Study finds long-term survival of human neural stem cells transplanted into primate brain

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A team of researchers in Korea who transplanted human neural stem cells (hNSCs) into the brains of nonhuman primates and assessed cell survival and differentiation after 22 and 24 months found that the hNSCs had differentiated into neurons at 24 months and did not cause tumors.

The study will be published in a future issue of *Cell Transplantation* but is currently freely available on-line.

The hNSCs were labeled with magnetic nanoparticles to enable them to be followed by magnetic resonance imaging (MRI). They did not use immunosuppressants. According to the researchers, their study is the first to evaluate and show the long-term survival and differentiation of hNSCs without the need for immunosuppression.

The researchers concluded that hNSCs could be of "great value" as a source for cell replacement and gene transfer for the treatment of Parkinson's disease, Huntington's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), spinal cord injury and stroke.

"Stroke is the fourth major cause of death in the US behind heart failure, cancer, and lower respiratory disease," said study co-author Dr. Seung U. Kim of University of British Columbia Hospital's department of neurology in Canada. "While tissue plasminogen activator (tPA) treatment within three hours after a stroke has shown good outcomes, stem cell therapy has the potential to address the treatment needs of those stroke patients for whom tPA treatment was unavailable or did not help."

Dr. Kim and colleagues in Korea grafted magnetic particle-labeled hNSCs into the brains of laboratory primates and evaluated their performance to assess their survival and differentiation over 24 months. Of particular interest was determining their ability to differentiate into neurons and to determine whether the cells caused tumorogenesis.

"We injected hNSCs into the frontal lobe and the putamen of the monkey brain because they are included in the middle cerebral artery (MCA) territory, which is the main target in the development of the ischemic lesion in animal stroke models," commented Dr. Kim. "Thus, research on survival and differentiation of hNSCs in the MCA territory should provide more meaningful information to cell transplantation in the MCA occlusion stroke model."

The researchers said that they chose NSCs for transplantation because the existence of multipotent NSCs "has been known in developing rodents and in the human brain with the properties of indefinite growth and multipotent potential to differentiate" into the three major CNS cell types – neurons, astrocytes and oligodendrocytes.

"The results of this study serve as a proof-of-principle and provide evidence that hNSCs transplanted into the non-human primate brain in the absence of immunosuppressants can survive and differentiate into neurons," wrote the researchers. "The study also serves as a preliminary study in our planned preclinical studies of hNSC transplantation in non-human primate stroke models."

"The absence of tumors and differentiation of the transplanted cells into neurons in the absence of immunosuppression after transplantation into non-human primates provides hope that such a therapy could be applicable for use in humans." said Dr. Cesar V. Borlongan, Prof. of Neurosurgery and Director of the Center of Excellence for Aging &

Brain Repair at the University of South Florida. "This is an encouraging study towards the use of NSCs to treat neurodegenerative disorders".

More information: Lee, S-R.; Lee, H. J.; Cha, S-H.; Jeong, K-J.; Lee, Y. J.; Jeon, C-Y.; Yi, K. S.; Lim, I.; Cho, Z-H.; Chang, K-T.; Kim, S. U. Long-term survival and differentiation of human neural stem cells in nonhuman primate brain with no immunosuppression. *Cell Transplant*. Appeared or available online: January 29, 2014. http://www.ingentaconnect.com/content/cog/ct/pre-prints/content-ct1117Antonucci2.

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