

Stem-like Cells from Peripheral Blood Restore Function

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Tampa, FL (July 7, 2003) — Rats with severe strokes recovered function following intravenous injections of stem-like cells obtained from circulating human blood — a finding that points to another potential cell therapy for stroke.

The study, by researchers at the University of South Florida Center of Excellence for Aging and Brain Repair, appears in today's issue of the journal *Cell Transplantation*.

The human blood donors were injected with granulocyte stimulating factor (G-CSF) to stimulate the release of stem-like cells from their bone marrow into the bloodstream before a blood sample was collected. These stem-like cells are known as peripheral blood progenitor cells.

"This is the first demonstration that G-CSF stimulated peripheral blood cells promote functional recovery after a stroke," said Alison Willing, PhD, assistant professor of neurosurgery and first author of the study. "We were putting these cells into animals 24 hours after a stroke and seeing significant behavioral improvement. The animals behaved almost normally on our tests, just as they had before the stroke. That's pretty amazing."

G-CSF stimulated peripheral blood cells have become an alternative treatment to bone marrow transplants for patients with blood cancers. They are easier to obtain, lead to faster recovery from chemotherapy and better survival.

Dr. Willing and her colleagues wanted to explore whether G-CSF treated peripheral blood cells might also be a treatment for central nervous system disorders. For the last few years, the USF Center for Aging and Brain Repair has been investigating alternatives to human embryonic stem cells, such as adult bone marrow stem cells and human umbilical cord blood (HUCB) cells, as treatments for stroke, spinal cord injury and other neurological disorders.

"Our findings suggest that mobilized peripheral blood cells might be a good candidate for early treatment of central nervous system disorders like stroke," said Paul R. Sanberg, PhD, DSc, professor of neurosurgery and director of the USF Center for Aging and Brain Repair. "They appear to be more readily accessible and easier to isolate than bone marrow and, like bone marrow, could be donated by patients for their own use."

In an editorial accompanying the USF study, authors Cesar Borlongan, PhD, and David Hess, MD, both of the Medical College of Georgia, also suggest that a patient's own peripheral blood stem cells might be a source of cell therapy for stroke. "Administration of G-CSF itself (an already FDA-approved drug) may mobilize progenitor cells from the bone marrow compartment into the peripheral blood where they can 'home' to the brain

and have a protective or restorative effect. This would avoid the need to isolate cells and reinject them."

For this pilot study, the USF team compared the effect of G-CSF stimulated peripheral blood cells with that of HUCB cells in a rat model for severe stroke. An earlier report by researchers at USF and Henry Ford Hospital in Detroit reported that intravenous injections of HUCB cells helped rats recover from strokes faster.

The USF team looked at three groups of rats induced to have symptoms of stroke.

The first group was intravenously injected with G-CSF stimulated peripheral blood cells 24 hours after a stroke. These cells were collected from the circulating blood of human blood donors through a process known as leukapheresis. Because the donors had received G-CSF before their blood was drawn, the resulting blood sample included a larger-than-normal population of immature, undifferentiated cells with the capacity to become any cell in the body, including neurons.

The second group was intravenously injected with HUCB cells 24 hours after the stroke.

The third group, a control, received no cellular treatment.

The researchers found that, following cell therapy, the stroke-induced hyperactive behavior of the rats was reduced to a pre-stroke level of normal activity. The improvement was similar whether the rats had been treated with peripheral blood cells or HUCB cells. Unlike humans, who are often paralyzed following a severe stroke, rats typically become abnormally active.

In addition, both the G-CSF stimulated peripheral blood cells and HUCB cells prevented the rats from developing stroke-associated motor asymmetry — the favoring of one side over another. The control rats displayed a significant increase in motor bias following stroke.

The researchers are unsure how these peripheral blood cells improve functional recovery, but they suspect the transplanted cells may secrete protective substances that prevent further brain damage rather than replacing already damaged neurons. One month, the length of the USF study, likely was not enough time for a stem-like peripheral blood cell to change into a replacement neuron and sprout functioning fibers in the brain, Dr. Willing said.

Dr. Willing and her colleagues are continuing to try to determine how the peripheral blood cells work, as well as the optimal time, method and number of cells to deliver following a stroke.