Growth factor in stem cells may spur recovery from multiple sclerosis

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A substance in human mesenchymal stem cells that promotes growth appears to spur restoration of nerves and their function in rodent models of multiple sclerosis (MS), researchers at Case Western Reserve University School of Medicine have found.

Their study appeared in the online version of Nature Neuroscience on Sunday, May 20.

In animals injected with hepatocyte growth factor, inflammation declined and neural cells grew. Perhaps most important, the myelin sheath, which protects nerves and their ability to gather and send information, regrew, covering lesions caused by the disease.

"The importance of this work is we think we've identified the driver of the recovery," said Robert H. Miller, professor of neurosciences at the School of Medicine and vice president for research at Case Western Reserve University.

Miller, neurosciences instructor Lianhua Bai and biology professor Arnold I. Caplan, designed the study. They worked with Project Manager Anne DeChant, and research assistants Jordan Hecker, Janet Kranso and Anita Zaremba, from the School of Medicine; and Donald P. Lennon, a research assistant from the university's Skeletal Research Center.

In MS, the immune system attacks myelin, risking injury to exposed

nerves' intricate wiring. When damaged, nerve signals can be interrupted, causing loss of balance and coordination, cognitive ability and other functions. Over time, intermittent losses may become permanent.

Miller and Caplan reported in 2009 that when they injected human mesenchymal stem cells into rodent models of MS, the animals recovered from the damage wrought by the disease. Based on their work, a clinical trial is underway in which MS patients are injected with their own stem cells.

In this study, the researchers first wanted to test whether the presence of stem cells or something cells produce promotes recovery. They injected mice with the medium in which mesenchymal stem cells, culled from bone marrow, grew.

All 11 animals, which have a version of MS, showed a rapid reduction in functional deficits.

Analysis showed that the disease remained on course unless the molecules injected were of a certain size; that is, the molecular weight ranged between 50 and 100 kiloDaltons.

Research by others and results of their own work indicated hepatocyte growth factor, which is secreted by mesenchymal stem cells, was a likely instigator.

The scientists injected animals with 50 or 100 nanograms of the growth factor every other day for five days. The level of signaling molecules that promote inflammation decreased while the level of signaling molecules that counter inflammation increased. Neural cells grew and nerves laid bare by MS were rewrapped with myelin. The 100-nanogram injections appeared to provide slightly better recovery.

To test the system further, researchers tied up cell-surface receptors, in this case cMet receptors that are known to work with the growth factor.

When they jammed the receptors with a function-blocking cMet antibody, neither the mesenchymal stem cell medium nor the hepatocyte growth factor injections had any effect on the disease. In another test, injections of an anti-hepatocyte growth factor also blocked recovery.

The researchers will continue their studies, to determine if they can screen mesenchymal stem cells for those that produce the higher amounts of hepatocyte growth factor needed for effective treatment. That could lead to a more precise cell therapy.

"Could we now take away the mesenchymal stem cells and treat only with hepatocyte growth factor?" Miller asked. "We've shown we can do that in an animal but it's not clear if we can do that in a patient."

They also plan to test whether other factors may be used to stimulate the cMet receptors and induce recovery.

Provided by Case Western Reserve University