

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

(January 22, 2019)

Division/Team Name: Technology and Development Team for Mammalian Genome Dynamics
(Kuniya ABE, 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 reaching the global standards for research by obtaining excellent achievements in the following points: (i) output and impact of research, (ii) specific missions such as research support and the RIKEN internal cross-collaboration program, and (iii) pioneering research fields, acquisition of intellectual property rights and commercialization, social enlightenment, merging of different fields, and social contributions etc.
- The Team is developing valuable initiatives for the development of novel resources by using techniques such as epigenotype analysis and genome modification to further clarify the control mechanisms of development.
- Through Wnt signal inhibition, they have established a highly efficient method for creating EpiSC lines, and have succeeded in the maintenance and homogenization of induced pluripotent stem (iPS) cells in an undifferentiated state. These have been used as a bioresource in quality control systems.
- The development of epiblast stem cell (EpiSC) and the cell phenotyping technology utilizing AI based on cell morphology are important for resource developments.

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

- The Team is conducting international collaborative research and producing research results of the global standards.
- Since the Team is collaborating with companies for technological development, the Team should consider strengthening further collaboration with industry.
- Not only creating an environment that can supply the naïve and the primed stem cells, but also the Team has made consistent achievements by publishing research article and reports.
- The Team has published some of their results by the joint research and development projects with companies and other institutions, by establishing cell lines for visualization of DNA methylation and generating a high-brightness luciferase genetic resource.

- As academic activities, the PI has served as the Secretariat of the International Mouse Genome Society since 2017. Moreover, he has been appointed three professor positions tasked with educational activities and has had a good record. The PI serves as a professor of the Cooperative Graduate School and the Collaborative Graduate School of the University of Tsukuba, Japan, and a visiting professor of the Universiti Sains Malaysia.
 - It is necessary to advertise their achievements and the possible applications by showing the numbers of resource distribution and of citation of their methodology papers.
 - How far actual developments can be made regarding distribution of resources to researcher communities within Japan and overseas and the promotion of joint research are issues for the next phase. It is necessary to clarify the objectives by making a road map of research plans.
- (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?
- A plan has been formulated in line with the issues pointed out for the achievements of the 3rd Mid- to Long-Term Plan. The Team plans to develop a cell image processing technology as a cross-sectional project within RIKEN. This plan is appropriate and takes advantage of each participating team.
 - The research plan is in line with the mission of the Bioresource Infrastructure Divisions "Understanding sophisticated biological phenomena, improving human health, and overcoming disease", and it may contribute to the development of BRC.
 - When the plans of the Team are accomplished, significant progress will be made to the current cutting-edge technologies including the analysis of higher-order functions at cell levels and whole body level of animals, and the analytical systems for disease-related gene networks. The results may, therefore, contribute to the development and production of mouse strains and human iPS cell lines in which a whole target pathway is collectively controlled.
 - The plan to construct a system that noninvasively assesses the state of iPS cell differentiation using time lapse imaging and machine learning is valuable. There is a high possibility that the construction of a gene expression control system, using CRISPRi and CRISPRa, will be widely used by the research community. If noninvasive detection of epigenomic changes can be achieved, it will greatly contribute to the research community.
 - The Team is putting significant effort into the development of advanced novel technologies, such as single-cell analysis and allele-specific gene expression analysis. It is appreciated, but they seem to be too much with introducing new technology. They must consider focusing and balancing their efforts.

- The Team is focusing on the development of technologies that standardize and analyze iPS and Germline Stem (GS) cells developed in Japan, which contributes to the Center's advancement. However, sufficient materials are not presented to evaluate if it actually contributes to the supply of resources and technologies from BRC.
- (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 would be appreciated if cell image processing technologies are actively promoted.
 - A new plan aims to develop a technology for detecting epigenomic changes in individual cells noninvasively and for analyzing the time-series changes as well as to develop bioresources relevant to these technologies. They are of great use for research on environment-genome interaction and aging process. These are highly anticipated areas of research that would enable the screening of influential environmental and aging factors.
 - The above project faces many issues in the supply of resources, including the research and development of core technologies and the development of EpiSC. The Team should focus on the proposed technological developments and consolidations.
 - The main research plans of this Team are epigenomic imaging and gene regulation. The both are highly needed. The Team should conduct the original research in order to be an international leader in this field.

2. SWOT Analysis

- (1) Are the results of the presented SWOT analysis valid?
- The results of the SWOT analysis are appropriate.
 - The hiring and keeping superb talent is necessary for the development of cutting-edge technology. However, when the staff members find out a good career to pursue, they should be pushed forward from the perspective of the development of young talent. Although this analysis is theoretically valid, this may be a difficult issue to resolve in practice.
 - It is better to clarify that which personnel is in charge of each objective and to define their role in each objective.
- (2) Are the countermeasures for the results of the SWOT analysis appropriate?
- The PI's term is limited, and it seems to be difficult to secure employees.
 - The project plans appropriately reflect the results of the "Weaknesses" analysis that "targets are diverse, and cannot necessarily be completed by his own team" and "the number of his staff is currently too small."

- From the various diverse project plans, it is important to select and focus on highly-original technological development. Moreover, it is also desirable that projects will include dissemination of the developed cutting-edge analysis technologies and resources to the research community.
- The response to the lack of human resources, by engaging in joint research within RIKEN is appropriate.

3. International collaboration

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

- This is being actively addressed, such as hosting a summer school.
- Individual joint research collaboration has been successful and highly appreciated over a long period.
- It would be beneficial if there were more international exchanges such as technical guidance and seminars.

4. PI assessment

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

- The PI is fulfilling his role in line with the BRC mission by contributing to three areas: (i) the production of novel resources, (ii) the development of technology to analyze resource characteristics, and (iii) internal collaboration within the center.
- It is necessary to appeal to companies and the research community on the utilization and potential applications of the developed technology and to promote its use as a resource.

(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 achievements of the PI's research and development have met the international standards based on these three perspectives:
- The dissemination of the information from their research, collaboration within RIKEN, and acquisitions of intellectual property rights have been sufficiently conducted.
- It is necessary to publicize these results.
- New technologies should be proactively introduced to companies.

- As for the contribution to society and social enlightenment, it should be proceeded by the whole center, not just by a single team.
- (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 PI is appropriately handling the management and operation of the Team. In addition, in the training and development of young talent, the PI has demonstrated accomplishments including researcher promotions, education of graduate students, and acceptance of international graduate students.
 - A more accurate evaluation will be possible if the information on the carrier path of alumni from the Team is available.
 - The replenishment of manpower is necessary to achieve the goals set out in the research plan in the 4th Mid- to Long-Term Plan.

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