

# FY 2024 Follow-up of WPI Program

By Program Committee

# March 2025

(This document reports on progress made under the WPI Program in FY 2023.)

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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 5 more centers have been launched by 2023. This 2024 follow-up report describes notable areas of progress in FY 2023 and new developments in FY 2024.

# A. 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

# **B. 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 nanoarchitetonics, National Institute for Materials Science

The sixth WPI center was launched under the "green innovation program" in 2010, and it is the 6<sup>th</sup> member of the WPI Academy.

- **I<sup>2</sup>CNER** 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, Institute of Science Tokyo (Formerly Tokyo Institute of Technology)

- **ITbM** on plant/animal biology and chemistry, Nagoya University

In 2017, the 11<sup>th</sup> 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
- SKCM<sup>2</sup> on knotted chiral metamatter, Hiroshima University
- **Bio2Q** on microbiome and quantum computing, Keio University

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

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



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.

# C. WPI Academy

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, IFReC and MANA from FY 2017 and recertified in FY2020, I<sup>2</sup>CNER 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.

# **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 its Chair, 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 2024, the Program Committee was held on 28-29 October in Tokyo. The main items of



28-29 October 2024 in Tokyo

business on Committee's agenda were (1) follow-up reviews of nine centers (IRCN, NanoLSI, ICReDD, ASHBi, QUP, PRIMe, SKCM<sup>2</sup>, Bio2Q, WPI-AIMEC), (2) report on WPI Academy centers, (3) report on gender balance in WPI Program, and (4) future plan of WPI.

#### 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: <a href="http://www.jsps.go.jp/english/e-toplevel/08\_followup.html">http://www.jsps.go.jp/english/e-toplevel/08\_followup.html</a>

#### 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-October 2024. 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**

The Academy site visit for recertification of World Premier status for I<sup>2</sup>CNER was held on site on 5-6 December 2023 by AD/PD, AO, AWG.

For the eight Academy-member centers (AIMR, iCeMS, IFReC, MANA, Kavli IPMU, IIIS, ELSI, and ITbM), site visits were held from December 2023 to February 2024. Attended by AD/PD and AO these site visits were carried out on-site with a duration of about 2 hours. Reports on the site visits were made to the Program Committee in its October meeting by AD/PD.

#### E. Follow up on the 2 Centers launched in 2017

#### E-1. IRCN

Center director: Takao HENSCH

Program officer: MISHINA Masayoshi, Ritsumeikan University

#### 1. Advancing research of the highest global level

IRCN researchers have intensively interacted and have produced high-quality publications. Elucidation of the synaptic mechanism of developmental disorder Angelman syndrome is outstanding. Notable achievements include: the mechanism of mechanic synaptic transmission caused by spine enlargements, the causal relationship between functional callosal connectivity and cognitive flexibility, the molecular mechanism of attention deficits associated with early life stress, the synaptic and gamma rhythm signature of critical period plasticity, distinct brain dynamics underlying the co-occurrence of autism and ADHD, the critical role of the feedback prediction error signal in autonomic detection of unpredicted stimuli, and the benefit of stochasticity in higher layers of deep neural networks. On the other hand, more focused efforts and concrete results are required to achieve center's goals of innovating neuro-inspired AI and revealing the origin of human intelligence.



**Research Highlight:** Early adversity induces attention deficits in male mice and boys, due to a persistent sleep loss. A dopamine receptor imbalance in the anterior cingulate cortex was further found to underlie the sex-specific cognitive vulnerability (Y. Makino et al. and T. K. Hensch, published in *Sci. Trans. Med.*, October 2024).

#### 2. Implementation as a WPI center

#### Generating fused disciplines:

The center's dynamic team science strategy has facilitated interdisciplinary

collaborations among developmental, computational and clinical neuroscience groups. Active collaborations through neuromodulation, critical period, social learning, predictive coding and intrinsic activity team sciences are seeking diverse seeds for next generation AI. The five teams are relevant to core, social and diverse intelligences.

#### **Realizing an international research environment:**

Under the leadership of Director Hensch, the globalization and creation of an international research environment in IRCN is very well established and highly achieved. Globalization of the center has been maintained through research networks with 15 overseas and 4 domestic partner institutes. IRCN re-started face-to-face gatherings such as international retreats and workshops, 33 international science salons and 4 international seminars for young researchers. IRCN hosted 18 guest researchers from abroad and lively discussions took place surrounding this vibrant group of prominent visitors. Neuro-inspired computation course has now been reopened in 2024.

#### Making organizational reforms:

The introduction of team science is an effective system reform breaking down barriers between PI labs of traditional departments. IRCN maintains a research network by enlisting 63 Affiliated Faculties (AFs) and 19 Associate Research Fellows who participate in weekly Salon seminars and collaborative research projects. IRCN has appointed a new female Administrative Director and a female Deputy Director, composing 33% of executives.

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

UTokyo has made commitments to maintain IRCN as a permanent institute within the UTokyo Institutes for Advanced Study (UTIAS) and to allocate 500M yen as an annual budget to it from FY2027 in a permanent fashion. Prof. Aihara has been named Executive Director with the specific mission to boost the AI incubator. Top computational AFs are now being promoted to Affiliate PIs and visiting Professors.

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

IRCN responded well to the recommendations of future plan, graduate education and strengthening computation group. But the responses to those of vision on neuro-inspired AI and origin of human intelligence were insufficient.

#### 3. Actions required and recommendations

1) Neuro-inspired AI: Revisiting the strategy for neuro-inspired AI is urgent. IRCN should

critically examine their approach and strategy toward neuro-inspired AI, considering the rapid progress in the field, and clarify its objectives to maximize its unique contributions at the intersection of neuroscience and AI. The center must clarify its milestones and progresses achieved. It should develop a focused vision that either aligns neuroscience research with modern AI advancements, or pivots towards more approachable directions in AI research. Organizing a workshop to discuss this issue in depth inviting experts from relevant disciplines is recommended.

- 2) Origin of human intelligence: IRCN should clearly describe its progress and overall strategy toward understanding the origin of human intelligence. We strongly recommend that the center develops a grand design and research strategy to elucidate the origin of human intelligence.
- 3) Organization reform: UTokyo has a responsibility to show bold and ambitious actions for organization reform as a Japan's leading university by using two WPI centers.
- 4) Diversity: Diversity is not satisfactory and should be improved as a priority challenge. IRCN should continue its effort to add PIs with diversity in both internationality and gender in mind.
- 5) Graduate education and fostering young scientists: Access to students in other schools including physical sciences and engineering is still limited. Stronger initiatives are needed to obtain cross-appointments for junior project PIs in appropriate departments.

