World Premier International Research Center Initiative (WPI)
FY2023 WPI Project Progress Report

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Research Center	Premium Research Institute for Human Metaverse Medicine		
Center Director	Kohji Nishida	Administrative Director	Takefumi Doi

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2024) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.
➢ Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

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

1. World-leading Scientific Excellence and Recognition
1-1. Advancing Research of the Highest Global Level

Premium Research Institute for Human Metaverse Medicine (WPI-PRIMe) challenges to create Patient bio-Digital Twins that will replicate biological phenomena and pathological processes in human organs in cyberspace. To achieve PRIMe's goal, first of all, we have articulated and shared the definition and the overall strategy to establish Patient bio-Digital Twins.

Definition of Patient bio-Digital Twin

The "Patient bio-Digital Twin" we are pursuing is a computational model comprising life phenomenon, particularly pathological processes, based on tracking changes in gene expression over time. It comprehensively incorporates hierarchical information across all body sites (spatial axis), as well as time axis information. We term this model, developed via organoid research, the "Patient bio-Digital Twin (PbDT)." This innovation will enable the spatial, hierarchical, and temporal prediction of all clinical life phenomena, leading to the realization of advanced personalized medicine.

Overall Strategy to Establish Patient bio-Digital Twin

Biological information (data sets relating to the macro hierarchy of individuals, organs or the environment: macro data sets) obtained from various sensing devices is accumulated. Macro information includes clinical information obtained in hospitals (e.g. blood test data, image data, data obtained from medical interviews) and sensing information obtained in daily life outside hospitals (e.g. information obtained through technologies such as IoT).The accumulated macro data sets are used for modelling of disease onset and progression in the target disease, via information and mathematical sciences, such as artificial intelligence (AI) and mathematical modelling. However, this model does not contain microscopic hierarchical information such as cellular and molecular information. Therefore, the molecular mechanisms underlying the pathological process are a black box. Therefore, at PRIMe, micro-hierarchical data are obtained from patient-derived organoid models. In particular, single-cell and spatial transcriptome analyses are performed to obtain data sets relevant to disease mechanisms. This micro-dataset is used to supplement the mechanistic information to the model constructed from the macro-dataset described above. This model's validity can be confirmed by comparing it with an external data-driven clinical model based on clinical information.

Based on the definition and strategy described above, several key research progress for creation of PbDT related to five target organ groups (Sensory, Hepato-biliary-pancreatic, Bone-cartilage, Cardiovascular, and Reproductive) including interdisciplinary fusion collaborations has been achieved. In addition, PRIMe researchers have developed widely applicable cutting-edge technologies in this fiscal year (e.g. Algorithm for library selection, DNA-barcode, and DNA-GPS).

*In the interest of patent application and intellectual property protection, since we did not want to publish a description of the specific strategy steps in "Overall Strategy to Establish Patient bio-

Digital Twin", we changed the description to one that describes the same content (Jan.17, 2025).

1-2. Generating Fused Disciplines

To advance research by fused disciplines, Center Director held one-to-one meeting with PRIMe PIs to exchange opinions at first. Next, we newly established the Research Steering Committee consisting of Center Director, Deputy Directors, and Core Researchers. This committee has been managing activities such as Progress Report Meeting, Next Generation Working Group, and PRIMe Retreat to share common concept and basic strategy to create Patient bio-Digital Twin. We also took additional measures to further generate fused disciplines (e.g. PRIMe Seminar Series/Omnibus Seminar Series and networking sessions where PRIMe members interact, PRIMe International Symposium, Interdisciplinary Lecture, Happy Hour, and Joint Research Grant).

2. Global Research Environment and System Reform

2-1. Realizing an International Research Environment

WPI-PRIMe has fostered collaboration with international research institutions by inviting world-class researchers from Japan, the U.S., Canada, and Mexico to serve as PIs. In addition, our institute has facilitated information exchange with researchers at the Institut Curie in France and the University of Dublin in Ireland.

Efforts to enhance the international recognition of PRIMe include organizing seminars and international symposiums, as well as inviting prominent researchers from abroad.

The fact that PI member Prof. Hayashi was selected as one of Nature's 10 researchers of the year has further amplified PRIMe's visibility.

PRIMe set up the EDI (Equity, Diversity and Inclusion) Committee and started to actively work on creating a system to discuss and improve the situation and ratio of female and foreigner researchers at PRIMe.

To attract the world's top young researchers, we have implemented a salary structure that exceeds the university's regulations. To support the advancement of young researchers' projects, we have established grants to provide research funds.

2-2. Making Organizational Reforms

PRIMe was the first department at Osaka University to hire faculty members affiliated with overseas institutions as part-time special appointed professor and special appointed associate professors. PRIMe has enabled researchers from overseas institutions, who were previously ineligible for employment under the Osaka University system, to participate in this program.

In addition, we have requested the university headquarters to establish a system to provide salary incentives to PRIMe PIs and the application for this system is on its way to being approved.

As previously mentioned in section 2-1, the University has implemented a new capped salary structure focusing on attracting top researchers globally.

3. Values for the Future

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

For domestic/overseas researchers and also for people from the industry, we held a two-day international symposium with more than 200 participants in total. For overseas people, we also provided information through the PRIMe website and SNS. We started SNS (Facebook and Twitter/X) in April 2024 and enriched our website content, as each media has a different audience. We also published some press releases with attractive research, which resulted in attracting more than 60 media attentions.

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

PRIMe has completed the internal procedures necessary to participate as a collaborative department in the Graduate School of Medicine, Osaka University.

In preparation for establishing the degree program, we have determined a schedule to build the program step by step while addressing center issues in collaboration with the university administrative office. We have opened the "Introduction to Human Metaverse Medicine" subject (lecture series) in graduate school in October 2023.

3-3. Self-sufficient and Sustainable Center Development

A new research building with a total floor area of 8,800 m^2 is scheduled to be constructed in 2026 on the Suita Campus, where most of PRIMe's members conduct their research, bringing all members together in a truly under-one-roof environment.

One tenured faculty post has been secured. In the future, we will increase university support for up to ten faculty positions.

1. World-Leading Scientific Excellence and Recognition

1-1. Advancing Research of the Highest Global Level

* Among the research results achieved by the center, concretely describe those that are at the world's highest level. In Appendix 1, list the center's research papers published in 2023.
* Regarding the criteria used when evaluating the world level of the center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

This section describes the definition and the overall strategy to establish Patient bio-Digital Twins at first, following key research achievements in FY2023 and the future research direction of the five target organ groups including interdisciplinary fusion collaborations.

Definition and Overall Strategy to Establish Patient bio-Digital Twin

The "Patient bio-Digital Twin" we are pursuing is a computational model comprising life phenomenon, particularly pathological processes, based on tracking changes in gene expression over time. It comprehensively incorporates hierarchical information (individual, organ, tissue, cellular, and molecular) across all body sites (spatial axis), as well as time axis information. We term this model, developed through organoid research, the "Patient bio-Digital Twin." This innovation will enable the spatial, hierarchical, and temporal prediction of all clinical life phenomena, leading to the realization of advanced personalized medicine (Figure 1).
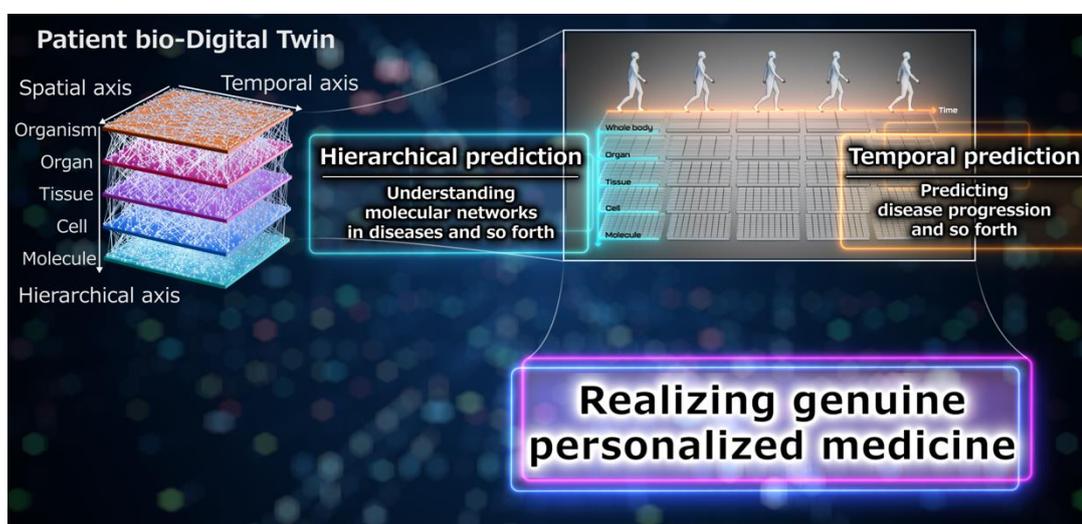

Figure 1. Definition of Patient bio-Digital Twin

The construction of the "Patient bio-Digital Twin" will take place in two phases. Initially, an organoid-based model, "Organoid bio-Digital Twin," will be created. Organoids will be induced from patient-derived iPS cells with multiple genetic backgrounds. We will induce organoids from iPS cells derived from patients with multiple genetic backgrounds, and then perturbations corresponding to environmental factors will be applied to these organoids with different genetic backgrounds to observe the transition of their states. Utilizing organoids enables us to record, accumulate, and model the effects of state-transitioning gene expression on a microscopic hierarchical axis (including tissue, cell, and molecule levels) and a temporal axis. This model is referred to as the Organoid bio-Digital Twin. We will pinpoint a set of biomarkers directly accessible from the patient and measurables within the organoid. Using this set of biomarkers, we can accurately map specific clinical conditions onto the Organoid bio-Digital Twin. The temporal evolution of the microscopic hierarchical axis can be forecasted as the organoid evolves in response to the mapped clinical condition. This predictive model represents the "Patient bio-Digital Twin (First-Generation)" with micro-hierarchical and temporal information (Figure 2).

In the second step, we outline the development of a "Patient bio-Digital Twin (Second-Generation)." Here, the "Organoid bio-Digital Twin" is mapped by multiple clinical information using a common set of biomarkers. This makes the "Organoid bio-Digital Twin" a model with information not only on the micro-hierarchical axis, but also on the macro-hierarchical axis (individuals and

organs). The "Patient bio-Digital Twin (Second-Generation)" is a model equipped with information spanning all hierarchical and temporal axes. This model's validity can be confirmed by comparing it with an external data-driven clinical model based solely on clinical information (Figure 3).
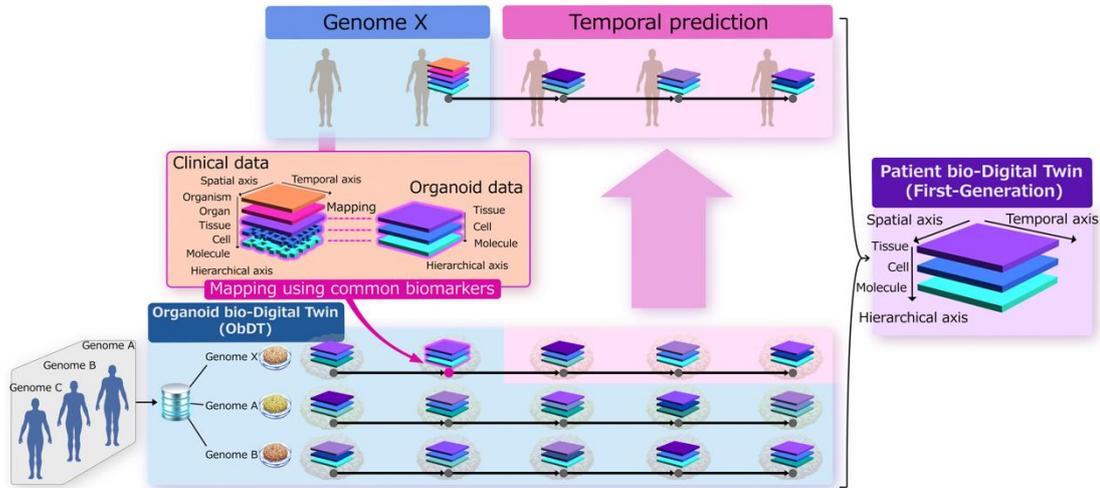

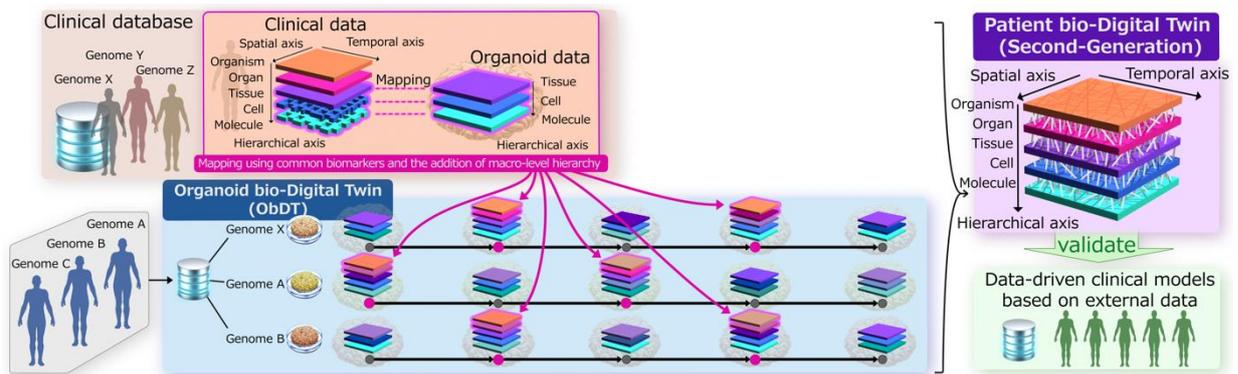**Figure 2.** Creation of Patient bio-Digital Twin (First-Generation)

Figure 3. Creation of Patient bio-Digital Twin (Second-Generation)

Sensory Group (Nishida, Nagahara, Yokota, Nemoto, and Yachie (A))

   This group is currently working on constructing the First-Generation of "Patient bio-Digital Twin" aimed at elucidating the pathology of intractable retinal diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD). Initially, we are developing a model called the "Organoid bio-Digital Twin" based on organoids. The construction of this Organoid bio-Digital Twin requires the evaluation of retinal disease models using retinal organoids derived from patients with different genetic backgrounds. Therefore, we are working on the development of disease models using retinal organoids.

