

Activities in BioResource Center

Evaluations

Evaluation by Council for Science and Technology Policy (CSTP), The Cabinet Office

In Octobers of 2006, 2007, and 2008, conferences of the Council for Science and Technology Policy (CSTP) were held, and core activities of independent administrative institutions in the field of science and technology for the budget request in each year were evaluated. RIKEN BioResource Center (RIKEN BRC) was highly evaluated in the conferences for their bioresource infrastructure activities and following views and comments were given.

<2006>

【Evaluation Overview】

Priority: S

Reason for priority:

- Satisfactory results have been achieved as planned as an infrastructure of life science in Japan. The bioresource infrastructure is an important issue that Japan should continue to actively promote.

Points to consider:

- Developing collaborations with Asian countries are necessary.
- Education and training of scientists and technicians for the next generation and communication with users is issues that RIKEN BRC should keep in mind as well.
- Attention must also be paid especially to intellectual property rights, especially in the relationship with other countries.
- Flexibility of selection of bioresources for preservation should be considered according to the research trend in the period. However, replacements should be based on legitimate evaluations.
- It is desirable to consider collaborating or integrating with the bioresource owned by other research institutes and related ministries such as Ministry of Health, Labor and Welfare, Ministry of Agriculture, Forestry and Fisheries and other Ministries.
- Roles of researchers in research and development and bioresource maintenance and management should be

balanced well.

- A possibility of user-charge should be examined.

【Committee Members】

Ryuzo UEDA	Director, Nagoya City University Hospital
Ryu OHSUGI	Professor, Graduate School, Tokyo University
Yuji KOHARA	Executive Director, Research Organization of Information and Systems
Takeshi KURATA	Director, Toyama Prefectural Institute of Health
Takashi GOJOBORI	Professor, National Institute of Genetics
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Kazumi NISHIJIMA	Mochida Pharmaceutical
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Tasuku HONJO	Professor, Kyoto University
Yuji MATSUZAWA	Director, Sumitomo Hospital
Yasushi MIYASHITA	Professor, The University of Tokyo
Eitaro MIWA	Professor, Tokyo University of Agriculture
Tomoko MIHOYA	Women's Nutrition University

<2007>

【Evaluation Overview】

Priority: S

RIKEN BRC was evaluated by documentary examinations

<2008>

【Evaluation Overview】

(The continuous project Thus, they are not graded. Priority: Equivalent to A)

- In order to promote the life science in Japan

comprehensively, RIKEN BRC needs to collect, preserve, and distribute the bioresource, develop related technologies, and educate researchers as a core institute of the resource.

- For permanent bioresource management, user-charge should be examined.
- The bioresource infrastructure activity is important as a foundation for the life science and it needs to be continuously conducted steadily and efficiently.
- In order to conduct the activity as steadily and efficiently as before, it is necessary not only to enhance stability of the activity but also improve a quality management system, keeping the global standards of the future bioresource in mind.

【Committee Members】

Masuo AIZAWA	Former President, Tokyo Institute of Technology
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Tasuku HONJO	Guest Professor, Kyoto University
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Ichiro KANAZAWA	President, Science Council of Japan

Ministry of Education, Culture, Sports, Science and Technology (MEXT) Independent Administrative Institution Evaluation Committee

In May 2007 and June 2008, conferences for the MEXT Independent Administrative Institution Evaluation Committee were held, and achievements of RIKEN BRC (bioresource infrastructure activity) in the Mid-term target period (from October 2003 to March 2008) were highly regarded as described below.

<Evaluations in Mid-term Target Period> (October 2003 to March 2008)

【Evaluation Overview】

Evaluation: S

Reason for Evaluation and Points to Consider:

- It was esteemed that RIKEN BRC compiled steady efforts to collect, preserve, and distribute the bioresource within the mid-term target period, which led BRC to gain worldwide recognition. The center largely surpassed the target numbers regarding any of animals, plants, cells, genes, and microorganisms. In addition to this accomplishment, we gave high praise to their contribution to spread the brand name of “RIKEN BioResource Center” by developing the activity efficiently in a short period. They fully achieved the mid-term goals.
- In terms of quality, BRC has a management system so that they can distribute the highest quality bioresource. Establishing infrastructures to supply ES cells and iPS cells is an unexpected accomplishment and believed to significantly contribute to advancement of the research.
- Their efforts that have established a world-leading biological resource center in five years should be appreciated. Since RIKEN BRC is able to develop technologies to collect and preserve the bioresource, collaborate with bioresource core facilities in other countries, and provide research institutes in other countries with bioresources, they surely become a research infrastructures of biology, life science, basic medical science, and clinical medicine and contribute to natural science of the 21st century. Considering a competition to consolidate an international research environment and a resource utilization frame, the future of the bioresource needs to be deliberated as a national strategy of Japan. However, so far, the mid-term goals such as conducting development researches of the resource, providing technical trainings, and adding higher value to the resource were all fully achieved. They proved more than expected.
- Many institutes in Japan have deposited the bioresources to RIKEN BRC, which has become an international core facility of the bioresource. RIKEN BRC started supplying mouse iPS cells swiftly, resulting in providing 80 institutes with the cells within two months. The operation policy of the director and visions of BRC are being brought to realization.
- RIKEN BRC rescued bioresources from institutions such as Institute of Development, Aging and Cancer, Tohoku University. RIKEN BRC also contributed to establishing

Asian networks. RIKEN BRC and Jackson Laboratory cooperated with each other and established the rule of intellectual property and established the mouse federation. They built up what is called a one-stop database (one-stop shop) network. Although RIKEN BRC ranks second for their size, they have the best technology to preserve the bioresource and take leadership in technology harmonization. RIKEN BRC should not let the United States to hold all the defact standards. RIKEN BRC is valued for their commitment bringing enhancement of the network in Asia and improvement of the entire life science study in Asia.

