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

Host Institution	Osaka University	Host Institution Head	Shojiro Nishio
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 2025) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

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

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

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) aims to develop Patient bio-Digital Twins that will replicate biological phenomena and pathological processes in human organs in cyberspace. Towards realizing the Patient bio-Digital Twins, our key research achievements in FY2024 of the five major target organ groups are described below.

Sensory Group: 1) systematically organized clinical information from patients with retinitis pigmentosa (RP) collected over an extended period to establish a data platform required for model construction. **2)** developed a mathematical disease progression prediction model that estimates future changes in visual function by using multiple parameters derived from clinical data as inputs. **3)** identified cellular populations involved in RP pathogenesis and potential therapeutic target candidates by integrating multilayered analyses of retinal organoids generated from patient-derived cells with computational approaches based on gene regulatory networks.

Hepato-Biliary-Pancreatic Group: 1) expanded iPSC-derived human liver organoids (HLOs) to multiple donors including metabolic dysfunction-associated steatohepatitis (MASH) and conducted drug exposure assays using previously developed donor-mosaic population panel to examine responses across different genotypes. **2)** based on data from 1), investigating drug mechanisms of action, stratified by genetic background using polygenic scores and creating gene regulatory networks associated with metabolic dysfunction to conduct in-silico drug assay. **3)** developed new liver organoid can recapitulate complex liver structure to enable advanced disease modeling (**Nature,** in press) and found a novel RNA transfer phenomenon that may be associated with disease causalities or progression (**PNAS**). **4)** established a pipeline to assess real-time metabolic flux in HLOs using hyperpolarized Nuclear Magnetic Resonance (NMR) spectroscopy.

Cardiovascular Group: 1) completed comprehensive omics analyses on heart specimens from restrictive and dilated cardiomyopathy pediatric patients to identify key disease specific pathways. **2)** developed an innovative mathematical model (**PLOS Digital Health**) to bridge the gap between Engineered Heart Tissue (EHT)-based disease model (**Development Growth & Differentiation**) and clinical ECG recordings. **3)** constructed a model that estimates mechanical performance based on input parameters such as the presence or absence of gene repair, gene expression patterns, and other patient attributes. **4)** optimized mRNA cardiac delivery for therapeutics (**J. Control Release**).

Bone-Cartilage Group: 1) established conditions for utilizing novel MRI datasets from 4,000 participants, linked with genotype data gathered at Tohoku Medical Megabank Organization to conduct fine-grained stratification of osteoarthritis (OA) subclasses (data-driven approach). **2)** collected cartilage tissue data (scRNAseq etc) from over 44 patients exhibiting biochemically diverse OA patient etiologies. **3)** identified molecular signaling network of resting, proliferating and hypertrophic chondrocytes using scRNAseq data from mouse growth plate model, which is applicable to chondrocytes from OA patients. **4)** established organoid experiment system using mechanical stress as perturbation to recapitulate OA patient's cartilage.

Reproductive Group: **1)** constructing human mature ovarian cortex from iPS cells that hold dormant oocytes (four out of the six steps have been completed toward the differentiation of ovarian tissue). **2)** developed an imaging system for quantifying follicular size and number. **3)** identified IGF-INS signaling pathway to activate dormant oocytes. **4)** preparing to utilize over 500 clinical serum samples, linked to each patient information undergoing infertility treatment.

1-2. Generating Fused Disciplines

To advance interdisciplinary research, we reconstructed the Research Steering Committee by adding female researchers and experts conversant in both experiments and mathematical modeling. This committee has been managing activities such as Joint Research Grant, PRIMe Retreat, and Progress Report Meeting for strengthening fused disciplines. We formed a partnership with The Systems Biology Institute as one of Satellites, to provide strong support for the creation of a bio-Digital twin. We took additional measures to generate fused disciplines (PRIMe Seminar Series and networking sessions, International Symposium, Happy Hour, and Lunch Meetup).

2. Global Research Environment and System Reform

2-1. Realizing an International Research Environment

As shown in Appendix 2, since the recruitment of new members last year, PRIMe has continued to attract world-class researchers. We have recruited Abugessaisa from RIKEN and Yachie (A) from The Systems Biology Institute as PIs to strengthen our information and mathematical sciences.

We commenced a concrete collaborative research with the Curie Institute. In addition to the existing partners, we started joint research with Morita's laboratory at the University of Texas.

The EDI (Equity, Diversity, and Inclusion) Committee, established last year, held discussions and compiled a declaration on promoting EDI within PRIMe. Additionally, lectures and workshops on unconscious bias were conducted to raise awareness and facilitate to ensure diversity.

Hayashi, who was selected as one of Nature's 10 in 2023, was selected as one of TIME 100 in 2024, raising the international recognition of the center.

2-2. Making Organizational Reforms

In 2023, we proposed to the university headquarters the establishment of a system to provide salary incentives to principal investigators (PIs), and as a result, this first-of-its-kind system was approved by Osaka University in 2024. Additionally, we applied for an increase in the allowance for deputy center directors, which is not currently available in other departments.

In order to achieve gender balance, our center held an open-call female-only recruitment, and we secured two female researchers. Furthermore, as a result of discussions at an overseas forum, we were able to obtain candidates for foreign female researchers.

3. Values for the Future

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

For researchers and industry actors, we held an international symposium in March, 2025. As for overseas activities, we presented at Science in Japan Forum hosted by JSPS in June, 2024.

We also provided information through the PRIMe website and SNS in both English and Japanese.

To serve the general public in Japan, 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, including the WPI Science Symposium on November 14, 2024. We also published a Newsletter "Nexus" for the general public, which is available online.

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

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.

Following its launch in 2023, the 'Introduction to Human Metaverse Medicine' subject has been continued in FY2024 with ongoing improvements based on feedback and review. In April 2024, we launched the Human Metaverse Medicine graduate course as a Graduate Program for Advanced Interdisciplinary Studies, following the completion of preparations in the previous year.

3-3. Self-sufficient and Sustainable Center Development

Suita Agora 2, with a floor area of 8,850 m^2, is scheduled for completion in March 2027, and many of PRIMe's laboratories will be consolidated in this building.

Originally, one tenured faculty position has been secured, and another has been added for the FY2025. In the future, we plan to hire up to 10 faculty members.

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

1. World-Leading Scientific Excellence and Recognition

1-1. Advancing Research of the Highest Global Level

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

This section describes key research achievements in FY2024 across the five target organ groups with focus on interdisciplinary fusion collaborations. It also includes perspective, mathematical model planned to use, and implementation for Patient bio-Digital Twins.

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

We aim to construct a "Patient bio-Digital Twin (PbDT)" that integrates multi-layered and time-resolved biological phenomena observed in clinical ophthalmology. The PbDT is designed as a comprehensive model capable of digitally reproducing each patient's disease state to support prognosis prediction and estimation of therapeutic effects. Target diseases include major causes of visual impairment such as retinitis pigmentosa (RP), age-related macular degeneration, and glaucoma, with RP model development currently progressing ahead of the others.

In the first phase of the project, long-term clinical data collected from RP patients are being systematically organized to establish a foundation for model construction. This effort enables the development of a structured data framework suitable for handling individualized longitudinal clinical information.

In the second phase, we are developing a disease progression prediction model that uses the organized clinical data as input. RP is characterized by the stepwise degeneration of photoreceptors, leading to progressive loss of visual function, making early prediction of disease progression clinically valuable. To address this, multiple clinically obtainable parameters from each patient are incorporated into a mathematical modeling framework that estimates temporal changes in visual function. The resulting model is expected to provide individualized prognostic insights and contribute to the optimization of therapeutic interventions.

In the third phase, to deepen understanding of the molecular basis of RP, retinal organoid experiments using patient-derived cells are being conducted. Retinal organoids are three-dimensional tissue models induced from patient cells and are well suited for replicating disease pathology. Using this experimental platform, multi-omics analyses—such as gene expression profiling, chromatin accessibility analysis, and proteomic analysis—are performed to identify disease-associated cellular populations and molecular features. By integrating these high-dimensional data, the group is also pursuing the identification of factors involved in disease progression and potential therapeutic targets.

By integrating information across diverse layers—including clinical data, mathematical modeling, cellular models, and multi-omics analyses—the project seeks to establish a digital twin framework for ophthalmic diseases. Through this integrated approach, the research aims to advance understanding of patient-specific disease mechanisms and create a foundation that supports the development of personalized medicine in ophthalmology.

Hepato-Biliary-Pancreatic Group (Takebe, Nemoto, Negoro, and Yachie (A))

The immediate goal of bio-digital twin for Hepato-Biliary-Pancreatic Group is to achieve "Prediction of disease onset and progression" and "Prediction of drug efficacy". Metabolic dysfunction-associated steatohepatitis (MASH), previously known as NASH, exhibits patient-specific disease progression, influenced by both genetic background and individual life-style factors. Liver Bio-Digital Twin (BDT), that can infer, project and predict the pathogenic biological trajectory would help account for these complex variables, enabling the identification of the most effective strategy for each patient. The developed liver BDT will then serve as a foundational building block for the Organoid-based Patient Digital Twin (OPDT). The OPDT 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 BDT framework. Electronic health record (EHR) data collected from patients diagnosed with MASH will be entered into the simulation platform to a patient-specific bio-digital twin that can inform the possible pathogenic trajectory and therapeutic strategy, including personalized drug selection. The patient's bio-digital twin will be calibrated by the latest EHR data to increase its accuracy reiteratively. We envision that the patient's bio-digital twin will realize

personalized medicine facilitated by robust clinical and mechanistic evidence through an accessible online platform. To achieve our goal, several projects are being conducted in parallel, as outlined below.

1. Population organoid panels for personalized, optimal drug selection: To quantitatively understand how individuals respond to environmental stress and drugs at the population level, we have developed a high-throughput, en masse population panel of iPSC-derived human liver organoids (HLOs). In this Population organoid Panel (PoP), HLOs from diverse genetic backgrounds are exposed to fatty acids in a single petri dish, mimicking lifestyle-related excess energy intake in a controlled manner (Kimura et al., **Cell**, 2022). Using the same technology, we are conducting drug exposure assays (e.g., FXR agonist, PPAR agonist, and LXR inverse agonist) to examine responses across different genotypes. Building on the original PoP, this expanded study now includes HLOs from healthy Japanese panel, adult MASH panel, and a control panel. These panels are currently undergoing single-cell RNA sequencing (scRNAseq), along with proteomic and metabolomic analysis of the culture medium (see 2. below). With the aid of demultiplexing algorithms (Figure 1a), we obtain gene expression profiles for all participants, both before and after drug administration to HLOs (Figure 1b). Based on these data, we investigate drug mechanisms of action, stratified by genetic background using polygenic scores (PGS) related to steatosis (e.g., elevated BMI, ALT, AST) and DMET (Drug Metabolism Enzymes and Transporters, e.g., CYP gene mutations). Gene regulatory networks associated with metabolic dysfunction—including de novo lipogenesis, fatty acid oxidation, cholesterol transport, mitochondrial metabolism, and insulin signaling—are modeled using a hybrid approach combining knowledge-based methods, machine learning (SCENIC and CellOracle), and deep neural networks (a transformer-based method: scGPT. See Figure 1c). To enable personalized, optimized drug selection, we conduct in silico perturbative drug assays using the constructed regulatory network. These simulations explore variable drug doses and targets, stratified by genotype based on PGS.

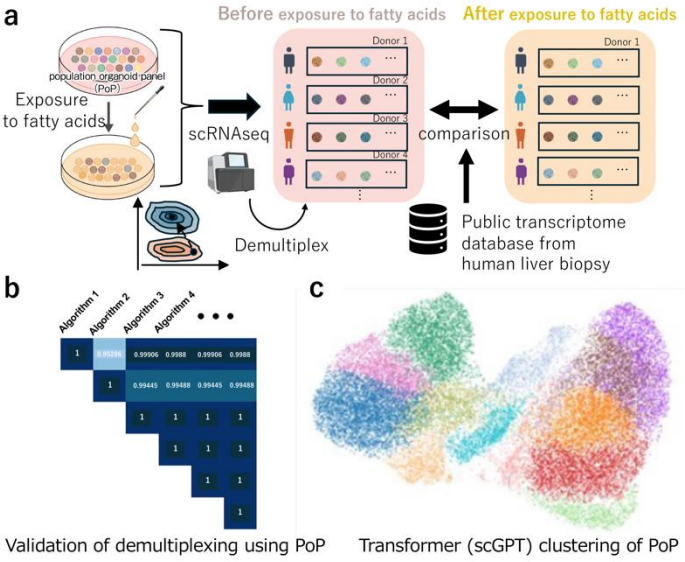

Figure 1. Construction of organoid panels from over one hundred donor samples

To further model spatial complexity of liver function in metabolic diseases, we have also developed new liver organoid can recapitulate complex liver structure to enable advanced disease modeling and found a novel RNA transfer phenomenon that may be associated with disease causalities or progression.

2. A pipeline for hyperpolarized NMR-based organoid metabolomics: Understanding the metabolic signature of MASH patient-derived liver organoids is crucial for predicting MASH trajectory and connecting it with clinical datasets to aid liver bio-digital twin development. We established a pipeline to assess real-time metabolic flux in HLOs using

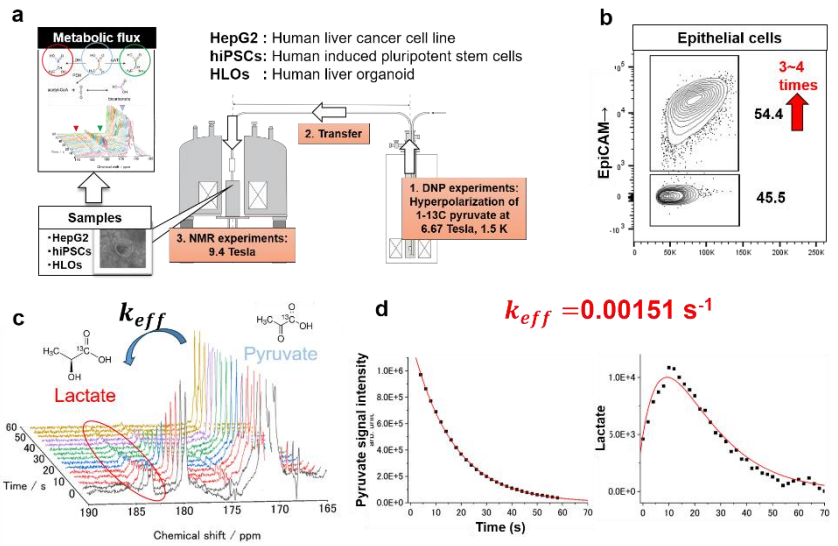

Figure 2. Assessment of HLOs using NMR spectroscopy

hyperpolarized Nuclear Magnetic Resonance (NMR) spectroscopy, which captures rapid (<1 min) metabolic alterations using isotope-labeled precursors. iPSC-derived HLOs were harvested and placed in a sample chamber where metabolic reactions were monitored (Figure 2a). Hyperpolarized ^{13}C pyruvate was used to trace pyruvate-to-lactate conversion. To more closely reflect in vivo liver status, we refined our differentiation protocol to generate higher-order liver organoids containing over half epithelial components (hepatocyte/cholangiocyte) (Figure 2b). These organoids enabled measurement of pyruvate-to-lactate metabolism, and the reaction rate constant (Keff) was successfully calculated based on time-course signal intensity (Figure 2c and d).

Cardiovascular Group (Miyagawa, Kashino, and Tsukada)

The initial goal is constructing a computational model that can reproduce the mechanical and electrical activities of iPSC-derived EHT for each individual subject to serve as a basis for constructing organoid-based patient digital twin hearts (OPDTH). This includes generating an electrical signal, or organoid ECG (OECG) that the EHT will generate.

The ultimate goal is to extend the model to the organ level to develop patient-specific digital twins that can forecast disease progression and guide the selection of optimal therapeutic interventions.

We have also continuously studied the implementation of the bio-Digital twin. In the future, we envision a robust integration of our digital twin platform into clinical practice. By combining patient-specific data with our advanced modeling techniques, the platform will provide clinicians with a transformative tool for personalized diagnosis and treatment planning. When a patient presents with cardiovascular problems, the system will quickly generate a comprehensive digital twin of the patient's heart, capturing both electrical and mechanical functionalities. This real-time digital representation will enable physicians to simulate various therapeutic interventions, predict potential risks and optimize treatment strategies tailored to the individual's unique condition. In addition, the platform will incorporate decision support algorithms that leverage big data analytics and machine learning to continuously refine its predictive accuracy as more clinical data becomes available. In practice, patients will undergo a series of non-invasive assessments, such as advanced imaging and biometric monitoring, to provide the necessary input data. This integration will not only streamline diagnostic processes, but also facilitate early detection of abnormalities, leading to improved patient outcomes. Ultimately, by bridging the gap between experimental models and real-world clinical practice, our digital twin technology will translate cutting-edge research into everyday patient care, paving the way for proactive and precisely tailored treatment.

1. Omics Profiling: Uncovering Disease-Specific Pathways for RCM and DCM.

We performed comprehensive omics analyses on cardiac tissue samples from four pediatric patients for each of our initial target diseases - restrictive cardiomyopathy (RCM) and dilated cardiomyopathy (DCM). These analyses enabled us to identify key disease-specific pathways, and we are now in the process of validating these findings in vitro. Specifically, we are using patient-derived iPSC-cardiomyocytes and iPSC-EHTs to evaluate the phenotypic improvements induced by inhibitors targeting these pathways.

2. Advancements in Mathematical Modeling: Tensor Cardiography (TCG).

We have developed an innovative mathematical model, Tensor Cardiography (TCG), which conceptualizes electrocardiograms (ECGs) as sequences of probability density functions derived from cumulative Gaussian functions that model transitions in action potentials (Tsukada et al., **PLOS Digital Health,** 2024). This approach is designed to reconstruct the dipolar fields resulting from collective action potentials through time-series point processes, thereby enabling the synthesis of ECG signals from iPSC-EHT data. TCG represents a significant step toward bridging the gap between EHT-based disease models (Hasegawa et al., **Development Growth & Differentiation,** 2024) and clinical ECG recordings, ultimately facilitating the realization of comprehensive cardiac digital twins.

