

Evaluations and Comments
13th Meeting of the
RIKEN BioResource Center Resource Committee of Genetic Materials
(April 8, 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 Gene Engineering Division currently preserves almost four million genetic strains and these, including libraries of scientifically important species, are important asset for future life science research.
- The amount of genetic material that is being distributed is increasing, and these resources are considered important and essential components of current life science research, both domestically and internationally.
- The number of research papers produced has increased and we consider that the distributed materials have contributed to an increase in the amount of high quality research. Thirty-two patent applications were submitted in the last five years. These research papers and patent applications represent only a small fraction of the amount of research; we assume that dozens of times the volume of research using the bioresources distributed by the Gene Engineering Division is being performed behind the scenes, which suggests that the Division is helping achieve results based on a scientific foundation.
- On the BioResource Center (BRC) website, there are links between libraries within the Center and with databases at other institutes, which indicates that consideration has been given to users' convenience.

(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?

- Approximately 25% of genetic materials distributed by the Gene Engineering Division are for research institutes overseas. The Division is making steady progress in its aim to become an international base of genetic materials.
- On the other hand, effective advertisement is necessary to acquire overseas users, because many institutes overseas may not know about the BRC.
- Distribution to industry totals only a few percent compared to that to academia; however, this is not surprising given the closed nature of technology development in for-profit organizations. The Division's bioresources have been functioning very well in relationships with for-profit organizations.
- The Gene Engineering Division has been collecting, preserving, and developing genes of enzymes derived from termites and filamentous fungi, which is a basis of bioethanol production. This work is valuable with respect to coping with the risk of global warming. Resources related to cellulase genes have already been used, which indicates the possibility of a profitable return from this project to the public, and we also consider that the Division provides hope to the public.
- The BRC supports many important domestic and international research projects and the importance of the BRC has increased. These research projects contribute to the future life and health of the "general public." From this viewpoint, we believe that the BRC returns sufficient profit to society and provides hope to the public.

(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?**
- We appreciate the development of adenoviral vectors that can be made visible by the expression of multiple proteins and fluorescence. Their utility may, however, be limited because users are required to manipulate the vectors themselves.

- One matter to be emphasized for the resource infrastructure project is that the Kyoto Encyclopedia of Genes and Genomes (KEGG) database of Kyoto University and the clone list of the BRC were linked and released to the public, based on suggestions from resource committee members.
- The Gene Engineering Division promptly performs quality tests for deposited research materials and takes appropriate measures in cooperation with a depositor if a problem is detected. An assessment system has also been established. The Division is trusted because of its well-organized quality control.

(3) Other matters

- **Education and training**
 - **Collaborations within BRC and within RIKEN**
 - **Collaborations inside and outside Japan**
 - **Public relations activities**
- The Gene Engineering Division should consider increasing the number of training opportunities and improving the content of training when many applicants desire it.
 - Biomass-related enzymes are managed as an intra-RIKEN project and the Gene Engineering Division is also involved in the project.
 - The Gene Engineering Division has been distributing materials to and exchanging information with 703 domestic institutes since 2001, and it has been playing an invaluable role as a hub to promote domestic research.
 - The website of the Division has been drastically improved and it is now easier to access the information and links that users require. The Division is actively engaged in exhibitions at various scientific conferences.
 - The Division has been making steady efforts to enhance local understanding and to draw children's attention to science by holding public exhibitions in Tsukuba City and organizing facility visits by junior high school and high school students, which gained public favor.

(4) Response to items pointed out previously

- **Concerning the use of resources that are entangled with private company licenses, the**

RIKEN BRC should pave the way.

