



FY 2023 Follow-up of WPI Program

By Program Committee

March 2024

(This document reports on progress made under the WPI Program in FY 2022.)

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In 2007, the Japanese government launched an ambitious initiative to create globally visible and internationally opened research centers. This program, World Premier International Research Center Initiative (abbreviated WPI), has, pursuant to the program’s mission stated in 2007, successfully launched 13 centers over the 14-year period from 2007 to 2020. In 2020, a new mission was initiated that advances further the principles of the original WPI mission. The Launching of centers under the New Mission began in 2021, and 4 more centers have been launched by 2022. This 2023 follow-up report describes notable areas of progress in FY 2022 and new developments in FY 2023.

A. Highlights in FY 2023

A-1. Launching a new center

In 2023, MEXT made an open call for WPI center proposals under a new center scheme; a WPI CORE center which develops to a full-sized center through a stage gate process, and a WPI Multiple HOST center which is jointly proposed by multiple host institutions. After a vigorous selection process that ran from February to September of 2023, the Program Committee selected a new center in the Multiple HOST center category “Advanced Institute for Marine Ecosystem Change (AIMEC)” established jointly by Tohoku University and Japan Agency for Marine-Earth Science and Technology.

A-2. Meetings in person after 3 years of Pandemic

After three years since the winter of 2020, the COVID-19 Pandemic has eased in 2023, taking advantage of which the site visits to WPI centers in the summer were conducted on site, and the Program Committee meeting in the fall were held in person in Tokyo.



PRIME’s site visit in August 2023

B. WPI Outline

In 2007, Ministry of Education, Culture, Sports, Science and Technology (MEXT) launched the WPI Program aimed at establishing internationally open and globally visible “World Premium Institutes” in Japan. The background was:

- Increasing worldwide competition in generating new research outcomes and in recruiting talented scientists.
- Strong need felt for more efficient forms of funding to advance fundamental and innovative sciences, which are essential to building knowledge-based societies.
- The advent of research excellence initiatives designed to encourage outstanding research by providing large-scale and long-term funding.

To sharply focus the aim of the Program, the following Mission was given to the WPI centers.

- Advancing to the highest pinnacle of globally leading-edge research
- Creating interdisciplinary domains
- Establishing international research environments
- Reforming research organizations

MEXT supports the WPI centers within the following context.

- Up to ¥700 million a year per center in principle
(Up to about ¥1.3 billion a year for centers launched in and before 2010)
- Research money is not included.
- Support for 10 years (5-year extension is applicable for centers launched in or before 2012)

In 2020, the New Mission, advancing on the principles of the original mission above, was formulated, namely,

- World-Leading Scientific Excellence and Recognition
 - The Highest Level of Research Impact
 - Expanding Knowledge Frontiers through Interdisciplinarity and Diversity
- Global Research Environment and System Reform
 - Harnessing Talent and Potential through Global Brain Circulation
 - Interdisciplinary and Inter-Organizational Capacity Building
 - Effective, Proactive and Agile Management
- Values for the Future
 - Societal Value of Basic Research
 - Human Resource Building: Higher Education and Career Development
 - Self-Sufficient and Sustainable Center Development

The launching of centers under the New Mission started from 2021. MEXT supports these

WPI centers within the following context.

- Up to ¥700 million a year per center in principle
- Research money is not included.
- Support for 10 years

In 2023, MEXT introduced a new scheme of WPI center development while maintaining the new mission; a WPI CORE center which develops to a full-sized center through a stage gate process, and a WPI Multiple HOST center which is jointly proposed by multiple host institutions.

- For a WPI CORE center, up to ¥500 million a year per center in principle before the stage gate and thereafter up to ¥700 million a year per center in principle
- For a Multiple HOST center, up to ¥1,000 million a year per center in principle

C. WPI Centers

Nine WPI centers were launched during the first 10 years of the WPI Program.

The first five WPI centers launched in 2007 are now all members of the WPI Academy.

- **AIMR** on materials and mathematics, Tohoku University.
- **Kavli IPMU** on the origin of Universe, The University of Tokyo.
- **iCeMS** on cell biology and materials, Kyoto University
- **IFReC** on immunology, Osaka University
- **MANA** on nanoarchitectonics, National Institute for Materials Science

The sixth WPI center was launched under the “green innovation program” in 2010, and it is the 6th member of the WPI Academy.

- **I²CNER** on energy, Kyushu University

Three WPI centers were launched in 2012, and they are now all in the WPI Academy.

- **IIIS** on sleep, University of Tsukuba
- **ELSI** on the origins of Earth and life, Tokyo Institute of Technology
- **ITbM** on plant/animal biology and chemistry, Nagoya University

In 2017, the 11th year of the WPI Program, two WPI centers were added:

- **IRCN** on origin of intelligence, The University of Tokyo
- **NanoLSI** on nano life science, Kanazawa University

In 2018, two more centers were launched:

- **ICReDD** on chemistry and information, Hokkaido University
- **ASHBi** on human biology, Kyoto University

In 2021, one new center was launched under the New Mission:

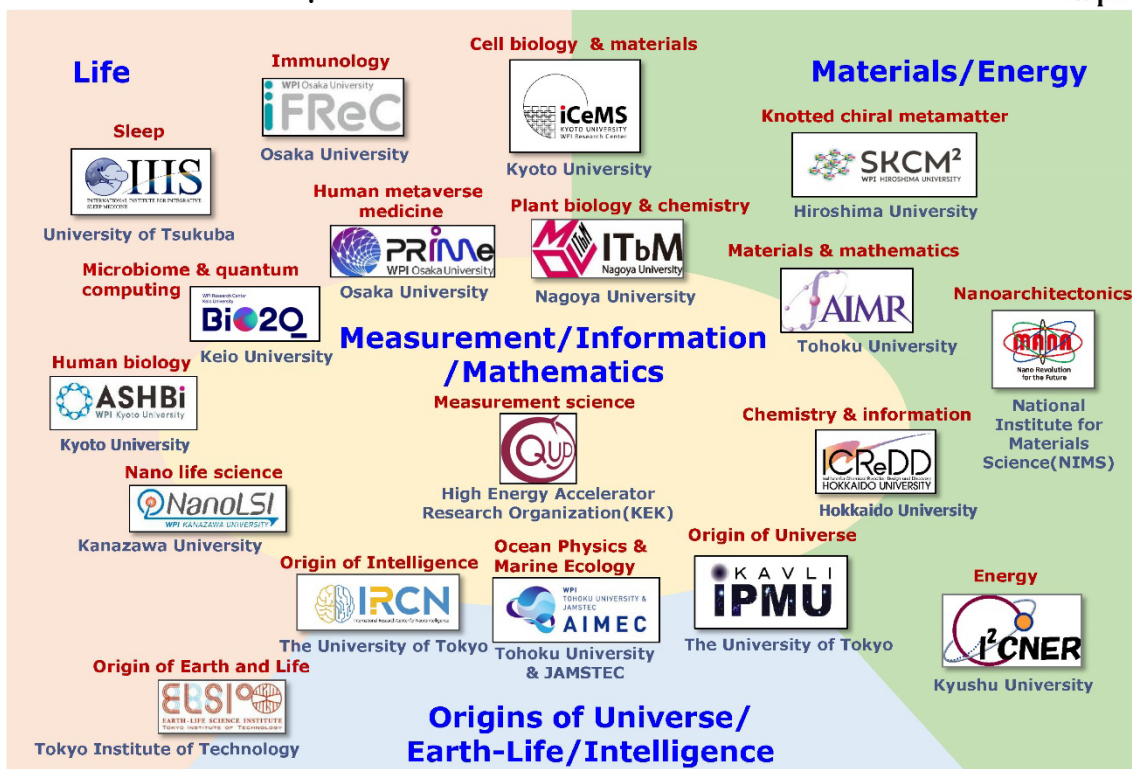
- **QUP** on measurement science High Energy Accelerator Research Organization (KEK)
 In 2022, three new centers were launched under the New Mission:

- **PRIME** on human metaverse medicine, Osaka University
- **SKCM²** on knotted chiral metamatter, Hiroshima University
- **Bio2Q** on microbiome and quantum computing, Keio University

In 2023, the 17th year of the WPI Program, one new Multiple HOST center was launched under the New Mission:

- **AIMEC** on ocean physics and marine ecology, Tohoku University and Japan Agency for Marine-Earth Science and Technology

Science Map of WPI centers



As shown above, the sciences explored by the 18 WPI centers extend from Origins of the Universe, Earth-Life, and Intelligence, Life, Materials/ Energy, and Measurement /Information/ Mathematics.

D. Follow-up framework

The WPI Program carries out a robust follow-up system comprising the international Program Committee, program director (PD), deputy program director (DPD), program officers (POs),

and working groups (WGs). Since 2017, an academy director (AD), academy officers (AOs), and Academy working groups (AWGs) have been put in place to oversee the follow-up activities of the WPI centers that are members of the WPI Academy.

Program Committee

WPI Program committee continued its operation under Dr. HAMAGUCHI; four members left the committee at the end of March 2023, and five members joined in April and June of 2023. The Committee members and their affiliations are listed in the following website:

https://www.jsps.go.jp/english/e-toplevel/07_committee.html

In FY 2023, the Program Committee held meetings on 15, 19-20 September and on 24-25 October. The September meeting was held on-line, whereas the October meeting was in-person in Tokyo. The main items of business on Committee's agenda in its September meeting were (1) the selection of new WPI centers. In its October meeting, they were (2) reports by the new center directors on their vision (iCeMS, I²CNER, Kavli IPMU), (3) follow-up reviews of eight centers (IRCN, NanoLSI, ICR²DD, QUP, PRIME, SKCM², Bio2Q), (4) report on WPI Academy centers, and (5) future plan of WPI.



Program committee in October 2023 in Tokyo

PD, DPD, POs and WGs

PD: Dr. UKAWA Akira has been serving as Program Director since April 2017.

DPD: Dr. KAIBUCHI Kozo has been serving as Deputy Program Director Since April 2022.

POs: Being experts in the research areas of each center, they chair site visits and prepare site-visit reports by compiling the comments of the site-visit team members.

WGs: Assembled for each WPI center, these groups principally consist of 3 domestic and 3 international experts in areas that cover the center's activities.

PD, DPD, POs and WG members and their affiliations are listed in the following website:

http://www.jsps.go.jp/english/e-toplevel/08_followup.html

AD, AOs and AWGs

AD: Dr. UKAWA Akira, Program Director, has been in this position since April 2021.

AOs: Being experts in the research areas of the member centers, they chair site visits and prepare site-visit reports for the Program Committee.

AWGs: Assembled for each WPI center, these groups principally consist of 2 domestic and 1 international expert in areas that cover the center's activities.

