillaume Bourque	Using comparative epigenomics to better understand non-coding DNA	RIKEN invited presentation
Mar. 30, 2019	Mototsugu Eiraku	Self-organization of patterned functional tissues from pluripotent stem cells	119th International Titisee Conference:Tissue formation and regeneration: from molecules to models, lake Titisee, Germany

3. Major Awards

- List up to 10 main awards received during FY 2018 in order from the most recent.
- For each, write the recipient's name, the name of award, and the date issued.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
May15, 2018	Seishi Ogawa	Medal with Purple Ribbon
Oct.27, 2018	Tadashi Isa	Honorary Fellow of Indian Academy of Neuroscience (IAN), awarded at the IAN Meeting
Nov.8, 2018	Mitinori Saitou	Academic Award of the Mochida Memorial Foundation

Appendix 2 FY 2018 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 or in the proposal for newly selected centers in FY2018, attach a “Biographical Sketch of a New Principal Investigator”(Appendix 2a).

<Results at the end of FY2018> **Principal Investigators Total: 12**

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	48	Professor Kyoto University Institute for Advanced Study, Kyoto University	MD, PhD 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	
Vice director Tadashi Isa	58	Professor Graduate School of Medicine, Kyoto University	MD, PhD 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 Yasuaki Hiraoka	41	Professor Kyoto University Institute for Advanced Study, Kyoto University	PhD 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	
Head of the Single-cell Genome Information Analysis Core Takuya Yamamoto	41	Associate Professor, Department of Life Science Frontiers, Center for iPS Cell Research & Application, Kyoto University	PhD Molecular Biology, Bioinformatics	80%	Oct.30, 2018	Usually stays at the center and participates in the center's activities as Executive Board member	
Guillaume Bourque	42	Associate Professor Human Genetics, McGill University	PhD Bioinformatics, Genomics, Epigenomics	25%	Oct.30, 2018	Stays at Kyoto University 3 times per year for 3-4 weeks (total ~11 weeks)	Currently recruiting both Japanese and foreign staff

Mototsugu Eiraku	44	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	51	Professor Department of Stem Cells and Human Disease Models Research Center for Animal Life Science, Shiga University of Medical Science	PhD Developmental Biology, Developmental Engineering	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
Misao Fujita	49	Program-Specific Professor Center for iPS Cell Research and Application, Kyoto University	MS MPH PhD Bioethics	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
Takashi Hiiragi	51	Group Leader Developmental Biology, European Molecular Biology Laboratory	MD, PhD Developmental Biology	20%	Oct.30, 2018	Stays at the center every 1-2 months and participates in the center's activities	Setting up the laboratory, recruiting co-PI
Seishi Ogawa	56	Professor Pathology and Tumor Biology,Graduate School of Medicine,Kyoto Univerisity/ Guest professor Department of Molecular Hematology, Karolinska Institute	MD, PhD Molecular Oncology	90%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	
Hideki Ueno	51	Professor Department of Microbiology, Icahn School of Medicine at Mount Sinai, NY, USA	MD, PhD Immunology	95%	Oct.30, 2018	currently in preparation: will stay at the Center for approximately 3 months per year; at the satellite in Mount Sinai for 9 months per year	Plan to recruite young scientists in the Center and/or the satellite
Motoko Yanagita	49	Professor Graduate School of Medicine, Kyoto University	MD, PhD Nephrology	70%	Oct.30, 2018	Usually stays at the center and participates in the center's activities	

Principal investigators unable to participate in project in FY 2018

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken
Anne Ferguson-Smith	Arthur Balfour Professor of Genetics and Head of the Department of Genetics, University of Cambridge	-	Could not spare enough time and effort to ASHBi due to the duties at the current institution.	Join as the Senior Academic Mentor to provide necessary advices to the research at ASHBi

Appendix 3-1 FY 2018 Records of Center Activities

1. Researchers and center staffs, 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.

Prof. Anne Ferguson-Smith, Arthur Balfour Professor of Genetics and Head of the Department of Genetics, Cambridge University, has joined ASHBi as the Senior Academic Mentor instead of Principal Investigator.