   *For the sake of intellectual property protection, we will keep descriptions and figure undisclosed (Jan. 17, 2025).

1. Development of Disease Models Using Retinal Organoids (Nishida)

   This year, we have already created a retinal disease model for RP. In RP2 knockout retinal organoids, which involve one of the genes responsible for RP, we observed a decrease in the density of CRX-positive photoreceptor cells (Figure 4). This result indicates that we have successfully replicated the pathology occurring in human diseases (unpublished). Additionally, in preparation for developing a disease model for AMD, we are in the process of creating retinal organoids with a knockout of the CFH gene, which is implicated in the onset of AMD.

2. Development of Data-Driven Clinical Models for Retinal Diseases (Nishida, Yokota, Nagahara)

We are advancing the development of clinical prediction models for both RP and AMD. For RP, the clinical parameter that best reflects disease progression is the visual field as measured by kinetic visual field tests. However, in the clinical practice of ophthalmology, the results of kinetic visual field tests are primarily in analog form. Therefore, we have developed an algorithm that recognizes the results of kinetic visual field tests as images and converts them into digital information (unpublished) (Nishida, Yokota).

*Descriptions have been deleted from the viewpoint of intellectual property protection (Jan. 17, 2025).
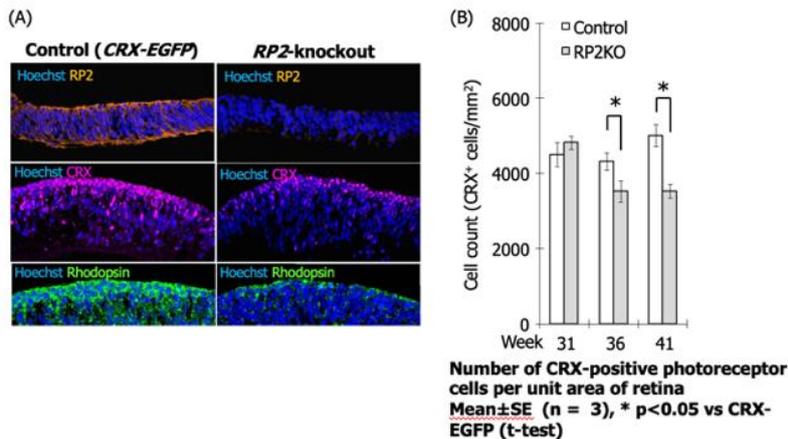

Figure 4.
Retinal organoids with knockout of RP2, the gene responsible for RP, had reduced photoreceptor cells. (A) Immunohistochemical Images of Retinal Organoids. CRX is an early photoreceptor marker, and Rhodopsin is a rod photoreceptor marker. (B) The density of CRX-positive cells at weeks 31, 36, and 41 post induction of retinal organoids.

Hepato-Biliary-Pancreatic Group (Takebe, Nemoto, Hwa, and Kashino)

The first goal of this group is to build hepatic molecular-state simulator, Liver bio-Digital Twin, i.e. First-Generation of Patient bio-Digital Twin, that can infer, project and predict the pathogenic biological trajectory under the interplay of genetic and environmental factors associated with metabolic dysfunction associated steatohepatitis (MASH) in digital space. The developed liver BDT will then serve as a foundational building block for the Patient bio-Digital Twin. The Patient bio-Digital Twin is designed to predict pathogenic trajectories in patients by integrating clinical diagnostics data and molecular states of the liver, obtained from both, liver and liquid biopsies, with the liver bio-Digital Twin framework. Our centerline hypothesis is that pediatric *versus* adult-onset MASH patient-specific organoid panel can distinguish the transition from simple steatosis to inflammation.

*Undisclosed due to descriptions containing unpublished data (Jan. 17, 2025).

To achieve this goal, the group has been focusing on the following three key progress made in the first year. First we have collected more than 20 patients derived PBMC and successfully reprogrammed into iPSCs harboring 120 clones in total from both domestic and international partner hospitals. Secondly, based on population liver organoids (PLO) technology (*Cell* 185: 4216-4232 (2022)), we used various algorithms developed for extracting donor information by single cell RNAseq and systematically identify different donors from PLO. Finally, we have applied newly-developed the trajectory inference technology to create a system that allows us to intuitively visualize differentiation structures while also explicitly quantifying the uncertainty of the differentiation inference. We will use collective methodologies to explore the predictive ability of MASH-related features in various donors, and benchmark against patients' clinical information in the following year. These progresses made a strong basis for scalable interrogation in building Liver bio-Digital Twin, potentially applicable to broader disease states.

*Descriptions and Figures including unpublished data have been deleted from the viewpoint of intellectual property protection and patent application and replaced by the modified descriptions (Jan. 17, 2025).

Cardiovascular Group (Miyagawa, Kashino, Tsukada, and Okada (M))

The first goal of this group is to build an algorithm to generate the Organoid-based ECG (OECG) waveforms. The OECG waveforms can predict cardiac dysfunction and arrhythmia development in

digital space under the interaction of genetic and environmental factors from the onset of cardiomyopathy to heart failure. The developed OECG waveforms will serve as a foundational building block for the First-Generation of Patient bio-Digital Twin Heart. The Patient bio-Digital Twin Heart is designed to predict pathogenic trajectories in patients by integrating clinical data and molecular states of the heart obtained from liquid biopsy with the OECG waveforms. To this end, we have first worked on constructing human iPS cell-derived engineered heart tissue (EHT) model *in vitro* (Figure 5) and reproducing

(A)
Pillar

EHT

6.5 mm

(B)
Pillar
EHT

δ

$$\delta = \frac{\$\%}{\&'} (\quad (I = \frac{!}{"\#} d^{\#})$$

L = Pillar length (12 mm)
E = Young's modulus (1.7 MPa)
d = Pillar head diameter (1.2 mm)

(*Develop Growth Differ*. 2024)

Figure 5.
(A) Fabrication of EHT (B) Force calculation formula

cardiomyopathy pathology using the EHT. Our first target is pediatric restricted cardiomyopathy (RCM) and dilated cardiomyopathy (DCM) as we have chronological data on these patients from the time of diagnosis, and the disease occurred in childhood which makes sense to reproduce a model using current iPSC technology from a maturity perspective. This fiscal year, NTT group (Kashino and Tsukada) and our group published the paper on a pathological model of RCM using the EHT (*Develop Growth Differ*. 2024). In this study, we generated iPS cells from a patient with the TNNI3 R170W mutation and succeeded in capturing the relaxation impairment at the level of cardiomyocyte and EHT, which is one of the main clinical features of RCM. In addition, we have generated iPSC lines from other 3 patients with RCM with different gene mutations and 4 patients with DCM and are now using these iPSCs to recapitulate the pathology and analyze disease progression in the EHT. Furthermore, all these patients have already undergone heart transplantation and we have the patients' own heart specimens at the time of transplantation. We are working with Okada (M) to verify pathological level of EHT by comparing the spatial transcriptome data of these clinical specimens and to elucidate the pathogenesis of the disease by obtaining sequential data on EHTs. So far, we have accumulated clinical data of more than 50,000 cases in the Osaka Cardiovascular Research group (OSCAR) database, and we have a large number of clinical specimens of failing hearts because Osaka University Hospital is one of the leading heart transplantation facilities in Japan. These are unique assets that cannot be obtained from other institutions and we are planning to utilize them in the development of the Patient bio-Digital Twin Heart.
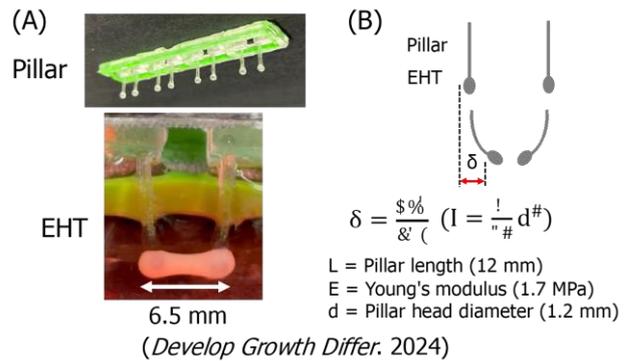
Bone-Cartilage Group (Tsumaki and Nemoto)

To construct a First-Generation of Patient bio-Digital Twin for osteoarthritis of the knee, this group employ following approaches to integrate both macro- and micro-level information obtained from the patients.
1. To create an algorithm to map the correlation between patient-derived iPS cell-derived cartilage organoid omics data and diseased cartilage scRNA-seq data along with the joint fluid proteomic data from the same patient.
2. To classify patients into several classes based on clinical symptoms and the above integration of omics data.
3. To infer and verify prognosis of newly diagnosed patients using models obtained from clinical symptoms, patient-derived iPS cell-derived cartilage organoid data and joint fluid proteomic data.

The following information will be acquired as necessary to construct a Patient bio-Digital Twin of osteoarthritis of the knee.
Macro layer/hierarchical information.
   1. Patient Information; age, gender, medical history, clinical symptoms, and complications.
   2. Blood test results, knee radiographs, knee MRI, knee CT, genomic DNA and SNPs.
Micro layer/hierarchical information.
   3. Proteomic analysis of joint fluid
   4. Histology and patient cartilage scRNA-seq data of cartilage discarded during joint

replacement surgery.

5. Cartilage organoids are differentiated from patient-derived iPS cells and subjected to mechanical and metabolic stress to obtain omics data.

The clinical research procedure was established and approved by the Osaka University Hospital Ethics Committee and we have already begun obtaining macro and micro information on the patients. For scRNA-seq of patient lesion cartilage, we completed a protocol to search for conditions to make single cells by enzymatic digestion of the extracellular matrix of cartilage tissue and to add hashtags. We actually performed scRNA-seq and obtained data. The analysis is conducted in collaboration with Nemoto's group with WPI-PRIMe (Figure 6, left). For the establishment of patient-derived iPS cells, we obtained patient blood samples and requested the production of iPS cells in accordance with the establishment of the PRIMe iPSC Core Facility.

We established a method to apply mechanical stress to iPS cell-derived cartilage organoids. We performed bulk RNA-seq analysis on 2 mm diameter cylindrical iPS cell-derived cartilage organoids subjected to various weights in a three-dimensional cyclic mechanical load culture system. The transcriptome analysis was performed in collaboration with Nemoto's group to obtain mechanical load weights corresponding to physiological loads such as walking and hyper-physiological loads that induce osteoarthritis, respectively (Figure 6, Right). This enabled the setting of conditions for perturbation by mechanical stress.
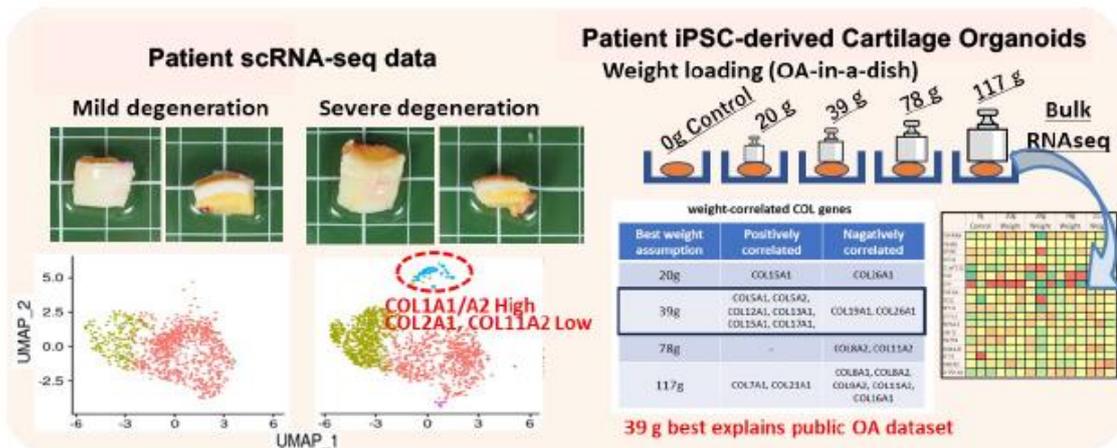

Figure 6. Patient scRNA-seq data and Weight loading for iPSC-derived cartilage organoids

Reproductive Group (Hayashi, Hwa, and Yokota)

For the construction of the First-Generation of Patient bio-Digital Twin in reproductive organs, our group has been dedicated to:
(1) Induction of ovarian somatic cells from human iPS cells
(2) Refinement of culture conditions allowing long-lived dormant oocytes in culture
(3) Development of an imaging system to comprehensively quantify the ovarian follicles (with Yokota G).