3. From iPSC-EHTs to a Digital Twin Platform.

To implement TCG in high-throughput assays, we are currently designing and optimizing a platform equipped with flexible electrodes for recording EHT action potentials, in conjunction with a chronic stimulation system to promote tissue maturation. Using pilot data, we currently reconstruct ECG waveform and validate against clinical ECG recordings.

4. Digital Modeling of Organoid-Level Activity.

To achieve our initial goal of constructing an organoid-level mechanical and electrical activity model for individual patients, it is essential to precisely quantify the corresponding parameters specific to each subject. Accordingly, we have developed two novel measurement methods. One is

a vision-based approach based on the Phase Only Correlation (POC) technique, which allows for sub-pixel resolution measurement of the dynamic properties of iPSC-EHT contraction and dilation from video recordings. The other is an approach to measure object "hardness" as acoustic impedance with 3D resolution at the cellular level. Using these approaches, we have constructed a model that estimates mechanical performance based on input parameters such as the presence or absence of gene repair, gene expression patterns, and other patient attributes. To bridge the gap between cellular-level dynamics and macroscopic signals such as the ECG, we also developed an interconversion model that correlates parameters representing cardiomyocyte state with ECG features.

5. Development of mRNA Therapeutics: Optimizing Cardiac Delivery Strategies.

As one of the therapeutic intervention options for the ultimate goal, we are investigating the potential of mRNA therapeutics for heart failure, and we have recently established an efficient method for their delivery to the heart (Handa et al., **J. Control Release**, 2025). In our studies, lipid nanoparticles (LNPs) encapsulating firefly luciferase (FLuc) mRNA were delivered to rabbit hearts via intracoronary (IC) catheterization and the results were compared to intravenous (IV) and intramyocardial (IM) administration. Notably, IC administration resulted in significantly higher mRNA expression in both healthy and ischemia-reperfusion models, with a broader distribution that extended to remote myocardial regions. Histological analysis confirmed FLuc expression in both cardiomyocytes and vascular cells. In addition, IC administration of VEGF mRNA-LNPs significantly reduced infarct size and improved cardiac function. These findings highlight IC delivery as a minimally invasive and clinically viable strategy for cardiac mRNA-LNP delivery.

<u>Bone-Cartilage Group (Tsumaki and Nemoto)</u>

Osteoarthritis (OA) of the knee affects over 300 million people globally due to cartilage degeneration, and represents a pressing social challenge in aging societies. OA is a chronic, life-long condition influenced by confounding risk factors -from genetic SNPs to patients' lifestyles- being one of subjects that gain benefit from the development of a bio-Digital Twin (Figure 3). Our goal is to create mathematical/machine learning models for (i) "Prediction of disease onset and progression" and (ii) "Prediction of drug efficacy". Our approach uses both in vivo and in vitro datasets currently being collected by our group: (a) Novel MRI datasets from 4,000 participants, linked with genotype data (SNP microarray) gathered at Tohoku Medical Megabank Organization (ToMMo), (b) Patients' cartilage tissue obtained as excised medical disposal after Total Knee Arthroplasty (TKA), along with associated clinical data, (c) Chondrocytes differentiation in mouse growth plate cartilage, and (d) Patient-specific iPSC-derived cartilage organoid.

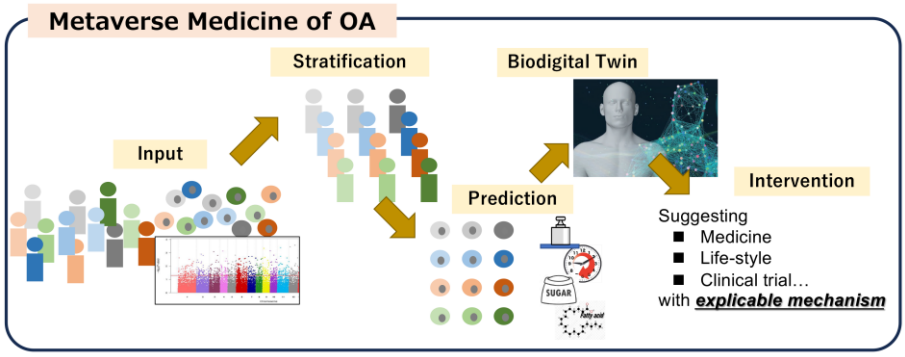

Figure 3. Schematic model of OA bio-Digital Twin, which will be used for clinical intervention upon treatment of the patients

For the first goal (i), we aim to conduct fine-grained stratification of OA subclasses based on genotypes and clinical measurements (such as X-ray, MRI, and blood tests). Using the novel 4,000-participant MRI-genotype ToMMo dataset, we will adopt a data-driven approach by leveraging Convolutional Neural Network (CNN) models developed as part of the Foundation of the National Institute of Health Biomarkers Consortium Osteoarthritis Project. This project was established for identifying the most responsive imaging biomarkers for knee MRI images. Building on these well-established deep neural network models, we aim to integrate MRI imaging data with previously unexplored genetic (SNP) and blood biomarkers. The combination of these novel biomarkers could enable detailed stratification of the general populations, including both OA patients and at-risk individuals, ultimately allowing for unprecedented accuracy in predicting disease onset and progression.

To achieve the second goal (ii), we aim to bridge in vivo level information with molecular-level insights into the disease mechanisms. In collaboration with Osaka University Hospital Department of Orthopaedic Surgery, we have accumulated cartilage tissue data from over 44 patients exhibiting biochemically diverse patient etiologies. By integrating scRNAseq data from these cartilage tissues with corresponding X-ray images and blood test results, we will identify key gene regulatory networks for each stratified cluster defined in the first goal (i). This effort is further strengthened by the use of animal models and our cartilage organoid models, which are a core strength of our research. Specifically, our mouse growth plate model has identified improved molecular signaling network of resting, proliferating and hypertrophic chondrocytes using single cell RNAseq data. These findings are expected to be applicable to chondrocytes from OA patients. Additionally, iPSC-derived cartilage organoid for all patients involved in this study are being developed in collaboration with iPS Cell Core Facility of PRIMe, along with the clinical data. To induce OA-like phenotypes in the organoid, we have imposed an OA-related stress factor using weight bearing experiments, which successfully demonstrated that several stress responsive genes are regulated by this mechanical stress (Figure 4). Furthermore, we observed that the chondrocytes subpopulation and cell-cell interaction in degenerated organoid behave similarly to those in OA patients (Figure 5). Based on the scRNAseq data with TF database (including motif ranking datasets), we are currently modeling regulatory networks using both database-driven approaches (in collaboration with the Curie Institute) and unbiased machine learning methods such as SCENIC, which infers directed TF networks from scRNAseq data, followed by TF motif enrichment analyses (cisTarget analysis). The resulting regulatory network will then be used in silico perturbation experiments in personalized drug screening assays, stratified by the disease subtypes defined in the first goal (i).

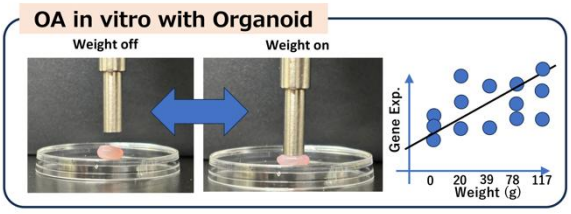

Figure 4. Stress responsive genes are up regulated in correlation to weight bearing, which partially represents the onset of OA.

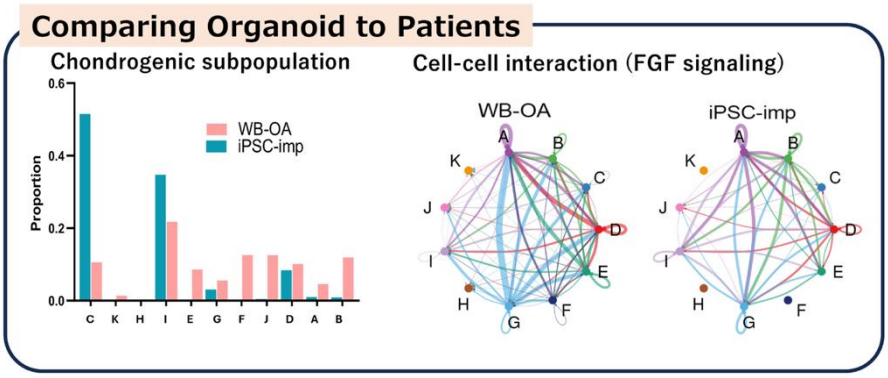

Figure 5. Degenerated organoid (iPSC-imp) show similar chondrogenic subpopulation (left) and cell-cell interaction (right) to OA patients' cartilage (WB-OA).

In summary, in vitro analysis using organoids will provide data to improve the molecular signaling network so the responsive differentiation against certain perturbations can be modeled and experimentally tested. With the established model, we will be able to predict disease onset and progression in cellular level, so that drug efficacy can also be assessed in the cellular level for its mode of action.

<u>Reproductive Group (Hayashi, Hwa, and Yokota)</u>

To construct the first-generation patient bio-digital twin of reproductive organs, we will establish a human ovarian organoid system capable of testing oocyte lifespan using human serum samples. Through quantification of oocyte longevity and multi-omics analysis, this organoid system will generate datasets to model ovarian function, forming the basis for predicting female reproductive lifespan (Figure 6). To achieve this, our group has been focusing on: (1) Inducing ovarian somatic cells from human iPS cells, (2) Refining culture conditions that support long-lived dormant oocytes in vitro, (3) Developing an imaging

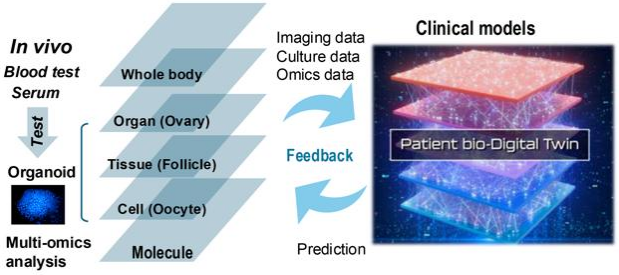

Figure 6. Overview of patient bio-Digital twin in reproductive organs

system for comprehensive quantification of ovarian follicles, and (4) Collecting patient serum and cells.

In this FY2024, we identified a culture condition that maintains dormant oocytes—serving as an oocyte reservoir—for several months in a mouse ovary organoid model (paper in preparation). This finding provides a foundation for optimizing the culture conditions needed for human ovary organoids. To produce human ovary organoids, we have made progress in inducing intermediate mesoderm and potential precursors of gonadal somatic cells, demonstrating appropriate marker gene expression (Figure 7). Building on these results, we will continue refining the differentiation conditions for ovarian somatic cells. For quantitative validation of the ovary organoids, we have been developing an imaging system capable of extracting multiple parameters such as oocyte size, number, and location. So far, the system allows accurate counting and sizing of oocytes (Figure 8) (paper in preparation). We plan to further enhance this system to incorporate time-lapse imaging of ovary organoids. In addition, we discovered that IGF signaling plays a critical role in maintaining oocyte dormancy in the mouse model. Given that the mouse model harbors the identical IGF1 receptor mutation found in humans, IGF signaling is a strong candidate pathway influencing female reproductive lifespan. Meanwhile, in collaboration with the Department of Gynecology and Obstetrics at Osaka University Hospital, we are preparing to utilize over 500 clinical serum samples linked to patient information from individuals undergoing infertility treatment.

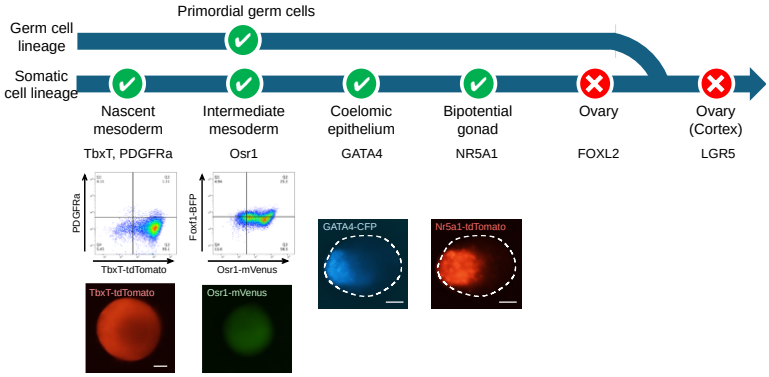

Figure 7. Induction of human ovarian organoids: The induction of ovarian tissue differentiation for organoid generation requires a five- or six-step differentiation process. Currently, four of these steps have been completed.

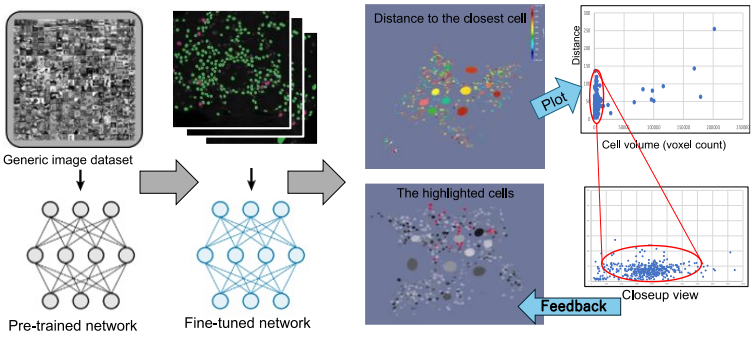

Figure 8. Development of an imaging system for quantifying oocytes: To segment oocytes, we fine-tuned a pre-trained CNN using an annotated dataset. The annotation dataset was generated by expert biologists. This system enables automatic segmentation and analysis of various cell types, tailored to the needs of researchers.

Cutting Edge Technologies developed in PRIMe

In addition to the interdisciplinary approaches to develop patient bio-Digital twins described above, Quantum Science groups have developed cutting-edge technologies which might be applicable for creation of Human Metaverse Medicine as described below.

1) Negoro's group (Quantum measurement) has been developing hyperpolarization technology (including amelioration of experimental materials) that can improve the sensitivity of magnetic resonance imaging (MRI)/nuclear magnetic resonance (NMR). Notably, this technology is an example of interdisciplinary fusion research within PRIMe, visualizing the metabolic process in organoid to understand disease models at the quantum mechanical level. Please also see Hepato-Biliary-Pancreatic Group described above (Figure 6).

Science Advances (2024) DOI: 10.1126/sciadv.adp2533
Journal of Physical Chemistry Letters (2024) DOI: 10.1021/acs.jpclett.4c01456
Journal of the American Chemical Society (2024) DOI: 10.1021/jacs.4c01050

2) Harada's group (Quantum sensing) developed methods to control and monitor local intracellular temperature and studied how noninvasive temperature changes affect neuronal differentiation in neuron-like cells using infrared lasers. They discovered that neuronal differentiation

involves intracellular thermogenesis linked to transcription and translation. These results are expected to bring a new angle on intracellular heat as an important factor in understanding physiological and pathological processes of organoid disease models in PRIMe and its medical applications.

Nature Communications (2024) DOI: 10.1038/s41467-024-47542-8
Adv Exp Med Biol (2024) DOI: 10.1007/978-981-97-4584-5_7

Platform for Human Metaverse Medicine

We develop a platform and dashboard design to support the deployment of bio-Digital twins in virtual spaces, aiming to bridge gaps between experts and non-experts and enable collaborative decision-making. Since no existing platform fully meets the complex requirements—such as multi-scale, multimodal (e.g., multi-omics, multi-AI), and real-time visualization capabilities—we are exploring existing platforms and data formats. As a practical step, we have tested Omniverse using CT scan data of the Cardiovascular system (DICOM format), converted to USD via ParaView, enabling multi-user 3D visualization. Pilot studies also include CAD-based simulations of myocardial activity and 3D modeling for EHT bioassay platforms. Real-time synchronization is essential for cardiovascular digital twins. To support this, we are developing the Tensor Cardiography (TCG) to derive action potentials from ECG data, preparing for future metaverse applications.

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."

First of all, **Center Director held one-to-one meeting with PRIMe PIs (mostly with interdisciplinary collaborators)** to advance research by integrating disciplines through establishment of mathematical models for target diseases. It was decided that, in addition to Takebe and Nagahara, **Yachie (A) and Hayashi will be appointed as Deputy Directors from April 1st, 2025** to support the Center Director. Mentioned four Deputy Directors (two dry researchers and two wet researchers) will effectively and collaboratively promote the fusion of different fields. Abugessaisa (PRIMe PI and Big Data and Computing Core) also held another one-to-one meeting with PRIMe PIs in Organoid biomedical sciences related to the 5 major target organs and collected information of experimental data to develop PRIMe integrated database including tracking, storage, and protection (also refer to Section 5, Response to (4) in detail).

To further strengthen team bonds in PRIMe and also according to FY2024 Follow-up of WPI-Program, **we changed Research Steering Committee member** by adding three female researchers and two experts conversant in both experiments and mathematical modeling. Please also see Section 5, Response to (1). This renewed committee has been managing three major activities as follows to advance research in fused disciplines.

A) **PRIMe Joint Research Grant**

The PRIMe Joint Research Grant was established to foster interdisciplinary research within PRIMe. It provides basic funding for a one-year interdisciplinary collaboration research project with the responsible investigator being a PRIMe junior researcher (excluding PIs and Professors). In FY2024, seven researchers were selected by the review committee in PRIMe and a total of 5 million yen was allocated. In addition, during the 4th PRIMe Retreat (March 15, 2025), a presentation session was held for this year's successful applicants to present and receive feedback. The committee plans to continue the grant program for FY2025, and in addition to new applications, it also plans to accept continued applications from FY2024.

