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Editorial

Standardization of Stem Cells for Practical Application

Masanori Terai*

Department of Judotherapy, Tokyo Ariake University of Medical and Health Sciences, Japan

***Corresponding author**

Masanori Terai, Department of Judotherapy, Faculty of Health Sciences, Tokyo Ariake University of Medical and Health Sciences, Tokyo 135-0063, Japan, 2-9-1 Ariake, Koto-ku, Tokyo 135-0063, Japan, Tel: 81-3-6703-7061; E-mail: terai@tau.ac.jp

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For future application of cell-based therapies, a stable and sufficient source of clinically applicable cells will be essential. Such cells will need to retain their normal function without impairment, and should be stable and safe for supply to various medical fields, such as regenerative medicine in which transplanted cells are used to repair organs or tissues that have lost their growth function. Seven years have passed since induced pluripotent stem (iPS) cells were first obtained from mice (1). Since then, iPS cell research has been progressing at a remarkable speed, and we are now on the threshold of clinical application of the world's first human iPS cells. In the adult human, however, hematopoietic stem cells, mesenchymal stem cells and adult pluripotent stemcells exist. These stem cells derived from autologous cells have high potential value for stem cell-based therapies for incurable or lifestyle-related diseases.

Human iPS cells and mesenchymal stem cells have pluripotent ability to differentiate into bone, cartilage, fat, heart, nerve, liver and skeletal muscle (2-6). Mesenchymal stem cells are derived from bone marrow in the patient's body itself, and therefore pose no immunological or ethical problems. However, it is difficult to obtain sufficient numbers of cells from mesenchymal stem cells derived from bone marrow, and there is a limit to the treatment of patients with reduced bone regeneration capacity, osteoporosis or rheumatoid arthritis, or for reconstruction of wide defects, using currently available methods. The situation is similar for mesenchymal stem cells, such as those derived from umbilical cord blood or peripheral blood, and hematopoietic stem cells. Basic biological studies have clarified the properties of hematopoietic stem cells, mesenchymal stem cells and adult pluripotent stem cells. Currently, problems related to cell number can be solved by gene transfer without chromosomal abnormalities (5). It has been reported that cells with chromosomal abnormalities can maintain their ability to differentiate depending on the type of gene transferred (6).

Human iPS cells are at a more advanced stage and their clinical application is expected. Human iPS cells are made from a patient's own cells, and thus present no immunological or ethical problems. It is believed that it will be possible to obtain iPS cells in sufficient numbers for treatment and reconstruction of extensive defects. The establishment of iPS cells appears to be associated with telomere elongation and activation of telomerase. However, we have reported that chromosomal abnormalities are present in some clones of iPS cells, and that their telomeres are shortened (7). The heterogeneity of telomerase expression in iPS cells suggests that cellular senescence could be controlled by the chromosomes of individual cells, and that short telomeres arising as a result of limiting levels of telomerase predispose chromosomes to instability. Chromosome abnormalities have not been observed in clones of iPS cells without shortening the telomere (7). If iPS cells are applied for cell therapies in the future, reprogramming techniques considering the expression of specific genes in individual cells will be needed.

In the future, with a view to clinical application, there will be a need to analyze in detail problems such as chromosomal abnormalities in both mesenchymal stem cells and human iPS cells. Standardization of various stem cells is now a priority for practical application.

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