Creating ideal neural cells for clinical use

April 13 2009

Investigators at the Burnham Institute for Medical Research (Burnham) have developed a protocol to rapidly differentiate human embryonic stem cells (hESCs) into neural progenitor cells that may be ideal for transplantation. The research, conducted by Alexei Terskikh, Ph.D., and colleagues, outlines a method to create these committed neural precursor cells (C-NPCs) that is replicable, does not produce mutations in the cells and could be useful for clinical applications. The research was published on March 13 in the journal *Cell Death and Differentiation*.

When the C-NPCs created using the Terskikh protocol were transplanted into mice, they became active neurons and integrated into the cortex and olfactory bulb. The transplanted cells did not generate tumor outgrowth.

"The uniform conversion of embryonic stem cells into neural progenitors is the first step in the development of cell-based therapies for neurodegenerative disorders or spinal injuries," said Dr. Terskikh. "Many of the methods used to generate neural precursor cells for research in the lab would never work in therapeutic applications. This protocol is very well suited for clinical application because it is robust, controllable and reproducible."

Dr. Terskikh notes that the extensive passaging (moving cells from plate to plate) required by some protocols to expand the numbers of neural precursor cells limits the plasticity of the cells, can introduce mutations and may lead to the expression of oncogenes. The Terskikh protocol avoids this by using efficient conversion of hESCs into primary neuroepithelial cells without the extensive passaging.

The scientists were able to rapidly neuralize the hESCs by culturing them in small clusters in a liquid suspension. The cells developed the characteristic "rosettes" seen in neuroepithelial cells. The C-NPCs were then cultured in monolayers. Immunochemical and RT-PCR analysis of the cells demonstrated that they were uniformly C-NPCs. Whole-genome analysis confirmed this finding. Immunostaining and imaging showed that the cells could be differentiated into three distinct types of neural cells. The team then demonstrated that the C-NPCs differentiated into neurons after transplantation into the brains of neonatal mice.

This research received funding from the National Institutes of Health and the California Institute for Regenerative Medicine.

Source: Burnham Institute (news : web)