For Recruitment of young PIs, Dr. Cantas Alev, currently an Assisant Professor at CiRA, is joining ASHBi as a new PI from July 2019.

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, 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
Research Center for Animal Life Science, Shiga University of Medical Science	Masatsugu Ema	

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes

2. Holding international research meetings

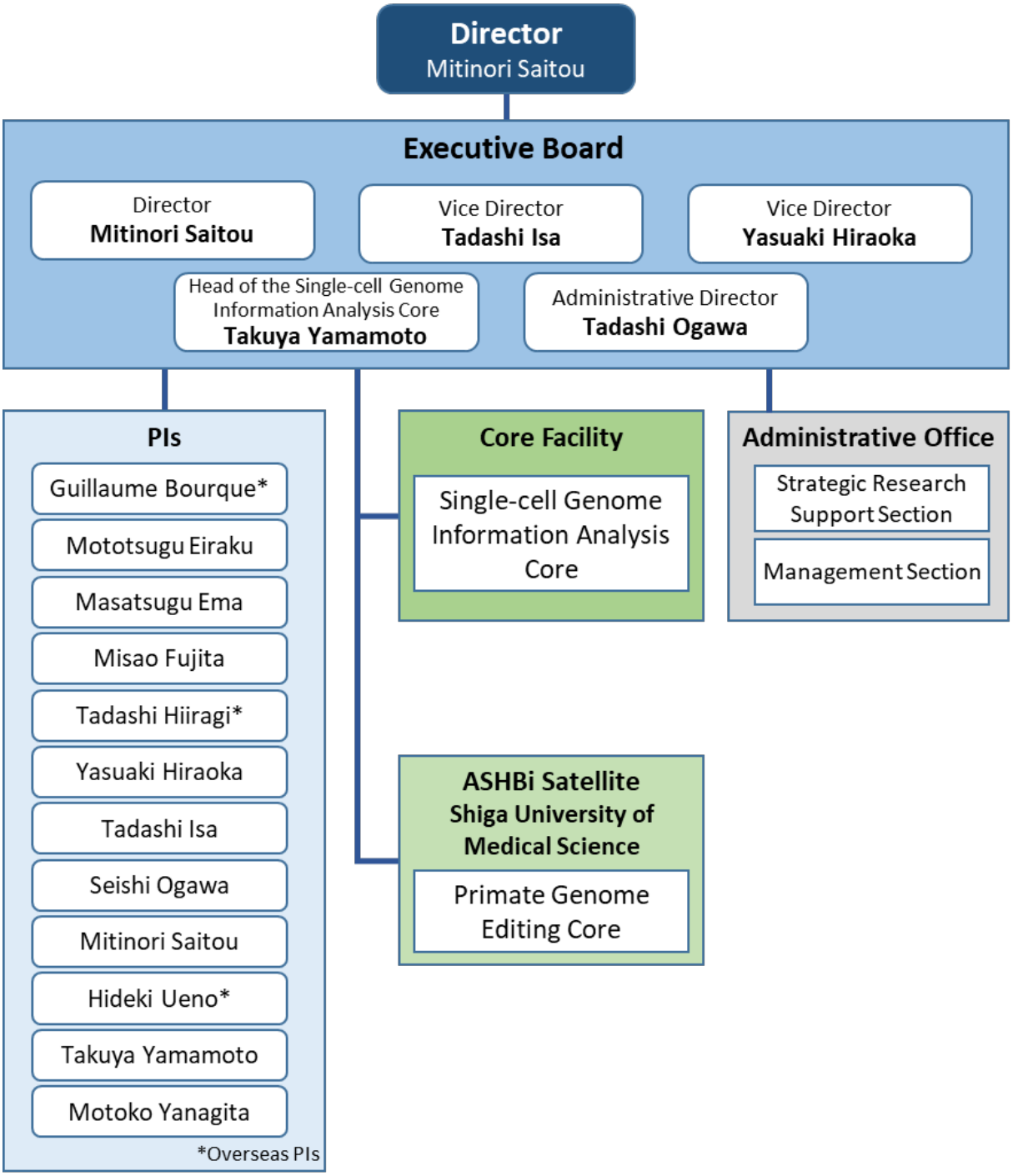
- Indicate the number of international research conferences or symposiums held in FY2018 and give up to three examples of the most representative ones using the table below.

