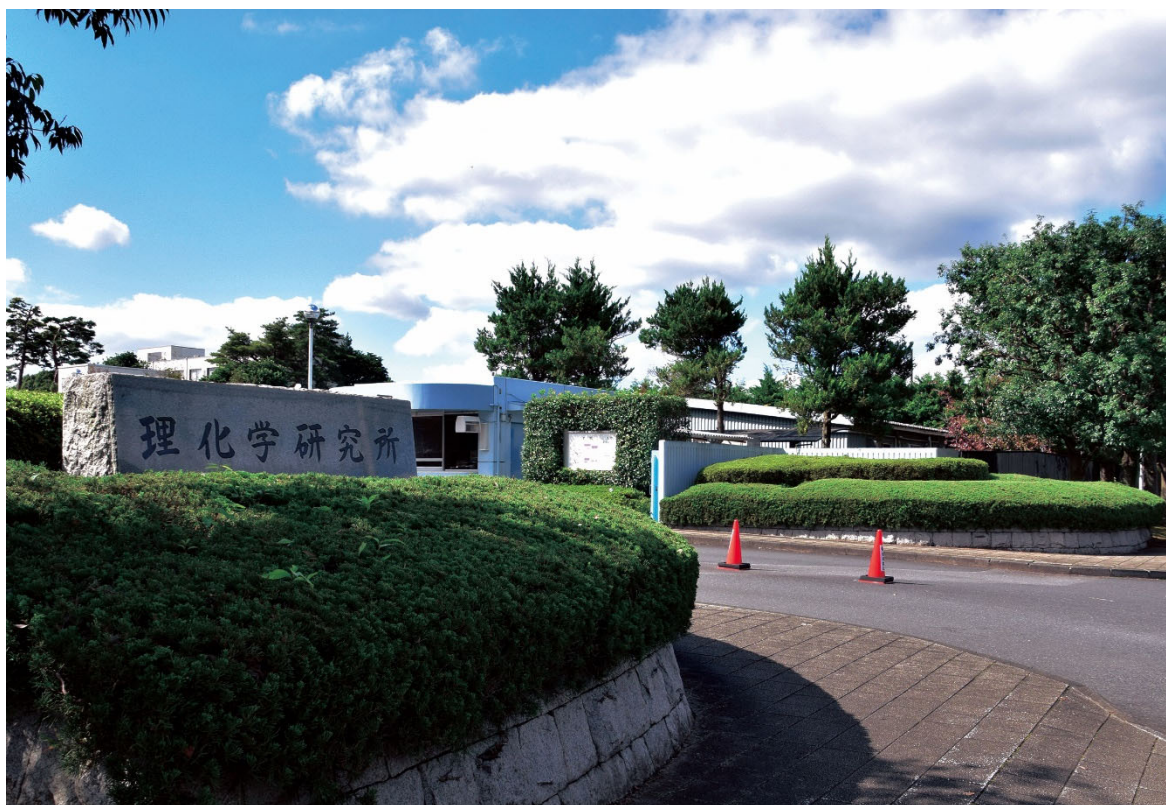


# The Report

The 8th RIKEN BioResource Research Center  
Advisory Council

May 16 – 19, 2023



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## Evaluation and Advice

### Introductory Comments

BRC Advisory Council (BRAC) believes that RIKEN BioResource Research Center (BRC) continues to operate at the forefront globally in the provision of a diversity of *in vivo* (mice, plants, cells, microbes) and *in vitro* (gene materials) bioresources to the wider biological and medical sciences community in Japan and beyond. This activity is allied to internationally-recognized research and development efforts to support the acquisition, analysis, and dissemination of bioresources for research and discovery (R&D) in medicine, health, and the environment. BRC is recognized as one of the leading centers worldwide for biological resources with not only a high impact in Japan, but also internationally. The vision and leadership shown by Dr. Shiroishi and his senior colleagues both in responding to the 2019 BRAC recommendations set alongside the successful operations and R&D activities of the 4<sup>th</sup> Mid- to Long-Term Plan period underpin a highly successful period of both resource provision and resource research from 2018 to 2023. This provides a strong platform for the proposed new policies and strategic direction that are foreseen for the 5<sup>th</sup> Mid- to Long-Term Plan period (2025-2031). Furthermore, despite the very difficult situation during the pandemic, BRC continued to operate responsibly as a national resource center. Their achievements in collecting, archiving, and distributing bioresources in the light of this challenge were exemplary.

***TOR1. Evaluate the responses to the 2019 BRAC recommendations.***

The responses to the 2019 BRAC recommendations are both comprehensive, rigorous, and robust. Importantly, **they emphasize the critical importance of R&D as a driver for outstanding resource acquisition, development, rigorous quality control and dissemination – a critical point which the BRAC supports very strongly.** The juxtaposition of resources with R&D is at the center of all internationally leading resource centers and Dr. Shiroishi is quite right to emphasize this dimension.

The BRAC strongly supports the achievements made for contributing to society

and the research-community within Japan and overseas. In particular, recognizing the importance of phenotyping for maximizing the scientific value of all bioresources and their translational potential is meritorious. The BRAC welcomes the assignment of the Mouse Phenotype Analysis Team to the Key Technology Development Program. This reassignment will ensure the utility of mouse models for disease and therapeutic studies, which is critical for proposed future strategic developments in and research application of mouse mutant resources. Moreover, the continual renewal of the BRC website is key to all the activities and essential to broaden outreach to diverse scientific communities. On this note, bringing the wild-derived mouse strain database, “Mog+”, to BRC is part and parcel of consolidating key data for BRC resources at a single-entry point.

With respect to meeting standards of other major international bioresources, excellent progress has been made in adopting FAIR principles and RRIDs. BRC is to be applauded for the careful attention this has received.

Establishing multiple routes for regular feedback from users has been implemented dynamically and thoughtfully. It is a key element to any resource-based activity, and the senior leadership has clearly thought deeply about improvements and new strategies in this area.