B) **PRIMe Retreat**

We held PRIMe Retreat twice within this fiscal year (September 5 and March 15, gathering 70 and 57 participants respectively). Through these Retreats, we not only strengthened the shared understanding of PRIMe vision but also organized special activities as follows: **ELSI group work** focusing on workshop for Patient and Public Involvement (PPI) with PRIMe Researchers, **Joint Research Grant Reports** (described above), **Educational Lectures** (Lecturers: Yachie (A) and Abugessaisa), and our **first-Equity, Diversity, and Inclusion (EDI) Workshop** entitled "Creating a Workplace to Achieve Diversity: How to Break the Habit of Bias?" (Please see also Section 3-2 in detail).

C) **Progress Report Meeting**

A total of eight Progress Report Meetings (the 6th to the 13th meeting) were held in FY2024. This

FY, in addition to the major target organ groups, the Core Facilities (iPSC and Big data and computing), ELSI, and Quantum groups also presented their research, while keeping the style of simultaneous presentations by interdisciplinary collaborators. Initially, the participants were mainly members of the Research Steering Committee. However, from the 10th meeting, participation became open to all PRIMe members, and the meetings were expanded to include not only PIs but also next-generation researchers to encourage discussion for interdisciplinary fusion research.

The following ongoing activities to generate fused disciplines have been conducted since last FY.
1) **PRIMe Seminar Series/Omnibus Seminar Series**: Inviting outstanding researchers to present and holding networking sessions where PRIMe members interact (total 15 seminars throughout FY2024).
2) **PRIMe International Symposium:** The 3rd International Symposium (March 14, 2025) inviting researchers from Japan and overseas to facilitate the integration research conducted at PRIMe. Interdisciplinary fusion research by next-generation researchers in PRIMe were also introduced via flash talks and poster session program during this symposium.
3) **Happy Hour and Lunch Meetup**: Monthly events allowing sharing ideas for the creation of bottom-up fused research among young and senior researchers of all fields in the CoMIT building.

New PRIMe Satellite

Since Yachie (A) is also affiliated with The Systems Biology Institute (SBI, President: Hiroaki Kitano), **we formed a partnership with SBI as one of PRIMe Satellites** and will recruit two additional foreign researchers (specially appointed researcher, part-time employee) in FY2025 to propel the establishment of mathematical models for target diseases. Because SBI is a non-profit private research institution with the aim of promoting systems biology research and focuses on rapid translation of basic research to practical outcomes for both business and clinical applications, the establishment of this partnership is expected to provide strong support for the creation of a bio-Digital twin.

Expansion of research space

Before establishing the actual under-one-roof condition in Suita Agora 2 (see Section 3-3), as shown in Figure 9, we renovated and rearranged allocation of "wet" and "dry" researchers in CoMIT building in Suita Campus for sharing better vision and generating stronger fused disciplines.

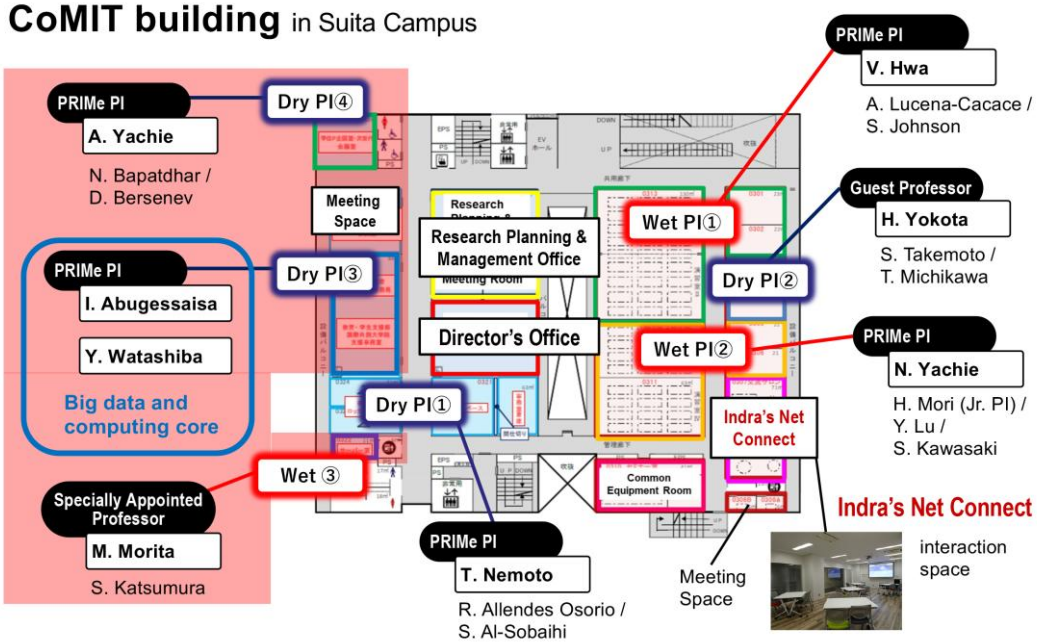

Figure 9. Further expansion of research space (pink area)

2. Global Research Environment and System Reform

2-1. Realizing an International Research Environment

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

・Further initiatives based on leading-edge research and international exchange experience

As shown in Appendix 2, since the recruitment of new members last year, PRIMe has continued to attract world-class researchers. This year we have recruited Imad Abugessaisa from RIKEN and Ayako Yachie from SBI (The Systems Biology Institute) as PIs to strengthen our information and mathematical sciences.

In terms of collaboration with overseas research institutions, in addition to the existing partner institutions, we have started a joint research project with Masahiro Morita's laboratory at the University of Texas. Sakie Katsumura, a female researcher at Morita's laboratory, joined us as a guest associate professor. She also received the JSPS Grant-in-Aid for Scientific Research in 2025 for her joint research with PRIMe.

In October 2024, 10 people from the University of Groningen in the Netherlands, including the Rector and Director, visited our institute and discussed about the creation of digital health projects, graduate school education, double degree programs, and a possible research collaboration based on organoid and data science.

・Efforts to promote diversity within the center

For internal activities, the EDI (Equity, Diversity, and Inclusion) Committee, launched last year, finalized and published the EDIB Statement on our website after a series of discussions. Another activity was a workshop on unconscious bias by Hideko Nishioka, Deputy Director of the Center for Diversity & Inclusion at Osaka University, at the PRIMe Retreat, by which took steps to raise awareness of the importance of diversity at PRIMe.

In order to accelerate recruitment of overseas researchers and female researchers, as mentioned earlier, we hired Imad Abugessaisa as a foreign PI and Ayako Yachie as a female PI. We also hired Antonio Lucena-Cacace and Sean Johnson in Hwa's laboratory, Mohamed Marzouk Sobaih in Shinobu's laboratory, and Thibaud Sotin in Takebe's laboratory as foreign researchers. These new recruitments have contributed to ensuring diversity of PRIMe. In addition, we held an open-call female-only recruitment for professors and associate professors to balance the ratio of gender among researchers. We would like to continue such recruitment as needed.

We explore research in Human Metaverse Medicine in cooperation with overseas research institutes. Our PIs are conducting joint research at Cincinnati Children's Hospital Medical Center, the University of British Columbia, and National Autonomous University of Mexico, which are beginning to bear fruitful success. We also organized symposiums to enrich our diverse research environment: as a result, Laurence Calzone of the Curie Institute, one of the speakers of our symposium, visited Nemoto's Laboratory to conduct joint research on a model of the gene expression regulatory network of chondrocytes. Furthermore, we participated in the Science in Japan Forum held in Washington DC to introduce the activities of PRIMe and exchange information on interdisciplinary fusion research; moreover, we found a candidate for foreign female researcher as PI.

・Initiatives and achievements to become a center for young researchers from around the world

In order to support the development of young researchers and promote interdisciplinary fusion research within the center, a joint research grant was launched at the end of FY2023, and seven projects received grant support. The results of this grant program were presented at the March retreat, where the projects were confirmed and verified. In FY2024, we plan to maintain the current grant funding and increase the total amount of grant support.

For the purpose of enabling young researchers to actively present at international conferences, etc., we have established a fund to support foreign travel expenses, and secured the financial resources.

In addition, with the intention of attracting world-class researchers, we continue to employ them on a salary structure that exceeds the university's regulations.

Additionally, we were able to achieve substantial research results by publishing internationally-noted research papers such as Makoto Negoro and Akinori Kagawa's "Development of technology leading to ultra-sensitive MRI diagnosis", Yukinori Okada and others' "Report on improving the accuracy of genetic risk prediction for type 2 diabetes", and "Development of software to quantify escape from X-chromosome inactivation from single-cell RNA-seq data", and Takanori Takebe et al. "Discovery that transfer of mRNA between cells reprograms the fate of pluripotent stem cells", and Kohji Nishida et al. "Successful clinical research on transplanting corneal epithelial cell sheets created from iPS cells".

Moreover, in order to develop our basic research into the applications through collaborations with companies, we have established two joint research chairs, (1) a chair to study metabolic disease signal control with Atransen Pharma, and (2) a chair to study organoid toxicology with Suntory. We are also aiming to develop applications in various ways through international collaborations.

2-2. Making Organizational Reforms

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

At Osaka University, a position allowance is paid as a management supplement, however PRIMe was attempting to introduce a system that was not bound by the conventional method of operation, such as a salary system entirely based on competency. In 2023, we proposed to the university headquarters that a system be established to provide salary incentives to PIs. As a result, in 2024, this system was approved for the first time at Osaka University and have successfully increased the number of full-time international researchers at PRIMe.

PRIMe, unlike other departments engages in a broad range of interdisciplinary research.

To enhance management capacity, we have decided to increase the number of deputy directors from two to four. We also applied for the establishment of a deputy director allowance, which had not been approved by other departments.

As mentioned previously, in order to achieve gender balance, our center held an open-call female-only recruitment, and we were able to secure two female researchers. Furthermore, as a result of networking at forums overseas, we were able to obtain candidates for foreign female researchers.

Osaka University will continue to fully support various system-level reforms necessary for the development of PRIMe.

PRIMe is one of the International Advanced Research Institutes (same as WPI-IFReC), and is positioned as an independent department at Osaka University. The Center Director of PRIMe is also given special top-down executive authority, unlike the heads of other departments.

In order to achieve gender balance within PRIMe, lectures were given by faculty members from the Center for Diversity & Inclusion of Osaka University to raise awareness of diversity among PRIMe members.

In addition, Osaka University has established a system whereby researchers can use external funding to cover the costs of their accompanying children when they travel for academic conferences or other purposes, so that their research activities are not disrupted even when they are raising children.

We received a request from PRIMe members to use credit cards for payment, and negotiations were held with Osaka University. And at the end of 2024, the University accepted the request of PRIMe, reformed its system, and a corporate credit card was introduced at Osaka University.

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.

Our branding plan was established in FY2023, which we planned with a branding consultant (Figure 10). This year, our main goal was to reach out to the general public, and we achieved this

goal through several approaches, as shown below.

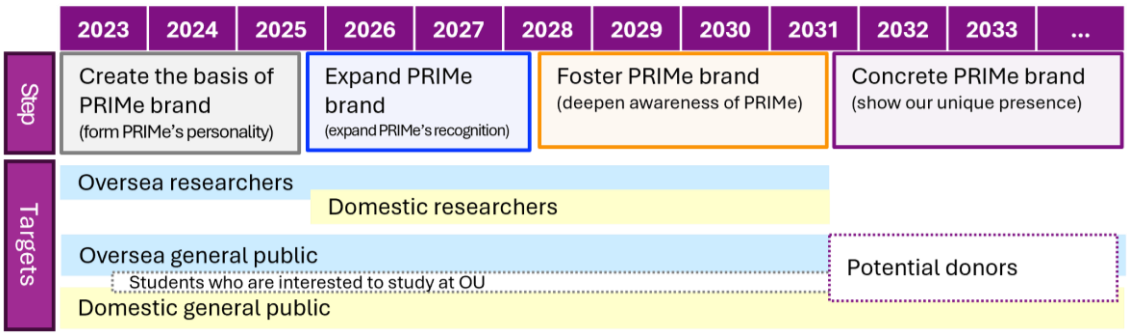

Figure 10. WPI-PRIMe Branding plan (Long Term Overview)

(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 researchers and industry actors, we held an international symposium (Onsite on March 14, 2025) For overseas, our researchers presented their research at the Science in Japan Forum hosted by JSPS (Hybrid on June 13, 2024). We also provided information through the PRIMe website and SNS in both English and Japanese (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 (November 16, 2024). We also published a Newsletter "Nexus" for the public, which is available online.

(2) Ongoing public engagement (for details of each event, refer to Appendix 7)

Since we started SNS (Facebook and Twitter/X) in April 2023 and constantly enriched our website, we hired new PR staff to facilitate our promotion toward general public through these different channels. By encouraging our researchers, we achieved to issue 8 press releases with their affiliation "WPI-PRIMe" included, whereas there were only 3 such releases last year. Therefore we succeeded in increasing the number of media coverage of our researchers.

In addition, Kishimoto's group (ELSI research) organized a Patient & Public Involvement (PPI) event on July 20, 2024. This event was part of the outline of their proposal presented at our symposium in FY2023; the result was reported in the next symposium.

(3) PI Selected as TIME 100

By the end of 2023, Nature selected our PI Katsuhiko Hayashi as one of "Nature's 10", the ten people who helped shape science that year. His research paper published in Nature (Murakami et al., **Nature**, 2023) was one of the most widely reported results. In April 2024, he was selected as TIME 100: the most influential People of 2024. At the same time, he was invited to TED talk in Vancouver, which the movie is open to the public (https://www.ted.com/talks/katsuhiko_hayashi_a_mouse_with_two_dads_and_a_new_frontier_for_biology). His research result continuously attracts people all over the world.

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

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

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 educational programs and have continuously updated and improved them.

Collaborative department of the Graduate School

PRIMe completed the necessary procedures to serve as a collaborative department in the Graduate School of Medicine, enabling its faculty members to supervise graduate students. In FY2024, this framework was further utilized, with three dedicated PRIMe faculty members formally joining the

collaborative department and taking on the role of enrolling and supervising graduate students.

Ph.D. programs

In preparation for establishing the degree program, we have determined a schedule to build the program step by step while addressing major issues in collaboration with the university administrative office (Figure 11). Following its launch in 2023, the 'Introduction to Human Metaverse Medicine' subject (2 credits) — offered to PhD students and covering cyber, physical, ethical, and social perspectives — has been continued in FY2024 with continuous improvements based on feedback and review. In April 2024, we launched the Human Metaverse Medicine graduate course as a Graduate Program for Advanced Interdisciplinary Studies (more than 7 credits), following the completion of preparations in the previous year. This program includes the 'Introduction to Human Metaverse Medicine' subject (2 credits) as a required core course and features a selection of thirteen elective courses covering a diverse range of subjects, including Medicine, Life Sciences, Biosensing & Biomeasurement, Bioinformatics, Medical Statistics, and Bioethics, all related to "Human Metaverse Medicine". Building on the planning initiated in FY2023, we are continuing our efforts in FY2024 to establish the Human Metaverse Medicine Ph.D. program (Integrated Doctoral Program) starting in April 2027, as well as a double degree program scheduled to begin in October 2026.

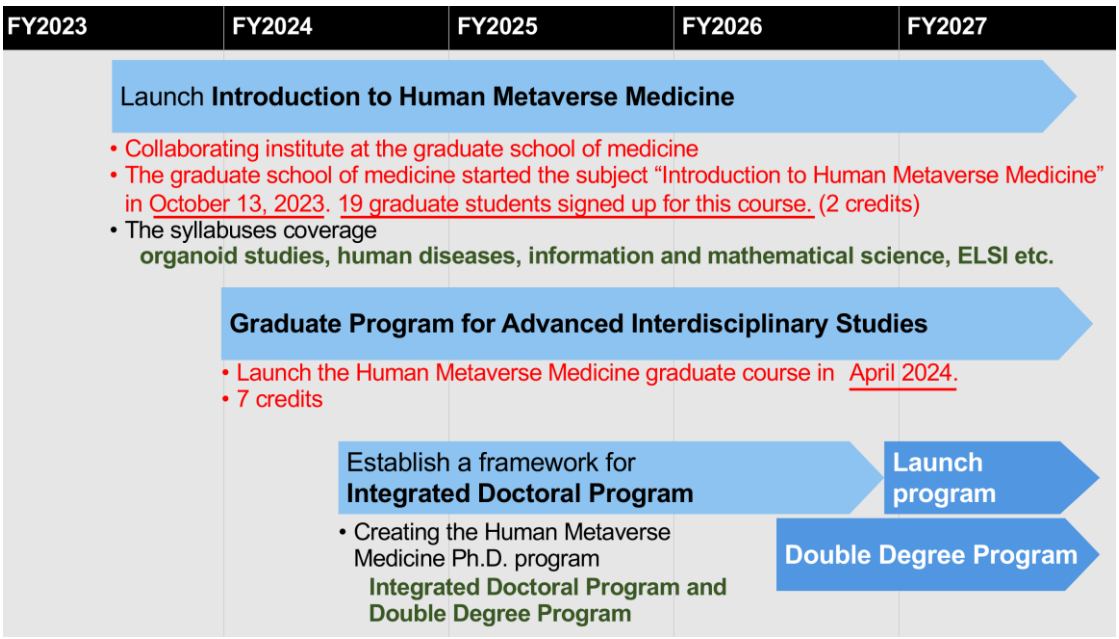

Figure 11. Time schedule of establishing the degree program

Support scholarships/research grants

Nine PhD students from PRIMe were awarded scholarships/research grants in 2024 from SPRING (Support for Pioneering Research Initiated by the Next Generation), Osaka University Next Generation Researcher Development Project supported by JST.