FY 2018: 1 meeting

Major examples (meeting titles and places held)	Number of participants
Mar.11, 2019 ASHBi Kickoff Symposium at Shirankaikan, Kyoto University	From domestic institutions: 146 From overseas institutions: 5

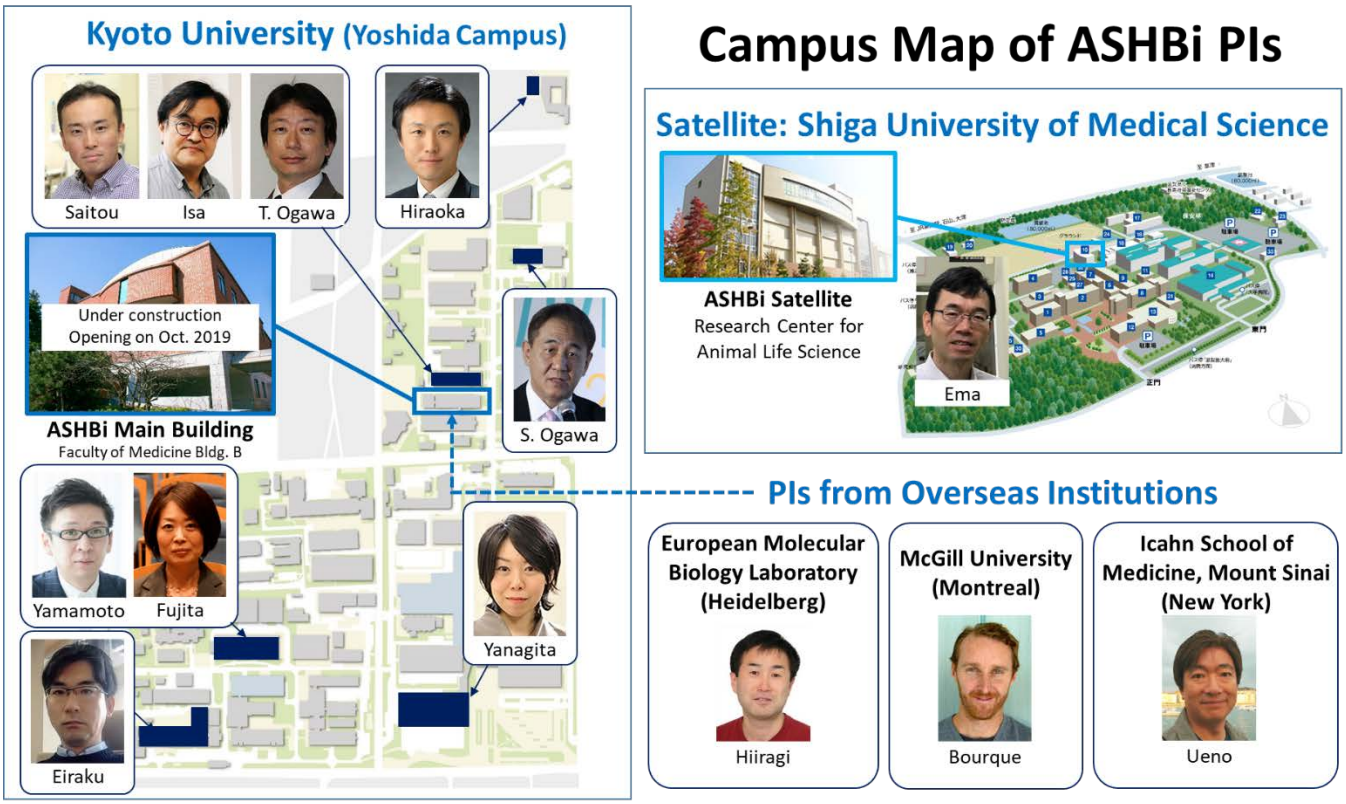
3. Diagram of management system

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



4. Campus Map

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



5. Securing external research funding*

External research funding secured in FY2018

Total*: **660,870,261 yen**

**Amount(yen) shown in this section stands for the amount which are proportionally distributed according to effort ratio of each PI from the original secured amount unless otherwise specified.*