Future Direction of the Center Based on the Evaluation Results:

- It is essential to maintain the system to collect, preserve, and distribute the bioresource with long-term and well-planned strategies for the future and for scale of the resource center. Especially, “standardization” is an issue that has an influence on a course and possibility of Japan in various fields. RIKEN BRC should make a strong appeal that the standardization for bioresource management and utilization is an important national strategy. The situation will not move ahead unless the government, the Council for Science and Technology Policy, Science Council of Japan and industries share common beliefs. The industries, government, and academia should recognize the necessity of making efforts to take the initiative for standardization to survive in the international research competition.
- We pay respect to RIKEN BRC for their strengthening their presence as a core facility by accumulating steady efforts such as quality control and developing the preserve methods. RIKEN BRC is expected to provide world’s highest life science foundation as an influential infrastructure.
- RIKEN BRC is now the biggest institution in Japan of this kind. We would like RIKEN BRC to be one and only institution in the world. RIKEN BRC is expected to strategically develop and produce fruitful results in the next term.
- Enhancement of research and development capability is anticipated due to participation of a team transferring from the former Genomic Sciences Center.
- It is desirable and important to take all measures so that the bioresource center activity will fully develop as a core

facility of Japan.

【Committee Members】

Kazue KURIHARA	Professor, Institute of Multidisciplinary Research for Advanced Materials, Tohoku University
Takao KASHITANI	The Japan Institute of Certified Public Accountants
Yoshio OKAMOTO	Mitsubishi UFJ Research & Consulting
Kiyonari INAMURA	Professor, Kansai University of International Studies
Yoichi OKABE	Deputy President, The Open University of Japan
Shigeyuki KOIDE	The Yomiuri Shimbun Holdings
Junichi SONE	NEC
Osamu TAKAI	Professor, Nagoya University
Mitsuaki YOSHIDA	Guest Professor, Graduate School of Frontier Sciences, The University of Tokyo

<2006>

【Evaluation Overview】

Rank: A

Points to consider:

- RIKEN BRC is considered as the one of the world’s three largest center for the animal, plant, cell and gene bioresources. RIKEN BRC should be evaluated highly since it secures a firm position as a world leading bioresource center.
- RIKEN BRC produces significant results of the research and development activities in regarding with the advanced quality control technology, growth and preservation technology, and characterization and analysis of function. RIKEN BRC plays a role in intellectual infrastructure in Japan and yields excellent results in the field of the bioresource.
- On the other hand, explanations on necessary quantity to be collected and preserved for each bioresource, bioresource collecting methods, and necessary scale are not sufficient with respect to the activities of collecting, preserving, and distributing the biological resources. Also, it is required to provide explanations of quality management and cost

reduction for the preservation and resulting effects in detail.

【Committee Members】

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Shigeyuki KOIDE	The Yomiuri Shimbun Holdings
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<2007>

【Evaluation Overview】

Rank: S

Points to consider:

- The number of the bioresources collected, preserved and distributed in 2007 reached the largest for any of the animals, plants, cells, genes and microorganisms since BRC was established. The results largely exceeded the target numbers and made a huge contribution to spread the name brand of RIKEN BRC. In addition to these, RIKEN BRC established a quality management system, which enabled RIKEN BRC to supply the highest quality bioresources.
- RIKEN BRC established a quality management unit and obtained and maintained the international quality management standard ISO9001. RIKEN BRC gained worldwide recognition as a biology resource center which offered the highest quality since they promoted the quality management of the cell materials and microorganisms and also set up a backup facility with installing liquid nitrogen tanks for preserved resources in a frozen state.
- RIKEN BRC set up and started operating a research infrastructure for human iPS cells and other stem cells. RIKEN BRC built a system to smoothly utilize academic institutions and industries, which were considered to be distinguished achievements. It should be noted that accumulation of technologies and trust resulted in the

distribution of mouse iPS cell to over 80 institutes. Their prompt responses to requests were appreciated as well.

- Through unrelenting efforts on collecting, preserving and distributing the bioresources, RIKEN BRC strengthened their confidence domestically and internationally. Because of the trust, iPS and ES cell distribution was a sign of trust in RIKEN BRC, while the national effort will be made to promote the iPS research.
- The number of the collected, preserved, and distributed bioresources increased by 17% from the last year and marked the highest record in the past, achieving satisfactory results which greatly surpassed the target. As seen in their efforts that RIKEN BRC diversified the activities into several sections such as development of preservation and transportation technology and securement of bioresources and their direction is focusing on continuance for more 100 years was apparent. Meanwhile, the activities to collect, preserve and distribute the bioresources is obviously an issue related to the national strategy, while standardization of bioresources in the industries, international planning and frame setting are needed to be considered. RIKEN BRC is expected to take a prompt initiative and project strategies, involving the government, business communities and legislative body. We would like RIKEN BRC to conduct public relations activities with these issues in mind.
- The number of collected, preserved, and distributed bioresources successfully increased and exceeded the annual plan. This is an indication that RIKEN BRC obtained credibility for their activities at BRC and highly regarded. However, RIKEN BRC should be aware that scale expansion is not always a good result.

Ministry of Education, Culture, Sports, Science and Technology

Research Revolution (RP2002) Evaluation of National Bioresource Project

In March 2008, a conference of National Bioresource Project Evaluation Committee was held. The activities of RIKEN BRC (experimental animal: mouse, experimental plant: *Abrabidopsis*, cell material: human and animal cell culture, genetic material: DNA etc.) were highly valued as stated below.

<Evaluation of the First Term> (from 2002 to 2006)**【General Comments】**○ **Experimental animal: Mouse**

The core facility marked the world's second-largest number of the mouse strain collections and built up a worldwide infrastructure of the mouse resource center. RIKEN BRC organized an excellent system to collect, preserve and distribute the high-quality mouse strains. MTA is easily accessible and widely used both domestically and internationally. RIKEN BRC also put efforts into transfer of the technology. They own great databases and dispatched information efficiently, and offer unique mouse strains of high-quality, which are highly ranked internationally. Their contribution to life science is considered to be significant. RIKEN BRC plans to increase values of their resources by adding characteristic information especially of phenotypes. It is anticipated that they can easily achieve the goal, which is to develop the world's most advanced mouse resource center by 2010.

Comprehensively, this activity is evaluated to accomplish extremely excellent results.