In the meantime, we are considering appropriate perturbations that provide parameters for bridging between organoid-based data and clinical/patient data. Based on our research and collaboration with Hwa G, these perturbations would be derived from serum samples linked to infertility patient information, as over 500 samples from infertility patients have been stored at Osaka University Hospital. Followings are detail of progress in this fiscal year.

(1) Induction of ovarian somatic cells from human iPS cells

We have established appropriate reporter human iPS cell lines for the induction of ovarian tissues. The culture conditions for the induction of common precursors, which have the potential to
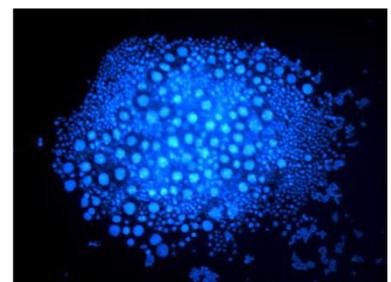

Figure 7. Dormant oocytes (blue) in cultured organoid

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differentiate into all ovarian somatic cells, have been nearly determined.

(2) Refinement of culture conditions allowing long-lived dormant oocytes in culture

   For the first time, we have determined the culture conditions that allow oocytes to remain dormant for a long time period using mouse fetal ovaries and ovarian organoids (Figure 7).
   *Undisclosed due to descriptions containing unpublished data (Jan. 17, 2025).

(3) Development of an imaging system to comprehensively quantify the ovarian follicles

   In collaboration with Yokota G., we developed the first version of an imaging system that can quantify histological information, such as the number, size, and circularity of oocytes, as well as their distance from the nearest oocyte, the ovarian surface, and blood vessels, etc. (Figure 8). This will serve as a foundational technology providing quantitative information for the bio-digital Twin in the ovary.
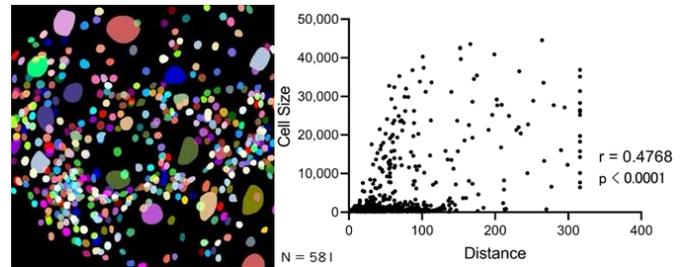
   *Because descriptions are contained unpublished data, we will keep them undisclosed (Jan. 17, 2025).

Figure 8. An image converted from histological sections (left) and quantification of oocyte size and distance from the nearest oocyte (right).

Cutting-edge Technologies Developed in PRIMe

   In addition to the interdisciplinary approaches to develop Patient bio-Digital Twins described above, PRIMe researchers have developed widely applicable cutting-edge technologies in this fiscal year as described below:

1. **Nemoto** (PRIMe PI) established ACIDES (Accurate Confidence Intervals for Directed Evolution Scores) that combines statistical inference and *in-silico* simulations to improve performance estimation in the library selection process by attributing accurate statistical scores to individual variants.
   Nature Communications (2023) DOI: https://doi.org/10.1038/s41467-023-43967-9

2. **Schiebinger** (PRIMe and UBC) proposed DNA-GPS (global positioning system), a theoretical framework for large-scale optics-free spatial genomics that combines ideas from mathematical cartography and positional indexing. DNA-GPS has the potential to achieve scalable spatial genomics for multiple measurement modalities, and by eliminating the need for optical measurement, it has the potential to position cells in three-dimensions (3D).
   Cell Syst. (2023) DOI: 10.1016/j.cels.2023.08.005

3. **Yachie (N)** (PRIMe PI and UBC) presented a new multi-kingdom genetic barcoding system, CloneSelect, in which a target cell clone can be triggered to express a reporter gene for isolation through barcode-specific CRISPR base editing. This novel CRISPR-barcode genetics platform provides many new ways of analyzing and manipulating mammalian, yeast, and bacterial systems.
   bioRxiv (2023) DOI: https://doi.org/10.1101/2023.01.18.524633

4. **Morita** (PRIMe and Univ. of Texas Health Center), collaborating with Okada (M), compiled comprehensive data on organelle contacts and structures in human cancers and succeeded to integrate high-dimensional, multimodal information, encompassing organelle morphology and omics data. These intricate molecular signatures can be applied for stratification of organoids and patients utilizing sophisticated techniques, such as artificial intelligence (AI).
   Manuscript in preparation

1-2.   Generating Fused Disciplines
* Describe the content of measures taken by the center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields. If any, describe the interdisciplinary research/fused discipline that have resulted from your efforts to generate fused disciplines. You may refer to the research results described concretely in "1-1. Advancing Research of the Highest Global Level."

To advance research by fusing disciplines, **Center Director held one-to-one meeting with PRIMe PIs** to exchange opinions at first. Next, we newly established the **Research Steering Committee** consisting of Center Director, Deputy Directors, Nemoto (Algorithm development), Abugessaisa (Data Processing), Nakagawa (Manager of iPSC Core), Hayashi (Organoid Science of Reproduction), and Sakurada (Digital Advisor). This committee has been managing three notable activities described below to share common concept and basic strategy to create Patient bio-Digital Twins. Please also see section 5, Responses to (1) and (2).

A) **Progress Report Meeting**: We organize the meeting once a month focusing one research group to deeply discuss (usually take two hours) about not only progress of research but also milestone to establish bio-Digital Twin. First of all, we started from the five target organ groups (Sensory, Hepato-biliary-pancreatic, Bone-cartilage, Cardiovascular, and Reproductive). Basically, not only core PIs of each group present their researches, interdisciplinary collaborators also give presentations and induce more active discussions.

B) **Next Generation Working Group**: We hold study group once a month among core next generation researchers in PRIMe (currently 14 members) to share ideas and create bottom-up interdisciplinary research among these researchers.

C) **PRIMe Retreat**: We held PRIMe Retreat twice within this fiscal year (a two-day retreat from September 1st and 2nd and one-day retreat on March 2nd, gathering 49 and 59 participants respectively). We strengthened the shared understanding of PRIMe vision and our team bonds.

Based on those activities, we shared common concept of Patient bio-Digital Twins among PRIMe researchers and set strategic approach as described in section 1-1 and section 5 Response to (4), and we also took additional measures described below to further generate fused disciplines.

1) **PRIMe Seminar Series/Omnibus Seminar Series**: Inviting outstanding researchers to present and holding networking sessions where PRIMe members interact (total 14 seminars during this fiscal year).

2) **PRIMe International Symposium**: The 2nd International Symposium (February 29 and March 1, 2024) inviting researchers from Japan and overseas to introduce the vision of PRIMe and to facilitate the integration research conducted at PRIMe.

3) **Interdisciplinary Lecture**: Exchanging and expanding basic knowledge between wet and dry researchers.

4) **Happy Hour**: Monthly event allowing sharing ideas for the creation of bottom-up fused research between young and senior researchers of all fields at the Special Interaction Space (Indra's Net Connect) in CoMIT building.

5) **Joint Research Grant**: Special grants for young researchers providing research funds to support their interdisciplinary projects.

Those initiatives described above enhanced to generate Fused Disciplines described in section 1-1.

2. Global Research Environment and System Reform

2-1. Realizing an International Research Environment

* Describe what's been accomplished in the efforts to raise the center's recognition as a genuine globally visible research institute, along with innovative efforts proactively being taken in accordance with the development stage of the center, including the following points, for example:
- Efforts being developed based on the analysis of number and state of world-leading, frontline researchers (in Appendix 2); exchanges with overseas entities (in Appendix 4); number and state of visiting researchers (in Appendix 5)
- Proactive efforts to raise the level of the center's international recognition and to obtain diversity within the center including gender balance.
- 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)

・Appendix 2 illustrates how WPI-PRIMe has brought together world-leading researchers from Japan, the U.S., Canada, and Mexico to serve as PIs, fostering collaborative partnerships with these esteemed international research institutions. In addition, our institute has facilitated information exchange with researchers at the Institute Curie in France and the University of Dublin in Ireland

(outlined in Appendixes 4 and 5). Collaborative research is underway with Cincinnati Children's Hospital (USA) on developmental disorders, The University of British Columbia (Canada) on barcode gene-related research, National University of Mexico (Mexico) on epithelial cell modeling, Institut Curie (France) on computational biology and University of Dublin (Ireland) on systems biology.

・Efforts to enhance the international recognition of PRIMe include organizing seminars and international symposiums, as well as inviting prominent researchers from abroad (refer to Appendix 5). The fact that PI member Prof. Hayashi was selected as one of Nature's 10 researchers of the year has further amplified PRIMe's visibility.

To ensure our commitment to diversity, we have a policy of prioritizing the recruitment of female and foreigner for faculty positions. However, recognizing that the representation of female and foreigner remains insufficient, we are exploring the possibility of establishing specific quotas for female scientists and implementing recruitment procedures in the future. Additionally, PRIMe set up the EDI (Equity, Diversity and Inclusion) Committee and started to actively work on creating a system to discuss and improve the situation and ratio of female and foreign researchers at PRIMe.

Furthermore, we aim to improve the pool of candidates by proactively engaging with international partner institutions, among other strategies, to attract qualified individuals who contribute to a balanced gender ratio.

・To attract the world's top young researchers, we have implemented a salary structure that exceeds the university's regulations. To support the advancement of young researchers' projects, we have established grants to provide research funds. Moreover, recognizing the importance of interdisciplinary collaboration, we have established the Next Generation Working Group aimed at catalyzing fusion research among scholars across wet and dry fields. This initiative serves to elevate the capabilities of young researchers by facilitating the exchange of shared information and knowledge, eventually, enhancing their expertise levels.

When the new buildings (Suita Agora 2) funded by university bonds are completed in 2026, most members of the center will be able to conduct research together. In the interim, we will create an environment, as shown in the Figure 11, to encourage maximal communication between wet and dry researchers.

Furthermore, two core facilities will be established to enable the center members to conduct research efficiently and achieve results smoothly.

(1) iPS cell Core Facility (Nakagawa)

A 400 m^2 laboratory, serving as the iPS Cell Core Facility, has been established on the second floor of the Graduate School of Medicine. The facility specializes in the establishment and storage of human iPS cells. Additionally, barcoded iPS cells are produced and utilized for experiments to align cell lines. A dedicated researcher and technical experts (Nakagawa and Doi) have been assigned to manage operations within this facility.

(2) Big Data and Computing Core Facility (Nagahara, Abugessaisa and Watashiba)

This facility was established to standardize and manage data obtained from clinical tests and organoid experiments. Computer servers were installed in the Cybermedia Center at Osaka University, where ONION and the supercomputer (SQUID) will be used to build the bio-Digital Twin. Alongside the assignment of researchers (Nagahara: chief, Abugessaisa: data processing, Watashiba: data storage) to oversee this project, support will be provided by professors at the Cybermedia Center (Date and Furihata) and the director of the medical information department at the hospital (Takeda).

2-2. Making Organizational Reforms

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

Attempts to reform the system.

In many cases, when asking outstanding overseas researchers to join a center, it proves

challenging for them to relocate from their positions abroad. Often, it is also difficult to hire them through cross-appointment. In such conditions, they are often compelled to give up their participation. However, PRIMe was the first department at Osaka University to hire faculty members affiliated with overseas institutions as part-time special appointed professor (Yachie (N)) and specially appointed associate professors (Domínguez-Hüttinger, Schiebinger and Shakiba). PRIMe has enabled researchers from overseas institutions, who were previously ineligible for employment under the Osaka University system, to participate in this program.

In addition, we have requested the university headquarters to establish a system to provide salary incentives to PRIMe PIs and the application for this system is on its way to being approved.

As previously mentioned in section 2-1, the University has implemented a new capped salary structure focusing on attracting top researchers globally. This initiative represents a significant departure from prior regulations and is a result of PRIMe's acceptance into the WPI program. This strategic move signifies the effort to reform the university's system. With this new structure, the University can now offer competitive salaries commensurate with those offered by leading international institutions, enabling us to recruit talented researchers.

Host institution's commitment to the system reforms.

Osaka University is committed to fully supporting the various system reforms that are essential for the development of PRIMe. Furthermore, PRIMe is recognized as a world-leading research organization overseen by the President of Osaka University and is regarded as an independent department. In addition, the PRIMe Center Director has been granted special top-down executive authority that other department heads do not possess and is responsible for promoting original research and managing the center. Osaka University will reallocate faculty positions from current departments and provide the necessary space for PRIMe. Additionally, during the WPI support period, existing organizations within Osaka University will be reorganized to consider the establishment of another new organization that will realize PRIMe's mission. Furthermore, as mentioned above, Osaka University is in the process of approving a new system of salary incentives for PRIMe PIs.

