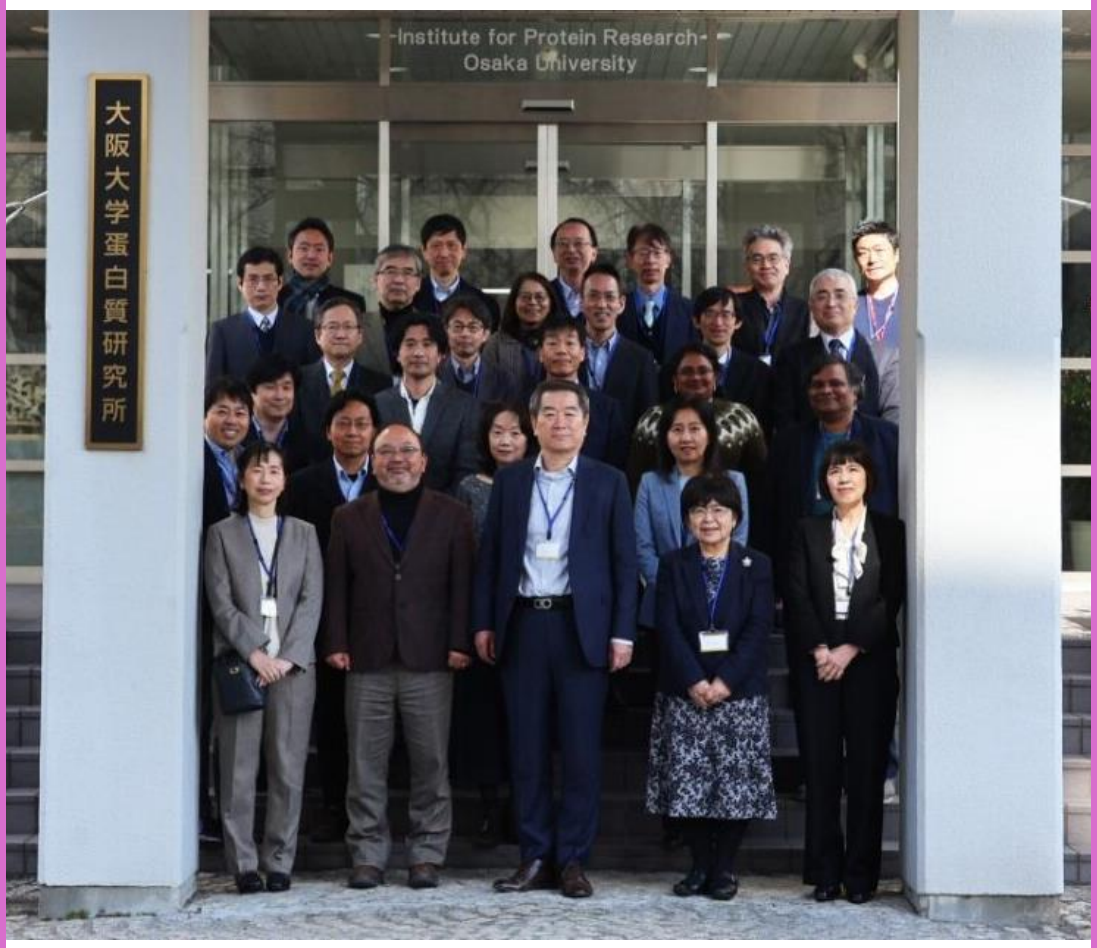
External Review Report
of
Institute for Protein Research

2023



INSTITUTE for PROTEIN RESEARCH
OSAKA UNIVERSITY

March 2024 Issued

Preface

The Institute for Protein Research (IPR) was established in 1958 based on the Faculty of Science and the Faculty of Medicine of Osaka University as a Joint-use Research Organization under the supervision of Prof. Shiro Akabori as its first director. Since its establishment, IPR has been leading protein science, a key field of life sciences based on interdisciplinary research in chemistry, biology, physics, and medical science. In addition to our research, IPR has been working as a hub of protein sciences for many laboratories worldwide.

At its establishment, IPR consisted of three divisions: Organic Chemistry, Physical Chemistry, and Protein Metabolism, but with advances in protein science and life science, IPR has expanded to cover a broader range of research fields. To respond to the rapid progress of life science in recent years, IPR reorganized the Research Center for Next-Generation Protein Sciences in October 2020, and established the Advanced Data Science Center for Protein Research in October 2022, aiming to serve as a core center for life sciences based on protein structural information. Now IPR has grown into an organization consisting of 16 laboratories in five research divisions (including the Endowed Chair), five laboratories in the Research Center for Next-Generation Protein Sciences, and five laboratories in the Advanced Data Science Center for Protein Research.

Since its establishment, IPR has been active as a Joint-use Research Organization where many researchers can visit and conduct research by sharing IPR's facilities, equipment, and research know-how from all over Japan. In April 2010, IPR was certified as a Joint Usage / Research Center for Protein Research by the Ministry of Education, Culture, Sports Science and Technology. IPR continues its invigorate activities and is committed to contributing to the protein research community IPR's activities involve programs such as "Domestic Collaborators," "International Collaborative Research," and "IPR Fellows" that promote research activities, "IPR Seminars" that support organizing seminars to provide a place for forming a community and exchanging information, the programs that support the use of the forefront large facilities such as SPring-8 synchrotron radiation beamline, high-magnetic field NMR machines, and cryo-electron microscopes. IPR also operates a protein structural database (Protein Data Bank) that is fundamental for protein research. IPR continues to serve as a research center for life sciences, focusing on protein science.

The database project, PDBj (Protein Data Bank Japan) serves as one of the three regional data centers of the Worldwide Protein Data Bank (wwPDB) organization, registers data and provides various services in Asia and Oceania. Additionally, the Synchrotron Radiation Beamline has been promoting various international collaborative research activities, such as the formation of an Asia-Oceania

structural biology network through an academic agreement with the National Synchrotron Radiation Research Center in Taiwan, as well as other international collaborative research programs.
IPR has international academic exchange agreements with 17 research institutions and has increased its presence.
While conducting cutting-edge research, IPR faculty members actively provide lectures and practical training to 120 students from the Faculty of Science, Faculty of Medicine, Faculty of Engineering, Graduate School of Science, Graduate School of Medicine, Graduate School of Frontier Biosciences, and Graduate School of Engineering, Osaka University. In addition, about 30 postdoctoral researchers are involved in various research projects.

For the projects that IPR carried out from FY2016 toFY2021, we received the highest rating of Category S with the following comments:

> *As a core center for protein science, IPR makes its facilities, equipment, materials, and data available for shared use, including the world's most powerful cryo-electron microscope, instruments essential for protein structure analysis, and the operation of protein databases, and actively conducts collaborative use activities. IPR has achieved excellent research results, including numerous publications, and is making efforts to further improve its core competence as a research center by promoting interdisciplinary research, reorganizing research organizations, and forming an international joint laboratory, as well as by responding to the interim evaluation results. In the future, further efforts are expected to be made to focus on specific areas of research to make the facility unique, and to conduct advanced research in protein science using computational science and data science, such as prediction of 3D structures.*

IPR has conducted external reviews in the past at critical times when it was deemed necessary to review its research activities and structure. This external review was conducted prior to the interim evaluation of the Joint Usage / Research Center scheduled for FY2024, to obtain an external evaluation of the activities of IPR, as well as the Advanced Data Science Center for Protein Research (ASPiRE) which was launched in 2022 to promote advanced protein science research. This external review was conducted from December 2023 to March 2024 with the dedicated cooperation of 12 academic experts inside and outside Japan.

IPR conducted the External Review Committee Meeting (on-site and online) on January 29-30, 2024, and received evaluations from the following perspectives regarding the status of activities and functions related to the IPR's Joint Usage / Research Center.

[Evaluation Items]

1. Research Activities

For the laboratories responsible for the review, are the goals of the research and the research themes and methods based on those goals appropriate?

2. Budget and Organization

   Is the management of the Joint Usage / Research Center properly organized? And is its support system functioning properly?

3. The Joint Usage / Research Center Activities

   Are the activities of the Joint Usage / Research Center appropriately implemented?

4. Education

   Is IPR engaging in fostering its undergraduate/graduate students, young researchers, and foreign researchers by utilizing the programs of the Joint Usage / Research Center?

5. External funding and other research expenses

   Is IPR making efforts to secure the necessary research funding for research activities?

6. Information Disclosure and Social Relationships

   Is IPR offering information about its research activities sufficiently to society?

7. International Exchanges

   As a university-affiliated research institute and as a Joint Usage / Research Center, does IPR engage in sufficient international exchange activities?

[General Discussion]

- Are IPR's research activities and organization appropriate, including the recent reorganization?
- Is IPR's future direction orientated toward protein or life science prospects?

This review report summarizes the above external evaluation and describes IPR's future actions. We will take these evaluations and recommendations made by the committee members seriously and incorporate them into our future efforts.

March 2024

Mariko Okada

Professor, Mariko Okada
Director, Institute for Protein Research

Atsushi Nakagawa

Professor, Atsushi Nakagawa
Chair, Review Committee of IPR

EXECUTIVE SUMMARY

This is the executive summary for the final report of the 2023 External Review (ER2023) of the Institute for Protein Research (IPR), Osaka University, organized by the External Review Committee consisting of 12 distinguished international and domestic researchers in protein science.

During the two-day on-site visit to the IPR in Osaka, the ER2023 committee members extensively had in-depth reviews and discussions with the directors of the IPR, its affiliated research centers, and PIs in all research groups to examine their recent activities. The ER2023 committee mainly focused on the following activities and their performances from April 2019 to December 2023 from the viewpoint of the IPR's roles as a leading research institute and a Joint Usage / Research Center.

Main topics of this external evaluation by the ER2023 committee:

1. Research Activity
2. Activities as a Joint Usage / Research Center
3. Education
4. Information Disclosure and Social Relationship
5. International Exchange

The evaluation also provides observations (comments, thoughts), suggestions, and recommendations for each topic. Overall, ER2023 committee members conclude that:

Research Activity:

The IPR demonstrates excellent international presence, research accomplishments, and strategic initiatives. The committee recommends maintaining a proactive approach to adapting to emerging research trends, investing in emerging areas, enhancing internal collaboration, establishing a future planning committee, and balancing tradition with cutting-edge research. The launch of ASPiRE is seen as a proactive approach to adapting to emerging research trends, although its outcomes need further evaluation.

Activities as a Joint Usage / Research Center:

The Joint Usage / Research Center of IPR, as a core for protein research in Japan, operates as a successful Joint Usage / Research Center, acknowledged for its significant achievements and proper functionality with well-established management and user support systems. The committee admires the center's exemplary performance and recommends further expanding collaborations for groundbreaking discoveries in these facilities.

SPring-8 and PDBj are the examples of the IPR's outstanding assets. They are also acting as the assets for global collaborations and the provision of research platforms for high-end protein research. However, concerns include a decreasing trend in collaborations after 2018 and the need for constant funding for high-end facilities. The committee appreciates IPR's efforts but raises budgetary concerns and suggests the consideration of charging systems for facility usage to supplement government support, aligning with current practices at many universities.

Education:

The committee praises the IPR's commendable efforts in cultivating the intellectual landscape of young scientists in the intricate field of protein life science. Its effective programs have educated and successfully nurtured the budding talents that form the backbone of the scientific community. The committee also acknowledges and commends the IPR's steadfast commitment to student education, citing a noteworthy increase in student numbers over the preceding four years.

Recognizing the potential for further advancement, the committee puts forth insightful recommendations. These include augmenting scholarships for Ph.D. students through collaborative initiatives with Osaka University, ensuring a robust influx of promising doctoral candidates. Moreover, an imperative call is made to broaden the horizons of the postdoctoral research program, with a keen focus on fostering diversity among international fellows. This strategic expansion is pivotal for sustaining a vibrant and globally representative community of researchers.

While acknowledging the enriching seminar milieu conducive to on-site learning, the committee underscores the necessity for diplomatic negotiations with the Faculty of Science. This effort is crucial to address perceived limitations in assigning undergraduates to IPR and to promote an inclusive educational environment.

Information Disclosure and Social Relationship:

The committee appreciates the uniqueness of IPR's outreach activities but propose more inclusive endeavors transcending generational boundaries for broader societal impact. Additionally, the committee emphasizes the need for participant feedback to ensure program satisfaction. Furthermore, the committee suggests that IPR could enhance transparency and public perception by adopting an open election system for director and professor positions, leading to information disclosure.

International Exchange:

The IPR has successfully engaged in collaborative research with researchers from diverse countries, indicating satisfactory international exchange activities for an affiliated research institute and the Joint

Usage / Research Center. The institute's commitment to global scientific cooperation is evident through its involvement in joint research projects, academic exchange agreements, and international joint labs. Furthermore, IPR's public offering programs, supporting International Collaborative Research, non-proprietary usage of Synchrotron Radiation Beamline, and MicroED collaborative research, exemplify its dedication to fostering international scientific exchange and development.

Although the IPR has an outstanding role in facility usage and database access, there is a notable concentration of international beamline allocation to Taiwan. The committee recommends that the IPR develop close relationships with more countries worldwide for research and human resource exchange to ensure sustained growth.

Conclusions and Other Recommendations

The committee has acknowledged that the IPR possesses the ambition and potential to establish itself as a world-leading research institute. The accomplishments of the IPR faculties are highly commendable and underscore the institute's significant contributions to protein science. However, collaboration within the IPR is relatively limited. The committee suggests encouraging collaborative research within the institute to develop it further and take advantage of diverse research experts in the IPR.

IPR boasts an excellent array of facilities crucial for advancing cutting-edge research in protein sciences. However, the management of most of these facilities is overseen by associate professors, who ideally dedicate their time and efforts to their research endeavors. Hiring specialized personnel to manage these resources would alleviate the burden on academic staff and enhance the overall functionality and utilization of the facilities. Such support would ensure that the equipment is maintained at optimal performance levels and is readily available for researchers, thereby maximizing the investment and contributing to more robust and efficient scientific outcomes. The government must recognize the importance of funding the purchase of such high-caliber equipment and ensuring adequate resources for its ongoing management. A more sustainable management model of IPR's facility infrastructure, supported by adequate government funding, is needed to provide the longevity and effectiveness of these valuable resources.

Acknowledgments:

The ER2023 committee members acknowledge all the IPR members for helpful, clear, comprehensive interviews, documentation, presentations, and answers to follow-up questions. As far as the ER2023 committee members could assess, the IPR was transparent and internally self-consistent. The ER2023 committee members note that logistical support was outstanding—many thanks to Director Mariko Okada, Prof. Atsushi Nakagawa, and the ER2023 administration office.

