

**The 15<sup>th</sup> Committee for Cell Resource  
Evaluation and Suggestions**

(April 12, 2016)

**Cell Engineering Division**

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◎: Compulsory report items ○: Major report items ●: Optional report items

◎ 1-1a. *Have sufficient results been achieved? (The BRC's standing in the world, contribution to society.)*

- From the following perspectives, it can be evaluated as meeting expectations:
  1. The BRC is a world-renowned hub among cell providing institutions.
  2. Since quality management is a major precondition for providing cells, this is the most important item. The current stance should be continued.
  3. Results are showing a nearly consistent upward trend. This is evaluated highly.
- The Committee points out and makes suggestions to produce sufficiently enhanced performance in the future:
- (1) An extremely massive number of disease-specific iPS cells have been deposited, but few of them are used. Some suggestions are provided below:
- It is necessary to create a venue that will be appealing to many researchers and promote use of the cells.
- The users' technology, etc., is not prepared to deal with iPS cells, which are much more fastidious than ordinary cells such as cancer cells, so it is hoped that there are established venues for dissemination of technology during university education and other training.
- Most researchers may be hesitant to pursue this field, due to the complexity of research ethics screening in research involving disease-specific iPS cells, so it may be necessary to promote use by offering support for the creation of documents.

- (2) It is hoped that collaboration with new teams and new locations will be conducted to establish a system in which newly deposited cells and newly developed cells can be put to use as soon as possible.
- (3) When analyzing and evaluating performance with cell deposition and so on, it will be more convincing if not only the institution's own performance, but also data that compares the BRC's performance with the performance and characteristics of other major world-class cell banks, is added.

© *1-1b. Responses to previous comments and advice*

- From the following perspectives, it can be evaluated as adequately addressed:
  1. Infrastructure focused on disease-specific iPS cells is a move in the right direction.
  2. A total of 158 diseases, with 1,568 cell lines from 446 patients, have been deposited, and we believe that it will be extremely significant if iPS cells for all diseases are organized.
- The Committee points out as follows:
  1. It is believed that a very large budget and a large number of personnel will be needed for the ES/iPS cell infrastructure. The BRC will need further systems and infrastructures that will enable it to implement intensive resource preparation, and if this is designated as a national project, then construction of a support system that reflects the importance of the project will be essential.

○ *1-2. Is the self-analysis of strengths and weakness adequate?*

- From the following perspectives, it can be evaluated as adequately analyzed:
  1. It will be a major task to gather the following four types of cells: 1. ES/normal iPS cells, 2. Genome editing cells that insert disease-specific genes into them, 3. Disease-specific iPS cells, and 4. repaired iPS cells with mutated genes. Since these cells are the most basic, further hard work is expected.
- The Committee offers the following suggestions for further improvement:
  1. Concentration on iPS cells is in the foreground, but it would be desirable to consider promoting usage by providing a more

user-friendly environment, particularly by providing technological advice.

- For some portions that are deemed insufficient, the Committee points out and makes suggestions as follows:
  1. It is thought that the abundance of the BRC's resources is a strength, but it may be necessary to perform further analysis of the decrease in the number of cells provided in FY2015 and to prepare a more user-friendly environment. Moreover, the number of varieties of diseases-specific iPS cells has increased, but the number of provisions has not. This fact should be analyzed and it is required to prioritize preparation of the resources that are most needed.
  2. There is insufficient persuasive data as to why certain characteristics are defined as strengths or weaknesses. Once comparisons with similar institutions (the world's major cell banks) and the degree to which sample-incidental information is desirable, or whether it is extremely useful, are presented, only then it is possible to discuss current shortcomings and so on.

© 1-3. *Is the plan reasonable for the medium to long term?*

- From the following perspectives, it can be evaluated as sufficiently presented:
  1. The Committee highly approves the orientation toward having human disease-specific iPS cells and derivative cells (derivative human ES cells, disease-specific iPS cells created through genome editing, etc.), and differentiation-marker expressed iPS cells as the main focus of activities. The Committee requests that the BRC commit people and resources to these areas.
- The Committee points out and makes suggestions for further improvement as follows:
  1. ES and iPS cells are mentioned as examples of source of derivative cells, but these cells are also highly useful as function-retaining cells, such as those from primary cultures. And since it is quite possible that ES/iPS derivative cells will be used in future research, preparation of them should be considered.