PRIMe Seminar series

We held the PRIMe Seminar Series/Omnibus Seminar Series for FY2024, as following: Speakers: J. Kere (Karolinska Institutet), K. Nakashima (Kyushu University), J. Auwerx (EPFL), J. Chan (National University of Singapore), K. Kamimoto (Washington University), S. Goto (Tokai University School of Medicine, Keio University), J. Wu (UT Southwestern Medical Center), T. Kitajima (RIKEN), T. Duchaine (McGill University), M. Gu (Cincinnati Children's Hospital Medical Center), N. Hamazaki (University of Washington), T. Yamashita (Chubu University), T. Furukawa (Nagoya University Hospital), R. Kawaguchi (The University of Tokyo, Kyoto University), M. Ruscone (Barcelona Supercomputing Center)

Seminars were open to graduate students and young researchers in Osaka University.

Postdoctoral training

We have designed and created postdoctoral and advanced postdoctoral programs to train young

researchers for PRIMe. Basic funding support 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 twice a month throughout FY2024 to facilitate communication and exchange ideas and experience among students, young researchers, and PIs, thereby providing an interdisciplinary research environment at PRIMe for young researchers.

Fostering researchers with a view to achieving gender plans and attracting female researchers to the center.

PRIMe has established the EDI (Equity, Diversity, and Inclusion) Committee, which has been engaged in discussions on developing a code of conduct concerning EDIB (Equity, Diversity, Inclusion, and Belonging). As part of its activities, the committee organized an EDI Workshop during the PRIMe 4th Retreat held in March 2025, in collaboration with the ELSI team of PRIMe. The workshop addressed gender issues, beginning with a keynote lecture by Prof. Hideko Nishioka of the Osaka University Center for Diversity & Inclusion, followed by group discussions among PRIMe members. Through this event, participants deepened their awareness and understanding of EDI.

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.

Research Space

Osaka University will use the proceeds from the sustainability bond to construct a new research building, Suita Agora 2, with a total floor area of 8,850 m^2, on the west side of the Faculty of Medicine and Graduate School of Medicine building. This building is scheduled for completion in March 2027, and will be used primarily by PRIMe, bringing together many of PRIMe's laboratories in a single building to create an 'under-one-roof' research environment.

Personnel Support

Originally, one tenured faculty position has been secured, and another has been added for the FY2024. In the future, we plan to hire up to 10 faculty members.

We employed four permanent administrative staffs in the PRIMe administrative department.

Osaka University has been selected for the Japan Science and Technology Agency's (JST) Support Program for Research and Development of Human Resources in Science and Technology (SPRING). The University is supporting doctoral students at PRIMe in challenging academic research, helping them to enhance their skills as researchers, and encouraging them to play an active role in a variety of career fields.

Financial support

In 2024, ¥700 million was allocated as administrative cost support.

In addition, PRIMe signed joint research agreements with two companies in 2024 and established joint research chairs. Osaka University fully supports such initiatives with companies.

Other

The Osaka University Office of Management and Planning provides consultation and support for base management when necessary. In addition, the Co-creation Bureau provides advice on issues related to collaboration with companies and intellectual property, as well as support and coordination for negotiations on intellectual property rights with overseas institutions.

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.

Building a network among URAs at WPI centers

In September 2024, URA meeting between WPI-PRIMe and WPI-ASHBi was held on the campus of Kyoto University, taking advantage of overlapping research areas in life science and geographical proximity between the two centers. The purpose was to share initiatives and explore possibilities for future collaboration. PRIMe and ASHBi exchanged views on research support systems, early-career

researcher development, outreach strategies, and event management. Discussions covered various topics, including support mechanisms across research stages, external funding acquisition, and creation of interdisciplinary fusion research. The lab tour organized by the ASHBi URA team helped highlight common issues shared by both WPI centers and contributed to a meaningful discussion. We aim to leverage these personal networks to enhance collaboration and share practical issues between both centers' URAs.

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 and recommendations (1-5) are as follows.

1) Research Steering committee:
The addition of an expert conversant in both experiments and mathematical modeling is strongly recommended.

Response to 1)

According to recommendation, we revised Research Steering Committee by adding three female researchers (Yachie (A), Shinobu, and Shimada) and two experts conversant in both experiments and mathematical modeling (Yachie (A) and Abugessaisa) (Figure 12).

This renewed Research Steering Committee has been managing PRIMe Joint Research Grant, PRIMe Retreat, and Progress Report Meeting as its major activities to foster research of fused disciplines. Please see also Section 1-2.

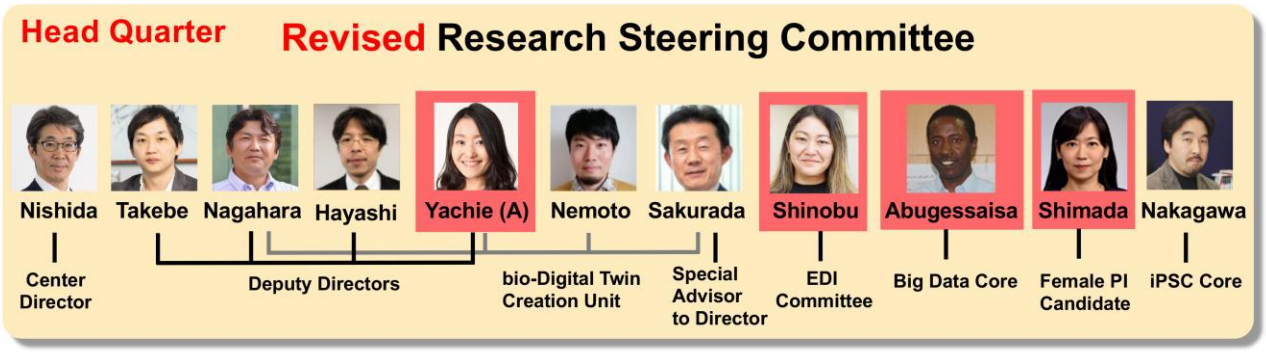

Figure 12. Revised Research Steering Committee

2) Bio-Digital twin creation unit and big data core:
This unit and core is a major step forward from last year. More PIs are needed to actively participate in mathematical modeling for each organoid system. Progress in research activities on the bio-Digital twin made by integrating experiments and mathematical modeling should be mainly presented in next year's site visit.

Response to 2)

The Figure 13 below shows the goals of what should be predicted by the mathematical models to create a bio-Digital twin for each organoid group's target disease. This Figure also shows the PRIMe PIs and researcher that should be actively involved in designing the predictive mathematical models. Please also refer to Section 1-1 about mathematical modeling in detail for each organoid group. At the FY2025 site visit, each group will make a presentation focusing on their progress in mathematical modeling.

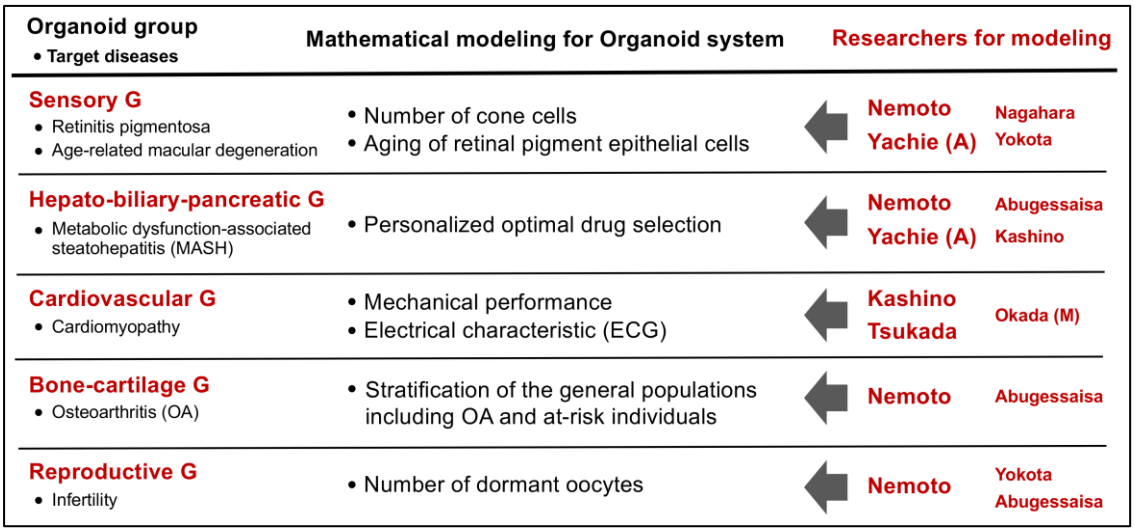

Figure 13. Mathematical modeling and responsible dry researchers for each group

3) A common framework for bio-Digital twin:
The research steering committee and the creation unit are to design a common framework for mathematical modeling and a roadmap for the human bio-Digital twin.

Response to 3)

As shown in Figure 14 below, predictive mathematical models are basically designed using clinical data. Each organoid group sets the goal of what should be predicted for the target disease (described above in Figure 13) and designs its own mathematical model to achieve their objectives (Section 1-1). Furthermore, by integrating micro experimental data using organoids, we challenge to construct a prediction model that includes macro to micro hierarchies and temporal prediction (human bio-Digital twin). Notably, it is necessary for each group to adopt different integration methods for integrating the macroscopic mathematical model with the microscopic data derived from organoid experiments (Figure 14, Right part).

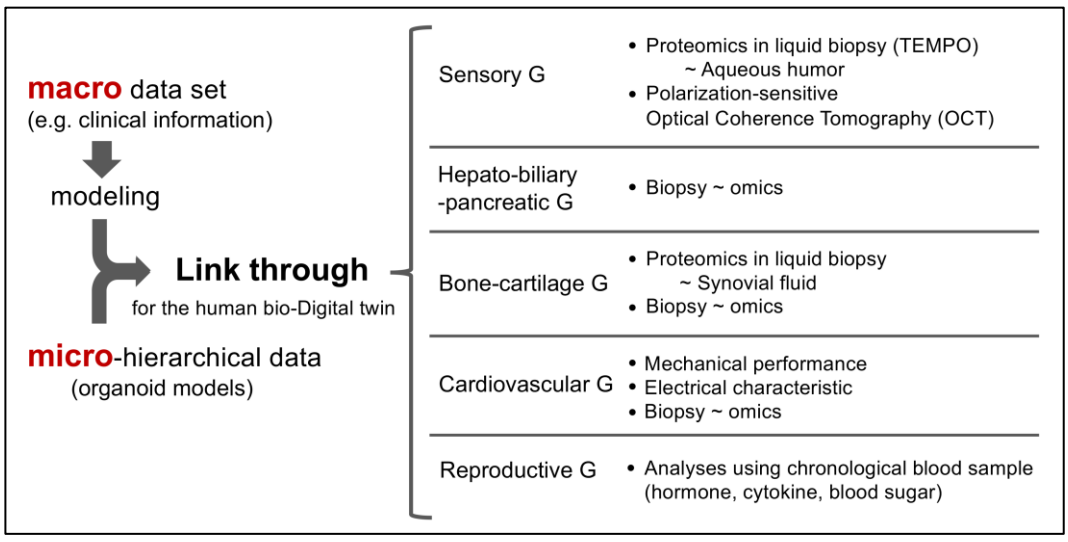

Figure 14. Common framework for human bio-Digital twin

4) Data standardization:
Standardized protocols for experimental and mathematical analyses should be set for cohesive integration into bio-Digital twins.

Response to 4)

The computational environment for generating bio-Digital twins is designed as a data-centric computing infrastructure that integrates the Osaka University D3 Center's storage service "ONION" with various computational resources. The configuration of the data management infrastructure and its data flow are illustrated in Figure 15. The metadata management system provides two main functions: one for collecting, storing, and managing the data with metadata, and another for data search using metadata. Data stored in ONION-object is saved using the encryption functionality provided by ONION-object. Regarding data usage, the infrastructure supports not only direct access to ONION-object but also enables high-speed access by using ONION-file as a cache. The framework of the metadata management system has been developed in collaboration with the Joint Research Laboratory for Integrated Infrastructure of High Performance Computing and Data Analysis of D3 Center at Osaka University. Furthermore, the logical structure of metadata has been designed through a case study involving research using ophthalmological data.

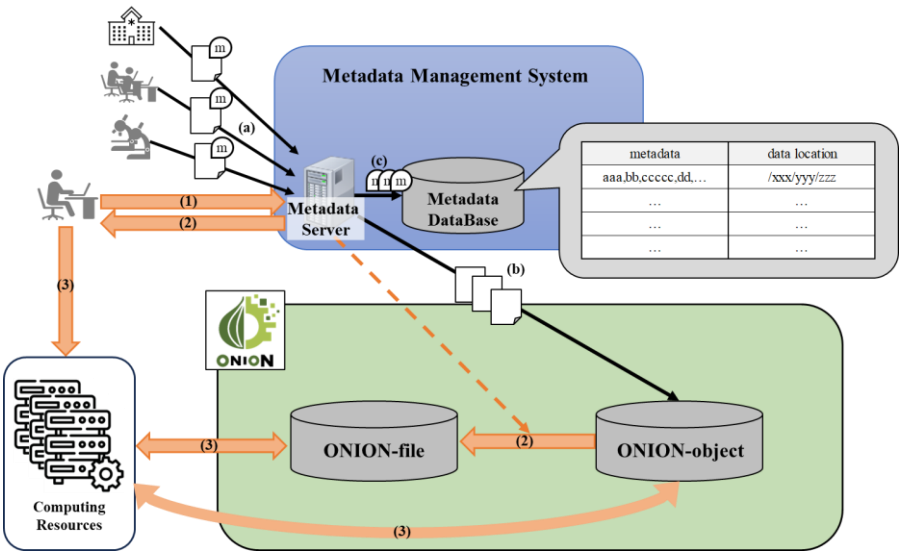

Figure 15. The configuration of the data management infrastructure and its data flow

Main category	Sub-category	Sub-subcategory
Experiments protocols	Protocols for sample collection & storage.	Standardization of ethical application Whole blood collection & storage protocol Tissue collection & storage protocol PBMC extraction protocol PBMC stocking protocol Tissue staining protocol Eye fluids (Protocol for protein extraction, storage, and shipment)
	Protocol for iPSC generation*	iPSC establishment and culture protocol iPSC quality tests protocol iPSC function tests protocol iPSC stocking protocol
	Protocol for iPSC derived organoid	Protocol for organoid development (Retina, liver, heart, ovary, cartilage, etc.)
	iPSC derived organoid quality test protocol	qPCR, scRNA-seq, Bulk RNA-seq
	Data analysis standards for Organoid data	RNA extraction protocol RNA quality control protocol Sequence library preparation protocol QC of the cDNA QC of the sequenced libraries Sequencing quality protocol QC protocol of the mapping Protocol for analysis of scRNA-seq Statistical analysis of scRNA-seq data Protocol for analysis of TEMPO
Protocols for Organoid data analysis and mathematical modeling	Standardized protocol for Statistical Analysis Standardized protocol mathematical & Machine Learning (ML) analysis	Predefined methods for hypothesis testing & subgroup analysis
		Microscopic image analysis protocol
		Mathematical Modeling Modeling Protocols (ODE, Stochastic, binary model, etc.) Model sharing (SBML, CellML, COMBINE) Integration of mathematical models Validation and verification protocol (in silico, in vitro)
		Numerical analysis standards
		ML analysis protocols Integration of multimodal data
Standardized protocols for data management, integration & sharing	FAIR principles ; Documentation of software versions, parameters, and scripts	Repositories File formats

*Standard protocol already developed and in use at the iPSC core facility.

Table 1. The set of protocol categories

WPI-PRIMe certainly recognizes the importance and requirements of standardized protocols for sample collection, iPSC generation, iPSC-derived organoid generation, processing, analyzing, and integration into bio-Digital twins. To meet these requirements, currently we identified a set of tentative categories of standard protocols covering experiments and modeling process. Some of the protocols have already developed and conducted in PRIMe. The set of protocol categories are listed on the Table 1 and standardized protocols for the experiments and modeling in detail will be presented during the FY2025 site visit.

5) International and gender balance:
PRIMe should continue its effort to meet the requirements for international and gender balance of PIs, postdocs, and students.

Response to 5)

To meet requirements for international and gender balance, in this FY, we had recruited one female PI (Yachie Ayako, also as one of Deputy Directors) and promoted one foreign researcher (Imad Abugessaisa) to PI. Four additional foreign researchers (Antonio Lucena-Cacace, Sean Johnson, Mohamed Marzouk Sobaih, and Thibaud Sotin) were recruited. Moreover, it was decided that one female foreign PI (Robabeh Rahimi), three foreign researchers (Nishad Bapatdhar, Dennis Bersenev, and Vikas Pandey), and one female researcher (Yukiko Himeno) will be hired in FY2025.

For the purpose of accepting postgraduate students in PRIMe, we completed procedures to allow PRIMe dedicated PIs (Nemoto and Abugessaisa) and Jr. PI (Mori) to participate in education and research as supervisors at the Graduate School of Medicine, Osaka University.

The following improvement activities to address this issue have been ongoing since last fiscal year. 1) Open-call female-only recruitment for several positions. 2) Innovative salary structure that exceeds the university regulations. 3) PRIMe Joint Research Grant.

These topics (International and gender balance) are regularly discussed in the **PRIMe EDI committee** to solicit ideas and summary of these ideas is promptly reported to the Executive Committee Meeting for further consideration. In addition, the **1st PRIMe EDI workshop** was held on 15th March 2025 during PRIMe Retreat in collaboration with the Center for Diversity & Inclusion of Osaka University with the aim of effectively improving the situation and raising the awareness of PRIMe researchers regarding international and gender balance (Please see Section 3-2 in detail).