#### E-2. NanoLSI

Center director: FUKUMA Takeshi Program officer: NAKANO Akihiko, RIKEN

#### 1. Advancing research of the highest global level

NanoLSI is making steady progress in research. The level of Bio-SPM research continues to be at the world-top level. Nanoendoscopy-AFM has now enabled examining elasticity change of nuclear envelope under various conditions. Collaboration with cell biology experts appears to be going well. Integration of AI for automated operation and data analysis of high-speed AFM looks promising to ensure versatility. Toward measurement of metabolites, molecular sensors for 1-MNA and lactate have improved their sensitivity and specificity, which would be good for out-cell use, but more efforts are encouraged to make them practical for in-cell nanoendoscopic use. Discussion with clinical researchers is also advisable. Attempts to use designer EVs for therapeutic immunoregulation purposes are very impressive. Computational analysis has led to interesting results on the interpretation of high-speed AFM data. In 2023, NanoLSI published 193 papers and obtained 1.3 billion JPY grants, indicating continued high level of scientific activities.



**Research Highlight:** Examples of the proteins studied using high- speed AFM technology and computational analysis. **A:** SaCas9 in action (Puppulin *et. al.*, ACS Nano 2023, vol. 17, 5, 4629), **B:** A proposed gating mechanism of a Na+ channel by formation of inter-channel network (left) and its disconnection (right). (Sumino *et.al.*, Nat Commun. 2023, vol14,7835), **C:** Sequential HS-AFM images of rat CaMKIIa. Arrowheads indicates kinase domains with arbitrary numbers. Arrows indicate the kinase domains in motion Frame rate, 3.3 frames/s. (Tsujioka *et. al.*, 2023, Sci. Adv., vol. 9, eadh1069)

# 2. Implementation as a WPI center Generating fused disciplines:

Transdisciplinary Research Promotion Grants (TDRP-G) of bottom-up and top-down have worked well to accelerate fusion of disciplines. The themes of top-down grants have been shifted from "proof of concept" and "exploring applications" to several promising subjects such as nuclear elasticity by in-cell AFM and cell database by high-speed SICM, which are expected to bear fruits. NanoLSI also appears to be gradually broadening targets to nano-level understanding on cellular and medical life science in a more interdisciplinary manner, by newly developed techniques not only Bio-SPM.

Different styles of meetings, luncheon meetings, T-meetings, NanoLSI colloquia, and NanoLSI symposia, have also been effective in promoting interdisciplinary research. Take T-meetings for example: About 61% of meetings led to possible collaborative projects and 37% resulted in actual collaboration, among which 82% are ongoing and 44% have already resulted in publications, talks and grant applications.

#### Realizing an international research environment:

Internationalization has been promoted at a good pace with productive scientific outcomes emerging from international collaborations. 42% of publications are internationally coauthored, which appears reasonable. A concern remains about having lively exchanges of ideas and know-hows between researchers at NanoLSI and those overseas, which have perhaps declined a little since the unfortunate disruption caused by COVID-19. More substantial collaborations are desired to recover. Bio-SPM Summer School, Bio-SPM Collaborative Research, and NanoLSI Visiting Fellows Program are all running well, which are important for the world-wide recognition of NanoLSI. The Summer School attracts about 30 participants from over 10 countries annually, showcasing NanoLSI's high visibility. The newly set-up Nanoprobe Life Science Forum is also nice and should be advertised more widely.

#### Making organizational reforms:

NanoLSI and Kanazawa University have already made significant reforms in research and education systems. Nano Life Science Division of the Graduate School of Frontier Science Initiative enrolls 17 master's course students and 36 doctorate course students as of April 1st, 2024. Kanazawa University was selected for J-PEAKS (Program for Forming Japan's Peak Research Universities) in 2023, which will benefit and strengthen NanoLSI.

Regarding the gender balance issue, NanoLSI is making steady efforts. The ratio of female researchers has increased from 12% in 2017 to 23-24% now. NanoLSI has

updated its Research Center Proposal, strategically planning to increase the female researcher ratio to 25% or more at the end of FY 2026 and further to 35% onward. The plan is also to increase the female PI number, from one to two. An international call for female-only tenure-track Jr. PI is going on. It is appreciated that the center is seriously addressing this problem.

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

The continued support by President Wada of Kanazawa University is very important and valuable. 12 of 22 tenured researcher positions currently held at NanoLSI will be made permanent as discretionary posts for the president. High activities of Jr. PIs are a good sign for the future. Fostering and securing next-generation researchers is also important and outreaching to high-school and even younger students is expected to be fruitful in the long run. Regarding the financial sources, it is good for NanoLSI to consider relations with industry. Several private companies appear to be getting interested and involved, so efforts should continue to develop better relationships. Acquiring a large amount of external funding is a strength of the center; however, the ultimate transition to mostly external funding will need careful planning.

The scientific mission of NanoLSI to establish "Nanoprobe Life Science" is unique because it is based on the state-of-the-art Bio-SPM technology of the center. Towards the next decade of the center, candid discussions should be made among current and prospective members as to how the targets of the center can be extended or shifted and what new disciplines or expertise will be required. At the same time, the great advantage of having the world-top Bio-SPM technology should continue to be at the core.

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

As always, NanoLSI has responded to the follow up of the previous year very sincerely. The most important message that continues to be raised is to "answer still-unanswered questions in life science."

#### 3. Actions required and recommendations

- Continue further efforts to answer questions that are not easily addressed by methods other than Bio-SPM. Keep and strengthen interactions with expert researchers in cell biology.
- 2) Continue efforts to develop molecular sensors for practical use in nanoendoscopy.
- Continue to grow global presence and increase awareness of the NanoLSI activities world-wide.

- 4) Continue to better the gender balance and carry out the strategy as planned.
- 5) Start earnest discussions for the future plan of NanoLSI beyond the  $11^{th}$  year.

# F. Follow up on the 2 Centers launched in 2018

# F-1. ICReDD

Center director: MAEDA Satoshi Program officer: TATSUMI Kazuyuki, Nagoya University

## 1. Advancing research of the highest global level

ICReDD is intended to focus on the interface between theoretical and experimental chemistry with a particular focus on new reaction discovery. Remarkable progress has been made in the past few years in advancing research, creating a new paradigm for reaction discovery and expanded the scope of designing chemical reactions. Their publications with the highest quality are a testament to the high productivity of the Centre.

The center's research activities have been substantially intensified by the commitments of information scientists. There is a notable utilization of big data analysis and artificial intelligence tools for tackling large scale systems, broadening the scope of chemical reactions to more complex targets.

The seven Flagship Projects have been reorganized to six, which has been done so effectively that these projects now act as a powerful driver for research focus, methodological advances and validated reaction discoveries. The bottom-up projects, which have been proposed and organized by young members of ICReDD have also functioned as unique and fresh projects.



Virtual Ligand-Assisted Optimization (VLAO)



**Recent Highlight [Left]** Virtual Ligand-Assisted Optimization: A Rational Strategy for Ligand Engineering (ACS Catalysis 2024. DOI: 10.1021/acscatal.4c06003) **[Right]** Catalytic Asymmetric Fragmentation of Cyclopropanes (Science 2024. DOI: 10.1126/science.adp9061)

# 2. Implementation as a WPI center Generating fused disciplines:

ICReDD has been planned to conduct research through collaborative efforts across different disciplines in theoretical chemistry, synthetic chemistry, and information science since the early stage of the project. The introduction of a unique scheme for fusion research between chemists and clinicians has opened up a new phase of collaborative research achievements. A notable outcome includes substantial progress in spatial transcriptomics of glioblastoma and reprogramming of intestinal stem cells. The set-up of a "Clinical Platform for Chemical Reactions" has aided this fusion research.