2. The current human resources system was mentioned, but if the mid- and long-term plans include the administrative system, in addition to collected cell materials and research, it will be necessary to consider taking a broader view, including a vision for satellite organizations and a vision for collaboration with outside organizations.
- For some portions that are deemed insufficient, the Committee points out and makes suggestions as follows:
    1. It is reasonable to expect that human disease-specific iPS cells and derivative cells will increase sharply. However, at the same time, animal cells, including all kinds of mouse cells, will tend to decrease.

© 2a. *Have appropriate fields been earmarked for future prioritization?*

- From the following perspectives, it can be evaluated as generally sufficient:
  1. These policies are reasonable because better cell incidental information greatly enhances the usability and reliability of cells for the user and also there are strong societal demands for a focus on the development of cells for drug discovery.
  2. The Committee agrees with the idea of establishing two new teams, the Higher-order Cell Characterization Team and the Drug-discovery Cellular Basis Development Team.
- The Committee points out and makes suggestions for further improvement as follows:
  1. The direction of emphasis, such as the increasing sophistication of incidental information about disease-specific iPS cells and the provision of differentiated cells, is correct, but user-friendliness and adaptability to cryopreservation differ greatly depending on the degree of differentiation. Since greater advances in technology development are still required in this respect, it will be important to conduct joint research and collaborate with specialized institutions. The question of how to use limited human, financial, and time resources to bring this about will be an issue.
  2. The gene expression profiling of cancer cells can easily change, depending on factors such as the culture conditions, so it will be necessary to conduct strict analyses based on standard protocols. It

would be better to profile cancer-related genes, rather than gene expressions, and use them as resource-incidental information.

3. When developing drug-discovery cells, incorporating researchers from companies and working together with them should be considered, instead of just offering the cells to companies (incentives such as giving priority user rights may be conceivably offered to companies that provide funds and human resources). This will make it possible for the BRC to be strongly competitive at a time when there are constraints on human resources and funding.

- For some portions that are deemed insufficient, the Committee points out and makes suggestions as follows:
  1. The time frame is unclear. In order to make use of Japan's strengths, particularly in iPS cells, and to contribute to applied research in drug discovery, etc., it is essential to deal with this immediately. Riken has a major role to play.

© 3-2. *Are the policies for future resource infrastructure and technology development appropriate?*

- From the following perspectives, it can be evaluated as appropriate:
  1. In connection with cell depositions up until now, the BRC has created a resource infrastructure that is more than sufficient, but it is also vital to make use of experiences with the cell resources to develop new cell resources. It will be necessary to put into place a strategy of proactively manufacturing resources that are often needed but have not been supplied, and plans are getting started on this kind of research and development, so the Committee definitely hopes that they will advance.
- The Committee points out and makes suggestions for further improvement as follows:
  1. Since "it is difficult to conduct detailed differentiation capacity analysis for all cells," the Committee suggests that consideration be given to the possibility of a "crowd sourcing" function. In other words, researchers come to the bank for a certain period (under the guidance of the bank) and analyze the differentiation capacity using standard

methods, or offer cells, the details of whose differentiation capacity are unknown, and have the user share differentiation capacity analysis results with the bank.

2. The Committee considers the concept of a Drug-discovery Cellular Basis Development Team to be important, so the Committee requests that this intention be conveyed to Director Yamanaka of the CiRA at Kyoto University as soon as possible, so that the direction of research can be worked out as soon as possible.
3. Having no medical information or information about differentiation capacity included is rather senseless. Even if the total number decreases, the Committee requests that the BRC proceed according to the proposal.

### *3-3. Innovation hub*

#### *○ (iii) Continuous operation and attracting new users*

- It can be evaluated as generally sufficient, but the Committee points out and makes suggestions as follows for further improvement:
  1. The Committee requests that the BRC look at case studies, including those from institutions overseas, to see whether there are any new approaches that are completely different from conventional methods.
- For some portions that are deemed insufficient, the Committee points out and makes suggestions as follows:
  1. There will be an urgent need, not only for guidance on ES cells, but also for creating an environment that promotes the use of iPS cells. The Committee suggests that it would be a good idea to put a system in place that can offer guidance on culturing iPS cells at research base universities all over Japan.