AD and AOs and their affiliations are listed in the following website:

https://www.jsps.go.jp/english/e-toplevel/18_academy.html

Site Visits

Site visits to the WPI centers receiving ongoing funding were conducted during the period of July-September 2023. Taking advantage of the easing of the COVID-19 pandemic after 3 years, all the site visits were carried out on-site. They had full agendas over 2 days including presentations by the center directors and the heads of the host institutions, presentations by the PIs, and poster sessions by researchers. The reports on the site visits were submitted to the Program Committee and disclosed to the respective centers.

WPI Academy Site Visits

For the nine Academy-member centers (AIMR, iCeMS, IFRcC, MANA, I²CNER, Kavli IPMU, IIIS, ELSI, and ITbM), site visits were held from November 2022 to March 2023. Attended by AD, AO with PD and DPD, these site visits were carried out online with a duration of about 2 hours. Reports on the site visits were made to the Program Committee in its October meeting by AD.

E. Future plan of the WPI Program

In this year's October meeting of the Program Committee, Mr. NISHIYAMA Takashi, Director of Basic and Generic Research Division of Research Promotion Bureau of MEXT, presented MEXT's plan of further sustainable support for the development of WPI centers.

F. Follow up on the 2 Centers launched in 2017

F-1. IRCN

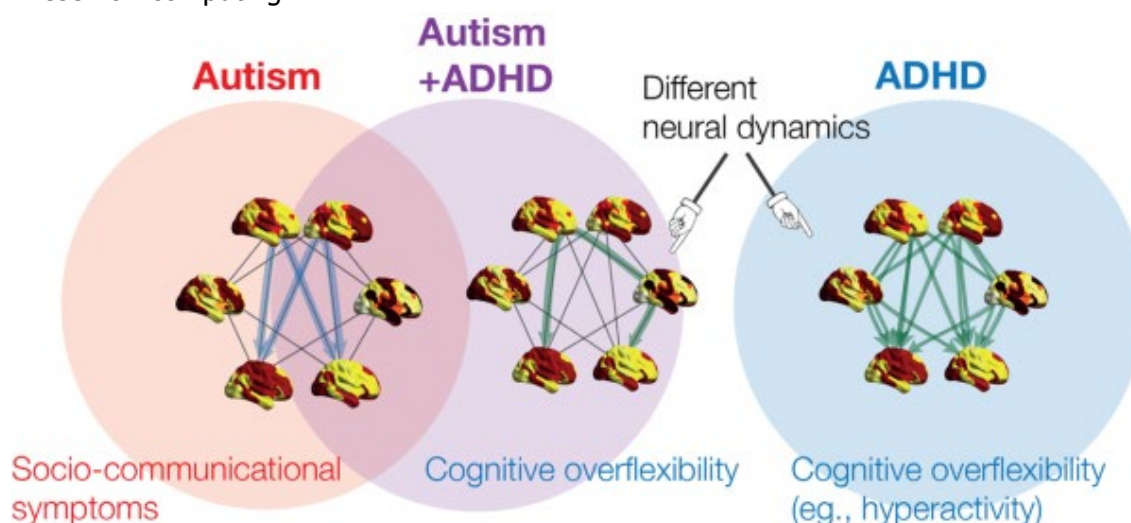
Center director: Takao HENSCH

Program officer: MISHINA Masayoshi, Ritsumeikan University

1. Advancing research of the highest global level

IRCN is tackling the challenging question of how human intelligence (HI) arises by establishing principles of brain development, unraveling the etiology and treatment of mental disorders, and innovating neuro-inspired artificial intelligence (AI).

Using a bottom-up team science strategy, IRCN researchers have intensively interacted and produced high-quality publications. Among IRCN's impressive achievements, its findings on a modular strategy for developing hierarchical visual networks is particularly outstanding. Its achievements in elucidating the initial synaptic events underlying critical period plasticity, inflexible brain dynamics in autism, and the pharmacological manipulation of visual neuroplasticity are also commendable. Its integration of neurodevelopment findings into computation models is emerging as exemplified by reservoir computing.



Recent Highlight Children with autism spectrum disorder (ASD) show cognitive rigidity and tend to persist in specific thoughts and behaviors, whereas those with ADHD exhibit unstable cognition and have difficulty in concentrating. Despite such contrasts, clinically, the two prevalent neurodevelopmental disorders are often reported to co-exist in the same individual and sometimes treated as an overlap of the two conditions. Applying novel energy landscape analysis published in *eNeuro* on July 6, 2023, Principal Investigator (Associate Professor) Takamitsu Watanabe and Mr Daichi Watanabe, an undergraduate internship student from UC Berkeley, found that such an ASD+ADHD condition is not a simple merging of pure ASD and pure ADHD; rather, the condition is a biological subtype of ASD, and its cognitive instability is underpinned by unique brain dynamics that are not seen in pure ADHD. These findings indicate that the comorbidity of ASD and ADHD would need a bespoke diagnosis and treatment

2. Implementation as a WPI center

Generating fused disciplines:

The center's approach of flexibly organizing teams based on shared topics is proving to be quite successful. This dynamic team science strategy strongly facilitates interdisciplinary collaboration among the developmental neuroscience, human/clinical, and computation groups.

We saw a number of publications that emerged from these collaborations, including on improvement of reservoir computing by adjusting the excitatory-inhibitory balance based on their findings regarding critical period development and on exploration of brain states of psychosis using dynamical network biomarkers.

Realizing an international research environment:

The ratio of overseas PIs now stands at 19% (3/16). The ratio for all overseas researchers is 34% (46/137). These numbers satisfy the requirement of the WPI Program, though the ratio of PIs can be improved by adding one or two more foreign PIs.

Throughout the COVID-19 pandemic, IRCN made effort to maintain its international presence through its International Science Salons and by sustaining MOUs with 16 foreign brain research organizations. Reflecting this effort, IRCN hosted 6 researchers who were on sabbatical leave. An office suite was prepared to welcome these foreign professors during their sabbatical stays.

Making organizational reforms:

The Director's Office was established to provide more agile oversight of day-to-day issues. The center's Steering Committee was expanded to include all PIs. Its five core facilities continued to provide research services and technologies. IRCN has re-started its internship programs that host foreign students.

IRCN is in a "quasi" under-one-roof environment and maintains extensive research networks by enlisting 54 Affiliated Faculty members and 21 Affiliated Research Fellows.

Few junior PIs participated in the university's graduate training programs. Disconnection between young PIs and graduate students is a problem that must be officially addressed as soon as possible.

The flexible, collaborative organization enabled by "team science" appears to be well in motion and producing active collaborations across PIs. The university's proposal to place IRCN within the Graduate School of Medicine is incompatible to advancing reform as it requires abolishing the open, flat and interdisciplinary structure of IRCN and putting its

faculty into a traditional hierarchical structure. This will severely downgrade IRCN's attraction as an international hub for brain research.

Effort to secure the center's future development over the mid- to long-term:

UTokyo has secured a permanent budget for retaining 10 full-professor equivalents for IRCN.

The plan for a new Life Innovation Building to house IRCN was presented based on the "Basic Concept for Revitalizing UTokyo Hongo Area," but the building schedule to be completed by 2029 is very slow.

UTokyo has proposed placing IRCN within the Graduate School of Medicine as the future plan for the center. That transition would take 4 years up to 2027 to complete, requiring IRCN's team structure to adapt to the department style of the School of Medicine. This proposal is completely counter to the requirement of WPI Program for UTokyo, the host institution, to establish IRCN as an independent and autonomous institute within its organization. IRCN's open and interdisciplinary structure, which embodies the system reform intended by WPI, will be forced to bend back to a traditional hierarchical structure. If this happens, IRCN will lose its essential character as a WPI center. UTokyo should seriously reconsider its future plans for IRCN.

To foster junior PIs, it will be essential to allow them access to graduate students as soon as possible.

IRCN needs a strategy to develop diversity, especially regarding the participation of female scientists.

Center's response to the follow-up results of last year:

Strengthening the Computation Group

The presented list of researchers intended to enhance the center's computational aspects seems somewhat inflated and lacks a clear focus.

Milestones

What IRCN's milestones will be in coming years is not sufficiently articulated. It will need to provide more specific goals for treating mental disorders and innovating neuro-inspired AI.

Future plan for IRCN

UTokyo's proposal to place IRCN within the Graduate School of Medicine as the future plan for IRCN is very unsatisfactory.

Graduate education

UTokyo and IRCN should take stronger initiatives for obtaining cross-appointments of junior PIs in appropriate departments so as to allow their engagement in graduate education.

3. Actions required and recommendations

- 1) Placing IRCN within the Graduate School of Medicine runs completely counter to the WPI Program's requirement that UTokyo should establish IRCN as an independent and autonomous institute within its organization. The open and interdisciplinary structure of IRCN's faculty, which embodies the system reform intended by the WPI program, will be forced to bend back to a traditional hierarchical structure. UTokyo should seriously reconsider its future plans for IRCN. If nothing else, it should keep IRCN within the University of Tokyo Institutes for Advanced Study (UTIAS) and secure the positions, budget and building sufficient for its sustainable operation, as in the case of Kavli IPMU.

It is agreeable that UTokyo has reconsidered a future plan for keeping IRCN within UTIAS. UTokyo should clarify its fundamental policy as to how it intends WPI centers to transform the university.

- 2) Strategies must be implemented that will enable young PIs to accept graduate students. IRCN and UTokyo should take stronger initiatives for obtaining cross-appointments of junior PIs in appropriate departments so as to allow them to effectively supervise graduate students and deliver lectures in interdisciplinary fields. It will also be valuable for IRCN to develop more aggressive promotion strategies for younger and female scientists.
- 3) IRCN should clearly describe its progress and overall strategy toward understanding the origin of human intelligence. IRCN's milestones for coming years are not sufficiently articulated. It will need to provide more specific goals for treating mental disorders and innovating neuro-inspired AI.
- 4) The presented list of researchers intended to enhance the center's computational aspects seems somewhat inflated and lacks clear focus. Given the rapid advancements in AI technologies such as generative AI, a vision for neuroscience research that aligns with these advancements is desired. Understanding the brain through the lens of modern AI technologies can provide profound insights and novel directions in the field.

- 5) Considering explosive development of AI and its impacts on society, economy and science, IRCN should clarify its vision on neuro-inspired AI including ethical and social issues. Within the context of a need for milestones and alignment of neuroscience research with recent advances in AI, IRCN may consider writing a forward-looking position paper which presents, from its perspective, views on important progress/discoveries and next steps for neuroscience and AI.

