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Human stem cells aid stroke recovery in rats

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Neural cells derived from human embryonic stem cells helped repair stroke-related damage in the brains of rats and led to improvements in their physical abilities, according to a new study by researchers at the Stanford University School of Medicine.

This study, to be published in the Feb. 20 issue of the journal PLoS ONE, marks the first time researchers have used human embryonic stem cells to generate neural cells that grow well in the lab, improve a rat's physical abilities and consistently don't form tumors when transplanted.

Though the authors caution that the study is small and that more work is needed to determine whether a similar approach would work in humans, they said they believe it shows the potential for using stem cell therapies in treating strokes.

Senior author Gary Steinberg, MD, PhD, the Bernard and Ronni Lacroute-William Randolph Hearst Professor in Neurosurgery and Neurosciences, said that with 750,000 people having strokes in the United States each year, the disease creates a massive burden for people, their families and the medical system.

"Human embryonic stem cell-based therapies have the potential to help treat this complex disease," Steinberg said, adding that he hopes the cells from this study can be used in human stroke trials within five years.

Human embryonic stem cells are able to form any cell type in the body.

Pushing those cells to form neurons rather than other types of cells has been a substantial hurdle, as has avoiding the cells' tendency to form tumors when transplanted. Because embryonic stem cells are still immature and retain the ability to renew themselves and produce all tissue types, they tend to grow uncontrollably into tumors consisting of a mass of different cells.

First author Marcel Daadi, PhD, a senior scientist in Steinberg's lab, said the team overcame both obstacles by growing the embryonic stem cells in a combination of growth factors that nudged the cells to mature into stable neural stem cells. After six months in a lab dish, those neural stem cells continued to form only the three families of neural cells — neurons, astrocytes and oligodendrocytes — and no tumors.

Convinced that the cells appeared safe, Daadi and co-author Anne-Lise Maag, a former Stanford medical student, transplanted those cells into the brains of 10 rats with an induced form of stroke. At the end of two months, the cells had migrated to the damaged brain region and incorporated into the surrounding tissue. None of those transplanted cells formed tumors.

Once in place, the replacement cells helped repair damage from the induced stroke. The researchers mimicked a stroke in a region of the brain that left one forelimb weak. This model parallels the kinds of difficulties people experience after a stroke.

Testing at four weeks and again at eight weeks after the stem cell transplants showed the animals were able to use their forelimbs more normally than rats with similarly damaged brain regions that had not received the transplants.

"The great thing about these cells is that they are in unlimited supply and are very versatile," Daadi said. The neural cells the group generated grew

indefinitely in the lab and could be an ongoing source of cells for treating stroke or other injuries, he added.

In previous studies, Steinberg and others have implanted cells from cord blood, bone marrow, fetal and adult brain tissue or derived from mouse embryonic stem cells into stroke-damaged rats, but none of those cell types appear as promising as the cells in this study, the researchers said. Those cells are not as easy to produce in large scale for the appropriate quality assurance program to meet a sufficient patient population for multi-center clinical trials.

Before researchers can begin testing these neural cells in human stroke patients, Steinberg and Daadi said they need to verify that the cells are effective in other animal stroke models and don't form tumors. They are working with industry groups to grow the cells in accordance with U.S. Food and Drug Administration guidelines, which would be necessary before they could move on to human trials.

Citation: Daadi MM, Maag A-L, Steinberg GK (2008) Adherent Self-Renewable Human Embryonic Stem Cell-Derived Neural Stem Cell Line: Functional Engraftment in Experimental Stroke Model. PLoS ONE 3(2): e1644. doi:10.1371/journal.pone.0001644 (www.plosone.org/doi/pone.0001644)

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