- 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,” and for “joint research projects” 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)	214,927,021 yen
Commissioned Research Projects	337,478,577 yen
Joint Research Projects	108,464,663 yen
Total* (total for above mentioned)	**660,870,261 yen**
Others (Donation funds, etc)	*47,800,969 yen*
Grand Total including donations etc.	*708,671,229 yen*

[Acquired large-scale research grants (35,000,000yen+ in secured amount)]

Organization	Fund name	PI	Funding amount (Secured amount)
JSPS	KAKENHI Specially Promoted Research	Mitinori Saitou	110,000,000 yen
AMED	Project for Cancer Research and Therapeutic Evolution (P-CREATE)	Seishi Ogawa	68,856,154 yen
AMED	Practical Research for Innovative Cancer Control Project	Seishi Ogawa	38,269,230 yen
AMED	Practical Research for Innovative Cancer Control Project	Seishi Ogawa	35,000,000 yen
AMED	Research Center Network for Realization of Regenerative Medicine: Centers for Clinical Application Research on Specific Disease/Organ(Type A)	Mototsugu Eiraku	35,000,000 yen

[Large-scale donation funds in FY 2018]

Fund name	PI	Funding amount
Pythias Fund	Mitinori Saitou	47,447,296 yen

Appendix 3-1a FY 2018 Records of Center Activities

1. Researchers and other center staffs, satellites, partner institutions

1-1. Number of researchers and other center staffs

* Fill in the number of researchers and other center staffs 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 2018	Final goal (Date: month, year)
Researchers from within the host institution	8	8	11
Researchers invited from abroad	4	3	4
Researchers invited from other Japanese institutions	1	1	1
Total principal investigators	13	12	16

b) Total members

	At the beginning of project		At the end of FY2018		Final goal (Date: month, year)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	13		38		58	
Overseas researchers	4	31%	10	26%	18	31%
Female researchers	3	23%	9	24%	17	29%
Principal investigators	13		12		16	
Overseas PIs	4	31%	3	25%	5	31%
Female PIs	3	23%	2	17%	4	25%
Other researchers	0		26		42	
Overseas researchers	0	-	7	27%	13	31%
Female researchers	0	-	7	27%	13	31%
Research support staffs	2		3		20	
Administrative staffs	3		12		14	
Total number of people who form the "core" of the research center	18		53		92	

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	11	1
	Principal investigators (no. of persons): 7	31	4
	Other researchers (no. of persons): 7	7	7
	Research support staffs (no. of persons): 2	1	1
	Administrative staffs (no. of persons): 17	11	4
	Subtotal	61	17
Project activities	Research startup cost	3	3
	Cost of satellite organizations (no. of satellite organizations):1	30	30
	Cost of international symposiums (no. of symposiums):1	1	1
	Rental fees for facilities	6	6
	Cost of outreach activities	2	2
	Cost of consumables	4	2
	Cost of Core Facility	19	19
	Cost of general service expenses	45	40
	Other costs	7	7
	Subtotal	117	110
Travel	Domestic travel costs	0.5	0.5
	Overseas travel costs	0	0
	Travel and accommodations cost for invited scientists (no. of domestic/overseas scientists): 0/3	1.3	1.3
	Travel cost for scientists on transfer (no. of domestic/overseas scientists): 1/0	0.2	0.2
	Subtotal	2	2
Equipment	Cost of buildings	168	106
	Cost of equipment	465	465
	Subtotal	633	571
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1		
	KAKENHI	212	0
	Commissioned research projects, etc.	330	0
	Joint research projects	108	0
	Ohers (donations, etc.)	47	0
	Subtotal	697	0
Total		1510	700

Costs (Million yens)

WPI grant in FY 2018	700
Costs of establishing and maintaining facilities	106
Establishing new facilities	0
Repairing facilities (Number of facilities: , 1,500m²)	106
Others	0
Costs of equipment procured	465
NovaSeq6000	158
FACS Aria Fusion Cell Sorter	90
Biomek i7 Hybrid	50
NextSeq550	45
Others	122

*1. Funding sources that include government subsidies (including Enhancements promotion expenses (機能強化促進経費), 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

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons)		
	Other researchers (no. of persons)		
	Research support staffs (no. of persons)		
	Administrative staffs (no. of persons)		
	Subtotal	6	0
Project activities	Subtotal	30	30
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal	11	
Total		47	30

Appendix 4 FY 2018 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2018 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. 2019 and not described in Appendix 1.

