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Stem cells found to play restorative role when affecting brain signaling process

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A study by a Korean team of neuroscientists has concluded that when mesenchymal stem cells (MSCs; multipotent structural stem cells capable of differentiation into a variety of cell types) are transplanted into the brains of mice modeled with Alzheimer's disease (AD), the cells stimulate neural cell growth and repair in the hippocampus, a key brain area damaged by AD. The finding could lead to improved AD therapies.

The study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line as an unedited early e-pub.

Neuroscientists know that Alzheimer's disease is caused by the presence of amyloid-B (AB) "plaques" and "tangles" in the brain's network of neurons. Recently, a protein signaling pathway called "Wnt" (Wingless-type mouse mammary tumor virus (MMTV) related integration site family) which plays a role in embryonic development as well as the development of some diseases, such as cancer, has been linked to Alzheimer's disease. Researchers speculate that an interruption in the Wnt pathway signaling process caused by the AB plaque buildup may have an impact on potential brain cell renewal processes, called neurogenesis. Evidence has indicated that the Wnt signaling pathway plays an important role in the pathogenesis of AD.

This study was carried out to determine if MSCs benefitted neurogenesis in the hippocampus by "modulating" the Wnt pathway in such a way that that the MSCs are able to differentiate into neuronal progenitor cells (NPCs) that could help rebuild the affected areas of the brain.

"Recent studies have shown that MSCs express various proteins related to the Wnt pathway," said study co-author Dr. Phil Hyu Lee, Department of Neurology, Yonsei University College of Medicine in Seoul, South Korea. "It has also been determined that MSCs derived from bone marrow produce biologically active Wnt proteins that may counteract the negative influence of AB on neuronic activity."

The authors report that MSC treatment of AD in cellular and animal models significantly increased hippocampal neurogenesis and enhanced neuronal differentiation of NPCs.

"Our data suggest that the modulation of adult neurogenesis and neuronal differentiation to repair the damaged AD brain using MSCs could have a significant impact on future strategies for AD treatment," the researchers concluded.

A number of laboratory histological tests confirmed that MSCs enhanced the expression of beneficial reactions. In addition, behavioral analysis showed that MSC treatment produced significantly reduced numbers of memory errors in the treated animals.

The researchers concluded that "MSC administration significantly augments hippocampal neurogenesis and enhances differentiation of NPCs into mature neurons in AD models by augmenting the Wnt signaling pathway."

"This study provides evidence that MSCs can manipulate the Wnt pathway to promote recovery in AD." said Dr. Paul R. Sanberg, distinguished professor at the Center of Excellence for Aging and Brain Repair, Morsani College of Medicine, University of South Florida, Tampa, FL. "Further studies may reveal such mechanism of action for MSCs in other neurological disorders."

More information: Oh, S. H.; Kim, H. N.; Park, H-J.; Shin, J. Y.; Lee , P. H. Mesenchymal stem cells increase hippocampal neurogenesis and neuronal differentiation by enhancing the Wnt signaling pathway in Alzheimer's disease model. *Cell Transplant.* Appeared or available online: March 7, 2014. www.ingentaconnect.com/content … nts/content-CT1059Oh

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