○ **Experimental plant: Arabidopsis**

Although RIKEN BRC started later than ABRC (the United States) and NASC (England) as a resource center of Arabidopsis which is one of the most important model plants, RIKEN BRC is now playing a role as one of the world's three major institutions regarding the collection volume. RIKEN BRC also proceeds with collection of full length cDNA. Consequently, RIKEN BRC earns recognition as a global resource center which collects and supplies high-quality resource. From the fact that RIKEN BRC received an award from the academic conference for their activities, it can be seen that they are acclaimed by the researcher communities for their supply condition and contribution to the plant research field. RIKEN BRC has become an ideal resource center for NBRP, which sufficiently represents the importance of the resource type, quality and quantity to be maintained.

RIKEN BRC's future plans include to reinforce and expose additional information on such as genomic analysis and wild strain character analysis, and to improve quality management technologies, showing that they are making advances steadily in order to reach the highest level in the world. It is necessary

to discuss the system of activity on other plant cell cultures which is a unique product of RIKEN BRC.

Comprehensively, this activity is evaluated to accomplish extremely excellent results.

○ **Cell Material: Animal Cell Culture, Cancer Cell, Human Cell**

The core institute in charge of this resource has a long history and have collected, preserved and distributed cell lines including many cancer cell lines. In these years, RIKEN BRC aggressively deals with collecting and preserving some new cell types such as human cord blood cells and ES cells. These new activities are admirable. RIKEN BRC works on quality management, collaboration with similar projects of other institutes, and reexamination of the system in a positive and serious manner on the issues and opinions raised in the evaluation committee. In order to make full use of the resource, RIKEN BRC is expected to strengthen their cooperation with researcher communities. We would like to keep an eye on their future transition.

In this activity, although quantitative goals are sufficiently achieved, RIKEN BRC will be required to organize and prioritize researchers' requests, within the limited expense and space.

Comprehensively, this activity is evaluated to show favorable results.

○ **DNA: Animal and Microorganism**

Their goals of the first term for collection, preservation and distribution were achieved and consequently RIKEN BRC is recognized as a world-class DNA resource organization. RIKEN BRC make efforts to improve resource quality by collecting resources endemic to Japan and providing additional information, as well as enhance public relations activities. RIKEN BRC is thought to be a model core institute of a national bioresource project. Through providing strategic maintenance of the resources in wider range including microorganisms, seeking preservation method of increasing resources, dividing tasks with other resource institutes in Japan and other countries, enhancing cooperation, RIKEN BRC is anticipated to evolve as a DNA resource core facility further and to be essential for the domestic and international biology research.

Comprehensively, this activity is evaluated to accomplish

extremely excellent results.

【Committee Members】

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Naoki OGASAWARA	Executive Director / Vice President, Nara Institute of Science and Technology
Chieko KAI	The Institute of Medical Science, The University of TOKYO
Masatoshi TAKEICHI	Director, RIKEN Center for Developmental Biology
Satoshi TABATA	Deputy Director, Kazusa DNA Research Institute
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Evaluation on BioResource Center by the Resource Committee

○ Resource Committee of Experiment Animals

【Proposal for future policy】

<The 6th meeting> (February 2nd, 2007)

1. Types of resources to be collected and distributed

- (1) Setting up various lineups of the genomic DNA of mouse strains may be required.
- (2) Setting up various lineups of the models of human diseases including the ENU mutant strains.
- (3) Collecting ES cells derived from inbred mouse strains is valuable. Genetically modified ES cells from which already knockout mice had been generated were not to be collected as ES cells, but to be collected and preserved as knockout mice. Other genetically modified ES cells which have not been used to generate knockout mice may

have difficulty in collection from researchers, due to being under the development, or may be considered to have problems in generation of the mice.

- (4) For a while, tissues and organs must be distributed one by one if requested within a manageable level. Due to the cost and labor of collecting organs and tissues, the freezing facilities for frozen samples and quality issues, distribution of tissues and organs requires a careful consideration and estimation of the future demands, cost and its effects.

2. Strategy to attain the highest level in the world

- (1) It is advised to collect the mouse strains based on unique Japanese research achievements, such as research on the brain, cancer, immune systems and other outstanding research achievements, that are leading the world in science. It is also important to disseminate information of the strains through the International Mouse Strain Resource (IMSR) to scientists around the world.
- (2) It is desired to collect Cre-transgenic strains that enable spatiotemporal regulation of genetic manipulations. The establishment of useful Cre collection must be conducted while paying attention to the current overseas trend in the knockout mouse projects and the generation of Cre-lines.
- (3) The choice of the background strains (B6/J v.s. B6/N) is a critical issue in the functional genomics. RIKEN BRC needs to demonstrate the scientific evidence of the difference of the strains and pay attention to needs of the world scientists.
- (4) It is recommended to collect visualizing models which enable us to observe biological events as fluorescent signals in vivo. It is also important to develop novel devices and technologies for in-vivo imaging using those visualizing models, and disseminate the advanced technologies to users through the training course.

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3. Development project

- (1) Recovery rates of each cryopreserved strains must be disclosed on the website to demonstrate the technical level of the BRC.
- (2) It is essential to establish cryopreservation techniques for embryos and sperm of a wide range of strains including wild-derived strains and other low-surviving strains.
- (3) The development of an inexpensive transportation method for embryos and sperm is required.
- (4) The health monitoring tests should be performed by the BRC itself. However, it is necessary to verify the results

regularly by third party organization.

4. Sub facilities and cooperation facilities

(1) Nine facilities had been assigned as sub-facilities to create advanced “hot” mouse resources. Although the adequate budget was given in the past five years, the results, especially deposition were insufficient. The strict evaluation must be conducted by the members, consisting of the Resource Committee of Experimental Animals who represents the research community (Some experts may be added if required).

(2) As the policy for sub-facilities after 2007, a proposed plan was approved by the Resource Committee of Experimental Animals that the BRC will publicly call applicants for research and development programs to create novel genetically-modified mouse strains (100 strains per year) with immediate demand by the research community of the priority areas in Japan.

