Issue Number 4 June 2008

BioResource now !

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Yukio Nakamura
Cell Engineering Division, RIKEN BioResource Center

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What is web accessibility ?

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- WGR http://www.shigen.nig.ac.jp/wgr/
- JGR http://www.shigen.nig.ac.jp/wgr/jgr/jgrUrlList.jsp

Announcements

(Details are available at : http://www.nbrp.jp/)

- Training for the Use of Technology in the Latest Bioresources Call for Participation (plants and *Arabidopsis thaliana*)
  Application Period : June 18 (Wed) - July 4 (Fri) , 2008
- The 79th annual meeting of the Zoological Society of Japan in Fukuoka
  Date : September 5 (Fri) to September 7 (Sun) , 2008
  Venue : Fukuoka University

Introduction to Resource Center No.25

National Bioresource Project on "Human and animal cells"

Yukio NAKAMURA General Manager,
Cell Engineering Division, RIKEN BioResource Center

Introduction

Most conventional cell banks have been collecting, preserving, and distributing cell lines derived from human tumor cells and cultured cells derived from animal tissues. However, the RIKEN Cell Bank has initiated maintaining and distributing various other cells (Fig. 1). Moreover, the generation of induced pluripotent stem (iPS) cells is currently the central topic in cell-related research. The RIKEN Cell Bank initiated the distribution of mouse iPS cells in March 2008 (Fig. 2), and is currently preparing to distribute human iPS cells.

1 General cell line materials

The Cell Bank activities at the Institute of Physical and Chemical Research (RIKEN) were initiated in 1986 (inaugurated as "RIKEN Gene Bank"). Since then, we have aggressively collected and maintained cell materials and have established a system to rapidly distribute over 1,300 cell lines (if we receive a request before 17:00 hours on Thursday, we can dispatch it on Tuesday the following week). Moreover, we have cooperated with the Cell Resource Center for Biomedical Research at the Institute of Development, Aging and Cancer, Tohoku University, since 2003; all the cell lines that were collected, stored, and distributed by this center were transferred to our division, which will be distributed henceforth. Our division has already initiated the distribution of many cell lines; these cell lines are available for distribution and are listed on our homepage.

- Uncultured cells
  - Human cord blood
- Short-term cultured cells
  - Human mesenchymal stem cells
  - Fibroblasts : both human and animal-derived
- Long-term cultured cells
  - Embryonic stem (ES) cells : human, ape, and mouse
  - Induced pluripotent stem (iPS) cells : human (preparation underway) and mouse
  - Human cell lines : mainly derived from human tumor cells
  - Animal cell lines : Mouse, rat, fowl, etc.
- Cultured cells mainly for gene analysis
  - Cells derived from normal Japanese individuals and patients : Epstein-Barr virus (EBV)-transformed B-cells
  - Sonoda-Tajima collection : cells derived from various races and nations in the world
  - Goto collection : cells derived from Werner syndrome patients

Fig. 1: Types of cell material distributed by the Cell Engineering Division, RIKEN BioResource Center. The human-derived fibroblasts include cells having differentiation potency, such as mesenchymal stem cells, osteoblasts, and cartilage precursor cells.

2 Human somatic stem cells

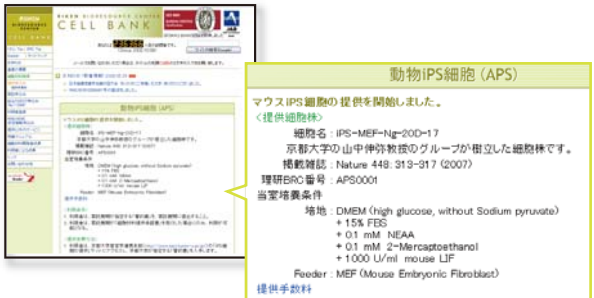
Somatic stem cells are the principal cells used in research in regenerative medicine. Currently, we collect, maintain, and distribute human cord blood and mesenchymal stem cells (Fig. 1).

There is a possibility that various types of somatic stem cells other than hematopoietic stem cells are contained in the bone marrow. However, it is difficult to collect human bone marrow cells. On the other hand, the content of hematopoietic stem cells in the human cord blood is almost the same as or more than that in the bone marrow. Moreover, there is also the possibility that various types of somatic stem cells other than hematopoietic stem cells are contained in the human cord blood. Therefore, the human cord blood is considered as a primary research resource for research in regenerative medicine.

3 ES cells

The revised Guidelines for Derivation and Utilization of Human Embryonic Stem Cells issued by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) allow the establishment of a distribution organization for human ES cells. In April 2008, our division was designated as the sole distributor of human ES cell lines by MEXT. Therefore, we are pursuing the preparation for distribution of ES cells.

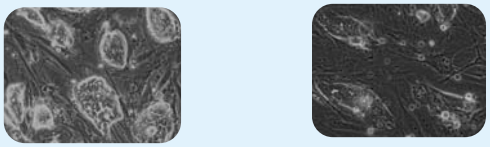
Before cells derived from human ES cells can be used clinically, preclinical studies are necessary, such as implanting differentiation-induced cells from primate ES cells into experimental primates. Therefore, our division distributes ES cell lines derived from primates (common marmoset). However, since basic research using mouse ES cells is still considered important, our division distributes various types of mouse ES cell lines, such as those derived from C57BL/6 mouse or those established by the nuclear transfer technique.



The homepage including the list of human and animal cells is available at http://www.brc.riken.jp/lab/cell/

4 iPS cells

The technology used to establish iPS cells, invented by Professor Shinya Yamanaka of Kyoto University, is the most advanced technology that is attracting global attention. Research on the application of this technology to the ongoing research in various biological fields is being actively pursued. We have already initiated the distribution of mouse iPS cells (Fig. 2) and are currently preparing for the distribution of human iPS cells.