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

1. Refereed Papers

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

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

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

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

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

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

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

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

A. WPI papers

[1. Original articles]

1 Ishikawa-Yamauchi, Y; Emori, C; Mori, H; Endo, T; Kobayashi, K; Watanabe, Y; Sagara, H; Nagata, T; Motooka, D; Ninomiya, A; Ozawa, M; Ikawa, M; Age-associated aberrations of the cumulus-oocyte interaction and in the zona pellucida structure reduce fertility in female mice. Communications Biology 7. (2024) DOI: 10.1038/s42003-024-07305-z

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8 Yamamoto, K; Namba, S; Sonehara, K; Suzuki, K; Sakaue, S; Cooke, NP; Higashiue, S; Kobayashi, S; Afuso, H; Matsuura, K; Mitsumoto, Y; Fujita, Y; et al.; Genetic legacy of ancient hunter-gatherer Jomon in Japanese populations. Nature Communications 15. (2024) DOI: 10.1038/s41467-024-54052-0

9 Kaneda-Nakashima, K; Shirakami, Y; Hisada, K; Feng, SF; Kadonaga, Y; Ooe, K; Watabe, T; Manabe, Y; Shimoyama, A; Murakami, M; Toyoshima, A; Haba, H; et al.; Development of LAT1-Selective Nuclear Medicine Therapeutics Using Astatine-211. International Journal of Molecular Sciences 25. (2024) DOI: 10.3390/ijms252212386

10 Osorio, RSA; Kosugi, Y; Nyström-Persson, JT; Mizuguchi, K; Natsume-Kitatani, Y; A modern multi-omics data exploration experience with Panomicon. Bioinformatics Advances 4. (2024) DOI: 10.1093/bioadv/vbae147

11 Kondo, Y; Saito, Y; Seki, T; Takakusagi, Y; Koyasu, N; Saito, K; Morimoto, J; Nonaka, H; Miyanishi, K; Mizukami, W; Negoro, M; Elhelaly, AE; et al.; Directly monitoring the dynamic in vivo metabolisms of hyperpolarized 13C-oligopeptides. Science Advances 10. (2024) DOI: 10.1126/sciadv.adp2533

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Digital Health 3. (2024) DOI: 10.1371/journal.pdig.0000273

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29 Maeda, S; Sakai, S; Takabatake, Y; Yamamoto, T; Minami, S; Nakamura, J; Namba-Hamano, T; Takahashi, A; Matsuda, J; Yonishi, H; Matsui, S; Imai, A; et al.; MondoA and AKI and AKI-to-CKD Transition. Journal of the American Society of Nephrology 35. (2024) DOI: 10.1681/ASN.0000000000000414

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32 Inukai, M; Sato, H; Miyanishi, K; Negoro, M; Kagawa, A; Hori, Y; Shigeta, Y; Kurihara, T; Nakamura, K; Cocrystalline Matrices for Hyperpolarization at Room Temperature Using Photoexcited Electrons. Journal of the American Chemical Society 146. (2024) DOI: 10.1021/jacs.4c01050

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36 Sepulveda-Rincon, LP; Wang, YF; Whilding, C; Moyon, B; Ojarikre, OA; Maciulyte, V; Hamazaki, N; Hayashi, K; Turner, JMA; Leitch, HG; Determining the potency of primordial germ cells by injection into early mouse embryos. Developmental Cell 59. (2024) DOI: 10.1016/j.devcel.2024.01.022

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41 Hasegawa, M; Miki, K; Kawamura, T; Sasozaki, IT; Higashiyama, Y; Tsuchida, M; Kashino, K; Taira, M; Ito, E; Takeda, M; Ishida, H; Higo, S; et al.; Gene correction and overexpression of TNNI3 improve impaired relaxation in engineered heart tissue model of pediatric restrictive cardiomyopathy. Development Growth & Differentiation 66. (2024) DOI: 10.1111/dgd.12909

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[2. Review articles]

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48 Naito, T; Okada, Y; Genotype imputation methods for whole and complex genomic regions utilizing deep learning technology. Journal of Human Genetics 69. (2024) DOI: 10.1038/s10038-023-01213-6

[3. Proceedings]

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50 Quach, S; Lewis, K; Iwasawa, K; Milton, Y; Guillot, A; Ahmed, YA; Takebe, T; Behncke, RY; Rezvani, M; SAT-180 Targeting neutrophil injury-pathways and fibrogenesis in non-parenchymal immune tissue-like liver organoids generated from human induced pluripotent stem cells. Journal of Hepatology 80. S302-S303. (2024) DOI: 10.1016/s0168-8278(24)01071-7

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[4. Other English articles]

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DOI: 10.1038/s41562-024-02019-y

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B. WPI-related papers

[1. Original articles]

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58 Imaoka, S; Kashiyama, N; Yoshioka, D; Saito, S; Kawamura, T; Kawamura, A; Matsuura, R; Misumi, Y; Toda, K; Miyagawa, S; Clinical outcomes of modified left ventricular assist device driveline management. Journal of Artificial Organs. (2024) DOI: 10.1007/s10047-024-01482-8

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60 Watanabe, T; Kawamura, T; Harada, A; Taira, M; Yoshioka, D; Shimamura, K; Watabe, T; Shimosegawa, E; Ueno, T; Miyagawa, S; Human induced pluripotent stem cell-derived cardiomyocyte patches ameliorate right ventricular function in a rat pressure-overloaded right ventricle model. Journal of Artificial Organs. (2024) DOI: 10.1007/s10047-024-01479-3

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65 Kanai, M; Sakimoto, S; Suzue, M; Shiozaki, D; Okazaki, T; Shiraki, A; Nishida, K; Maruyama, K; Usui, S; Sato, S; Matsushita, K; Maeno, T; et al.; Long-term risk factors for poor visual outcomes in patients with epiretinal membrane and open-angle glaucoma: a retrospective study. Scientific Reports 14. (2024) DOI: 10.1038/s41598-024-80020-1

66 Koyama, J; Morise, M; Furukawa, T; Oyama, S; Matsuzawa, R; Tanaka, I; Wakahara, K; Yokota, H; Kimura, T; Shiratori, Y; Kondoh, Y; Hashimoto, N; et al.; Artificial intelligence-based personalized survival prediction using clinical and radiomics features in patients with advanced non-small cell lung cancer. BMC Cancer 24. (2024) DOI: 10.1186/s12885-024-13190-w

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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 2024 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
Mar. 19, 2025	Vivian Hwa	Human IGF1R Insufficiency: Insights into Human Growth and Development Using Pluripotent Stem Cell Models	The 2025 Gordon Research Conference on IGF and Insulin System in Physiology and Disease, CA, USA
Jan. 16, 2025	Ai Shinobu	Cross-scale computational analysis of EGFR mutations in lung cancer through molecular dynamics and mathematical modeling	IPR International Conference 2025, Hyogo, Japan
Dec. 3, 2024	Makoto Negoro	Quantum Hyperpolarized MRI and Quantum Controller for Spin and Superconducting Qubits	Impurity Spins for Quantum Information Science and Technologies, Okinawa, Japan
Nov. 13, 2024	Takanori Takebe	Organoid guided Hepato-Biliary-Pancreatic Bioengineering (Keynote)	The International Conference on Biofabrication 2024, Fukuoka, Japan
Nov. 8, 2024	Yoshikatsu Kanai	Pharmacology of amino acid transporter LAT1 (SLC7A5): Roles in pathogenesis and targeting for drug discovery	The 25th Korea-Japan Joint Seminar on Pharmacology (KJJSP), Jeju Island, Korea
Oct. 9, 2024	Yukinori Okada	Statistical genetics elucidates disease biology, personalized medicine, and drug discovery	The Nature Conference on Human Genetics and Genomics: Maximizing Power to Address Complexity and Human Health, Beijing, China
Jul. 17, 2024	Katsuhiko Hayashi	State-Of-The-Art-Lecture: Reconstitution of Germ Cell Lineage and Gonadal Environment Using Pluripotent Stem Cells	2024 57th Annual Meeting – Society for the Study of Reproduction, Dublin, Ireland
Jun. 13, 2024	Kohji Nishida	The Human Metaverse Medicine Envisioned by PRIMe	The 27th Science in Japan Forum, Washington DC, USA
May 16, 2024	Takanori Takebe	Complementing Human Organoids for Vascular Discovery (Keynote)	Vascular Discovery 2024, Chicago, USA
Apr.19, 2024	Katsuhiko Hayashi	In Vitro Gametogenesis: Advancing Understanding and Application	UBC SBME Seminar, Vancouver, Canada

3. Major Awards

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

Date	Recipient's name	Name of award
Mar. 26, 2025	Yukinori Okada	Japanese Society of Allergology, *Allergology International* Sanofi Award（日本アレルギー学会 サノフィ優秀論文賞 Allergology International 誌部門）
Mar. 14, 2025	Yukinori Okada, Qingbo Wang, Ryuya Edahiro	The 2024 RIKEN EIHO Award (RIKEN Significant Achievement Award)
Feb. 19, 2025	Masahiro Morita	Cancer Prevention and Research Institute of Texas, Individual Investigator Research Awards
Dec. 17, 2024	Kenji Kamimoto	17th Inoue Science Research Award
Sep. 27, 2024	Nozomu Yachie	14th Frontier Salon Nagase Prize, Grand Prize
Sep. 12, 2024	Takanori Takebe, Ryo Okabe, Toyofumi F. Chen-Yoshikawa, Yosuke Yoneyama, Yuhei Yokoyama, Satona Tanaka, Akihiko Yoshizawa, Wendy L. Thompson, Gokul Kannan, Eiji Kobayashi, Hiroshi Date	2024 Ig Nobel Prize in physiology
Aug. 22, 2024	Makoto Negoro, QuEL, Inc.	MEXT Minister's Award of the 2024 Award for Academic Startups
Jun. 12, 2024	Katsuhiko Hayashi	The Tokyo Academy of Physics Award Academic Year 2024, 7th Award Recipient
May 18, 2024	Hideto Mori	Funai Information Technology Award for Young Researchers
Apr. 16, 2024	Takanori Takebe	1st KOBE PRIZE Young Investigator Awards

Appendix 2　FY 2024 List of Principal Investigators

NOTE:

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

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

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

	<Results at the end of FY2024>					Principal Investigators Total: 20	
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	62	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	38	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 Hajime Nagahara	51	Professor,D3 Center, Osaka Univerisity	PhD,Computer vision, machine learning	70	Nov.11,2022	stays at the center about 15 times a month	
Noriyuki Tsumaki	60	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	66	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)	
Katsuhiko Hayashi	53	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	57	Professor,Graduate School of Medicine, Osaka University	MD, PhD,Cardiovascular surgery, Regenerative medicine, Medical AI	80	Nov.11,2022	usually stays at the center	

Takahiro Nemoto	38	Associate Professor,Premium Research Institute for Human Metaverse Medicine, Osaka University	PhD,Data science, Algorithm development	100	Nov.11,2022	usually stays at the center	
Ai Shinobu	43	Associate Professor,Premium Research Institute for Human Metaverse Medicine, Osaka University	PhD,Molecular dynamics, simulation	100	Nov.11,2022	usually stays at the center	
Yukinori Okada	44	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	
Imad Abugessaisa	51	Professor,Premium Research Institute for Human Metaverse Medicine, Osaka University	PhD,Computer Science	100	Dec.1,2024	usually stays at the center	
Yoshie Harada	65	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	
Makoto Negoro	42	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	
Astuo Kishimoto	54	Director, D3 Center, Osaka University	PhD,ELSI, Risk assessment	30	Nov.11,2022	stays at the center about 7 times a month	
Hideo Yokota	56	Team Leader, Advanced Photonics Center, Riken	PhD,Image Processing	20	Nov.11,2022	joins event or videoconference from another institution occasionally	
Kunio Kashino	57	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	
Elisa Domínguez-Hüttinger	40	Research Associate,National Autonomous University of Mexico	PhD,Bioengineering	8	Nov.11,2022	joins event or videoconference from another institution occasionally	

Ayako Yachie	45	President and CEO, SBX BioSciences, Inc., SBI	PhD,Media and Governance	10	Feb.1,2025	joins event or videoconference from another institution occasionally	
Shingo Tsukada	59	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	
Nozomu Yachie	44	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	

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

Principal investigators unable to participate in project in FY 2024

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

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) Ayako Yachie (45)

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

Guest Professor, PRIMe, Osaka University
President & CEO, SBX BioSciences, Inc. (CANADA)
VP Research Service, SBX Corporation (JAPAN)
Senior Scientist, The Systems Biology Institute (JAPAN)

Academic degree and specialty

Ayako Yachie Ph.D. Media & Governance (Systems Biology Program)

Effort **10%**

* 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

2024-present **Guest Professor**, PRIMe, Osaka University
2023-present **Vice president of Research service,** SBX Corporation, Japan
2020-present President & CEO, SBX BioSciences, Inc., Canada
2018-present **Senior Scientist**, The Systems Biology Institute, Japan
2019-2023 Director of Research, SBX Corporation, Japan
2018-2019 Deputy Director of Research, SBX Corporation, Japan
2016-2018 **Adjunct Professor (Cross-appointment)**, Institute of Biomaterials and Biomedical Engineering (IBBME), University of Toronto, Canada
2015-2018 Researcher, The Systems Biology Institute, Japan
2011-2015 **Postdoctoral research fellow**, Institute of Biomaterials and Biomedical Engineering (IBBME), University of Toronto, Canada
2007-2012 **Research Assistant Professor**, School of Medicine, Department of Biochemistry, Keio University, Japan
2007 **Ph.D. System Biology Program**, Graduate School of Media and Governance, Keio University, Japan (Supervisor: Prof. Masaru Tomita)
2004 **M.S. System Biology Program**, Graduate School of Media and Governance,Keio University, Japan (Supervisor: Prof. Masaru Tomita)

Achievements and highlights of past research activities

She dedicated her efforts on developing methodologies and models for cellular metabolic simulations in her PhD. At the Stem Cell Bioengineering Lab in University of Toronto, she developed a methodology to predict stem cell state transitions with a stochastic Boolean model by representing the Signal-Gene Regulatory Network derived from large-scale gene expression data, and validated the model-driven hypothesis. After returning to Japan, in industry settings, she led numerous joint research as well as software and platform development projects with various companies, including pharmaceutical and healthcare companies. Specializing in the integration of a wide range of information technologies, including mathematical modeling, deep learning, machine learning, generative AI including large language models, she builds predictive models utilizing various types of data such as molecular quantitative data, text data, image/video data, sensor data, and real-world data.

Achievements

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

a) Recipient of international awards: none
b) Member of a scholarly academy in a major country: none

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field: none
d) Editor of an international academic journal: none
e) Peer reviewer for an overseas competitive research program (etc.): none

(2) Receipt of major large-scale competitive funds (over the past 5 years)
None

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations) (Citations are referenced using data from Web of Science)

1. Akiyoshi R, Hase T, Sathiyananthavel M, Ghosh S, Kitano H, **Yachie A.** Noninvasive, label-free image approaches to predict multimodal molecular markers in pluripotency assessment. *Sci Rep*. Jul 9;14(1):15760, 2024. Citations: 1.
2. Takeshi Hase, Samik Ghosh, Ken-ichi Aisaki, Satoshi Kitajima, Jun Kanno, Hiroaki Kitano, **Ayako Yachie**. DTox: A Deep neural network-based in visio lens for large scale Toxicogenomics data. *J Toxicol Sci*. 49(3):105-115, 2024. Citations:2.
3. Shuo Jiang, Daniel Evans-Yamamoto, Dennis Bersenev, Sucheendra K Palaniappan, **Ayako Yachie-Kinoshita.** ProtoCode: Leveraging Large Language Models for Automated Generation of Machine-Readable Protocols from Scientific Publications. *SLAS Technology.* Apr 24:100134, 2024. Citations: 2.
4. Hitomi Sano, Anton Kratz, Taiko Nishino, Haruna Imamura, Yuki Yoshida, Noriaki Shimizu, Hiroaki Kitano, **Ayako Yachie**. Nicotinamide mononucleotide (NMN) alleviates the poly (I: C)-induced inflammatory response in human primary cell cultures. *Sci Rep.* 13: 11765, 2023. Citations: 6.
5. **Yachie-Kinoshita, A.**, Onishi, K., Ostblom, J., Nakanishi, M., Posfai, E., Rossant, J., and Zandstra, PW. Modeling signaling-dependent pluripotent cell states with Boolean logic to predict cell fate transitions. *Mol Syst Biol*., 14:e7952, 2018. Citations: 36.