In line with the advice to develop and implement novel resources and research fields for the long-term perspective for the 5<sup>th</sup> Mid-to-Long-Term Plan, Dr. Shiroishi and his senior colleagues have thoughtfully considered longer-term strategic developments with vision and imagination. In their response to questions on new resources and research fields, they carefully considered how to develop their operational, analytical, and integrative approach to the big datasets being generated at BRC. For instance, initiation of a collaboration with Research Digital Transformation (DX) Foundation Team will allow them to integrate and apply DX activities across data acquisition, management, analytical, and dissemination processes. Moreover, it is welcome that Machine Learning (ML) and Artificial Intelligence (AI) approaches are being promoted by the Integrated Bioresource Information Division. It will be important to recognise that these approaches, which will transform the ability to enhance high dimensional datasets and provide biological solutions, will require additional expertise and human resources at

**BRC. While collaboration and outreach are essential with current projects and in-house expertise, the development of a critical mass of experts within the Integrated Bioresource Information Division will serve BRC well in the long-term.**

To understand global research trends, it is welcome to see that BRC is utilizing specific open source and *de facto* standard software solutions to implement AI/ML approaches to data management. These will be valuable tools and assets for strategic planning, which is critical for a successful 5<sup>th</sup> Mid- to Long-Term Plan period.

BRC is playing an ever-increasing role in Japan in the development of novel disease models for the study of human disease (delivered through the activities of the Experimental Animal Division, Next Generation Human Disease Model Team and the two iPSC focused Teams). This is an excellent and critical strategic path forward. In parallel, as the response outlines, the ongoing planning for improvements to facilities and infrastructure for mouse resources, including a new mouse resource building, are particularly important goals that will underpin the future success of BRC across the 5<sup>th</sup> Mid- to Long-Term Plan period.

The BRAC welcomes the focus on improvements in outreach as well as the introduction of DX approaches to enable regular assessments and audits of barriers to successful resource acquisition, development, and dissemination. This will have a powerful impact on BRC's continued application of the bioresource circulation cycle and any roadblocks that impede its success.

**In summary, the response to the 2019 BRAC recommendations is excellent with an outstanding period of operational success, allied to several critical strategic developments which presage the longer-term plans stretching into the 5<sup>th</sup> Mid- to Long-Term Plan period.**

**TOR2.** Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).

### **The Current Position**

BRC retains its very strong position as a provider of diverse *in vivo* and *in vitro* resources to biological, medical, and agricultural sciences both within Japan and internationally. This position has been strengthened by some realignment of the scientific divisions. There are 3 overarching programs at BRC:

- *Bioresource Infrastructure Program*, that focuses on collecting and preserving cutting-edge bioresources, while conducting relevant R&D. The five bioresources and the Integrated Bioresource Information Division that make up this Program are one of the most unique and outstanding features of BRC.
- *Key Technology Development Program*, that develops key underpinning technologies for preservation and Quality Control (QC) of bioresources. **As of May 2023, the reassignment of the Mouse Phenotype Analysis Team from the Bioresource Frontier Program to the Key Technology Development Program is very welcome as this will underpin the strategic goal of generating novel mouse models for the study of human disease and the development of novel therapeutic strategies.**
- *Bioresource Frontier Program*, that conducts bioresource-related research and discovery, which consists of 4 highly successful and productive scientific Teams. The Technology and Development Team for Mammalian Genome Dynamics was sunsetted with the retirement of Dr. Abe, and, as stated above, the Mouse Phenotype Analysis Team was reassigned.

Overall, the structure and organization of BRC are well set. BRC is an integral and vital part of the Ministry for Education, Culture Sports, Science and Technology (MEXT) National BioResource Project (NBRP).

### **Achievements**

There were numerous achievements during this period, with some notable accomplishments that are worth emphasizing:

1. The development and implementation of a web-based system that enables comprehensive search of resources is highly commendable.
2. The repositories are expanding well. Overall, BRC ranks within the top 3 public repositories worldwide. The enhancement of QC is a major contribution to the quality of the repositories, and their attractiveness to users, both of which promise to increase utilization and enrichment of the bioresources.
3. The quality and utility of the repositories are clearly demonstrated not only by the uptake of bioresources by Japanese scientists but also by those internationally (>20% of bioresource distribution is overseas). Moreover, the large number of papers (from 9.4% of BRC-provided resources) and patents (2.8% of BRC-provided resources) produced from BRC repositories strongly underpins the key role of BRC within NBRP and Japan's wider science agenda.
4. The refreshed website along with the establishment of FAIR principles and the use of RRIDs have all contributed to a landscape of improved outreach and accessibility.
5. BRC organized and hosted IMGC2023 in Tsukuba with many participants from abroad, one of the first major international conferences since the COVID-19 pandemic.
6. Advanced cryopreservation and reproductive technologies are routinely used at BRC, which contributes significantly to its overall operational efficiencies and effectiveness and emergency preparedness.
7. The emphasis on development of bioresources to assist in infectious disease research to counter future pandemics is welcome, and in particular the ability to provide relevant mouse lines, cell lines, and gene materials. This will likely require replacement, revision, and/or upgrade of the current mouse and laboratory facilities to accommodate research on highly contagious human pathogens such as SARS-CoV-2.
8. The strong position of BRC in the global landscape and its worldwide recognition is exemplified and underscored by participation in key international consortia, such as the International Mouse Phenotyping Consortium (IMPC) and Asian Mouse Mutagenesis Resource Association (AMMRA).
9. The concept of "bioresource circulation" is highly innovative and will likely lead to expanded use of extant bioresources and the deposition of newly

derived derivatives. This will greatly extend the scientific utility and impact of bioresources donated to BRC.

10. The move toward DX is promoted but is still in an early stage of development; there remain several aspects of this concept still to be addressed and implemented (see plans in TOR 3).
11. The four research and development Teams have all been highly successful, generating not only high-profile publications but also new technologies and bioresources (e.g., iPSCs of human diseases) that are used by the research community. In addition, the research programs serve as a rich and rigorous training ground for graduate students and new young scientists early in their careers.
12. There has been significant development of and dramatic increases in the size and distribution of world-class bioresources (plant materials, cell cultures, and microbes) that are available and accessible for use by research scientists in basic science and agriculture, with a focus on the environment and food production.

Also commendable during the current period is the director's initiative to conduct a Strengths / Weaknesses / Opportunities / Threats (*SWOT*) analysis of BRC (see Appendix). A few notable points from that analysis are described here:

*Strengths*: The strategic organization of 5 highly quality-controlled bioresources operating under BRC administrative umbrella is unique in the world. The concept of "bioresource circulation" further takes advantage of this organization and promises even more success in the future.

*Weaknesses*: Particular attention to two weaknesses in the report will be critical to address for ensuring the future success of BRC.