(3) The applicants of the above program are asked to propose the design of genes constructs for genetic modifications using a specific format, produce and submit the recombinant gene constructs to BRC. Both developer organizations and genes to be modified should be selected by the Resource Committee of Experimental Animals (adding experts if required).

(4) BRC orders third parties to make mouse strains in C57BL/6N for immediate distribution to the research community.

5. Change in fees

(1) After the transition of national universities to National Universities corporations, universities have tried to calculate every necessary cost to provide their service and resource, and have begun to charge users fees as reimbursement to the universities. Accordingly, it is inevitable that RIKEN BRC revised and increased distribution fees. However, we would request RIKEN BRC to consider some solutions which can care for low budget laboratories.

(2) Since the BRC is a not-for-profit government funded institution, components of the distribution fee must be disclosed to users.

<The 7th meeting> (January 24th, 2008)

1. Roadmap of Experimental Animal Division

(A five-year roadmap considering the ideal situation plan for

the following 100 years)

(1) The mouse strains are invaluable property and research resources generated through a vast investment of scientific research funding. The establishment of such resources must be conducted by the nation, and strongly supported by the research community.

(2) The maintenance of bioresources and improvement of their quality can only be achieved by successive presence of persons with affection to bioresources.

(3) To pursuit efficiency of the operation, collecting and preserving only mouse strains with the highest demand is the easiest way to manage; however, that attitude has no value for the infrastructure development and the mouse resource center. It is important for the resource center to have attitude of collecting and preserving anything and everything.

2. Management of collected and preserved amounts required for each bioresource, the method of collecting bioresources, and required scales

(1) It is necessary to clarify the criteria for selecting mouse strains to be kept alive, and whether or not it is managed based on the frequency of request. If the economic value and impact of research results by users are properly assessed, we can persuade public regarding the importance of the bioresource.

(2) Inbred strains, especially from the viewpoint of permanence, should be preserved as embryos. For other strains with commercially available B6 backgrounds, such as transgenic and knockout mice, can be efficiently preserved as frozen sperm.

(3) Since the survival rate of cryopreserved sperm is still not consistent, ICSI or other equivalent systems are essential to promote utilization of frozen sperm.

(4) Bioresources can not be restored once they are lost. Thus, bioresource should be cryopreserved instead of discarded. It should be emphasized that the information associated with cryopreserved embryos and sperm should be kept properly.

3. Commission

(1) Value of live mice is superior to cryopreserved embryos. Because live mice can be used immediately in experiments and frozen embryos take much time and labor for recovery. Including depreciation expenses, the cost of a mouse is more than several hundred thousand yen, thus the increase

in fees for live mice is reasonable and not a problem.

(2) Users of mice and rats feel disinclined when the fees exceed 10,000 yen. The users community feels genetically-modified animals, commercially available at 20,000 to 50,000 yen are too expensive for academic users, only for for-profit users. Therefore, 10,000 yen is a reasonable price.

4. Disclosure of research achievement which used resources provided by the National Bio Resource Project (NBRP)

(1) For clear notification of resource origin, the description in the materials and methods section is more appropriate than a description in the acknowledgement. Clear indication of description and examples for users are required.

(2) A formal letter should be sent to the journal editors requesting not to accept manuscripts without appropriate description of the origin of the resources as a measure against users those who does not describe resource origin.

(3) BRC must survey publications by users, and examine whether the origin of resources are described or not. If not, BRC should urge them to describe the resource origin in the coming paper.

5. Others

(1) In cooperation with The Jackson Laboratory, the BRC should play a leading role in the nomenclature of strains, based on the international rules. The search engines on the Web must support strain names according to the standard nomenclature rule, former names and revised names. We would request the Bio Resource Center to play a leading role in the establishment of the defacto standard for the phenotypic description method.

(2) The Gene trap lines developed by Dr. Ishida (Nara Institute of Science and Technology) require additional information about the trapped genes, detailed phenotypic description and so on. It is not realistic to carry out mycoplasma infection testing on 260 trap lines at once. It is advised that such quality tests must be done if requested. Besides, it may be possible to eliminate mycoplasma infection through passages in culture, if the mycoplasma is not the mouse mycoplasma.

(3) We discussed about preserving a duplicate of mouse resources among international resource centers. FIMRe member organizations agreed to the policy that each repository does not hold a duplicate mouse resource from another repository due to the intellectual property issues.

Furthermore, the amount of mouse resources has exceeded the limitations of capacity of each repository to preserve overlapping strains. Therefore, international collaboration of resource centers is considered to be necessary. Facilitation of distribution and the transportation methods have been discussed in the FIMRe.

【Committee Members】

Toshio ITO	Deputy Director, ICLAS Monitoring Center, Central Institute for Experimental Animals (2007~)
Ryo KOMINAMI	Professor, Graduate School of Medical and Dental Sciences, Niigata University
Toshihiko SHIROISHI	Professor, Mammalian Genetics Laboratory, Genetic Strains Research Center, National Institute of Genetics
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Kenichi YAMAMURA	Professor, Institute of Molecular Embryology and Genetics, Kumamoto University
Minesuke YOKOYAMA	Professor, Center for Bioresource-based Researches, Brain Research Institute, Niigata University
Hikomichi YONEKAWA*	Vice-President, The Tokyo Metropolitan Institute of Medical Science, Tokyo Metropolitan Organization for Medical Research

*Chairperson



○Resource Committee of Experimental Plants

【Proposal for future policy】

<The 6th meeting> (January 26th, 2007)

1. Types of resources to be collected and distributed
 - (1) The RIKEN BRC should respond to the request from other core plant resource institutes for the backup of cDNA.
 2. Strategy to attain the highest level in the world
 - (1) To improve the quality of the Arabidopsis resource, collecting resource-associated information and creating databases including published papers may be needed.
 - (2) For information searches relevant to resources, it is said that Google and other search engines have started collecting associated technical vocabulary, and ELSEVIER has fully systemized published academic journals and has been providing them as a subscription service to universities at high prices. Therefore, the development of information services, under the circumstances described above, is considered to be important.
3. Development project
 - (1) Time and energy might be heavily involved in technology development and innovative research relating to biological resources, therefore, securing high-quality staff and researchers is very important.
 - (2) In the stream of university innovation, faculties specialized in bioresources have been established in both undergraduate and graduate schools. Securing stable staff in cooperation with such universities and research institutes as Ministry of Agriculture, Forestry and Fisheries of Japan is considered important.
 - (3) As for the training of research technicians and coping with downsizing of staff, in cooperation with biotechnology colleges, educating technical know-how to students and recruiting outstanding staff to RIKEN BRC will be appropriate.
4. Change in fees
 - (1) As for distribution of resources, when too much emphasis is placed on beneficiary liability, then it is more likely to be perceived as business, thereby, the nature of the resource project is likely to be distorted. To keep the balance between the collection of actual expenses and idea of non-profit is important.
 - (2) For the improvement of life science, it is important to design the base framework for the principle of actual expenses and non-profit based on situation of each resource at the bioresource bank.