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

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

In FY2023, we spent three months discussing with a branding consultant with experience in PR planning for financial/insurance/technology/apparel companies how to develop a strategy to make WPI-PRIMe an outstanding global institute. Over the next few years, we plan to increase PRIMe's visibility to the public, including researchers worldwide, and to begin fundraising to secure donations for the next decade. This year, our main goal was to reach out to the general public, and we achieved this goal through several approaches, as shown below.

WPI-PRIMe Branding Plan (Long Term Overview)

(1) Events for each target (for details of each event, refer to Appendix 6)
Based on the branding plan, we planned an online/onsite approach to reach each target. For

domestic/overseas researchers and also for people from the industry, we held a two-day international symposium with more than 200 participants in total. For overseas people, we also provided information through the PRIMe website and SNS (see (2) for details).

For the domestic public, we held a Science Café with WPI-IFReC, especially for high school students and their parents who are interested in studying at Osaka University. We also collaborated with other WPIs to increase the presence of our research through onsite/online/hybrid events, including the WPI Science Symposium. In addition, Center Director Nishida gave a lecture at *Koan-ki* (洪庵忌), an annual event based on the memoirs of Japanese doctor *Ogata Koan* (緒方洪庵), which was uploaded to YouTube. The video has been viewed nearly 2,000 times by the general public.

(2) Ongoing public engagement

Continuous communication with the public is important, so we have increased the number of channels through which we communicate with the public. We started SNS (Facebook and Twitter/X) in April 2024 and enriched our website content, as each media has a different audience. The PRIMe website (https://prime.osaka-u.ac.jp/) was renewed last summer, and we publish the same information in different channels to provide the latest news to the public. The PR film created by JSPS was released on YouTube in February 2024, which may expand the audience we can reach. We also published some press releases with attractive research, which resulted in attracting more than 60 media attention (see Appendix 7).

In addition, Kishimoto's group (ELSI research) planned to build a Patient & Public Involvement (PPI) platform for WPI-PRIMe. They presented the outline of their proposal at the WPI-PRIMe International Symposium poster session and are now communicating with researchers and URAs about the next step to achieve their goal.

(3) Selected as Nature's 10

In 2023, researchers from our institute brought many outstanding research results to the public. Dr Katsuhiko Hayashi's research paper published in Nature (K. Murakami et al. Nature 615, 900-906; 2023) was one of the most widely reported results. It reported that his laboratory had successfully produced eggs using cells from male mice. This news was broadcast by NHK (Japan), BBC (UK), ABC (US) and other major mass media. His research paper was significant enough to be mentioned in related articles and news for the time being. At the end of 2023, Nature selected Dr Hayashi as one of "Nature's 10", the ten people who helped shape science that year. It showed how much his result had influenced scientists, and also how much the public was interested in his research.

3-2. Human Resource Building: Higher Education and Career Development
* Describe the content of measures taken by the center to foster young researchers, including doctoral students, through their participation in a research system that creates new interdisciplinary domains within a rich international environment.

PRIMe is making efforts to foster the next generation researchers with advanced expertise in "Human Metaverse Medicine" as well as a bird's-eye view of the entire field. In addition, it is necessary to build the foundation of "Human Metaverse Medicine" to create broader impacts in various academic fields and to develop interdisciplinary collaboration. To this end, we have created the following educational programs.

Collaborative department of the Graduate School

PRIMe has completed the internal procedures necessary to participate as a collaborative department in the Graduate School of Medicine, Osaka University. As a result, faculty members belonging to PRIMe have been able to accept, supervise, and examine graduate students since April 1, 2023.

Ph.D. programs

In preparation for establishing the degree program, we have determined a schedule to build the program step by step while addressing center issues in collaboration with the university administrative office (Figure 9). We have opened the "Introduction to Human Metaverse Medicine" subject (lecture series) in graduate school (2 credits) in October 2023. The syllabuses cover cyber,

physical, ethical, and social perspectives. 19 Ph.D. students signed up for this course in 2023. We have also completed the process to launch the Human Metaverse Medicine graduate course as a Graduate Program for Advanced Interdisciplinary Studies (> 7 credits) starting in April 2024. We are also working to create the Human Metaverse Medicine Ph.D. program (Integrated Doctoral Program) starting in April 2027 and a double degree program in October 2026. Further, we are preparing to open the lecture series to graduate students and young researchers outside the Center, including graduate students of the World-leading Innovative & Smart Education program (WISE) and Leading Graduate programs.
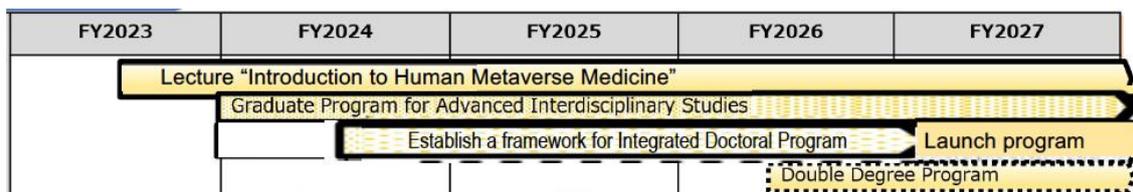

FY2023	FY2024	FY2025	FY2026	FY2027

Lecture "Introduction to Human Metaverse Medicine"
Graduate Program for Advanced Interdisciplinary Studies
Establish a framework for Integrated Doctoral Program — Launch program
Double Degree Program

Figure 9. Time schedule of establishing the degree program

Seminar series
We held the Interdisciplinary Human Metaverse Medicine seminars for 2023 fiscal year.
(Speakers: S. Pasca (Stanford University), M. Saitou (Kyoto University), N. Shakiba (The University of British Columbia), M. Ebrahimkahni (Pittsburg University), K. Sakurada (Keio University), G. Schiebinger (The University of British Columbia), H. Asahara (Tokyo Medical and Dental University), B. Kholodenko (University College Dublin), S. Uchida (Kyushu University), Y. Morishita (RIKEN), M. Morita (University of Texas), S. Ogishima (Tohoku University), Y. Suzuki (Tokyo University), E. Kawakami (Chiba University), I. Abugessaisa (RIKEN))
They were open to graduate students and young researchers outside the Center.

Postdoctoral training
We have designed and created postdoctoral and advanced postdoctoral programs to train young researchers for PRIMe. Funding basis will be guaranteed in collaboration with the Support for Pioneering Research Initiated by the Next Generation (SPRING) program of Osaka University.

Students, young researchers, PI gathering
We held regular informal meetings (Happy Hour and Networking) approximately three times a month for 2023 fiscal year to facilitate students, young researchers, and PIs to communicate and exchange ideas and experience, thereby providing an interdisciplinary research environment at PRIMe for young researchers.

3-3.   Self-sufficient and Sustainable Center Development
* Describe the state of implementation of the host institution's mid-to-long term measures for supporting the center toward becoming self-sufficient and sustainable after the 10-year funding period ends, such as reforming the host institution's organization, providing personnel with priority allocation of tenured posts to the center, providing fundamental financial support, and material support including land and buildings.

In the present, as stated in the "OU Master Plan 2027", the University's mid-to-long-term management vision, as the world's most innovative university, is to create "a society where each member leads a meaningful and fulfilling life." Osaka University is currently developing the OU (Osaka University) Ecosystem, which embodies a systematic co-creation with society to solve social issues. The world that PRIMe aims to create, "a world where all diseases are conquered and everyone can live a long and healthy life," is consistent with "a society where every member leads a meaningful and fulfilling life." PRIMe was established as one of the WPI centers to foster the university's mid-term goals, mid-term plans, and the OU Master Plan 2027. In addition, as one of the world's leading research centers in new academic fields, the University will provide full support for the necessary institutional reforms and the development of research implementation systems to realize a world class research environment and to ensure that such activities can be sustained even

after this support ends.

Facility Support

Regarding facilities, the University has already raised the same amount of funds through the 1st National University Corporation Bond (Sustainability Bond, nicknamed "Osaka University Social Creation Bonds that Foster a Purpose of Life") (bond amount: 30 billion yen) on April 28, 2022. The fund raised by the bond issue will be used to implement various projects under the "OU Master Plan 2027" with the aim of realizing "a society where each member leads a meaningful and fulfilling life". A new research building (Suita Agora 2) with a total floor area of 8,800 m^2 is scheduled to be constructed by this fund in 2026 on the Suita Campus, where most of PRIMe's members conduct their research, bringing all members together in a truly under-one-roof environment. Until then, approximately 1,500 m^2 of space within the Graduate School of Medicine has been reserved for incoming external researchers.

Personnel Support

One tenured faculty post has been secured. In the future, we will increase university support for up to ten faculty positions.

Osaka University has been selected by the JST (Japan Science and Technology Agency) as a Support for Pioneering Research Initiated by the Next Generation (SPRING) support project. In this programme, PRIMe's doctoral students are supported in their challenging and interdisciplinary researches and in their development as researchers, while being encouraged to work in a variety of careers.

Financial Support

More than 700 million yen (about 4.64 million in US dollars) has been provided in FY2023 and will continue to be provided each of the following years to reinforce the management.

We plan to establish comprehensive collaboration agreements and joint research contracts with corporations. Such kind of model has provided a sustainable foundation for the operation of IFReC, which serves as a reference for PRIMe. Osaka University fully supports such initiatives.

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

5. Center's Response to Results of Last Year's Follow-up
* Transcribe the item from the "Actions required and recommendations" section in the site visit report and the Follow-up report, then note how the center has responded to them.
* If you have already provided this information, indicate where in the report.

Our responses to the Actions required and recommendations (1-7) are as follows.

(1) There is a strong need for PRIMe to clearly articulate and share a common vision/concept on biodigital twins among all its PIs. This requires intense discussions led by a "Steering committee", including the director and deputy directors, some young scientists and a medical ethics expert. The role of the steering committee would be to design a vision/concept of biodigital twins, formulate a strategic roadmap and flagship projects for the mid (within 5 years) and long terms (10 years or more).

Response to (1).

First of all, **the center Director had one-to one meeting with PRIMe PIs** to reconcile opinions and newly established **Research Steering Committee** consisting of the Center Director, Deputy Directors, and Core Researchers (Figure 10 and also refer to section 1-2). This committee has so far managed to hold seven times Progress Report Meeting (2hr/group) to share common concept and basic strategy to create Patient bio-Digital Twins [refer to section 1-1 and section 5, Response to 4)] and has been developing augment for strategic roadmap and flagship projects (mid and long terms). We plan to include ELSI researchers into this committee in the near future

(2) Deputy director Okada, who is familiar with both wet and dry research, should be put in a position where she can take more leadership in facilitating discussions and can guide the process of interdisciplinary fusion more actively. Hiring an additional PI who has the expertise and background that would help to develop biodigital twins is as an option for enhancing the center's vision and possibly attracting more international collaborations.

Figure 10.
Research Steering Committee and Leadership in Fusion

Response to (2).

Unfortunately, Deputy Director Okada (M) will resign as both Deputy Director and PI of PRIMe from April 2024 due to convoluted reasons. However, Okada (M) will continue to constantly support PRIMe as an official Science Advisor. We appointed Nagahara to take charge of Deputy Director position and the chief of Big data and computing core facility. We additionally recruited Yasuhiro Watashiba to manage PRIMe data storage in this core facility. After thorough discussions with Okada (M), to take leadership in facilitating discussions and guide the process of interdisciplinary research more effectively, we established a system (Figure 10) which is not managed through one person but through the cooperation with **Research Steering Committee, Matching coordinator** (URA, Imamura) who can contact with both dry and wet researchers frequently and receive requests from researchers following coordinate matching discussion, and **Science Advisor** [Okada (M)]. We additionally recruited Imad Abugessaisa and Ayako Yachie who have strong background that help to develop bio-Digital Twins and further established **bio-Digital Twin Creation Unit** (Nagahara, Sakurada, Yachie (A), and Abugessaisa) to process data from micro to macro and strengthen to build up Patient bio-Digital Twins (Figure 10). Since Yachie (A) is also belonging to Systems Biology Institute (SBI), we are planning to form a partnership with SBI as one of PRIMe Satellites. Importantly, Okada (M) is still able to support PRIMe to attract international collaborators as a Science Advisor.

(3) There is urgent need for a dialog between PIs doing experiments, including organoid and clinical studies, conducting mathematical analyses, and developing advanced technologies to see how their sciences can be integrated. In particular, integration of the surrogate model (data-driven model) for clinical data, and of the causal model (hypothesis-driven model) for human organoids should be designed and implemented.

Response to (3).

To induce active and frequent dialogues between PRIMe PIs for integration of their sciences, we implemented several direct activities as follows:
· **One to one meeting of Center Director with PRIMe PIs**
· **Progress Report Meeting** and **PRIMe Retreat** as described detail in section 1-2
· **PRIMe Seminar Series/Omnibus Seminar Series** followed by **Networking** (14 times in this fiscal year) as described in section 1-2
· **Happy Hour** and **Interdisciplinary Lecture** (once a month) as described in section 1-2
· **2nd WPI-PRIMe International Symposium** "Frontiers in Human Metaverse Medicine" as described in Appendix 6.

As a result of these dialogues, the integration of the surrogate model (data-driven model) for clinical data, and of the causal model (hypothesis-driven model) for human organoids was designed and described in section 1-1 and section 5, Response to (4) below. Importantly, based on these

dialogues, 18 collaborative research works in PRIMe have been initiated in this fiscal year. We are also planning to hold meetings including basic researchers in PRIMe and clinical doctors in Osaka University Hospital for interactive communications and mutual understanding.