#### Realizing an international research environment:

At the end of FY 2024, 47% of researchers were foreign nationals. Very active participation of the foreign PIs in the research, together with a large number of foreign researchers, has created a truly international environment at ICReDD. The increasing number of researchers from established top-institutes in Europe and the USA are now highly visible in ICReDD's daily activities. Inauguration of the "List DX Catalyst Collaboration Research Platform" as an integral part of ICReDD must be an advantage not only for ICReDD's research activities but also for its international reputation as a top institute.

#### Making organizational reforms:

As Centre has grown in size, the management structure has also been expanded and strengthened. The Administrative Director has been of significant management help for then Center Director Maeda, allowing him to allocate more of his time on research leadership. The President of Hokkaido University has been very enthusiastic in promoting the activity of ICReDD. With these people in place, ICReDD now appears to be a smooth-running operation, and the ICReDD Director appears to feel more comfortable in leading the institute as one of the top research institutes in the world.

ICReDD has been making a continuous effort to increase the ratio of females to males, where a career-conscious approach has been adopted in which female researchers are hired at every level from postdocs to junior researchers to senior PIs. The ratio has been steadily increasing from 7% in 2018 to 19% in 2024, with a target of 25%. However, this number is still far from a satisfactory level, and further efforts are needed.

**Effort to secure the center's future development over the mid- to long-term:** Hokkaido University has made substantial commitments, financially and with regard to organization issues, in order to give ICReDD an excellent opportunity to sustain its research program after the WPI funding ends by integrating ICReDD as a substantial component of the future plans for Hokkaido University. The university is now showing a staffing plan roadmap for FY 2028, which consists of 16 PIs, 19 faculty members, and 29 postdocs funded by Hokkaido university, totaling 64 researchers, which is the same number as at present.

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

The center has responded to the follow-up results of last year in a serious manner with sincerity. They have acted diligently in responding to the recommendations from last year on scientific misconduct. Hokkaido University has finalized the report of its investigation committee (2023/09/12), which has been made public (2023/09/20), and MEXT has completed its formal recognition of the misconduct and disciplinary action at the end of FY 2023. ICReDD and Hokkaido University have both been implementing measures to prevent the reoccurrences of misconduct.

#### 3. Actions required and recommendations

- Continue the effort to achieve top-level science through fusion of computation/ informatics/ experiment. Flagship projects are full of seeds for achieving pioneering breakthroughs in chemical reaction design and discovery.
- 2) Continue the effort to improve gender balance at all levels, particularly at the PI level.
- 3) Speed up the planning of the ICReDD (MANABIYA)-based new graduate school.
- 4) International interactions of junior researchers from ICReDD are an area to improve. It is recommended that supporting systems be established to encourage ICReDD's young PIs, young scientists and even graduate students to take advantage of opportunities for international exposure to enhance their value early in their scientific careers.

#### F-2. ASHBi

Center director: SAITOU Mitinori Program officer: OKANO Hideyuki, Keio University

## 1. Advancing research of the highest global level

ASHBi has established itself as a leader in human biology research, with 16 PI groups and over 360 publications. Its innovative use of non-human primate models has significantly advanced studies in early embryonic development and clinical medicine. Notably, the flagship kidney disease project by the Yanagita group has earned high praise, while Fujita's group has drawn attention for its ethical research incorporating traditional Japanese childbirth practices.



Unravelling CD4 T cell diversity by active enhancer mapping and their role in immune disease (Murakawa G, *Science*, 2024);

According to Japanese folklore, 7th of July is the only day of the year when the two stars, Altair and Vega – Hikoboshi and Orihime, can meet at the Milky way. Similarly, in our genome, enhancers "meet" promoters at the necessary times to regulate the expression of genes...

# 2. Implementation as a WPI center Generating fused disciplines:

The ASHBi research center focuses on integrating biology with mathematics, data science, and ethics, a rare fusion in academia. Notable achievements include the globally recognized RECODE algorithm, with over 220,000 downloads, aiding many research areas including germ cell biology. Ethics, led by Fujita's group, spans areas like fetal tissue research and consultation, strengthening public support and tissue donation efforts. Breakthroughs in axioloid technology and ethical deliberations on the 14-day rule position ASHBi as a global bioethics leader, tackling issues beyond the scope of even ISSCR.

#### Realizing an international research environment:

The recruitment of foreign PIs has surpassed the initial target of 20%, reaching an impressive 25%. This achievement reflects significant progress in enhancing diversity within the institution, where 41% of researchers are from overseas and 27% are women. Among the

graduate student body, the representation of diversity is equally noteworthy, with 30% of students being international and 31% being women, successfully meeting the set target ratios for inclusivity.

#### Making organizational reforms:

Kyoto University (KU) is committed to supporting its researchers, securing PI employment beyond 2028, and planning a new building for ASHBi. While collaboration among flagship projects is strong, some PIs work in relative isolation. KU also aims to increase women in senior roles and foster a more gender-friendly environment to promote inclusivity.

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

We appreciate the host institution's efforts toward sustainability, including maintaining PI members, supporting post-doctoral employment, preserving SignAC's core functions, and funding ASHBi after MEXT support ends. While securing PI employment post-2028 is commendable, KU must address budget cuts by seeking additional research funding. Continuous KU support and developing a new ecosystem, including tenure-track positions and a new building, are essential. Strategies to secure public or private funding, ideally through industry endowments, are necessary despite the challenges.

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

The Center has addressed last year's follow-up findings with notable progress.

The <u>Monkey Project</u> continues to explore DISC1 in transgenic monkeys, but as suggested by the Working Group, it will be conducted as basic research to explore the neural basis of neuropsychiatric disorders.

In <u>Mathematics</u>, the scRNA analysis software's 220,000 downloads highlight its impact, though widespread adoption may require a user-friendly GUI developed by professionals.

Ethics concerns have been effectively addressed by ASHBi.

The <u>Clinical Science team</u> excels in hereditary kidney disease research using GM macaques but faces challenges in applying these models to psychiatric disorders, indicating a need for new biomarkers.

<u>Diversity</u> efforts show steady improvement, with increased female and non-Japanese representation.

# 3. Actions required and recommendations

#### **Reevaluating the NHP Project**

ASHBi has made remarkable progress in human developmental biology and the establishment of primate-based models, alongside groundbreaking research into hereditary diseases caused by single-gene mutations. However, as many human diseases are polygenic, there is a pressing need to advance research into genetic regulation in polygenic diseases to address their complex nature.

#### **Focusing on Human-Specific Biological Features**

A deeper focus on identifying human-specific biological traits through non-human primate studies is crucial. Enhancing multi-omics analysis—particularly for proteins and metabolites will enable a more comprehensive understanding of cellular function. Additionally, to ultimately understand what makes us human, the group should recognize the importance of integrating investigations of social and psychological dimensions to gain a more holistic understanding of human biology in its future direction.

