Establishment of induced pluripotent stem cells from Werner syndrome fibroblasts

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Associate Professor Akira Shimamoto and Professor Hidetoshi Tahara at the Graduate School of Biomedical & Health Science in Hiroshima University, Professor Koutaro Yokote at the Graduate School of Medicine in Chiba University, Visiting Professor Makoto Goto at the Medical Center East in Tokyo Women's Medical University, and collaborators including the staff at the Cancer Chemotherapy Center in the Japanese Foundation for Cancer Research, Tottori University, and Keio University established induced pluripotent stem (iPS) cells from the fibroblasts of Werner Syndrome patients.

These results were published in *PLOS ONE* in an article entitled "Reprogramming Suppresses Premature Senescence Phenotypes of Werner Syndrome Cells and Maintains Chromosomal Stability over Long-Term Culture."

Werner syndrome is characterized by the premature appearance of features associated with normal aging and cancer predisposition. This syndrome occurs frequently in Japan, affecting 1 in 20,000 to 1 in 40,000 people. The therapeutic methods for this disease are very limited and it is expected that iPS cells can be used for the development of innovative therapies.

Dr. Shimamoto and his collaborators analyzed patient-derived iPS cells and found that telomeric abnormalities in the fibroblasts of these patients, which were caused by the lack of WRN helicase encoded by the gene responsible for Werner syndrome, were recovered in the iPS

cells generated from these patients. Furthermore, Dr. Shimamoto found that the expression levels of aging-related genes, including those encoding cell cycle inhibitors and inflammatory cytokines, in the patient-derived iPS cells were the same as those in normal iPS cells, even though the expression levels of these genes in the fibroblasts of the patients were higher than those in normal fibroblasts.

Dr. Shimamoto said, "So far, the use of patient cells was restricted to blood or dermal cells in basic research. The iPS cells that we have established will provide an opportunity for drug discovery for the treatment of Werner syndrome and also help with better understanding of the mechanism of this disease. In addition, the mutated WRN gene in patient-derived iPS cells can be corrected by genome editing. This advantage will be help in the development of new gene and cell therapies for Werner syndrome."

Provided by Hiroshima University