(4) Standardized protocols for experimental and mathematical analyses should be set for cohesive integration into biodigital twins. Hiring a specialist researcher who can lead this effort and manage the resulting data should be considered.

Response to (4).

As suggested, we hired Yachie (A) and Abugessaisa as a specialist researcher. We also hired Watashiba (effort 100% work for PRIMe) specifically to manage the resulting data collaborating with Department of Medical Informatics and Cybermedia Center in Osaka University. Standardized protocols for experimental (iPSC generation) and mathematical analyses have been set.
*But for the sake of intellectual property protection, we will keep them undisclosed (Jan.17, 2025).

(5) PRIMe is strongly recommended to systematically accelerate the recruitment of foreign and female researchers beyond the WPI requirements.

Response to (5).

As described in Section 2-1, although we have maintained a policy of prioritizing the recruitment of female and foreign researchers for faculty positions, the representation of female and foreigner still remains insufficient. To address this issue, we are planning to open positions to female only. We also try to openly recruit candidates through international partner institutions to attract qualified individuals who contribute to increase foreign researchers and desired gender balance ratio. In addition, to attract the world's top young researchers, we have implemented the following improvement activities to elevate the capabilities of young researchers and enhance their expertise level. 1) Innovative salary structure that exceeds the university regulations. 2) Special grants for young researchers providing research funds to support their interdisciplinary projects. 3) Next Generation Working Group catalyzing interdisciplinary research among young researchers. We have newly established an **Equity-Diversity-Inclusion (EDI) committee** and are constantly discussing these matters and soliciting ideas.

(6) Research space allocation should mix "wet" researchers (experimentalists) and "dry" researchers (theorists) on the same floor for better vision sharing and activity fusion. This should be taken into account in the design of the new building.

Response to (6).

The "Suita Agora 2" research building (8,800 m^2), to be built by 2026 using the university bond will be secured mainly for PRIMe and mixing of research space allocation for "wet" and "dry" researchers on the same floor will be taken into account in the design of the new building. Moreover, the building will include an open collaborative space where center members can interact, discuss, and meet new people in a relaxed atmosphere.

Before establishing the actual under-one-roof condition, as shown in Figure 11, we renovated and rearranged allocation of "wet" and "dry" researchers in CoMIT and Techno-Alliance Complex building in Suita Campus for better vision sharing and activity fusion.

Figure 11. Renovation and allocation of research space

(7) The host university should clarify how it will make administrative staff positions permanent after WPI funding ends.

Response to (7).

Osaka University has an organization called the International Advanced Research Institute, to which belongs three research centers: two WPI centers (IFReC and PRIMe) and the Center for Quantum Information and Quantum Biology (QIQB). Currently, each of the three centers has its own independent administrative structure, but we believe that the integration of the administrative divisions into one as the World-Leading Research Organization will make it possible to treat them as an administrative organization of the university and ensure its permanence.

At present, the four administrative staff members in PRIMe are not funded by the WPI grant but by the university budget as permanent positions. In the near future, Osaka University would like to support other staff members, such as URAs, regardless of WPI funding.

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

1. Refereed Papers
- List only the Center's papers published in 2023. (Note: The list should be for the calendar year, not the fiscal year.)

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

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

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

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

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

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

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

A. WPI papers
[Original articles]

1.   Murakami, K; Hamazaki, N; Hamada, N; Nagamatsu, G; Okamoto, I; Ohta, H; Nosaka, Y; Ishikura, Y; Kitajima, TS; Semba, Y; Kunisaki, Y; Arai, F; Akashi, K; Saitou, M; Kato, K; Hayashi, K. Generation of functional oocytes from male mice in vitro. ***Nature*** *615*. (2023) DOI 10.1038/s41586-023-05834-x

2.   Nemoto, T; Ocari, T; Planul, A; Tekinsoy, M; Zin, EA; Dalkara, D; Ferrari, U. ACIDES: on-line monitoring of forward genetic screens for protein engineering. ***Nature Communications*** *14*. (2023) DOI 10.1038/s41467-023-43967-9

3.   Ogawa, Y; Lu, YG; Kiyozumi, D; Chang, HY; Ikawa, M. CRISPR/Cas9-mediated genome editing reveals seven testis-enriched transmembrane glycoproteins dispensable for male fertility in mice. ***Andrology***. (2023) DOI 10.1111/andr.13564

4.   Abe, K; Yamashita, A; Morioka, M; Horike, N; Takei, Y; Koyamatsu, S; Okita, K; Matsuda, S; Tsumaki, N. Engraftment of allogeneic iPS cell-derived cartilage organoid in a primate model of articular cartilage

defect. **Nature Communications** *14*. (2023) DOI 10.1038/s41467-023-36408-0

5. Kamioka, J; Sasaki, K; Baba, K; Tanaka, T; Teranishi, Y; Ogasawara, T; Inoie, M; Hata, KI; Nishida, K; Kino-oka, M. Agent-based approach for elucidating the release from collective arrest of cell motion in corneal epithelial cell sheet. **Journal of Bioscience and Bioengineering** *136*: 477-486. (2023) DOI 10.1016/j.jbiosc.2023.10.003

6. Tomofuji, Y; Kishikawa, T; Sonehara, K; Maeda, Y; Ogawa, K; Kawabata, S; Oguro-Igashira, E; Okuno, T; Nii, T; Kinoshita, M, et al. Analysis of gut microbiome, host genetics, and plasma metabolites reveals gut microbiome-host interactions in the Japanese population. **Cell Reports** *42*. (2023) DOI 10.1016/j.celrep.2023.113324

7. Al Reza, H; Farooqui, Z; Al Reza, A; Conroy, C; Iwasawa, K; Ogura, Y; Okita, K; Osafune, K; Takebe, T. Synthetic augmentation of bilirubin metabolism in human pluripotent stem cell-derived liver organoids. **Stem Cell Reports** *18*: 2071-2083. (2023) DOI 10.1016/j.stemcr.2023.09.006

8. Fujiwara, Y; Miki, K; Deguchi, K; Naka, Y; Sasaki, M; Sakoda, A; Narita, M; Imaichi, S; Sugo, T; Funakoshi, S; Nishimoto, T; Imahashi, K; Yoshida, Y. ERRγ agonist under mechanical stretching manifests hypertrophic cardiomyopathy phenotypes of engineered cardiac tissue through maturation. **Stem Cell Reports** *18*: 2108-2122. (2023) DOI 10.1016/j.stemcr.2023.09.003

9. Hino, T; Omura, SN; Nakagawa, R; Togashi, T; Takeda, SN; Hiramoto, T; Tasaka, S; Hirano, H; Tokuyama, T; Uosaki, H; Ishiguro, S; Kagieva, M; Yamano, H; Ozaki, Y; Motooka, D; et al., An AsCas12f-based compact genome-editing tool derived by deep mutational scanning and structural analysis. **Cell** *186*. (2023) DOI 10.1016/j.cell.2023.08.031

10. Tanaka, H; Okada, Y; Nakayamada, S; Miyazaki, Y; Sonehara, K; Namba, S; Honda, S; Shirai, Y; Yamamoto, K; Kubo, S; Ikari, K; Harigai, M; Sonomoto, K; Tanaka, Y. Extracting immunological and clinical heterogeneity across autoimmune rheumatic diseases by cohort-wide immunophenotyping. **Annals of the Rheumatic Diseases** *83*: 242-252. (2024) DOI 10.1136/ard-2023-224537

11. Greenstreet, L; Afanassiev, A; Kijima, Y; Heitz, M; Ishiguro, S; King, S; Yachie, N; Schiebinger, G. DNA-GPS: A theoretical framework for optics-free spatial genomics and synthesis of current methods. **Cell Systems** *14*. (2023) DOI 10.1016/j.cels.2023.08.005

12. Kawakami, E; Saiki, N; Yoneyama, Y; Moriya, C; Maezawa, M; Kawamura, S; Kinebuchi, A; Kono, T; Funata, M; Sakoda, A; Kondo, S; Ebihara, T; Matsumoto, H; Togami, Y; Ogura, H, et al., Complement factor D targeting protects endotheliopathy in organoid and monkey models of COVID-19. **Cell Stem Cell** *30*. (2023) DOI 10.1016/j.stem.2023.09.001

13. Imoto, H; Rauch, N; Neve, AJ; Khorsand, F; Kreileder, M; Alexopoulos, LG; Rauch, J; Okada, M; Kholodenko, BN; Rukhlenko, OS. A Combination of Conformation-Specific RAF Inhibitors Overcome Drug Resistance Brought about by RAF Overexpression. **Biomolecules** *13*. (2023) DOI 10.3390/biom13081212

14. Matsuzaki, T; Kawano, Y; Horikiri, M; Shimokawa, Y; Yamazaki, T; Okuma, N; Koike, H; Kimura, M; Kawamura, R; Yoneyama, Y; Furuichi, Y; Hakuno, F; Takahashi, SI; Nakabayashi, S; Okamoto, S; Nakauchi, H; Taniguchi, H; Takebe, T; Yoshikawa, HY. Preparation of mechanically patterned hydrogels for controlling the self-condensation of cells. **Star Protocols** *4*. (2023) DOI 10.1016/j.xpro.2023.102471

15. Miyanishi, K; Sugiki, T; Matsui, T; Ozawa, R; Hatanaka, Y; Enozawa, H; Nakamura, Y; Murata, T; Kagawa, A; Morita, Y; Fujiwara, T; Kitagawa, M; Negoro, M. Protein-Ligand Interaction Analyses with Nuclear Magnetic Resonance Spectroscopy Enhanced by Dissolution Triplet Dynamic Nuclear Polarization. **Journal of Physical Chemistry Letters** *14*: 6241-6247. (2023) DOI 10.1021/acs.jpclett.3c01002

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

- List up to 10 main presentations during FY 2023 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
Nov. 17, 2023	Takanori Takebe	Organoid & tissue-engineered graft in LT	Asian Transplantation Week 2023, Seoul, Korea
Oct. 7, 2023	Ai Shinobu	Extensive Sampling of Protein-inhibitor Binding Landscapes using Molecular Dynamics Simulations	The 6th International Conference on Molecular Simulation (ICMS) 2023, Taipei, Taiwan
Sep. 19, 2023	Takanori Takebe	Stem cell technology for studying hepatology and hepatitis viruses	2023 International HBV Meeting, Kobe, Japan
Aug. 31, 2023	Mariko Okada	A computational platform for Patient-specific Modeling	OKO International Symposium 2023 Mathematical Biology from Genes to Cells to Humans, Kyoto, Japan
Jun. 19, 2023	Nozomu Yachie	Biotechnologies to tackle stem cell and developmental biology questions	The 16th Annual Meeting of the Japanese Society for Epigenetics, Tokyo, Japan
Jun. 16, 2023	Takanori Takebe	ISSCR Outstanding Young Investigator Award Lecture: Understanding Interconnectedness in Liver Development and Disease	International Society for Stem Cell Research (ISSCR) Annual Meeting, Boston, USA
Jun. 8, 2023	Nozomu Yachie	HD Video Recorder of the Cell	8th Annual Meeting of the Japanese Society for Genome Editing, Tokyo, Japan
Jun. 5, 2023	Mariko Okada	Encoding and Decoding of NF-κB Nuclear Dynamics and Cell Fate Regulation	The Uehara International Symposium 2023: Tokyo, Japan
May 17, 2023	Mariko Okada	Encoding and decoding of NFBk transcriptional regulation	Cell Signalling and its Therapeutic Implications (CSTI-2023), Victoria, Australia
May 13, 2023	Yukinori Okada	How to utilize genomics in dermatology	1st International Societies for Investigative Dermatology Meeting (ISID2023), Tokyo, Japan

3. Major Awards

- List up to 10 main awards received during FY 2023 in order from the most recent.
- For each, write the date issued, the recipient's name, and the name of award.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
Mar. 28, 2024	Yukinori Okada	Ishidate-Ueno Award 2023, Chugai Foundation for Innovative Drug Discovery
Mar. 21, 2024	Takanori Takebe	Society Award 2024 in Basic Research, The Japanese Society for Regenerative Medicine
Mar. 15, 2024	Makoto Negoro (joint research group: Fujitsu Limited, RIKEN, National Institute of Advanced Industrial Science and Technology, National Institute of Information and Communications Technology, Osaka University, Nippon Telegraph and Telephone Corporation)	Prime Minister's Award of the 53rd Japan Industrial Technology Awards, The Nikkan Kogyo Shimbun Ltd.
Feb. 6, 2024	Takanori Takebe	2024 Vilcek Prize for Creative Promise in Biomedical Science, The Vilcek Foundation
Dec. 20, 2023	Nozomu Yachie	The 20th JSPS Prize, Japan Society for the Promotion of Science
Dec. 14, 2023	Hideto Mori	The 40th Inoue Research Award for Young Scientists, Inoue Foundation for Science
Dec. 13, 2023	Katsuhiko Hayashi	Nature's 10, Nature
Nov. 1, 2023	Kohji Nishida	The 2023 Medical Award of the Japan Medical Association, Japan Medical Association
Sep. 29, 2023	Kensuke Goto	The Bronze Award of the 11th Wakamoto Conference of Advanced Medicine of Ophthalmology; WACAMOTO, Wakamoto Pharmaceutical Co., Ltd.
May. 31, 2023	Yukinori Okada	The EULAR 2023 Abstract Award in Basic Science, The European Alliance of Associations for Rheumatology

