Burnham team is successful in stem cell study

by Terri Somers

SAN DIEGO - Scientists at the Burnham Institute for Medical Research said they have used human embryonic stem cells to treat a genetically linked degenerative disease by significantly preserving function and prolonging life in mice.

Evan Snyder, Burnham Institute for Medical Research

Their findings offer insights into a biological pathway that affects a broad array of diseases, which combined afflict one in 5,000 people, said Evan Snyder and Jean-Pyo Lee, the Burnham scientists.

In a peer-reviewed article in the journal Nature Medicine, published online Sunday, the San Diego-based scientists write that they implanted two types of stem cells - human neural stem cells taken from a developing brain and human embryonic stem cells coaxed to become neural stem cells - into mice with Sandhoff disease, a deadly degenerative childhood affliction.

Children with Sandhoff, a form of Tay-Sachs disease, are deficient in an enzyme that helps the body metabolize lipids, a fatty material. A buildup of lipids destroys brain cells that control and coordinate body movement and leads to the deterioration of the brain and spinal cord. Children with the disease often don't see their sixth birthday.

When stem cells were implanted in mice, the onset of symptoms was delayed, well-being and motor function were preserved, and life span was extended 70 percent, according to the article.

The study showed the stem cells migrated throughout the brain, with some replacing damaged nerve cells and transmitting nerve impulses.

This is the first evidence that stem-cell-derived nerve cells may integrate electrically and functionally into a diseased brain, Snyder said.

The transplanted cells also boosted the brain's supply of the enzyme Hex, the housecleaning substance that reduces lipid accumulations.

The treatment also dampened the inflammation that typically occurs in the brain as a result of most degenerative diseases. Inflammation is also thought to play a role in disease progression.

"Our study offers the first evidence that (human embryonic stem cells) employ multiple mechanisms - not just cell replacement - to benefit disease," said Snyder, who runs Burnham's stem cell program.

When the stem cells were transplanted into mice who were also given a drug that permitted the enzymes in the stem cells to work more efficiently, the life span of the mice doubled.

This part of the study highlights how future therapeutic use of stem cells against degenerative disease will likely be multidimensional, using the cells as the glue to hold everything together, Snyder said.

"Our studies suggest that functional neuronal replacement can be complemented and, under some conditions, eclipsed by a range of other stem cell actions that nevertheless exert a number of critical stabilizing forces," Snyder said.

Neither of the human embryonic stem cells created tumors, the article says. And the scientists also noted that they saw no negative reactions by the mouse immune system, which are often prompted by transplanting foreign cells into a body.

The article is the culmination of a long-standing collaboration between the Burnham scientists and Frances Platt and Mylvaganam Jeyakumar of Oxford University in England.

The scientists noted that the stem cells they used were coaxed to evolve and survive in a solution that does not contain animal cells and would therefore likely be acceptable to the Food and Drug Administration. All new drugs and therapies in the United States require FDA approval.

While Sandhoff is a rare disease, it is one of a broad type of diseases in which the body cannot metabolize lipids. Since its genetic link is known, scientists use it in researching an array of other diseases in which the genetic cause still has not been identified.

The Burnham scientists hope their work with Sandhoff disease, for which there is no cure, lays the groundwork for clinical trials.

"Dr. Snyder's team has extended the promise of stem cell therapies to children with special needs, including those with Sandhoff disease," said Fia Richmond, the Santa Barbara, Calif., founder of Children's

Neurobiological Solutions, whose son has an undiagnosed neurological disorder.

"The CNS Foundation is proud to have contributed major funding for this project on behalf of the 14 million special-needs children in the United States alone."

Other funding for the four-year study came from the National Institutes of Health, Oxford University, the Wellcome Trust and private philanthropies, including National Tay-Sachs and Allied Diseases Foundation, the Late-Onset Tay-Sachs Foundation, the A-T Children's Project, the Barbara Anderson Foundation for Brain Repair, Project A.L.S., March of Dimes and Hunter's Hope.

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