Overseas Satellite : None as of Mar. 31, 2019

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2018. 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 : None as of Mar. 31, 2019

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2018					

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2018					

Appendix 5　FY 2018 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.

Total:　18

	Name	Age	Affiliation (Position title, department, organization)	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)
1	Bernard de Massy	60	Research Director, Univ Montpellier, 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	Apr.06, 2018	Seminar
2	Thongchai Sooksawate		Associate Professor, Chulalongkorn University, Thailand	PhD Neuroscience	Associate Professor of Department of Physiology and Pharmacology 2007 Nagai Award Thailand for Science Research	Jun.21-Jul.20, 2018	collaborative studies
3	Keisuke Yonehara		Principal Investigator DANDRITE, Aarhus University, Denmark	PhD Neuroscience	Head of Yonehara Group (Spatially Assymmetric Neural Circuits in Visual System), DANDRITE 2016 Swiss OphthAWARD 2016 AIAS Associate 2015 Japan Neuroscience Society Young Investigator Award 2014 ERC Starting Investigator 2014 Max. M. Burger Prize, Friedrich Miescher Institute for Biomedical Research 2013 Visual Neuroscience Young Investigator Award	Jul.23, 2018	discussion and seminar
4	Jerome Sanes		Professor Brown University, USA	PhD Neuroscience	Professor of Depratment of Neuroscience, Director of Magnetic Resonance Imaging Research Facility 2018 President's Award for Excellence in Faculty Governance, Brown University 2015-2016 Fulbright Scholar Award, Franco-American Commission 1995 Honorary Master of Arts, Brown University 1979 National Research Service Award	Jul.23, 2018	discussion and seminar

5	Yuji Naya		Professor Pekin University, China	PhD Neuroscience	Investigator of Center for Life Sciences, IDG/McGovern Institute for Brain Research and Department of Psychology at Peking University 2003 Japan Neuroscience Society Young Investigator Award	Jul.30, 2018	discussion and seminar
6	Motomi Osato	55	Associate professor, National University of Singapore	PhD Cell Biology	Principal Associate of Cancer Science Institute of Singapore, and Research Associate Professor of Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore Professor of International Research Center for Medical Sciences, Kumamoto University, Japan '2016 Wong Hock Boon – Singapore Medical Association Charity Fund Outstanding Mentor Awards 2012- Gene Associate Editor	Jul.30, 2018	short-term stay for the seminar and discussion
7	Hiroyuki Kato		Assistant Professor, University of North Carolina	PhD Neuroscience	Head of Kato Lab, Department of Psychiatry and the Neuroscience Center at UNC Chapel Hill 2018 Pew Scholar in Biological Sciences	Aug.01, 2018	discussion and seminar
8	Aya Takeoka		Principal Investigator NERF, Belgium	PhD Neuroscience	Principal Investigator of Takeoka Lab at NERF, powered by IMEC, KU Leuven and VIB and Assistant professor at the Department of Neurosciences, KU Leuven	Aug.03, 2018	discussion and seminar
9	Masanori Nakayama	43	Group leader, Max Planck Institute for Heart and Lung Research	MD	Group Leader of Laboratory for Cell Polarity and Organogenesis	Aug.06, 2018	short-term stay for the seminar and discussion
10	Rebecca Brown		Research Fellow University of Oxford	PhD Practical Ethics	Research Fellow of Oxford Uehiro Centre for Practical Ethics She has done interdisciplinary research which incorporates empirical research and philosophical theory in order to address practical questions in social policy and public health.	Aug.27, 2018	short-term stay for the seminar and discussion
11	Neil Levy	51	Professor Macquarie University/ Senior Research Fellow, University of Oxford	PhD Practical Ethics	Professor of philosophy at Macquarie University, Sydney and Senior Research Fellow at the Uehiro Centre for Practical Ethics, University of Oxford He has published widely on many topics in philosophy, ranging from philosophy of mind to bioethics. He has published more than 150 articles in refereed journals, and 7 books.	Aug.27, 2018	short-term stay for the seminar and discussion