External review of Institute for Protein Research (FY2023)

Committee Members

Chairperson

Bong-Jin LEE (Dean of College of Pharmacy, Ajou University, Korea)

【Division of Protein Chemistry】

*Tatsuya SAWASAKI (Professor, Ehime University)

Keiko SHIMAMOTO (Specially Appointed Manager, Suntory Foundation for Life Sciences)

Hee-Jung CHOI (Professor, Seoul National University, Korea）

【Division of Protein Structural Biology】【Research Center for Next-Generation Protein Sciences】

*Bong-Jin LEE (Dean of College of Pharmacy, Ajou University, Korea)

Yuriko YAMAGATA (President, Shokei University, Shokei University Junior College)

Takeshi MURATA (Professor, Chiba University)

【Division of Integrated Protein Functions】

*Sen TAKEDA (Professor, Teikyo University)

Tatsumi HIRATA (Professor, National Institute of Genetics)

Jun SUZUKI (Professor, Kyoto University)

【Division of Protein Network Biology】【Advanced Data Science Center for Protein Research】

*Shoji TAKADA (Professor, Kyoto University)

Kenta NAKAI (Professor, The University of Tokyo)

Chandra VERMA (Senior Principal Investigator, A*STAR, Singapore)

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*Overall Review Member

AGENDA

Date: January 29 (Mon) - 30 (Tue), 2024

Venue: 1F Auditorium, 2F Large Meeting Room (#212), 2F Medium Meeting Room (#202), 4F Seminar Room (#415), 7F Seminar Room (#712)

DAY 1

10:00 – 10:10	**Welcome Speech**: *Dir./Prof. Mariko Okada* **Introduction of Reviewers** *Moderator: Prof. Atsushi Nakagawa* Room: Large Meeting Room (#212)	Attendees
Overall Review (15 min presentation + 10 min Q&A) Room: Large Meeting Room (#212)		
10:10 – 10:35	**Overall activities of IPR** *Dir./Prof. Mariko Okada*	• All Reviewers • All PIs
10:35 – 11:00	**Activities of Joint Usage / Research Center** *Prof. Yoshie Harada*	
11:00 – 11:25	**Research Center for Next-Generation Protein Sciences** *Prof. Atsushi Nakagawa*	
11:25 – 11:50	**Advanced Data Science Center for Protein Research** *Prof. Nobuyasu Koga*	
11:50 – 12:05	**Discussion**	
12:05 – 12:15	**Group Photo (Entrance)**	• All Reviewers • All PIs
12:15 – 13:30	**Lunch Break (Auditorium)**	
Review of Research Group Activities (10-15 min presentation & 5 min Q&A)		
Division of Protein Chemistry *Moderator: Prof. Toshifumi Takao* Room: 4F Seminar Room (#415)		• Each Reviewer • Takao • Hojo • Harada • Takagi • Suzuki
13:30 – 13:50	Laboratory for Protein Organic Chemistry: *Prof. Hironobu Hojo*	
13:50 – 14:10	Laboratory for Nanobiology: *Prof. Yoshie Harada*	
14:10 – 14:30	Laboratory for Protein Synthesis and Expression: *Prof. Junichi Takagi*	
14:30 – 14:50	Laboratory for Protein Profiling and Functional Proteomics: *Prof. Toshifumi Takao*	
14:50 – 15:05	Laboratory for Physical Biology: Assoc. *Prof. Madoka Suzuki*	
Division of Protein Structural Biology/Research Center for Next-Generation Protein Sciences *Moderator: Prof. Takayuki Kato* Room: 2F Medium Meeting Room (#202)		• Each Reviewer • Kato • Kurisu • Nakagawa • Matsuki • Miyanoiri • Okumura
13:30 – 13:50	Laboratory for Protein Crystallography: *Prof. Genji Kurisu*	
13:50 – 14:10	Laboratory for CryoEM Structural Biology: *Prof. Takayuki Kato*	
14:10 – 14:30	Laboratory for Supramolecular Crystallography: *Prof. Atsushi Nakagawa*	
14:30 – 14:45	Laboratory for Molecular Biophysics: Assoc. *Prof. Yoh Matsuki*	
14:45 – 15:00	Laboratory for Ultra-High Magnetic Field NMR Spectroscopy: *Assoc. Prof. Yohei Miyanoiri*	
15:00 – 15:15	Laboratory for Biomolecular Analysis: *Assoc. Prof. Nobuaki Okumura*	

Division of Integrated Protein Functions *Moderator: Prof. Akira Shinohara* Room: 7F Seminar Room (#712)		• Each Reviewer • Shinohara • Furukawa • Nakai
13:30 – 13:50	Laboratory for Molecular and Developmental Biology: *Prof. Takahisa Furukawa*	
13:50 – 14:10	Laboratory for Genome and Chromosome Functions: *Prof. Akira Shinohara*	
14:10 – 14:30	Laboratory for Advanced Brain Functions: *Prof. Takatoshi Hikida*	
14:30 – 14:45	Laboratory for Organelle Biology: Assoc. *Prof. Masato Nakai*	
Division of Protein Network Biology/Advanced Data Science Center for Protein Research *Moderator: Prof. Kenji Mizuguchi* Room:2F Large Meeting Room (#212)		• Each Reviewer • Mizuguchi • Okada • Koga • Sandhya
13:30 – 13:50	Laboratory for Cell Systems: *Prof. Mariko Okada*	
13:50 – 14:10	Laboratory for Computational Biology: *Prof. Kenji Mizuguchi*	
14:10 – 14:30	Laboratory for Protein Design: *Prof. Nobuyasu Koga*	
14:30 – 14:45	Laboratory for Biomolecular Modeling and Dynamics: *Assoc. Prof. Sandhya P. Tiwari*	
14:45 – 15:00	Laboratory of Protein Databases (PDBj): *Prof. Genji Kurisu*	
15:00 – 15:30	**Break (Auditorium)**	
15:30 –	Facility tour (NMR (solid/solution), Cryo-EM)	• Applicant
17:00 –	To Senri Hankyu Hotel	• All Reviewers • All PIs
17:30 –	Dinner (Senri Hankyu Hotel)	

DAY 2

10:00 – 10:40	**Session 1: Summary of Reviewers' Comments** Room: Auditorium	• All Reviewers • Okada • Nakagawa • Hojo
10:40 – 10:50	**Break**	
10:50 – 11:30	**Session 2: Overall Evaluation of Research Group Activities** Room: Each room	• Each reviewer • Each PI (Presenters)
11:30 – 11:40	**Break**	
11:40 – 12:35	**Overall Review, Q&A** *Moderator: Prof. Atsushi Nakagawa* **Closing remarks**: *Prof. Atsushi Nakagawa* Room: Auditorium	• All reviewers • All PIs
12:35 – 14:00	**Lunch Break (Auditorium)**	• All reviewers • All PIs
14:00	To Senri-Chuo Station	

Inside the Meeting (Large Conference Room)

Inside the Meeting Room (Auditorium)

Inside the Meeting (Each Division)

External Review FY2023

Evaluation Sheet (Activities of IPR)

Reviewers: Hee-Jung CHOI, Bong-Jin LEE, Tatsuya SAWASAKI, Shoji TAKAD, Sén TAKEDA

Based on the perspectives of:

1. the research activities and performance as the research institute, and
2. the functions and activities as the Joint Usage / Research Center,

please provide your evaluation and review for each topic described below. If you find any outstanding points, issues, or recommendations, we highly appreciate your comments. You do not need to fill out all topics, but please kindly provide as much information as possible.

1. Research Activity

[Evaluation Perspective]

- Are the IPR's research activity, performance and the composition of research divisions appropriate as an internationally-recognized protein life science research institute?
- Is the current IPR's vision appropriately set to meet the future advances in protein science, life science, etc.?

Commentary and Recommendations

[Reviewer #1]

In terms of research activities, accomplishments, and the composition of its research departments, the IPR has demonstrated a strong international presence and sufficient influence. In addition, the current vision of the institute is established with due consideration given to the future development of protein science and life sciences. By keeping this quality of activity, the IPR will be able to continue to lead protein research in Japan, as it is doing now.

[Reviewer #2]

IPR shows an excellent track record of publications in prestigious journals, underlining its significant contributions to protein science. The institute's provision of state-of-the-art facilities and advanced equipment further underscores its commitment to maintaining a cutting-edge research environment. A particularly notable achievement is IPR's strategic response to the evolving landscape of data-driven protein science, including novel protein design, which is rapidly growing research field globally. The establishment of the new ASPiRE division is a commendable step. This division, encompassing four new laboratories (Protein Design, Biomolecular Modeling and Dynamics, Protein Network, Drug Discovery Informatics) along with the existing Protein Databases lab (previously part of the Research Center for Next-Generation Protein Sciences), reflects a proactive and flexible approach to organizational structure. This reorganization allows IPR to stay at the forefront of global research trends and dynamically evolve in response to the shifting

landscape of protein science.

Looking forward, it is recommended that IPR continues to foster this adaptive approach, particularly by investing in emerging areas of protein science that show potential for significant impact.

[Reviewer #4]

This reviewer finds the IPR's overall research activity is obviously above average in terms of scientific performance. Each division constantly contributes to the progress of protein research in each specific field and continues to be productive, verified by high-quality publications over the past years. IPR covers broad areas in protein science ranging from structural biology to higher brain function of mammals, making it possible to be a hub for the protein-oriented research both in domestic and international research network. Moreover, basic research, ideas and concept appear to transform or sublime to be a full-fledged applied sciences that are buttressed by the traditional and master techniques in protein chemistry that have been developed, refined and handed down during the long history of IPR.

When we take a look at equal opportunity action or diversification of faculty, this reviewer finds the status quo of IPR copes well with the standard requirements from the society as we can see from the breakdown of faculty recently employed here, though continued efforts are required to maintain and foster a mind of diversity.

Whilst my general impression on IPR is a very positive one, there are a couple of advice that would be ideally reconsidered by a decision-making committee of IPR to improve the performance as well as to assure the sustainability of IPR.

First, it would be better to have in-house research seminar that can expedite collaborative research between different expertise in IPR thorough exchanging basic ideas. As collaborative research is going quite actively with external facilities, this reviewer does not find it difficult to have in-house collaborations, if each member of IPR bears in mind what in-house collaboration means. It does not necessarily mean that substantial collaboration on a specific theme through and through, but technical or conceptual collaboration will do. According to vis-à-vis hearing from not a few staff scientists during my stay in IPR, this reviewer finds himself noticing that there is no real opportunity such as seminar or retreat that make all affiliates in IPR know about research contents explained by PIs by themselves of each division. What one can do as a next step is to prepare a platform for promoting in-house collaboration to take advantages of expertise blanketing broad area of protein research. A good example for that is an initiative of in-house funding platform taken by Prof. Koga from ASPiRE. This has a great potential to promote internal collaboration in the long run, while it appears rather reserved now.

Second, it is advisable to have a kind of active future planning committee to set short-, mid-, and long- term goals of IPR with special references to the recruitment of staff, direction of research, re-organization of

division, and financial issues. Committee should include a couple of external members to gather and blush up proposals and idea that potentially contributes to a continued development of IPR.

Third, perspectives for running the organization in mid-term is very important to balance the tradition and cutting-edge research field. On one hand, IPR should keep heritages of protein chemistry as fundamentals of institute, such as proteomics and organic chemistry. On the other hand, IPR has to deconstruct and reorganize the current division at least to keep abreast of age, and ideally take an initiative of protein research globally. This reviewer heard that 8 leading PIs are going to be retired from IPR in the coming 5 years. Taking this into account, it may be high time to reconsider the restructuring of organization by taking the advantages of this opportunity to foster the development of new research area.

[Reviewer #5]

Evaluating the whole activities of the IPR, I am convinced that the overall research activity of the IPR is outstanding and at the world-level.

For the long-term direction, I am impressed that the IPR realizes nice balance between the conservation and the revolution/change. As a single national institute focusing on protein science in Japan, the IPR keeps the position of the center of protein science, with current focus in structure biology. At the same time, the IPR keeps changing driven by scientific development. More recently, the IPR launched the data-oriented center, ASPiRE, which perfectly meets the current need in protein science. As such, this new center, ASPiRE, plays an important role. Its organization looks good, but obviously, it is too early to assess its outcome.

2. Activities as a Joint Usage / Research Center

[Evaluation Perspective]

- Are the activity and performance as a Joint Usage / Research Center appropriate?
- Are the management and user-support system properly arranged and functioned as a Joint Usage / Research Center?

Commentary and Recommendations

[Reviewer #1]

The IPR has more than enough activities and achievements as the Joint Usage / Research Center, and is functioning properly. The IPR is fully functioning as a core for protein research in Japan. The management system and user support system as the Joint Usage / Research Center have been appropriately established and are functioning properly. If the government adds more budget, I can further expect that this institute will be a driving force in protein research in Japan.

[Reviewer #2]

The Joint Usage/Research Center at IPR has demonstrated exemplary performance, particularly evidenced by the publication of excellent research results in top-tier journals such as 'Cell' (2021) and 'Nature Structural

& Molecular Biology' (2019, 2021, 2023). This success is notably attributed to the effective utilization of IPR's state-of-the-art facilities, including the X-ray beamline, NMR, and cryo-EM. These tools have been instrumental in advancing research and fostering collaborative projects with industry partners and international scholars, showcasing the center's role as a hub of innovation and practical application.

Moving forward, it is recommended that the center continue to build on these strengths by further expanding its collaborative endeavors. This could involve establishing more diverse partnerships, both within academia and across different industry sectors worldwide. Doing so could broaden the scope of research and increase the potential for groundbreaking discoveries and technological advancements.

Additionally, considering the rapid evolution of scientific technology, regular assessments and upgrades of the center's equipment and facilities (supported by government) are essential. Keeping pace with the latest advancements will ensure that the center remains at the forefront of research capabilities.

[Reviewer #4]

To this reviewer's understanding, there are two outstanding assets in IPR, both of which contribute to the expertise of protein research: Spring-8 and Protein Databank Japan (PDBj). In addition, series of NMR and cryo-EM instrumentations reinforce the fundamentals of IPR, all of which live up to the reputation of IPR as a center of protein research in Japan. The stats show that those facilities are working very busy, operated not only by the faculty of IPR, but also by many collaborators around the globe.

In terms of fostering researchers in the field of protein life science, the fundamentals of IPR provide young scientists with an opportunity to carry out forefront research that will be inaccessible at their own affiliations. Technically, IPR provides 8 types of platforms for collaborators, which enables them to be easily accessible to high-end protein research facilities without going through any particular issues in operating and applying those instrumentation.

Regarding protein informatics, PDBj covers over 30% of world-wide registry of protein databank, whose entries appears to be on an increasing trend after 2015. Moreover, the number of accessions to PDBj has been drastically increased, reaching at over 170 million annually in 2022. Taking those stats into account, IPR can be evaluated as a major joint user research center of protein in the world.