F-2. NanoLSI

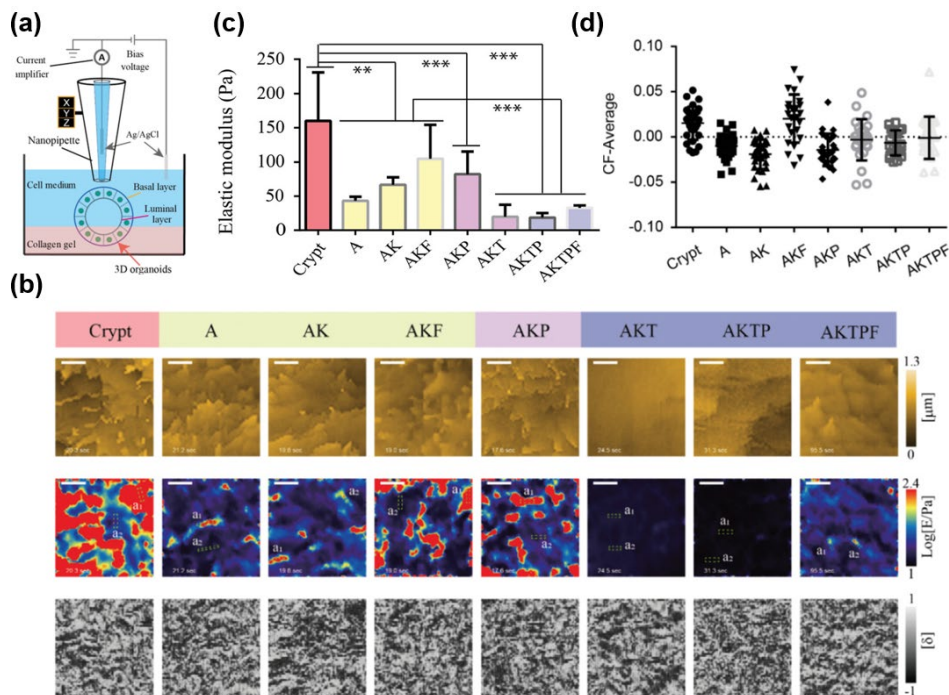
Center director: FUKUMA Takeshi

Program officer: NAKANO Akihiko, RIKEN

1. Advancing research of the highest global level

NanoLSI is continuing its excellent activities in science. In the Center's PI list, Prof. Ando and Prof. Mikhailov retired and were succeeded by Prof. Kodera and Prof. Beta, respectively. Dr. Sato has joined as an Associate PI. Six Jr. PIs who have joined NanoLSI since 2019 are now well integrated into the research environment and are producing good outputs. In FY 2022, PIs of NanoLSI published 106 original articles, of which 45 came from international collaborations, and 26 are top 10%.

Solid progress has achieved marked results in several areas. The high-speed AFM has become even faster due to efforts to reduce the response times of cantilevers, and the 10-fold improvement of temporal resolution now allows observing the dynamics of actin filaments and microtubules at 70-100 frames/s. Analyses by AFM and SICM on the stiffness of the plasma membrane and the nuclear envelope have revealed intriguing changes during cancer metastatic transition, raising many mechanistic questions that



Recent Highlight Mapping Nanomechanical Properties of Basal Surfaces in Metastatic Intestinal 3D Living Organoids with High-Speed Scanning Ion Conductance Microscopy (HS-SICM) **(a)** HS-SICM setup for 3D cell measurement. **(b)** Snapshots of time-lapse images of height, elastic modulus and local correlation factor of in genotype-defined (A, AK, AKF, AKP, AKT, AKTP, and AKTPF) 3D organoids of metastasis cancer cells and normal Crypt cells. **(c)** Elastic moduli and **(d)** local correlation factors in genotype-defined 3D organoids.

Wang et al., *Small* (2023), vol.19 (9), DOI: 10.1002/sml.202206213

await fruitful collaborations with cell biologists. Supramolecular chemistry has succeeded in developing a new sensor system that enables nanomolar detection of 1-MNA as a cancer marker.

2. Implementation as a WPI center

Generating fused disciplines:

To encourage interdisciplinary research, the Transdisciplinary Research Promotion Grant (TDRP-G) is now accepting both top-down (since FY 2021) and bottom-up (since FY 2018) proposals in good balance. T-meetings are operating very well, now often held voluntarily. Matching up young researchers of two different groups, they lead to collaborations.

Realizing an international research environment:

Due to COVID-19, there was a serious physical disruption of communication and exchange between researchers at NanoLSI and those overseas. Now that the pandemic is over, this situation improves and active international interactions have resumed. Applications to the Bio-SPM Summer School and for Bio-SPM Collaborative Research have bounced back to the pre-COVID level.

Making organizational reforms:

NanoLSI and Kanazawa University have already implemented a set of significant reforms during the first half of the WPI funding period. These reforms are to be continued. As of April 2023, 24 master's course students (13 domestic and 11 overseas from 7 countries) and 32 doctorate course students (10 domestic and 22 overseas from 8 countries) are enrolled. These numbers will further expand in FY 2024.

The laboratory tours taken on day 2 of the visit gave us a good and impressive opportunity to see how the NanoLSI building (completed in 2020 during COVID) is organized and how people are working there together.

Effort to secure the center's future development over the mid- to long-term:

President Wada of Kanazawa University expressed a clear and concrete commitment to support NanoLSI even after WPI funding ends, including in terms of personnel and infrastructure maintenance and development. A mechanism for retaining foreign PIs should be considered, perhaps by cross appointments, after WPI funding ends.

The total amount of external funds in FY 2022 granted to NanoLSI was 1.36 billion JPY. The increase in funding continuing from FY 2018 indicates the high evaluation of NanoLSI's research, which will be of strong support in securing the Center's future.

Kanazawa University has a plan to build a new building, "Experimental Research Center for Envisioning the Future," for industry-academia collaboration and verification of basic research results. Part of its space will be used for expanding NanoLSI's activities.

Center's response to the follow up results of last year

As always, NanoLSI has responded to the WG's follow-up recommendations of the previous year very sincerely. Balancing top-down and bottom-up projects has been effectively adjusted, for example, by monitoring the outputs of TDRP-G. To involve more early-stage students, NanoLSI PIs and Jr. PIs are now actively giving lectures and courses to undergraduate students. Female ratio of researchers has increased from ~10% to ~20% in the past 3 years. Among the foreign students at NanoLSI, 58% are now female. The joining of Dr. Hanae Sato from USA as an Associate PI is also good news. Industry collaborations and non-biological applications are also being pursued.

3. Actions required and recommendations

NanoLSI is achieving good progress in developing high-end SPM technologies at a top world level.

It is now time to apply these technologies to answering still-unanswered questions in life sciences, not just to cancer research. Stiffness and elasticity of membranes are one of the promising targets, and collaborations with experts in cell biology will be key to gaining mechanistic insights.

To realize true nanoendoscopy, continued efforts will be needed in developing sensor systems that can be of practical use in measuring metabolites and other parameters in and around living cells.

The Center should continue its efforts in basic research to integrate nano-scale observation and measurement techniques into a new research field and, at the same time, begin to consider broader applications of its technologies to non-expert scientists and the non-academic community by seeking further collaborations with industry in the future.

Improvement of gender balance should also be continued with a strategy. A program to invite senior female and international scientists on a short-term basis to participate in seminars and give presentations may also help in improving this balance.

To expand NanoLSI's international networking, it may also be a good idea for the Center to seek more connections to other overseas research institutions.

G. Follow up on the 2 Centers launched in 2018

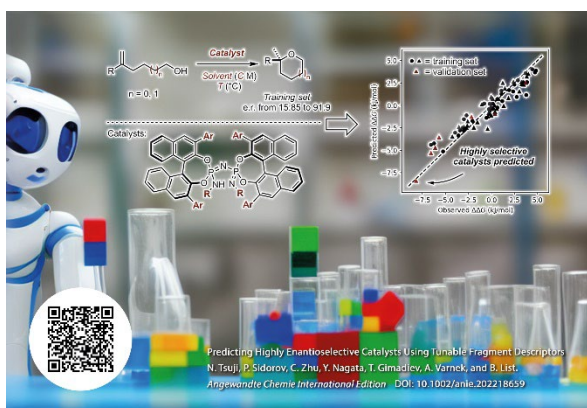
G-1. ICReDD

Center director: MAEDA Satoshi

Program officer: TATSUMI Kazuyuki, Nagoya University

1. Advancing research of the highest global level

At the interim evaluation of ICReDD last year, significant progress was recognized in advancing research on chemical reactions. Toward the second half of its funding period, theoretical chemists, synthetic chemists, and information scientists will continue to collaborate for the creation of a new paradigm for reaction discovery and for expansion of the scope of designing chemical reactions. The seven Flagship Projects had been used as key drivers for the research focus in the first five years, and they have now been reorganized to six projects. The road map of new six projects is explicitly described, and they are complementary to the existing/new bottom-up projects, which are proposed and organized by young members. Particularly noteworthy are 1) application of AFIR to a full theoretical design of chemical syntheses of useful fluorinated compounds etc., 2) use of AFIR for transition-metal catalysis, enantioselective catalysis, and organocatalysis, 3) mechanochemical synthesis, and 4) functionalization of gels and their clinical application.



Recent Highlight [Left] Predicting Highly Enantioselective Catalysts Using Tunable Fragment Descriptors (*Angew. Chem. Int. Ed.* 2023. DOI: 10.1002/anie.202218659)

[Right] In Situ and Real-Time Visualization of Mechanochemical Damage in Double-Network Hydrogels by Prefluorescent Probe via Oxygen-Relayed Radical Trapping (*J. Am. Chem. Soc.* 2023. DOI:10.1021/jacs.2c13764)



2. Implementation as a WPI center

Generating fused disciplines:

From the very beginning of ICReDD, the research has been conducted based on the strong collaboration of theoretical chemists, synthetic chemists, and information scientists. In particular, collaborative efforts of theoretical chemists and synthetic chemists have been very successful on creating a new paradigm for reaction discovery. More recently, information scientists have accelerated their contribution to ICReDD, strengthening the collaborative

capacity of the institute. The fusion of computational and information science has resulted in the AFIR Database designated as SCAN, which is now a powerful tool to design new reactions. Furthermore, in an attempt to apply new chemical materials to cancer diagnosis, close collaboration of chemists, biochemists, and medical staffs has been sought for, and the new consortium (Clinical Platform) is organized for chemists in ICRéDD and for clinicians in Faculty of Medicine and Medical School of Hokkaido University.

Realizing an international research environment:

At the end of FY2022, 45% of researchers are foreign nationals, which is satisfactory.

Inauguration of "List DX Catalyst Collaboration Research Platform" in the structure of ICRéDD is certainly an advantage not only for the Center's research activity but also for its international reputation as an institute. "Fusion Research Office" in the new building also facilitates international research environment.

Making organizational reforms:

- 1) The Administrative Director has provided significant management help for Center Director Maeda, allowing him to concentrate himself more on the research leadership. The President of Hokkaido University has been very enthusiastic in promoting the activity of ICRéDD.
- 2) "List DX Catalyst Collaboration Research Platform" has been inaugurated within the organizational structure of ICRéDD, and the research laboratory is set in the new ICRéDD building. This is significant for ICRéDD, as it will be a welcome boost to the visibility of the institute within the world. In fact, Prof. Benjamin List, Nobel Laureate of chemistry in 2021, understands very well the mission and objectives of the institute as a PI and as the head of the new platform, and he has been well aligned with Center Director Maeda on the vision of ICRéDD.
- 3) ICRéDD is regarded as a core in Hokkaido University in promoting "Grand Challenge Research Strategy", a newly established top-down organizational reform, where the collaborative research platforms create a flexible and dynamic research organization to conduct cutting-edge fusion research.

