

The 17th Resource Committee of Experimental Animals
Evaluation and Suggestions

(January 22, 2019)

Division/Team Name: Experimental Animal Division

Division Head: Atsushi YOSHIKI

1. Achievements and plans for the Division

(1) Have the current achievements reached the standards of those made by the major international bioresource centers?

● Collection, Preservation, and Distribution

Experimental Animal Division reached the highest global standard in all aspects as mouse repository such as the numbers of preserved and distributed mouse strains and the variety of collections. Approximately 250 mouse strains are collected annually. As of FY2018 nearly 8,500 strains have been collected and after the 18-year operation since its foundation. The Division is evaluated that it has become one of the top 3 major mouse repositories in the world together with the Jackson laboratory holding 9,000 strains in the US and the European Mouse Mutant Archive (EMMA) with 6,000-7,000 strains in Europe. The Division has made a particularly large contribution to the collection of the unique mouse strains developed in Japan. Since the start of its operation, BRC as a whole has provided a total of 5,099 overseas institutions in 71 countries with its bioresources, including mice to 800 institutions in 39 countries.

● Quality control (QC)

The Division also reached the highest standard in QC. They have advanced the QC of mouse strains by implementing original genetic and microorganism tests. Furthermore, a high level of microbial tests is being developed by the support from FY2018 National BioResource Project (NBRP) “Fundamental technology upgrading program”.

● User’s outcome

Mouse users have published 870 papers and 37 patents using the mouse lines since the start of operation. Over 80% of papers were published in high-impact journals with an impact factor of 3 and above (IF 3+).

(2) Have sufficient achievements been made for contributing to society and to the research community within Japan and overseas?

● The Division provides 300-500 mouse strains in Japan and to overseas constantly each year.

- The number of publications made by users of these mouse strains, and the number of mouse strains provided to industry and patents established by R&D with the resources, all demonstrated that the Division has made a very significant contribution to the research community in Japan and overseas, as well as to the industry. Apparently, those facts reflect their high level of QC.
 - The Division has been correcting information required for genetical QC and cleaning-up microbial contaminations. This improvement contributes to high accuracy in animal research and improves the animal welfare.
 - It is highly evaluated that the Division developed with a company a PCR Test Kit for genetical QC based on the Division's original method and made the kit commercially available to research community through the company.
 - The Division is contributing to improvement, expansion of applications, and safety assessments of genome editing technologies, by improvements in fundamental technologies and generation of disease models in the NBRP project and the international consortium.
 - The Division is contributing to the society through a variety of outreach activities in regard to the recognition of the importance of bioresources.
 - Active involvement and contribution to international collaboration such as those from the International Mouse Phenotyping Consortium (IMPC) are encouraged. From now on, it is necessary to provide Japanese and international research communities with information from previous large-scale mouse mutagenesis programs as their novel properties could be useful and relevant for current researches.
 - It is difficult to evaluate the production and provision of mouse models which reflect genomic information for patients with rare and intractable diseases because of the limited number of such mouse strains at present. However, we hope such mouse models should contribute to society and the patient community in the future.
 - It is recommended that the Division will make full use of the results of the QC tests as in feedback for depositors and users as well as disclosure of information associated with resources. In the future, it is recommended to further strengthen the collaboration between researchers and related institutions, in order to improve community relationship.
- (3) Are current activities and plans based on the results of the 3rd Mid- to Long-Term Plan or the achievements in the previous position? Are they in line with the BRC's 4th Mid- to Long-Term Plan (7 years from 2018 to 2024)? Are they appropriate and do they contribute to the development of the center?
- The Division is contributing to the development of BRC by fulfilling their important mission of collection and distribution of genetically-modified mice as bioresources. It is obvious that the Division is internationally appreciated as the Division is not just collecting mouse resources but conducting high level genetical and microbial QC.

- The current activities and plans with the major objectives of “Understanding sophisticated life phenomena, improving human health, and conquering diseases” consist of the core of the 4th Mid to Long-Term Plan and will serve as the driving force for the development of BRC.
 - Based on the results of the 3rd Mid- to Long-Term Plan, the Division plans to generate and supply more sophisticated disease models by incorporating state-of-the-art imaging technology, gene expression analysis technology, and physiological and morphological analyses. This plan is consistent with the center's mission.
 - As was in the 3rd Mid- to Long-term Plan, collaboration with teams within BRC is recommended in the current 4th Mid- to Long-Term Plan. The present plan will contribute to the advancement of BRC by accelerating new technical development through increase of collaboration with other institutions that possess similar technology.
 - Because the Division’s collaborations with research communities are currently limited, more effort is required to expand. To accelerate the progress of the development plan and thereby contribute to the center’s advancement, the Division must strengthen the cooperation with other institutions that possess genome editing and other technologies, and must listen to the opinions of clinicians on what kinds of mouse models should be generated.
 - Genome editing allows simple knock-out and knock-in mice to be generated by any researcher, so the Division should try to distinguish BRC’s resources from others.
 - While it is understandable that resource operation will take time, the Division head is encouraged to make future improvements in the quality and number of paper publications, in which the Division head is the corresponding author.
 - A clear explanation of the position or role of this Division in the IMPC is required.
- (4) What are resources to be developed and research/ technological development to be undertaken in addition to those currently planned in the initial 4th Mid- to Long-term Plan?
- It is difficult to determine what kind of mouse strains should be collected as it depends on user’s need. However, the dissemination of information on previously collected and archived resources is required.
 - It is recommended to generate and supply new highly versatile mouse strains in response to the growing needs.
 - Since further human resources and financial support are necessary to advance the planned technological and research developments, the Division should draw a road map and ensure its proper implementation.
 - The Division should search the needs of the institutions which are studying aging mice and supply necessary aged mice.