- a. Building and infrastructure maintenance. A new mouse resources building is paramount and a fundamental building block for the future. The new design should take into account best practices for modern mouse facilities worldwide. Development plans should integrate horizon scanning of future mouse genetics needs and developments.
- b. Maintaining Scientific Leadership. The impending retirement of several leaders of the Bioresource Infrastructure Divisions is a challenge to the



continuity and future scientific development of BRC. Consideration should be given to international and female candidates during recruitment.

*Opportunities:* The implementation of DX and use of AI/ML analyses will have a profound impact on operations, utilization, productivity, and success of BRC. To maximize this opportunity, BRC should consider the feasibility of developing relevant expertise in-house in order to enhance a dynamic and productive data science environment.

*Threats:* The possibility of the next pandemic or other natural disasters (e.g., earthquake) puts not only BRC but all of Japan at risk. BRC has instituted and tested a thoughtful Business Continuity Plan to address preparation strategies (e.g., off-site backup storage) and mitigate the potential impacts of future disasters.

**In summary, over the 4th Mid- to Long-Term Plan period BRC has delivered a series of noteworthy, globally recognized, and singular achievements and successes from resource provision and infrastructure, to key technological developments and frontier research programs. There remain a few issues to consider and address as the new strategic plan for the 5<sup>th</sup> Mid- to Long-Term Plan period unfolds. However, BRC has already established an exceptionally strong platform upon which to further build and develop strategies and policies for the next period.**

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. BRC has a clear and appropriate priority list for future focused activities that reflect societal and environmental areas unique and/or supportive to Japanese interests, particularly where these are currently assessed to be unattractive, difficult, or unavailable to other research centers. These selected areas will be in addition to the continuity and development of existing resources and will fill critical and timely gaps. **The balance and distribution of work in terms of the generation of new resources across priority areas in the Health and**

**Medical Research domain and the Environment and Food Research domain will need to be regularly re-assessed. For example, but certainly not exclusively, research on induced pluripotent stem (iPS) cells for dementia should specifically be enhanced, including external support from institutions such as the Center for iPS Cell Research and Application (CiRA) at Kyoto University.**

2. The ongoing digitization of mechanisms and processes supports a more efficient and effective resource environment, particularly for donations and distribution. Following on from the disruptive effects of COVID-19 and the global rise of online activities, it is a critical time to capitalize and consolidate digital ‘ways of working’. This is a very appropriate time to be considering the use of AI/ML. Clear forward planning and suitable platforms are already in place and suitable discussion has occurred across the entire organization. This will help to capitalize on opportunities from these highly disruptive technologies. **Some units are already actively engaged in providing and utilizing novel tools, and increased uptake must be encouraged.**
3. The concept of Transformative Research Innovation Platform of RIKEN platforms (TRIP), introduced by RIKEN HQ, is a next generation principle to support and incentivize the move from digitization into full data interoperability across the diverse high-quality bioresources at BRC and beyond. This approach when added to appropriate social networking services (SNS) will have the added benefits of increased visibility both domestically and abroad. **Uptake and investment in these resources will require careful consideration when set against current commitments and available capital including human resources which currently may not suffice. The BRAC encourages collaboration with appropriate researchers inside or outside of BRC to maximize interaction with TRIP.**
4. BRC showed a significant and serious intention for future construction and renovation of the physical infrastructure with a corresponding request for suitable budgets that will enable and enhance critical operations. **Renovation is very timely and includes careful consideration of continuity of activities and resource evacuation and should keep in mind measures to protect against adventitious pathogens and infectious diseases when designing the new mouse facility.**

5. General and specific disaster planning is being taken very seriously through engaging responsive policies such as the Business Continuity Plan. Possible disruptions include chronic and time-unpredictable events such as COVID-19; acute and stochastic threats such as earthquakes; emerging social threats such as economic and political events; and more directed threats such as IP infringement.
6. Maintaining a cadre of outstanding scientific leadership in the face of several retirements is essential for future continuity and will benefit from active support such as specific promotion and application guidance, workshops, and personalized feedback, alongside a suitable breadth of marketing and outreach both internally and externally. Mentoring approaches and active monitoring using established practices against gender bias also help to address the gender gap in recruitment processes.

**In summary, the future strategic and operational plans at BRC are excellent. It will be critical to regularly appraise the introduction of new resources and research programs, thus ensuring a balanced approach that reflects the available capital and infrastructure whilst always taking advantage of available outside expertise and community requirements.**

## **Comments for Divisions and Teams**

### **1 Experimental Animal Division**

**(Division Director: Atsushi Yoshiki)**

***TOR1. Evaluate the responses to the 2019 AC recommendations.***

- 1 Sufficient measures have been taken to address the issues raised at the last advisory council.
- 2 To accurately evaluate BRC's contribution to the research community, the collection rate of user publications needs to be improved. A publication search system using AI is expected to be developed soon to drive a virtuous cycle of bioresources.
- 3 There is still room for improvement, such as increasing collaborations with other facilities, including NBRP Human Pathogenic Virus Centers, and forging links between disease models and disease names.

***TOR2. Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).***

- 1 The BRAC believes that appropriate action has been taken to address the points raised thus far.
- 2 The SARS-CoV-2 mouse models should be improved through collaboration with other facilities, including NBRP Human Pathogenic Virus Centers, and by linking the mouse models to human cases.
- 3 As a core NBRP facility, the Division is well-established as a major mouse repository in Asia. Based on its role as an active member of IMPC, the BRAC judges BRC to be a mouse resource center that meets high international standards.
- 4 The BRAC is satisfied that the Division plays an active role in international exchange as a national center and as an international hub, and the BRAC thinks it is commendable that the Division has been engaged in a university program for both international and domestic graduate students.
- 5 While progress has been made in improving gender balance, the Division needs to further increase the representation of female and/or overseas

investigators and researchers. This applies to all of BRC, not only this Division.

- 6 The BRAC would like to see an emphasis on finding ways to sustain the personnel of this Division.

***TOR3.*** Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.

- 1 The efforts made by this Division to differentiate itself from other centers is one of its strengths. This has been accomplished by prioritizing the collection of unique mouse strains and planning the publication of their phenotypic data.
- 2 The Division has an adequate plan to enrich mouse resources with valuable information. Collaboration with the mouse phenotyping Division is important to achieve this goal.
- 3 Based on the mission of “Providing the most advanced and highest level bioresources to researchers around the world,” a system that allows collaboration with the Divisions of BRC and the Integrated Bioresource Information Division must be created to better promote bioresource businesses.