However, when we take a look at the status quo in detail, there are several negative factors that have to be addressed to sustain and strengthen the leading roles of IPR. First, the total number of collaborations takes on a decreasing trend after 2018, while the number of international ones is increasing. As for the number of users, it remains relatively constant during this period except for 2021, non-collaborative users stay on a same trend. Considering one of the important roles of IPR as a center for joint research, it is advisable to encourage collaborative research to broaden the coverage of research area. Second, international beamline allocation appears to be deviated to Taiwan accounting for ca. 10%, while the sector for all other countries

adds up only to 1 %. Although there might be some geographical barrier in collaborating with IPR, it is ideal to recruit more countries all over the world from the standpoint expediting multidisciplinary research. Third, measures to maintain constant funding to maintain the high-end facilities have to be considered in a proactive manner to assure the position of IPR to be a pivot of protein research, such as an introduction of charging system to the users depending on the affiliation. Considering rapidly exchanging, volatile time we are confronting nowadays, proactive measurements are indispensable to further strengthen the power of IPR.

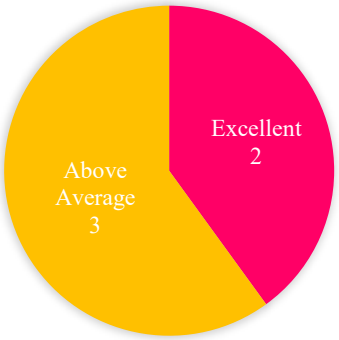
[Reviewer #5]

I see that the IPR made tremendous effort to serve as the Joint Usage / Research Center, which I appreciate to. To maintain the service and keep the facilities top-leveled, the budget is the issue. Government support is desired, but cannot be too much, either. I thought the IPR can seriously think of charging systems for usage of facilities. I hope it would not be too expensive. But, it can be non-free. Nowadays, many Universities have charging systems, as far as I know.

3. Education

[Evaluation Perspective]

- In terms of fostering researchers in the field of protein life science through Joint Usage / Research Center, are the programs appropriately arranged?
- In terms of fostering young researchers (undergraduate students, graduate students, post-doctoral fellows, and foreign researchers) in the IPR, is the education appropriately provided?



Commentary and Recommendations

[Reviewer #1]

As an institution for fostering researchers in the field of protein life science through the Joint Usage / Research Center, the IPR has established sufficient programs and an appropriate systems, and has demonstrated a satisfactory achievement.

[Reviewer #2]

IPR significantly contributes to the education and training of the next generation of scientists in the field of protein life science, offering a range of programs and opportunities for students and researchers. To further enhance this educational role, it is recommended that IPR, through Osaka University, provides more scholarship opportunities for PhD students, to recruit more PhD students.

Additionally, although the IPR New Research Exploration Program is commendable (it is not clear whether it supports postdoctoral fellows), an expansion of the postdoctoral research program to support the independent research of both domestic and international postdoctoral fellows would be an excellent step (Government should provide more funding for this purpose). By nurturing a diverse and dynamic community of researchers, IPR can continue to make substantial contributions to the field.

[Reviewer #4]

According to the stats, the number of students shows an increasing trend during the COVID19 pandemic, and the total amount of scholarship increased steadily. Considering the expected roles of IPR as a center for fostering researcher in protein science of broad meaning, the goals of IPR appears to have been successfully attained at least during last couple of years in terms of figures. Furthermore, this reviewer witnessed that quite a few students belong to each lab and contribute to the scientific output to some extent. However, as there was no detailed information, such as syllabus and course guidebook, given during the review round, this reviewer is not able to evaluate precisely the quality of education both in terms of lectures and laboratory course for all sectors of students. Taking the environment of IPR into account, where many seminars are held every week, students are provided with enough chance to learn the cutting-edge research. In this sense, educational activities in IPR are likely given on site in each lab and they would be ideal teaching materials for students, judging from the high-quality scientific products from IPR.

One comment that comes up in my mind is a recruiting system. During my stay in IPR, I've heard that there is a restriction in the number of undergraduates allocated to IPR. The fact that only 8 undergraduates belonging to Faculty of Science can choose labs in IPR appears to be a kind of enclosure, which should be ideally changed through negotiation on the basis of educational collaboration and development of IPR.

[Reviewer #5]

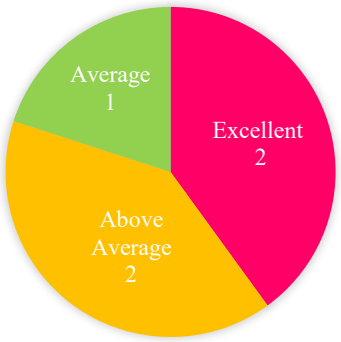
The IPR made much effort to education of students in IPR. I am very impressed that the number of students steadily and markedly increased in the last 4 years. I hope this continues.

I did not see the fostering program of protein science for the community run by the IPR (Possibly, I just missed it). Summer and/or winter schools for comprehensive protein science, for example, can be great for the community. Such schools can also be effective as a tool of recruiting students from other Universities. Once video recorded, lectures in these schools can be delivered via YouTube or others.

4. Information Disclosure and Social Relationship

[Evaluation Perspective]

- Is the IPR sufficiently communicating with the societies about the IPR's activities?



Commentary and Recommendations

[Reviewer #1]

The IPR has adequate outreach activities to the public, including academic societies and high school students.

[Reviewer #2]

IPR sufficiently communicates with the societies about the IPR's activities through its website, both in English and Japanese.

[Reviewer #3]

Not only a lecture for high-school students, but a lecture for general people is needed for PR (promotion) of IPR for the social relationship. PR of IPR research result is important in increasing the support from government.

[Reviewer #4]

Regarding the outreach activity, this reviewer feels nothing particular that is superior to other institutions. While IPR offers special programs and lectures to high school students, more generalized activities not confined to specific generations should be considered to be recognized as a pro bono institute influencing the society. From the standpoint of evaluation, this reviewer would like to give just a brief comment on an outreach activity to high school students. Although it is highly evaluated to facilitate the participation of younger generation to get involved in the protein research, it would be better to know the feedback from the participants whether or not they have satisfied with the program.

When it comes to information disclosure, IPR places annual reports and review reports of every four years open to the public on its website. This is a de facto international standard for universities and research institutions. IPR can be at the vanguard of information disclosure, if election system of director as well as professor is open to the public. To this reviewer's eye, a system for electing Director of IPR though mutual selection is appealing compared to the candidature system. For academic organization, candidature system often does not work well, where only those aspiring for power tend to stand for the position.

5. International Exchange

[Evaluation Perspective]

- Are the IPR's international exchange activities satisfactory as an affiliated research institute and a Joint Usage / Research Center?

Commentary and Recommendations

[Reviewer #1]

The IPR has been conducting collaborative research with researchers in a very diverse range of countries. These facts indicate that IPR's international exchange activities are satisfactory enough for an affiliated research institute and the Joint Usage / Research Center.

[Reviewer #2]

IPR's engagement in a broad spectrum of international collaborations is commendable. Its involvement in joint research projects, academic exchange agreements, and international joint labs demonstrates a strong commitment to global scientific cooperation. Additionally, IPR's public offering programs, which support International Collaborative Research, non-proprietary usage of Synchrotron Radiation Beamline, and MicroED collaborative research, are exemplary initiatives that showcase the institute's dedication to fostering international scientific exchange and development.

[Reviewer #4]

As commented in sections 1 and 2, most of the stats shows an outstanding role of IPR both in facility usage and database access. However, international beamline allocation is concentrated to Taiwan accounting for circa 10%, whereas that for all other countries account for around 1 %. Possibly, very close relationship of IPR with Academia Sinica account for this, it is ideal to recruit more countries all over the world to promote the research and human resource exchange, which will ensure a continued growth of IPR.

[Other]

If you have any additional comments or recommendations other than those mentioned above, please describe them here.

[Reviewer #1]

The IPR is a strong supporter of protein research, especially in Japan. This contribution is very significant, and many domestic researchers have benefited from it. However, because of the amount of effort that is required to make up for this, collaboration within the IPR appeared to be relatively limited. For the further development of this institute, I would like to encourage collaborative research within the institute.

[Reviewer #2]

This review has clearly demonstrated that the Institute of Protein Research (IPR) possesses the ambition and potential to establish itself as a world-leading research institute. The accomplishments of the IPR faculties are highly commendable and underscore the institute's significant contributions to the field of protein science.

IPR boasts an excellent array of facilities, which are crucial for advancing cutting-edge research in protein sciences. However, it is notable that the management of this equipment is currently overseen by associate professors, who ideally should be dedicating their time and efforts to their own research endeavors.

It is essential that the government recognizes the importance of not only funding the purchase of such high-caliber equipment but also ensuring adequate resources for its ongoing management. This includes covering expenses related to device repairs, updates, and most importantly, the salaries of dedicated staff members tasked with facility management. Hiring specialized personnel to manage these resources would alleviate the burden on academic staff and enhance the overall functionality and utilization of the facilities. Such support would ensure that the equipment is maintained at optimal performance levels and is readily available for

researchers, thereby maximizing the investment and contributing to more robust and efficient scientific outcomes.

In summary, this reviewer is highly impressed with the accomplishments of the IPR faculties, but there is a clear need for a more sustainable management model of IPR's facility infrastructure, supported by adequate government funding, to ensure the longevity and effectiveness of these valuable resources. This reviewer appreciates the opportunity to have undertaken the review.

[Reviewer #3]

IPR have shown very good activities in the field of protein science. IPR has excellent two centers, such as "Research Center for Next-Generation Protein Science" and "Advanced Data Science Center for Protein Research". These two centers have shown good achievement in protein science research.

Because IPR has Synchrotron beam line, high-resolution Cryo-EM, Micro-ED and Ultra-high magnetic field NMR facilities, IPR could lead protein science in the world. Because these facilities was open to foreign scientists, an international collaboration was increased and this international collaboration greatly contributed to protein science research in the world. The comments for the future development of IPR are as follows.

Recently, female scientists are increasing in the world and have shown an important role and good achievement in the scientific field. In IPR, the number of female faculty members has been slightly increasing until 2022. But the percentage of female faculty members is under 20 %. Therefore, an effort to increase the number of female faculty members is needed, Because IPR has excellent facilities and good scientists, more collaborations with overseas scientists are recommended. International collaboration is one of an important factor in the evaluation of institute or university by the rating agency (QS, Times etc.) Development fund-raising by alumni or industry is needed for the development of IPR. Also, I recommend Bioventure company will be founded by IPR faculty members. This company can give a research grant and strong academia-industry relationship. NMR is very important facility in protein science research. IPR has 950 MHz NMR machine which is most large NMR in Japan and in Asia. In this year, 1200 MHz (1.2 Giga Hz) machine will be installed in Korea Basic Science Research Center. Therefore, I recommend that IPR will try to purchase more larger NMR Machine than 950 MHz machine.

[Reviewer #5]

Regarding the diversity and inclusion initiatives, I am very pleased to see that the ratio of female faculties increased dramatically, based on the IPR's several strategies. This would influence, to a good direction, other Departments and Universities in Japan.

The new center ASPiRE is a promising direction. In its organization, it would be great if the center can recruit a proper IT group dedicated to machine-learning. Cross-appointing to Professors in Osaka University can be a possibility, I thought.

I saw that the Research Center for Next-Generation Protein Science makes much effort to the service as Joint Research Center. Some of the laboratories are run by Associate Professors, who can be fixed-term employed, I guess (I am not very sure, though). Especially in this case, I thought the IPR should take care of their effort to the service.

The IPR has many prominent structural biologists who determine new structures quite steadily. Given that, I thought it would be nicer if there is one group in the IPR dedicated to the state-of-the-art all-atom MD simulations. As soon as a new protein structure is determined, they can examine its functional dynamics by MD.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Protein Organic Chemistry

Name of Reviewers: Hee-Jung Choi, Keiko Shimamoto, Tatsuya Sawasaki

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- The research goals of this laboratory are well-aligned with the objectives of IPR, demonstrating a clear approach to their scientific inquiries. As a member of a premier institution in protein life sciences, the lab's research focus is appropriately established to contribute meaningfully to the field.
- Synthesis of large size proteins and synthesis of uniquely modified proteins utilizing this technology.

Commentary and Recommendations:

- This laboratory has made commendable achievements in the field of protein synthesis research, particularly in areas such as protein synthesis involving glycosylation and phosphorylation, and cyclic peptide synthesis. These areas are critical to advancing our understanding of protein functionality and potential therapeutic applications, so it is recommended to leverage their research outputs to explore and answer complex biological systems through collaborations, which will greatly enhance the impact the lab's research.
- They have established techniques for the precise chemical synthesis of proteins modified with glycans and lipids. Technical abilities to synthesize such difficult proteins by using combination of various types of condensation reactions and newly developed protecting groups should be highly evaluated. Lipid-modified peptides and proteins are expected to be powerful tool for elucidating functions of hydrophobic proteins. However, at this stage, the purpose of synthesis in life science is not so clear. Supplying functional molecules directing chemical biology, such as isotope labeling for NMR and the introduction of click/photoresponsible tags for identification of their target molecules will be expected.
- This laboratory has very unique peptide synthesis and fusion technologies, and their research is very promising. However, it is unclear what kind of impact these technologies will have on research, and what kind of impact they will have on related research fields. It is necessary to set more clearly defined goals for the research, and further effective utilization of the

technologies of this laboratory is desirable.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- The current review reveals no immediate areas requiring urgent attention in terms of research achievements and contributions.
- Collaborations with researchers who will actively use this technology to advance science.

Commentary and Recommendations:

- The research output of this laboratory is commendable, with 11 publications as a corresponding author, and 13 invited lectures both domestically and internationally over the last 5 years. This reflects good research conducted in their respective fields.
- Establishing techniques for the chemical synthesis of proteins modified with glycans and lipids, and supplying synthesized samples to biological experiments contribute to the advancement of protein chemistry. However, at this stage, biological studies using these samples seem to be limited. I recommend them to collaborate with cell biologists in the future.
- The number of research achievements is not a problem at all. I think it is important to develop more high-impact research in the future. I think this LAB has enough potential to do so. For this purpose, I think it is important to find research partners from within and outside the institute who can make good use of this technology.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- The current assessment indicates no immediate areas requiring attention in terms of the group's contribution to the Joint Usage / Research Center.
- Promoting the technology to researchers in diverse fields.

Commentary and Recommendations:

- This laboratory has demonstrated a commendable level of engagement in collaborative efforts, evidenced by its participation in 10 international collaborations. Such endeavors enhance its research capabilities through diverse perspectives and expertise. Additionally, the lab's

contribution of 6 seminars to IPR is noteworthy. These highlight the lab's active role in engaging with the scientific community within the framework of the Joint Usage/Research Center.

