Transplanted human stem cells prolong survival in mouse model of rare brain disease

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A new study finds substantial improvement in a mouse model of a rare, hereditary neurodegenerative disease after transplantation of normal human neural stem cells. The research findings, published by Cell Press in the September 4th issue of the journal *Cell Stem Cell*, show that the transplanted cells provided a critical enzyme that was missing in the brains of the experimental mice and represent an important step toward what may be a successful therapeutic approach for a currently untreatable and devastating disease.

Infantile neuronal ceroid lipofuscinosis (INCL), commonly known as Batten disease, is a fatal neurodegenerative disease in children. It is caused by a mutation in the gene that makes a crucial enzyme called palmitoyl protein thioesterase-1 (PPT1). A deficiency of PPT1 in the brain causes the abnormal accumulation of a cellular lipid storage material called lipofuscin, which leads to neuron death, a decline in cognitive and motor skills, visual impairment, seizures and premature death. Unfortunately, intravenous enzyme replacement therapy is not a viable treatment approach as it is nearly impossible to get the PPT1 enzyme into the brain.

Although there is currently no effective treatment for INCL, it has been hypothesized that transplanted donor cells might be able to secrete the needed enzyme directly into the host brain. A mouse model of INCL that mimics many aspects of the human disease has been developed and provides an excellent experimental model for testing whether a human neural stem cell transplant may be a beneficial disease treatment. Dr.

Nobuko Uchida from StemCells, Inc., in Palo Alto, California led a study that tested this hypothesis with banked human neural stem cells that had been purified, expanded, and preserved.

"We took a novel approach and transplanted normal, nontumorigenic, and nongenetically modified human neural stem cells to deliver the deficient enzyme in the mouse model of INCL," explains Dr. Uchida. "We transplanted self-renewing human neural stem cells because, theoretically, these transplants can provide life-long production of the missing enzyme." Dr. Uchida and colleagues found that the purified human neural stem cells engrafted to the brain of INCL mice, migrated extensively, and produced enough PPT1 in the host mice to elicit significant improvement. Specifically, the INCL mice exhibited reduced lipofuscin, widespread neuroprotection, and a delayed loss of motor coordination.

"Early intervention with neural stem cell transplants into the brains of INCL patients may supply a continuous and long-lasting source of the missing PPT1 and provide some therapeutic benefit through protection of endogenous neurons," concludes Dr. Uchida. "These data support our rationale for continued development in humans and the potential for a medical breakthrough in this deadly disease." Notably, StemCells, Inc., recently reported positive results from the first Phase 1 clinical trials assessing the safety of these human neural stem cells as a potential treatment for Batten disease.

Source: Cell Press (news : web)