## **2 Experimental Plant Division** **(Division Director: Masatomo Kobayashi)**

***TOR1.*** Evaluate the responses to the 2019 AC recommendations.

1. The Experimental Plant Division has completely responded to the 2019 BRAC recommendations about their activities.
2. The Division has been collecting Arabidopsis natural variations, their genome data (GWAS analysis) and phenotype measured with the RIKEN Integrated Plant Phenotyping System (RIPPS), and further developing a possible new model candidate.
3. The Division has collected Arabidopsis mutants for CLE-peptide encoding genes generated by genome editing technology. All lines are open for distribution. CLE peptides are critical hormone that plays pivotal roles in plant development and physiology.

4. The Division has also improved transformation efficiency of *Brachypodium distachyon* which is one of new model candidates.
5. All these activities are an important part of the responses.

**TOR2.** *Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).*

1. As one of the three major resource centers for Arabidopsis in the world, the achievements of the Division have exceeded expectations.
2. The quality control of resources has been more than adequate. Precise quality control of resources is a distinguished feature of this Center and sets it apart in the world.
3. Bioresource circulation of plant material works well as an important function of resource center.
4. The BRAC would appreciate further attention to the uniformity of seed material in order to obtain reliable data for phenotypic analysis.
5. Education and training materials for young staff will also be useful for increasing public understanding and support of resource projects.
6. Despite the difficult situation during the COVID-19 pandemic, the contribution of the Division to research achievement in the international community is notable.
7. The Division has been acquiring genome sequences using NGS and phenome analysis, and plans to build a new database useful for GWAS analysis.
8. The Division has discovered a symbiotic fungus that promotes plant growth and the growth of cultured cells. Progress in important research directly related to BRC activities is also expected to be significant in the future.
9. Phenome data on the Exp-Plant Catalog increase the value of the resources.
10. Despite the difficulties during COVID-19, the Division actively worked on international collaboration to be a hub for international plant resource projects.
11. The Division Director is a member of the Multinational Arabidopsis Steering Committee.
12. The 33rd International Conference on Arabidopsis Research (ICAR2023) will be held in June 2023 in Japan. The Division and the Director are working as

one of the many organizers of the ICAR2023 which could lead to further progress in this field.

13. The sustainability of personnel in the future is important. A successor for the Division Director and career paths for young researchers and technicians should be considered an issue for BRC as a whole.
14. Dissemination of information and public relations that bring about momentum for resource projects is also suitable.
15. Improving visibility both domestically and internationally by using social media will become more important for public relations activities.

***TOR3.** Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.*

1. Further analysis of a new data set of Arabidopsis is important, but careful handling is required for profiling data by RNA-seq analysis of whole plants. The result of RNA-seq analysis is different from genome data because the gene expression is quite sensitive to environmental conditions. On the other hand, RNA-seq data from cultured cells may be more useful to users because they are less influenced by the environment.
2. Research results are truly desirable for both the resource center and the center's researchers. Research projects based on the role of the bioresource center should be prioritized in the future.
3. Plans are suitable for three major projects, namely Arabidopsis seeds, plant cultured cells, and research infrastructure of biological interactions.
4. The importance of Arabidopsis research is increasing more than considered. It is advisable to discuss the expected role of *Brachypodium* and other different materials.
5. Continuous efforts for collecting resources from retirees are desirable to prevent the loss of resources produced in Japan.
6. The development of cryopreservation technology is being carried out carefully. Continuous efforts that will lead to the establishment of efficient preservation technology for long term storage of resources and disclosure of such developed technologies are recommended.

7. As for *Marchantia*, it may be a good service to present a contact point for the *Marchantia* domestic research community and/or to upload video protocols to the BRC website.
8. Application of AI to search research papers in which BRC resources were used is outstanding and highly appreciated.

### **3 Cell Engineering Division**

**(Division Director: Yukio Nakamura)**

***TOR1. Evaluate the responses to the 2019 AC recommendations.***

1. The Division did the following to address the BRAC recommendations: 1) Initiated distribution of cell lines derived from human iPS cells; 2) Began a bank of patient blood cells; 3) Used patient-derived iPS cells to analyze genes that cause amyotrophic lateral sclerosis (ALS).
2. It is impressive that such progress has been made regarding these activities. Because BRC possesses a variety of bioresources in one center it is one of the world's most valuable bioresource centers. Therefore, the BRAC strongly recommends taking advantage of the whole BRC through rigorous collaboration among different Divisions.

***TOR2. Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).***

1. The achievements of the Division regarding cell resources, particularly disease-specific iPS cells, can be considered high by world standards in all aspects (number of collections, quality control, and number of distributions), and it is a world leading cell repository. As a result, many papers and patents have been published by users. Cell resources are expected to be made more useful for domestic users, and especially for overseas users, by further developing the features and strengths of the Division, such as having the world's largest bank of disease-specific iPS cells.
2. As a part of their efforts to expand iPS cell banking, the Division has conducted



genetic analyses of disease-specific iPS cells. The analyses, and the disclosure of the results through a web catalogue, are very useful for users.

3. iPS cells that express differentiation markers under the promoters of tissue-specific genes are quite useful. Generation of similar ES cells will be useful as well. Because it is time- and cost-consuming work, the BRAC strongly recommends a community-targeted questionnaire for which tissue-specific promoters should be selected.
4. Public relations and outreach activities are being carried out suitably. In the future, the Division should focus on public relations that target young investigators. In addition, the BRAC strongly recommends using public relations to help increase the number of depositors and the number of hospitals that deposit patient blood cells.
5. Considering the number of cell resources deposited, the Division's efforts to keep up the cell bank have been carried out very efficiently, with a relatively small number of staff. However, the career paths for the staff seem unclear. Examples of cell bank staff who successfully moved to other academic institutions or companies would likely help promote recruitment of new employees.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. The Division's plan to collect and provide cell resources that research community will need in the near future is good and appropriate. However, the human resources, budget, and infrastructure needed to achieve this plan should be the first priority, making sure that the necessary resources can be secured.
2. Undertaking the following projects is both appropriate and important: 1) building a patient blood bank and a cancer organoid bank and 2) establishing a platform to analyze cell morphology. Regarding the project 2), collaborating with experts in the relevant fields is necessary, especially because the field has been advancing rapidly. It is important to inform cooperating organizations that the ethical review process can be done by the central IRB and RIKEN.
3. The number of ES/iPS cell users is small because the high skill required for the work drives up the cost. If the methods for ES/iPS cell cultures become

easier and the cost becomes more reasonable, many more researchers will be able to use these cells. Therefore, the BRAC recommends that basic researches develop such methods. Overall, distributing various kinds of differentiated cells derived from ES/iPS cells is desirable.

