Stem cell-based transplantation approach improves recovery from stroke

June 19 2014

Stroke is a leading cause of death and disability in developed countries, and there is an urgent need for more clinically effective treatments. A study published by Cell Press June 19th in *Stem Cell Reports* reveals that simultaneous transplantation of neural and vascular progenitor cells can reduce stroke-related brain damage and improve behavioral recovery in rodents. The stem cell-based approach could represent a promising strategy for the treatment of stroke in humans.

"Our findings suggest that early cotransplantation treatment can not only replace lost cells, but also prevent further deterioration of the injured brain following ischemic stroke," says senior study author Wei-Qiang Gao of Shanghai Jiaotong University. "With the development of human embryonic and induced pluripotent stem cell technology, we are optimistic about the potential translation of our research into clinical use."

The most common kind of stroke, known as ischemic stroke, is caused by a blood clot that blocks or plugs a blood vessel in the brain. Although a medicine called tissue plasminogen activator can break up blood clots in the brain, it must be given soon after the start of symptoms to work, and there are no other clinically effective treatments currently available for this condition. Stem cell transplantation represents a promising therapeutic strategy, but transplantation of either neural progenitor cells or vascular cells has shown restricted therapeutic effectiveness.

In the new study, Gao teamed up with colleagues at Shanghai Jiao Tong

University, including Jia Li, Yaohui Tang, and Guo-Yuan Yang, to test whether cotransplantation of both neural and vascular precursor cells would lead to better outcomes. They induced ischemic stroke in rats and then simultaneously injected neural and vascular progenitor cells from mice into the stroke-damaged rat brains 24 hours later. The transplanted precursor cells turned into all major types of vascular and brain cells, including mature, functional neurons. The resulting vascular cells developed into microvessels, while the grafted neural cells produced molecules known to stimulate the growth of both neurons and vessels.

"This is the first study to use embryonic stem cell-derived vascular progenitor cells together with neural progenitor cells to treat ischemic stroke," Gao says. "These two types of progenitors generate nearly all types of brain cells, including endothelial cells, pericytes/smooth muscle cells, neurons, and astrocytes, resulting in better restoration of neurovascular units and better replacement of the lost cells in the stroke model. A previously reported cotransplantation approach published in the journal *Stem Cells* in 2009 (DOI: 10.1002/stem.161) was limited because it did not use vascular precursor cells capable of turning into all major types of vascular cells important for recovery. Our findings here suggest that cotransplantation of the two types of cells that restore the neurovascular unit more effectively is a better approach for the treatment of ischemic stroke."

Two weeks after stroke, rats that had undergone cotransplantation showed less brain damage and improved behavioral performance on motor tasks compared with rats that had been treated with neural progenitor cells alone. "Our findings suggest that cotransplantation of neural and vascular cells is much more effective than transplantation of one cell type alone because these two cell types mutually support each other to promote recovery after stroke," Gao says.

More information: *Stem Cell Reports*, Li et al.: "Neurovascular

Recovery via Co-transplanted Neural and Vascular Progenitors Leads to Improved Functional Restoration after Ischemic Stroke in Rats." www.cell.com/stem-cell-reports … 2213-6711(14)00153-2

Provided by Cell Press