- Synthetic proteins with modifications were provided to researchers inside and outside IPR to promote collaborative research. However, these collaborations were personal, and compounds were not commonly used. It would be even better that their techniques will be widely appealed to biologists. Since MS facilities will be moved to their Lab from Takao's Lab, their contribution to IPR or protein life science communities will be enhanced by the combination of synthesis and analysis.
- I have the impression that this laboratory does not have a high level of activity in the Joint Usage / Research Center's Programs. Although this may be a limited need, there are probably researchers who need this laboratory's unique technology, so more active involvement is required.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- While this laboratory provides valuable educational opportunities to graduate students, the ratio of doctoral to master's students suggests a potential area for growth. Doctoral students play a crucial role in advancing research and maintaining academic rigor. Therefore, it's recommended to implement strategies aimed at increasing the enrollment and retention of doctoral candidates.
- Consultation with an Intellectual Property Officer.

Commentary and Recommendations:

- The lab's active engagement in providing research guidance to both graduate and undergraduate students is commendable. In terms of funding, the lab has successfully secured sufficient resources to support its research endeavors. The lab's active involvement in numerous

international joint research projects is another notable achievement. Such international collaborations broaden the scope and impact of the lab's research, contributing to the global scientific community.

- Competitive fundings have been steadily obtained. Although the number of students earning doctoral degrees is a few, one is working as an assistant professor. Previously enrolled staff has moved out into an industrial company. Thus, fostering young researchers/students is properly managed.
- This lab also performs well in education duty. There seems to be little commitment to intellectual property. It is a unique, useful, and good technology that can be sufficiently IPO.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- As a contributing member of IPR, renowned for its status as a world-class institute in protein life sciences, this laboratory has consistently demonstrated its ability to produce excellent research outputs. The lab's involvement in a wide array of collaborative projects is a testament to its dynamic approach and commitment to scientific advancement. Moreover, the lab's clear and forward-looking vision aligns well with the goals of IPR.
- Protein synthesis and modification based on organic chemistry is one of the advantages of IPR. It is desirable to accelerate collaborations with cell biologists, rather than just developing synthetic methods, to clarify the purpose of synthesis.
- This laboratory has unique technology for peptide synthesis. This is a wonderful thing, but I have the impression that the development of their research is limited. In other words, the technology of this laboratory should be utilized more. For this purpose, it seems necessary to communicate with researchers in various research fields to understand their needs.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Nanobiology

Name of Reviewers: Hee-Jung Choi, Keiko Shimamoto, Tatsuya Sawasaki

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- The Laboratory of Nanobiology has developed novel technologies for monitoring biomolecules at the single-cell level. However, an area that requires further focus is the practical application of these technologies to actual biological questions. While the technological advancements are impressive, leveraging them to explore and answer complex biological phenomena could greatly enhance the impact and relevance of the lab's research.
- Collaboration with experts in cell differentiation.

Commentary and Recommendations:

- The Laboratory of Nanobiology's development of the real-time single cell secretion assay platform, alongside its work in quantum biosensing and intracellular temperature measurement, demonstrates a clear alignment with long-term research goals and an innovative approach. As mentioned above, it is recommended that the laboratory actively seeks opportunities to apply them to real-world biological contexts. This could involve understanding disease mechanisms, cellular communication, or biomolecular processes under various physiological conditions. Collaborations with other research groups within the institute or partnerships with external biological research entities are advised to ensure a comprehensive approach to these complex questions. By extending the application of their technologies to tangible biological research, the laboratory can enhance its contribution to the field of nanobiology and further cement its position as a leader in this area.
- The technology to precisely measure intracellular temperature is very unique and is expected to contribute to cell biology and biophysics. Further development of measurement and control technology is expected. However, at this stage, applications are still limited and it has not been proven whether these phenomena are universal. It would be even better if they could develop from model cells and find objects whose physiological significance becomes clear.
- The laboratory has developed a very unique technology that can measure the temperature of a localized region of a cell. However, because the cells being targeted are limited to neurons, the

generality of the new finding that the temperature changes found affect cell differentiation is unclear. Therefore, collaboration with a cell differentiation laboratory is needed for further analysis.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- While the current review reveals no immediate areas requiring urgent attention in terms of research achievements and contributions, it is advisable to continuously monitor emerging trends and challenges in the field of nanobiology.
- It is desirable to develop research on diseases, for example, whether temperature changes are occurring in cancer cells.

Commentary and Recommendations:

- The achievement of publishing 18 research papers in the past five years is indeed commendable, reflecting the lab's active contribution to the field. It is noteworthy that many of these publications have been made by Professor Madoka Suzuki as the corresponding author, a testament to his significant role in this lab's research endeavors. It is also observed that the Harada lab's research, particularly in the area of intracellular temperature sensing, is transitioning smoothly into the Suzuki lab. This transition appears to be a strategic move, leveraging the strengths and expertise of both labs to advance this line of research.

  Looking ahead, there is a keen anticipation for the culmination of the ongoing research projects, especially as Professor Harada approaches retirement. It is hoped that this period will be marked by successful completion of their accumulated research, thereby cementing the lab's legacy and contributing significantly to the advancement of their scientific field.
- By introducing temperature-sensitive fluorescent polymers or nanodiamonds into cells, they have been able to visualize the intracellular temperature. They found that suppressing transcription and translation decreases heat production, and conversely, providing heat increases neurite outgrowth. It would be interesting to explore whether this is due to general increases in all reaction rates or acceleration of specific reactions in neurons. They are expected to apply their technology to other cells.
- I think the laboratory could have more of an impact because of its unique perspective in developing research.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage /

Research Center's programs?

Area(s) that need(s) further attention:

- In the future, it would be beneficial to conduct more collaborative research in connection with the Joint Usage/Research Center. Leveraging the resources and expertise available through the center can enhance the scope and impact of the research, fostering more integrated and innovative scientific inquiries.
- A project to introduce this technology is needed.

Commentary and Recommendations:

- Given the nature of the research, it is anticipated that fluorescence microscopy, a shared resource, is extensively utilized. While there are commendable domestic collaborations in place, expanding these collaborations to the international level would be highly advantageous. International collaborations bring diverse perspectives and expertise, which can significantly enrich research outcomes and lead to breakthroughs in the field.
- The development of basic technology for intracellular temperature measurement and one-cell immune response analysis is being promoted through collaborative research. However, research is conducted between individual laboratories, and the ripple effect on the community is not remarkable. If physiologically significant research targets are found, collaboration with biologists can be widely expected.
- From the current data, I had thought that the needs for this technology did not match the Joint Usage / Research Center's Programs, but this lab is conducting a reasonable number of joint research projects.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- Consultation with an Intellectual Property Officer.

Commentary and Recommendations:

- This laboratory has demonstrated a strong commitment to education by successfully securing and training a considerable number of graduate students. The notable accomplishment of guiding Professor Madoka Suzuki to become an independent researcher further highlights the laboratory's effective role in nurturing the next generation of scientists. This indicates a significant contribution to the field in terms of educational impact and mentorship.

  Additionally, the bilingual organization of the laboratory's website in both English and Japanese is commendable. Therefore, information about the lab is shared well internationally. Since detailed information regarding research funding is missing in this material, no commentary is given for research funding.
- Collaborative research with inside and outside the institute is progressing to expand the scope of research. Students successfully have obtained doctoral degrees. A staff member has been promoted and has become independent.
- This lab also performs well in education duty. There is a lack of explanation regarding intellectual property efforts. Although intellectual property of this technology may be difficult due to the industrial application aspect, it would be better to ensure a system for consultation.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group’s research?

Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- The internal collaboration of this laboratory is commendable and this laboratory has demonstrated an appropriate vision for its future direction.

  As previously mentioned, one of the lab's notable strengths is the development of novel technologies. It is highly recommended that these technologies be further applied to broader biological systems. Doing so could greatly enhance the practical and real-world impact of the laboratory's work. Collaborations, both domestic and international institutions, will be key in achieving this application. Such collaborative efforts can provide new insights, access to diverse expertise, and opportunities to test and refine these technologies in various biological contexts.

  In summary, while the laboratory is well-positioned with its effective internal collaboration and clear future vision, maximizing the application of its novel technologies in biological systems

through collaborative research should be a primary focus. This approach will ensure the laboratory continues to thrive and make significant contributions to the scientific community.

- Dr. Suzuki has become independent, but they have a good collaborative relationship in research and education. They can continue to promote projects focusing on intracellular thermal measurement.
- Since this lab has a unique perspective and approach, it is most important to find a good research partner who can utilize this technology and develop it broadly and deeply for future research directions.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Protein Synthesis and Expression

Name of Reviewers: Hee-Jung Choi, Keiko Shimamoto, Tatsuya Sawasaki

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- The three missions presented by this laboratory align well with the objectives of IPR and are being effectively pursued. These missions represent appropriate and well-defined research goals, demonstrating the lab's commitment to contributing to the scientific objectives of IPR.
- It is enough to promote the research that is underway, without giving any advice.

Commentary and Recommendations:

- Protein production is an important step in structural biology and in vitro biochemistry research, and this laboratory has demonstrated commendable expertise in addressing the challenges associated with protein production. Their proficiency in this area has facilitated significant research into the mechanisms of signaling pathways, showcasing their ability to apply technical know-how to complex biological problems.

  Furthermore, the lab's utilization of protein engineering techniques, particularly the innovative LassoGraft technology, in designing novel protein drugs is noteworthy. This approach not only exemplifies the laboratory's skill in protein engineering but also its potential for making impactful contributions to therapeutic development.
- Three research missions of the Lab, the supply of required proteins, elucidation of the structure and function of complex receptor proteins, and the development of proteins with new functions, are very clear and being vigorously promoted. They should be highly evaluated as cutting-edge and high-level research in the world class.

  The know-how to overcome difficulties in protein synthesis/expression has certainly been accumulated. LassoGraft technology, in which functional peptides obtained with the RaPID system are incorporated into antibodies or other proteins, is being industrially applied as a powerful biomedical strategy of easily adding new functions to antibodies.
- This LAB has three missions as its research pillars: technology development, basic research, and applied research, and they work in tandem to advance research based on very good research management. I hope that the lab will continue to proceed research with this quality, and I am

confident that this will contribute greatly to the advancement of this institute.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- The current review reveals no immediate areas requiring urgent attention in terms of research achievements and contributions.
- I have nothing to advise you, as you have been more than adequate in your perspectives and vision in addressing protein research as well as technology development.

Commentary and Recommendations:

- The research output of this laboratory is commendable, with publications in prestigious journals such as Science Translational Medicine, Nature Chemical Biology, and Nature Communications. This reflects the high quality and impact of the research conducted in their respective fields.
- Through protein making technology, they significantly contribute not only to academia field but also to the general public.
- The contribution of this laboratory in the field of protein life science is very significant. Especially in protein engineering and protein production, the ideas and know-how from this laboratory have been widely spread. This laboratory is an opinion leader in the field.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- The current assessment indicates no immediate areas requiring attention in terms of the group's contribution to the Joint Usage / Research Center.
- I feel that the support system regarding the Joint Usage / Research Center's programs would be even stronger if this laboratory had additional manpower support, such as technical staff and post-doctoral fellows.

Commentary and Recommendations:

- The active involvement of this lab in the institutional activities of the Joint Usage / Research Center is commendable. Notably, this lab has been involved in diverse range of collaborative studies, both domestic and international, further highlighting its commitment to global scientific

engagement and interdisciplinary research.

- A number of high-level collaborative projects are underway.
- The lab is well advanced in its collaborative research with national and international partners, and I can judge that the lab is contributing to the Joint Usage / Research Center's programs to a greater extent than anticipated.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- The current review indicates no immediate areas requiring attention in terms of the group's contribution to education, research funding, information disclosure, and international exchange.
- The status quo is sufficient.

Commentary and Recommendations:

- This laboratory has demonstrated remarkable success in producing outstanding researchers, reflecting its strong commitment to high-quality education and mentorship. The lab's active engagement in providing research guidance to both graduate and undergraduate students is particularly commendable. In terms of funding, the lab has successfully secured sufficient resources to support its research endeavors. This financial stability is crucial for maintaining the lab's research momentum and pursuing innovative projects. The lab's active involvement in numerous international joint research projects is another notable achievement. Such international collaborations broaden the scope and impact of the lab's research, contributing to the global scientific community.
- A large amount of research funding and patents were acquired. Notably, Prof. Takagi, with Prof Suga of the University of Tokyo, founded a venture company. The company is developing biopharmaceuticals in new modalities to solve unmet medical needs, with LassoGraft technology.

This will be one of the successful examples of Osaka University-launched venture, which will attract attentions from general public.

- The educational activities, acquisition of external funds, international exchanges, and disclosure of information to society have all contributed more than enough to date. I hope that you will continue to proceed with these activities for the further progress of the institute.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- As a contributing member of IPR, renowned for its status as a world-class institute in protein life sciences, this laboratory has consistently demonstrated its ability to produce excellent research outputs. The lab's involvement in a wide array of collaborative projects is a testament to its dynamic approach and commitment to scientific advancement. Moreover, the lab's clear and forward-looking vision aligns well with the goals of IPR.
- Research is being conducted at a very high level, and they can be evaluated as a laboratory that can communicate the significance of protein research to the world.
- As mentioned above, this laboratory is outstanding in its current research quality and future research vision. Even with the quality as it is, the laboratory will be able to demonstrate a sufficient presence in the field of protein life science research. As a comment not on this laboratory but on this institute, this institute should make better use of the research resources such as protein engineering and protein expression technologies that this laboratory has, because those technologies that this laboratory has are the foundation of protein research. At present, this institute does not seem to be making good use of them, so I dare to make this comment.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Protein Profiling and Functional Proteomics

Name of Reviewers: Hee-Jung Choi, Keiko Shimamoto, Tatsuya Sawasaki

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- The research goals of this laboratory are well-aligned with the objectives of IPR, demonstrating a clear approach to their scientific inquiries.
- Installing high-spec mass spectrometry machines

Commentary and Recommendations:

- This laboratory has made achievements in the field of protein Mass Spectroscopic analysis. This area is important for advancing our understanding of protein function within the cellular context.
- Conventional LC-MS has become popular in many Labs, but native MS or measurement of post-translationally modification still requires advanced techniques. This Lab has contributed to protein science through its development.
- The research results to date have been highly impactful and industry-leading. However, I have the impression that it has become difficult to develop research that leads the research field because the performance of mass spectrometry machines has become outdated. Since the mass spectrometry machines are very expensive, the positioning of mass spectrometry analysis in IPR should be clarified.
-

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- The current review reveals no immediate areas requiring urgent attention in terms of research achievements and contributions.
- Support system as IPR if it is difficult to purchase mass spectrometry equipment.

