

Evaluations and Comments

13th Meeting of the

RIKEN BioResource Center Resource Committee of Cellular Materials

(April 9, 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 number of units distributed by the Cell Engineering Division has increased to 6,000 units/year in recent years, and distribution to overseas makes up more than 10% of that total. Factors supporting this increase are the creation of a standard distribution system and technology development for quality control and standardization.
- The rich variety of cells prepared and the infrastructure leadership that the Cell Engineering Division takes, most notably with its iPS cells, make it a cell bank that is renowned throughout the world. It supports research by distributing cells and information to researchers, thus contributing to society and enabling excellent outcomes.
- As for infrastructure policy, the Division practices strict quality control of general-purpose cells, including human cancer cells lines, and plans to further prioritize international collaboration on quality control. Therefore the Division is commended for its correct infrastructure policy.
- The policy under which it has already begun developing genome-edited cells and disease-specific iPS cells, demand for which is projected to grow in the future, is also correct. These cells are expected to be used for academic research, medical care, and in industry. The Division is therefore to be praised for the foundation of academics and its contribution to the industrial world.
- The number of research papers published in a year that are known to use cells distributed by

the Division has reached 700. In light of search method limitations, the actual number is believed to be even greater. Based on the fact that the overall quality of research papers using cells from Japan has improved in recent years, the contribution made by RIKEN BRC would appear to be quite substantial.

(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 Cell Engineering Division is steadily distributing cells to the industrial world too, but it will be necessary to do a survey of trends to determine what kind of cells industrial users want the Division to prepare.
- Distribution to users outside Japan totaled 13% in FY2013. Expectations for the Division going forward are that it will enhance the collection of disease-specific iPS cells, together with the fact that research is increasing in Asian nations, further increase the Division's international contribution.
- The Division's position of actively preparing disease-specific iPS cells inspires great hope for citizens in general and especially patients suffering from hard-to-cure diseases.
- Preparation of cells used in disease research, such as disease-specific iPS cells, offers hope for discovering new pharmaceuticals for treating hard-to-cure diseases.

(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?**
- The Cell Engineering Division is to be commended for establishing cell misidentification testing with STR polymorphism analysis. RIKEN BRC would also win praise internationally if it indicated that cell misidentification testing is reliably performed.
- In terms of quality control, the Division has established a quality management system and earned ISO 9001 certification. This was found to be very important and useful for ensuring

reliability and stability, which are essential aspects of resource projects.

- The Cell Engineering Division accepts commissions to perform analysis for quality inspections, which helps to raise the level of bioscience in Japan.

(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 Cell Engineering Division periodically hosts technical training on human embryonic stem cells and human iPS cells and provides technical instruction to many researchers. These efforts are highly commended.
 - Perhaps the Division could partner with the RIKEN Program for Drug Discovery and Medical Technology Platforms on the use of cells in applied research, such as drug discovery. This would be a way of collaborating within RIKEN.
 - Collaboration within Japan includes close partnerships with the Japanese Society for Regenerative Medicine, the Japanese Tissue Culture Association, and others. By such means, the Division is engaged in very active initiatives. It has a particularly close relationship with the Kyoto University Center for iPS Cell Research and Application (CiRA). Based on this foundation, it has built a system to establish disease-specific iPS cells and at the same time accept deposits of them. This is especially deserving of mention.
 - Internationally, several North American and European countries are beginning projects to prepare disease-specific iPS cells. The Division will need to consider international partnerships while firmly securing its own intellectual properties.
 - The Cell Engineering Division has built cooperative relationships with the world's major cell banks to eliminate cell misidentification, and is engaged in awareness-raising initiatives, etc. This too is highly commendable.
 - Resource projects should increasingly take place in an international framework. Thus it is important to foster next-generation resource personnel throughout Asia and over a wider area, creating an enthusiasm for elevating BRC standards until they become the world standard.
 - It is necessary to perform PR initiatives to make division operations and results better known

to industry and encourage its use of Division services. To that end too, it would be useful to call attention to successful examples of industrialization and to take the initiative in collaborating with the RIKEN Program for Drug Discovery and Medical Technology Platforms.

- The Division is asked to work to increase understanding among corporate researchers (especially those from pharmaceutical companies) by having them take part in lab tours to observe the actual facilities and listen to lectures.

(4) Response to items pointed out previously

- There is a gradually growing awareness that researchers cannot present their results at academic conferences and in research papers unless they use cells distributed by RIKEN BRC other Cell banks. On the international side, the Cell Engineering Division is to be commended for working to raise awareness of misidentified cells as a member of the International Cell Line Authentication Committee (ICLAC).
- The attitude of prioritizing which cells to prepare is quite understandable. The Division will need to seriously consider its stance on preparing disease-specific iPS cells going forward. The issues it must address are accurately tracking user needs and balancing the types and numbers of disease-specific iPS cells on deposit. At the same time, it must craft a long-term response to the question of what to do about preparing normal iPS cells that will serve as controls. RIKEN BRC should decide at what scale it will prepare iPS cells, including collecting genome-edited cells. In light of future growth in basic research and the pharmaceutical industry in Japan, the iPS cell project should go forward as the core of RIKEN BRC's cell bank projects.
- RIKEN BRC will need to step up its efforts to secure a budget for large-scale preparation in its disease-specific iPS cells project.

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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- It is hoped that cells distributed by RIKEN BRC will become the standard cells for research in Japan. For that purpose also, the Cell Engineering Division is expected to perform even more thorough quality control and grow into its role as a world-leading organization.
 - It is important to prepare many varieties of disease-specific iPS cells, as well as iPS cells from healthy people, covering different ages and both genders. Detailed characterization, including differentiation potential analysis, is important as part of the quality control of iPS cells. It is also desirable that the Cell Engineering Division partner with industry as necessary to enable it to practice such high-level quality control. The above projects would be worthy of a “specified national research and development corporation.”
 - Cell research is developing at a faster and faster pace, making it possible that new groups of resources will be developed in the next five years. A system for preparing such cells, setting the standards for quality, and providing a steady supply of resources is the indispensable foundation for the advancement of new research and development of new pharmaceuticals and medical treatments.
 - The Division should consider measures to ensure that its resources are used by industry and turned into commercial products. For example, its distribution of disease-specific iPS cells leads to results in the research development of new pharmaceuticals and test agents. This consideration is the key to tomorrow’s big leaps forward. It could also consider speeding up the industrialization process by sharing BRC technology and providing information to industry as part of joint research. To that end, it might establish consortiums or collaborative research groups.
 - It is also important to patent the cells distributed and to establish patent rights, etc. It is hoped the Cell Engineering Division will solicit opinions from industry and build a cell bank project that is easy for users to use.

(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?**

- The Cell Engineering Division plans to perform STR polymorphism analyses of general-purpose cells and to establish a database based on that, as well as to perform high-level characterization, including differentiation potential analysis, of disease-specific iPS cells and genome-edited cells. This technology development is indispensable to pursuing cell bank projects in future and is thus commended.

(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 Cell Engineering Division is constantly re-examining its projects, and is clearly aware of those that should be ended, those that should be temporarily suspended, those that should be steadily continued, and those that should be newly undertaken.
- The human umbilical cord blood project is to be commended for taking demand into account and reducing the scale of its collection. It will continue to be important in the future to firmly grasp demand trends in the research community.
- Embryonic stem cells are likely to be used as controls for iPS cells, so it will be necessary to expand this collection in future, both from animals and humans. In addition, it is believed that genome-editing technology will enable researchers to make embryonic stem cells with a variety of disease-related genetic defects, so the Division should actively prepare these embryonic stem cells.