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Immune system helps transplanted stem cells navigate in central nervous system

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By discovering how adult neural stem cells navigate to injury sites in the central nervous system, UC Irvine researchers have helped solve a puzzle in the creation of stem cell-based treatments: How do these cells know where to go?

Tom Lane and Kevin Carbajal of the Sue and Bill Gross Stem Cell Research Center found the answer with the body's immune system.

Their study not only identifies an important targeting mechanism in transplanted stem cells but also provides a blueprint for engineering stem cell-based therapies for multiple sclerosis and other chronic neurological diseases in which inflammation occurs. Results appear in this week's early online edition of the Proceedings of the National Academy of Sciences.

"Previously, we've seen that adult neural stem cells injected into the spinal column knew, amazingly, exactly where to go," said Lane, Chancellor's Fellow and professor of molecular biology & biochemistry. "We wanted to find what directed them to the right injury spots."

The researchers used adult neural stem cells to treat mice with a disease similar to MS that destroys myelin, the protective tissue coating on nerves, causing chronic pain and loss of motor function. Adult neural stem cells have shown the ability to change - or differentiate - into oligodendrocytes, the building blocks of myelin, and repair or replace affected tissue.

In the mice, inflammatory cells - reacting to the virally induced nerve damage - were observed activating receptors on the adult neural stem cells. These CXCR-4 receptors, in turn, recruited chemokine proteins called CXCL-12 that guided the stem cells to specific sites. Chemokines are produced in acute and chronic inflammation to help mobilize white blood cells.

As the stem cells migrated through the central nervous system, they began to transform into the precursor cells for oligodendrocytes. Latching onto their repair sites, they continued the differentiation process. Three weeks after the initial treatment, 90 percent of the cells had grown into fully formed oligodendrocytes.

In earlier work, Lane and colleagues demonstrated that adult neural stem cell treatments improved motor function in mice with chronic MS symptoms.

"In this study, we've taken an important step by showing the navigational cues in an inflammatory environment like MS that guide stem cells," said Lane. "Hopefully, these cues can be incorporated into stem cell-based treatments to enhance their ability to repair injury."

Chris Schaumburg and Joy Kane of UCI and Dr. Robert Strieter of the University of Virginia participated in the study, which received support from the National Institutes of Health and the National Multiple Sclerosis Society.

Lane recently received a Collaborative MS Research Center Award from the National Multiple Sclerosis Society to assemble a team to investigate the use of cell replacement therapy to regenerate MS-ravaged nerve tissue.

Provided by University of California - Irvine