Commentary and Recommendations:

- The research output of this laboratory is commendable, with 11 publications as a corresponding author, and 13 invited lectures both domestically and internationally over the last 5 years. This reflects good research conducted in their respective fields.
- Native MS method was applied to capture the complex of enzyme-nucleic acid-metal ion. They captured unstable enzyme reaction intermediates as complexes by mass spectrometry and analyzed the reaction mechanism, which is commendable. Unfortunately, the number of published papers as a corresponding author is not so many for these years because he had few students before his retirement. However, he has contributed to protein identification through collaborative works as an expert in mass spectrometry.
- The Lab has a high previous research record and has reported a number of high impact papers. I consider the activity in the last few years in this Lab to be not high compared to other labs in the Institute currently. This may be due to the fact that the boss is approaching retirement, but essentially it seems to be due to the absence of a clear direction in the utilization of mass spectrometry analysis in this institute.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- It seems necessary to consider the position of mass spectrometry in the Joint Usage / Research Center's Programs.

Commentary and Recommendations:

- This laboratory's longstanding collaboration with the CIGB in Cuba is a testament to its commitment to international scientific partnerships. This collaboration has undoubtedly yielded valuable insights and advancements. However, to further enhance the lab's research scope and impact, it would be beneficial to explore collaborations with a more diverse array of laboratories.
- Contribution to protein identification through the Joint Usage / Research Center's programs as an expert in mass spectrometry for a long time is obvious. It may be necessary to consider taking over the advanced MS technology after Professor Takao's retirement. It would be desirable to establish an MS department in the Research Center for Next-generation Protein Sciences and invite a new PI.
- In the Joint Usage / Research Center's Programs, the analysis of protein modification identification is active, but the studies presented were not the most recent. Therefore, it was not possible to understand the activities of the past 5 years.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- I think it is recognized as a highly regarded research from abroad, given the large number of students from China. I think that this Lab needs to be promoted to other Asian countries as well.

Commentary and Recommendations:

- more information needed for comment.
- Although students who belonged to the Lab were small, international students successfully received Ph.D. They have also won awards for their conference presentations. Thus, educational activities have been appropriate. It is regrettable that few grants have been awarded.
- The education through research is being done, as the results of research in which students are the first authors can be adequately confirmed.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- As the PI approaches retirement in March, it seems that the lab's recent research output may not be as robust as that of other labs. However, it is important to acknowledge the lab's significant achievements over the years, particularly in the field of mass spectrometry (MS). The lab has a commendable track record of utilizing MS to produce excellent research results. This legacy of

high-quality research should not be overshadowed by the natural decrease in output typically associated with the transition period leading up to retirement. The lab's contributions to the field, especially through its MS-based studies, have laid a strong foundation for future research and have significantly advanced our understanding in this area. To ensure the continuation of the lab's strong legacy in this field, it is hoped that a younger MS expert will be hired.

- Although this is not the problem with this lab only, measures need to be taken to avoid a decline in activity due to a lack of students in the lab before professor's retirement. This problem is particularly acute at the institute, because only a few students come from the faculty. Is it possible that IPR supports to hire PD or temporary staff?
  As mentioned in other items, mass spectrometry is essential for identification of modified proteins and spatio-temporal analysis. We would like to recommend the addition of the MS facility (including PI level staff) to the Joint Usage / Research Center.
- Although this lab has made several important biological discoveries using mass spectrometry analysis, I cannot judge them due to a deficiency in explanation of their commitment to intellectual property. Also, since the lab is closing this March, it is not constructive to discuss the future of this Lab. The most important thing is for this institute to make a vision for the future of instrumentation for mass spectrometry analysis.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Supramolecular Crystallography

Name of Reviewers: Yuriko YAMAGATA, Bong-Jin Lee, Takeshi MURATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- This group has achieved world-class results in the field of supramolecular crystallography, determined the structures of many biologically important proteins, and contributed to the advancement of research in that field. Furthermore, the group has operated the Spring-8 beamline and supported the development of protein crystallography in Japan.
- A new beamline (BL44XU) was constructed to enable the structural analysis of supramolecular complexes, and this has led to the successful elucidation of many important and complex protein structures.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- This group has achieved world-class results in the field of supramolecular crystallography, determined the structures of many biologically important proteins, and contributed to the advancement of research in that field. Furthermore, the group has operated the Spring-8 beamline and supported the development of protein crystallography in Japan. (Same as above comments.)
- In addition to constructing beamlines, development of production technologies for complex and challenging protein complexes has also been achieved, enabling the successful structural analysis of many membrane proteins.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage /

Research Center's programs?

Area(s) that need(s) further attention:

- Based on the Spring-8 II project, the establishment of the IPR beamline should be considered.

Commentary and Recommendations:

- They have been involved in the management, operation, and user support of BL44XU for many years.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- Large budgets continue to be obtained. The beamline has been well promoted.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- This group has led protein crystallography in Japan.
- This lab showed good activities in all areas. This lab has shown good competitiveness in the protein science field. But some activity should be pointed out for the future development of this lab. Output (publications) from the IPR Beamline had increased until 2020. But, during 2021~2023, publications were decreased comparing with 2020 publications. PDB deposition was

also decreased during this period. The reason of this decrease should be analyzed. Also, more industry-academia collaboration is needed

- Conducting education for young researchers and students in IPR, which encompasses structural analysis technologies, is crucial for producing researchers who will carry the future of structural biology in Japan. Therefore, it is of great importance for IPR to construct and operate the latest and most advanced X-ray beamlines. Even after your retirement, it is hoped that the unique BL44XU beamline will continue to be developed and operated sustainably, fostering outstanding beamline scientists and engineers.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Protein Crystallography

Name of Reviewers: Yuriko YAMAGATA, Bong-Jin Lee, Takeshi MURATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- Structure and function relationship at the atomic level in various types of photosynthesis.

Commentary and Recommendations:

- Integrated/hybrid structural research including neutron crystallography is amazing.
- Research focusing on photosynthetic membrane protein complexes and dyneins has outlined specific goals, such as elucidating the mechanisms of energy conversion and motility.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- This group can advance its current research.
- Using correlational structural analysis, detailed mechanisms of photosynthesis-related proteins have been elucidated. Development of technologies such as MicroED is also being pursued.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- Enhancing PDBj

Commentary and Recommendations:

- Not only managing the Protein Data Bank Japan (PDBj), but also overseeing the Cambridge Crystallographic Data Centre (CCDC)

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- Prof. Kurisu has obtained the Grant-in-Aid for Transformative Research Areas (A) as a head investigator.
- Large budgets continue to be obtained.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- This lab showed good activities in all areas. This lab has shown good competitiveness in the protein science field. But some activity should be pointed out for the future development of this lab as follows: More industry-academia collaboration is needed.
- Managing the PDBj in IPR is a pride for Japan. While it may be challenging, it would be greatly appreciated if the management of the PDBj could continue in IPR.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Cryo EM Structural Biology

Name of Reviewers: Yuriko YAMAGATA, Bong-Jin Lee, Takeshi MURATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- This group has determined the structures of highly impact protein complexes and these results will contribute to the treatments of infectious diseases in the future.
- I would have liked to see a vision for the planned main focus on research into olfactory receptors.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- I think it is better that this group choose the target protein complexes newly in addition to flagella motor of salmonella.

Commentary and Recommendations:

- Outstanding results have been achieved in structural studies of flagella and ADE using cryo-EM.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- This group has determined the structures of protein complexes using cryo-EM, in response to requests from many researchers. And also, the development of cryo-EM technique is ongoing.
- Vigorously advancing the management, operation, and support of cryo-EM.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- Cryo-EM workshops were organized for research including Company's ones.
- Contributing to the development of the field and the education of students by organizing cryo-EM workshops.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- The laboratory is starting up smoothly, especially cryo-EM equipment has been installed, and the number of students is increasing, so I can expect the laboratory to develop in the future.
- Cryo-EM is very power-pool and important tool in protein science research field. This lab published many papers in high impact factor journals. Recently, International collaboration is important for the evaluation of university or institute. I recommend more international collaboration to this group because this group has very good cryo-EM facilities. Also, more industry collaboration and industry grants are needed for this group. Because IPR does not have the most high-resolution EM. I recommend that IPR will try to purchase more advanced new high-resolution EM.
- Not only the development of grid preparation techniques but also the automation and

acceleration of analysis, as well as the development of new analytical methods, are anticipated to significantly advance the field of structural biology. Structural analysis of olfactory receptors is also expected. Conducting education for young researchers and students in IPR, which encompasses structural analysis technologies, is crucial for producing researchers who will shape the future of structural biology in Japan. Therefore, it is very important for IPR to be equipped with the latest and most advanced cryo-electron microscopes to fulfill this role. Please make every effort to achieve this.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Ultra-High Magnetic Field NMR Spectroscopy

Name of Reviewers: Yuriko YAMAGATA, Bong-Jin Lee, Takeshi MURATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- They are developing new methods and labeling techniques for solution NMR to reduce the limitations on molecular weight and sensitivity, aiming to enhance the value creation of NMR.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- They have successfully performed structural analysis on large proteins using the RO-SAIL method.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- They are continuously providing operational and management support for large-scale NMR facilities.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- Continuously promote the utility of liquid NMR and please make efforts to secure large-scale funding. This will likely attract students synergistically as well.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- High-field NMR shows very important role in the NMR field and will be more developed in the future. This NMR technique can broaden application of the bioscience research. Fragment-based drug discovery by NMR can give a useful information for drug discovery of pharmaceutical company. This lab. has good academia-industry collaboration. The research topics are relatively large considering the number of lab members. Therefore, the number of lab. members, such as student numbers, should be increased. Although JMR is a good Journal, I recommend this lab members try to submit their research result to high impact journal.
- Conducting education for young researchers and students in IPR, which encompasses structural analysis technologies, is crucial for producing researchers who will carry the future of structural biology in Japan. It is important to be installed the latest and most advanced 1.2GHz NMR in IPR, aiming to nurture researchers who will lead future NMR studies.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Biomolecular Analysis

Name of Reviewers: Yuriko YAMAGATA, Bong-Jin Lee, Takeshi MURATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- They actively provide support for techniques like protein sequencing and mass spectrometry.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- Biomolecular analysis tool, such as MASS can be used to discover biomarker. Therefore, this lab. can have a good the academia-industry collaboration. Because this lab. does not have students for research, it is needed to increase student numbers in order to broaden research topics.
  Although JMR is a good Journal, I recommend this lab members try to submit their research result to high impact journal.
- Conducting education for young researchers and students in IPR, which encompasses structural analysis technologies, is crucial for producing researchers who will carry the future of structural biology in Japan. It is important to be installed the latest and most advanced mass spectrometry in IPR, aiming to nurture researchers who will lead structural studies.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Molecular Biophysics

Name of Reviewers: Yuriko YAMAGATA, Bong-Jin Lee, Takeshi MURATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- This group is highly commendable for its development of solid-state NMR, In Cell NMR, and Dynamic Nuclear Polarization (DNP) technique that will be very useful for future advances in structural biology.
- They are advancing technology development towards the ambitious goal of elucidating the states of membrane proteins and amyloids within cells using solid-state NMR.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- They have developed a helium-temperature Dynamic Nuclear Polarization (DNP) system and successfully increased its sensitivity by 4000 times.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- Please continue to promote solid-state NMR, aiming to expand its user base.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- Continuously promote the utility of solid-state NMR and please make efforts to secure large-scale funding. This will synergistically attract students as well.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- Solid-state NMR plays very important role in the NMR field and will be more developed in the future. DNP technique can broaden academic application in the bioscience research. This lab. has good academia-industry collaboration and industry grant. The research topics are relatively large considering the number of lab members. Therefore, the number of lab members, such as student numbers, should be increased. Although JMR is a good Journal, I recommend the lab members try to submit their research results to high impact journal.
- Conducting education for young researchers and students in IPR, which encompasses structural analysis technologies, is crucial for producing researchers who will carry the future of structural biology in Japan. It is important to develop and operate the latest and most advanced solid-state NMR and DNP devices in IPR, and to train researchers who are proficient in using next-generation solid-state NMR.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Molecular and Developmental Biology

Name of Reviewers: Jun Suzuki, Sén TAKEDA, Tatsumi HIRATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- Structure analysis of identified proteins may help further characterization of their regulation mechanisms.

Commentary and Recommendations:

- Prof. Furukawa's research on development of retina and brain has been developed through identification of core transcriptional factors to determine the cell types. By combining their own research tools (mice genetics) with single cell RNAseq analysis, their research has been further developed. In some cases, even ES cells are used to see development of neurons.
- Each research group sets unique goals, all of which directs towards the fundamental questions in biology. However, the topics are very diversified covering from molecular level to a higher brain function and behaviour. **Dr. Furukawa**'s lab investigates neural function by making the most of retina, which is one of the best systems to cover broad topics of neuroscience from development, differentiation to special sensory function. Technically, his topics cover neuronal differentiation, synaptic formation, visual function revealed by electrophysiology, and protein transport with special references to the cilia of photoreceptors. Taking advantages of single cell analysis of transcriptome, he successfully identified genes critical for determining the cell fate into photoreceptors or amacrine cells. From another standpoint, knockout of retina-specific gene brought about abnormal visual perception. Taking the facts into account that neurodevelopmental disorders such as autism spectrum disorders (ASD) show occasionally hypersensitive to sensory inputs, Dr. Furukawa's viewpoint has potential to uncover the mechanism of ASD through multidisciplinary strategy. Moreover, investigation on the connecting cilium of photoreceptor reveals the molecular mechanism of ciliary transport, which would be a target of drug discovery to treat retinal degeneration. His team constantly publishes high quality papers supported by many graduate students, who are the source of younger scientists leaving the nest to become full-fledged expert. Though it is a personal interest, focusing on the retinal ganglion cells may pave the way into clarification of pathogenesis for

glaucoma.

- This group constantly publishes high-quality work in various journals using mouse models. While their activities appear somewhat wide-ranging, it is likely they will converge towards the focused research goal in the near future.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- If protein function can be categorized at molecular level, cellular level, and at animal level, Prof Furukawa's research is strong and more focused on at cellular and animal levels. Understanding at molecular level has a space to be developed with collaboration.

Commentary and Recommendations:

- Currently, it is easier to know comprehensively which genes or protein are expressed at particular stages or cell types during development. Important points are to clarify how these proteins function at cellular level. In this meaning, Prof. Furukawa's group has a strategy to utilize genetic approaches and clearly show their role on development in detailed analysis.
- As stated in the previous section, most of the labs significantly contribute to the advancement of protein research, which can be evaluated by the list of publication, acquisition of grants and international collaborations. Dr. Furukawa's alumni include quite a few people who joined industrial fields. This will expedite interdisciplinary research as well as expand the scopes of research significantly. While my general remarks are excellent, this reviewer thinks the score fluctuates depending on the team being evaluated.
- This face-to-face meeting revealed an exciting fact that this group is actively pursuing in-house collaborations with protein science labs. Their published successes alone would not hint at these hidden efforts and experimentation, which might have underscored the lab's activities. What I mean is that some biologists are genuinely open to exploring protein science collaborations. It is vital for IPR to actively cultivate an environment that fosters these seeds of collaboration. For that, efficient communication among labs will be needed. I also feel that the presentation style can be adjusted to understand each other.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- Because Prof. Furukawa is distinct in the field of retina development, it is encouraged to show and share his tools with scientists in the field, but currently the tools are not easier to see from outside. By having a platform (that might be named as e.g. EyePR, Eye Protein Research Tools) in IPR, tools are easier to be found and accessed.

