

**Evaluations and Comments**  
**13<sup>th</sup> Meeting of the**  
**RIKEN BioResource Center Resource Committee of Experimental Animals**  
**(April 10, 2014)**

**1. Achievements**

**(1) Are there any activities or achievements worthy of special mention?**

**(a) Is the Division functioning adequately as an infrastructure for science? What are its plans and achievements? What of the quantity and quality of its users' output (number of papers)?**

- The Experimental Animal Division is steadily achieving its objective based on an appropriate development policy. The Division is known worldwide as a mouse resource center whose users have produced outcomes. The division's activity is to be evaluated qualitatively and quantitatively.
- In particular, it has a substantial collection of mouse models for human diseases, as well as tissue-specific Cre and reporter mice.
- The number of items distributed is declining. This is partly because fewer live mice are being distributed, while distribution of frozen embryos and sperm is increasing. However, the causes of the decline in Japan in particular need to be explained, and countermeasures need to be taken. The number of users in Japan is shown for each of four categories, including universities. There seems to be some unequal distribution among the user categories. There also seems to be room for growth among users, e.g., among companies with large-scale animal testing facilities.
- Publications by users have become significantly high in quantity and quality. This result reflects the Division's steady activity to build up the resource infrastructure up to now.
- If mice distributed by the Division were presented at a glance with information such as the number of distributions and user's publications, this would further increase usability.

It is not an easy task to explain correctly and plainly deposited strains, especially human disease models, for ordinary users to approach, but the Division needs to make an effort to do

so.

**(b) Is the Division functioning adequately as an infrastructure for society? What are its industry and international contributions? Is it returning the fruits of its achievements to the Japanese people, and has it stimulated people's imaginations?**

- The Division has served as a core facility of mouse resources for Japan, whose national policy is to be a world leader in science and technology, and has provided an enough function as social infrastructure, but even greater achievements are expected than those done to date.
- The Division makes significant contributions internationally. It has distributed many resources to academia outside Japan, and is actively involved in FIMRe, IMSR, AMMRA, and IMPC.
- It has distributed relatively few resources to the industry compared to the academia. It is essential to appeal to each industrial company individually to boost use of mouse resources.
- It is important for the Division to contribute internationally by taking advantage of RIKEN BRC's features and playing a specific role, rather than playing a broader role than the Division has done in the past.
- The Division does a great deal to give back to the community. It takes PR initiatives, especially in Tsukuba City, and offers facility tours for junior and senior high school students. It should enrich these activities by, for example, providing a permanent exhibition to disseminate interesting life sciences among students.

**(2) R&D, technology development, resource development, characterizations and quality control**

- **Have these activities been effectively applied in advancing BRC's bioresource infrastructure program?**
- **Have advanced and innovative results been produced?**
- Research and technology development up to now: The Division has constantly implemented resource development, characterization, and quality control, which have contributed to the bioresource project.
- Research and technology development are indispensable for up-grade of the resource

infrastructure and raise-up of staff motivation.

- Microbiological quality has been appropriately maintained by adequate quality control programs. The results have been evaluated as steady state. When wrong mice were distributed, measures were taken promptly after the problem was discovered. The Division has also responded appropriately to claims, but it will be necessary to take adequate measures to prevent such problems from recurring. The majority of errors were by researchers who deposited resources, but the blame is sure to fall on RIKEN BRC. The Division must make every effort to establish better communication with depositors and ensure allele-specific genotyping of genetically-engineered mice.
- If the Division merely collects and supplies resources, all of its technologies and other resources will become obsolete. The funds necessary for research and technology development should be secured for future.
- The Division has obtained an outstanding result in reproductive technology which allows efficient collection of ova from wild-derived strain mice using anti-inhibin serum injection for embryo cryopreservation in collaboration with the Bioresource Engineering Division. This achievement is highly evaluated.
- The Division recently started to produce knockout mice using genome-editing technology, such as the CRISPR/Cas9. However, a more efficient collaboration is urgently needed to speed up the production.

### **(3) Other matters**

- **Education and training**
  - **Collaborations within BRC and within RIKEN**
  - **Collaborations inside and outside Japan**
  - **Public relations activities**
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- The Division actively shares tasks and collaborates with FIMRe, IMSR, AMMRA, IMPC, and so on to promote use of mouse resources effectively.
  - An example of collaboration within the Center is a partnership with the Bioresource Engineering Division for cryopreservation and with the Technology and Development Team for Mouse Phenotype Analysis for the IMPC.
  - PR initiatives include setting up booths at academic conferences. The Division is proactive in

basic science fields, but needs more effort toward medical science and industry and so on.

