

Researchers focus on human cells for spinal cord injury repair

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For the first time, scientists discovered that a specific type of human cell, generated from stem cells and transplanted into spinal cord injured rats, provide tremendous benefit, not only repairing damage to the nervous system but helping the animals regain locomotor function as well.

The study, published today in the journal [PLoS ONE](#), focuses on human astrocytes – the major support cells in the central [nervous system](#) – and indicates that transplantation of these cells represents a potential new avenue for the treatment of [spinal cord](#) injuries and other central nervous system disorders.

Working together closely, research teams at the University of Colorado School of Medicine and University of Rochester Medical Center have made a major breakthrough in the use of human astrocytes for repairing injured spinal cords in rats.

"We've shown in previous research that the right types of rat astrocytes are beneficial, but this study brings it up to the human level, which is a huge step," said Chris Proschel, Ph.D., lead study author and assistant professor of Genetics at the University of Rochester Medical Center. "What's really striking is the robustness of the effect. Scientists have claimed repair of [spinal cord injuries](#) in rats before, but the benefits have been variable and rarely as strong as what we've seen with our transplants."

There is one caveat to the finding – not just any old astrocyte will do. Using [stem cells](#) known as human fetal glial precursor cells, researchers generated two types of astrocytes by switching on or off different signals in the cells. Once implanted in the animals, they discovered that one type of human astrocyte promoted significant recovery following spinal cord injury, while another did not.

"Our study is unique in showing that different types of human astrocytes, derived from the exact same population of human precursor cells, have completely different effects when it comes to repairing the injured spinal cord," noted Stephen Davies, Ph.D., first author and associate professor in the Department of Neurosurgery at the University of Colorado School of Medicine. "Clearly, not all human astrocytes are equal when it comes to promoting repair of the injured central nervous system."

The research teams from Rochester and Colorado also found that transplanting the original stem cells directly into spinal cord injured rats did not aid recovery. Researchers believe this approach – transplanting undifferentiated stem cells into the damaged area and hoping the injury will cause the stem cells to turn into the most useful cell types – is probably not the best strategy for injury repair.

According to Mark Noble, director of the University of Rochester Stem Cell and Regenerative Medicine Institute, "This study is a critical step toward the development of improved therapies for spinal cord injury, both in providing very effective human astrocytes and in demonstrating that it is essential to first create the most beneficial cell type in tissue culture before transplantation. It is clear that we cannot rely on the injured tissue to induce the most useful differentiation of these precursor cells."

To create the different types of astrocytes used in the experiment,

researchers isolated human glial precursor cells, first identified by Margot Mayer-Proschel, Ph.D., associate professor of Genetics at the University of Rochester Medical Center, and exposed these precursor cells to two different signaling molecules used to instruct different astrocytic cell fate – BMP (bone morphogenetic protein) or CNTF (ciliary neurotrophic factor) .

Transplantation of the BMP human astrocytes provided extensive benefit, including up to a 70% increase in protection of injured spinal cord neurons, support for nerve fiber growth and recovery of locomotor function, as measured by a rat's ability to cross a ladder-like track.

In contrast, transplantation of the CNTF astrocytes, or of the stem cells themselves, failed to provide these benefits. Researchers are currently investigating why BMP astrocytes performed so much better than CNTF astrocytes, but believe multiple complex cellular mechanisms are probably involved.

"It is estimated that astrocytes make up the vast majority of all cell types in the human brain and spinal cord, and provide multiple different types of support to neurons and other cells of the central nervous system," said Jeannette Davies, Ph.D., assistant professor at the University of Colorado School of Medicine and co-lead author of the study. "These multiple functions are likely to all be contributing to the ability of the right human astrocytes to repair the injured spinal cord."

With these results, the Proschel and Davies teams are moving forward on the necessary next steps before they can implement the approach in humans, including testing the transplanted human astrocytes in different injury models that resemble severe, complex human spinal cord injuries at early and late stages after injury.

"Studies like this one bring increasing hope for our patients with spinal

cord injuries," said Jason Huang, M.D., associate professor of Neurosurgery at the University of Rochester Medical Center and Chief of Neurosurgery at Highland Hospital. "Treating spinal cord injuries will require a multi-disciplinary approach, but this study is a promising one showing the importance of modifying human [astrocytes](#) prior to transplantation and has significant clinical implications."

Provided by University of Rochester Medical Center

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