**The 5th Review Committee of Experimental Animals (A)**
**Evaluation and Suggestions**

**(January 22, 2019)**

**Division/Team Name: Technology and Development Team for Mouse Phenotype Analysis (Masaru TAMURA, Team Leader)**

1. Achievements and plans for the Team

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

- The Team is playing an important role in line with BRC's mission. The Team has been participating in the International Mouse Phenotype Consortium (IMPC) and its research projects are reaching the standards of the major bioresource centers in the world.
- In the IMPC project promoted by collaboration of 20 research institutions and funding agencies in 14 countries and regions worldwide, RIKEN BRC has been sharing the work of phenotypic analysis of 250 lines of knockout mice.
- It is difficult to operate constantly a phenotyping pipeline of high standard, but the Team has been carrying out well. The followings are highly appreciated as achievements in the research and development of phenotype analysis of the mouse: 1) results of the IMPC Early Adult Pipeline, the IMPC Late Adult Pipeline, and the IMPC Embryonic Lethal Pipeline; 2) the development of a new imaging technology for micro X-ray CT imaging; and 3) the development of method for high-resolution imaging. Achievements of the above results and developments can be highly commended.

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

- The IMPC's results were published in the well-known high impact journals, indicating that the Team is performing competently.
- It seems necessary to examine whether the IMPC's results are being well-utilized by Japanese researchers.
- By providing Japanese researchers with opportunity to analyze their mouse strains by the world-class phenotyping pipeline via the “Japan Mouse Clinic,” the Team has been contributing to the Japanese research community, and to the strengthening of the Japanese research.
- The Team is disseminating the phenotyping methods named “SHIRPA” as well as advanced imaging technology of X-ray micro-CT.

- Phenotypic analyses at the Japan Mouse Clinic have exceeded 150 mouse lines developed by researchers out of BRC, and the number of deposit lines is steadily increasing. However, the number of publications of the results of these lines is currently limited. This requires improvement.

（3） Are they appropriate 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?

- In the 4th Mid- to Long-Term Plan, this group is expected to play an important role in fulfilling the center's mission of international contribution and collaboration. Based on the results of the 3rd Mid- to Long-Term Plan, the Team's efforts will be centered on the IMPC. Regarding development of new disease model animals, it is anticipated that the Team will support the center's activities through joint research and the provision of technology to research groups within Japan and overseas.
- Current activities and plans include phenotyping gene knockout mice, from the embryonic stage to old age, using a world-class phenotyping platform. This concurs with the 4th Mid- to Long-Term Plan, and it will provide great contributions to the center's advancement.
- The continuous phenotyping with the comprehensive pipeline, development of telemetry analysis for behavior phenotype align with the 4th Mid- to Long-Term Plan. The plans are considered to be appropriate and contribute to the center's development. Moreover, based on their unique achievements, development of high-resolution soft tissue X-ray micor-CT analysis and new contrast agents for the X-ray micro-CT is promising plan with high originality. These proposed developments are expected to raise quality standards, and the resulting analytical methods will be used widely among the research community.
- The Team plans to produce physiological, behavioral and morphological phenotype data, which improves the quality of bioresources. These resources are expected to be widely utilized by the research community.

（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?

- New plans include developing new technologies to detect longitudinal change of phenotype and to comprehensively analyze mouse resource characteristics as follows: 1) analysis of physiological change with ageing (telemetry analysis); 2) analysis of behavioral change; 3) analysis of morphological change; and 4) the development of a new contrast agent for X-ray CT and method of gene expression imaging. Phenotypic information on disease model mice, which will be obtained by these new technologies, is expected to advance and improve quality of the mouse resources.

- The development of a behavioral phenotype pipeline is much-needed by the society. Yet, it is also necessary to fully consider cost-efficacy. It is thus recommended that telemetry analysis should progress concurrently. It is desirable to devise a system incorporating industry-academia collaboration. Moreover, such a system ought to advance joint research with engineering departments of domestic universities that are carrying out related technological development.
- Regarding high-resolution soft-tissue X-ray CT analysis, and the development of new contrast agents, it is necessary to consider ways of strengthening collaboration with the disease research community and promoting resource use.
- The timely updating of equipment is an important topic. The Team should make efforts for continuous equipment renewal using various methods (such as the free loan of equipment developed through joint research).
- Though it was a topic of debate in the 3rd Mid- to Long-Term Plan, it is important to establish beneficiary charge system for the on-demand phenotyping by Japan mouse clinic that is conducted to accommodate requests from outside scientists, for continuation of its operation. The charge system should be examined.

2. SWOT analysis

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

- They are generally adequate. The issues to be resolved have become clear.
- The development of young talent is an important topic. Superb young talent will not come if they cannot envision a subsequent career path. Accordingly, the PI must help young researchers to develop a clear career path.

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

- The Ogura's laboratory in BRC is doing an excellent job carrying out talent development. In this regard, it should be referred to as a model case.
- It is also necessary to appeal to disease researchers, including the medical community, to further improve resource promotion.
- While some operations can be automated, e.g., imaging analysis. On the other hand, there is an urgent need to fulfil those duties (such as dissection) that cannot be replaced by machine. Therefore, intense deliberation has been directed towards allocations within the budget, and the improving plan is reasonable. It is recommended that some of running costs will be secured by the AMED project, academic-industry collaboration, beneficiary charge and others.
- The issues of securing and developing young talent are concerns shared by universities. Examining their salary and the content of duties are necessary steps in resolving these issues.

3. International collaboration

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

- The Team is participating in the IMPC and AMMRA/AMPC, and is also committed to ensuring a presence in Asia. Thus, the Team is functioning well as an international science and technology hub.
- Data from the Japan mouse clinic could be more useful and utilized more often if the data are linked to those of the MGI and IMPC.

4. PI assessment

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

- Considering the PI’s participation in the IMPC, his role is in line with the BRC’s mission.
- The Team leader is contributing to the BRC's mission by directing development of novel methods such as X-ray micro-CT technology, and the development of contrast agents.
- The Team leader needs to respond to the self-evaluation regarding delayed publication of the results of Japan mouse clinic.

（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

- The PI is performing satisfactorily in terms of the above all three perspectives.
- When a new technology is developed, it must actively be transferred to commercial entities.
- The results of international joint research have been published in high-impact international journals. Research support, RIKEN internal collaboration, and social education activities are also being carried out steadily. Such activities are satisfying international standards.
- IMPC is exceptionally important in establishing research infrastructures, although the result of each project of IMPC has little impact. On this point, it is excelling. If the method of phenotype analysis with telemetry were developed, the committee hope that it will be international standard protocol.
- Due to the lack of documentation, the achievements of the acquisition and commercialization of intellectual property is unclear.

- Regarding social outreach on science, it is necessary to strengthen activities which focus on a broad range of research fields.

(3) Is the PI appropriately tackling the management and operation of the Team? In addition, does the PI make efforts for training and development of young talent?

- The Team lacks a sufficient number of researchers who are able to conduct phenotyping of large number of mice. Securing new talent and developing young talent has not progressed in these early stages. It is necessary to improve on this. There are issues in the mechanism for recruiting new talent. Young talents will not come if they are not sure they can build a career path. It is necessary for the PI to create career paths for them.
- The PI has acquired competitive funding and he is giving technical classes and lectures.
- Phenotype data is likely to be used more widely by the research community in the future. Therefore, it seems necessary to further strengthen information dissemination not only to basic biology researchers, but also to clinical researchers.

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