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

-none

Appendix 2a Biographical Sketch of a New Principal Investigator

Name (Age) Imad Abugessaisa（51）

Affiliation and position (Position title, department, organization, etc.)
Specially Appointed Professor, WPI-PRIMe, Osaka University

Academic degree and specialty

2008 PhD Computer Science, Linköpings universitet, Sweden

2005 MSc Geoinformatics, Linköpings universitet, Sweden

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

Research and education history

2024-present Specially Appointed Professor (full time), WPI-PRIMe, Osaka University, Japan
2020-2024 Senior research scientist, RIKEN, Japan
2014-2020 Senior research scientist, RIKEN, Japan
2012-2014 Assistant Professor, Karolinska Institutet, Sweden
2010-2012 Post Doctoral Researcher, Karolinska Institutet, Sweden

Achievements and highlights of past research activities

1. Created an integrated expression atlas of miRNAs and their promoters in human and mouse in primary mammalian cells, establishing a foundation for detailed analysis of miRNA expression patterns and transcriptional control regions. de Rie D, **Abugessaisa I**, et al., ***Nat Biotechnol.*** *35(9):872.* 2017 [PMID: 28829439].
2. Developed a reference transcription start sites (TSSs) for human and mouse. refTSS consists of genomic coordinates of TSS peaks, their gene annotations, quality check results, and conservation. **Abugessaisa I**, et al., ***J Mol Biol.*** *431(13):2407-2422.* 2019**.** [PMID: 31075273].
3. Developed SkewC, a novel quality-assessment tool, to identify skewed cells in scRNA-seq experiments. **Abugessaisa I**, et al, *iScience 25(2).* 2022. [PMID: 35146392].
4. Contributed to the development of FANTOM5 sample annotations and web resources. **Abugessaisa, I.**, et al, ***Nucleic Acids Research*** *49(D1);D892-D898.* 2021. [PMID: 33211864].
5. Development of single-cell RNA-seq database for human and mouse. Abugessaisa I, et al., ***Nucleic Acids Research*** *46(D1); D781-D787.* 2018. [PMID: 29045713]

Achievements

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

a) Recipient of international awards: none
b) Member of a scholarly academy in a major country: none
c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field:
- European Society for Translational Medicine conference October 2013, Mondorf Parc Hotel, Mondorf-les-Bains, Grand-Duchy of Luxembourg.
- Invited speaker International Mammalian Genome Society (2015), Yokohama, JAPAN
- The 39th Annual Meeting of the Molecular Biology Society of Japan (2016), Yokohama, JAPAN
- Invited lecture for graduate students in PhD program in Genomics and Precision Medicine & PhD in Biological and Biomedical Sciences, College of Health and Life Sciences, HBKU, Qatar (2019).
- Guest lecturer, PhD course in the application of single-cell genomic analysis in research of early embryo development; EU-funded MATER project for doctoral education at Karolinska Institute, (2022).

d) Editor of an international academic journal: none
e) Peer reviewer for an overseas competitive research program (etc.): none

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

1. GHIT Fund (Global Health Innovative Technology Fund), JAPAN,2020-22 (**PI**) ¥28,593,793
2. JSPS, KAKENHI, 2020-24 (**PI**) ¥4,290,000
3. GHIT Fund (Global Health Innovative Technology Fund)**,** JAPAN, 2024-26 (**PI**) *****¥ 60,000,000 ** Awarded but not contracted yet.*

(3) Major publications (Titles of major publications, year of publication, journal name, number of citations) (Citations are referenced using data from Web of Science)

Peer-reviewed journals: Original papers

1. **Abugessaisa I**, Hasegaw a A, Noguchi S, Cardon M, Watanabe K, Takahashi M, Suzuki H, Katayama S, Kere J, Kasukawa T. SkewC: Identifying cells with skewed gene body coverage in single-cell RNA sequencing data. *iScience* Jan 15;25(2):103777. 2022. doi: 10.1016/j.isci.2022.103777. [**PMID**: 35146392]. Citations: 4(10)
2. Woogeng IN, Kaczkowski B, **Abugessaisa I**, Hu H, Tachibana A, Sahara Y, Hon CC, Hasegawa A, Sakai N, Nishida M, Sanyal H, Sho J, Kajita K, Kasukawa T, Takasato M, Carninci P, Maeda A, Mandai M, Arner E, Takahashi M, Kime C. Inducing human retinal pigment epithelium-like cells from somatic tissue. *Stem Cell Reports* Feb 8;17(2):289-306. 2022. doi: 10.1016/j.stemcr.2021.12.008. Epub 2022. Jan 13. [**PMID**: 35030321]. Citations: 6(10)
3. Gomez-Cabrero, D., Walter, S., **Abugessaisa, I.**, et al., FRAILOMIC initiative(2021), A robust machine learning framework to identify signatures for frailty: a nested case-control study in four aging European cohorts. *Geroscience* 43(3), 2021. doi: org/10.1007/s11357-021-00334-0 [**PMID**: 33599920]. Citations: 35. (44)
4. **Abugessaisa, I.**, Ramilowski, J., Lizio, M., Severin, J., Hasegawa, A., Harshbarger, J., Kondo, A., Noguchi, S., Yip, C., Ooi, J., Tagami, M., Hori, F., Agrawal, S., Hon, C., Cardon, M., Ikeda, S., Ono, H., Bono, H., Kato, M., Hashimoto, K., Bonetti, A., Kato, M., Kobayashi, N., Shin, J.W, de Hoon, M., Hayashizaki, Y..; Carninci, P.; Kawaji, H.; Kasukawa, T.,(2021), FANTOM enters 20th year: expansion of transcriptomic atlases and functional annotation of non-coding RNAs. *Nucleic Acids Research* 49, D1 (D892–D898), 8 January 2021. doi: org/10.1093/nar/gkaa1054. [**PMID**: 33211864]. Citations: 64 (101)
5. **Abugessaisa, I***., Noguchi, S*., Hasegawa, A., Kondo, A., Kawaji, H., Carninci, P., Kasukawa, T., refTSS: A reference dataset for human and mouse transcription start sites. *Journal of Molecular Biology* 431(13):2407-2422, 2019. [**PMID:** 31075273]. Citations: 55. (99)
6. Quistrebert, J., Hässler, S., Bachelet,D., Mbogning,C., Musters, A., Tak,P.P., Wijbrandts,C.A., Herenius,M., Bergstra, S.T., Akdemir,G., Johannesson,M., Combe, B., Fautrel,B., Chollet-Martin, S., Gleizes,A., Donnellan,N., Deisenhammer,F., Davidson,J., Hincelin-Mery, A., Dönnes,P., Fogdell-Hahn,A., De Vries, N., Huizinga, T., **Abugessaisa,I.**, Saevarsdottir,S., Hacein-Bey-Abina, S., Pallardy, M., Broët,P., Mariette, X., on behalf of the ABIRISK Consortium, (2018), Incidence and risk factors for adalimumab and infliximab anti-drug antibodies in rheumatoid arthritis: a European retrospective multicohort analysis. *Seminars in Arthritis and Rheumatism* 48(6), 2019. [**PMID:** 30420245]. Citations: 47. (72)
7. Lizio, M., **Abugessaisa, I.**, Noguchi, S., Kondo, A., Hasegawa, A., Hon, C., de Hoon, M., Severin, J., Oki, S., Hayashizaki, Y., Carninci, P., Kasukawa, T., Kawaji, H., Update of the FANTOM web resource: expanded resource of transcriptome atlas. *Nucleic Acids Research* 47(D1), 2019. [**PMID:** 30407557]. Citations: 162. (233)
8. **Abugessaisa I**, Noguchi S, Böttcher M, Hasegawa A, Kouno T, Kato S, Tada Y, Ura H, Abe K, Shin JW, Plessy C, Carninci P, Kasukawa T. SCPortalen: human and mouse single-cell centric database.

Nucleic Acids Res 46(D1):D781-D787, 2018. doi: 10.1093/nar/gkx949. [**PMID**: 29045713]. Citations: 41. (59)

9. **Abugessaisa I**., Noguchi S., Hasegawa A., Harshbarger J., Kondo A., Lizio M., Severin J., Carninci P., Kawaji H. and Kasukawa T. FANTOM5 CAGE profiles of human and mouse reprocessed for GRCh38 and GRCm38 genome assemblies. *Nat scientific data* 4. 2017. [**PMID**: 28850105]. Citations: 56. (75)
10. de Rie D., **Abugessaisa I**., Alam T., et al., An integrated expression atlas of miRNAs and their promoters in human and mouse. *Nature Biotechnology* 35(9) 872, 2017. [**PMID:** 28829439]. Citations: 397. (622)
11. Hon CC, Ramilowski JA, Harshbarger J, Bertin N, Rackham OJ, Gough J, Denisenko E, Schmeier S, Poulsen TM, Severin J, Lizio M, Kawaji H, Kasukawa T, Itoh M, Burroughs AM, Noma S, Djebali S, Alam T, Medvedeva YA, Testa AC, Lipovich L, Yip CW, **Abugessaisa I**, Mendez M, Hasegawa A, Tang D, Lassmann T, Heutink P, Babina M, Wells CA, Kojima S, Nakamura Y, Suzuki H, Daub CO, de Hoon MJ, Arner E, Hayashizaki Y, Carninci P, Forrest AR,. An atlas of human long non-coding RNAs with accurate 5' ends. *Nature* 543 (7644) 199, 2017. [**PMID:** 28241135]. Citatioins: 721. (1066)
12. Lizio. M, Harshbarger. J, **Abugessaisa. I**, Noguchi. S, Kondo. A, Severin. J, Mungall. C, Arenillas. D, Mathelier. A, Medvedeva. YA, et al. (2017): Update of the FANTOM web resource: high resolution transcriptome of diverse cell types in mammals. *Nucleic Acids Res* 45(D1), 73D737-D743. 2017. [**PMID:** 27794045]. Citations: 83. (113)
13. **Abugessaisa, I**., H. Shimoji, S. Sahin, A. Kondo, J. Harshbarger, M. Lizio, Y. Hayashizaki, P. Carninci, F. consortium, A. Forrest, T. Kasukawa and H. Kawaji. FANTOM5 transcriptome catalog of cellular states based on Semantic MediaWiki. *Database,* 2016. [**PMID:** 27402679]. Citations: 38 (84)
14. Arner, E., C. O. Daub, K. Vitting-Seerup, et al. (2015). Transcribed enhancers lead waves of coordinated transcription in transitioning mammalian cells. *Science* 347(6225), 2015. DOI: 10.1126/Science.1259418 [**PMID:** 25678556]. Citations:426. (640)
15. Lizio, M., J. Harshbarger, H. Shimoji, J. Severin, T. Kasukawa, S. Sahin, **I. Abugessaisa,** S. Fukuda, F. Hori, S. Ishikawa-Kato, C. Mungall, E. Arner, J. Baillie, N. Bertin, H. Bono, M. de Hoon, A. Diehl, E. Dimont, T. Freeman, K. Fujieda, W. Hide, R. Kaliyaperumal, T. Katayama, T. Lassmann, T. Meehan, K. Nishikata, H. Ono, M. Rehli, A. Sandelin, E. Schultes, P. 't Hoen, Z. Tatum, M. Thompson, T. Toyoda, D. Wright, C. Daub, M. Itoh, P. Carninci, Y. Hayashizaki, A. Forrest and H. Kawaji. Gateways to the FANTOM5 promoter level mammalian expression atlas. *Genome Biology* 16, 2015. [**PMID:** 25723102]. Citations: 580. (930)
16. Gomez-Cabrero, D., **Abugessaisa, I.,** Maier, D., Teschendorff, A., Merkenschlager, M., Gisel, A., Ballestar, E., Bongcam-Rudloff, E., Conesa A., and Tegnér, J., Data integration in the era of omics: current and future challenges. *BMC Systems Biology* 8, 2014. [**PMID:** 25032990]. Citations: 249. (528).
17. **Abugessaisa*, I**., et al., Iron regulatory pathways differentially expressed during *Madurella mycetomatis* grain development in *Galleria mellonella*, 2025. **(*Accepted Nature Communications*).**
    * Corresponding author

Editor of a textbook

1. **Abugessaisa, I**., Kasukawa, T. (eds) Practical Guide to Life Science Databases. Springer, Singapore. https://doi.org/10.1007/978-981-16-5812-9_9 (200)

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

Media coverage & press release of my research

1. Medicinsk Vetenskap , T-MedFusion project interview - Medicinsk Vetenskap nr 1 2012,
2. RIKEN press release, Continuously extensible database provides insights into our cells
3. RIKEN press release, FANTOMデータベースの最新アップデートーゲノム科学に貢献してきた20年にわたる基盤的活動ー

Appendix 3-1 FY 2024 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

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

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

Special mention

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

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	
The Systems Biology Institute	Ayako Yachie	Newly installed

< 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		

1-3. Postdoctoral Positions through Open International Solicitations

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

Fiscal year	Number of applications	Number of selections
FY 2024	2	1
	〈 1 , 50 %〉	〈 0 , 0 %〉

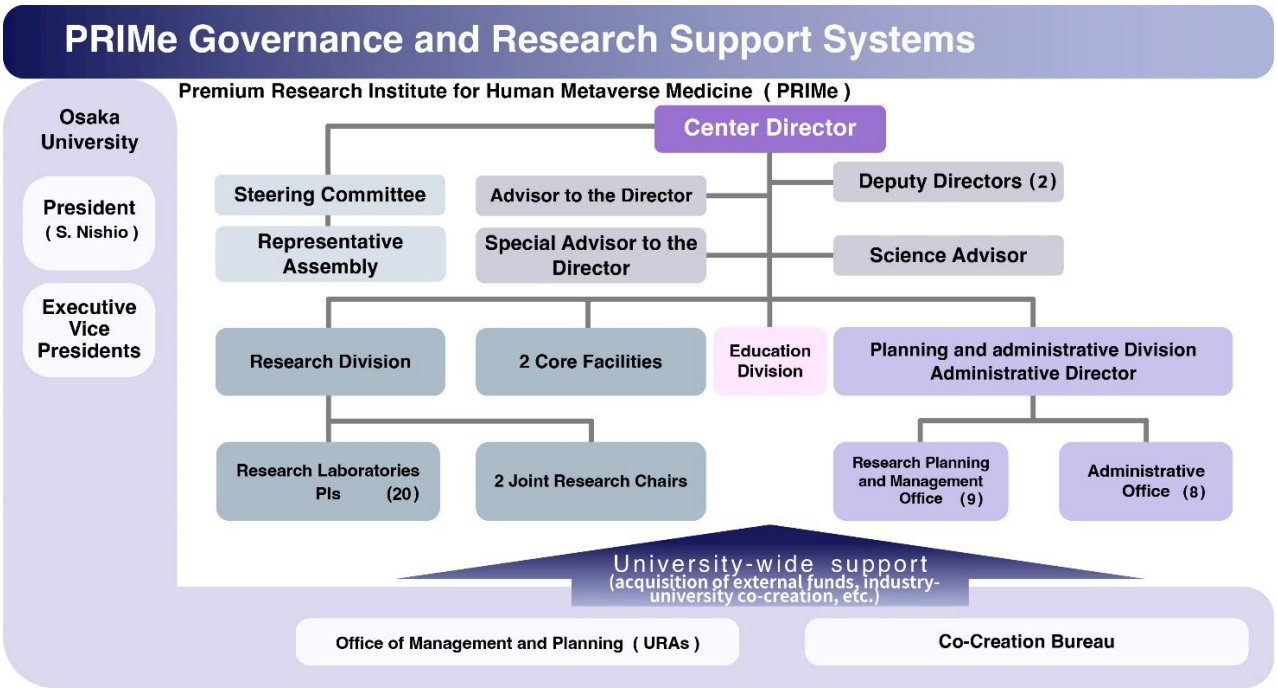
2. Holding international research meetings

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

FY 2024: 1 meetings	
Major examples (meeting titles and places held)	Number of participants
Osaka University Symposium, 3rd WPI-PRIMe International Symposium -Towards Patient Bio-Digital Twin-, Osaka International Convention Center, Osaka, Japan	From domestic institutions:106 From overseas institutions: 8

3. Diagram of management system

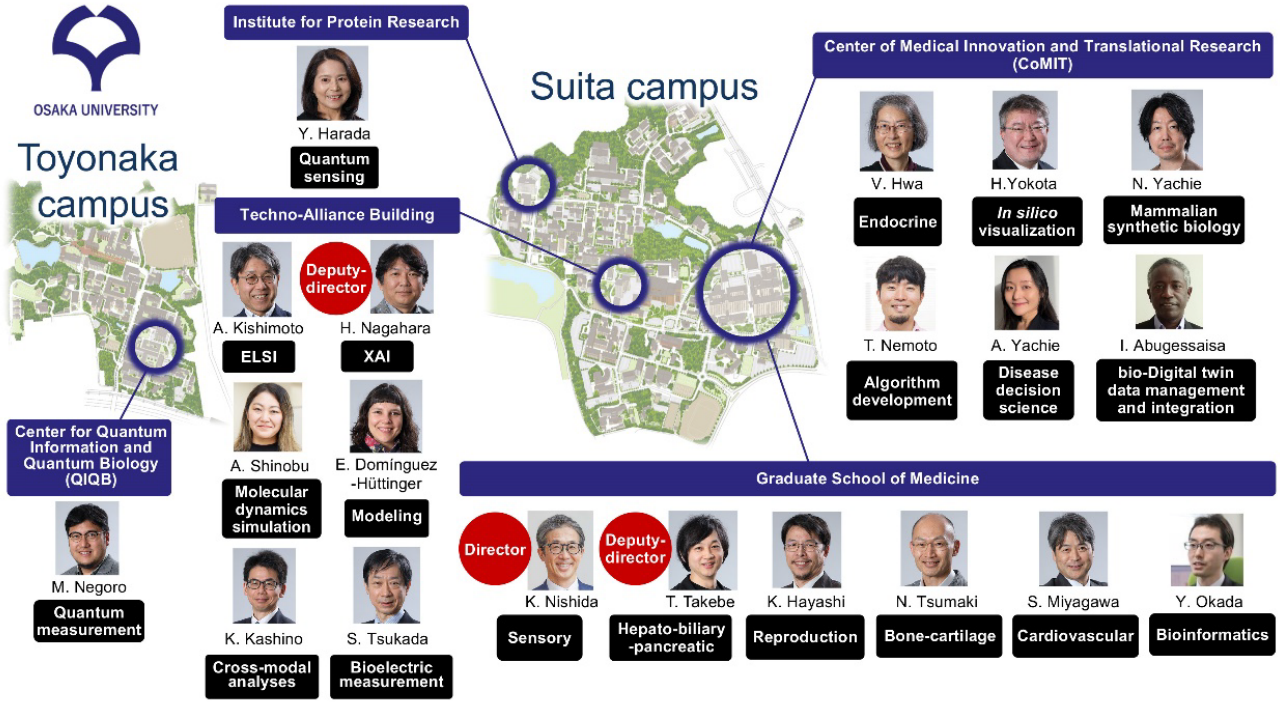
- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such 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).