Effort to secure the center's future development over the mid- to long-term:

Hokkaido University has presented a strong and concrete support plan for the future of ICRéDD.

- 1) The new 4-story 5,500 m² ICRéDD building opened, where the two-story "Fusion Research Office" brings together researchers from different disciplines.
- 2) In order to maximize the impact of ICRéDD in terms of contribution to industry and

commercialization opportunities, “The Mitsui Chemicals - ICRéDD Innovative Chemical Reaction Design Laboratory” has been established in the new building.

- 3) Positions of 10 Senior PIs and 6 Young PIs are, and will be, allocated to ICRéDD by Hokkaido University in order to maintain ICRéDD as a permanent institute. It is not very clear at this stage, however, whether the 10 PI positions will belong solely to ICRéDD or to elsewhere in Hokkaido University.

Center’s response to the follow-up results of last year

The center has adequately and positively responded to the follow-up results of last year. In particular, the following Items are seen as very positive outcomes; 1) to set explicitly its goals and roadmaps for the Flagship Projects and the bottom-up projects, 2) to elucidate the nature of the cancer stem cells that ICRéDD has derived from their interactions with hydrogels, closer collaborations with experts in fundamental cancer biology and pathology are needed, and 5) to make every effort of investigation on the scientific misconduct that occurred at ICRéDD and on the reforms that the university will undertake to prevent reoccurrences.

3. Actions required and recommendations

- 1) Continue the efforts to achieve the top-level science through fusion research of theoretical/ informational/experimental sciences. The flagship projects as well as the bottom-up projects have been a very effective promoters for this purpose.
- 2) Continue the efforts to fulfill the gender balance at every level in line with the policy of Hokkaido University.
- 3) Continue the efforts to establish the staffing plan to guarantee that ICRéDD will maintain 10 PI positions of its own.
- 4) It is recommended that ICRéDD and Hokkaido University aid “List DX Catalyst Collaboration Research Platform” to promote additional funds from funding agencies both in Japan and in Germany, e.g., JSPS and DFG.
- 5) ICRéDD is recommended to bring in more researchers and students from established top-institutes abroad, e.g., those in Europe and in the USA.
- 6) One mission of MANABIYA for spreading the methods of “computation-aided chemical reaction design” is fine, but the planning and setting-up for MANABIYA-based new graduate school needs to be much accelerated.
- 7) Hokkaido University is asked to conduct reforms in order to prevent reoccurrences of the scientific misconduct that occurred at ICRéDD, and the members at the center are asked to share deep understanding on research ethics and proper scientific conduct.

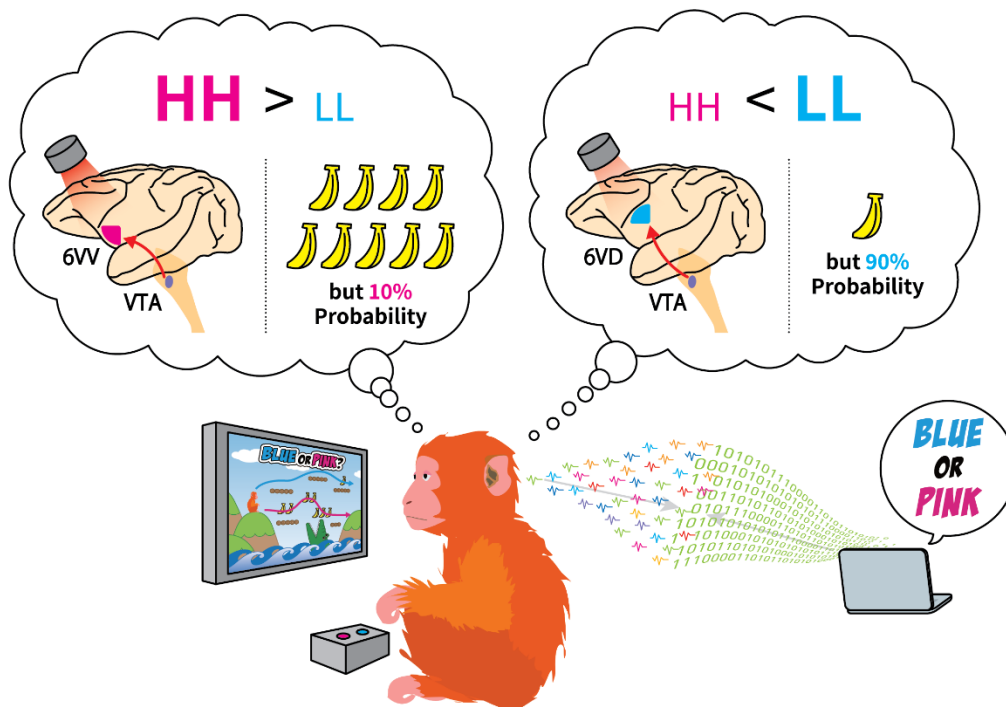
G-2. ASHBi

Center director: SAITOU Mitinori

Program officer: OKANO Hideyuki, Keio University

1. Advancing research of the highest global level

ASHBi aims to understand biological traits that define humanity, using this knowledge for disease treatment. Focusing on genome regulation and disease modeling, they have published more than 200 influential WPI papers in five years. Recently, we observed enhanced coherence in ASHBi's research. Their five flagship projects, particularly one on early primate development, show promise in understanding the human essence. We emphasize the significance of ASHBi's nonhuman primate research for global biomedical advances and recommend focused discussions to maximize its medical impact, especially in kidney and psychiatric disorders.



Recent Highlight Lighting the Circuits to Risky Decision-Making (Isa G, Science, 2024)

2. Implementation as a WPI center

Generating fused disciplines:

Fusion of biology and mathematics: ASHBi's efforts to merge mathematics with biology have seen substantial progress. They've set up a specialized mathematics team comprising data science and mathematical modeling experts, not limited to Kyoto University. This team has pioneered advanced algorithms like RECODE for minimizing noise in scRNA-seq analysis and tools vital for biological data examination, like scEGOT and the

topological embedding method for scMC-3C.

Fusion of bioethics and life science: ASHBi's Bioethics Group is making international waves, partnering with organizations such as ISSCR. They have led discussions on sensitive topics, including human fetal and postmortem tissue research, stem cell-based embryo studies, synthetic embryos, and the controversial 14-day rule for human embryo research.

Realizing an international research environment:

ASHBi's internationalization and diversity have grown significantly, recruiting two foreign/female Principal Investigators (PIs) and promoting foreign/female postdocs via their Employment Support Program. Continuing these efforts is crucial for international collaborations and enhancing ASHBi's global prominence.

Making organizational reforms:

Kyoto University (KU) is supporting ASHBi's organizational reforms, including a top-down decision-making system. To sustain the Institute beyond the WPI program. A) **Personnel Support:** KU will give five tenured professorship positions to ASHBi. By the end of 2021, two were filled, and three more are expected by April 2024; B) **Financial Support:** KU will redirect indirect funding from its two WPI centers to a special budget for the centers.

Effort to secure the center's future development over the mid- to long-term:

Kyoto University (KU) has prioritized ASHBi's long-term growth with several initiatives: A) After WPI funding concludes, KU will allocate a special budget to maintain ASHBi's Administrative Office and Research Acceleration Unit; B) ASHBi's successful practices, core facilities like SignAC, will be incorporated into broader KU system reforms, signaling a major overhaul of the university's research administration and support structure.

Center's response to the follow-up results of last year

ASHBi is dedicated to understanding the fundamental essence of what makes us human. They have actively promoted the integration of various disciplines and launched 5 Flagship Projects, while conducting regular progress checks and in-depth evaluations at the Principal Investigator (PI) level. With an ambition to become a global nexus for human biology, ASHBi is pushing to diversify its team by increasing the number of foreign and female PIs, junior researchers, and postdocs.

3. Actions required and recommendations

- 1) **(Monkey Project):** There is opportunity for the Center's non-human primate research to be very impactful in tackling human diseases. To address the issue of insufficient supply and high cost of macaque monkeys, ASHBi is considering having its satellite at

Shiga University of Medical Science breed the macaque monkeys. The size of the satellite's facility and its current monkey count will need to be assessed toward obtaining a consistent research supply. On the other hand, sufficient ethical reflection should be shown in their work on genetically modified non-human primates.

- 2) **(Mathematics):** ASHBi has created advanced analysis systems like RECODE and V-Mapper. The goal should now be to set these systems as global benchmarks in biological data analysis.
- 3) **(Ethics):** ASHBi appears able to become a leader in creating ethical guidelines for research, particular in the domain of stem and germ cells. Eventually, it should share this knowledge internationally.
- 4) **(Clinical Science):** ASHBi should develop "Better Cures for Disease". It is expected that ASHBi will advance research plans aimed at developing new therapies for diseases based on human biology. They should not be satisfied with just developing genetically modified monkey models of human diseases but should proactively investigate ways to develop innovative therapeutic strategies using the monkey models they develop.
- 5) **(Diversity):** The Center's female and non-Japanese ratios are reasonably good. However, considering the fields related to the Center's research, ASHBi could aim at a higher percentage of female researchers. While ASHBi stated that they are going to recruit more females, they did not tell us much about their plan to increase female researchers in the Center. ASHBi needs to take an even more concerted and strategic approach to encouraging gender diversity, especially at the PI level.
- 6) **(Support from Kyoto University):** Kyoto University considers ASHBi and SignAC as exemplary models of research organizations and plans to expand them to university-wide system reforms and promises continuing financial support for that.

