

Stem cell advance a step forward for treatment of brain diseases

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Scientists have created a way to isolate neural stem cells – cells that give rise to all the cell types of the brain – from human brain tissue with unprecedented precision, an important step toward developing new treatments for conditions of the nervous system, like Parkinson's and Huntington's diseases and spinal cord injury.

The work by a team of neuroscientists at the University of Rochester Medical Center was published in the Nov. 3 issue of the [Journal of Neuroscience](#). Neurologist Steven Goldman, M.D., Ph.D., chair of the Department of Neurology, led the team.

The latest paper marks a six-year effort by Goldman's team to develop a better way to isolate pure preparations of neural stem cells directly from the human brain. These stem cells can renew themselves and have the potential to become a number of brain cell types – for instance, oligodendrocytes that might help people with multiple sclerosis, or neurons to help people with Parkinson's disease. But after the first few months of human embryonic development, they become rare in the brain, and it's challenging for scientists to find, isolate and manipulate them. Yet those challenges must be met if stem cells are to live up to their promise as treatments for a host of human diseases of the nervous system.

So far, most efforts aimed at isolating human fetal stem cells have entailed cultivating brain tissue in tissue culture in the laboratory for months, then separating out the stem cells for study. In addition, today's

techniques don't separate out just stem cells; typically, similar cells known as progenitor cells, which have already committed to becoming a certain type of cell, are also captured. The difference is crucial for scientists who often prefer to capture only uncommitted neural stem cells, whether to treat brain diseases requiring the replacement of multiple cell types or to better understand their function.

The Goldman lab's new technique snags only neural stem cells and does so directly from brain tissue. The technology saves months of time and labor in the laboratory and also gives scientists a clearer look than ever before at exactly how stem cells operate in the brain.

In its studies, Goldman's team found some surprises. As expected, certain classes of genes encoding for proteins active in mouse neural stem cells – such as members of the Notch and WNT families – were highly active. But when the scientists looked more closely, they found that the freshly isolated neural stem cells expressed some genes from these families that were previously virtually unknown in humans, and which had never before been implicated in human brain function. At the same time, some of the genes that are important and active in mouse neural stem cells proved not to be so in the human cells.

"While research in mice and other animals serves as a guide, ultimately you have to study human tissue and humans to really understand disease in people," said Goldman, who is also co-director of Rochester's Center for Translational Neuromedicine. "While the general signaling pathways active in mice and people are very similar, the individual genes are quite different. This is not something we would have predicted. It's a good demonstration that you can't use mouse studies to fully dictate what kinds of therapeutics should be used in people."

The ability to gather human cells more efficiently should aid potential treatments built around transplanting stem cells. In the last few years a

couple studies using human neural stem cells in the nervous system have begun in children with incurable brain diseases known as pediatric leukodystrophies. But the field is in its infancy, and Goldman believes that the cell types currently being used will soon be replaced by more effective types of transplantable stem and progenitor cells.

The new technology is built around a piece of DNA that codes for a protein known as Sox2, which has long been recognized as a key stem cell gene. Since the gene is active only in stem cells, finding a way to see and isolate cells with an active Sox2 gene is the key.

To track it down, the team identified the DNA sequence, known as an enhancer, that determines whether Sox2 is active in neural stem cells. The scientists took that piece of DNA, coupled it to a gene that makes cells emit light of a particular wavelength, and then packaged the resulting synthetic DNA into a virus. They used the virus to deliver the synthetic DNA to neural stem cells in the brain tissue. The technique compelled neural stem cells – and only the [stem cells](#) – to emit light of a certain color, which in turn allowed a laser-based system to tag and capture just those cells. The result was a pure population of human [neural stem cells](#), the first such population ever purified so specifically or directly.

Provided by University of Rochester Medical Center

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