#### **Building a Sustainable Research Foundation**

Sustaining ASHBi's innovative research requires long-term support for its Research Acceleration Unit and core facilities. Financial support from Kyoto University will be pivotal in ensuring the institute's future, particularly for completing the new building, which will serve as a cornerstone of ASHBi's research infrastructure.

# **G.** Follow up on the Centers launched in 2021 G-1. QUP

Center director: HAZUMI Masashi

Program officer: TSUNETA Saku, Chiba Institute of Technology

#### 1. Implementation as a WPI center

# 1) World-Leading Scientific Excellence and Recognition Advancing research of the highest global level:

"SpaceTES" has been treated as a Flagship Project in QUP. Its aim is to deliver a flight TES detector system to the JAXA's LiteBIRD mission, whose objective is to make groundbreaking cosmological measurements. The TES detector for the LiteBIRD mission has very specific and high-level performance, reliability, and verification requirements as compared with the TES for ground-based applications. Space-level system engineering, quality control and project management, which would be different from previous KEK projects, are required for the "SpaceTES" project. It has not been clearly presented by QUP where the "SpaceTES" project is in terms of the ultimate flight model requirements and specifications.

The current Systemology Support Section is to support the conceptual design of a few infant projects. It has proved its usefulness within QUP, but not in the sense of the original proposal.

QUP's second flagship project candidate, the QUP-Kamioka-DM project, has been



#### "CIGS semiconductor detector" detects individual charged particles

The Cu(In,Ga)Se<sub>2</sub> (CIGS) semiconductor is well-known for its self-repair mechanism against radiation damage. It has attracted substantial attention for applications in high radiation environments, such as in particle detectors and cameras. We have succeeded in detecting Xe ions with the fabricated CIGS detector. This is the first detection of single particle beam using CIGS semiconductors in the world. We have also confirmed that the detector recovers from radiation damage by heat treatment. **Left)** QUP CIGS particle detector and CIGS solar cell. **Right)** Charge distribution of the Xe ions detected by the CIGS detector. (K. Itabashi et al. Nucl. Instrum. Methods A 1067 (2024) 169637.)

delayed and will only start to produce data in 2025. The project is still in candidate phase. The PI-led projects, including the Casimir force, the NV diamond sensor, radiationhardened detector, and the data acquisition (DAQ) and analysis do not yet possess sufficient strength to be world leading.

#### Generating fused disciplines:

There is cooperation between different efforts. An example is the use of the optical TES detectors in the topical area of the dark matter search experiments proposed in QUP. The integration within the center, however, is still not on a very high level, and synergy is not exploited at every possibility. Within QUP, the group which appears most likely to generate fused disciplines is the Theory group. However, it is not clear to what extent these directions are actually new.

# 2) Global Research Environment and System Reform Realizing an international research environment:

While the ratio of foreign researchers has reached 34%, there are only 35 researchers at present with 12 from overseas. The majority of the foreign PIs do not stay in Japan for a long period of time, and there is only one foreign PI residing at site. A global research environment is difficult to be realized with such a small number of resident foreign researchers. The number of foreign post-doctoral fellows and graduate students also seems to be small. It is disappointing that there have been no resident Japanese scientists staying at the Berkeley site and vice versa, no long-term non-Japanese visitors staying at the Tsukuba site. QUP should seriously consider how to make its environment more attractive for researchers and students.

#### Making organizational reforms:

QUP leadership should have had more conversations on all aspects of QUP with KEK Director General, and a consensus approach should have been presented to improve QUP performance. The Program Committee has a deep concern that QUP will not be able to evolve fast enough to be truly competitive on the world stage in just a few years. It is not clear that Japan or the broader scientific community gains significantly from having QUP continue in its present style. Unless more researchers are based in-house, it is hard to imagine QUP having the overarching impact as the initial proposal envisioned.

#### 3) Values for the future

#### Societal Value of Basic Research:

Though the QUP leadership did not provide concrete examples of why the work at QUP benefits society in tangible ways, the outreach program has been expanded compared to previous years. Public lectures and other ongoing efforts are an important contribution

to the public and industrial sector. It is not clear that these occasional activities exert long-term positive, persistent effects to society. There is still room for improvement.

#### Human resource building: higher education and career development:

Human resource building is far from satisfactory. QUP offers internships for graduate students and post-docs with about 20 participants per year. It is unclear how many of these students will subsequently participate as graduate students or post-doctoral fellows. More efforts to attract them are needed.

#### Self-sufficient and sustainable center development:

Though the new Director General of KEK assured that he remains committed to support QUP during and beyond the 10-year WPI funding period of QUP, the research program of the center does not fully align with the expectations of the host institution KEK. QUP will not be a sustainable center unless its activities are in line with KEK. Thus, close communication between KEK and QUP is necessary.

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

The Center's response to the recommendations is incomplete, and several of the comments made by the Program Committee one year ago are reiterated now. The role of systemology has been clarified to some extent, but it is questionable whether this is really in line with the original objectives and whether it is designed to realize the vision of QUP.

#### 3. Actions required and recommendations

Overall concern with the state of progress of QUP continues this year, necessitating the Program Committee to make a similar set of comments and recommendations. The general view of the Program Committee is that QUP has not yet converged on a convincing strategy to implement its overarching vision. For this reason, in the near term, QUP needs to re-evaluate the vision it put forward at its inception ("to bring new eyes to humanity") and define it more clearly or put forth a new vision which is compelling at the world-leading level in each and all of the WPI missions required by WPI. It is good that KEK has acknowledged these comments by the Program Committee by taking the initiative to make major changes in the QUP.

The institutional strategy to enable this vision should be made clear at all levels. They must develop a new research focus that can only be achieved through fusion of different fields and points of view, so as to make major inroads toward solving some big problem that will be exciting to the world research community. As a part of such reform, an intention was expressed by the KEK Director General to move away from the LiteBIRD

project. Though this is in line with the Program Committee's comments, it should be kept in mind that any decision involves and affects the international LiteBIRD study efforts outside QUP and a larger international community of CMB scientists.

The QUP leadership should have a serious discourse with the KEK leadership to work out a concrete plan for improvement that will reflect the spirit as well as each and all of the requirements of the WPI Program. Moreover, the WPI center must serve as a catalyst for transforming the culture and systems of KEK. KEK should study several successful WPI centers and use that study to pro-actively implement new transformational processes.

# H. Follow up on the Centers launched in 2022

## H-1. PRIMe

Center director: NISHIDA Kohji Program officer: KURODA Shinya, The University of Tokyo

# 1. Implementation as a WPI center

# (1) World-Leading Scientific Excellence and Recognition Advancing research of the highest global level:

PRIMe has consistently demonstrated exceptional scientific excellence by advancing research that meets the highest global standards, including the organoids analysis to model specific diseases, the innovative technology such as barcoding system and establishment of the iPSC core.

Establishing the research steering committee on the bio-Digital twin, the big data core, and the bio-Digital twin creation unit by recruiting new PIs is highly appreciated. Close interaction between these three parties is required to form a unified global strategy to achieve the ambitious goal of human metaverse medicine/bio-Digital twin.