H. Follow up on the Centers launched in 2021

H-1. QUP

Center director: HAZUMI Masashi

Program officer: TSUNETTA Saku, National Astronomical Observatory of Japan

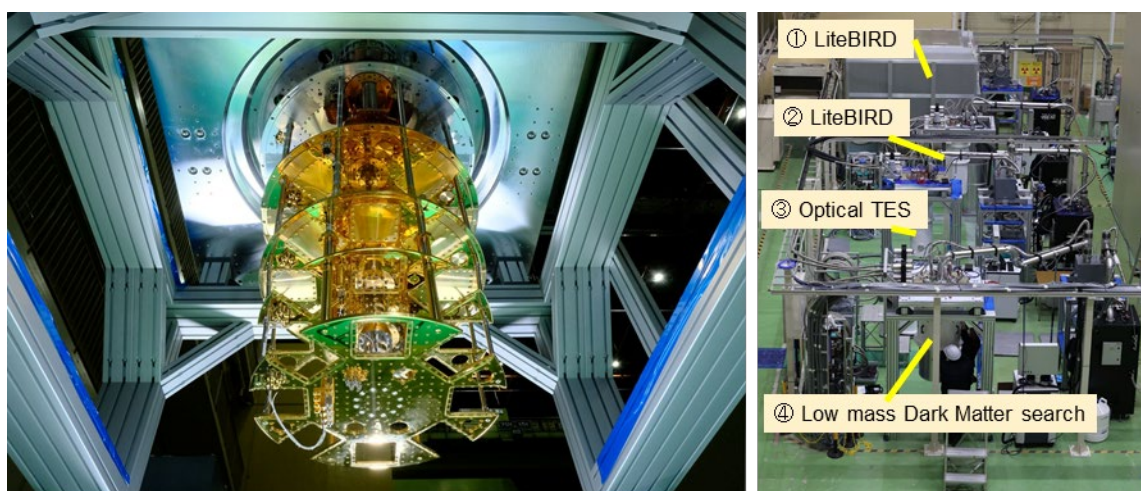
1. Implementation as a WPI center

(1) World-Leading Scientific Excellence and Recognition

Advancing research of the highest global level:

Development of novel measurement principles for particle physics and cosmology with broader societal applications in the longer term is the scientific vision of QUP. It is clarified that the QUP's SpaceTES for the LiteBIRD Project is responsible for the design, fabrication, test and delivery of the TES detector system to JAXA's LiteBIRD flight mission. There are a number of serious concerns with this project. The higher-level JAXA-led project has not yet been well defined and therefore all the external interfaces are poorly defined including the overall schedule and the budget acquisition prospect. Within QUP, experience of developing space hardware is limited to very few people. The QUP-Kamioka-DM (Dark Matter) project, a new flagship project candidate, has been proposed, having two phases (exploratory and more sophisticated experiment phases). This second-stage project, however, is still in a preliminary stage. The Casimir force project is very interesting but needs clearer objective and stronger plan. The PI-led rad-hard project and collider project need more coherence and synergy with the objective of QUP.

Overall, there does not seem to be a systematic approach to developing novel quantum field measurement systems, resulting in slowness in developing flagship projects and a lack of cohesiveness in the research agenda presented.



Recent highlight QUP cryo-facility: Four dilution refrigerators were installed for the QUP detector

Generating fused disciplines:

It turns out that systemology was a system-engineering methodology, and a solid system engineering support group is being put in its place, which will be essential for implementing the SpaceTES Project. The director proposed that systemology also be applied to more infant and ambiguous research activities. The concept of systemology does not appear to be coming together.

QUP has initiated the QUPosium/Workshops, QUP week, and QUP Synergy Summit. It is too early to know whether these new activities will lead to important progress in technology and discoveries. Overall, the fusion with other disciplines is still relatively moderate.

(2) Global Research Environment and System Reform

Realizing an international research environment:

With PIs from abroad spending only a week/year at the center in FY2022, and the total number of researchers still being at the low number of 30 by the end of FY2022, which is well below the planned number, international PIs and researchers do not appear to be well integrated into the QUP project. Serious effort is needed to recruit foreign researchers both at the PI level, which was in last year's recommendations, and at a junior level. Without this effort, it will be difficult for QUP to attain international standing and attractiveness for young researchers from overseas.

Making organizational reforms:

It is not clear whether QUP has implemented any system improvements to enhance its transparency. Questions include: What is the decision-making system? What is the relation between the QUP Director and KEK Director-General? How is QUP's administration organized, and what role is the administrative director playing?

KEK Director-General did mention that KEK would support QUP without commenting on its own organization reform plan stimulated by QUP. It is important for KEK to find sufficient incentive to support QUP. To make its support for QUP sustainable, KEK will need to identify the actual merit of accommodating QUP within its organization.

(3) Values for the future

Societal Value of Basic Research:

Outreach activities to society should be more emphasized. An outreach expert to promote public awareness on the societal value of QUP is needed.

The idea to directly include the industry sector in the project is new and could lead to

inventions developed interactively with society. Incorporating more diverse groups including non-Japanese industries will increase the effectiveness of this approach.

Human resource building: higher education and career development:

QUP has started an internship program for graduate students and postdocs called QUPIP. However, we do not see clear presence of PhD students, and with QUPIP, people do not stay at QUP for more than three months. More effort is needed to set up an education system that is attractive to students and young researchers, and that triggers a system change in the graduate education of KEK. A numerical target should be established.

QUP's initial proposal stated dispatch of young researchers to the Berkeley Satellite for an extended period to foster researchers with an international perspective. We need to see that this happens.

Self-sufficient and sustainable center development:

Director-General Yamauchi explained KEK's support plan for QUP's sustainability. There are a number of issues regarding the self-sufficient and sustainable development of the center. The role that KEK wishes QUP to play in its reform is not clearly explained. The number of positions is insufficient for QUP to become self-sustained; more positions will be needed. It is not clear whether the renovated building has sufficient space to house all PIs, including those from abroad, "under-one-roof".

2. Center's response to the follow up results of the last year

QUP management took last year's recommendations very seriously and made a significant effort to implement them, including structural changes to the organization, and de-emphasis of some activities. While this has resulted in improvements, the state of progress is not satisfactory. Regarding the LiteBIRD project, a new set of technical and programmatic concerns has emerged including the funding issue to be resolved with wider stakeholders of KEK, JAXA and MEXT. Regarding project-Q, the QUP-Kamioka DM project is proposed as a candidate. It appears that the project is still in the defining phase. A clear path for the technology, methods, and goals needs to be worked out to see if the project will be competitive and worthwhile as a second flagship project.

3. Actions required and recommendations

The WPI Program Committee is seriously concerned with the state of progress at QUP. The activities reported do not show convincing quality, breadth and strength required to achieve the WPI mission. The identity and role of QUP, justifying a new center within the host institution KEK, is not becoming any clearer. WPI Program Committee advises QUP

and KEK, as the host organization, to seriously consider the following points. The Program Committee expects to receive clear and concrete responses on these points from QUP and KEK at next year's Program Committee meeting.

- 1) There is very urgent need to establish a clear and credible research agenda that is coherent and systematic for achieving QUP's scientific vision, namely, to develop novel measurement principles for particle physics and cosmology with longer term societal impacts.

The SpaceTES for the LiteBIRD Project is more into the engineering phase than the basic research phase suited to WPI. To the extent that this project is to be pursued by QUP, it requires a clear internal and external interface definition, definitive plan for AIV (Assembly, Integration, Verification) with quality assurance and system engineering, and the necessary team staffing to deliver the flight TES system to JAXA. The funding to build the TES flight system must be clarified with KEK, JAXA and MEXT.

The QUP-Kamioka-DM Project should develop a concrete plan for building the proposed facility at Kamioka and establish a strategy with a realistic plan and timeline for actual payloads (especially phase 2 and "plan B" for phase 2) to detect light dark matter. The novelty and superiority of this project among the multitude of DM projects has to be established.

In addition to SpaceTES and QUP-Kamioka-DM, serious consideration has to be given to the PI-led projects including the Casimir force, rad-hard and collider physics projects to ensure their strength and coherency with QUP's objectives.

- 2) The concept of systemology is not coming together. QUP should design much more concretely the application and extension of system engineering (aka systemology) to its research projects with fusion among disciplines in mind. QUP should also establish success criteria for the systemology section to gauge its effectiveness.
- 3) Very strong efforts should be made by QUP's leadership to recruit foreign researchers and integrate them into QUP's activity. This includes additional foreign PIs residing on site and junior researchers including postdocs and graduate students. QUP should aim at levels higher than the WPI numerical target. Assuring the quality of personnel and promoting their long-term residence at QUP in Japan is also essential. To achieve this, QUP should examine what attractive features it can provide to foreign researchers.
- 4) QUP Internship Program (QUPIP) requires much more ideas and effort for it to exert a change in KEK's education system. The program should be made more attractive

and better known to young researchers worldwide, along with having a relevant financial support scheme. QUP should dispatch young (Japanese) researchers to its Berkeley Satellite for extended periods to foster researchers with international perspectives, as stated in its proposal.

- 5) QUP should make stronger, more persistent outreach efforts to promote public awareness of its societal value. Collaboration with diverse companies will be effective in disseminating the value of basic research to society.
- 6) KEK Director-General should make KEK's support plan into an official statement so as to guarantee its execution of QUP's operation after WPI funding ends.
- 7) The new building to be built by 2025 should have enough space to truly house all PIs and researchers under-one-roof. It should have an attractive design, one that realizes the kind of open and international environment envisioned by WPI.
- 8) As a WPI center, QUP is expected to develop a clear and unique identity, which is not an extension of KEK, in both its science, as a research organization, and its education. QUP and KEK should make clear and concrete statements on their views regarding this matter.

I. Follow up on the Centers launched in 2022

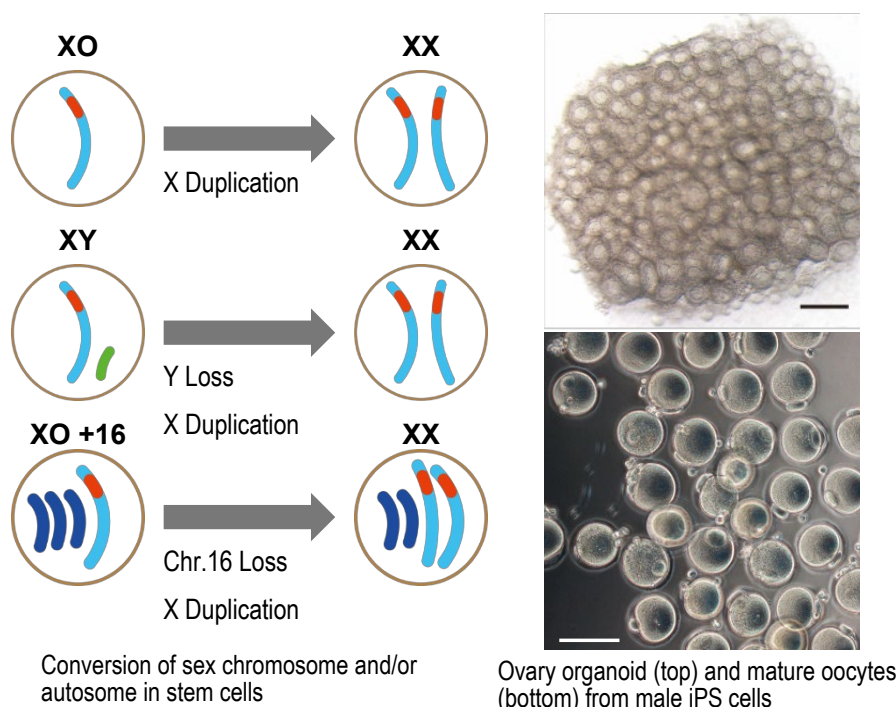
I-1. PRIME

Center director: NISHIDA Kohji

Program officer: KURODA Shinya, The University of Tokyo

1. Efforts to improve points indicated as requiring improvement in application review and results of such efforts

(1) PRIME has attempted to coordinate research on digitizing life and medical phenomena. However, a shared vision of a concept of biological twins and a common research direction/roadmap for biodigital twins are still lacking. (2) A strategy related to cross-talk in inter-organ networks was presented, but verification is still pending. (3) While the idea of setting up a cloud-based data infrastructure is appreciated, there is a significant concern about the lack of coordination between experimental researchers, mathematical/ information scientists and advanced technology teams. (4) The role of partner institutions was not explained clearly during the site visit.