12	Takaharu Ichimura	55	Associate Biologist, Instructor Harvard Medical School	PhD	Instructor of Renal Division, Brigham and Women's Hospital, Harvard Medical School	Sep.07, 2018	short-term stay for the seminar and discussion
13	Neil Hunter		Professor, University of California Davis, USA	PhD Microbiology Molecular Genetics	Professor of Department of Microbiology and Molecular Genetics, College of Biological Sciences and Department of Cell Biology and Human Anatomy, School of Medicine 2016 Elected to the American Association for the Advancement of Science 2016 Elected Fellow of the American Academy of Microbiology 2013 Investigator of the Howard Hughes Medical Institute 2013 CBS Faculty Research Award 2009-2014 Chancellor's Fellow 2009 Early Career Scientist of the Howard Hughes Medical Institute 2007 UCD Mutant Mouse Regional Resource Center Award 2006 France-Berkeley Fund Award 2005 March of Dimes - Basil O'Connor Award 2004-2006 Concern Foundation - Young Investigator Award 2003-2006 Damon Runyon Cancer Foundation - Scholar Award 1997-2001 Wellcome Trust - Prize Travelling Postdoctoral Fellowship 1993-1996 Wellcome Trust - Prize PhD Studentship	Nov.09, 2018	Seminar
14	Yasuhiro Yamauchi	44	Junior researcher, University of Hawaii at Manoa, USA	PhD Developmental Biology	Junior researcher at Monika A Ward's Lab, Department of Anatomy, Biochemistry and Physiology	Nov.15-Dec.14, 2018	short-term stay for joint research
15	Masaru Ito		Postdoc, University of California Davis, USA	PhD Microbiology Molecular Genetics	Post Doc at Neil Hunter's lab, Department of Microbiology and Molecular Genetics, College of Biological Sciences	Nov. 19-Dec.21, 2018	short-term stay for joint research

16	Arthur Caplan	69	Professor/ New York University School of Medicine	PhD Ethics, Bioethics, Research Ethics, Transplantation, Health Reform	Drs. William F. and Virginia Connolly Mitty Professor of Bioethics and Founding Head of Division of Medical Ethics, Department of Population Health 2016 Lifetime Achievement Award, American Society of Bioethics and the Humanities 2016 Rare Impact Award, National Organization for Rare Disorders (NORD) 2014 Public Service Award from the National Science Foundation/National Science Board 2011 Patricia Price Browne Prize in Biomedical Ethics 2008 "Ten most influential people in science" Discover Magazine 2001 “Person of the Year" USA Today McGovern Medal of the American Medical Writers Association Franklin Award from the City of Philadelphia He has served on a number of committees including the chair of the National Cancer Institute Biobanking Ethics Working Group, chair of the Advisory Committee to the United Nations on Human Cloning.	Dec.14, 2018	short-term stay for the seminar and discussion
17	Yuki Oka		Assistant Professor Caltech, USA	PhD Neuroscience	Principal Investigator of Oka Lab and Assistant Professor of Biology and Chen Scholar, Division of Biology and Biological Engineering 2018 Ajinomoto Award for Young Investigators in Gustation or Oral Chemosensation 2016 Klingenstein-Simons Fellowship Award 2016 McKnight scholar 2015 Searle Scholar 2008 Excellent Young Investigator Award (Inoue Foundation)	Dec.25, 2018	discussion and seminar
18	Herbert Edelsbrunner	61	Professor, IST Austria	PhD Computational Geometry and Topology	Professor of Mathematics at Institute of Science and Technology Austria Alan T. Waterman Award (NSF)	Jan.7-11, 2019	Short-term stay for joint researh and discussion. Participation in the workshop