Commentary and Recommendations:

- Because the group's strength is mouse genetics, mice tools are shared well with the research community.
- Since this division is composed of labs different from those providing IPR with basic analytical techniques, informatics or high-end facilities, contribution to joint usage/research seems to be hard to appreciate. However, 3 departments out of 4 included a power point slide illustrating their involvement in this subject. While some of those activities would be preferably classified as collaborations with external facilities, rather than joint usage/research center having connotation of more assisting or rear-guard position, this reviewer finds the overall activities are accepted as a favorable factor contributing to the reputation of IPR. This reviewer recommends all the lab head to include materials that correspond precisely to the evaluation axis preset by IPR.
- This group has contributed Joint Usage / Research Center's programs. They organize IPR seminars, and provide genetically modified mice globally.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- Although homepage is well designed, unfortunately quality of some member photos is quite low. It is recommended to replace them with new one. Taking photo outside in sunny days will

show their face expression brighter.

Commentary and Recommendations:

- The group includes two female staff scientists (International and domestic Assistant professors) and international students, thus contributes to the diversity of the institute. Homepage is well organized and appealing. CREST and Moonshot should be also recognized.
- Generally speaking, this reviewer finds that each department fosters young researchers from all categories and is up to the level of expectations from IPR and Osaka University. When it comes to the acquisition of research funding, some departments do not explicitly state the exact name of grant they have acquired. As far as this reviewer concerned, Dr. Furukawa's and Dr. Shinohara's group must be financially prosperous by judging from their activities and achievements, though there is no description on this subject at all. Information disclosure and social relationship appear to be on average for all the labs. For international exchange, all labs actively collaborate with foreign countries represented by the number of foreign students.
- Many students have been educated in this lab.

5. Comprehensive Evaluation

[Evaluation Perspective]

A. Are internal collaboration and/or IPR framework nicely utilized in the group's research?
B. Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- Prof. Furukawa's research is distinct enough in the research field. Internal collaboration seems like not much for this group, but at the same time, internal collaboration happens when each interest matches between different groups. It should not be forced by the institute. If it is forced, it becomes service, but not research collaboration. I rather suggest having a framework to set up some small goals to be achieved by the institute. For instance, "Understand and control photo system". The plant chloroplasts use light to generate a metabolite while the eye system use light to see outside. Light can be also used to control protein functions such as PA-GFP and channel rhodopsin. In such framework, scientists from different fields or groups exchange ideas freely, and this may be more important to facilitate science. I can say, inspiration-based collaboration.
- Concerning item A, this reviewer's general impression is that the division seems to be rather independent from other divisions as applied biology. According to Dr. Furukawa's explanation, he was also eager to have a collaboration with other divisions, while joint usage was not

realized due to discrepancies in mutual research interests. Nowadays, it is often said that we confront deep valley or obstacles among each highly developed expertise, and they prevent us from understanding each specialty in detail and make us blind to the field outside one's expertise. To overcome this and facilitate collaborations, university research administrators (URA), who liaise with different specialists to achieve effective collaboration, should be placed properly as shared staff, though this reviewer is familiar with the issue of budget in national universities. However, URA is able to set a framework of collaboration between division of integrated protein science and other division focusing on protein analysis, even if an initiative was not taken by the leaders of integrated protein science. Regarding the item B, most of the departments have their own future perspectives that can be evaluated as excellent.

- This group's excellence in their own field is evident. Furthermore, their proactive search for protein science collaborations elevates their standing. A successful collaboration will hold immense potential for IPR.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Genome and Chromosome Functions

Name of Reviewers: Jun Suzuki, Sén TAKEDA, Tatsumi HIRATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- Research area is important to be explored, but also classic. Integrating new technologies such as CRISPR screening and proximity biotin-labeling may facilitate Prof Shinohara's research by identifying core components of RAD51.

Commentary and Recommendations:

- Since Prof. Shinohara started to work by cloning cDNA of RAD51, an important gene for homologous recombination, he has intensively worked on RAD51 to understand molecular mechanisms of the protein on homologous recombination. Research done by this group has been proceeded well and productivity is enough. Also Prof. Shinohara collaborates with IPR members to determine protein structure.
- Each research group sets unique goals, all of which directs towards the fundamental questions in biology. However, the topics are very diversified covering from molecular level to a higher brain function and behaviour. **Dr. Shinohara**'s project sets genome stability as a main topic of research, with an emphasis on the homologous recombination. He is a leading scientist in genome stability and contributed greatly to this field after he discovered Rad51, a crucial molecule in recombination over 30 years ago. Based on this molecule, his research has been developed to have a link with various associated proteins, whose function is involved in immunity and reproductive system. Presentation of unpublished data pertaining to these molecules were exciting one, making us convinced that his research is coherent for many years in terms of protein molecule-based study. This will lead to the elucidation of aetiology of female infertility. This reviewer would like to emphasize his proactive attitude to have in-house collaborations with other departments in IPR. For example, with a participation of Prof. Nakagawa and Prof. Kato, Dr. Shinohara has successfully submitted lines of evidence that dynamic conformational changes are responsible for carrying out precisely homologous recombination. This reviewer finds him as a role model for facilitating the in-house collaborations. Regarding the publication and grant acquisition, his group attains great

achievements during past 5 years, all of which should be highly appreciated as a great contributor to IPR. This reviewer would like to know about the appointments of his lab alumni to any academic position, after leaving his lab.

- This group has constantly published solid papers in scientific journals and their research goal is crystal clear. It is also obvious that this group promotes diversity in IPR.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- Through deep understanding of homologous recombination, it will be great if new technology to artificially control the process appears.

Commentary and Recommendations:

- Current trend is to understand the biological phenomenon as network by comprehensive analysis. On the other hand, understanding mechanisms of specific biological process such as homologous recombination is also important. In this meaning, the group has advanced the research area.
- As stated in the previous section, most of the labs significantly contribute to the advancement of protein research, which can be evaluated by the list of publication, acquisition of grants and international collaborations. Dr. Shinohara and Hikida had also an interface with clinical and pharmaceutical area, starting from their target molecules. While my general remarks are excellent, this reviewer thinks the score fluctuates depending on the team being evaluated.
- I am particularly impressed by this group's strong drive to integrate protein science into their research. Given the natural synergy between this research field and structural biology, collaborative efforts within IPR hold immense potential for impactful results. While DNA research collaborations with structural biology often yield high-impact publications, success is not guaranteed. Nonetheless, the collaboration between this group's activities and protein science makes them prime candidates for investment. Successful in-house collaborations could deliver groundbreaking, globally impactful findings, solidifying IPR's leadership. Therefore, I strongly advocate for IPR to develop support mechanisms for fostering such internal collaborations.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage /

Research Center's programs?

Area(s) that need(s) further attention:

- One of the ways to contribute to the protein life science communities is to share the research tools and knowledge for homologous recombination.

Commentary and Recommendations:

- Homologous recombination is an important research area where a lot of senior researchers have retired. In this meaning, Prof. Shinohara is expected to explore the field by conducting cutting-edge science and to contribute to the society.
- Since this division is composed of labs different from those providing IPR with basic analytical techniques, informatics or high-end facilities, contribution to joint usage/research seems to be hard to appreciate. However, 3 departments out of 4 included a power point slide illustrating their involvement in this subject. While some of those activities would be preferably classified as collaborations with external facilities, rather than joint usage/research center having connotation of more assisting or rear-guard position, this reviewer finds the overall activities are accepted as a favorable factor contributing to the reputation of IPR. The degree of contribution varies with each department, while there was no explicit statement from Laboratory of Genome-Chromosome Function. However, taking the multidirectional contributions of this lab into account, and judging from the on-site presentation during the external review, this reviewer assumes its active participation in Joint Usage/Research Center's program. This reviewer recommends all the lab head to include materials that correspond precisely to the evaluation axis preset by IPR.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- In the website, it is recommended to put photos so that students/researchers outside can have an image or atmosphere of laboratory and research life in Japan.

Commentary and Recommendations:

- The group includes two female staff scientists (Associate professor and postdoc) and many international students, thus contributes to the diversity of the institute.
- Generally speaking, this reviewer finds that each department fosters young researchers from all categories and is up to the level of expectations from IPR and Osaka University. When it comes to the acquisition of research funding, some departments do not explicitly state the exact name of grant they have acquired. As far as this reviewer concerned, Dr, Furukawa's and Dr. Shinohara's group must be financially prosperous by judging from their activities and achievements, though there is no description on this subject at all. Information disclosure and social relationship appear to be on average for all the labs. For international exchange, all labs actively collaborate with foreign countries represented by the number of foreign students.
- Fostering foreign and female researchers is highly appreciated.

5. Comprehensive Evaluation

[Evaluation Perspective]

A. Are internal collaboration and/or IPR framework nicely utilized in the group's research?
B. Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- The group has collaborated with structural biologist in the institute to know the protein structure. In this meaning, internal collaboration is ongoing well. I expect that Prof. Shinohara develops his curiosity-driven research on homologous recombination and greatly impacts on the research field.
- Concerning item A, this reviewer's general impression is that the division seems to be rather independent from other division as applied biology except for Dr. Shinohara's team. His collaborations with groups for protein structure substantiate the joint usage/research center's policy as mentioned above, and therefore is judged as excellent. Nowadays, it is often said that we confront deep valley or obstacles among each highly developed expertise, and they prevent us from understanding each specialty in detail and make us blind to the field outside one's expertise. To overcome this and facilitate collaborations, university research administrators (URA), who liaise with different specialists to achieve effective collaboration, should be placed

properly as shared staff, though this reviewer is familiar with the issue of budget in national universities. However, URA is able to set a framework of collaboration between division of integrated protein science and other division focusing on protein analysis, even if an initiative was not taken by the leaders of integrated protein science. Regarding the item B, most of the department have their own future perspectives that can be evaluated as excellent.

- I hope to see a successful collaboration of genome DNA research and protein science in the near future.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Advanced Brain Functions

Name of Reviewers: Jun SUZUKI, Sén TAKEDA, Tatsumi HIRATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- Compared to neural circuit study, molecular study seems like not much done.

Commentary and Recommendations:

- Prof. Hikida's group is strong in the research field of decision making. Especially, at neural circuit level, Prof. Hikida's group has explored how decision is made through dopamine receptors at thalamus when mistakes happened. This research is quite original.
- Each research group sets unique goals, all of which directs towards the fundamental questions in biology. However, the topics are very diversified covering from molecular level to a higher brain function and behaviour. While **Dr. Hikida's** selection of research topic is very intriguing in terms of neuroscience, especially higher cognitive function of the brain, it appears to lack an interface with IPR's other laboratories and departments. On the other hand, his topic attracts many young scientists as his research direction is one of the hottest topics in basal ganglia function of broad meaning, especially in terms of neural circuit for the reward system. He set a goal of research to dissect the molecular mechanism of psychiatric disorders such as addiction, schizophrenia and so on. Taking advantages of cutting- edge techniques in molecular biology and optogenetics, his team is going to study a neural circuit for integrating various sensory modality. This reviewer find that the setting of his research goal directs towards the elucidation of the decision-making process mediated by various sensory inputs, just being similar to the somatic marker hypothesis proposed by Antonio R. Damasio, while the approaches taken by Dr. Hikida are original ones. On one hand, his study opens a new avenue in brain function research. On the other hand, it may be important to think about the strategy how to weave his team into IPR's framework of research smoothly.
- This group has published research papers constantly well and received a good track record of obtaining grants. Therefore, the research goal and topic seem to be quite appropriate as an individual lab. At the same time, I feel that it is possible that this group steers a little more toward integration with protein science in collaboration with other labs. Such a research focus could be

greatly beneficial for this division's long-term success.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- Dopamine signaling has been studied extensively in the world and structural analysis has been performed. So, rather, Prof. Hikida may be able to seek the space for protein study to generate new tools to control neuronal function through designing reporter proteins/systems.

Commentary and Recommendations:

- Proteins function in cells, 2. Cells function in tissues, and 3. Tissues function in individual (animal). Prof. Hikida's research is strong at tissue level, especially how dopamine receptors regulate behaviors.
- As stated in the previous section, most of the labs significantly contribute to the advancement of protein research, which can be evaluated by the list of publication, acquisition of grants and international collaborations. Dr. Furukawa's alumni include quite a few people who joined industrial fields. This will expedite interdisciplinary research as well as expand the scopes of research significantly. From another standpoint, both Dr. Shinohara and Hikida had also an interface with clinical and pharmaceutical area, starting from their target molecules. While my general remarks are excellent, this reviewer thinks the score fluctuates depending on the team being evaluated.
- I understand that it is not easy that this research field combines with protein science. However, there are many interesting questions that can be solved by protein science, and this group can provide these questions in more appealing way to other IPR members. **Effective communication with other IPR members**, highlighting how protein science could answer this group's key questions, can pave the way for fruitful collaborations within the institute. The current situation, though productive, may miss opportunities for greater impact. **Encouraging exploration of collaborative avenues with protein science experts, even without immediate collaboration,** should foster interdisciplinary understanding each other.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- Commentary and Recommendations: It is not clear how Prof. Hikida contributes to Joint Usage without oral presentation: e.g. tool, knowledge, or mice sharing.

Commentary and Recommendations:

- Prof. Hikida seems like contributing to the protein life science through Joint Usage in terms of numbers of collaboration.
- Since this division is composed of labs different from those providing IPR with basic analytical techniques, informatics or high-end facilities, contribution to joint usage/research seems to be hard to appreciate. However, 3 departments out of 4 included a power point slide illustrating their involvement in this subject. While some of those activities would be preferably classified as collaborations with external facilities, rather than joint usage/research center having connotation of more assisting or rear-guard position, this reviewer finds the overall activities are accepted as a favorable factor contributing to the reputation of IPR. The degree of contribution varies with each department, while there was no explicit statement from Laboratory of Genome-Chromosome Function. However, taking the multidirectional contributions of this lab into account, and judging from the on-site presentation during the external review, this reviewer assumes its active participation in Joint Usage/Research Center's program. This reviewer recommends all the lab head to include materials that correspond precisely to the evaluation axis preset by IPR.
- This group contributes to collaborations with people outside IPR and gives IPR seminars frequently. These activities can be regarded as institutional activities of the Joint Usage/ Research Center.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- Without availability in web site, it is not easy to judge.