Recent Highlight PRIME PI Katsuhiko Hayashi and colleagues achieved successful mouse oogenesis reconstitution, converting both autosomes and sex chromosomes. This technology enables the production of functional oocytes from male cells. It will serve as the foundation for creating a human ovarian organoid system from iPS cells of patients with sex chromosome abnormalities or aneuploidy.

Nature (2023) DOI: [10.1038/s41586-023-05834-x](https://doi.org/10.1038/s41586-023-05834-x)

2. Implementation as a WPI center

(1) World-Leading Scientific Excellence and Recognition

Advancing research of the highest global level:

PRIME has assembled researchers of high quality in a multi-disciplinary area that spans biomedical research, clinical medicine, mathematical sciences, and advanced technologies. At the same time, there is a significant lack of a shared, concrete vision for the center project's main aim: creating biodigital twins. To remedy this situation, there is a strong need to form a "steering committee" that defines the concept of biodigital twins, and generate a roadmap for integrating each team into a cohesive whole for researching biodigital twins. The steering committee would include the director and deputy directors, and perhaps some young PIs and an ELSI expert to spur their early participation in leadership.

A very important element for establishing biodigital twins is the managing and sharing of data. A unified plan for data generation, verification and sharing is urgently needed.

Generating fused disciplines:

Regular and deep discussions among PRIME members are crucially needed so as to fuse organoid research with computational modeling. The "steering committee" described above would be a good arena for conducting such discussions. Deputy director Okada, who is familiar with both wet and dry research, should be put in a position where she can take more leadership in facilitating discussions and can guide the process of interdisciplinary fusion more actively. Recruiting an additional PI who makes 100% effort to developing biodigital twins should be considered. The new PRIME building, to be completed by 2026, will provide a co-location for 'wet' and 'dry' researchers, greatly facilitating their integration under one-roof.

(2) Global Research Environment and System Reform

Realizing an international research environment:

The center currently falls short of meeting WPI requirements for international representation and diversity among its PIs and researchers. The center should recognize the importance and benefits that well-diversified research leadership and a diverse group of researchers can bring, and make a concerted effort to increase the number of foreign PIs and female PIs at the center.

Many of the foreign and cross-appointed PIs are not spending adequate time at PRIME, which is an issue given their importance to the center.

Making organizational reforms:

PRIME has instituted a top-down decision-making process, led by the director, which includes budgetary and personnel decisions. It has also set up an administration system with 5 URAs for research support.

(3) Values for the future

Societal Value of Basic Research:

PRIME's outreach includes Nature Index announcements, a dedicated website, symposia, and high-school programs. There is a need, however, for a well-formulated strategy to disseminate the value of "Human Metaverse Medicine", and PRIME should establish strong interaction with patient groups and the public.

Human resource building: higher education and career development:

Graduate program for human Metaverse and a Ph.D. program will start by 2027. An inspiring environment for Junior PIs exists. Further planning and concrete measures are required, however, including a concrete support plan for graduate students, greater attention to attracting foreign students, and clearer program definitions, especially in interdisciplinary education like bioinformatics.

Self-sufficient and sustainable center development:

Osaka University supports PRIME with a new building, faculty positions, and JPY 700M in management costs. Concerns exist about the permanency of the administrative staff position after WPI funding ends.

3. Actions required and recommendations

- (1) There is a strong need for PRIME to clearly articulate and share a common vision/concept on biodigital twins among all its PIs. This requires intense discussions led by a "Steering committee", including the director and deputy directors, some young scientists and a medical ethics expert. The role of the steering committee would be to design a vision/concept of biodigital twins, formulate a strategic roadmap and flagship projects for the mid (within 5 years) and long terms (10 years or more).
- (2) Deputy director Okada, who is familiar with both wet and dry research, should be put in a position where she can take more leadership in facilitating discussions and can guide the process of interdisciplinary fusion more actively. Hiring an additional PI who has the expertise and background that would help to develop biodigital twins is as an option for enhancing the center's vision and possibly attracting more international collaborations.
- (3) There is urgent need for a dialog between PIs doing experiments, including organoid

and clinical studies, conducting mathematical analyses, and developing advanced technologies to see how their sciences can be integrated. In particular, integration of the surrogate model (data-driven model) for clinical data, and of the causal model (hypothesis-driven model) for human organoids should be designed and implemented.

- (4) Standardized protocols for experimental and mathematical analyses should be set for cohesive integration into biodigital twins. Hiring a specialist researcher who can lead this effort and manage the resulting data should be considered.
- (5) PRIME is strongly recommended to systematically accelerate the recruitment of foreign and female researchers beyond the WPI requirements.
- (6) Research space allocation should mix "wet" researchers (experimentalists) and "dry" researchers (theorists) on the same floor for better vision sharing and activity fusion. This should be taken into account in the design of the new building.
- (7) The host university should clarify how it will make administrative staff positions permanent after WPI funding ends.

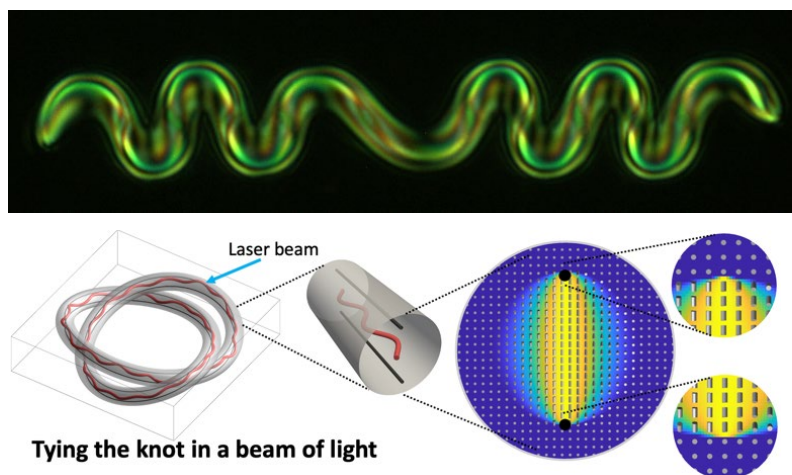
I-2. SKCM²

Center director: Ivan SMALYUKH

Program officer: YASHIMA Eiji, Nagoya University

1. Efforts to improve points indicated as requiring improvement in application review and results of such efforts

- 1) The director stayed in Hiroshima fulltime for the first year of the SKCM² center, committing an admirable effort to achieving a successful start of the SKCM² project. He should, however, make it clear how much time he will stay in Hiroshima over the next couple of years.
- 2) The foreign PIs' effort numbers have improved. To accommodate long-term stays of foreign PIs and the center director at SKCM², a new building dedicated to SKCM² for providing them space and providing the availability of a suitable international school for their children are urgently needed.
- 3) The center director has done an excellent job of launching SKCM². He has established an initial set of operating rules and a top-down decision structure to promote internationalization and system reform.



Recent highlight

[Top] A polarizing optical micrograph of a defect configuration with Möbius strip topology, called "möbiuson", in a chiral nematic liquid crystal. Upon supplying energy as electric pulses, möbiusons exhibit rotational and translational motions, as well as topological cargo-carrying abilities controlled by tuning amplitude and frequency of applied fields.

(H. Zhao et al, *Nature Physics* 2023. <https://doi.org/10.1038/s41567-022-01851-1>).

[Bottom] Optical axis patterns with singular vortex lines with Möbius strip topology robustly steer beams of light, including into knots. They may find technological uses in beam steering, telecommunications, virtual reality implementations and anticounterfeiting.

(C. Meng et al, *Nature Materials* 2023. [doi:10.1038/s41563-022-01414-y](https://doi.org/10.1038/s41563-022-01414-y)).

2. Implementation as a WPI center

(1) World-Leading Scientific Excellence and Recognition

Advancing research of the highest global level:

The director has successfully brought in diverse groups of expert PIs from different foreign institutions and from Hiroshima University (HU), along with a strong view of gender diversity at all levels of the center. He has assembled research teams of experimentalists and theoreticians from various disciplines to develop a world-leading research center to create the new field of “knotted chiral meta matter”.

The research approach and principles being put forward by SKCM² appear to be good, and there are a large number of very impressive research projects being undertaken. Several reports have been published in good journals during the first year, but it's important to know how much of the reported research is driven by the center director versus the center as a whole. SKCM² should present the center's research achievements as a whole next year.

Generating fused disciplines:

The center has 18 excellent senior and talented young PIs from diverse disciplines of chemistry, physics, biology and mathematics. It has assembled research teams and has implemented a number of measures including shared space and daily coffee time to promote collaborative projects across disciplines. At present, fusion studies are still in the developing stage. The center director should carefully monitor progress in the key areas supported within the center to ensure that they evolve into topics with genuine connections to the intellectual core of the center.

(2) Global Research Environment and System Reform

Realizing an international research environment:

As of September, of this year, SKCM² had 66 members of whom 44 (66%) are from abroad. It is impressive to see the involvement of many early career researchers and students from abroad. The support provided young scientists to spend time in overseas labs is significant to creating additional opportunities for collaboration and also to expanding the minds of young Japanese scientists.

In order for overseas PIs and the center director to stay at HU for long-term periods and promote productive collaborative research activities, there is a need to solve the serious problem of an international school being located a long distance from the campus. This is a basic infrastructure problem outside of major cities in Japan, which needs to be solved. President Ochi is now actively working to bring an international

school closer to the campus.

Making organizational reforms:

The many system reforms initiated at SKCM² under the strong leadership of the center director, who is a non-Japanese researcher, and with strong support of President Ochi are very encouraging. The host university should continuously support this effort in various ways so that the director's vision can be realized in SKCM² and can lead the reform of HU.

(3) Values for the future

Societal Value of Basic Research:

Strategic efforts are being taken to reach out to leading institutions such as MIT in attracting postdocs to the center. Meaningful outreach is also being taken to attract potential young scientists in schools and communities. These include the hiring of an in-house science writer.

The center director emphasized the goal of SKCM² achieving societal impacts by tackling problems related to sustainability. However, the potential of the center's research to make sustainable impacts is not obvious; it should be more clearly articulated in the center's research mission and plans.

Human resource building: higher education and career development:

SKCM² has initiated an interdisciplinary graduate program to train students in a fashion that enables them to cross boundaries of isolated disciplines of science. The details of the program are still being developed. It will be necessary to confirm the progress made in the future, including an increase in the number of female students. Toward improving gender balance in fields of science and engineering at SKCM², one of the Deputy Directors is actively engaged in related outreach.

The director's declaration to publish 1,000 papers per year and have 10,000 cumulative impact factors might be not be conducive to a healthy research culture for advancing good science. It would be better not to set unnecessary quantitative goals.

