Researchers restore neuron function to brains damaged by Huntington's disease

May 29 2012

Researchers from South Korea, Sweden, and the United States have collaborated on a project to restore neuron function to parts of the brain damaged by Huntington's disease (HD) by successfully transplanting HD-induced pluripotent stem cells into animal models.

Induced pluripotent stem cells (iPSCs) can be genetically engineered from human somatic cells such as skin, and can be used to model numerous human diseases. They may also serve as sources of transplantable cells that can be used in novel cell therapies. In the latter case, the patient provides a sample of his or her own skin to the laboratory.

In the current study, experimental animals with damage to a deep brain structure called the striatum (an experimental model of HD) exhibited significant behavioral recovery after receiving transplanted iPS cells. The researchers hope that this approach eventually could be tested in patients for the treatment of HD.

"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.

The study, published online this week in *Stem Cells*, found that transplanted iPSCs initially formed neurons producing GABA, the chief inhibitory neurotransmitter in the mammalian central nervous system, which plays a critical role in regulating neuronal excitability and acts at inhibitory synapses in the brain. GABAergic neurons, located in the striatum, are the cell type most susceptible to degeneration in HD.

Another key point in the study involves the new disease models for HD presented by this method, allowing researchers to study the underlying disease process in detail. Being able to control disease development from such an early stage, using iPS cells, may provide important clues about the very start of disease development in HD. An animal model that closely imitates the real conditions of HD also opens up new and improved opportunities for drug screening.

"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.

Huntington's disease (HD) is a neurodegenerative genetic disorder that affects muscle coordination and leads to cognitive decline and psychiatric problems. It typically becomes noticeable in mid-adult life, with symptoms beginning between 35 and 44 years of age. Life expectancy following onset of visual symptoms is about 20 years. The worldwide prevalence of HD is 5-10 cases per 100,000 persons. Key to the disease process is the formation of specific protein aggregates (essentially abnormal clumps) inside some neurons.

More information: "Neuronal Properties, In Vivo Effects and Pathology of a Huntington's Disease Patient-Derived Induced

Pluripotent Stem Cells" www.ncbi.nlm.nih.gov/pubmed/22628015

Provided by Van Andel Research Institute