<The 7th meeting> (January 25th, 2008)

1. Roadmap of Experimental Plant Division
(A five-year roadmap considering the ideal situation plan for the following 100 years)
 - (1) By clearly assigning the Arabidopsis as a model in the crop research, Arabidopsis resources will be regarded as research tools not only for basic study but also for agricultural study; thus the anticipatory perspective for next 100 years can be developed. From this point of view, roles and significance of the plant resources and other research foundation must be established through the development of the research strategy to address the food shortage issue.
 - (2) Considering the Arabidopsis as a model of crops, the systematic consolidation database (SABRE) is particularly important. We would like the RIKEN BRC to take in the consideration to combine the array data of model plants and crops with SABRE.
2. Management of collected and preserved amounts required for each bioresource, the method of collecting bioresources, and required scales
 - (1) For the management of resources that are not used often enough, the development of technology that enables long term preservation of resource is considerably important.
 - (2) For the epoch-making resources, it is not enough to wait until establishment of such resource in the community; it is important for RIKEN BRC to actively develop these resources by the organization itself.
3. Commission
 - (1) After the discussion on the international standard, the revision of distributing fees was approved without any specific disagreements.
4. Disclosure of research achievement which used resources provided by the National Bio Resource Project (NBRP)
 - (1) Ordinal disclosure of used journalistic form is not seen as a problem. Ingenuity of abbreviation is required for the Ministry of Education, Culture, Sports, Science and Technology.
5. Others
 - (1) The improvement of transformation technology such as establishment of knock-in plant is required in plant science. We would like the BRC to collect information on such technology and take it into consideration in the future.

【Committee Members】

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Kiyotaka OKADA*	Director-General, National Institute for Basic Biology
Yasunari OGIHARA	Professor, Kihara Institute for Biological Research, Yokohama City University
Hiroshi KAMADA	Professor, Graduate School of Life and Environmental Sciences, University of Tsukuba
Makoto KAWASE	Director, Genebank, National Institute of Agrobiological Sciences (2008)
Nobuharu GOTO	Honorary Professor, Miyagi University of Education
Kazuo SHINOZAKI	Director, Plant Sciences Center, RIKEN
Satoshi TABATA	Deputy Director, Kazusa DNA Research Institute

*Chairperson

○Resource Committee of Cellular Materials**【Proposal for future policy】****<The 6th meeting> (January 16th, 2007)**

1. Types of resources to be collected and distributed

- (1) We would like the RIKEN BRC to determine how many cell lines for each kind of cell material are required to be prepared as an immediately available material.
- (2) We would like the RIKEN BRC to start “stem cell bank” as soon as possible, i.e., bank of human ES cells and induced Pluripotent Stem (iPS) cells.
- (3) As for mouse ES cells, there exist many kinds of cell line that have been established with the intention to produce gene modified mice. In addition, gene modified human ES cell lines have also been established. Since such cell lines are valuable, we would like the RIKEN BRC to collect and distribute them.

2. Strategy to attain the highest level in the world

- (1) To collect cell resources effectively, participation and cooperation of related academia is necessary.
- (2) In relation to drug efficacy test, the experiments using experimental animals will be replaced with the

experiments using human stem cell-derivatives. Thus, the banking of human ES cells and human iPS cells is very important.

- (3) In the near future, clinical grade human ES cells and human iPS cells will be required. The technologies relating to clinical grade human stem cells should be developed.

3. Development Project

- (1) The characteristics of cell lines are not stable following passages. Thus, the analyses of characteristics should be performed periodically.
- (2) Gene expression profiling analysis of immortalized cell lines possibly leads to various applications as well as determining the derived tissues. Therefore, we would like the RIKEN BRC to actively perform this.
- (3) Ethical procedures to obtain human umbilical cord blood from the RIKEN BRC should be simplified, i.e., approval of institutional ethical committee of user institute be replaced with another procedure.
- (4) We would like the RIKEN BRC to collect information about human ES cells established in foreign countries relating to intellectual property right and procedures to use them.
- (5) The achievements of researches using the cell materials distributed by the RIKEN BRC should be collected in earnest.

4. Sub facilities and cooperation facilities

- (1) Cooperation with other divisions in the RIKEN BRC is important, e.g., cooperation with the animal division relating to animal cells derived from wild-type mouse.
- (2) Cooperation with other institutions in the RIKEN is also important e.g., cooperation with Center of Developmental Biology relating to stem cell bank.
- (3) As of 2008, the priority of collecting cell materials was decided by the Resource Committee. In other words, the Resource Committee selected the institutions that would deposit an important cell material.

5. Change in fees

- (1) There is no objection on changing the fees to reimburse handling and shipping costs.

<The 7th meeting> (January 24th, 2008)

1. Roadmap of the Cell Engineering Division

(A five-year roadmap considering the ideal situation plan for the following 100 years)

(1) Quality control of cell materials is very pivotal. The RIKEN BRC should obtain a reliability from research community so that research community can use the cell materials in the RIKEN BRC as the best cell materials for research.

(2) Collaboration with other domestic institutions is important.

(3) Collaboration with foreign institutions is also important, in particular with the institutions in Asia.

(4) Propagation of standard culture method is also an important mission of the RIKEN BRC. Thus, the RIKEN BRC should establish a training course of cell culture.