Appendix 6 FY2018 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2018 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2018 (number of activities, times held)
PR brochure, pamphlet	Brochures: ASHBi brochure, WPI brochure vol.14, KUIAS 2018 brochure, AAAS brochure(Science Transcending Boundaries) Flyer: ASHBi Kick off Symposium
Lectures, seminars for general public	Mar. 11, 2019 ASHBi Kickoff Symposium
Teaching, experiments, training for elementary, secondary and high school students	N.A.
Science café	N.A.
Open houses	N.A.
Participating, exhibiting in events	N.A.
Press releases	Sep.20 2018 Research result of Prof. Saitou on Science (Kyoto University) Oct.10 2018 ASHBi selected for WPI Program by MEXT(Kyoto University) Oct.30 2018 Establishment of ASHBi at KUIAS(Kyoto University, KUIAS) Nov.22 2018 Research result of Prof. Eiraku on Sciences Advances (Kyoto University) Jan.08 2019 Research result of Prof. Ogawa on Nature (Kyoto University) Jan.18 2019 Research result of Prof. Yanagita on Kidney International (Kyoto University) Mar.11 2019 ASHBi Kickoff Symposium
Publications of the popular science books	N.A.
Others ( )	

*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.

Appendix 7 FY 2018 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2018 resulting from press releases and getting reported.

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	Sep. 20, 2018	news website 1	[Washington Post] "The 'game-changing' technique to create babies from skin cells just stepped forward" - Introduction of the recent research result published in Science by Prof. Saitou
2	Sep. 21, 2018	newspaper 8	[Asahi Shimbun Sep.21, The Kyoto Shimbun Sep.21, Sankei Shimbun Sep.21, Chunichi Simbun Sep.21, Nihon Keizai Shimbun Sep.21, Nikkann Kogyo Simbun Sep.21, Mainichi Shimbun Sep.21, Yomiuri Shimbun Sep.21] - Introduction of the recent research result published in *Science* by Prof. Saitou
3	Sep. 21, 2018	news website 1	[Chincago Tribune] "'Game-changing' technique to create babies from regular cells just stepped forward" - Introduction of the recent research result published in Science by Prof. Saitou
4	Sep. 24, 2018	news website 1	[Smithsonian.com] "'Scientists Create Immature Human Eggs Out of Blood Cells For the First Time" - Introduction of the recent research result published in Science by Prof. Saitou
5	Oct. 14, 2018	news website 1	[The Guardian] "Reproduction revolution: how our skin cells might be turned into sperm and eggs" - Introduction of the recent research result published in *Science* by Prof. Saitou
6	Nov. 21, 2018	news website 1	[Phys.org] "Team uncovers the underlying mechanisms of 3-D tissue formation" - Introduction of the research result published in *Science Advances* by Prof. Eiraku
7	Nov. 22, 2018	newspaper 2	[Nikkan Kogyo Shimbun Nov.22, Mainichi Shinbun Nov.23] - Introduction of the research result published in *Science Advances* by Prof. Eiraku
8	Nov. 23, 2018	news website 1	[Cell Science] "Cellular Mechanosensing Key for 3D Formation" - Introduction of the research result published in *Science Advances* by Prof. Eiraku
9	Jan. 2, 2019	news website 1	[genomeweb]"Cancer Driver Gene Mutations Rise with Age in Otherwise Normal Esophageal Tissue" - Introduction of the research result published in *Nature* by Prof. S. Ogawa
10	Jan. 3, 2019	newspaper 6	[Asahi Shimbun Jan.3, The Kyoto Shimbun Jan.3, Sankei Shimbun Jan.3, Nihon Keizai Shimbun Jan.3, Mainichi Shimbun Jan.6, Yomiuri Shimbun Jan.7] - Introduction of the research result published in *Nature* by Prof. S. Ogawa
11	Jan. 22, 2019	newspaper 2	[Yomiuri Shimbun Jan.22, The Kyoto Shimbun Jan.25] - Introduction of the research result published in *Kidney International* by Prof. Yanagita
12	Jan. 30, 2019	news website 1	[One Zero by Medium] "Inside the Experiment That Could End Infertility" - Interview of Prof. Saitou and an introduction of a new technology to create egg and sperm cells from iPS cells published in *Science*.
13	Mar. 11, 2019	television 1	[NHK Kyoto] ASHBi Kickoff Symposium at Kyoto University.
14	Mar. 12, 2019	newspaper 1	[The Kyoto Shimbun] Establishment of new institute(ASHBi) at Kyoto University and its research goals.