4. Public relations and outreach activities have been carried out to an appropriate degree. In the future, public relations focused on attracting young investigators should be enhanced. In addition, the BRAC strongly recommends public relations and outreach activities to increase the number of depositors and hospitals that deposit patient blood cells. The labor shortage in the fields of scientific research is a very serious problem in Japan, including the field of bioresource banking. Continued employment and development of human resources are critical for maintaining bioresource banking.

#### 4. **Microbe Division**

**(Division Director: Moriya Ohkuma)**

***TOR 1. Evaluate the responses to the 2019 AC recommendations.***

1. Each recommendation has been adequately addressed. Regarding matters that are in the process of being dealt with or that should be dealt with in the future, the current actions and future plans for dealing with them are adequate. Additionally, efforts to update these actions and plans are steadily ongoing. Some actions led to new outcomes that have been highly praised.
2. The Division has responded adequately to Advice 1: “Reinforcing R&D for functional genomics, phenotyping, data analysis, enhancing the collection, integration, dissemination of genomic, phenotypic data and information on existing bioresources.” Evidence for this evaluation comes in part from their development of the system that lists yeast strains based on their phenotypes, and the development and dissemination of the “List of microbial resources.”
3. The Division has also responded well to Advice 2: “Comparative genomics of bioresources with natural diversity”. Specifically, the Division has contributed to the *GCM 10K type strain sequencing project* (38% for JCM), providing a large number of strains.

***TOR2.*** Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).

1. The annual strain deposition rate of 755 (mean rate from 2018-2022, as calculated by HO) is a steady increase. The mean percent of overseas depositions was 73% per year (mean percent from 2018-2022, as calculated by HO). The Division contributed 38% of sequenced strains (the largest numbers involving 25 microbial bioresources) to the *GCM 10K type strain sequencing project*. These achievements clearly show that the Division is a major international collection center for cultures.
2. The quality control, including the QC test before acceptance, high levels of distribution (mean of 4,989 and 33% from 53 overseas countries between 2018 and 2022), and the type-strain holdings for prokaryotic species (#2 in the world) show that the Division is trusted by researchers around the world.
3. Because Asian countries have abundant microbial resources, the Division is expected to be a core hub for microbial research in Asia. This has been well established through the cycle of accepting depositions of new species, publishing papers about the deposited strains, provision of strains, and papers authors by the users.
4. The Division made technical developments to isolate and keep symbiotic and difficult-to-cultivate microorganisms such as DPANN, a superphylum of Archaea. This will be viewed highly worldwide and is expected to contribute to R&D.

***TOR 3.*** Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.

1. The following plans to maintain their world-leading type-strain holding status, to enrich useful resources for the environment and health science, and to expand the numbers of microbial symbiont resources and difficult-to-cultivate microorganisms, are judged as very important for meeting future demands for microbial cultures and further microbial R&D, including genomic research.

2. Research DX is indispensable for the science and technology of the future, and there will be a phase in which the quality and quantity of data will determine the speed and success of research. In this respect, the Division's efforts to expand the information infrastructure composed of genome/omics data, source of origin, phenotypic characteristics, and publications are very important.
3. Planning the sustainability of reliable activity (such as human resource development) is not just a problem for the Division, but a problem for the entire BRC.

**5. Gene Engineering Division**  
**(Division Director: Yoshihiro Miwa)**

***TOR1.** Evaluate the responses to the 2019 AC recommendations.*

Overall, Gene Engineering Division (there after “the Division”) responded sincerely and adequately to the 2019 AC recommendation.

1. The BRAC welcomes the introduced high-throughput sequencers (HTSs) for short read and long read sequencing and the preparation of a procedure for Quality Control with HTSs.
2. The promotion of research DX, using digital files instead of papers in deposition and distribution procedures, constructing databases, and developing an AI system to search for new genetic resources from publications are much needed changes. The Division also began new internal study meetings to improve the abilities of the Division's staff.
3. While the activities on the social education were suspended due to the COVID-19 pandemic in 2020, it resumed after 2021, with the Tsukuba Ph.D. kids' program and Lectures for high school students.
4. Two young members, one Research Scientist and one Technical Staff were recruited. In addition, a personnel selection process is currently underway for recruiting another R & D Scientist.
5. The newly appointed PI started a joint research project to develop new resources with a wide-range of collaboration with researchers not only of BRC but also with universities.

**TOR2.** *Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).*

1. The high-quality bioresources collected in accordance with the Mid- to Long-Term Plan play a significant role in life science research and in the development of industrial activities. In addition, the Division is actively collecting bioresources that respond to research trends and needs, strengthening and streamlining quality control to improve quality, and appropriately implementing the maintenance of information dissemination to attract users.
2. Maintaining high quality through quality control effort is an important achievement and a major characteristic of the Division. As an effort to ensure the accuracy of genetic resource information, the BRAC highly commends the establishment of a system that enables confirmation of the entire sequence during quality control at the time of deposit.
3. The expansion of resources deposited by world-renowned Japanese researchers will lead to further activation of research, consequently these resources will become one of Japan's strong points.
4. As one of the five Divisions of BRC in the NBRP of MEXT, the Division has made significant contributions to the project. The achievement has reached the level of the world's major bioresource centers. The BRAC is looking forward to further efforts to exceed the world standards.
5. Although the impact of the COVID-19 pandemic on the operations may have been significant, the management has been appropriate.
6. In order to function as an international hub, the BRAC would like to see the Division collaborates with overseas resource centers and collects resources from other countries, especially from Asia. In order to attract new users from overseas and increase the level of use for further improvement, it is necessary to publish papers using bioresources provided by the Division and disseminate information to overseas communities using the bioresources, and it is desirable to further increase opportunities for technological development on a joint research basis or on an independent basis.
7. Regarding information dissemination and public relations, the BRAC commends the website renovation, e-mail news dispatch, information

dissemination at various symposia and other events, and information dissemination to the community alternatively the online technical training system. As the website alone is no longer sufficient, additional SNS support may be useful and needs to be considered.

