Patient-derived Induced Pluripotent Stem Cells Advance Research

Researchers in Korea, Sweden, and the United States have been working with a line of induced pluripotent stem cells derived from a donor with Juvenile Huntington's disease. Induced pluripotent stem cells are produced by using genetic engineering or chemical means to cause an adult cell to revert to an earlier stage of development. Pluripotent means that the stem cells have the potential to become any one of a variety of types of cells. We first reported on the development of these iPSCs in 2008 (http://www.hdsa.org/images/content/1/1/11500.pdf). Most recently, the researchers have used the cells to see if they can treat the disease in a neurotoxin rat model and are also using the cells to better understand the progression of the disease.

Rats were injected with quinolinic acid in the striatum, the area of the brain most severely affected by Huntington's disease. Induced pluripotent stem cell neural precursors were introduced seven days later. The day before transplantation and every two weeks following transplantation, the animals were given three behavioral tests to see if they experienced functional recovery. These were the stepping test, the staircase test and the apomorphine-induced rotation test.

The animals were followed for twelve weeks. They continued to achieve functional recovery. The animals were sacrificed at twelve weeks post-transplantation. The transplanted precursors appeared to have become GABAergic projection medium spiny neurons as needed. No cell overgrowth or tumors were found.

However, had the animals been followed for a longer period of time, evidence shows that the HD protein in those cells would have begun to cause damage. Neonatal rats which had been injected with induced pluripotent stem cells from this line developed HD pathology at 33 weeks. As with humans, as the animals aged, their brains could no longer cope with the challenges presented by the mutant protein. To be used for treatment in human patients, the mutated gene in the induced pluripotent stem cells will need to be corrected before transplantation.

"The unique features of the iPSC approach means that the transplanted cells will be genetically identical to the patient and therefore no medications that dampen the immune system to prevent graft rejection will be needed," said Jihwan Song, D.Phil. Associate Professor and Director of Laboratory of Developmental & Stem Cell Biology at CHA Stem Cell Institute, CHA University, Seoul, South Korea and co-author of the study.

In addition, the induced pluripotent stem cells are providing insights into the progression of the disease. "Having created a model that mimics HD progression from the initial stages of the disease provides us with a unique experimental platform to study Huntington's disease pathology," said Patrik Brundin, M.D., Ph.D., Director of the Center for Neurodegenerative Science at Van Andel Research Institute (VARI), Head of the Neuronal Survival Unit at Lund University, Sweden, and co-author of the study.

Reference:

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- *Marsha L. Miller, Ph.D., June 13, 2012*