- The Gene Engineering Division has been actively negotiating the licensing of materials, such as fluorescent proteins, from private companies that possess their rights, and taking appropriate measures.
- We were told that it is necessary to carefully handle the transfer of products to private companies because of issues of proprietary rights. On the other hand, because the transfer can put pressure on the private sector, this matter should be discussed between the BRC and private companies.
- **The RIKEN BRC should request that the BRC gene catalog number appear on KEGG.**
 - It should particularly be mentioned that the link between the KEGG database at Kyoto University and the clone list of the web catalog of the Gene Engineering Division was released to the public and that clone searching has become easier.
- **Training should be provided for very special techniques that are available only at the RIKEN BRC.**
 - The Division has been doing its best by selecting appropriate subjects for daily duties, as well as by making an effort to provide training for handling adenoviral vectors and training in the protein expression method and enzyme activity measurement method for biomass-related enzymes.
 - Training for very special techniques that are available only at the RIKEN BRC is desirable at a higher level, and for most advanced research, such as induced pluripotent stem (iPS) cells and clustered regularly interspaced short palindromic repeats (CRISPR), if possible.
- **RIKEN's organization has been drastically changed and the RIKEN BRC will be reviewed five years from now. The BRC should, however, demonstrate its direction as a center in approximately three years' time.**
 - The BRC has been taking appropriate measures for the matters that were pointed out by the previous assessment: 1) Prior to the RIKEN Advisory Council discussion in November 2014, each team within the BRC and the Bioresource committee should discuss the direction and 2) As a precondition, invite comments from the research

community about the importance of bioresources. The problem is how the latter action should be performed promptly.

- **The RIKEN BRC provides prompt feedback to users with information from the depositors, a follow-up service that similar resource centers are not thought to offer.**
 - We judge that the BRC provides much more careful follow-up of research materials that they distribute compared to other bioresource centers. To continue this service, it is important to maintain a close liaison with the depositors, and the BRC should persuade the depositors to better cooperate.

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?**

- The Gene Engineering Division has a plan to prepare resources that are closely related to future health policy and drug development, such as the preparation of disease-specific iPS cell libraries and sources of gene groups related to cancer, as well as to psychiatric and neurological fields. In addition, the Division will develop preservation methods for resources and enhance this information.
- To provide research support that is available only from the RIKEN BRC, the BRC should aim to provide proactive support, through which the BRC adopts rapidly developed research technologies worldwide and provides them to researchers, and custom-made support, through which the BRC manufactures and provides the highest quality research materials upon request from the most advanced domestic researchers. For this purpose, it is essential to establish a liaison system with researchers who are familiar with advanced technologies,

such as CRISPR. Dramatic results are anticipated by this plan.

- If genetic materials are useful for the formation of a society with sustainable development or for environmental conservation, the Division should prepare them as resources. Resources of enzyme gene groups related to the fixation of carbon dioxide and atmospheric nitrogen would be worth considering.
- The Division should consider cDNA sets of various species as new resources that should be prepared with the greatest priority in the future. Because the CRISPR/Cas9 technique is predicted to be widely used, guide RNA vectors for this technique would be useful resources.
- The rapidity and economy of development of research and technologies and the validity of research materials will be more important in the future. The Japanese government should plan to establish the BRC as a basic infrastructure and develop it permanently under a policy of promoting science and technology.

(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?**
- This resource project is very important and essential domestically and internationally to keep technology research and development advanced and innovative, for the purpose of establishing academic, innovation, and social infrastructures.
- Preparation of biomass-related enzymes is anticipated to be effective in bioethanol production. However, collaborations with companies will also be necessary in the future for practical application.
- To spread the technique that uses adenoviruses more widely, the Division has a plan to develop expression vectors for simultaneous multiple protein expressions, which we assume many researchers desire.
- The Division's judgment looks reasonable at this moment. The Division should, however, review its plans appropriately, because the advancement of technologies related to genome, mutant mouse preparation, and multiple sample analysis is rapid.

(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 review is reflected in the current plan, especially in the genome field.
- Advanced technologies, such as visualizing technologies, have already provided excellent results, and diversification of visualizing technologies is also included in the current plan. This reflects the attitude of the Division toward embarking on this plan during the solving of licensing-related issues.
- With respect to CRISPR/Cas9, an advanced technology, leading practical strategies through liaison should be given considerable weight, as should the collection and distribution of Cas9 and guide RNA for each species.
- The Gene Engineering Division should make a shift to preserve resources that are rarely requested for distribution and, in contrast, should conduct research and development so that new resources that will be requested often for distribution are modified into more usable forms and enhance the system of distributing the resources.