Appendix 2 FY 2023 List of Principal Investigators

NOTE:

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

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

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

		<Results at the end of FY2023>					Principal Investigators Total: 19
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 Kohji Nishida	61	Professor, Graduate School of Medicine, Osaka University	MD, PhD Stem cell biology, Regenerative medicine, Ophthalmology	90	Nov.11,2022	usually stays at the center	
Deputy-Director Takanori Takebe	37	Professor, Center for Stem Cell and Organoid Research and Medicine, Director for Commercial Innovation, Cincinnati Children's Hospital Medical Center, Graduate School of Medicine, Osaka University	MD, PhD Organoid medicine, Organ development, Regeneration	30	Nov.11,2022	stays at the center about 7 times a month	
Deputy-director Mariko Okada	61	Professor, Institute for Protein Research, Osaka Univeristy	PhD Systems biology	45	Nov.11,2022	stays at the center about 10 times a month	
Katsuhiko Hayashi	52	Professor, Graduate School of Medicine, Osaka University	PhD Reproductive genetics, Ovarian organoids	70	Nov.11,2022	stays at the center about 15 times a month	
Shigeru Miyagawa	56	Professor, Graduate School of Medicine, Osaka University	MD, PhD Cardiovascular surgery, Regenerative medicine, Medical AI	80	Nov.11,2022	usually stays at the center	
Noriyuki Tsumaki	59	Professor, Graduate School of Medicine, Osaka University	MD, PhD cartilage, Regenerative medicine	70	Nov.11,2022	stays at the center about 15 times a month	
Vivian Hwa	65	Professor, Premium Research Institute for Human Metaverse Medicine, Osaka University	PhD Growth deficiency disease, Genetics	100	Nov.11,2022	usually stays at the center (work at home)	
Yukinori Okada	43	Professor, Graduate School of Medicine, Osaka University	MD, PhD Bioinformatics, Machine learning, Omics analysis	50	Nov.11,2022	stays at the center about 10 times a month	

Name	Age	Position	Degree / Field	%	Date	Stay at center	
Hajime Nagahara	50	Professor, Institute for Datability Science, Osaka Univerisity	PhD Computer vision, machine learning	70	Nov.11,2022	stays at the center about 15 times a month	
<u>Nozomu Yachie</u>	43	Associate Professor, School of Biomedical Engineering (SBME), The University of British Columbia	PhD Synthetic biology, Information science	15	Nov.11,2022	working at home twice a month	
Takahiro Nemoto	37	Associate Professor, Premium Research Institute for Human Metaverse Medicine, Osaka University	PhD Data science, Algorithm v development	100	Nov.11,2022	usually stays at the center	
Ai Shinobu	42	Associate Professor, Premium Research Institute for Human Metaverse Medicine, Osaka University	PhD Molecular dynamics simulation	100	Nov.11,2022	usually stays at the center	
Makoto Negoro	41	Associate Professor, Center for Quantum Information and Quantum Biology/Osaka University	PhD Magnetic resonance, Quantum computer	35	Nov.11,2022	stays at the center about 7 times a month	
Yoshie Harada	64	Professor, Institute for Protein Research, Osaka Univeristy	PhD Quantum sensing, Live imaging	70	Nov.11,2022	stays at the center about 15 times a month	
Astuo Kishimoto	53	Director, ELSI Center, Osaka University	PhD ELSI, Risk assessment	30	Nov.11,2022	stays at the center about 7 times a month	
<u>Elisa Domínguez-Hüttinger</u>	39	Research Associate, National Autonomous University of Mexico	PhD Bioengineering	8	Nov.11,2022	joins event or videoconference from another institution occasionally	
Hideo Yokota	55	Team Leader, Advanced Photonics Center, Riken	PhD Image Processing	20	Nov.11,2022	joins event or videoconference from another institution occasionally	
Shingo Tsukada	58	NTT Fellow, NTT Bio-Medical Informatics Research Center, NTT Basic Research Laboratories	PhD Bio-digital twin, Bio-Medical Informatics&ICT	20	Nov.11,2022	joins event or videoconference from another institution occasionally	
Kunio Kashino	56	Senior Distingished Researcher, NTT Bio-Medical Informatics Research Center, NTT Basic Research Laboratories	PhD Bio-digital twin, Bio-Medical Informatics&ICT	20	Nov.11,2022	joins event or videoconference from another institution occasionally	

*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
N/A				

Appendix 2a　Biographical Sketch of a New Principal Investigator
(within 3 pages per person)

Name (Age)

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

Academic degree and specialty

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

Research and education history

Achievements and highlights of past research activities

Achievements

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

　a) Recipient of international awards

　b) Member of a scholarly academy in a major country

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

　d) Editor of an international academic journal

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

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

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

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

Appendix 3-1 FY 2023 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions
1-1. Number of researchers in the "core" established within the host institution
- Regarding the number of researchers at the Center, fill in the table in Appendix 3-1a.

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

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
RIKEN Center	Hideo Yokota	
NTT	Kunio Kashino Shingo Tsukada	
The University of British Columbia	Nozomu Yachie	
National Autonomous University of Mexico	Elisa Domínguez-Hüttinger	

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
Systems Biology Ireland at University College Dublin		
Institut Curie		
Cincinnati Children's Hospital Medical Center		
Department of Psychiatry and Behavioral Sciences at Stanford University		

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

FY 2023: 1 meetings	
Major examples (meeting titles and places held)	Number of participants
WPI-PRIMe International Symposium: Frontiers in Human Metaverse Medicine At Saji Keizo Memorial Hall, Osaka University Nakanoshima Center On February 29th - March 1, 2024	From domestic institutions: 183 From overseas institutions: 28

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).

Management and Support System of the Center

Director :	Kohji Nishida
Deputy Director :	Takanori Takebe, Mariko Okada
Administrative Director :	Takefumi Doi
PIs :	Katsuhiko Hayashi, Vivian Hwa, Shigeru Miyagawa, Noriyuki Tsumaki, Hajime Nagahara, Nozomu Yachie, Yoshie Harada, Makoto Negoro, Shingo Tsukada, Takahiro Nemoto, Yukinori Okada, Kunio Kashino, Ai Shinobu, Hideo Yokota, Astuo Kishimoto, Elisa Domínguez-Hüttinger
Research Support Staff (URAs) :	Maki Tani, Ryu Imamura, Bidadi Haniyeh, Cui Chenlu, Takako Igi
Administrative Staff :	Shingo Murakami, Hiroko Umeda, Naohisa Kido, Aya Hirono, Itsuro Takami, Satomi Utsunomiya, Tomoko Tsuchida, Saori Hayakawa, Tomoko Takahashi, Emi Maeda, Hisano Nakajima, Reiko Tanaka

(Name list as of March 31, 2024)

In order to facilitate the smooth operation of the center, the Steering Committee was established as a forum for discussions on research plans, basic policies for administration, PI personnel matters, and important matters related to administration. In addition, the Representative Assembly was established to deliberate on faculty appointments, annual plans, and other matters. Furthermore, by holding Executive Committee with the delegates, the Planning Office, and administrative staff as members, the center is structured to be managed through collaboration between faculty and staff.

4. Campus Map

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

This map shows the location of our PIs' laboratories on Osaka University campus.

5. Securing external research funding*

External research funding secured in FY2023

 Total: 693,447,104 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.

[Acquired large-scale research grants (over 35,000,000yen per year)]

Organization	Fund Name	PI	Funding amount (yen)
AMED	Medical research and development promotion grants	Kohji Nishida	59,500,000
AMED	R&D Promotion for National Issues	Kohji Nishida	47,000,000
JSPS	Grant-in-Aid for Transformative Research Areas (A)	Katsuhiko Hayashi	37,400,000
AMED	Platform Program for Promotion of Genome Medicine	Yukinori Okada	197,850,000
JST	Moonshot Research & Development Program	Yukinori Okada	60,000,000
AMED	Translational research program	Noriyuki Tsumaki	69,000,000
AMED	Medical research and development promotion grants	Shigeru Miyagawa	43,000,000
JST	CREST (Strategic Basic Research Programs)	Nozomu Yachie	40,000,000

Appendix 3-1a FY 2023 Records of Center Activities
Researchers and other center staff
Number of researchers and other center staff

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

a) Principal Investigators

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

(number of persons)

	At the beginning of project	At the end of FY 2023	Final goal (Date: November, 2027)
Researchers from within the host institution	11	13	13
Researchers invited from overseas	4	3	4
Researchers invited from other Japanese institutions	5	3	3
Total principal investigators	20	19	20

b) Total members

		At the beginning of project		At the end of FY 2023		Final goal (Date: November, 2027)	
		Number of persons	%	Number of persons	%	Number of persons	%
Researchers		20		40		61	
	Overseas researchers	3	15	9	23	19	31
	Female researchers	5	25	8	20	18	30
Principal investigators		20		19		20	
	Overseas PIs	3	15	2	11	4	20
	Female PIs	5	25	5	26	6	30
Other researchers		0		19		36	
	Overseas researchers	0	###	5	26	11	31
	Female researchers	0	###	3	16	10	28
Postdocs		0		2		5	
	Overseas postdocs	0	###	2	100	4	80
	Female postdocs	0	###	0	0	2	40
Research support staffs		7		7		9	
Administrative staffs		3		15		17	
Total number of people who form the "core" of the research center		30		62		87	

	At the beginning of project		At the end of FY 2023		Final goal (Date: November, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	0		11		21	
Employed	0	-	0	0.0	5	23.8

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

Appendix 3-2　Project Expenditures

1) Overall project funding

* In the "Total costs" column, enter the total amount of funding required to implement the project, without dividing it into funding sources.

* In the "Amount covered by WPI funding" column, enter the amount covered by WPI within the total amount.

* In the "Personnel," "Project activities," "Travel," and "Equipment" blocks, the items of the "Details" column may be changed to coincide with the project's actual content.

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center director and administrative director	30	16
	Principal investigators (no. of persons):16	102	31
	Other researchers (no. of persons): 24	95	85
	Research support staff (no. of persons):5	36	36
	Administrative staff (no. of persons):5	62	37
	Subtotal	325	205
Project activities	Research startup cost (no. of persons):4	59	59
	Preperation costs for new laboragories and iPS Cell Core Facility	71	71
	Rental fees for facilities / Cost of utilities	94	29
	International symposium related cost : (no. of symposiums):1	11	11
	Public relations or advertising cost	7	7
	Personnel Dispatch cost	6	6
	Costs of consumable for office and others	18	18
	Subtotal	266	201
Travel	Domestic travel costs	8	7
	Overseas travel costs	19	18
	Travel cost for scientists on transfer	4	4
	(no. of domestic scientists):8		
	(no. of overseas scientists):2		
	Subtotal	31	29
Equipment	Basic equipment	222	222
	Equipment for iPS Cell Core Facilities	40	40
	Equipment for Offices	3	3
	Subtotal	265	265
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. [1]	12	0
	KAKENHI	58	0
	Commissioned research projects, etc.	602	0
	Joint research projects	3	0
	Ohers (donations, etc.)	30	0
	Subtotal	705	0
Total		1592	700

Costs (Million yens)

WPI grant in FY 2023	700
Costs of establishing and maintaining facilities	27
Establishing new facilities	0
Repairing facilities	
CoMIT Bldg, 767㎡	15
Techno Alliance Bldg, 770㎡	2
Center for Medical Research and Education Building, 423㎡	10
Costs of equipment procured	309
Equipments for PI Laboratory	44
Ultra Low Temperature Freezer	
Cooling centrifuge(2)	
Autoclave(4)	
Laboratory table(7) etc.	
Basic equipments	222
Experimental animal anaesthesia equipment(2)	
PCR System(2)	
Microscope(3)	
Compute server(2) etc.	
Equipment for iPS Cell Core Facilities	40
Clean bench(2)	
CO2 incubator(2)	
Microscope digital camera(2) etc.	
Equipment for Offices	3
Workstation	
Projector	
Data storage	

*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.

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):5		
	Other researchers (no. of persons):2		
	Research support staff (no. of persons):0		
	Administrative staff (no. of persons):0		
	Subtotal	0	0
Project activities	Subtotal		
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal		
Total		0	0

*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

Osaka University -2   Premium Research Institute for Human Metaverse Medicine

Appendix 4 FY 2023 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2023 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2024 and not described in Appendix 1.

Overseas Satellite 1   The University of British Columbia (Total: 1 papers)

1)(9)Hino, T; Omura, SN; Nakagawa, R; Togashi, T; Takeda, SN; Hiramoto, T; Tasaka, S; Hirano, H; Tokuyama, T; Uosaki, H; Ishiguro, S; Kagieva, M; Yamano, H; Ozaki, Y; Motooka, D; Mori, H; Kirita, Y; Kise, Y; Itoh, Y; Matoba, S; Aburatani, H; *Yachie, N*; Karvelis, T; Siksnys, V; Ohmori, T; Hoshino, A; Nureki, O. An AsCas12f-based compact genome-editing tool derived by deep mutational scanning and structural analysis. Cell ;186(22):4920-4935. (2023) DOI 10.1016/j.cell.2023.08.031

Overseas Satellite 2   National Autonomous University of Mexico (Total: 0 papers)

2. Status of Researcher Exchanges
- Using the below tables, indicate the number and length of researcher exchanges in FY 2023. Enter by institution and length of exchange.
- Write the number of principal investigator visits in the top of each space and the number of other researchers in the bottom.