- Mouse resource database should be developed in BRC, incorporating information on human diseases. Items to be considered are:
 - Improvements in the dissemination of information on previously collected and archived mouse strains
 - Integration of resource information for similar mouse strains, and
 - Link mouse strains with relevant cell lines such as human iPS/ES cell lines and genetic materials.

2. SWOT Analysis

(1) Are the results of the presented SWOT analysis valid?

- The results of the SWOT analysis are generally reasonable.

(2) Are the countermeasures for the results of the SWOT analysis appropriate?

- It is important to disseminate the information associated with mouse resources, as mentioned in the Weaknesses in supplying the resources, and it is recommended to incorporate the linkage to Mouse Genome Informatics (MGI) at the Jackson Laboratory in the US as well as to the information accumulated in our nation.
- Based on the foundation that the Division has built, comprehensive plans and policies are appropriate countermeasures to the results of the SWOT analysis.
- In regard to grasping users' needs and improving service as mentioned in the enhancement of the Strength, it is recommended that future analysis of users' data is necessary for marketing. This would include mouse models that are frequently requested and research fields that can be widely utilized.
- Publishing papers should be the countermeasure for the Weakness.
- To ensure the BRC's continuation, the Division should diversify the sources of income to secure financial resources and limit the threats, and they should develop Human Resource, and employment systems to ensure successors. More specific policies must be made and presented.

3. International collaboration

(1) Is the international collaboration being actively addressed, and is the Division functioning as a hub of international science and technology?

- International collaboration has been carried out through information dissemination, such as through the International Mouse Strain Resource (IMSR) portal.

- The Division is recognized as one of the three major mouse repositories, together with The Jackson Laboratory in US and EMMA in Europe. Furthermore, the Division has functioned as an international hub of science and technology, as the Editorial Policies in “Nature” introduced the Division as a representative supplier of research materials for reproducible research.
- Besides the international collaboration as in the IMPC, the Division is functioning as an international hub and a leader in Asia, pioneering unique collection of mouse resources containing genetic variations that correspond to variants in human populations.
- It is recommended that the Division should increase their international presence by focusing on Japan's strengths, high-level collaboration within RIKEN, and active dissemination of information in Japan and overseas.

4. PI assessment

(1) Is the PI fulfilling the role in line with the BRC mission?

- As clearly demonstrated by the numbers of collected mouse strains and those distributed in Japan and overseas, Dr. Yoshiki is fulfilling the PI's role in line with the BRC mission and he has had an excellent achievement.
- The PI leads the Division that has acted from both the global and local aspects, by addressing global issues, as an international hub organization, and local issues, such as the development of models for rare and incurable diseases which specifically affect Japanese. The PI is fulfilling its role in line with the BRC's mission.
- The BRC has been renamed as the Bioresource Research Center while spread of genome editing technologies are boosting interests and needs of general researchers toward bioengineering. We recommend that the PI should promote advanced technological developments as a world-class national research and development institute. We hope BRC will accomplish its missions during the 4th Mid- to Long-Term Plan.

(2) Do the PI's achievements in research and development (R&D) satisfy international standards in light of the following three aspects? (i) Results output and impact, (ii) Contribution to specific missions of each laboratory regarding research support and collaborative exchange programs within RIKEN, (iii) Pioneering new fields of research, acquisition, and commercialization of intellectual property rights, social education for science, the fusion of different fields, and social contribution

- (i)
 - Their highly reliable genetical and microbial QCs have been appreciated by more than 1,300 institutions from Japan and overseas. There have been nearly 1,000 publications from

researchers who have used their resources, of which almost 80% have been published in IF 3+ journals and are considered to be high-impact results.

- Their achievements in collection, preservation, and distribution of mouse strains are highly evaluated.
- Publication of papers by the PI as a corresponding author will be addressed for future evaluation.
- (ii)
 - The Division is steadily supporting researchers within BRC and collaborating with those in other RIKEN research centers.
 - Considering the overall scale, there is still room for further development in RIKEN's internal cross-collaboration programs, as well as the collaborations with labs in Wako, Kobe, and Yokohama campuses.
- (iii)
 - Recognition by general public is not so high, as compared to their contribution to the scientific community. But this is reasonable, considering the difficulties with disseminating the information due to the presence of activists opposing animal experiments.
 - It is recommended that the PI should make a plan of marketing research in the medical and pharmaceutical industries.
 - Their active efforts towards enlightening the general society on animal experiments are encouraged as their social contribution.
 - Considering recent decline of interest in sciences in primary education, it is recommended that the Division should make contributions to giving knowledge to elementary, middle and high school students and enlightening them.
 - It is difficult to evaluate their achievements in light of "interdisciplinary collaborations."
- (3) Is the PI appropriately tackling the management and operation of the Division? In addition, does the PI make efforts for training and development of young talent?
 - The PI smoothly operates the Division with a total of nearly 70 staff members.
 - In training the next generation of talent, it is important to consider aspects of international gender diversity.
 - Although there are issues in the entire field of animal research, it would be ideal to train personnel for both management operations and research activity.
 - The training and development of young researchers have not yet produced sufficient results. More efforts are needed in the development of human resources, in further cooperation with universities and research institutions both in Japan and overseas.

End