- Japanese scientists have led the world in developing and improving the reproductive technology such as in vitro fertilization and cryopreservation, which has become the world standard. RIKEN BRC has also been part of this effort, and the Division should use PR to the international community.

#### **(4) Response to items pointed out previously**

- It is important that the Division explains and calls attention to the earlier-mentioned IMPC initiatives to users, and at BRAC this June, it should explain its efforts and results in increasing the recovery rate of frozen embryos.
- Collection and preservation were accomplished in keeping with the original plan. So the budget cuts did not have a major impact on the project overall.

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

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

**(a) Can dramatic advances be expected from their strategies and plans for the next 5 to 7 years?**

- **Will they be able to function as an essential infrastructure for science, innovation, and society?**
  - **Are there any new resources that they should place priority on collection?**
  - **What kinds of results and effects can be expected?**
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- High priorities include expanding the Division's collection of tissue-specific Cre and reporter mice, as well as developing human disease models as counterparts to human disease-specific iPS cells.
  - Verification of Cre driver mice is expensive and labor-intensive, so it is essential to have ample funding. The Division must decide on its policy before proceeding, e.g., whether to spread its funding wide and thin, or to prioritize.
  - In the research community in Japan, recognition of the Division's results to date is not

particularly high. The Division would seem to need a more effective recognition-building plan for its results.

- As far as deposits are concerned, the Division needs to emphasize the BRC's unique characteristics by narrowing the focus of its collection. This will help the BRC establish its clear position globally. It is also important to use the Japan Mouse Clinic's imaging technology to search for the phenotypes of disease models.
- The Division should actively collect resources from the most advanced research fields in Japan. However, if the BRC aims to be a world leader, the Division should try to collect resources of wide fields to some extent so that the Center has a complete collection.
- Resource projects support the research infrastructure, so they should be firmly developed and maintained as a national policy. Therefore, the plan seems worthy of a "specified national research and development corporation."
- The direction expected of specified national research and development corporations is to focus on a narrow target and advance a specific subject. While a resource organization aims to respond to a wide range of research needs and establish an infrastructure steadily to support advanced researches, which is a very important assignment.

**(b) Can dramatic advances be expected from their research and technology development plans for the next 5 to 7 years?**

- **Are these plans effective and essential to promoting BRC's resource infrastructure?**
- **Can advanced and innovative results be expected?**
- There is great interest in collecting disease model mice, especially in collecting and developing disease models associated with iPS cells. However, the style and direction through which the two methods contribute to research are diametrically opposed. It will be necessary to carefully consider the potential for realizing outcomes through collaboration between the two.
- Development of treatment models is also important in that this gives back to society.
- Expanding the collection of Cre and reporter mice, and creating new knockout mice using the CRISPR/Cas9 system in collaboration with IMPC, among other initiatives, are useful and indispensable resource infrastructure projects carried out by the Center. Genome editing

technology is advancing day by day, and the Division's plan to collaborate within the Center to create, maintain, and distribute outstanding disease models will likely lead to great outcomes. In order to encourage more distribution of resources, it is very important that the Division develops resource-related information and upgrades its searching system. Additionally, because PR is a key to encouraging demand for resources, the Division must make a greater effort to collaborate with the information group.

- Needless to say, even resource infrastructure projects have to pursue advanced research and technology development and not fall behind.
- It would also be a good idea to clarify what policies RIKEN BRC has for participation in IMPC, which is funded in North America and Europe.
- The division should not be content with its current level of technology. One example is how to further improve the cryorecovery technology. It is important to have an attitude and a system that lets it work accurately with the rapidly developing research and technology.

**(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 evaluation is reflected. The best known point is the wide-ranging organizational reform and the change in content of each team within the bioresource R&D program. The Division is to be commended for having re-examined projects and outlined those that should be continued, and those that should be ended.
- The Division is commended for emphasizing targets with a richer range of content than just the number of specimens collected.
- The Division is operating appropriately despite its budget cuts.
- Even if the Division does not dispose of deposited strains that have not been used, reorganizing their listings is important, since it would promote more efficient use.
- Although there are few basic resource programs that should simply be ended, Division's programs as a whole have been reviewed and improved.