Overseas Satellite 1: The University of British Columbia

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023					0
	2				2

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	3	3			6
	4				4

Overseas Satellite 2: National Autonomous University of Mexico

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023					0
					0

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023		2			2
					0

Appendix 5　FY 2023 Visit Records of Researchers from Abroad

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

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

Total:　15

	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	Sergiu P. Pasca	42	Professor, Psychiatry and Behavioral Sciences - Sleep Medicine, Stanford University	USA	Medical Doctor MD, Ph.D Neuroscience, Biology, Stem Cell	ISSCR Momentum Award, International Society for Stem Cell Research (2024) Doctor Honoris Causa (D.H.C.), Hatieganu Medical School (2023) Sumitomo/Sunovion Prize, International College of Neuropsychopharmacology (2023) Knight of the Order of Merit, The Chancery of Orders (2023)https://profiles.stanford.edu/sergiu-pasca https://www.pascalab.org/	2023/6/27-29 (3 days)	・Lecture at PRIMe Omnibus Seminar ・Research Meeting
2	Nika Shakiba	35	Assistant Professor,School of Biomedical Engineering, University of British Columbia	CANADA	Stem Cell Bioengineering Ph. D.	Micheal Smith Health Research BC Scholar Award 2021-2026 Allen Distinguished Investigator 2022-present Structured Quartet Research Ensemble 2020-2021 Posddoctoral Fellowship 2018-2020 https://bme.ubc.ca/?directory=nika-shakiba	2023/7/18-31 (14 days) 2024/2/28-3/4 (6 days) Total：20 days	・Participation in the 56th Japanese Society of Developmental Biology ・Lecture at PRIMe Omnibus Seminar ・Participation in JST PRESTO "Multicellular" program International Workshop ・Participation in WPI-PRIMe International Symposium ・Participation in WPI-PRIMe Retreat ・Research Meeting
3	Mo Reza Ebrahimkhani	45	Associate Professor, Bioengineering, University of Pittsburgh	USA	physician scientists (M.D.)	European Association for Study of Liver Sheila Sherlock recipient of several research awards including NIH RO1s, Mayo Clinic accelerated regenerative medicine award, the New Investigator Award from Arizona Biomedical Research Council, NSF Recode program award and Charles E Kaufman Foundation initiative award. fellowshiphttps://www.engineering.pitt.edu/people/faculty/mo-reza-ebrahimkhani/ https://www.ebrahimkhanilab.bio/members	2023/7/19-31 (13 days)	・Participation in the 56th Japanese Society of Developmental Biology ・Lecture at PRIMe Omnibus Seminar ・Participation in JST PRESTO "Multicellular" program International Workshop ・Research Meeting
4	Schiebinger Geoffrey Robert	35	Assistant Professor, Department of Mathematics, University of British Columbia	CANADA	Statistics, PhD	Maud Menten New Principal Investigator Prize in Genetics, 2021. CIHR Project Grant, 2021. New Frontiers In Research Exploration Grant, 2020. NSERC Discovery Grant, 2020.https://personal.math.ubc.ca/~geoff/	2023/8/20-24 (5 days) 2024/2/28-3/4 (6 days) Total：11 days	・Lecture at PRIMe Seminar Series ・Participation in WPI-PRIMe International Symposium ・Participation in WPI-PRIMe Retreat

5	Boris Kholodenko	67	Professor, Systems Biology, University College Dublin	Ireland	Ph.D. in Biophysics	Royal Irish Academy Gold Medal for Natural Sciences, 2021. FEBS National Lecture, 2020. Royal Society of Chemistry Theophilus Redwood Award, 2019. Elected Member of Academia Europaea, 2018. FEBS Medal, 2016.https://people.ucd.ie/boris.kholodenko	2023/11/8 (1 day)	·Lecture at PRIMe Omnibus Seminar
6	Masahiro Morita	45	Assistant Professor, Department of Molecular Medicine and Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center at San Antonio	USA	PhD in Biochemistry and Biophysics	2022/12 45th Annual Meeting of MBSJ Travel Award, MBSJ, Chiba, Japan 2022/07 American Cancer Society Research Scholar Grant – ACS, USA 2022/06 Max and Minnie Tomerlin Voelcker Fund Research Project Grant – San Antonio, TX, USA 2022/03 CPRIT Individual Investigator Research Award – CPRIT, Austin, TX, USA https://barshopinstitute.uthscsa.edu/team-member/morita-masahiro/	2023/12/3-12/24 (22 days) 2024/2/27-3/3 (6 days) Total：28 days	·Lecture at PRIMe Omnibus Seminar ·Participation in WPI-PRIMe International Symposium ·Participation in WPI-PRIMe Retreat
7	Laurence Calzone	46	Research Engineer, Department of Computational Biology, Institut Curie	France	Ph.D Systems biology	None https://institut-curie.org/personne/laurence-calzone	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
8	Loic Thomas Chadoutaud	26	Ph.D student,Institut Curie, Department of Computational Biology	France	Ph.D student No specialty	None https://institut-curie.org/team/barillot	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
9	Thomas Edgar Walter	49	Director of Centre, Department of Computational Biology, Institut Curie	France	Ph.D in Computer Science	None https://thomaswalter.github.io/	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
10	Alexander Robert Bernier	28	Academic Associate, Center of Genomics and Policy,McGill University	Canada	Ph.D in Law	None https://computationalgenomics.ca/cgp-team/	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
11	Zhaoshi Jiang	50	CEO, BioMap US	USA	Ph.D in Genome Science	None https://www.biomap.com/en/team	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
12	Arvind Sivaramakrishna Ramanathan	51	Associate Professor, Institute for Stem Cell Science and Regenerative Medicine (in Stem)	India	Ph.D in Chemistry	None https://www.instem.res.in/faculty/arvind	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium

13	Megan Jayne Munsie	57	Group Leader, The University of Melbourne, Melbourne Medical School	Australia	Ph.D in Stem cell Biology	None http://stemcellsaustralia.edu.au https://pursuit.unimelb.edu.au/individuals/professor-megan-munsie	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
14	Johan Henri L Auwerx	65	Head of Laboratory, Laboratory of Integrative system Physiology, Swiss Federal Institute of Technology in Lausanne	Switzerland	MD and PhD in Molecular Endocrinology	Danone International Nutrition Award, the Oskar Minkowski Prize, the Morgagni Gold Medal, and the Marcel Benoist Prize. https://www.epfl.ch/labs/auwerx-lab/index-html/team/	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium
15	Emmanuel Maurice Louis Barillot	58	Research unit director, Institut Curie, Department of Computational Biology	France	PhD in biomathematics and genomics	None https://institut-curie.org/personne/emmanuel-barillot	2024/2/28-3/2 (4 days)	·Participation in WPI-PRIMe International Symposium

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- 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.

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NTT	Kunio Kashino Shingo Tsukada	
The University of British Columbia	Nozomu Yachie	
National Autonomous University of Mexico	Elisa Domínguez-Hüttinger	

< Partner institutions>

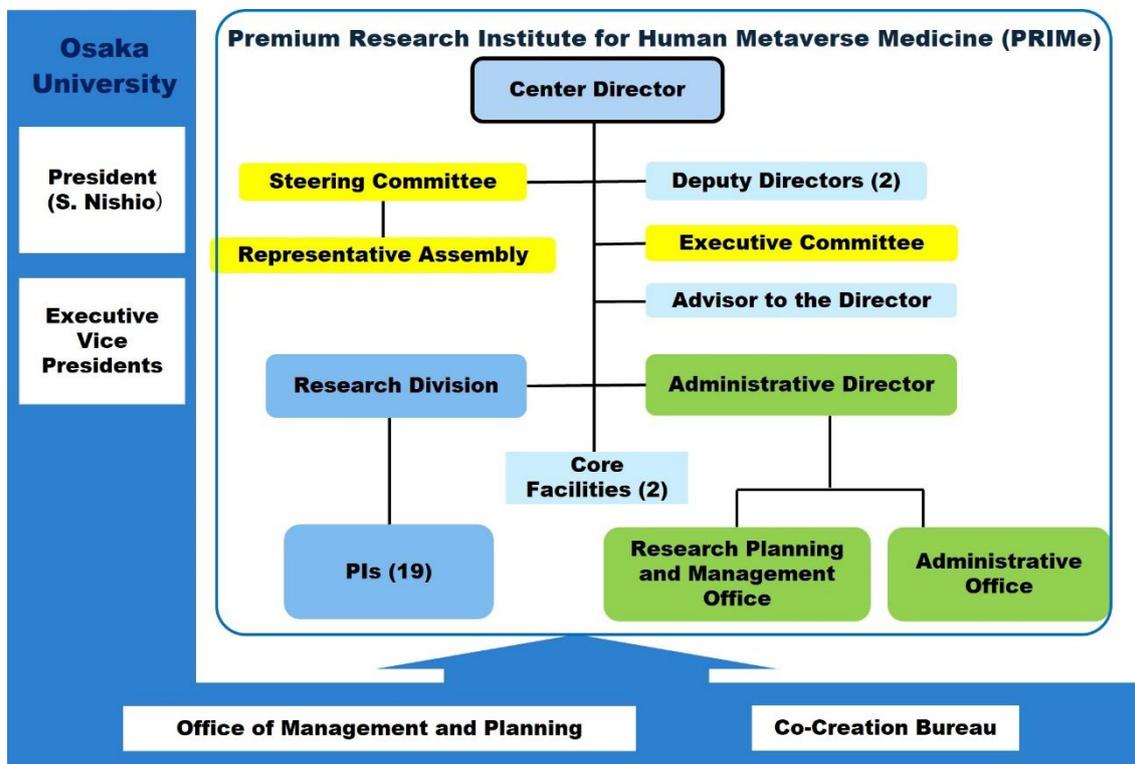| Institution name	Principal Investigator(s), if any	Notes
Systems Biology Ireland at University College Dublin		
Institut Curie		
Cincinnati Children's Hospital Medical Center		
Department of Psychiatry and Behavioral Sciences at Stanford University		

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

FY 2023: 1 meetings	
Major examples (meeting titles and places held)	Number of participants
WPI-PRIMe International Symposium: Frontiers in Human Metaverse Medicine At Saji Keizo Memorial Hall, Osaka University Nakanoshima Center On February 29th - March 1, 2024	From domestic institutions: 183 From overseas institutions: 28

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).
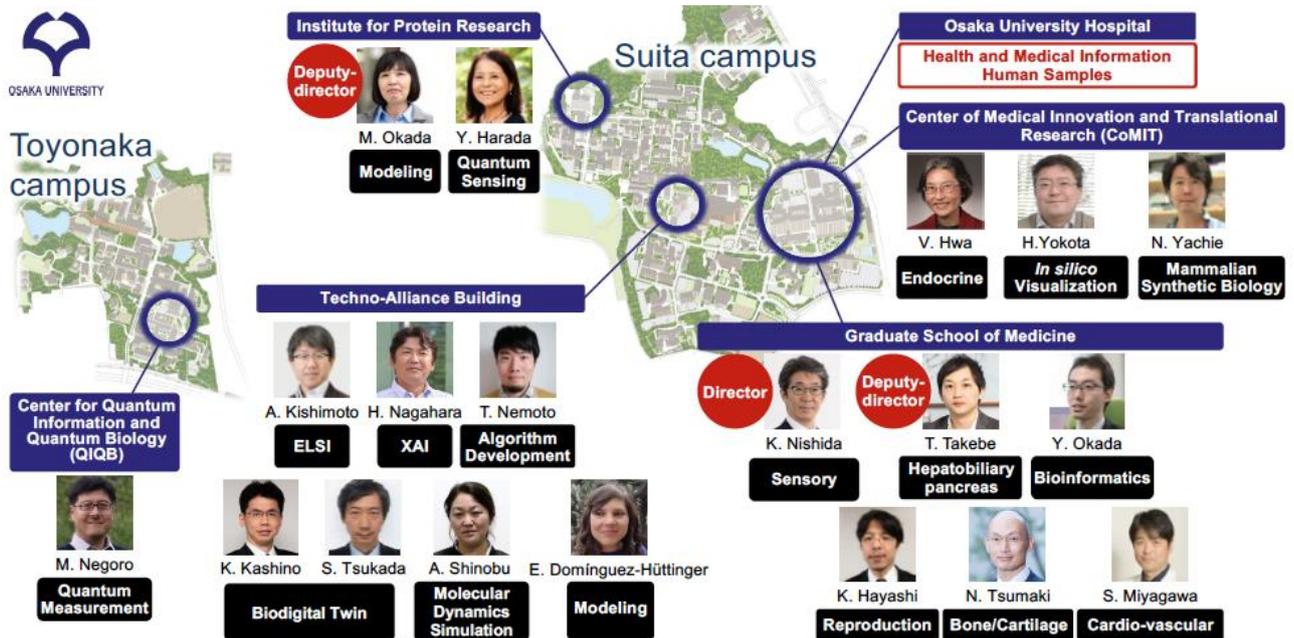

Management and Support System of the Center

Director :	Kohji Nishida
Deputy Director :	Takanori Takebe, Mariko Okada
Administrative Director :	Takefumi Doi
PIs :	Katsuhiko Hayashi, Vivian Hwa, Shigeru Miyagawa, Noriyuki Tsumaki, Hajime Nagahara, Nozomu Yachie, Yoshie Harada, Makoto Negoro, Shingo Tsukada, Takahiro Nemoto, Yukinori Okada, Kunio Kashino, Ai Shinobu, Hideo Yokota, Astuo Kishimoto, Elisa Domínguez-Hüttinger
Research Support Staff (URAs) :	Maki Tani, Ryu Imamura, Bidadi Haniyeh, Cui Chenlu, Takako Igi
Administrative Staff :	Shingo Murakami, Hiroko Umeda, Naohisa Kido, Aya Hirono, Itsuro Takami, Satomi Utsunomiya, Tomoko Tsuchida, Saori Hayakawa, Tomoko Takahashi, Emi Maeda, Hisano Nakajima, Reiko Tanaka

(Name list as of March 31, 2024)

In order to facilitate the smooth operation of the center, the Steering Committee was established as a forum for discussions on research plans, basic policies for administration, PI personnel matters, and important matters related to administration. In addition, the Representative Assembly was established to deliberate on faculty appointments, annual plans, and other matters. Furthermore, by holding Executive Committee with the delegates, the Planning Office, and administrative staff as members, the center is structured to be managed through collaboration between faculty and staff.