**Recent Highlight** Nemoto's group developed the algorithm ACIDES in collaboration with the group at Institut de la Vision in France to analyze protein screening experiments. By combining a statistical model that describes highly dispersed NGS noise with a mathematical model for protein screening, they made it possible to determine the statistical errors in protein screening experiments with unprecedented accuracy.

*Nature Communications* (2023) DOI: <u>https://doi.org/10.1038/s41467-023-43967-9</u>

# Generating fused disciplines:

The integration of experimental studies (particularly organoid research) and

computational science for the digital twin is the critical aspect of the center. This activity should be accelerated by close interaction between the research steering committee, the bio-Digital twin creation unit and big data core to develop a roadmap toward human bio-Digital twins.

## (2) Global Research Environment and System Reform

#### Realizing an international research environment:

The numbers of overseas researchers and female researchers are still limited. Continuous efforts are needed to increase the representation of international and female PIs/researchers.

#### Making organizational reforms:

Many activities for organizational reforms have been initiated, including one-on-one meetings with the director, progress reports, PRIMe Retreat, PRIMe Seminar, happy hour, and interdisciplinary lectures. PRIMe has introduced a program to provide financial assistance to graduate students. A new core facility was established for the production of patient-derived iPS cells.

#### (3) Values for the future

#### Societal Value of Basic Research:

PRIMe has implemented a branding plan, including practices such as utilizing social media and issuing press releases. They have also initiated patient and public involvement activities. These ELSI activities will be continued and should receive broader interest in the center in the future.

#### Human resource building: higher education and career development:

PRIMe has launched educational initiatives, including its Lecture Course of Introduction to Human Metaverse Medicine in 2023 and Graduate Program for Advanced Interdisciplinary Studies "Human Metaverse Medicine" in April 2024. Consideration could be given to establishing tandem education for graduate students and postdocs from experimental and theoretical groups co-supervised by PIs from both disciplines, and career development program for students and post-docs.

#### Self-sufficient and sustainable center development:

A new building, Suita Agora 2, with a floor space of 8,850 m<sup>2</sup>, will be primarily dedicated to housing PRIMe and is scheduled for completion in 2026-2027. Osaka University supports PRIMe with a new building, faculty positions, and JPY 700M in management costs. Establishing a core facility on iPS cells is very positive.

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

In response to the last year comments by WG, PRIMe launched the research steering committee, big data core, and bio-Digital twin creation unit by recruiting the new PIs. Data standardization is still needed to be prepared.

#### 3. Actions required and recommendations

PRIMe has already conducted excellent research activities in organoid and advanced technology. Fusion research toward building the bio-Digital twin is the highlight of PRIMe as a WPI center which should receive accelerated attention. Thus, most of the recommendations are related to the bio-Digital twin, as follows

1) Research Steering committee:

The addition of an expert conversant in both experiments and mathematical modeling is strongly recommended.

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.

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.

4) Data standardization:

Standardized protocols for experimental and mathematical analyses should be set for cohesive integration into bio-Digital twins.

5) International and gender balance:

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

# H-2. SKCM<sup>2</sup>

Center director: Ivan SMALYUKH

Program officer: YASHIMA Eiji, Nagoya University/ National Tsing Hua University

#### 1. Implementation as a WPI center

# (1) World-Leading Scientific Excellence and Recognition Advancing research of the highest global level:

SKCM<sup>2</sup> has excellent senior and junior PIs with diverse expertise and each appears to be doing excellent research. However, much of the work was mostly continuations or fragments of previous work done independently by the PIs at their home universities/institutes.

Many papers have been published by PIs and a large number of affiliate members in 2023 with SKCM<sup>2</sup> in the affiliation name. However, there are still few papers that can be considered as original research unique to SKCM<sup>2</sup>.



**[Top]** Hsu and colleagues combined advanced structural biology tools to experimentally verify the AI prediction of the smallest and most complex 7\_1 knot protein structure known in the protein universe. Hsu also reviewed the state-of-the-art of folding and functions of topologically knotted proteins. Hsu *et al.*, *J. Biol. Chem.* (2024). <u>https://doi.org/10.1016/j.jbc.2023.105553</u> & Hsu, *Curr. Opin. Struc. Biol.* (2023). <u>https://doi.org/10.1016/j.sbi.2023.102709</u>

**[Bottom]** In helical ferromagnets and liquid crystals, skyrmions arise due to chiral interactions. Computer simulations show that achiral hard banana-shaped particles can form 2D or 3D liquid crystal skyrmion phases with potential applications in photonics and memory devices.

R. Subert, G. Campos-Villalobos and M. Dijkstra, *Nat. Commun.* **15**, 6780 (2024). <u>https://doi.org/10.1038/s41467-024-50935-4</u>

The initial research concept presented by SKCM<sup>2</sup> was promising, but after two years, it remains at the idea stage with no major achievements. In fact, the director's presentation did not clearly show what scientific achievements and notable scientific breakthroughs have been made by the center researchers as a whole in the past year. The center director should seriously and concretely present the research strategies and activities on which the center focuses.

The lack of a clear scientific program is a serious concern, as the center risks becoming a collection of small collaborations without substantial progress, resulting in numerous unfocused engagements.

The number of researchers staying at Hiroshima is currently rather small. Foreign PIs need to stay longer at the center. Hiroshima University (HU) should play a central role as the hub of all the activities and should immediately provide research space for foreign PIs until the time when the new research building is completed.

#### Generating fused disciplines:

There have been great efforts to promote fusion research, but actual fusion research is still limited at this stage. This requires serious attention from the director and his senior colleagues. The center director effectively engages young researchers, but it is time to demonstrate concrete synergy effects and establish a clearer identity for the center.

The center has made serious efforts to establish efficient interactions between pure mathematicians and chemists, physicists, biologists, and material scientists, by inviting young active researchers to participate in the challenge. However, the results are still at the idea stage with notable achievements yet to come after two years. The center should clearly outline the academic concepts and specific goals of how such fusion research between mathematicians and scientists can contribute to the development of the new research field of "knotted chiral meta matter".

It is time for the center director to set scientific strategies and measures to converge and identify a unique character of the center in research excellence and become an internationally recognized hub.

# (2) Global Research Environment and System Reform

## Realizing an international research environment:

SKCM<sup>2</sup> appears to be very international with good gender diversity. However, most of the international members remain at home universities/institutions.

HU has secured funding for a new research building to be completed by the end of 2025 to realize the "under one roof" vision.

#### Making organizational reforms:

The introduction of a metrical system for bonus has not been well received and should be reviewed.

Active engagement is seen to recruit female researchers to make good gender balance. A clear explanation of how this WPI project contributes to university reform would be valuable.

# (3) Values for the future

#### Societal Value of Basic Research:

The research topics at SKCM<sup>2</sup> are widely scattered under the word "sustainability". However, it is not clear how knotted theory and chirality together with other disciplines will have a significant impact on sustainability. This stems from the fact that fusion research oriented towards significant impact on sustainability is not evident at this stage.