(5) The standard culture procedures should be established in the RIKEN BRC.

(6) The importance of quality control of cell materials should be announced to research community, e.g., relating to mycoplasma infection and culture cross-contamination.

2. Management of collected and preserved amounts required for each bioresource, the method of collecting bioresources, and required scales

(1) We would like the RIKEN BRC to determine how many cell lines for each kind of cell material are required to be prepared as an immediately available material.

(2) A number of the antibody-producing cell lines (hybridoma cell lines) are present in Japan. We would like the RIKEN BRC to preserve them.

(3) Technologies relating to iPS cells are very important. Thus, the RIKEN BRC should establish a training course of technologies relating to iPS cells.

(4) In the use of iPS cells, ethical matters should also be taken into account, e.g., the experiments prohibited in Japan relating to the use of human ES cells must be prohibited in the use of human iPS cells.

3. Fees

(1) There is no objection on changing the fees to reimburse handling and shipping costs.

4. Disclosure of research achievement which used resources provided by the National Bio Resource Project (NBRP)

(1) There is no objection on adding following Section in the MTA.

The RECIPIENT agrees to expressly describe that “the BIOLOGICAL RESOURCE (the resource name) was provided by the RIKEN BRC through the National Bio-Resource Project of the MEXT, Japan” in Materials and Methods or in the Acknowledgement in any publication

reporting the use thereof. The RECIPIENT also agrees to send a copy of such publication to the RIKEN BRC. The RIKEN BRC may disclose publicly, copy or otherwise use such publication to demonstrate the contribution by the RIKEN BRC.

【Committee Members】

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*Chairperson



○ **Resource Committee of Genetic Materials**

【Proposal for future policy】

<The 6th Gene Engineering Committee> (Jan. 19, 2007)

1. Types of resources to be collected and distributed

(1) Regarding the NIA/NIH mouse 15K and 7.4 K cDNA cloned sets, the user is restricted because of the necessity of wider space for the storage and higher costs for the storage of these samples. Therefore it might be better to divide and group the specific cloned sets with different biological function to generate the “Set Bank”.

(2) Regarding the new banking of gene-products, we need to collect the information related to peptide, protein, sugar, lipids and so on. Moreover we need to collect the information of other Institutes in Japan like RIKEN Frontier, AIST and the oversea to collect these materials. We also need to collect the information of the required technologies and preservation system for banking.

(3) Regarding the banking of peptide and protein, we need the higher skills and experiences to deal with to add the higher quality to the resource.

2. Strategy to attain the highest level in the world

(1) Regarding the banking of peptide and protein, it might be a good choice to be deposited by a group of “Protein 3000” in Yokohama RIKEN as this national project has already been completed in Japan.

(2) The scales of resources in RIKEN DNA bank are really expanded including not only the DNA but also the other genetic materials. Thus we need to focus upon to select the appropriate resources more to operate the banking activity normally.

(3) We need to discuss about the political aspects how to direct the DNA banking and how to cooperate with other groups within and outside RIKEN with the officers in MEXT and RIKEN.

3. Development project

(1) As for the preservation of the genetic materials, the preservation of DNA materials in tank of liquid nitrogen is safer as compared with that of the freezer. Moreover if the new system of the freeze-drying of the DNA materials will be established, it might be beneficial in terms of the safety and the cheap-cost as well as the space for the stock.

(2) Regarding the banking of peptide and protein, the higher technology is required to distribute these materials safely and with higher quality. Thus, it might be very careful to

initiate this project if we will decide to go.

(3) Although the proteins, the sugars and other materials as the experimental tools have been available in the market, we must to think about the specific way without redundancy to deliver them to the users. It might be useful for the users if their qualities are more stable and cheap.

(4) Regarding the banking of protein, it is necessary for us to check the practical points whether or not this banking can contribute to the researcher community and how to perform the banking of protein materials.

4. Change in fees

(1) The price for sending the DNA materials is reasonable to change as indicated by RIKEN DNA bank.

<The 7th Gene Engineering Committee> (Jan. 11, 2008)

1. Roadmap of Gene Engineering Division

(A five-year roadmap considering the ideal situation plan for the following 100 years)

(1) It is difficult to attain the purpose to become the top of the world of banking centers without the equivalent budget (ask MEXT and RIKEN).

(2) In attempt to become the standardized bank in the world, we can cooperate with other banks in USA, EC and Asian, and exchange the DNA materials for sharing.

(3) The promoter bank has a great potential for developing well in a future. .

(4) Regarding the preservation and transportation system of the DNA materials, it is very important and critical for the future development of the banking technology. This problem should be solved as soon as possible.

2. Management of collected and preserved amounts required for each bioresource, the method of collecting bioresources, and required scales

(1) The idea of Set-Bank is reasonable. In general, the molecular cloning of the expressed cDNA clones, approximately 20 % of the genome is very difficult to isolate and characterize for completion. We should think about other strategy to fill in this remaining gap for the completion. Thus it might be better to ask the prominent professor or the retired professors in Japan to let them to deposit their cloned DNA. We also can help to prepare the MTA and its related documents for registration. It is also required to introduce this announcement in the web site.

(2) Regarding the Set Bank of the transcription factors, the

number of the collection is around 500 to 600, which can cover most of the well-known factors.

(3) The DNA materials of EB-transformed lymphocytes of Mongoloid are very precious and suitable as the banking materials, which are useful for study of the population genetics.

3. Commission

(1) Regarding the revising the charge of commission, it is reasonable.

4. Disclosure of research achievement which used resources provided by the National Bio Resource Project (NBRP)

(1) It is critical to ask the research community to describe the source of materials in “Materials & Methods” section, or at least, in “Acknowledgements” on their published papers.

5. Others

(1) Regarding the Convention on Biological Diversity (CBD), it is highly possible that the working group of CBD will announce at the COP in Nagoya, 2010 to validate guideline of CBD by law within Japan. However its legalization will be no merits for Japan if USA will not be joined and agreed.

