

Evaluations and Comments

3rd Meeting of the RIKEN BioResource Center Review Committee (Technology and Development Team for Mammalian Genome Dynamics)

April 3, 2014

1. Achievements

(1) Has the Division, Team or Unit achieved sufficient results? Please evaluate and give us advice and suggestions from the following view point:

- **Has contribution been made to reinforcing BRC's raison d'être?**
 - **Have advanced, innovative results been achieved?**
 - **Have scientific results been produced?**
 - **Has there been social impact?**
 - **Has contribution been made to advancing BRC's resource infrastructure?**
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- The team produced successful results in three fields: bioimaging technology, genome polymorphism analysis, and stem cells. The development of bioimaging technology using three-dimensional internal structure microscope (3D-ISM) through joint research with Dr. Hideo Yokota, Team Leader of Riken in Wako, is of particularly high international originality and acclaim. Research on EpiSC cell analysis also seems very promising. These technological developments in general help to add values to bioresources and are therefore promising.
 - The research is of importance as part of bioresource frontier projects conducted within the framework of constantly advancing bioresource infrastructure. It has already made sufficient contributions and will certainly continue to do so in the future.
 - It has developed various, new imaging technologies, which made great contributions to a variety of fields. The 3D-ISM technology is particularly innovative and is expected to be put to a variety of applications in the future, e.g. adding values to reporter mice and Cre mice owned by BRC . The team also successfully established a method for epigenome (DNA methylation) analysis using a minute amount of cells, i.e. 100-cell, and appears to be making further advances in this direction.

- The team helps BRC achieve its purpose for existence. However, except for iPS, it is still necessary for the team to more clearly explain what they are doing, in order to clarify the difference between their research and other kinds of research conducted at universities. In other words, the team still has a little trouble explaining their contribution to the bioresource infrastructure.
- The discovery of large, germ cell-specific hypomethylated DNA domains is intriguing.
- Genome modification, i.e. epigenome analysis of germ cells may lead to dramatic changes in conventional concepts.
- Vps52 was identified as one of the causal genes of lethality in the t-complex region, which is one of the long-term pending issues in biology.
- The method to establish EpiSC cells by adding Wnt signal inhibitor enables highly reproducible EpiSC cell research. It is commendable in terms of academic achievement and highly praised in terms of novel development of bioresources.
- It was not clear how the research budget has been obtained.

(2) Other matters

- **Collaborations within BRC and within RIKEN**
 - **Collaborations inside and outside Japan**
 - **Public relations activities**
- A variety of research cooperation projects have been established at the Center or Riken, as well as in and outside Japan to develop advanced technologies, and these collaborative efforts have produced successful results.
 - Various research groups in Riken are engaged in a variety of cooperative projects, and highly acclaimed research papers have been published by these teams. It is worth mentioning that two joint research papers have appeared in the journal Science.
 - The cooperative efforts in Japan are commendable. However, it is necessary to make further efforts for international cooperation.
 - There is a feeling that although BRC has made many achievements, that fact is not sufficiently conveyed to the public. It may be better for Riken BioResource Center (BRC) to publicize its activities in a systematic manner as an organization, rather than by its field.
 - From the contents of the research, it seems that information is mainly provided through

academic papers. Although there is no problem per se with this approach, the problem is how to communicate this to the general public.

(3) Response to previous year's evaluation and advice

- You have properly addressed the issues that were pointed out by our previous recommendations, particularly about reinforcement of the imaging technology.
- Your response has been appropriate, as your proposal to promote research that specializes in epigenome analysis and imaging, as previously noted, has been materialized.
- A variety of new technological solutions have been developed to address the two tasks of epigenome analysis and imaging. This effort is praiseworthy.

2. Plans as RIKEN's proposed change of status to a new system for Independent Administrative Institutions

(1) Are their plans appropriate to the proposed change in RIKEN's status? Please evaluate and give us advice and suggestions from the following view point:

- **Can dramatic advances be expected from their strategies and plans for the next 5 to 7 years?**
 - **Should proposed plans be undertaken in BRC?**
 - **What topics are effective and essential to implementing BRC's resource infrastructure?**
 - **Can advanced and innovative results be expected?**
 - **Can achievements that will lead to innovation be expected?**
 - **Can a major impact on society be expected?**
 - **Are the proposed plans novel, do they have high priority, and are they sufficiently specific?**
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- The research aims to develop and improve imaging technology from the organismal level to the cellular level, which is appropriate. The development and improvement of imaging technology is expected to make contributions to a wide range of life science fields. Analysis of EpiSC cells is an important research theme not only for improving stem cell biology but also for enhancing the value of cell materials. Overall, these research plans are

commensurate with a non-profit national R&D organization.

- Epigenome analysis and imaging planned by this team are tasks to be tackled by BRC in developing bioresource infrastructure. 3D-ISM is a particularly innovative technology, and its results can be very impactful. Therefore, it has very high priority.
- This is a new type of research aiming to fuse genome information with new imaging technology. Although there are still many technical hurdles to overcome, it is sufficiently feasible to implement it as joint research inside Riken. The Abe Laboratory has established a unique position in Japan. If Riken is designated as a non-profit national R&D organization, the Laboratory should be able to promote highly promising projects.
- iPS can be considered as an indispensable topic for bioresource projects.

(2) Are suggestions made previously reflected in their current plans and strategies?

Have they endeavored to re-inspect their activities to date and made appropriate decision about what should be continued or discontinued?

- The previous recommendations have been fully incorporated into the efforts made to develop the imaging technology.
- The research themes have been more focused and implemented in response to the previous recommendations. The PDCA cycle seems to have been properly used.