The center director should clearly and more seriously articulate the center's research plans how research on "knotted chiral meta matter" can contribute to the realization of a sustainable society and what specific goals they are trying to achieve.

The outreach programs have been successfully implemented.

#### Human resource building: higher education and career development:

Many activities such as seasonal schools have been organized to attract students and young researchers across different disciplines. Young researchers are well taken care to be given opportunities and experiences in global circulation.

The center has initiated an interdisciplinary graduate program. However, the number of PhD students is still low and should be increased soon.

#### Self-sufficient and sustainable center development:

The host university is strongly committed to supporting the center's sustainable development in many ways, and in particular to helping the center build international connections at the university level.

A new research building will be built for SKCM<sup>2</sup> and will be completed in December 2025.

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

Many of last year's problems and issues remain unresolved.

 The director's presentation did not clearly show what scientific achievements and notable scientific breakthroughs were made by the center researchers as a whole during the past year.

- 2) The connection between the sustainability and the center's research mission and plans has not yet been clearly stated in the director's presentation.
- Fusion studies are still at the idea stage, with no notable achievements even after two years.
- 4) The director's appointments at HU and the University of Colorado, and a concrete intellectual property agreement between HU and the University of Colorado are still missing.
- 5) HU is very supportive and continues to discuss a difficult issue, the lack of suitable international schools near the campus, with a range of stakeholders.
- 6) The new research building for SKCM<sup>2</sup> will be completed in December 2025.

## 3. Actions required and recommendations

Many of the recommendations made last year are still unresolved. The Program Committee expects to receive clear and concrete responses to the recommendations below at the next year's Program Committee meeting.

- SKCM<sup>2</sup> should urgently establish a systematic and concrete research program unifying the diverse areas of research under the founding concept of "knotted chiral meta matter", without which the center will fragment into collaborations without substantial progress in any direction. It is very important to work quickly to prioritize key research topics and areas.
- 2) Foreign PIs need to stay longer at the center. HU should play a central role as the hub of all the activities. HU should immediately provide research space for foreign PIs until the time when the new research building is completed.
- 3) The center should clearly and more seriously articulate in the center's research plans how research on "knotted chiral meta matter" can contribute to the realization of a sustainable society and what specific goals they try to achieve.
- 4) Plans should be formulated to increase the number of Ph.D. students within the interdisciplinary graduate program.
- 5) The metrical system for bonus has not been well received and should be reviewed.
- 6) The cross-appointment of the center director at HU and the University of Colorado and a concrete intellectual property agreement between HU and the University of Colorado should be made immediately.

#### H-3. Bio2Q

Center director: HONDA Kenya Program officer: TAKAHASHI Ryosuke, Kyoto University

#### 1. Implementation as a WPI center

# (1) World-Leading Scientific Excellence and Recognition

#### Advancing research of the highest global level:

Bio2Q has clearly an internationally recognized leading position in contemporary human microbiome research and related areas. The advances made in the past year are impressive, including the level and quality of publications. The Q-core has made a strategic shift to focusing on "non-quantum" computational algorithms, while continuing its work on identifying biological problems amenable to quantum computing applications. The Q-core presented the potential and roadmap for applying AI to biomedical research in Bio2Q. However, with regard to application of quantum computing to biomedical field, further research and development are needed.

**Generating fused disciplines:** The fusion of microbiome research with other life sciences including neuroscience, organoids and lipidomic research in basic science disciplines holds great potential for advancing the scientific fields within Bio2Q. On the other hand, promotion of collaborations between clinical and basic sciences is necessary.



**Recent highlight**: Isolating and down-selecting commensal bacterial consortia from stool samples from healthy humans (left panel) led to identification of a consortia comprising 18 strains that specifically suppressed intestinal Enterobacteriaceae and alleviated *Escherichia*- and *Klebsiella*-driven intestinal inflammation in mice (ulcerative colitis model, upper right; inflammatory bowel disease model, lower right). **Furuichi et al**, *Nature 633*, 2024; https://doi.org/10.1038/s41586-024-07960-6; Adapted under CC BY 4.0.

# (2) Global Research Environment and System Reform

#### Realizing an international research environment:

The ratio of foreign PIs is 16%, and that for all researchers is 25% (8/32). These numbers are still below the WPI standard. The ratio of female researchers is 10% (2/20) for PIs and

22% (7/32) for all researchers. With the Bio2Q's target of 50% for all researchers, the numbers are still low. Bio2Q is taking a strategic approach for solving these Equality, Diversity and Inclusion (EDI) issues.

#### Making organizational reforms:

Bio2Q has put in place management arrangements to coordinate and drive system reforms in a consensual and progressive manner. Bio2Q has established 10 sets of internal regulations and bylaws so that it can operate as an autonomous center within Keio University.

#### (3) Values for the future

#### Societal Value of Basic Research:

Bio2Q has established a network of about 1000 researchers worldwide using LinkedIn. The center has held 20 open seminars, 1 symposium, and co-hosted 1 international and 1 domestic meeting for providing outreach to the scientific community.

#### Human resource building: higher education and career development:

Fourteen graduate students are enrolled in STaMP, a joint interdisciplinary international graduate program. The educational system is well conceived, with two mentors from different disciplines providing regular guidance. However, the educational and training content of STaMP is still under development.

#### Self-sufficient and sustainable center development:

A new research building will be constructed based on a six-billion-yen donation from the private sector. The university has provided funding for the installation of CryoEM from the research funds obtained through J-PEAKS.

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

- "Fusion": The center's researchers have seriously attempted to address the recommendations of last year, and in most cases have made substantial improvements along the suggested lines.
- 2) "Quantum computing": Bio2Q has reformulated its approach toward fusion of Q computing by hiring 2 key PIs in the Q core from the private sector and initially introducing generative AI technology for boosting its metabolome analyses while continuing to explore biological applications of quantum computing.
- 3) "Diversity goals": Bio2Q is taking a strategic approach for recruiting foreign and female researchers, and is making progress on this issue.
- 4) "Support from Host institution for sustainability": The top management of Keio

University succeeded in securing a donation of 6.0 billion yen from a company and showed a concrete plan for a new building for Bio2Q, which are in line with the WPI's overarching "under-one-roof" concept. Keio University will continue efforts to negotiate with the MEXT/Ministry of Education, Culture, Sports, Science and Technology in the next fiscal year to secure additional funding for the animal research building.

#### 3. Actions required and recommendations

- Efforts to generate fused discipline gave rise to notable progresses in Biology cores. However, collaboration between basic and clinical science is insufficient. It is recommended that Bio2Q enhance their collaboration with top-level clinical scientists in Japan and internationally.
- 2) The change in strategy from direct integration with quantum computing to integration with quantum computing by introducing generative AI techniques in the early stages and the hiring of two computational experts as new PIs for Q-Core, is a pragmatic approach. On the other hand, it is essential that the Center develop a strategy for reaching a visionary yet concrete project that develops quantum computing in the two bio cores. In this effort, Bio2Q could seek broader collaboration with emerging biomedical research initiatives in quantum computing across academia and industry. While Bio2Q has already established partnerships with organizations such as RIKEN and IBM, expanding these collaborations could further enhance its impact.
- Invest time into careful planning on how to use the CryoEM that will be installed in early 2025.
- 4) Demonstration of international PIs' involvement in Bio2Q is highly recommended. Further recruitment of international members is also necessary.
- 5) Increasing the number of both international and domestic female researchers should be prioritized.
- 6) The STaMP graduate school program represents an excellent example of fused disciplines with regard to young researcher education. However, a more comprehensive plan to foster the students should be shown.