8. Many progresses have been made, including efforts in deposit surveys, information dissemination to increase users and the number of resource distribution, improvement of business processes by using DX technology. Yet, the procedures and time period for deposition and distribution should be simplified and sped up to the same level as for Addgene (International level). The BRAC would like to see an acceleration of the computerization of resource operations to speed up the process for the users.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. The collection of bioresources and the development of new technologies in the planned project are appropriate. The bioresources to be maintained are appropriate because their quality is well controlled and their intellectual property and other rights are protected. Consequently, the bioresources can meet the demands of the industry as well as academic research.
2. Since the new Director is now appointed, it may be necessary to break down the issues and figure out the ideal image, goals, and timetable for each of 1) users, 2) depositors, 3) Gene Engineering Division, 4) outreach activities, and 5) international collaboration.
3. In the bioresource banking, it is important that there are personnel who are responsible for the long-term operation of the bioresources banking. The staff of the Division should be trained and employed on a long-term basis. The committee hopes that RIKEN's new personnel system will be enhanced to establish such a system that can contribute to the resource banking on a long-term basis.
4. The committee expects the collection and management of highly valuable bioresources with uniqueness and superiority originating in Japan, and the promotion of life science research integrated with computational science and information science in collaboration with domestic and overseas research

institutions.

5. The scrutiny of sequence information in NCBI and EBI, which many researchers use as reliable sources of information, and the optimization of genetic resource information are very important activities as an international response to correct errors that are overlooked by each institution.

## **6. Integrated Bioresource Information Division** **(Division Director : Hiroshi Masuya)**

**TOR1.** *Evaluate the responses to the 2019 AC recommendations.*

1. The opinions of the BRAC have been appropriately categorized and carefully addressed. Some of the issues such as research infrastructure development, security, and Business Continuity Plan (BCP) measures seem to be work in progress, but it is expected that the Division will be addressed by continued actions.
2. Both the number of website users and the number of searches have reached the level of major information centers worldwide. In particular, the development of Business Continuity Plan (RDF) data for bio-resources is unparalleled and will continue to be a leader in this field. To further utilize the advantages of data integration through RDF, collaboration with other organizations to improve user convenience is recommended.
3. The Division is taking the lead in integrating metadata from diseases to various species, leading to results in a variety of study fields. Maintaining the server while ensuring security and coordinating with RIKEN's policies is not easy, but steady progress is being made.
4. The Division plays an important role in the internationalization of BRC efforts and functions well as an international hub.
5. There seems to be a limit to personnel development within BRC. BRC should consider measures such as planning on-site lectures on IT education in cooperation with science-related university faculty and graduate schools.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

The Division's plan is appropriate, as it is in-line with the overall policies of the Center. In particular, the use of AI is expected to be in high demand from various study fields, and opportunities for collaboration should be created. The automatic extraction of bio-resource-related papers is an issue with high practical demands for NBRP. Therefore, it is expected to be put to practical use. The Division is expected to promote discussion and practice on how to utilize AI-related services that are continuously being released in life science. The following operations and activities are unparalleled.

- Data integration and standardization

Development of a cross-search system for five bioresources with an integrated knowledge base

- 1) Continuous enhancement of the knowledge base
- 2) Transfer and re-development of mouse genome variation database

- Improvement of web content

Update web content, delivery of email news, and maintenance of security and systems.

- 1) Grow access count
- 2) There was a thorough renewal of the website in 2020 and continuous improvement thereafter

- Big data analysis

- 1) Construction of a prototype of a cloud-based AI analysis platform and development of methodologies for big data analysis

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. The Division's plan is appropriate and solid. In particular, the promotion of international cooperation for RRID and the development of an online system for resource provision and deposition should be promoted in cooperation with other resource and information centers besides RIKEN. Since RDF and



ontologies generally have aspects of their true value that are difficult to understand and there are doubts as to whether they are truly practical, the challenge of predicting the future, whether successful or not, is considered significant in terms of clarifying the issues.

2. The Division is expected to make further efforts to decentralize servers, strengthen security, and operate them on a 24-hour basis. It is important to balance the use of external cloud services with the operation of RIKEN's internal storage servers (preservation of RIKEN's data).
3. To effectively promote the bio-resource cycle, information must play a central role in integrating national and international resource information and suggesting the next necessary resources from that information. The Division is expected to coordinate with various resource providers to expand new resource development projects as national projects.

## **7 Bioresource Engineering Division** **(Division Director: Atsuo Ogura)**

***TOR1. Evaluate the responses to the 2019 AC recommendations.***

1. The major issues raised by the previous review committee have been fully addressed, and the continued world-class research is highly commendable.
2. The Division has successfully developed cutting-edge technologies such as identification of genomic plasticity factor Rbl2 in 129 strains, development of hamster genome editing technology, elucidation of epigenomic characteristics of trophoblast stem cells (TSCs), improvement of intracytoplasmic sperm injection (ICSI) using spermatocytes, and blastomere cloning of common marmosets. Thus, the major points raised by the 2019 BRAC have been adequately addressed.

***TOR2. Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).***

1. Technical protocols and new technology series are posted on the website. Thus,

the Division has conducted adequate technology transfer.

2. The Division's mouse cryopreservation technologies and reproductive technologies are routinely used by the Experimental Animal Division, and thus they make a very significant contribution to the entire operation of BRC.
3. The Division contributes to BRC's global presence by conducting collaborative research with many overseas research institutions and by publishing outstanding research results in top journals.
4. Further expansion of the protocol collections on the web page is recommended.
5. Accepting high school students for laboratory tours is important for broadening basic public scientific knowledge, so it should be continued.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. Continuing the current activities will fully contribute to the development of the Center and bioresource projects.
2. The goals of the Division are appropriate. The developed technologies should be disseminated to other laboratories within BRC and to the rest of the world.
3. The BRAC would like to see more research that could increase the value of wild-derived mice. They are already valuable resources in our country and have many characteristics not found in standard laboratory mice. The BRAC hopes that these activities by the Division will make wild-derived mice recognized by researchers inside and outside Japan as Japan's unique bioresource.
4. As genetic modification technologies, including genome editing, are already mainstream, the BRAC is waiting for the next technological development. Our country's unique tools are expected to be generalized worldwide, along with the link to medical information and a trend toward decreasing "wet" experiments.