Self-sufficient and sustainable center development:

President Ochi's strong commitment to developing SKCM² as a sustainable institute is excellent. The support measures that he has introduced include financial support, research space in the existing building, 5 admin staffs, 5 new PI positions in the second half of the WPI funding period, and a plan to construct a new research building dedicated to SKCM². It is urgent that HU work closely with MEXT in obtaining

a budget for the building's construction.

3. Actions required and recommendations

Overall SKCM² has made a very good start in its first year of operation. There are some points that should be addressed for promoting further progress.

- 1) It may be too early to discuss its scientific achievements in the first year, but the center should present the original research achievements of its members as a whole next year.
- 2) The connection between the sustainability of society and the center's research mission and plans is not obvious and should be more clearly articulated.
- 3) Fusion studies are still in the developing stage. The center director should carefully monitor progress in the key areas currently supported within the center to ensure that they evolve into topics with genuine connections to the intellectual core of the center.
- 4) In relation to the director's appointments at HU and University of Colorado, a specific agreement needs to be exchanged on intellectual property assignment.
- 5) The lack of suitable international schools near the campus for supporting long-term stays of foreign researchers with family is a basic infrastructure problem outside of major cities in Japan. While this is an urgent problem, the solution will not be easy; we hope the host university will continue to work closely with the local community to find a solution as soon as possible.
- 6) There is an urgent need to construct a new research building for SKCM² as soon as possible, which will greatly contribute to productive interdisciplinary collaborative research, particularly by foreign PIs at HU.

I-3. Bio2Q

Center director: HONDA Kenya

Program officer: TAKAHASHI Ryosuke, Kyoto University

1. Efforts to improve points indicated as requiring improvement in application review and results of such efforts

The program committee raised four major concerns to be properly addressed.

1) Application of quantum computing to the biomedical field

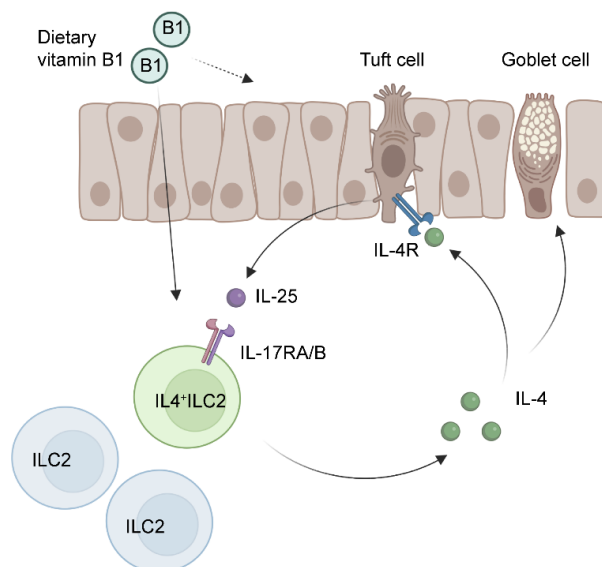
The computational researchers in the Q core started a discussion with biomedical researchers in the Bio1/2 cores to formulate a roadmap. Dr. Tuganbaev (Jr. PI) presented his attempt to leverage machine learning and quantum annealing computing for personalized drug efficacy optimization. Moreover, a senior quantum computing expert from IBM has been hired. A concrete roadmap, however, has yet to be presented.

2) Clarification of the relationship between microbiome and each organ

Top-down and bottom-up approaches using gnotobiotic techniques to clarify this relationship were described by Dr. Honda. Identification of bacterial consortia that mediate beige adipose cell induction achieved through the top-down approach and isolation of a bacterial metabolite specific to centenarians achieved through the bottom-up approach were given as examples.

3) Number of foreign PIs

Two PIs are currently invited to reside, and one Jr. PI is already residing, on site. It was decided to set a concrete target of having at least 5 international PIs or Jr. PIs residing on site. A global call is ongoing.



Recent highlight:

We identified a previously uncharacterized subset of group 2 innate lymphoid cells (ILC2s) constitutively expressing IL-4 in the mouse intestine and showed that dietary vitamin B1 has a crucial role in maintaining the interaction between tuft cells and IL-4+ ILC2s for intestinal homeostasis.

Cui et al, *J Exp Med.* 2023;220(8).

doi:10.1084/jem.20221773

4) Host institution's support

The top management of Keio University committed to constructing a new building with a floor space of 6050 square meters exclusively for Bio2Q on its Shinanomachi campus. This building is scheduled to be completed by 2027.

2. Implementation as a WPI center

(1) World-Leading Scientific Excellence and Recognition

Advancing research of the highest global level:

Biomedical research at Bio2Q is of very high quality. The discoveries on the metabolite and communities of microbiota using the gnotobiotic system (Director Honda), new techniques of 2D culture system of intestinal epithelia (PI Sato), the state-of-art technologies of lipidomics (PI Arita), CryoET analyses of synaptic proteins (Jr. PI Suzuki), and creation of marmoset model of Alzheimer disease (PI Sasaki) are particularly interesting and world-leading achievements in their respective research fields. However, it is not well explained how these research initiatives are connected to the research goals aimed at by the center. In particular, Bio2Q did not present a clear idea of how the quantum computer group could collaborate with the life science groups or of what its goals are.

Generating fused disciplines:

The fusion of microbiome research with neuroscience and other life sciences has made some progress. On the gut-brain axis focusing on the EEC, the neuro-regulation team is forming a nice collaboration with PI Sato's group, who has succeeded in developing organoids. On the other hand, translational approaches promoted by collaboration between basic and clinical researchers were not sufficiently discussed. The members of Bio1/2 cores should hold regular meetings to discuss ways to promote their collaboration under the leadership of the center director.

The collaboration between the Bio1/2 and Q core teams has an apparently more a fundamental problem: They speak different languages and still experience difficulties in mutual understanding. Joint seminars between these groups could be of some help but more concrete joint project planning is a necessity.

(2) Global Research Environment and System Reform

Realizing an international research environment:

Bio2Q has succeeded in recruiting world experts from abroad in establishing an international environment. Dr. Augustine, a renowned neuroscientist, will move to Bio2Q from Singapore and set up his lab as a PI. Dr. Aricescu (PI) at MRC is helping

Bio2Q to install a CryoEM, and Dr. Suzuki (Jr.PI) at MRC, who collaborates with Dr. Aricescu, is moving to Bio2Q to take initiatives in CryoEM studies. They plan to establish young researcher exchange programs between MRC and Keio in ensuing years.

On the other hand, whether English is used as the official language within the center and how the center supports foreign researchers were not elaborated in the presentations. Further effort is expected toward achieving the goal of making 30% of Bio2Q members foreign researchers.

Making organizational reforms:

Establishing a research center, independent and autonomous within the host institution, is a new experience for Keio University. The university's statutes have been changed to establish Bio2Q under the Keio Global Research Institute (KGRI), to define Bio2Q's independence with regard to decision making, and to establish the center's administration. Keio University is currently developing bylaws for Bio2Q. In recruiting excellent PIs from abroad, age and salary caps have been eliminated by decision of Keio's top management. The university has also committed to constructing a new building for Bio2Q on its Shinanomachi campus by 2027.

(3) Values for the future

Societal Value of Basic Research:

Bio2Q has huge potential to contribute to the sustainable growth of the human society with healthy longevity. As an example, several of the bacterial consortia developed in the Honda lab have been licensed to pharma/biotech companies. The 2D culture systems of organoids developed in the Sato lab have immediate and immense potential in the pharmaceutical industry.

Bio2Q has employed an international design company to develop a branding and design strategy and its center's logo. The name Bio2Q and its logo were registered as a trademark. As for outreach activities, Bio2Q members participated in the 11th WPI Science Symposium, explaining Bio2Q's activities to middle and high school students as well as to a general audience. Moreover, a Bio2Q Kickoff Symposium was held.

Human resource building: higher education and career development:

Bio2Q launched a joint interdisciplinary graduate English program, called STaMP (Science and Technology, and Medicine, Pharmacy), across the university's graduate schools of Medicine, Pharmaceutical Sciences, and Science and Technology. In FY

2022, STaMP held its first 5-day event "Workshop for Research Presentation Skills 2022". A researcher exchange program between the MRC and Keio is planned to be established by the Structure Analysis team (Drs. Aricescu and Suzuki) in the near future.

Self-sufficient and sustainable center development:

Keio University's top management communicated its plan to construct a new building dedicated to Bio2Q with a floor space of 6050 square meters at an estimated cost of about 5,500 million JPY. This plan is commendable as it strongly supports the activities of Bio2Q and fits with the WPI's overarching concept of "under-one-roof".

Keio's top management is well aware of the need to create a concrete plan for securing researcher positions and a financial basis for Bio2Q as a permanent organization under the financial conditions of a private university, which is very different from those of national universities.

3. Actions required and recommendations

- 1) The life science of Bio2Q is going extremely well. Individual research initiatives, including those of microbiome, organoid, lipidomics, synapse neurobiology and gene-engineered marmosets, are at world-leading levels. What is highly expected in the near future is to bring all of these initiatives together and to enhance fusion by having each Bio2Q member share the vision of director Honda. The center director will need to continuously help foster interactions during center operations by pointing out where collaborative connections still need to be established. Moreover, it is important to develop experimental and analytical techniques to understand the interactions between humans and microbiome at the molecular level. Furthermore, a data management plan for sharing data acquired from the center and the satellites would be helpful for future advancement.
- 2) Fusion of microbiome biology and quantum computing is still in its infancy and in a very challenging direction. But it will be a valuable challenge to tackle. To apply quantum computing to life science problems will require further advances in quantum computers combined with deep analyses on how problems can be solved. Finding practical but biologically relevant problems and solving them using quantum-inspired calculation is a good way to proceed. The commitment of both computational scientists and biologists is needed for this to succeed. Recruiting researchers from outside Bio2Q could be instrumental in bridging the biology cores and the quantum computing core. Moreover, it is important to keep open the

possibility of adjusting or even revising the roadmap in light of external developments, such as new advances in quantum computing in coming years and good usages of a hybrid-type computer.

- 3) Bio2Q aims to achieve the WPI goal of 20% non-Japanese PIs and 30% non-Japanese researchers in total. We encourage the center to take every possible measure to realize this goal. Bio2Q also aims to achieve 50% female researchers. This is a lofty goal which will require a strong, strategic recruitment plan. It is also not too early to begin planning career enhancement services for junior researchers to advance their future career development.
- 4) The host university should develop a strategy in the next year on how it will support Bio2Q after WPI program funding ends. Establishing an independent and autonomous research center is a new experience for Keio University. It is crucial to form a consensus on how Bio2Q will contribute to advancing the internationalization of Keio University, enhancing the university's global visibility, and delivering benefits to the university as a whole. The president and top management of Keio University should provide strong support in this effort.