# I. Follow up on the Centers launched in 2023 I-1. WPI-AIMEC

Center director: SUGA Toshio Program officer: SAITO Hiroaki, The University of Tokyo

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

Science-Society-Policy Interface: The UN Ocean Decade is a potential approach for engaging society, decision makers, and scientists within the global community. Establishing more collaborations with major organizations abroad such as UNESCO/IOC, PICES, WCRP would be useful for establishing AIMEC as the leading institute in marine science.

Higher education: Good progress has been made in developing the International Joint Graduate Programme in Earth and Environmental Science in collaboration with the University of Hawai'i.



to approximately 60°C for a few seconds before returning them to the sea.

# The Wisdom of Oyster Fishermen Achieves Three Goals at Once

"Hot water treatment" increases production, enhances product quality, and helps protect the marine environment.

# 2. Implementation as a WPI center

# (1) World-Leading Scientific Excellence and Recognition

# Advancing research of the highest global level:

The scientific activities of AIMEC are organized as 9 Units which together cover the 3 overarching themes of AIMEC. The scientific level of the Units is high, some being excellent. However, what seems to be lacking is the identification of "Grand Challenge" fusion research that will allow AIMEC to lead the development of change in how marine ecosystem research is done. Can we expect that by integrating Earth System Models (ESMs) with other units in AIMEC that AIMEC's ESM will become the best in the world in terms of performance in simulating marine ecosystems?

#### Generating fused disciplines:

AIMEC has made an internal call for "Fusion Science Activities (FSAs)", and 11 FSAs are underway. However, the relationship between the FSAs and AIMEC's three main themes have not yet been clearly defined. Further efforts are needed by AIMEC to develop "Grand Challenges" for real fusion science. Each research unit is encouraged to identify critical knowledge gap(s) for specific topics and formulate a plan for filling the gaps that includes insights and inputs from other research units through fusion science activities.

# (2) Global Research Environment and System Reform Realizing an international research environment:

As of October 2024, the ratio of international PIs to all PIs is 45% (10/22), and that of all researchers is 31% (18/58). The successful hiring of postdocs and researchers via the 2024 open call is expected to increase the percentage of international researchers. The recent hires of postdocs and researchers are mostly female, thereby improving gender balance and significantly advancing the goal of 30% female AIMEC participants by the end of FY2025.

It was unfortunate that many of the international PIs were not present at the site visit, and that their role and scientific contributions with AIMEC were not represented. The situation should be improved at the next site visit.

AIMEC should be more ambitious and should leverage its robust structure and funding so as to enhance its global leadership in marine ecosystems and climate research.

#### Making organizational reforms:

As AIMEC is jointly established by Tohoku University and JAMSTEC, each having its own rules and customs of governance, a major item to be addressed is the establishment of common rules and a mutual understanding of customs. This seems to have been accomplished by the sincere effort of the two host institutions, especially JAMSTEC.

Both host institutions should give attention to pro-actively finding ways to use this joint project to feed back into positive system reform more broadly in each institution.

#### (3) Values for the future

## Societal Value of Basic Research:

After ten years of research, what AIMEC products will transition to stakeholders, policy makers, and governments? Identifying these outputs will determine the societal benefits

of the basic research conducted by AIMEC. Knowing what these benefits will be requires identifying stakeholder needs now so that what is to be provided will be relevant and wanted. This will require AIMEC to engage in co-production and co-development with stakeholders so that their needs are known from the start.

#### Human resource building: higher education and career development:

AIMEC has an opportunity to train the next generation of students who will become an important legacy of the program. Reaching outside of traditional academic disciplines is important because the issues facing society require multi-sector solutions. In addition, AIMEC should consider developing capacities and strategic partnerships across all career stages so as to increase its disciplinary, scientific and cultural diversities.

#### Self-sufficient and sustainable center development:

Tohoku University and JAMSTEC have pledged strong support for AIMEC. The clear statement by the President of Tohoku University on the construction of the AIMEC building by FY 2028 is most welcome. This building will be essential for realizing the concept of a "Center of Under-One-Roof," as AIMEC is hosted by both Tohoku University and JAMSTEC.

There is also a mutual understanding of the need for tenure positions over the next decade. A long-term strategy to secure these tenure positions with full support from the host institutions needs to be developed.

Another path to sustainable center development is through engagement with industry partners and foundations. This will require AIMEC to have products that are relevant and needed by these partners.

#### 3. Actions required and recommendations

- Develop Grand Challenges immediately. Use the Grand Challenges to re-codesign a limited number of Fusion Science Activities that have clear integration across the units. In this process it is important not to neglect interfaces between AIMEC's work and other areas of earth systems and climate change modeling.
- 2) Identify knowledge gaps and barriers that will impede the ability of AIMEC to realize its goals in the short term and identify approaches for addressing these issues.
- 3) Expand the use of generative AI language models for knowledge synthesis and global leadership, including the recruitment of AI-related scientists.
- 4) Strengthen AIMEC's international leadership in marine ecosystems and climate research. Expand AIMEC's role of addressing grand challenge topics with other frontier science institutions. This involves not only seeking further international collaborations

but also making visible the role and activities of overseas PIs at AIMEC.

- 5) Develop a communication strategy and a comprehensive public engagement strategy, including with stakeholder communities.
- 6) Make continuous efforts for in-person communication, especially for students and young researchers located at the different sites within Tohoku University and JAMSTEC. Encourage young researchers and students to engage routinely in opportunities to consult beyond their own scientific group and scientific discipline.
- 7) Advance diversity and promote female scientists. Initiate actions and training to address unconscious bias and support female scientists. Initiatives such as unconscious bias training programs, mentorship opportunities for both male and female scientists, and recruitment strategies should be implemented so as to foster an inclusive research environment and establish AIMEC as a diversity leader in marine science.

#### J. Follow-up of the Academy centers

#### J-1. Recertification of I<sup>2</sup>CNER that joined the Academy in 2020

The Academy Working Group of I<sup>2</sup>CNER made a site visit on 5-6 December 2023, and the domestic members of the Program Committee carried out the recertification on 30 January 2024.

Since joining the WPI Academy in 2020, Director of I<sup>2</sup>CNER changed from Petros Sofronis to ISHIHARA Tatsumi in 2023. Science at I<sup>2</sup>CNER has progressed steadily with some very good achievements including nanomembrane-based direct air capture of carbon dioxide.