**8. Mouse Phenotype Analysis Division**  
**(Division Director: Masaru Tamura)**

***TOR1. Evaluate the responses to the 2019 AC recommendations.***

1. Responding to requests from the research community, the Team (Division) has appropriately developed phenotyping technologies and updated their equipment. A beneficiary-pay system with reasonable fees has also been implemented at the Japan Mouse Clinic (JMC). The BRAC gives the Team a high evaluation for this point.
2. In response to the previous advice from the BRAC, efforts have been made to increase the number of phenotyping results released by the JMC.

***TOR2. Based on the results of the Center's self-analysis, evaluate operations and R&D activities for the 4th Mid- to Long-Term Plan period (FY2018-2024)***

1. The Division has contributed to international efforts for mouse phenotyping, participating in the IMPC. The BRAC has evaluated the Team very highly on this point because the Team co-authored milestone papers published by the IMPC.
2. The BRAC considers the technological development of X-ray CT imaging methods to be among the best in the world, as it far exceeds the level achieved by many of the world's other major bioresource centers.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. The Division plans to advance phenotypic analysis and increase its efficiency by introducing automation and machine learning, and aims to collect a large amount of data with limited personnel. The Division should consider how to promote large-volume data analysis that will contribute to the development of the Bioresource Infrastructure Program.
2. In order to make high-resolution CT methods useful for a wide-range of users, it is essential to grasp the needs of the research community and provide

information regarding methods. In addition, the BRAC feels that the Division should consider proposing the phenotyping project that uses this technology in the IMPC.

3. The BRAC hopes that the Division will establish a system to take opinions from experts and requests from the research community for selecting target genes and phenotypes.

## **9 iPSC-based Drug Discovery and Development Team** **(Team Leader: Haruhisa Inoue)**

***TOR1. Evaluate the responses to the 2019 AC recommendations.***

1. The Team adequately responded to all issues raised at the last advisory council. Particularly, the BRAC values the development of the organoid model and the establishment of the assay system through collaboration with researchers in engineering fields.
2. At the last BRAC meeting in 2019 the team had only just been established and there were several concerns about how it could function and contribute as a member of BRC while being in the satellite site at Keihanna. However, the Team has done more than the BRAC expected and responded to each issue with a strong sense of action.

***TOR2. Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).***

1. The Team's achievements have been well-balanced between two major categories of research and development: 1) collaborative research themes based on specific needs and 2) the "Bioresource Frontier Program", which has been strategically set up in consideration of domestic and international trends. The Team is one of the best in world at what it does, especially in the neurological field. Numerous research projects using disease-specific iPS cells have been conducted, each with important results. In addition to

technological development, establishing 40 types of rare disease-specific iPS cells is a noteworthy achievement.

2. The Team is conducting appropriate research and development to promote the use of bioresources, with a focus on solving social issues related to drug development. Particularly, the Team has obtained highly successful results doing basic research aimed at developing and modeling methods of inducing cell differentiation that contributes to drug discovery research. The Team has also provided technical support to universities and companies for analysis of pathologies and evaluation of drug efficacy.
3. The BRAC gives the Team a high evaluation for managing such a large number of projects. The development of iPS cells derived from rare diseases is also progressing. However, it might be easier to understand the Team's accomplishments if they could produce materials that visualize the entirety of these contributions. It would also be helpful if they could explain how its organization helped make these contributions.
4. The Team hired foreign researchers and made presentations at international academic conferences. The Team is actively promoting its achievements at international conferences and making efforts to promote international exchange. The BRAC gives a high evaluation to the Team for leading the development of young researchers via themes that take advantage of the Team's characteristics and strengths.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. Labor shortages in Japan in scientific research fields is a very serious problem, including the field of bioresource banking. Continued employment and development of human resources (personnel) are critical for maintaining the bioresource banks.
2. The Team is expected to make a significant contribution to solving this problem by enhancing the significance and visibility of BRC's globally superior disease-specific iPS cell bank.
3. The BRAC suggests that the PI surveys and clarifies what needs to be done to promote the licensing of disease-specific iPS cells to academia and

industry (i.e., what kind of information is being requested? How smooth is the provision scheme?)

4. In the case of disease-specific iPSC cell resources, the most important obstacle is making sure that the cells can be properly induced to differentiate to the desired cell type by the user. Although the Team is already working vigorously on organoid differentiation, the BRAC would like the PI to determine the work processes that are left to the user after they receive the cells and make sure that users can use the resources as intended, with minimal effort.
5. In order to effectively deliver research results of a large number of diseases to pharmaceutical companies, it is necessary to visualize the research and development stages (phases) of each disease, and it is desirable to secure personnel who can grasp the entire project and support the PI.

#### **10. iPSC Cell Advanced Characterization and Development Team** **(Team Leader: Yohei Hayashi)**

**TORI. Evaluate the responses to the 2019 AC recommendations.**

1. All the issues pointed out in the last advisory council have been adequately addressed. However, the BRAC thinks that the Team should present a clearer explanation of what their aim termed “advanced characterization of iPSCs” means. The “basic characteristics” of iPSCs are pluripotency and self-replicating ability and the “advanced characteristics” may include stability or instability in maintaining pluripotency, and tendency to differentiate toward a specific differentiation lineage, or different epigenetic status. Although the results are preliminary, the Team has tackled this difficult issue and made some progress.
2. The establishments of disease-specific iPSC cells, pathological analysis, and further advancement into drug discovery have been successfully done. The BRAC appreciates each achievement, and at the same time expects the development of more fundamental technologies and platforms. In particular, the BRAC expects that “AI flow cytometry that enables cell classification without fluorescent labeling” will be a highly versatile technology.

3. The technological development is based on many unique ideas from a wide variety of fields, despite being led by a single PI. The BRAC full-heartily appreciates that all of these ideas are the result of a thorough knowledge of the cell-based research laboratory.
4. The BRAC gives a high evaluation to the establishment and deposition of several reporter iPS cell lines to the RIKEN Cell Bank. This is a significant contribution to research fields.
5. The BRAC also acknowledges that necessary items such as the development of reporter-visualized iPS cells have been addressed during this period.
6. Collaborations outside of RIKEN, including those overseas, are sufficient, but the BRAC would like the PI to strengthen collaborations (both information sharing and joint research) within BRC and with other RIKEN centers. The BRAC also would like the Team to further improve the bioresources and analysis systems and contribute to the community.