4.   Campus Map

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

This map shows the location of our PIs' laboratories on Osaka University campus.

5. Securing external research funding*

External research funding secured in FY2023

Total: 693,447,104 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.

[Acquired large-scale research grants (over 35,000,000yen per year)]

Organization	Fund Name	PI	Funding amount (yen)
AMED	Medical research and development promotion grants	Kohji Nishida	59,500,000
AMED	R&D Promotion for National Issues	Kohji Nishida	47,000,000
JSPS	Grant-in-Aid for Transformative Research Areas (A)	Katsuhiko Hayashi	37,400,000
AMED	Platform Program for Promotion of Genome Medicine	Yukinori Okada	197,850,000
JST	Moonshot Research & Development Program	Yukinori Okada	60,000,000
AMED	Translational research program	Noriyuki Tsumaki	69,000,000
AMED	Medical research and development promotion grants	Shigeru Miyagawa	43,000,000
JST	CREST (Strategic Basic Research Programs)	Nozomu Yachie	40,000,000

Appendix 7 FY 2023 List of Project's Media Coverage

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

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	Apr 3 2023	Newspaper 1	[Yomiuri Shimbun Apr 3] - Article referring to Prof. Hayashi's research result published in *Nature*
2	Apr 4 2023	Newspaper 1	[Mainichi Shimbun Apr 4] - Article of research result published in *Nature* by Prof. Hayashi
3	Apr 21 2023	Newspaper 1	[Mainichi Shimbun Apr 21] - Article about CHAT GPT by Prof. Kishimoto
4	Apr 25 2023	News website 1	[Nikkei Shimbun Digital Apr 25] - Article of research result published in *Nature Genetics* by Prof. Y. Okada
5	Apr 28 2023	News website 1	[DIAMOND Online Apr 28] - Article about CHAT GPT by Prof. Kishimoto
6	May 03 2023	News website 1	[NHK News May 3] - Article of research result published in *Nature* by Prof. Hayashi
7	May 16 2023	Newspaper 1	[Asahi Shimbun May 16] - Article about CHAT GPT by Prof. Kishimoto
8	May 22 2023	News website 1	[Asahi Shimbun Digital May 22] - Article about generative AI by Prof. Kishimoto
9	May 24 2023	Newspaper 2	[Asahi Shimbun, Nikkan Kogyo Shimbun May 24] - Article of research result by Prof. Y Okada
10	May 26 2023	Newspaper 1	[Nikkei Shimbun May 26] - Article of research result published in *Life Science Alliance* by Prof. Miyagawa
11	Jun 01 2023	Newspaper 1, News website 1	[Nikkan Kogyo Shimbun, Optronics Jun 1] - Article of research result published in *Life Science Alliance* by Prof. Miyagawa
12	Jun 05 2023	Newspaper 1	[Nikkan Kogyo Shimbun Jun 5] - Introduction about symposium of PRIMe by Director Nishida
13	Jun 18 2023	Newspaper 1	[Yomiuri Shimbun Jun 18] - Column about regenerative medicine by Prof. Nishida

14	Jun 26 2023	News website 1	[Nikkei Shimbun Digital Jun 26] - Article of research result published in *Nature* by Prof. Hayashi
15	Jun 28 2023	Newspaper 1	[Nikkei Shimbun Jun 28] - Article about ELSI by Prof. Kishimoto
16	Jun 30 2023	News website 1	[Nikkei Shimbun Digital Jun 30] - Article about ELSI by Prof. Kishimoto
17	Jul 04 2023	TV 1	[Nippon TV Jul 4] - Article of research result published in *Nature Communications* by Prof. Y Okada
18	Jul 06 2023	News website 2	[University Journal, QLifePro Jul 6] - Article of research result published in *Nature Communications* by Prof. Y Okada
19	Jul 13 2023	Newspaper 1	[Nikkei Shimbun Jul 13] - Article referring to Prof. Hayashi's research result published in *Nature*
20	Jul 19 2023	Newspaper 1	[Nikkei Shimbun Jul 19] - Article of research result published in *Cell Reports Medicine* by Prof. Y Okada
21	Jul 20 2023	Newspaper 1	[Yomiuri Shimbun Jul 20] - Article about AI by Prof. Kishimoto
22	Jul 26 2023	News website 1	[COURRiER Japon (Yahoo! News) Jul 26] - Article referring to Prof. Hayashi's research result published in *Nature*
23	Jul 28 2023	Newspaper 1	[Yomiuri Shimbun Jul 28] - Article about ELSI by Prof. Kishimoto
24	Aug 13 2023	Newspaper 1	[Nikkei Shimbun Aug 13] - Article referring to Prof. Hayashi's research result published in *Nature*
25	Sep 28 2023	News website 1	[npr Sep 28] - Article referring to Prof. Hayashi's research result published in *Nature*
26	Oct 06 2023	Magazine (Scientific) 1	[Cell Stem Cell Oct 6] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
27	Oct 06 2023	News website 1	[JIJI. COM Oct 6] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
28	Oct 10 2023	News website 1	[Nikkan Yakugyo Oct 10] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
29	Oct 12 2023	Newspaper 1	[Nikkan Kogyo Shimbun Oct 12] - Article of research result published in *Scientific Reports* by Prof. Nishida
30	Oct 12 2023	Newspaper 1	[Yomiuri Shimbun Oct 12] - Article of research result published in *Cell Stem Cell* by Prof. Takebe

31	Oct 13 2023	News website 1	[Nikkei Biotech Oct 13] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
32	Oct 16 2023	Newspaper 1	[Nikkan Kogyo Shimbun Oct 16] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
33	Oct 20 2023	Newspaper 1	[Nikkei Shimbun Oct 20] - Article of research result published in *Nature Communications* by Prof. Y Okada
34	Oct 23 2023	News website 1	[Nikkei Biotech Oct 23] - Article of research result published in *Nature Communications* by Prof. Y Okada
35	Oct 24 2023	News website 1	[QlifePro Oct 24] - Article of research result published in *Nature Communications* by Prof. Y Okada
36	Oct 25 2023	Newspaper 1, News website 1	[Nikkei Shimbun, 47 News Oct 25] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
37	Oct 28 2023	TV 1	[Ohayo Kansai(NHK) Oct 28] - Article of research result published in *Cell Stem Cell* by Prof. Takebe
38	Oct 31 2023	Newspaper 1	[Nikkei Shimbun Oct 31] - Article of research result published in *Annals of the Rheumatic Diseases* by Prof. Y Okada
39	Nov 01 2023	News website 1	[QLifePro Nov 1] - Article of research result published in *Annals of the Rheumatic Diseases* by Prof. Y Okada
40	Nov 04 2023	Newspaper 1	[Nikkei Plus 1 Nov 4] - Article about signs of disease by Prof. Nishida
41	Nov 07 2023	Newspaper 1	[Nikkei Sangyo Shimbun Nov 7] - Article referring to Prof. Hayashi's research result published in *Nature*
42	Nov 07 2023	Newspaper 1	[Nikkei Shimbun Nov 7] - Article of research result published in *Cell Reports* by Prof. Y Okada
43	Nov 08 2023	News website 1	[QLifePro Nov 8] - Article of research result published in *Cell Reports* by Prof. Y Okada
44	Nov 29 2023	News website 1	[Nikkei Biotech Nov 29] - Article of research result published in *Nature Communications* by Prof. Y Okada
45	Dec 07 2023	News website 1	[Gendai Business Dec 7] - Article about regenerative medicine by Prof. Miyagawa
46	Dec 10 2023	Newspaper 1	[Nikkei Shimbun Dec 10] - Article referring to Prof. Hayashi's research result published in *Nature*
47	Dec 13 2023	News website 1	[Nature's 10 Dec 13] - Article referring to Prof. Hayashi's research result published in *Nature*

48	Dec 14 2023	News website 1, Newspaper 4	[NHK News(NHK), Asahi Shimbun, Yomiuri Shimbun, Nikkei Shimbun, Sankei Shimbun Dec 14] - Article referring to Prof. Hayashi's research result published in *Nature*
49	Dec 18 2023	Magazine 1	[National Geographic Dec 18] - Article referring to Prof. Hayashi's research result published in *Nature*
50	Dec 21 2023	Newspaper 1	[Mainichi Shimbun Dec 21] - Article referring to Prof. Hayashi's research result published in *Nature*
51	Dec 24 2023	Newspaper 1	[Yomiuri Shimbun Dec 24] - Column by Prof. Hayashi, introducing Science report 2023
52	Dec 26 2023	Newspaper 1	[Nikkan Kogyo Shimbun Dec 26] - Article about Prof. M Okada's biography
53	Dec 28 2023	Newspaper 1	[Mainichi Shimbun Dec 28] - Article referring to Prof. Hayashi's research result published in *Nature*
54	Dec 28 2023	Newspaper 1	[Mainichi Shimbun Dec 28] - Artice about quantum computer by Associate Prof. Negoro
55	Jan 04 2024	News website 1	[Nippon Broadcasting System (Yahoo! News) Jan 4] - Article referring to Prof. Hayashi's research result published in *Nature*
56	Jan 04 2024	News website 1	[Nikkei Biotech Jan 4] - Article of research result published in *Nature Communications* by Associate Prof. Nemoto
57	Jan 05 2024	News website 1	[COULLiER JAPON Jan 5] - Article referring to Prof. Hayashi's research result published in *Nature*
58	Jan 05 2024	Newspaper 1	[Nikkei Shimbun Jan 5] - Article about Prof. Yachie's research result and his biography
59	Jan 11 2024	Newspaper 1	[Asahi Shimbun Jan 11] - Article referring to Prof. Hayashi's research result published in *Nature*
60	Jan 25 2024	News website 1	[Nikkei Biotech Jan 25] - Column about regenerative medicine by Prof. Nishida
61	Feb 02 2024	Newspaper 1	[Yomiuri Shimbun Feb 2] - Article about Nakanoshima Qross by Prof. Nishida
62	Feb 16 2024	News website 1	[National Geographic Feb 16] - Article referring to Prof. Hayashi's research result published in *Nature*
63	Mar 13 2024	Newspaper 1	[Sankei Shimbun Mar 13] - Article about Clinical trial by Prof. Miyagawa
64	Mar 14 2024	Newspaper 1, TV 1	[Yomiuri Shimbun, Good! Morning (TV Asahi) Mar 14] - Article about Clinical trial by Prof. Miyagawa

65	Mar 15 2024	Newspaper 1	[Nikkan Kogyo Shimbun Mar 15] - Article about Clinical trial by Prof. Miyagawa
66	Mar 19 2024	Newspaper 1	[Yomiuri Shimbun Mar 19] - Article referring to Prof. Hayashi's research result published in *Nature*
67	Mar 21 2024	Newspaper 1	[Yomiuri Shimbun Mar 21] - Article about generative AI by Prof. Kishimoto

ERRATA

Jan. 17, 2025

Page

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5   incorrect

Hepato-Biliary-Pancreatic Group (Takebe, Nemoto, and Kashino)

Correct

Hepato-Biliary-Pancreatic Group (Takebe, Nemoto, Hwa, and Kashino)

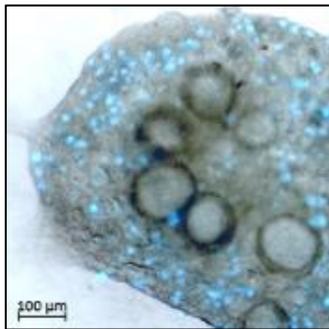
7   incorrect
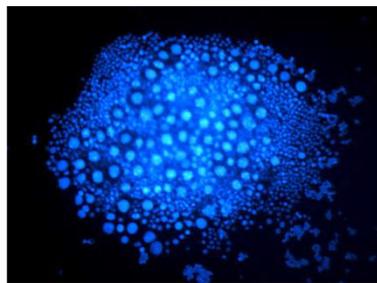

Figure 10. Dormant oocytes
(blue) in cultured organoid

correct

Figure 7. Dormant oocytes
(blue) in cultured organoid