Commentary and Recommendations:

- Prof. Hikida seems like obtaining enough budgets from different funding agency such as JSPS, AMED, and private foundations. Also contributing the diversity by hiring an international Assistant professor.
- Generally speaking, this reviewer finds that each department foster young researchers from all categories and is up to the level of expectations from IPR and Osaka University. When it comes to the acquisition of research funding, some departments do not explicitly state the exact name of grant they have acquired. Information disclosure and social relationship appear to be on average for all the labs. For international exchange, all labs actively collaborate with foreign countries represented by the number of foreign students.
- There seems to be many students in the lab. I am actually surprised to hear that the PI comes to the lab only once a week to manage the lab activities. It may be efficient but not the best way to run the lab. I hope that the lab will return back to normal operation soon.

5. Comprehensive Evaluation

[Evaluation Perspective]

A. Are internal collaboration and/or IPR framework nicely utilized in the group's research?
B. Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- As you know, protein functions in animal. In this meaning, having Prof. Hikida in the institute is meaningful. It is because protein scientists often see only proteins but not to see animals. On the other hand, animal scientists often see only animals but not see proteins. There is often a big gap in these two research fields. Considering protein aggregation, both scientists can easily work together because protein aggregation is process for protein assembly and aggregated proteins control cell/tissue behaviors in animals. In the case of Prof Hikida's research, the institutional small goal might be "Understand and control photo system". Channel rhodopsin in can control brain function and GFP-reporter system can visualize neuronal activity. Using brain as an output, cross-boundary collaboration might be possible.
- Concerning item A, this reviewer's general impression is that the division seems to be rather independent from other division as applied biology. Nowadays, it is often said that we confront deep valley or obstacles among each highly developed expertise, and they prevent us from

understanding each specialty in detail and make us blind to the field outside one's expertise. To overcome this and facilitate collaborations, university research administrators (URA), who liaise with different specialists to achieve effective collaboration, should be placed properly as shared staff, though this reviewer is familiar with the issue of budget in national universities. However, URA is able to set a framework of collaboration between division of integrated protein science and other division focusing on protein analysis, even if an initiative was not taken by the leaders of integrated protein science. Regarding the item B, most of the department have their own future perspectives that can be evaluated as excellent.

- Because the homepage is closed and the ResearchMap is not updated, evaluating the lab activities solely based on the submitted PowerPoint file was very challenging.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Organelle Biology

Name of Reviewers: Jun SUZUKI, Sén TAKEDA, Tatsumi HIRATA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- Prof. Nakai's work is mainly about protein complexes for protein import. This kind of research will have more impact on research fields with structural analysis.

Commentary and Recommendations:

- Mainly with graduate students without professional researchers, the group's achievement is enough, I think. Especially, Prof. Nakai has explored the field of protein import into chloroplast by identifying new proteins.
- Each research group sets unique goals, all of which directs towards the fundamental questions in biology. However, the topics are very diversified covering from molecular level to a higher brain function and behaviour. First, plant biology by Dr. Nakai is a kind of showcase of IPR's that has a unique position and policy in protein research field as his research focuses on plant cells, while most of the research topics in IPR and other institutions are usually animals. Since his group is rather small compared to others, explicit research goal is somewhat restricted, 'Elucidation of protein transport to chloroplast and their evolutionary history'. The topic appears to be an authentic protein research bridging protein function to structural biology, which has potential to accelerate in-house collaborations. However, while his group publishes high-quality papers, the number of publications is relatively low, especially in recent years. Although this reviewer does not know the details of his team as there was no on-site presentation by himself, I dare to point out that more achievements are required to be qualified enough as a member of IPR.
- I find that this group is active in research; articles have been published in top journals lately after a little fruitless period of time. Their research seems to be appreciated globally in scientific community. I am surprised to know that this group is run by only one faculty member.

2. Research achievements and resultant contributions to specific research area(s) in protein life

science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Area(s) that need(s) further attention:

- Protein import is a classical field of research and therefore it is hard to know what the missing piece or big question in the field is, without oral presentation.
- Laboratory for Organelle Biology

Commentary and Recommendations:

- Prof. Nakai seems like exploring the filed by identifying components of the protein import complex in chloroplasts.
- As stated in the previous section, most of the labs significantly contribute to the advancement of protein research, which can be evaluated by the list of publication, acquisition of grants and international collaborations. Regarding Dr. Nakai's team, this reviewer could not find out clear future direction of study at all. This should have been explicitly stated in the documents delivered before the review round. While my general remarks are excellent, this reviewer thinks the score fluctuates depending on the team being evaluated.
- I cannot identify current activities explicitly combining with protein science. Because this research field and protein science are a very good match, exploring avenues for such collaboration could be highly beneficial for both.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Area(s) that need(s) further attention:

- It is difficult to know what kind of Joint usage (material or knowledge sharing) was conducted without oral presentation.

Commentary and Recommendations:

- At least, outcome for research activity is apparent/obvious by judging from publication in the group.
- Since this division is composed of labs different from those providing IPR with basic analytical techniques, informatics or high-end facilities, contribution to joint usage/research seems to be hard to appreciate. However, 3 departments out of 4 included a power point slide illustrating their involvement in this subject. While some of those activities would be preferably classified as collaborations with external facilities, rather than joint usage/research center having

connotation of more assisting or rear-guard position, this reviewer finds the overall activities are accepted as a favorable factor contributing to the reputation of IPR. The degree of contribution varies with each department. This reviewer recommends all the lab head to include materials that correspond precisely to the evaluation axis preset by IPR.

- I cannot find contribution of this group through the Joint Usage / Research Center's programs.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Area(s) that need(s) further attention:

- Blog is a nice idea to communicate with people including students from outside, but currently available only in Japanese.
- Laboratory for Organelle Biology

Commentary and Recommendations:

- Blog is a nice idea to communicate with people from outside.
- Generally speaking, this reviewer finds that each department foster young researchers from all categories and is up to the level of expectations from IPR and Osaka University. When it comes to the acquisition of research funding, some departments do not explicitly state the exact name of grant they have acquired. However, it is hard to judge whether Dr. Nakai's lab is funded by external sources. This reviewer does not take it for granted that research funding is more important than achievements, sustainability for basic research would be guaranteed by constant fundings. Moreover, a source from external funding supports IPR's activity. In this meaning, this reviewer is rather curious about the financial status of Dr. Nakai's lab. Information disclosure and social relationship appear to be on average for all the labs. For international exchange, all labs actively collaborate with foreign countries represented by the number of foreign students.

- The number of students in the lab has increased lately. If the papers are published by students, education effort of young researchers can be more highly recognized.

5. Comprehensive Evaluation

[Evaluation Perspective]

A. Are internal collaboration and/or IPR framework nicely utilized in the group's research?
B. Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- Publication is enough in this smaller group consisting of only PIs, technical staff, and students. Research focus on protein complex involved in protein import is clear, and in this topic, internal collaboration in structural analysis seems like adequate in the future. However, as I described previously in Prof. Furukawa's part, it happens when two teams are interested in the project. Without oral presentation and Q&A, it is not easy to evaluate as excellent in total.
- Concerning item A, this reviewer's general impression is that the division seems to be rather independent from other division as applied biology. Nowadays, it is often said that we confront deep valley or obstacles among each highly developed expertise, and they prevent us from understanding each specialty in detail and make us blind to the field outside one's expertise. To overcome this and facilitate collaborations, university research administrators (URA), who liaise with different specialists to achieve effective collaboration, should be placed properly as shared staff, though this reviewer is familiar with the issue of budget in national universities. However, URA is able to set a framework of collaboration between division of integrated protein science and other division focusing on protein analysis, even if an initiative was not taken by the leaders of integrated protein science. Regarding the item B, most of the department have their own future perspectives that can be evaluated as excellent except for Laboratory for Organelle Biology.
- The lack of face-to face meeting made a comprehensive evaluation challenging. Despite such limitation, this group's recent publications show a commendable level of activity.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Cell Systems

Name of Reviewers: Kenta NAKAI, Chandra VERMA, Shoji TAKADA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Area(s) that need(s) further attention:

- Integration with the structural models.

Commentary and Recommendations:

- This group is exploring new fields of protein research. I like it.
- Excellent goal to integrate information at the cellular level. The PI is certainly excellent and qualified to continue making significant contributions in the field of systems biological approach to cell fate decisions. This is a world leading effort. PI is exploring a novel extension to the work: to use her models to report on post-translational modifications in the cell which will be a major contribution to the field and complement the in-cellulo experimental methods being developed. Indeed experimentally it is difficult to get time resolved data which the PIs systems approach of mathematical modelling of signalling networks should be able to report on and this will a significant advance in understanding intracellular biomolecular dynamics. Absolutely world class as evident from high impact publications. In addition, the NLP based modelling is bound to break new boundaries.
- The integrated approach of system biology to cell signaling in Okada lab is extremely impressive.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- Relatively few ‘big’ works in the last few years(?)
- The mathematical modelling of cell fate, signalling networks, NLP based models, use of ML/AI methods etc are world class efforts and clearly are opening up new vistas not only in fundamental understanding of intracellular landscapes, but also opens up the route to discovering new biology,

new regulatory mechanisms and clearly has already translated into areas as diverse as dentistry, skin, drug targets and patient stratification. Has significant number of research publications in international peer reviewed journals with high impact. This has resulted in a wide variety of collaborations – local and international and in a diverse range of topics reflecting the significance of the fundamental and necessary nature of the work of the PI.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- I think this group is a typical model for desired interdisciplinary research in the center.
- A significant number of activities including domestic and international collaborations, visiting researchers and exchanges etc has emerged as a result of the PI's work.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- Accepting many international students.
- As for the educational activities, excellent team has been assembled – faculty and graduate students and also an undergraduate student. In addition, has a diverse group of collaborators across the world in applying these fundamental methods to a range of problems from basic to clinical. Carried out considerable teaching and supervision of undergrad and grad students and also mentors international interns.

- As for the research funding, the group has successfully achieved significant funding, covers a range of topics from basics to applied from organizations ranging from JSST, JSPS, Uehara Foundation.
- As for the international exchanges, it is quite significant and diverse. Excellent in enabling international and national collaborations. This is also associated with several international exchanges.
- It is notable that the group has full of funding.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- Close to the 'Excellent' level. I have an impression that the collaboration between the labs in IPR (or even ASPIRE) has not begun fully.

  As a general comment, I think that the construction of the ASPIRE center was very nice (while the other center looks also promising). These organizations should become driving forces of the entire IPR in the future. It is too early to criticize its outcome. Work hard to prove these new attempts are indeed successful.
- Overall, excellent in all domains. Both as director of IPR and member of ASPIRE, has provided great leadership, mentoring in research, education and liaison. Is further expanding operations and making many more significant contributions with greater interdisciplinary efforts planned. These will emerge from both internal to APSPIRE/IPR, domestic and international collaborations.

  Has excellent vision among perspective of future directions. I would encourage continuing support and effort to further integrate across some aspects of different research groups. For example one area which can provide unique insights and be world leaders would be to integrate across the groups individual abilities that can illustrate at atomic level, how the intracellular signalling networks function in space and time and be modulated by post-translational modifications by integrating the functional dynamics of proteins and their interactions and how they will change with SNPs in different protein components of the network. This could really be a major milestone in the world and the current ASPIRE team has excellent capability to achieve this.
- I thought the recruitment of students in Okada Lab is very successful among other groups. I hope

the successful cycles can be transformed to other groups in IPR.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Computational Biology

Name of Reviewers: Kenta NAKAI, Chandra VERMA, Shoji TAKADA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- This group mainly focuses on computational research in the drug-discovery-related field/medical applications. I think this is a very promising approach.
- The research group is using database development, data integration, AI, machine learning and other modelling and simulations to lead a world class effort in protein life sciences. The research topics are clearly well thought out and very important including predicting toxicities of nanoparticles, ADMET properties of drugs, TCR-pMHC interaction predictions etc. Each of these has resulted in resources and/or high impact publications.
- Integration of data-driven science, AI, and simulations for drug discovery is truly a desired direction to go. This group covers broad range of bioinformatic analysis and modeling for the drug discovery and is very valuable.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- They keep high productivity, though there may not be many ‘remarkable’ achievements so far.
- Achievements of the group are excellent at an international level and has established the group with an excellent international reputation. Among the many projects, the excellent achievements of the PI in their ability to predict toxicity and ADME properties is of great significance to drug development and the MHC-peptide work for vaccine design. Nanoparticles toxicity prediction has great potential because of the huge interest in the world for drug delivery purposes and the PIs achievement is very notable and would be of significant interest to academics and industry. The development of DruMAP will be a great resource for the worldwide community. In addition,

critical analysis of their findings has resulted in the PI expanding the scope of investigations by for example inclusion of structural data. The research has been published in many internationally peer reviewed journals with high impact and several invited lectures.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- The lab shows representable activities in ASPIRE because their activities are based on the analyses of massive data.
- Several collaborations every year both national and international with a significant number from IPR, thus contributing significantly to the protein life science communities. Several international exchange students and staff and attracts many students with many resulting collaborations.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- This group accepted many students, including those from overseas. Successful collaboration with industries.
- As for the educational activities, the group has established an excellent reputation internationally. Mentors a significant number of international students and postdocs. Additionally gets several visiting researchers from the world. The group has also been mentoring an ASPIRE member Dr Tiwari by encouraging her to work with staff in his group.

- As for the research funding, the group has significant industry partnerships: Technopro, Astra Zeneca KK; the work is of great significance in the prediction of toxicity/ADME.
- As for Information Disclosure and Social Relationships, the group has given 36 invited lectures.
- As for the international exchange, the group has several collaborative research projects both nationally and internationally and with industry. The group has given 36 invited lectures.
- The group is having fairly many graduate students, but the majority is foreign students. It would be nicer if the group can recruit more Japanese students as well.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- Considering that the group has started their activity rather recently, their activity is rather impressive. I hope that they will tighten their links with industrial people because I believe that this will show a new model for the future of IPR.
- Excellent performance all round: research, mentorship, collaborations, outreach, industry collaborations. PI has great vision as is exemplified by excellent basic and applied research, including the plans for integrating work with others in ASPIRE has the potential to create some really groundbreaking discoveries and make significant contributions to basic and applied/translational sciences. The integration of resources developed by PI with those from other members of ASPIRE has excellent potential to result in a world leading platform.
- Dr. Mizuguchi joined the IPR relatively recently. We have to wait some years to see how the achievement done at IPR can lead to real drug discovery.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Protein Design

Name of Reviewers: Kenta NAKAI, Chandra VERMA, Shoji TAKADA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- I believe that this lab would become an iconic symbol of the new IPR.
- PI is clearly very good at designing novel proteins. The plan is very well thought out and will be very relevant to industry-pharma, sustainability, materials etc.
- Dr Koga has been so successful for designing protein structures, including oligomerization. Next challenge would be to design function in broad sense. Obviously, a hard target is to design enzyme activity. Combining with evolutionary approach seems promising.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- Excellent achievements are accumulating although they are performed at the group's previous affiliations.
- PI has been publishing (and undoubtedly will continue to publish) in high impact journals and also will contribute to innovations which clearly have been of great interest to industry. Will make significant contributions to life sciences especially in the areas of biomarker discovery, novel therapeutics etc.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- Obviously, it would be too early to evaluate their contributions; however, as I noted above, owning a lab for protein design would attract much attention to the center.
- There is excellent potential to engage with the other members. A collaboration with Dr Tiwari for example is planned which could illuminate significantly the role of intramolecular flexibility and complex formation as there is a vast resource of designed proteins that the PI has constructed. Feedback from the models of Dr Tiwari could point to new design principles. The work of the PI increasingly will also attract many more industries and research groups.
- Since it is a very new group, it is too early to assess this point.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- My suggestion is that they plan to boost a new avenue of protein-based industry (probably by launching a venture company).
- As director of ASPIRE, he oversees the various activities of ASPIRE which has witnessed several visiting students, researchers, collaborations of the team members in ASPIRE.
- The PI has attracted significant interest and funds from industry.
- As for the ASPIRE activity, a plan for collaboration with more than two groups would be a great idea. Especially, formation of a long-term team including young PIs is great.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction?