***TOR2.*** *Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).*

1. With regard to BRC's iPS-cell resources, this Team is making strong contributions that help BRC users, such as confirming the differentiation potential and introducing reporter genes. In addition, the Team is also providing technical support for the analysis of pathologies. Thus, the BRAC judges that the Team is operating appropriately in accordance with the 4th Mid- and Long-Term Plan.
2. From a broader perspective, this Team is working toward the goals of the 4th Term Plan period. The project proposals have been accepted as RIKEN, AMED, or Japan Society for the Promotion of Science (JSPS) projects, and active international exchange was conducted. The Team is also demonstrating true internationalization by hiring people from overseas to work in the Team.
3. The PI has high expectations for his future international activities, such as organizing a comprehensive collaboration with the University of Melbourne.
4. As the laboratory with a young PI, the BRAC appreciates that he supports the transfer of many students to academia. The PI also actively publicizes research outcomes. The Team actively accepts graduate students and provides

educational opportunities.

5. The Team is vigorously engaging in outreach activities and contributes to the research community, including the Japanese Society for Regenerative Medicine.
6. The Team actively applies for international exchange programs and has been accepted to several. The Team is making efforts to build a Team in which researchers from foreign countries can easily participate. This is exemplified by conducting lab meetings in English.

***TOR3.*** Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.

1. All of the plans for the remaining period are meaningful and attractive and will contribute to the development of BRC and the bioresource development project. On the other hand, the number of items to be implemented is quite large relative to the size of the Team. It may be a good idea to prioritize the contents of the projects according to the progress of research in the future. The plan shown in the presentation contribute to the development of the bioresource development project, but the BRAC would like the PI to share a more concrete and detailed plan.
2. The BRAC would like the PI to review the technologies that have been developed by this Team so far (including those conducted as research activities to be strengthened with competitive funds). The idea is explicitly to link them to the “advanced characterization of cells,” and if this cannot yet be done adequately, to devise ways to converge them to the “advanced characterization of cells” by generating additional data as needed.
3. Using the technology for highly efficient and successful knock-in, how about building a reporter system for expression of genes associated with differentiation tendencies reported so far and sorting at the level of strain selection or individual cells in a strain?
4. It is excellent that the PI is considering using the Web as a means of providing information. In addition to the resources, the BRAC would also like information related to the resources to be highly accessible.



## **11 Next Generation Human Disease Model Team** **(Team Leader: Takanori Amano)**

***TOR1. Evaluate the responses to the 2019 AC recommendations.***

1. Through active collaboration with clinical researchers, the Team was able to contribute to advances in clinical research by producing model mice that address diseases that are important to society and needed by the research community. In addition, the Team has worked on solving urgent issues such as knocking-in long DNA donors, and has a long-term vision for creating multifactorial disease models. Considering the above points, the BRAC judges that the Team has suitably responded to the issues that were raised at the last advisory council.

***TOR2. Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).***

1. The Team is currently clarifying whether Japanese Fancy Mouse 1 (JF1) has different characteristics from standard strains. The usefulness of JF1 will be further demonstrated by showing actual cases in which the same genetic mutation produces a different phenotype in JF1 than in the standard strain. Additionally, an easy-to-understand explanation of the usefulness and utilization of JF1 mice will be required.
2. The analysis of regulatory regions will become very important in the future. However, the probability of obtaining specific phenotypes is low with exhaustive mutant mouse production. The committee feels that narrowing down use of *in silico* analysis before mouse model production is important for increasing efficiency.

***TOR3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. The research plan is substantial and could be put to use for human disease research. Further, the results are expected to contribute to the bioresource project. The Team needs to have a vision for “next-generation human disease models” and to incorporate the Team’s original ideas and thinking.
2. The BRAC hopes the Team will collaborate more with clinical researchers and share best practices for collaboration between those researching disease genomes and those studying disease models.
3. However, the BRAC is concerned that the current research plan may be too ambitious in terms of the number of staff belonging to the Team and the amount research funding that the Team has obtained. It may be necessary to consider prioritizing the parts of the research plan based on current conditions.

## **12 Plant-Microbe Symbiosis Research and Development Team** **(Team Leader: Yasunori Ichihashi)**

***TOR 1. Evaluate the responses to the 2019 AC recommendations.***

1. The major comments and advice have been properly addressed.
2. As for the recommendation, “Although the Team is still in its inaugural year, the Team members, including young researchers and research assistants, seem to be working well. Young members should be mentored to ensure that they produce results relevant to the research Team,” the Team responded to the recommendation adequately and this is obvious by the fact that the development of young researchers is progressing smoothly (some have received awards for young researchers, as described below).

***TOR2. Based on the results of the Center's self-analysis, evaluate current operations and R&D activities (FY2018-2022) in the 4th Mid- to Long-Term Plan period (FY2018-2024).***

1. Consolidation into two research projects, “Symbiotic microbial resource” and “Digital twin in agriculture,” is evaluated to be in line with BRC’s 4th mid- to long-term plan.

2. The development of the digital twin in agriculture is remarkable and the cooperation with domestic academia and industry is developing well and has reached a sufficient level.
3. As for symbiotic microbial resources, the hope is to develop a million-screening technology and further isolate Arbuscular Mycorrhizal Fungi (AMF) from field soil. An opinion was given concerning the overlap between the AMF resources developed by this Team and the resources collected by the National Agriculture and Food Research Organization (NARO) Genebank. A future task will be to expand the resources that can be differentiated from those of the NARO Genebank.
4. This Team has become a domestic hub for the plant-microbe interaction collaboration, such as development of the digital twin in agriculture. The hope is that this hub function will expand from Asia to the world.
5. The Team comprises excellent young researchers. The development of young researchers is progressing smoothly, and some have received young researcher awards. This fact shows that the research environment of this Team is good and that its research projects are becoming more attractive.

***TOR 3. Evaluate the policies of the 5th Mid- to Long-Term Plan period (FY2025-2031) and recommend new directions for operations and R&D that should be implemented and promoted.***

1. This Team plans to further promote and develop the digital twin in agriculture and plant-microbe related bioresources, and their achievements are expected to contribute to the development of BRC project.
2. The development of the digital twin in agriculture is very important in terms of “green innovation.” To contribute to “green innovation,” this Team is expected to further accumulate research technology bases, publish results, and strengthen domestic and international networks.
3. This Team is encouraged to push forward with basic research and applied research without hesitation. The development of plant-microbe related bioresources by this Team will make a significant contribution to BRC even if it takes time.

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