Center Director:	Kohji Nishida
Deputy Director:	Takanori Takebe, Hajime Nagahara
Administrative Director:	Takefumi Doi
Advisor to the Director:	Katsuhiko Hayashi
Special Advisor to the Director:	Kazuhiro Sakurada, Hiromichi Mizuno
Science Advisor:	Mariko Okada
PIs:	Kohji Nishida, Takanori Takebe, Hajime Nagahara, Noriyuki Tsumaki, Vivian Hwa, Katsuhiko Hayashi, Shigeru Miyagawa, Takahiro Nemoto, Ai Shinobu, Yukinori Okada, Imad Abugessaisa, Yoshie Harada, Makoto Negoro, Astuo Kishimoto, Hideo Yokota, Kunio Kashino, Elisa Domínguez- Hüttinger, Ayako Yachie, Shingo Tsukada, Nozomu Yachie
Research Planning and Management Office:	Ryu Imamura, Maki Tani, Haniye Bidadi, Chenlu Cui, Takako Igi, Hisano Nakajima, Reiko Tanaka, Emi Maeda, Kana Okuno
Administrative Office:	Shingo Murakami, Chisato Nambu, Aya Hirono, Mari Sasaki, Hiroko Umeda, Natsumi Oonishi, Saori Hayakawa, Tomoko Takahashi

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 FY2024

Total: 506,195,756 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	Acceleration Program of R&D and Implementation for Regenerative Medicine and Cell and Gene Therapy	Kohji Nishida	59,500,000
AMED	Practical Research Project for Rare / Intractable Diseases	Kohji Nishida	47,000,000
AMED-CREST	Advanced Research & Development Programs for Medical Innovation	Takanori Takebe	321,440,000

Appendix 3-1a FY 2024 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

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

a) Principal Investigators

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

(number of persons)

	At the beginning of project	At the end of FY 2024	Final goal (Date: November, 2027)
Researchers from within the host institution	11	14	13
Researchers invited from overseas	4	3	4
Researchers invited from other Japanese institutions	5	3	3
Total principal investigators	20	20	20

b) Total members

	At the beginning of project		At the end of FY 2024		Final goal (Date: November, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	20		55		61	
Overseas researchers	3	15	15	27	19	31
Female researchers	5	25	12	22	18	30
Principal investigators	20		20		20	
Overseas PIs	3	15	3	15	4	20
Female PIs	5	25	5	25	6	30
Other researchers	0		29		36	
Overseas researchers	0	#DIV/0!	8	28	11	31
Female researchers	0	#DIV/0!	4	14	10	28
Postdocs	0		6		5	
Overseas postdocs	0	#DIV/0!	4	67	4	80
Female postdocs	0	#DIV/0!	3	50	2	40
Research support staffs	7		12		9	
Administrative staffs	3		17		17	
Total number of people who form the "core" of the research center	30		84		87	

	At the beginning of project		At the end of FY 2024		Final goal (Date: November, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students			11		21	
Employed			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	31	16
	Principal investigators: 16	103	64
	Other researchers: 31	168	168
	Research support staff: 5	38	38
	Administrative staff: 22	88	63
	Subtotal	428	349
Project activities	Research startup cost:4	8	8
	Preperation costs for new laboragories	21	21
	Rental fees for facilities / Cost of utilities	72	28
	International symposium related cost :1	4	3
	Costs of consumable for office and others	36	35
	Public Relations cost	2	2
	Core Facility operational cost	33	33
	Subtotal	176	130
Travel	Domestic travel costs	9	8
	Overseas travel costs	18	18
	Travel cost for scientists on transfer domestic: 2, overseas: 2	2	2
	Subtotal	29	28
Equipment	Spatial transcriptomics analyzer	109	109
	Equipment for iPS Cell Core Facilities	42	42
	Basic equipment	43	32
	Equipment for Big Data and Computing Core Facilities	10	10
	Subtotal	204	193
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	0	0
	KAKENHI	86	0
	Commissioned research projects, etc.	333	0
	Joint research projects	65	0
	Ohers (donations, etc.)	22	0
	Subtotal	506	0
Total		1343	700

Costs (Million yens)

WPI grant in FY 2024	700
Costs of establishing and maintaining facilities	8
Repairing facilities	8
Techno Alliance Bldg, 143㎡	4
Center for Medical Research and Education Building, 423㎡	2
CoMIT Bldg, 278㎡	2
Costs of equipment procured	198
Equipment for PI's labo	
Microscope(1)	1
Building fixtures(4)	4
Spatial transcriptomics analyzer(1)	109
iPS Cell Core Facility Equipment	42
PCR System(2)	
Thermomixture(1)	
Spectrophotometer(1)	
Thermal Cycler(1)	
Flow Sitemeter(1)	
Multi-beach soccer(1)	
Multi-Sample Holder(1)	
Density gradient fractionation system(1)	
Basic equipment	
Microscope(2)	32
Big Data and Computing Core Facility equipment	
Server(1)	10

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators		
	Other researchers		
	Research support staff		
	Administrative staff		
	Subtotal	0	0
Project activities	Subtotal		
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal		
Total		0	0

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

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

Appendix 4 FY 2024 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

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

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

1) (26) Nakane, T; Nakagawa, R; Ishiguro, S; Okazaki, S; Mori, H; Shuto, Y; Yamashita, K; ***Yachie, N***; Nishimasu, H; Nureki, O. Structure and engineering of Brevibacillus laterosporus Cas9. Communications Biology 7. (2024) DOI: 10.1038/s42003-024-06422-z

2)

Overseas Satellite 2 Universidad Nacional Autónoma de México (Total: 0 papers)

None

2. Status of Researcher Exchanges

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

Overseas Satellite 1: 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
FY2024	1	0	0	0	0
	0	0	0	0	0

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024	4	0	0	0	4
	1	0	0	0	1

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
FY2024	0	0	0	0	0
	0	0	0	0	0

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024	1	0	1	0	2
	0	0	0	0	0

Appendix 5　FY 2024 Visit Records of Researchers from Abroad

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

Total: 14

	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	Juha Kere	66	Professor,Department of Medicine, Huddinge, Karolinska Institutet	Sweden	Ph.D. Molecular genetics	Royal Society Wolfson Research Merit Award（UK） https://ki.se/en/research/research-areas-centres-and-networks/research-groups/embryonal-foetal-and-brain-development-juha-keres-research-group	2024/4/25-26(2 days)	・Lecture at PRIMe Seminar Series ・Research Meeting ・Guidance and advice
2	Johan Auwerx	66	Professor, School of Life Sciences,SV EPFL(Federal Institute of Technology in Lausanne)	Switzerland	M.D. Ph.D. Molecular Biology	Danone International Prize for Nutrition, 2009 https://www.danoneinstitute.org/nutrition-science-support/danone-international-prize-nutrition/johan-auwerx-2009-awardee EASD–Novo Nordisk Foundation Diabetes Prize for Excellence,2017 https://actu.epfl.ch/news/johan-auwerx-wins-the-2017-helmholtz-diabetes-awar/ -EMBO Membership,2003 -Academia Europaea Membership,2012 https://people.epfl.ch/johan.auwerx?lang=en	2024/6/4-5(2 days)	・Lecture at PRIMe Seminar Series ・Research Meeting ・Guidance and advice
3	Chii Jou Chan	47	Assistant Professor, Mechanobiology Institute, National University of Singapore	Singapore	Ph.D. Biological Physics	Marie Curie ITN ESR Fellowship (Ph.D.) – TRANSPOL (Grant number 264399) 2011 – 2014 https://www.ruhr-uni-bochum.de/mol-neurobio/TRANSPOL/ITN%20job-P13.pdf	2024/6/18-19(2days)	・Lecture at PRIMe Seminar Series ・Research Meeting ・Guidance and advice
4	Kenji Kamimoto	38	Associate Professor, Department of Developmental Biology, University of Washington	USA	Ph.D. Science	2024 Shimadzu Scientific Research Grant (Encouragement Award) https://developmentalbiology.wustl.edu/kenji-kamimoto-phd-has-been-awarded-a-one-year-award-by-the-sumitomo-foundation-in-japan/	2024/6/28(1day)	・Lecture at PRIMe Omnibus Seminar ・Research Meeting

5	Jun Wu	47	Associate Professor, Department of Molecular Biology, UT Southwestern Medical Center	USA	Ph.D. Life Science	2024 ISSCR Outstanding Young Investigator Award International Society for Stem Cell Research (ISSCR) https://www.isscr.org/isscr-news/tag/2024%2BAwards 2022 NYSCF–Robertson Stem Cell Investigator Award New York Stem Cell Foundation, https://nyscf.org/resources/two-nyscf-innovators-receive-prestigious-awards-from-international-society-for-stem-cell-research-isscr/	2024/9/25 （1day）	・Lecture at PRIMe Omnibus Seminar ・Research Meeting ・Guidance and advice
6	Thomas Duchaine	50	Professor, Faculty of Medicine and Health Science McGill University	Canada	Ph.D. Molecular Biology	Human Frontier Science Program (HFSP) Program Grant (2015) https://reporter.mcgill.ca/35220-2/	2024/11/24-12/5 (12 days)	・Lecture at PRIMe Seminar Series ・Research Meeting ・Guidance and advice
7	Mingxia Gu	38	Assistant Professor, UC Department of Pediatrics, Cincinati Childrens Hospital Medical Center	USA	Ph.D. Molecular and Developmental Biology	2020 American Heart Association (AHA) BCVS Louis N. and Arnold M. Katz Basic Science Research Prize for Early Career （Investigators Finalist） 2020 Elected Fellow of American Heart Association (FAHA) https://sessions.hub.heart.org/daily-coverage/article/21201809/welcome-new-2020-american-heart-association-fellows	2024/11/30-12/3(4 days)	・Lecture at PRIMe Omnibus Seminar ・Research Meeting ・Guidance and advice
8	Nobuhiko Hamazaki	37	Assistant Professor, Institute for Stem Cell＆Regenerative Medicine,University of Washington	USA	Ph.D. Developmental Biology and Bioinformatics	None https://nrid.nii.ac.jp/ja/nrid/1000010757008/	2024/12/12-13(2days)	・Lecture at PRIMe Omnibus Seminar ・Research Meeting ・Guidance and advice
9	Marco Ruscone	30	Postdoctoral researcher, Life Science Department, Barcelona Super Computing Center	Spain	Ph.D. Computational Biology	None https://www.bsc.es/ruscone-marco	2025/3/3 (1 day)	・Lecture at PRIMe Omnibus Seminar ・Research Meeting ・Guidance and advice

10	Edda Klipp	59	Professor,Institute of Biology, Humboldt-Universität zu Berlin	Germany	Ph.D. Theoretical Biophysics	Doctor honoris causa, Gothenburg University,Sweden,2009 Caroline-von-Humboldt Professorship,2016 https://www.hu-berlin.de/de/pr/nachrichten/archiv/nr1512/pm_151201_00	2025/3/13-15(3days)	・Participation in WPI-PRIMe International Symposium
11	Laurence Calzone	47	Research Engineer,Department of Computational Biology, Institut Curie	France	Ph.D. Systems biology	None https://institut-curie.org/person/laurence-calzone	2025/3/13-20(8days)	・Participation in WPI-PRIMe International Symposium ・Guidance and advice ・Research Meeting
12	David Sebastian Fischer	33	Associate Professor, AI in Systems Biology, Institute of Artificial Intelligence Medical University of Vienna	Austria	Ph.D. Computational Biology and Machine Learning	None https://ai4biomedicine.org/	2025/3/13-16(4days)	・Participation in WPI-PRIMe International Symposium
13	Sakie Katsumura	42	Assistant Professor, Department of Molecular Medicine,University of Texas Health Science Center at San Antonio	USA	Ph.D. Dentistry	None https://directory.uthscsa.edu/academics/profile/katsumura	2024/9/1-11(11days),2024/11/25-2025/1/7(44days),2025/3/12-24(13days) total:68 days	・Paticipation in WPI Site Visit ・Participation in WPI-PRIMe International Congerence and WPI-PRIMe Retreat ・Research meeting ・Participation in WPI-PRIMe International Symposium ・Running the seminar Series ・Participation in Annual Meeting ofthe Molecular Biology Society of Japan, Annual Meeting of the RNA Society of Japan
14	Ayako Yachie	45	SBX Bio Science President/CEO	Canada	Ph.D. Media & Governance	None https://nrid.nii.ac.jp/ja/nrid/1000010453549	2024/7/17-19(3days), 2025/3/13-16(4days) total: 7days	・Research meeting ・Participation in WPI-PRIMe International Symposium ・Participation in WPI-PRIMe Retreat ・Annual Meeting of the Molecular Biology Society of Japan

Appendix 6 FY2024 State of Outreach Activities

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

Activities	FY2024 (number of activities, times held)
PR brochure, pamphlet	8 (Pamphlet (English & Japanese), Newsletter "Nexus", International Symposium Flyer, International Symposium Poster, International Symposium program brochure, WPI Booklet, the 27th Science in Japan forum poster)
Lectures, seminars for general public	4 Cutting Edge Research from WPI: Lecture for Educators (Jul 23 2024) The 27th Science in Japan Forum (Jun 13 2024) PPI Workshop "Your PRIMe" (Jul 20, 2024) Osaka University Symposium, 3rd WPI-PRIMe International Symposium (Mar 14 2025)
Science café	1 (Osaka University Nakanoshima Festival (Dec 1, 2024))
Participating, exhibiting in events	5 Tokai Festa (July 13, 2024) Osaka University LINKS (July 16, 2024, introduced our institute with PR contents) WPI Science Symposium (Nov 16, 2024) Kagakuzanmai (Dec 25, 2024) Kita-Osaka Express Line Extension First Anniversary Festival (Mar 23, 2025, exhibited as Osaka University)
Press releases	8 Introduction of Research Result of Prof. Negoro and Assoc. Prof. Kagawa (May 17, 2024) Introduction to Research Result of Prof. Okada (Jun 11, 2024) Announcement to research collaboration between Osaka University (Prof. Tsumaki) and Astellas Pharma (Jul 22, 2024) Introduction to Research Result of Prof. Okada (Jul 30, 2024) Introduction to Research Result of Prof. Nishida (Nov 8, 2024) Introduction to Research Result of Prof. Takebe (Jan 29, 2025) Introduction to Research Result of Dr. Lu (Feb 28, 2025) Announcement of the WPI-PRIMe International Symposium (Mar 7, 2025)
Publications of the popular science books	3 Experimental Medicine "How to survive academia: methods and philosophy to enrich scientific research"(*実験医学2025年2月号～4月号:「アカデミアの泳ぎ方:理系研究を豊かにする各種技法と哲学」*) written by Prof. Yachie Nozomu (Published Jan 20, Feb 20 and Mar 19, 2025)
Others (Seminars for early career researchers in Molecular Dynamics Simulation)	16 IPR x WPI-PRIMe BioSim Talks: Sharing Insights in Computational Biology (Jul 3&19, Aug 1&23, Sep 6&27, Nov 11&22, Dec 6&20, Jan 10&24, Feb 26, Mar 3&17&26)
Others (interviews issued from other divisions in Osaka University)	5 Osaka University NewsLetter No.91 (Sep 2024, issued by Public Relations Division) Dialogue: Science & Technology (Oct 17, 2024, issued by Public Relations Division) OU Research Gazette No.4 (Nov 2024, issued by Public Relations Division) Global Outlook Vol.20 2024 (Dec 2024, issued by the Center of Global Initiatives) キラリと光る研究者 #004 (Mar 31, 2025, issued by Office of Management and Planning)

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

Outreach Activities and Their Results

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

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

- As a result of vigorously carrying out OO outreach activity, ¥OO in external funding was acquired.

(1) PPI Workshop "Your PRIMe"

PRIMe ELSI group (PI: Kishimoto) studies the ethical, legal, and social issues that PRIMe's research may pose to society. They also work with all types of stakeholders to explore how bio-Digital can be used to benefit individuals and society. In FY 2024, one of their main activities was to approach general public by field surveys, which led to plan the first public patient involvement (PPI) event called "Your PRIMe." This event was led by Itoh, Kishimoto, Kato and Cui with a short lecture from Center Director Nishida, and co-hosted by the ELSI center of Osaka University. The event logistics was supported by Research Management and Planning Office staff.

The Workshop participants varied in ages, genders and occupation, though highly interested in digital twins or medical topics. The participants were divided into several groups so they could talk in a small units. The Center Director gave a small presentation to provide information about PRIMe and what bio-Digital twin is, and the participants discussed the pros and cons in each group. The results illustrated a broad understanding of what the public expects and are concerned about BDT, accelerating PRIMe ELSI research leading it to the next step of conducting a larger population online survey about bio-digital twins (n=1,000 residents in Japan). Participants showed interest in PRIMe activities and the future of the healthcare system during the event, becoming one of the foundations for building trust with the public.

Figure 1. Photos of the PPI Workshop "Your PRIMe"

(2) Press Releases (PR) and Media Coverage

In FY 2024, we launched 8 press releases which is more than double compared to last year (3 press releases). The PR team encouraged PRIMe researchers to launch press releases by announcing them in the Steering Committee and communicating with them in internal exchange events. As a result, inquires regarding the press release became more frequent than before, including joint press release and press conference. This brought a positive effect on media coverage: the number increased about 20% compared to last year (see appendix 7 for detail of FY2024).

One domestic media coverage related to PRIMe outreach would be the broadcast of Science ZERO by NHK Educational TV. This program focuses on cutting edge science and technology which has potential to change the future society. It is a well-known program among individuals interested in science. The episode broadcasted on December 15, 2024, was about "the mystery of reproduction," and the guest was PRIMe PI Dr. Katsuhiko Hayashi("生殖"のミステリー!生き物の根源に挑む｜サイエンスZERO｜NHK website https://www.nhk.jp/p/zero/ts/XK5VKV7V98/episode/te/X6W4LV4Q83/). He has been spotlighted by the public since his research paper using cells from male mice to produce the eggs (K. Murakami et al. Nature 615, 900–906; 2023). In addition, he was on the "2024 TIME 100 List" by TIME (https://time.com/6964621/katsuhiko-hayashi-2/). Even this paper was published in 2023, his research still attracts the general public both domestically and overseas.