Mouse ES cells　　Mouse iPS cells

Fig. 2 : Mouse ES cells and iPS cells

Our division prepares various types of mouse ES cell lines such as those derived from C57BL/6 and having the potency to differentiate into germ cells and those established by the nuclear transfer technique. The mouse iPS cells distributed by our division are derived from the cell lines established by the research group led by Professor Shinya Yamanaka of Kyoto University (iPS-MEF-Ng-20D-17).

5 Human cells for gene analysis

In the current post-genome age, the demand for human cell materials used as "genome incubators" is high. When the same cell sample must be repeatedly used by many researchers, the cells must be immortalized (transformed); currently, the most popular immortalization method is the immortalization of B-cells using EBV. In collaboration with the National Institute of Radiological Sciences, our division distributes cells derived from normal Japanese individuals and patients. Further, we distribute the cells in the Sonoda-Tajima collection, which comprises cells derived from various races and nations around the world, as well as the cells in the Goto collection, which are derived from patients with progeroid syndromes (such as Werner syndrome) (Fig. 1).

6 Quality control and standardization of cell materials

We may assume that biological research at the end of the 20th century was mainly focused on the "manipulations of genes at will," whereas life science research in the 21st century will mainly focus on the "manipulations of cells at will," as represented by the technology used to establish iPS cells and its applications. However, there is the fact that present technical skill levels of researchers (including students) who culture cells are not acceptably high. Approximately 30% of the cells deposited at our bank are contaminated with mycoplasma (Fig. 3), and approximately 10% of the cells are misconceived as being other cells. Under such circumstances, studies which use cell materials that are simply exchanged among researchers without any standardization of the cell materials are considered unscientifically sound. Therefore, when research materials such as cell lines are produced, it is considered important to deposit them with a resource management authority. The authority performs quality control and standardization and researchers then use the standardized cell material. In the field of microbiology, it is considered a rule that microbe species are not recognized as valid research materials unless they have been deposited with 2 independent resource management authorities in the world. Thus, it seems that the time has come to consider similar rules for cell materials, which can be cultured for long periods, as is the case with those in microbiology. To this end, we have developed a quality management system that has acquired ISO 9001 certification.

Mycoplasma-negative cells　　Mycoplasma-positive cells

Fig. 3 : Examination of mycoplasma contamination using the DNA-staining method

In order to determine mycoplasma contamination, the mycoplasma DNA is detected through the polymerase chain reaction (PCR) technique. However, since commercially available primers cannot be used for all mycoplasma species, other methods of examination are used. One such method involves adding the culture supernatant of the sample cells to a medium containing Vero cells after which, the DNA of the cultured cells are stained.

- Negative cells: Only the nuclear region of the Vero cells is stained.
- Positive cells: Since large quantities of mycoplasma DNA are observed in the cytoplasm of the Vero cells, it is confirmed that the Vero cells are contaminated with microbes (mycoplasma).

10 minutes

Information Technology - 33 -

What is web accessibility ?

Recently, the concept of "barrier-free" which provides accessibility to the physically disadvantaged such as the elderly and handicapped individuals, and a step further, the concept of "universal design" where a product or service should be able to be used by everyone, have penetrated deeply into society. The universal design for Web sites is gauged in terms of "accessibility." The Japan Industrial Standards (JIS) regarding accessibility criteria for Web content were issued on June 21, 2004.

The technical manual, which is a reference book to be used to fulfill the abovementioned standards, is provided by the Japanese Standards Association at the following Web site.

http://www.jsa.or.jp/stdz/instac/commitee-acc/WG2/Docs/web-tech-repo/technical-report.html

In this manual, the requirements of the standards and concrete measures that can be taken to fulfill these standards are collectively

Let's use support tools !

Support tools that can be used to create highly accessible Web pages are available from IBM, FUJITSU, etc. Here, IBM's "aDesigner ver. 2.0" is introduced. The following are the 2 major functions provided in "aDesigner".

- Simulate hindrances faced by visually impaired users such as the visualization of voice browsers and simulate how users impaired with amblyopia, dyschromatopsia or cataracts will view the Web pages.
- Checks the Web page's compliance with various accessibility guidelines such as the abovementioned JIS and determine the level of usability by visually impaired users.

As an example, we performed a simulation to determine how a visually impaired user (eyesight, 0.5: deuteranomaly; lens permeability equivalent to that of a 40-50 year old) will view the home of CARD R-BASE (http://cardb.cc.kumamoto-u.ac.jp/transgenic/). The image on the left indicates the results obtained from the simulation; ❶ shows the original CARD R-BASE Web page used for the simulation; ❷ the results obtained from the simulation; ❸ and the evaluation results of the simulation thus indicating that, overall, the Web page is well-suited for handicapped users, while some content has room for improvement.

"aDesigner" can be downloaded from the following Web site. Please refer to the Japanese guide for the download and the FAQ link at the bottom of the page, if necessary.

http://www.research.ibm.com/trl/projects/acc_tech/adesigner.htm

(Gaku KIMURA)

Coming up in the next issue !
The special topic on resources discussed in the next month's issue will be "Ciona Intestinalis"

Editor's Note We are very grateful to the individuals engaged in the fight against intractable diseases, for their e-mails, encouragement for upgrading our information site on ES cells. The news of success in the establishment of iPS cells gives us further hope. The Riken BRC Cell Bank led by division head Dr. Nakamura immediately initiated the preparation of ES cells and iPS cells for distribution to institutions engaged in the latest researches. We eagerly await to see the impact of our efforts in future research. (Y.Y.)

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