PIs are gradually rejuvenated, leading to 25 PIs with 12 from abroad in 2023. Female PIs, however, remain few (2/25), requiring further effort to improve gender balance. Two new centers, Mitsui Chemicals Inc.- Carbon Neutral Research Center (MCI-CNRC) and Center for Energy Systems Design (CESD), are set up to strengthen industry and domestic collaborations. Kyushu University continues to strongly support I<sup>2</sup>CNER (16 positions, indirect costs, budget requests). The successful collaboration between Kyushu University and University of Illinois at Urbana Champaign is expanding to a broader agreement.

The Program Committee confirmed that I<sup>2</sup>CNER had maintained a standard of research and operation at a "world premier" level, and qualifies to continue as a member of WPI Academy.

# J-2. Follow-up of the Academy centers that joined the Academy in 2017 and 2022

#### AIMR

The research framework of "Advanced Target Project" continues to push "Mathematics-Material science Fusion", resulting in many publications in high impact journals. Global circulation of young researchers has been promoted using Joint Research Centers at University of Cambridge, University of Chicago, and Tsinghua University and the GI<sup>3</sup> Lab, a self-funded program that supports the dispatch and acceptance of researchers and students. The ratio of female researchers continues to improve steadily (5% in 2018, 12% in 2020, 19% in 2022), and G-RIPS (Graduate-level Research in Industrial Projects for Students) Program attracted many students.

#### **iCeMS**

Under Director UESUGI, iCeMS' research emphasizes "Understanding cellular selfassemblies and inventing self-assembling materials to solve global challenges". Exciting results are obtained by young PIs in cell biology, material science, and their fusion. iCeMS has 10 international laboratories collaborating with oversea institutes, of which 6 are KUapproved "On-site Laboratories" (VISTEC (Thailand), UCLA (US), Academia Sinica (Taiwan), Fudan University (China), A\*Star-IMRE (Singapore), MDI (New Zealand), and 4 are "Project Units" (INJA-IN BIO (India), SKAEM-JIL(China), iCeMS Taiwan Office, Small-Molecule Lab (France)), with which research collaboration and student exchange are promoted. "Venture Studio" is set up to accelerate start-up ventures from iCeMS (there are already 10 companies by 5 PIs).

#### **IFReC**

IFReC continues to be very productive in top-level immunology research. Human immunology is promoted through sharing of advanced instruments and usage support, resulting in substantial increase of sequence data and publications. Fostering of young researchers include "Advanced Postdoctoral Program" which attracts many excellent young researchers, and "Doctoral Program in Microbiology and Immunology" established jointly by IFReC and other Osaka university's research institutes, RIMD, CiDER, CAMaD, which started accepting students from Asian partner institutions. Global connections are strengthened and expanded from University College London and University of Bonn to include University of Melbourne.

#### MANA

MANA continues to produce top-level research based on the concept of "nanoarchitectonics" including many publications on quantum materials. The ratio of overseas researchers continues to be high at 43% (83/192), but the ratio of female researchers needs to be improved (20/192=10%). 6 MANA Satellites are functioning well in providing autonomous environment for young researchers and researcher exchanges.

Outreach is very active including MANA e-Bulletin and "Research Highlights" which successfully accessed wider audience.

#### **Kavli IPMU**

Director changed from OOGURI Hiroshi to YOKOYAMA Jun'ichi in November 2023. Research at Kavli IPMU continues at high level. Recent highlights include a slight yet definite offset in the cosmological parameter S<sub>8</sub> from Subaru HSC observation compared to that from Planck, and progress of Super-Kamiokande Gadolinium Project. Imagin-X, a startup making X-ray imagers for small animals, originating from Kavli IPMU, is doing well. Director Yokoyama is implementing his vision, including new collaborations with University of Portsmouth, hiring of excellent overseas researchers, and appointment of female Administrative Director candidate.

#### IIIS

Science activities are kept at high level covering many themes from basic mechanisms of

sleep to clinical relations between quality of sleep and health indicators. Junior PIs are actively engaged in research securing external fundings. International exchange of junior researchers and students are promoted with JSPS International Leading Research Project (RECONNECT) and internal grants. University of Tsukuba has placed IIIS as "World Leading Research Center" and provides strong support. Providing tenure posts to all PIs is progressing as planned. Further effort is needed to hire female PIs. Besides social/educational activities by requests from a variety of organizations including high school students, IIIS leadership is making conscious effort for media exposure, resulting in increased awareness of sleep science in society.

#### ELSI

Research on "Life on Planets" is making good progress. The recent highlights include a first detection of phosphate-rich ocean in Enceladus, and analysis of Ryugu samples brought back by Hayabusa2. The ELSI Graduate Course with 10 student enrollment (5 from abroad, 5 domestic) started 2 years ago. Collaboration of ELSI with industry has also started with a view to exploring a career path to ELSI Course graduates. Tokyo Institute of Technology merges with Tokyo Medical and Dental University in October 2024. The placement of ELSI in the organization of the new university, maintaining an independent status directly under the president, needs to be ascertained.

#### ITbM

Fusion research of synthetic chemistry and plant/animal biology characterizing ITbM is going very well. Recent highlights include the start of field trial of the Striga Project and development of highly potent CRY1 compounds. Five foreign PIs continue to work closely with their co-PIs. Two non-Japanese junior PIs have been recently hired. Exchanges of students and researchers with University of Munster started with JSPS International Leading Research Project (RECONNECT). ITbM emphasizes "Inclusive" as well as "Mix" in its operation, resulting in increased engagement of students and junior researchers in ITbM's activity and decision making.

#### K. Gender balance in WPI Program

Gender representation in Japanese academia shows significantly lower female participation compared to other developed nations, particularly in STEM fields. Within the WPI Program, female researcher participation has historically been around 15%, though showing recent improvement to over 20% in 2023. WPI Program Committee recommended for concrete policies for improving gender balance at WPI centers in its fall 2023 meeting. Centers were required to revise their project plans with proactive numerical goals for female researchers and comprehensive gender-balance improvement plans covering executive, PI, and

researcher positions; strategies for fostering and attracting female researchers; and institutional support systems.

Centers presented diverse approaches and targets. Strategies included appointing female leadership positions, implementing female-specific recruitment initiatives, establishing support systems such as childcare facilities and flexible work arrangements, creating mentorship programs, and developing outreach activities for female students. Host institutions have also implemented supporting measures, including unconscious bias training, dedicated funding for female researchers, and improved workplace facilities.

While progress is evident in many centers, sustained effort is needed to achieve improvement in gender balance across the WPI Program, particularly at leadership levels.

#### L. Future Plan of the WPI Program

In this year's October meeting of the Program Committee, NAKAZAWA Keita, Director of Basic and Generic Research Division of Research Promotion Bureau of MEXT, and AIKAWA Misa, Deputy Director, presented MEXT's reviewed proposal for further sustainable development of WPI centers, incorporating recommendations from last year's committee meeting.

#### M. Branding and outreach

In November 2024, the 13th WPI Science Symposium was held in Kyoto on the theme "Expansion of world through science". ASHBi of Kyoto University led in organizing the symposium. There were 301 attendants including 86 high school students. A poster session with a new format in which 28 posters by high school students were presented side by side with 18 posters by young WPI researchers provided a very stimulating arena for high school students to interact directly with young scientists of WPI centers.



Poster session with high school students