(3) Events (symposiums, seminars)

(a)Symposiums

In FY 2024, we had two important symposiums open to the public.

"The 27th Japan Science Forum: Conquering All Diseases by Metaverse-based Research" organized by the JSPS Washington Office, was held on June 13, 2024, in a hybrid format. The onsite venue was Washington Cosmos Club, located in the city center of Washington D.C. Approximately 70 participants joined this event from all over the world. The Forum kicked off by Center Director Nishida Kohji's Keynote Speech, followed by Takebe, Nemoto, Domínguez-Hüttinger and Yachie(N). Following their session, the panel discussion was moderated by Sakurada. This half day hybrid forum was joined by participants from onsite and online from the globe, and the whole session was closed in a warm atmosphere. This event introduced a new potential collaborator to expand our researchers' network, and we plan to move forward in the next fiscal year.

Figure 2. the 27th Science in Japan Forum Poster

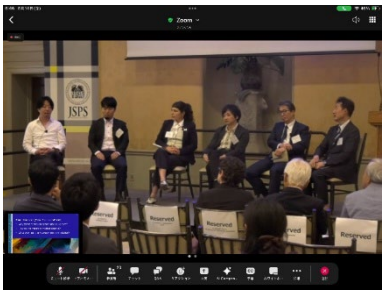


Figure 3. Photos of the 27th Science in Japan Forum (left: online, center and right: onsite)

On March 14, 2025, WPI-PRIMe 3rd international symposium "Towards Patient Bio-Digital Twin," was co-hosted by Osaka University and WPI-PRIMe. We were pleased to welcome over 110 attendees from both academia and industry, which was 10% increase compared to last year (last year was about 100 per day). The symposium showcased recent advancements in dry-lab research, with sessions focusing on biological modeling, bioinformatics, systems biology, and the emerging field of Bio-Digital Twin. Alongside the exceptional Keynote Lectures delivered by Prof. Gary Bader (University of Toronto) and Prof. Edda Klipp (Humboldt-Universität zu Berlin), we organized three unique sessions emphasizing an integrated approach to wet- and dry-lab research, wrapped up by the closing remarks from Prof. Takao Onoye, the Executive Vice President of our university. The program also had a poster session followed by an Exchange Event with the symposium participants, which accelerated the discussion through the whole day.

Figure 4. International Symposium Poster

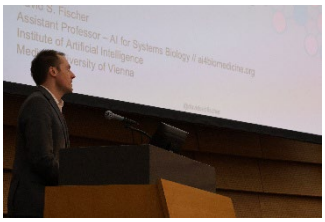




Figure 5. Photos of the WPI-PRIMe International Symposium

(b)Seminars

In FY 2024, we started a seminar series called "IPR x WPI-PRIMe BioSim Talks Sharing Insights in Computational Biology (an IPR seminar supported by WPI-PRIMe and ASPiRE)" co-hosted with Institute for Protein Research (IPR) in our university. The purpose of this seminar series was to promote computational biology education among our university, improve inter-center biomolecular researcher connections within Osaka region and enhance the quality of computational biological research. Apart from PRIMe Seminar Series and PRIMe Omnibus Seminars, this series was open to the public. The seminar was jointly organized by researchers from IPR and PRIMe, with Shinobu from PRIMe leading the planning and execution. This series was designed to attract young researchers such as graduate students and young staff. After having 3 times in onsite format, the organizers changed it to hybrid to encourage more researchers to participate from all over the world. Speakers were mainly invited from Kansai area, though their careers and methods varied which made the discussion part more enthusiastic. Organizers succeeded in expanding the researchers' network in this research field, which encouraged them to continue this seminar series in the next fiscal year.

Figure 6. The 1st BioSim Talk Poster



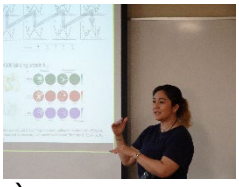


Figure 7. Photos of BioSim Talks (onsite venue)

Appendix 7 FY 2024 List of Project's Media Coverage

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

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	Apr 3 2024	Newspaper1	[Kyodo News Apr 3] - Prof. Miyagawa, article about his clinical trial of the iPS cardiomyocyte sheet to prevent serious dilated cardiomyopathy
2	Apr 15 2024	Newspaper1	[Nikkei Shimbun Apr 15] - Prof. Nishida, article about iPS cornea transplatation clinical trail starting at June
3	Apr 17 2024	Newspaper2	[Nikkei Shimbun, Sankei Shimbun Apr 17] - Prof. Takabe, article reporting his Kobe Prize Young Investigator Award
4	Apr 17 2024	Newswebsite1	[TIME Apr 17] - Prof. Hayashi, selected as "The most influential people of 2024" by TIME
5	Apr 18 2024	Newspaper2	[Nikkei Shimbun, Jiji Press Apr 18] - Prof. Hayashi, article reporting him selected as one of the TIME 100 members from Japan
6	Apr 19 2024	Newspaper1, TV1	[Asahi Shimbun, NHK news Apr 19] - Prof. Hayashi, article reporting him selected as TIME 100
7	Apr 22 2024	Newspaper1	[Mainichi Shimbun Apr 22] - Prof. Hayashi, article reporting his achievement which led to be selected as TIME 100
8	Apr 25 2024	Newspaper1	[Nikkan Kogyo Shimbun Apr 25] - Prof. Takebe, article reporting his award in Kobe Prize
9	May 7 2024	Newspaper1	[Mainichi Shimbun May 7] - Prof. Hayashi, article about his past research paper published in *Nature* (2023)
10	May 7 2024	Newswebsite1	[Nikkei Biotechnology and Business May 7] - Prof. Kato, article about his research paper published in *Frontiers in Genetics*
11	May 9 2024	Newspaper1	[Nikkei Shimbun May 9] - Prof. Harada, article about her research paper published in *Nature Communications*
12	May 9 2024	Newswebsite1	[Newswitch May 9] - Prof. Negoro, article with interview about quantum computer development in Osaka University and in Japan
13	May 10 2024	Newspaper1	[Nikkan Kogyo Shimbun May 10] - Prof. Harada, article about her research paper published in *Nature Communications*

14	May 13 2024	Newswebsite1	[TECH+ May 13] - Prof. Negoro, article about his research paper published in *Journal of the American Chemical Society*
15	May 14 2024	Newswebsite1	[TECH+ May 14] - Prof. Harada, article about her research paper published in *Nature Communications*
16	May 20 2024	Newswebsite1	[TECH+ May 20] - Prof. Negoro, article about his research paper published in *Journal of the American Chemical Society*
17	May 20 2024	Newswebsite1	[TECH+ May 20] - Assoc. Prof. Kagawa, article about his research paper published in *Journal of the American Chemical Society*
18	May 21 2024	Newspaper1	[Nihon Keizai Shimbun May 21] - Prof. Hayashi, article referring to his past research paper published in *Nature* (2023)
19	May 21 2024	Newspaper1, TV1	[Yomiuri Shimbun, news zero May 21] - Prof. Hayashi, article referring to his past research paper published in *Nature* (2023)
20	May 27 2024	Newspaper1	[Nikkan Kogyo Shimbun May 27] - Prof. Negoro, article interview as a researcher
21	Jun 3 2024	Newswebsite1	[Sankei News Jun 3] - Prof. Takebe, article reporting the ceremony of Kobe Prize which he received Young Investigator Award
22	Jun 15 2024	Newspaper1	[Yomiuri Shimbun Jun 15] - Prof. Y Okada, article about his research paper published in *Nature Genetics*
23	Jun 20 2024	Newswebsite1	[QLifePro Jun 20] - Prof. Kato, article about his research paper published in *Asian Bioethics Review*
24	Jul 17 2024	Newspaper1, Newswebsite1	[Nihon Keizai Shimbun, Nikkei Biotechnology and Business Jul 17] - Prof. Y Okada, article about his research paper published in *Nature Communications*
25	Jul 22 2024	Newspaper1, Newswebsite1	[Nihon Keizai Shimbun, Nikkei Biotechnology and Business Jul 22] - Prof. Tsumaki, article reporting the joint announcement by Astellas Pharma and Osaka University for the start of research collaboration
26	Jul 23 2024	Newswebsite1	[QLifePro Jul 23] - Prof. Y Okada, article about his research paper published in *Nature Communications*
27	Jul 24 2024	Newspaper1, Newswebsite1	[Nikkan Kogyo Shimbun, Nikkan Yakugyo Jul 24] - Prof. Tsumaki, article reporting the joint announcement by Astellas Pharma and Osaka University for the start of research collaboration
28	Jul 24 2024	Newswebsite1	[Nikkei Biotechnology and Business Jul 24] - Prof. Y Okada, article about his research paper published in *Nature Communications*
29	Jul 31 2024	Newspaper1	[Nihon Keizai Shimbun Jun 31] - Prof. Y Okada, article about his research paper published in *Nature Communications*
30	Aug 4 2024	Newspaper1	[Nihon Keizai Shimbun Aug 4] - Prof. Takebe, interview article in The STYLE "MyStory"

31	Aug 6 2024	Newspaper1	[Nihon Keizai Shimbun Aug 6] - Prof. Takebe, article referring to his previous achievement in successing to create iPS-derived liver organoid
32	Aug 7 2024	Newswebsite1	[Nikkei Biotechnology and Business Aug 7] - Prof. Nishida, article reporting the joint announcement from to Osaka University, Okayama University and Menicon about the approval of the new medical device
33	Aug 23 2024	Newspaper1	[Yomiuri Shimbun Aug 23] - Prof. Kato, leaving comment for epigenome reprogramming article
34	Aug 28 2024	Newswebsite1	[Yakuji Nippo Aug 28] - Prof. Negoro, article reporting him as the member of the team awarded as "Award for Academic Startups 2024" by MEXT, JST and NEDO
35	Aug 30 2024	Newspaper1	[The Science News Aug 30] - Prof. Negoro, article reporting him as the member of the team awarded as "Award for Academic Startups 2024" by MEXT, JST and NEDO
36	Sep 6 2024	Newspaper1	[Yomiuri Shimbun Sep 6] - Prof. Y Okada, article about his research paper published in *Cell Genomics*
37	Sep 11 2024	Newswebsite1	[Yakuji Nippo Sep 11] - Prof. Tsumaki, article reporting the kick-off of research collaboration by Astellas Pharma and Osaka University
38	Sep 11 2024	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Sep 11] - Prof. Y Okada, article about the research paper he joined and was published in *Journal of Neurology, Neurosurgery, and Psychiatry*
39	Sep 12 2024	Newswebsite1	[The Guardian Sep 12] - Prof. Takebe, article reporting him winning the IgNobel Prize
40	Sep 13 2024	TV6, Newspaper5	[NHK, Nippon Television NEWS NNN, CNN, Asahi Shimbun Breaking News, Asahi Shimbun, Nihon Keizai Shimbun, Yomiuri Shimbun, Nikkan Kogyo Shimbun Sep 13] - Prof. Takebe, article reporting him winning the IgNobel Prize
41	Sep 22 2024	Newspaper1	[Yomiuri Shimbun Sep 22] - Prof. Takebe, article interviewing him about IgNobel Prize
42	Sep 25 2024	TV1	[NHK G Gogo LIVE Newsoon Sep 25] - Prof. Takebe, broadcast reporting him winning the Ig Nobel Prize
43	Sep 25 2024	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Sep 25] - Prof. Y Okada, article about his reseach paper published in *Nature Genetics*
44	Sep 27 2024	Newspaper1	[Yomiuri Shimbun Sep 27] - Prof. Miyagawa, advertisement article reporting highschool students visiting Osaka University and Sumitomo Pharma
45	Oct 6 2024	Newspaper1	[Nihon Keizai Shimbun Oct 6] - Prof. Y Okada, leaving comments to the article about the secret of life longevity
46	Oct 7 2024	Newswebsite1	[Nikkei Biotechnology and Business Oct 7] - Prof. Y Okada, article about his research paper published in *Communications Medicine*
47	Oct 16 2024	Newswebsite3	[Jiji Press (Yahoo!News, goo News, BIGLOBE News), Jiji Medical, Nikkei Biotechnology and Business Oct 16] - Prof. Y Okada, article about his research paper published in *Nature Human Behaviour*

48	Oct 17 2024	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Oct 17] - Prof. Negoro, article about his research paper published in *Science Advances*
49	Oct 24 2024	Newswebsite1, Newspaper1	[Asahi Shimbun DIGITAL (Yahoo! News), The Science News Oct 24] - Prof. Y Okada and Prof. Kato, article related to their research paper published in *Nature Human Behaviour*
50	Nov 7 2024	Newspaper1	[Sankei Shimbun Nov 7] - Prof. Takebe, article referring to his IgNobel Prize award
51	Nov 11 2024	Newspaper1, Newswebsite1	[Yomiuri Shimbun, Asahi Shimbun DIGITAL Nov 11] - Prof. Nishida, article about his research paper published in *Lancet*
52	Nov 14 2024	Newswebsite1	[University Journal ONLINE Nov 14] - Prof. Nishida, article about his research paper published in *Lancet*
53	Nov 19 2024	Newswebsite1	[Nikkei Business Electronic Version Nov 19] - Prof. Takebe, interview article about his research related to his IgNobel Prize award
54	Nov 25 2024	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Nov 25] - Prof. Y Okada, article about his research paper published in *Nature Communications*
55	Nov 29 2024	Newspaper1	[Yomiuri Shimbun Nov 29] - Prof. Nishida, article reporting his lecture at a public event *再生医療の今と未来の医療を考える*(Thinking the present and future of regenerative medicine)
56	Nov 30 2024	Newspaper1	[Nihon Keizai Shimbun Nov 30] - Prof. Y Okada, article about his research paper published in *Nature Communications*
57	Dec 5 2024	Newswebsite1	[Nikkei Medical Dec 5] - Prof. Takebe, article related to his award for IgNobel Prize
58	Dec 5 2024	Newspaper1, Newswebsite2	[Yomiuri Shimbun, Yomiuri Shimbun(goo News), Asahi Shimbun Digital Dec 5] - Prof. Y Okada, article about his research paper published in *Nature Communications*
59	Dec 9 2024	Newswebsite1	[Kansai NEWS WEB (NHK) Dec 9] - Prof. Nishida, article and interview about his research paper published in *Lancet*
60	Dec 11 2024	Newspaper1	[Asahi Shimbun Dec 11] - Prof. Y Okada, article about his research paper published in *Nature Communications*
61	Dec 13 2024	Newspaper1	[Mainichi Shimbun Dec 13] - Prof. Y Okada, article referring to his research paper published in *Nature Genetics*
62	Dec 15 2024	TV1	[NHK E Dec 15] - Prof. Hayashi, broadcast in Science Zero related to his past research in *Nature* (2023)
63	Dec 15 2024	Newswebsite1, TV1	[Tereasa News (Yahoo! News), Asahi Broadcast (ABC News) Dec 15] - Prof. Nishida, interview about his research paper published in *Lancet*
64	Dec 16 2024	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Dec 16] - Prof. Hayashi, article reffering to his past reseach paper published in *Cell* (2011)

65	Dec 24 2024	Newswebsite1	[BIGLOBE News Dec 24] - Prof. Miyagawa, article reporting the press conference presenting the success of the trail of remote monitoring system detecting the patient's heart failure
66	Dec 27 2024	Newswebsite1	[Nikkei Medical Dec 27] - Prof. Miyagawa, article reporting his research group's success of the trail of remote monitoring system detecting the patient's heart failure
67	Jan 9 2025	Newswebsite2	[Nihon Keizai Shimbun Electronic Version, Nikkei Biotechnology and Business Jan 9] - Prof. Y Okada, article about his research paper published in *Nature Genetics*
68	Jan 20 2025	Newswebsite1	[The Huffington Post Japan Jan 20] - Prof. Miyagawa, article reporting the press conference presenting the success of the trail of remote monitoring system detecting the patient's heart failure
69	Jan 29 2025	Newswebsite1	[Nikkei Biotechnology and Business Jan 29] - Prof. Takebe, article about his research paper published in *Proceedings of the National Academy of Sciences(PNAS)*
70	Jan 29 2025	Newswebsite1	[Jiji Press News Jan 29] - Prof. Hayashi, reffering to his past research paper published in *Nature* (2023)
71	Feb 6 2025	Newswebsite1	[Nikkei Biotechnology and Business ONLINE Feb 6] - Prof. Y Okada, article about his research paper published in *Nature Communications*
72	Feb 22 2025	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Feb 22] - Prof. Y Okada, article about his research paper published in *Cell Genomics*
73	Mar 4 2025	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Mar 4] - Assoc. Prof. Lu Yonggang, article about his research paper published in Proceedings of the *National Academy of Sciences*(*PNAS)*
74	Mar 5 2025	Newswebsite1	[Nihon Keizai Shimbun Electronic Version Mar 5] - Prof. Y Okada, article about his research paper published in *Cell Genomics*
75	Mar 13 2025	Newspaper1	[Yomiuri Shimbun Mar 13] - Prof. Takebe, interview article related to his research activities and achievement winning the IgNobel Prize
76	Mar 24 2025	Newspaper1, Newswebsite1	[Yomiuri Shimbun, MSN Mar 24] Assoc. Prof. Lu Yonggang, article about his research paper published in *National Academy of Sciences(PNAS)*
77	Mar 26 2025	Newswebsite2, Newspaper1	[Yahoo! News, Kyodo News Mar 26] Assoc. Prof. Lu Yonggang, article about his research paper published in *National Academy of Sciences(PNAS)*
78	Mar 27 2025	Newspaper1, Newswebsite1	[Nikkan Kogyo Shimbun, Nihon Keizai Shimbun Electronic Version Mar 27] Prof. Harada, article about her research paper published in *Nano Letters*
79	Mar 27 2025	Newspaper1	[Asahi Shimbun Mar 27] Prof. Kishimoto, article reporting his keynote lecture at the ELSI event "ELSI University Summit"