【Committee Members】

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Sumio SUGANO	Professor, Graduate School of Frontier Science, The University of Tokyo (2007~)
Mamoru HASEGAWA	President-Director, DNAVEC Corporation
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(~2006)

*Chairperson



○Resource Committee of Microbial Materials

【Proposal for future policy】

<The 3rd Microorganisms Committee> (Jan. 26, 2007)

1. Types of resources to be collected and distributed

(1) To deposit new genera and species of microorganism, there may be a case when researcher's needs should be satisfied with research materials by ensuring consistency with ISO including 16S rRNA gene. It is necessary to establish a system, which allows for a finely balanced coexistence with the ISO management based on the factors outside the ISO concept.

(2) Archaea can only survive under an extreme environment or ultimate conditions; however, some archaea can also be seen in a normal environment. Since most of archaea are still unknown, superior cultural techniques are yet not established. Recently it was found that cultured archaea are only a part of them, and furthermore studies are expected.

2. Strategy to attain the highest level in the world

(1) In proposal of new type strains submitted International Journal of Systematic and Evolutionary Microbiology (IJSEM), the researchers must receive the issuance of JCM certification of deposited microorganism for deposition and availability of the type strain to new species proposed. The number of issuance in BRC-JCM is 2nd position in the world culture collections. It is necessary to extend the JCM activities collected, preserved and distributed the JCM microbial strains.

(2) In addition to the current strategy originated health and environment, BRC-JCM has become a core of culture collection in Japan for the research promotion with the transfer of the IAM microbial collection (2,700 strains)

from the Institute of Molecular and Cellular Biosciences, the University of Tokyo. It is necessary to include even “academically significant microorganisms” in our activity strategy.

- (3) Developing countries are requesting revision of the patent law in relation to CBD. The applications without a Certificate of Origin are not accepted for the patent application of microbial resources. Australia and Japan are showing their reluctance to their request. EU basically accepts it with a condition to stop accelerating excessive rules. Under such environmental conditions, it may be suggested that the Certificate submission for a patent may become a global system.
- (4) It was approved in a Cabinet meeting to propose a bid to hold the 10th Convention on Biological Diversity (COP 10) in 2010 in Nagoya (Aichi Pref.). RIKEN BRC may need to consider the PR activities including response to CBD at this time.
- (5) As mentioned above, in relation to a proposal of new species and CBD, the type strain proposed must be deposited with 2 culture collections before the submission of manuscript to IJSEM. In such cases, where the authority of the country doesn't approve from the viewpoint of CBD, there is a contradiction in that the country cannot issue permission. However, the above-mentioned cases are few even in Southeast Asia where it is strict. It is therefore not considered a big problem.
- (6) Japanese researchers have only a superficial understanding in terms of MTA. For instance, when microbial resources are received from overseas, researchers should be taken by checking rights status and carefully treating the research outcome in order not to waste study results.

3. Development project

- (1) The microbial identification at the level of bacterial strain is expected.
- (2) Although 16S rDNA sequence is an important indicator for quality management, they are eliminated from catalogs immediately after the analysis results show a difference to XXX. Such solution is not appropriate. Even in cases where they are actually distributed, it is important that all the users can receive the sequence results without changing scientific names. When information of microbial strains is incorrect, it should be taken care of immediately. On the identification of reference strains, however, many

users are interested in their activities in most cases. BRC-JCM should suggest that the information related to their resources and characteristics should be correctly described. It is important to provide their information to users accurately.

- (3) As for bacteria, since the homology ratio of 16S rDNA sequence is high within the same microbial groups, the differentiation may be difficult. It is necessary to consider that the 16S rDNA sequence analysis may not be taxonomically absolute.

4. Sub facilities and cooperation facilities

- (1) As for cooperation with other organizations, Suzuki Commissioner is currently appointed as the head of the Culture Collections Committee of Japan Society for Culture Collections (JSCC), and Benno GM is appointed as a chairman of the Society. It is important to enhance its coordination by making good use of such relationships.
- (2) In cooperation with other organizations, the first step is to enhance domestic cooperation, especially with NITE and MAFF. In international cooperation, it is necessary to enhance cooperation with Asian countries taking into account utilization of microbial resources.
- (3) Although NITE is working under the category of industrial microorganism, it is essential for both NITE and JCM to provide as many referential strains as possible rather than type strains as a culture collection.

5. Change in fees

- (1) As for “Change in the offer price”, there is no objection against the policy to advance the consideration on user's cost burden and actual cost burden when continuous operation of the resource activity is considered.

<The 4th Microorganisms Committee> (Jan. 29, 2008)

1. Roadmap of Japan Collection of Microorganisms

(A five-year roadmap considering the ideal situation plan for the following 100 years)

- (1) In order to maintain the world's highest standard, it is considered that not only a confirmation with 16S rDNA sequence for deposition and availability of the type strain but also an introduction of other genetic markers and ITS analysis. There are many cases where microbial species cannot be differentiated from 16S rDNA sequence. It is considered necessary to establish information transmitted to the world in these scientific areas.

(2) The slogan is "Provision of microbial resources in research of health and environment areas." It is considered necessary to survey how trends in the research areas of health and environment change after 5-10 years. It is also necessary to assess what microbial strains are associated with the above-mentioned slogan. In addition, it is necessary to collect appropriate microbial resources by assessing the inter-relationship between the trend of researchers' needs for microorganisms and microorganisms associated with the slogan.

(3) As for the roadmap, pathogenic bacteria of biosafety level (BSL) 2 collected should be prioritized and provided by clarifying the parts to be especially focused on during the collection.

2. Management of collected and preserved amounts required for each bioresource, the method of collecting bioresources, and required scales

(1) On preservation and maintenance of microbial resources, the preservation method in accordance with the researcher's needs for each microorganism should be improved. The requirements for appropriate methods according to the needs including stock management should be set. For instance, if a large number of strains are provided, the number of stock should be a large amount, otherwise the small amount of stocks are maintained.

(2) In many cases, pathogenic microorganisms are not preserved by the preservation organizations but are collected by organizations of each university. These pathogenic microorganisms may be scattered when the relevance professor retired. The number of such pathogenic microorganisms is expected to be approximately 500 strains every year for the next 5 years.

