MedicalXpress

Mysterious cells may play role in ALS

November 17 2010

(PhysOrg.com) -- By tracking the fate of a group of immature cells that persist in the adult brain and spinal cord, Johns Hopkins researchers discovered in mice that these cells undergo dramatic changes in ALS, also known as Lou Gehrig's disease.

A study reported November 17 online in *Neuron* shows that these cells, called NG2+, grow and expand rapidly during early life, eventually morphing into mature nervous system cells called oligodendrocytes. These "oligos" help speed the transmission of electrical impulses by providing insulation around nerve cells. This insulation, known as myelin, is disrupted in nervous system diseases such as multiple sclerosis.

The team tracked the fate of NG2+ cells in both normal mice and mice with a mutant form of the SOD1 gene that causes ALS. Using a stringent system that let them color-tag only NG2+ cells and then accurately locate these cells at various times in their development, the researchers found that NG2+ cells normally keep up a quiet program of dividing in adult tissues, sometimes replacing themselves and other times forming new oligos.

A slow and steady turnover of oligodendrocytes may be required throughout life to maintain myelin, says Dwight Bergles, Ph.D., associate professor in The Solomon H. Snyder Department of Neuroscience, Johns Hopkins University School of Medicine. However, the normal developmental program of NG2+ cells goes awry in the spinal cords of ALS mice.

“In the model ALS mice we studied, it’s as though NG2+ cells step onto a high-speed treadmill,” Bergles says. “They undergo explosive division, morph more readily into abnormal-looking oligodendrocytes and then, uncharacteristically, those differentiated cells quickly die. The brakes that normally hold these cells in check appear to be gone in ALS.”

Of special note are provocative data showing this cell type as the most proliferating cell population in the spinal cords of ALS mice, churning out even more oligodendrocytes than in normal mice, says Shin Kang, Ph.D, a research associate in The Solomon H. Snyder Department of Neuroscience.

“This suggests there is significant oligodendrocyte death even before anything else degenerates,” he explains, “which identifies a new and important player in the progression of this disease.”

All this frenetic oligodendrocyte-generating activity takes place in the central nervous system’s gray matter where other cells — the motor neurons — are dying. A body of research shows that after acute trauma to the central nervous system, a short-term upswing in NG2+ activity takes place that may help reduce the extent of damage. Whether this change in behavior of NG2+ cells is protective, or accelerates the death of motor neurons in ALS, is not yet known.

Earlier studies in lab-dish cultures showed that NG2+ cells acted like stem cells, capable of turning into the major cell types in the nervous system, suggesting that they could be harnessed to replace cells that died as a result of injury or disease. However, the Hopkins team saw no evidence that the cells become anything other than oligodendrocytes in both healthy animals and those carrying the ALS mutant gene.

“Although we found that the potential of these cells is more limited than previously thought, it might be possible to coax them to adopt different

fates," Bergles says. "We only need to know what factors are restricting their development in the intact nervous system."

"This goes much further than simply confirming a negative finding about these mysterious cells," adds Kang. "We've answered a question, but the new observation about the overgrowth could lead to an entirely new understanding of ALS."

Provided by Johns Hopkins University