J. A new WPI center launched in 2023

In 2023, MEXT made an open call for WPI centers under a new center scheme; a WPI CORE center which develops to a full-sized center through a stage gate process, and a WPI Multiple HOST center which is jointly proposed by multiple host institutions. After a vigorous selection process that ran from February to September of 2023, the Program Committee selected a new center in the Multiple HOST center category “Advanced Institute for Marine Ecosystem Change (AIMEC)” established jointly by Tohoku University and Japan Agency for Marine-Earth Science and Technology.

Headed by Professor SUGA Toshio, WPI-AIMEC aims to unravel the response and adaptation mechanisms of marine ecosystems to environmental and anthropogenic pressures by bringing together an interdisciplinary team of scientists from ocean physics, marine biology, climate science, data science and modelling. The center combines Tohoku University’s strength in basic academic research and education with JAMSTEC’s strength in missions-based research in advanced observation and modelling.

WPI-AIMEC started operation in October of 2023.

K. WPI Academy

K-1. Aims and members

Concurrent with the end of the 10-year support period for the initially established five WPI centers, a WPI Academy was launched by MEXT in 2017. Its aim is to enhance and amplify the WPI brand and to play a vanguard role in internationalizing and reforming Japan’s research environment by leveraging the WPI achievements attained so far.

Academy membership requires certification by the WPI Program Committee that a center has achieved “world premier” status. Centers, then, need to be recertified every 3 to 4 years by the WPI Program Committee, which determines whether they have maintained their “world premier” status.

Currently, the WPI Academy centers are: AIMR, iCeMS, IFRcC and MANA from FY 2017 and recertified in FY2020, I²CNER from FY 2020, Kavli IPMU from FY 2017 and recertified in FY 2021 at its final evaluation, and IIIS, ELSI and ITbM since FY 2022.

K-2. Change of the Director in I²CNER, iCeMS, and Kavli IPMU

Kyushu University, the host institution of I²CNER, proposed a change of the center director from Dr. Petros Sofronis to Dr. ISHIHARA Tatsumi. Following the procedure for changing WPI Academy center directors, a pre-evaluation by the AD, AO and DPD was conducted

on 13 January 2023, and a hearing by the domestic members of the Program Committee on 17 January 2023. The change was approved and Dr. ISHIHARA started his directorship on 1 April 2023.

Dr. ISHIHARA is an excellent chemist in catalyst field, well-known for his research on oxide ion conductors and solid oxide fuel cells. Under a rapidly changing global energy landscape, Dr. ISHIHARA will expand the carbon neutral research of I²CNER to include promising energy carriers such as ammonia.

Kyoto University, the host institution of iCeMS, proposed a change of the center director from Dr. KITAGAWA Susumu to Dr. UESUGI Motonari. A pre-evaluation by AD, AO and DPD was conducted on 22 December 2022, and a hearing by the domestic members of the Program Committee on 17 January 2023. The change was approved and Dr. UESUGI started his directorship on 1 April 2023.

Dr. UESUGI is an excellent scientist, well-known in the field of chemical biology. He aims to understand cellular self-assemblies to advance cell biology and create functional self-assembling materials to address global challenges. Additionally, he advocates for a new education framework that includes undergraduates and emphasizes diversity, equity and inclusion.

University of Tokyo, the host institution of Kavli IPMU, proposed a change of the center director from Dr. OOGURI Hiroshi to Dr. YOKOYAMA Jun'ichi. A pre-evaluation by AD, AO and DPD was conducted on 18 July 2023, and hearings by the domestic members of the Program Committee on 7 August and 13 October 2023. The change was approved and Dr. YOKOYAMA started his directorship on 1 November 2023.

Dr. YOKOYAMA is an excellent scientist, well known in the field of gravitation and cosmology. He will push the quest of Kavli IPMU for the fundamental laws of the Universe based on the comprehensive mathematical analysis of cosmological observation with emphasis on gravity. It is expected that Dr. Yokoyama vigorously pursues the reform of research and education system of University of Tokyo from Kavli IPMU.

K-3. Follow-up of the Academy centers

Follow-up of 9 WPI Academy centers, AIMR, iCeMS, IFRcC, MANA, I²CNER, Kavli IPMU, IIS, ELSI, and ITbM for the period of FY 2021 was conducted from November 2022 to March 2023. The findings were reported at the October meeting of the WPI Program Committee.

AIMR

The Advanced Target Project is effectively used to push Mathematics-Material science Fusion in which the mathematical science group functioned as the catalyst. This resulted in many publications with 10% in top-class journals. Global circulation of young researchers is promoted using the Global Intellectual Incubation and Integration Laboratory (GI³) Laboratory. The ratio of female researchers has improved to 21% (6% in 2018, 12% in 2020) and 6 female PIs. For Green Innovation (GX), "Open Innovation Center for Hydrogen Science" has been established under the Director, and co-creation research has started with industries. The Joint Research Centers at Cambridge University, University of Chicago, and Tsinghua University continued as satellites. Official Web Sites and international media coverages are promoted to outreach the "Math-Mat" brand of AIMR.

iCeMS

Fusion research of cell biology and materials science focusing on health, environment, and energy related themes is progressing well. Some notable achievements from young PIs include the dynamics of scramblase (Suzuki Jun), novel pi-electron systems with superior optoelectronics properties (FUKAZAWA Aiko), in Silico design of novel materials (Daniel Packwood) and many others. There are now 6 On-site Laboratories (VISTEC (Thailand), UCLA (US), Acad. Sinica (Taiwan), Fudan Univ. (China), A*Star (Singapore), MDI (New Zealand)) abroad, which are led by young PIs. The iCeMS Internship Program invited 4 undergraduates from abroad. Effort has continued to secure external funding and to launch startups. A large donation was secured this year with which hiring of female junior PIs is planned. Communication Design Unit has issued many press releases made with effective visual materials.

IFReC

Osaka University established a powerful framework for immunology and infectious diseases research by connecting IFReC with the newly established Center for Infectious Disease Education and Research (CiDER) and Center for Advanced Modalities and DDS (CAMaD). It has provided 6 posts to IFReC as well as extending the hiring of fixed term PIs to FY 2026. The Comprehensive Collaboration Agreement Grants and Collaborative Contracts spawned therefrom have provided a sustainable foundation for the operation of IFReC. Nurturing of young researchers is conducted with the "Young Lead Researcher" and "Advanced Postdoc" systems. In place of the "Singapore Immunology Network" which terminated in 2020, "International School on Advanced Immunology" with University of Bonn started in 2022. Outreach activities include publication of popular books on

immunology, the “Imuneco” journal, annual report and books for experts.

MANA

MANA continues to produce top-level results based on the concept of “nanoarchitectonics”. The host institution NIMS continues to support MANA strongly. Special fund from the NIMS President supports interdisciplinary research programs and postdocs. International research activity by young researchers has been boosted, leading to a high ratio (78.3%) of internationally authored publications. Research in quantum materials and neuromorphic system has been initiated to contribute to quantum technology innovation. MANA satellites with 7 Satellite-PIs are functioning as a hub for international talent circulation. Outreach is very active including MANA E-Bulletin, MANA Virtual City Workshop and “Nanocar Race II”, reaching both scientific community and society at large.

I²CNER

I²CNER has reorganized its divisions into 3 Thrusts (Advanced Energy Materials, Advanced Energy Conversion Systems, Multiscale Science and Engineering for Energy and the Environment) and 2 Platforms (International Collaborations and Partnerships, Societal Implementation and Industrial Collaboration). Scientific activity is sustained at high level with many publications. Senior PIs are gradually stepping down, replaced by new PIs, leading to 25 PIs with 12 from abroad in 2023. Kyushu University continues to strongly support I²CNER; in addition to 12 positions already provided to I²CNER, 4 more positions are under selection. Large external fundings are secured not only from Moonshot but also through active collaborative contract with industry. The collaboration with University of Illinois at Urbana Champaign Satellite continues to function well. In addition, Kyushu University and University of Illinois at Urbana Champaign have signed a strategic partnership.

Kavli IPMU

Internationally co-authored publications have increased from 50% in 2007 to 85% in 2021 at Kavli IPMU. Gadolinium experiment at Super Kamiokande started in 2022. Observations with Prime Focus Spectrograph (PFS) will start in 2024. Hyper Suprime-Cam (HSC) observation has finished in 2022, with many publications. Center for Data Driven Discovery has been established. 60% of researchers who worked at Kavli IPMU has gone on to tenure or tenure track positions abroad. Two foreign researchers obtained such positions in Japan. The five-year extension enabled Kavli IPMU to secure enough long-term funding for a stable operation with help from the University of Tokyo and Kavli Foundation. Effort for diversity includes establishing the C.-S. Wu Prize Postdoctoral Fellowship for female researchers, and participation in Kavli Foundation Science and

Society Program.

IIIS

In 2023, University of Tsukuba will place IIIS as “World Leading Research Center” and provide strong support. Tenure posts to all PIs are progressing as planned. Excellent results continue to emerge in prominent journals. Securing large external funds have been successful with the AMED Moonshot Project and JSPS International Leading Research Project (RECONNECT). International activities include the Annual International Symposia, and international talent circulation of graduate students and postdocs using Moonshot and RECONNECT programs. Outreach is pursued using EurekAlert! and interviews with science journalists to expose IIIS and its scientists to wider society.

ELSI

ELSI is expanding the scope from “Life on Earth” to “Life on Planets”. Research highlights includes analysis of Ryugu samples brought back by Hayabusa2, and organic chemical evolution on icy bodies. Noteworthy is the start of the ELSI Graduate Program with 10 student enrollments (5 from abroad, 5 domestic). ELSI is a permanent organization in International Research Frontiers Initiative (IRFI) of Tokyo Institute of Technology. Large external fundings have been secured with “Grant-in-Aid for Transformative Areas” and “International Leading Research (RECONNECT)”. International recruitment of postdocs is going well. New collaborative projects have been started with NASA, California Institute of Technology, University of Cambridge, and University of Cote d’Azur. Since 2019, the recruitment of foreign outreach specialist has boosted the international outreach, contributing to the recruitment of foreign researchers.

ITbM

Research is going well both in the existing projects such as Striga and clock diseases, and in new projects such as on mosquito hearing. Five foreign PIs continue to work closely with their co-PIs. Two foreign junior PIs have been recently hired, enhancing the international environment. ITbM is a permanent institution within Nagoya University Institute for Advanced Study, with 29 posts secured by 2022. 2 female and 2 foreign PIs or junior PIs recently joined. International activities have restarted including the annual international symposia and 2 “International Leading Projects” (RECONNECT). Postdoc applications has also rebounded in 2022. The final report to the WPI Program Committee on the research misconduct and the prevention measures has been submitted. The measures for nurturing openness, transparency, and inclusion for preventing research misconduct have been implemented.

L. Branding and outreach

In November 2023, the 12th WPI Science Symposium was held in Sapporo on the theme



“Research frontier driven by informatics.” ICRéDD of Hokkaido University led in organizing the symposium. The symposium was held in a hybrid fashion: 177 attended the symposium in person and 153 through internet.

Booth exhibition of WPI research centers