(3) In the area of environment research, it tends to collect microorganisms in specific environments such as ultimate, cold and hot environments. Issues directly involved in environmental problems are very difficult (i.e. currently, lignin decomposition of plant in biomass energy), making it an important subject to search extremophiles. It is considered necessary to review collection methods based on the research trends of current environment research.

(4) In the scientific areas of health and environment, which have already been recognized as key areas, it may be good to clearly explain how deposit and service of a microorganism contributed in activity results.

(5) It is considered that genomic information will be essential in research areas of microbiology; therefore, it is necessary to provide microorganisms to which genomic information with better quality is added.

3. Commission

(1) As for revising commission, no revision will be made this year, that is, the existing price will be applicable.

4. Disclosure of research achievement which used resources provided by the National Bio Resource Project (NBRP)

(1) There were no specific comments on the statement of study outcomes.

5. Others

(1) As for personnel training, we will look for a new connection to further strengthen connections with Tsukuba University and establish our independent specialty if possible. For example, majoring bioresource is considered to be ideal.

【Committee Members】

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○Resource Committee of Information

【Proposal for future policy】

<No. 5> (July 31st, 2007)

1. Types of resources to be collected and distributed

The following policies were proposed by the head of the Bioresource Information Division.

- i The priority should be placed on the information of resource newly collected by each resource [development] division.
- ii The information handled by the Bioresource Information Division must have resources. Therefore, in principal, the division should focus on information of BRC bioresources.
- iii Other information should be handled after analyzing the relationship with those of BRC bioresources.

The committee presented their opinions as follows over these issues.

- (1) The advantage of BRC database resides in that its information is based on bioresources. However, it would be even better if the database would cover the information of all bioresources of Riken.
- (2) It seems that the division will likely lose its chances by sticking to the BRC bioresources. If it can take in other resource information, it should take them in.

2. Strategy to attain the highest level in the world

The following policies were proposed by the head of the Bioresource Information Division.

- i Updating resource information is the key to increase the value of the resources and to determine their level. Therefore, it is needed not only to provide information of newly collected bioresources without delay, but also to collect and provide the latest information of the existing bioresources.
- ii More efforts should be made to collect and announce publications prepared by using BRC bioresources.
- iii The division should consider the timing of collecting and providing characteristics which it currently does not, with checking the cost-effectiveness, and in the co-operation with other resource [development] divisions.

The committee presented their opinions as follows over these issues.

- (1) To show the achievements and initiative of BRC, it is very important to announce publications prepared by using BRC bioresources.
- (2) It is needed to pay attention to license and security issues as well.

3. Development project

The following policies were proposed by the head of the

Bioresource Information Division.

- i The priority should be placed on software development accompanied with the launch of new bioresources or new types of characteristics from BRC resource divisions.
- ii The division should execute software development to enrich the information of BRC bioresource by finding the relation between resources and by co-operating with the relevant database of each resource.
- iii There is a possibility that, in process of the BRC project, the division will handle information of bioresources that are maintained outside of BRC. In that case, the division will need to cooperate resource centers/institutions that maintain those resources and their information.
- iv It is indispensable to take resource databases into the integrated database for life science to make it truly useful for lab scientists. The division will contribute data of BRC bioresources to the integrated database for life science.
- v The problem seen in the process of software development is to secure enough budgets and staff. Currently, however, these are mainly allocated to daily operations for resource distribution and are hardly allocated to the development.

The committee presented their opinions as follows over these issues.

- (1) The retrieval system should be made easy to use, even for non-specialists of the bioresources. Showing a simple outline of the system will also be helpful.
- (2) There are advances in the content of the web pages. Information on resource characteristics has especially been enriched. Since the web pages have acquired a lot of data and photos, which is one of the remarkable advances, the maintenance and update of these pages must be hard tasks.
- (3) Because the system may get heavier and slower as various search services are included, efficiency improvement should be considered with some criteria.
- (4) It would be very convenient if homology search is executable across various species.
- (5) Related to the previous item, it is very interesting to conduct homology search to BAC clones, because currently there is no homology search targeting such big segments as BAC clones. It is very critical to suitably handle information including intergenic regions from various species.
- (6) It seems that other institutes also have cDNA clones. Their sequence information can be found on internet. Such

information should be included in SABRE.

- (7) Under current conditions, it is very hard to obtain experienced staff from outside BRC. Nurturing human resources is required in order to secure manpower for developmental works. Also, it is required that scientists evaluate the staff for the maintenance of intellectual infrastructure.

<No. 6> (January 30th, 2008)

1. Roadmap of the Bioresource Information Division

(A five-year roadmap considering the ideal situation plan for the following 100 years)

- (1) BRC currently implements its activities under the The National BioResource Project. But BRC has not decided about the maintenance of the Japanese resources after the completion of the project's second term. Roadmaps are required to include such matters.
- (2) Resource-search technologies will become more important in the future. Carrying out a project relevant to the resource information technologies in the bioresource research and development programs is recommended.
- (3) It is difficult to standardize the resource characteristics data obtained at different laboratories, to make them comparable one another. It may be preferable to provide data as they are and to let users solve the problem.
- (4) One of the ways to cooperate with other databases is to participate in the integrated database for life science project. Since an almighty database is planning under the project, the division can do collaboration to integrate resource databases into the database as its user.

2. Management of collected and preserved amounts required for each bioresource, the method of collecting bioresources, and required scales

- (1) Since the Shiroishi Group of GSC will join to the BRC in April, it will be possible to generate large amounts of the phenotype and biochemical information as the mouse clinic and to provide standard phenotype analysis formats. BRC needs to progressively operate the phenotyping to create a de facto standard.
- (2) To collect information regarding user's publications prepared by using BRC bioresources, BRC should contact them regularly to survey their publications. How about developing a system that sends emails to users annually until they respond to us? For the future, it is necessary to

establish a new rule that users have to report the titles and journal names of their publications when an investigation came from BRC.

- (3) To increase the value of the brand of RIKEN BRC, the division needs to consider assigning ID numbers to BRC bioresources that can be recognized as the BRC numbers. Although conventional numbers may have to be left to keep the history of the bioresources, BRC can treat them as aliases.

【Committee Members】

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