If you have any opinions or suggestions regarding the future directions of their research, please kindly

share them with us.

Commentary and Recommendations:

- The high score is given not to their activities after coming to this institute but to my great hope for their future activities.
- The PI undoubtedly is excellent and the work that is emerging is amongst the best worldwide in the area of protein design. In addition, once the PI starts including ML/AI/LLM methods, the project will achieve a much higher level of applications and novel discoveries. In addition, there is immense potential of integrating the work both as director of ASPIRE and his own platforms with those of others in IPR to advance scientific research and directing an integration in his role as Director of ASPIRE. For example, combining the designs of proteins and assemblies with Dr. Tiwari's platforms to relate protein flexibility to functional motions and interactions and then to combine forces with the work on SNPs with Dr. Mizuguchi and finally to decorate the signalling networks of Dr. Okada could result in a fantastic integrated resource that can inform upon intracellular processes in unprecedented detail. The information would feedback into designing proteins with modified and unnatural amino acids too which will be of another great benefit to the international community.
- Recent outcomes from Koga's lab are fantastic, but most of them are from the previous position. We look forward to seeing the achievement done at IPR.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Biomolecular Modeling and Dynamics

Name of Reviewers: Kenta NAKAI, Chandra VERMA, Shoji TAKADA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- I think that their goal is appropriate but the PI should hurry up in recruiting new members to achieve the goal: how many staff can she employ?
- PI has just started but has a very good research plan. The plan will undoubtedly evolve with time and collaborations. The two main streams are modelling with analysis of SAXS, XFEL data; Understanding protein flexibility, allostery etc in the context of function. Both have immense potential to inform protein life science research.
- Dr. Tiwari just joined the IPR as a new PI so it is too early to judge her research in normal manner. It was not clear exactly what is her major research goal. She has many reasonable and promising themes planned as collaborations, but her own goal was not emphasized. It is very important to find a backbone research plan, a sort of dream, in the coming years.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- Of course, it is too early to discuss the achievements of this group. However, I could not recognize excellence in their approach.
- Currently the PI has already developed an IPR collaboration and an external collaboration with Hiroshima University. The PI has also written one review and several manuscripts are in progress with ASPIRE and external people. The results of these will be crucial in establishing a benchmark for the use of the PIs computational tools in advancing proteins life science research.
- Again, it is too early to assess this point. All atom molecular dynamics (MD) simulation is a potentially very valuable approach in the IPR because of many structural biologists who needs

MD analysis associated with the structure determination and because of lack of MD specialists in IPR.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- Considering the number of staff, I think that the PI is actively seeking collaborations (though they may not be through the programs of IPR).
- The PI already has been lecturing, serving as Masters thesis examiner, participating in Prof Mizuguchi's lab activities. PI is working on manuscripts with members of ASPIRE (Mizuguchi lab). The PI has plans to exploit and mine the vast resource of designed proteins with the Koga lab.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- These points are not bad, but considering the scale of the lab, the PI should not expand their miscellaneous activities at this stage, perhaps.
- Educational activities: PI has been working with postdoc in the Mizuguchi lab and has developed collaborations with Univ or Bergen, Universite Paris-Saclay and IIT Gandhinagar.
- Research finding: PI has received New Field Research Grant and has also been recipient of supercomputing hours at Cybermedia and TSUBAME

- Information Disclosure and Social Relationships: PI is organizer of IPR/ASSPIRE seminars and is on the organizing committee of IPR Retreat 2023.
- International exchanges: PI has already visited France, presented a poster at a conference for young modellers in Tolouse and gave an invited seminar in Paris. PI has organized the joint collaboration visit of Prof Nathalie Reuter from Norway.
- PI has begun to engage with students in the group of Prof Mizuguchi with his kind approval and mentoring. PI is exploring several routes to attract students. PI is participating in international conferences.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?

Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- I hope that this lab will be able to establish a solid position in ASPIRE/IPR soon.
- The PI is a recent addition but is already embarking on multiple projects both within ASPIRE/IPR and externally. The PIs platforms have excellent potential to inform upon the links between protein dynamics and function. Integrating her method with the designed proteins of the Koga lab, the SNPs of the Mizuguchi lab and inform upon the protein networks in signalling pathways from the Okada lab has excellent potential to advance protein life science research. It will attain much more momentum once the group is staffed towards which the PI is applying for grants and students. In addition, PI is developing collaborations with international partners.
- The group has no other members at the moment, which is a bit difficult situation especially as a young PI. To boost her group activity, it would be great if she can have at least one post-doc for a few years supported by the IPR.

External Review FY2023

Evaluation Sheet (Research Group Activity)

Name of the research group: Laboratory for Protein Databases (PDBj)

Name of Reviewers: Kenta NAKAI, Chandra VERMA, Shoji TAKADA

1. Research Goal and approach(s)

[Evaluation Perspective]

Does the research group set an appropriate research goal, select relevant research topic(s), and take appropriate approach(s) as a member of IPR, that is a world-class institute for protein life sciences?

Commentary and Recommendations:

- This lab could be a “raison d‘etre” of the data science-based center.
- An amazing and excellent effort for maintaining the PDB and associated databases to enable the community to mine and exploit structural biology research – its value to the relevant scientific community for advancing protein life sciences is beyond measure. There are significant plans in progress to link the PDB data with other data resources which will be quite a significant resource.
- This group has a special mission of managing the PDB, which is largely a service to the community. As users of PDB, I would really appreciate the effort of this group.

2. Research achievements and resultant contributions to specific research area(s) in protein life science

[Evaluation Perspective]

Do the achievements of the group contribute to the advancement of protein life science?

Commentary and Recommendations:

- I appreciate their effort in achieving the 31% contribution in wwPDB. However, we cannot be optimistic because this figure may be dropped significantly after PDBc goes smoothly.
- The achievements of this effort are tremendous and excellent. Research has focused on improved biocuration which has resulted in tremendous increase in deposited structures, increased efficiency; there was no impact of COVID-19 on the work which is an excellent testimony to the significance and robustness of this project. In addition there has been a tremendous effort in improving the quality of models of structures deposited which is very good for the community of users. The development of RDF to integrate across different databases will be an extremely useful resource for the community.

3. Contribution of the group to the institutional activities of the Joint Usage / Research Center

[Evaluation Perspective]

Does the research group contribute to the protein life science communities through the Joint Usage / Research Center's programs?

Commentary and Recommendations:

- The current situation may change drastically in the future.
- An increasing number of data submissions and its usage over the years. This is the aim of the data service and it is being accomplished in an excellent manner.

4. Others

Please give your comments and/or suggestions on other points as shown below,

(Educational activities)

・Fostering young researchers, including graduate students, post-doctoral fellows, and foreign researchers

(Research Funding from External Sources)

Research funding acquisition status, such as Grants-in-Aid for Scientific Research (KAKENHI), contracted research, industry-academia collaboration, etc.

(Information Disclosure and Social Relationship)

・Activities for updating the IPR website, lectures, public courses, etc.

(International Exchange)

・Activities for international joint research, organizing/participating in international conferences and meetings.

Commentary and Recommendations:

- so far so good
- Two young members have joined PDBj as lead annotator and annotation/validation servers for PDB China.
- Concerning "Information Disclosure and Social Relationship", the PDB is constantly updated and the worldwide effort includes workshops, lectures etc and has been an ongoing and extremely successful effort for years.
- International exchanges are a crucial part of the world wide PDB effort.
- The group owes major effort by specially-appointed people. I am not sure about their career path. Can they be permanently employed? In the near future, it would be more and more difficult to find great technical staffs. Stable employment would be desired.

5. Comprehensive Evaluation

[Evaluation Perspective]

Are internal collaboration and/or IPR framework nicely utilized in the group's research?
Does each laboratory or department have an appropriate vision and perspective for its future direction? If you have any opinions or suggestions regarding the future directions of their research, please kindly share them with us.

Commentary and Recommendations:

- In the post-AlphaFold2 era, the expected role of PDB will change significantly. If the PDBj team wants to have its independent policy from the one with its partners, they should propose it as soon as possible. In addition, the probable rise of PDBc is also a concern. I believe that the staff of PDBj should share a sense of crisis.
- This is a very critical part of protein life science research and it is a major public service. It consists of a significant number of staff from ASPIRE and IPR. It is continuing the momentum of its aims and their accomplishments. The RDF will incorporate other databases with other members including Mizuguchi and Koga labs. The development of OneDep system has clearly been a tremendous success. With the appropriate development of mining tools, ML/AI methods, it will be a great resource to include and enable integration of the models of the KOGA lab with the dynamics of the Tiwari lab and insights from the Mizuguchi lab and finally into the systems analysis of the Okada group. Has a fantastic potential of a well-integrated resource for the world wide community to efficiently mine and accelerate discoveries

External Review FY2023

Comments from the Reviewers on the Division of Protein Network Biology and the ASPiRE

Overall the output is quite amazing in terms of the science industry collaborations, outreach efforts The science is excellent and certainly at the leading and competitive edge in the world.

Division of Protein Network Biology

Laboratory for Cell Systems led by Dr. Mariko Okada focuses on system biology of cell fate decision mechanisms integrating experimental measurement and computational modeling. Laboratory for Computational Biology led by Dr. Kenji Mizuguchi works for drug discovery by database-driven and AI based approaches. Both labs show extremely high-level research activities. Notably, a good balance between academic and basic researches and collaborations with academic groups and industries is impressive.

We would like to suggest the following possibilities:

1) Increase links with local clinicians to perhaps be able to use their capabilities to help clinical decision making – especially with regards to SNPs in the local populations and their effects on drugs; maybe initiate this coupling into a national Precision Diagnosis/Medicine Program (if one does not exist)
2) Increase center links with biotech and industry along with those already arising out of individual networks that already are excellent (maybe have open days and invite biotech/pharma)
3) Explore joint PhD students with other countries (model could be the ARAP program offered by ASTAR, Singapore) and explore whether pharma would be interested in joint PhD students (model could be CASE studentships in the UK)

ASPiRE

ASPiRE aims at putting forward protein-centric data-driven studies, which perfectly meets the current need in protein science. As such, this new center, ASPiRE, plays a key role in the IPR. Its organization looks good overall: The five groups cover rational protein design, analysis of protein dynamics and protein network, drug discovery, and building/managing protein database.

The most exciting aspect we find is the potential for integrating across scales in space and time ranging from protein structures (SNPs), dynamics to cellular pathways (brings together all the 5 presentations) is very exciting because the tools are uniquely in place at ASPIRE and the integration capabilities exist – this will excitingly inform upon things such as post-translational modifications (PTMs) and their influence on structures, associations and phenotypes – thus opening new avenues in drug discovery –

which so far has not really been able to include the effects of PTMs. This will be a great defining unique character of ASPIRE which will certainly be world leading and guiding. It is an effort that certainly would blossom with as long-term assurance of funding.

We would like to suggest the following going forward:

4) It would be great if the center can recruit a proper IT group dedicated to machine-learning /AI. Cross-appointment to other Schools in Osaka University can be a possibility.
5) Keep an eye on developments in Quantum Computing especially in the field of structure manipulations in biology; keep talking with industry leaders in this area to keep updated with developments, especially in Quantum ML-AI. While these are long term, innovations can happen and the dynamic may suddenly change

Organaizaion

Director 所長

Faculty Meeting	教授会
Administrative Council	運営協議会
Panel on Joint Usage/Research	専門委員会
Research Divisions	**研究部門**
● Division of Protein Chemistry	蛋白質化学研究部門
Laboratory for Protein Organic Chemistry	蛋白質有機化学研究室
Laboratory for Nanobiology	蛋白質ナノ科学研究室
Laboratory for Protein Synthesis and Expression	分子創製学研究室
Laboratory for Protein Profiling and Functional Proteomics	機能・発現プロテオミクス研究室
Laboratory for Physical Biology	蛋白質物理生物学研究室
● Division of Protein Structural Biology	蛋白質構造生物学研究部門
Laboratory for Molecular Biophysics	機能構造計測学研究室
Laboratory for Protein Crystallography	蛋白質結晶学研究室
Laboratory for CryoEM Structural Biology	電子線構造生物学研究室
Laboratory for Supramolecular Crystallography	超分子構造解析学研究室
● Division of Integrated Protein Functions	蛋白質高次機能学研究部門
Laboratory for Molecular and Developmental Biology	分子発生学研究室
Laboratory for Genome and Chromosome Functions	ゲノム・染色体機能研究室
Laboratory for Advanced Brain Functions	高次脳機能学研究室
Laboratory for Organelle Biology	オルガネラバイオロジー研究室
● Division of Protein Network Biology	蛋白質ネットワーク生物学研究部門
Laboratory for Cell Systems	細胞システム研究室
Laboratory for Computational Biology	計算生物学研究室
Laboratory for Infection Systems	感染病態システム研究室
Special Research Facilities	**附属施設**
● Research Center for Next-Generation Protein Sciences	蛋白質次世代構造解析センター
Laboratory for Ultra-High Magnetic Field NMR Spectroscopy	高磁場NMR分光学研究室
Laboratory for Synchrotron Radiation Research	高輝度放射光結晶解析研究室
Laboratory for High Resolution Cryo-EM	高分解能クライオ電子顕微鏡研究室
Laboratory for Biomolecular Analysis	生体分子解析研究室
Open Space Laboratory for Advanced Protein Science	産学・国際連携研究室
● Advanced Data Science Center for Protein Research	蛋白質先端データ科学研究センター
Laboratory for Protein Design	蛋白質デザイン研究室
Laboratory for Biomolecular Modeling and Dynamics	生体分子動態モデリング研究室
Laboratory of Protein Databases	蛋白質構造データバンク構築研究室
Laboratory for Protein Network	蛋白質ネットワーク研究室
Laboratory for Drug Discovery Informatics	創薬インフォマティクス研究室
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Project Team of Joint Usage / Research Center	拠点プロジェクト班
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