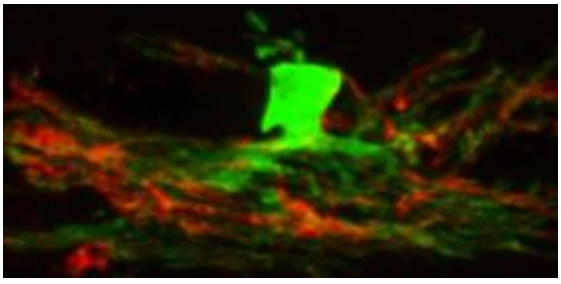
A new program for neural stem cells

May 12 2011



Transplantation of reprogrammed neural stem cells into the brains of genetically modified mice, which cannot form myelin. The stem cells develop oligodendrocytes (green), which form myelin (red). Credit: Max Planck Institute for Brain Research

German researchers succeed in obtaining brain and spinal cord cells from stem cells of the peripheral nervous system.

Neural stem cells can do a lot, but not everything. For example, brain and spinal cord cells are not usually generated by neural stem cells of the peripheral nervous system, and it is not possible to produce cells of the peripheral nervous system from the stem cells of the brain. However, researchers from the Max Planck Institute for Brain Research in Frankfurt and the Max Planck Institute of Immunobiology and Epigenetics in Freiburg have now succeeded in producing central nervous system cells from neural stem cells of the peripheral nervous system. They found that if peripheral stem cells are maintained under defined growth conditions, they generate oligodendrocytes, which form

the myelin layer that surrounds the neurons found in the brain and spinal cord.

The mammalian nervous system consists of a central (brain, spinal cord) and peripheral nervous system (e.g. nerves and sensory ganglia). Although the two systems are very closely interlinked, they differ anatomically and consist of different cell types. The cell types of the peripheral nervous system originate from precursor cells in the embryo called the neural crest. To date, it was believed that these neural crest stem cells could generate the neurons and support cells, known as glial cells, of the peripheral nervous system, but not the cells of the central nervous system.

Environmental conditions clearly determine the kind of cells into which the neural crest stem cells develop. Together with colleagues from Paris, the Freiburg- and Frankfurt-based scientists succeeded in demonstrating that, under modified conditions, these stem cells can also generate cells of the central nervous system. They exposed stem cells from the peripheral nervous system of embryonic or postnatal mice to different culture conditions. In addition to neurons, the neural crest stem cells also developed into different types of glial cells of the central nervous system, including oligodendrocytes and astrocytes. "The culture medium reprograms the neural crest stem cells in such a way that they change their identity. This worked without genetic modification of the cells," explains Hermann Rohrer from the Max Planck Institute for Brain Research.

Factors in the culture medium clearly activated a different genetic program so that cell types developed from the stem cells, which normally would not. The scientists do not yet understand the precise factors at work here. However, there are some indications that fibroblast growth factor (FGF) is involved in this transformation.

In the brains of mice at different developmental stages, the reprogrammed stem cells mainly developed into oligodendrocytes, which form the myelin layer around the neurons of the central nervous system and are, therefore, indispensable for the transmission of electrical stimuli. Transplantation experiments carried out by the researchers on genetically modified mice that do not produce myelin and have severe neurological defects proved that the new oligodendrocytes can also assume this task. "The reprogrammed stem cells can form cells of the central nervous system, and the new cells can permanently integrate into this system," says Verdon Taylor of the Max Planck Institute of Immunobiology and Epigenetics.

It is not yet clear, to what extent these basic research findings will contribute to the development of cell therapy for humans. This would require that similar stem cells are present and accessible in the peripheral nervous system of humans, and that these can be propagated and reprogrammed in culture. "At present, we only know that these stem cells in mice also have the potential to produce oligodendrocytes," says Hermann Rohrer. The scientists would now like to investigate in greater detail which molecular mechanisms are responsible for the reprogramming of the stem cells, whether neural crest stem cells also exist in the peripheral nervous system of adult mice and what kind of conditions are required to enable the reprogramming of these cells.

More information: Peripheral nervous system progenitors can be reprogrammed to produce myelinating oligodendrocytes and repair brain lesions, Ellen Binder, Marion Rukavina, Hessameh Hassani, Marlen Weber, Hiroko Nakatani, Tobias Reiff, Carlos Parras, Verdon Taylor, and Hermann Rohrer, Journal of Neuroscience, April 27, 2011, DOI:10.1523/JNEUROSCI.0129-11.2011

Provided by Max-Planck-Gesellschaft