Cause of nerve fiber damage in multiple sclerosis identified

October 16 2006

Researchers have identified how the body's own immune system contributes to the nerve fiber damage caused by multiple sclerosis, a finding that can potentially aid earlier diagnosis and improved treatment for this chronic disease.

The study reveals how immune system B-cells damage axons during MS attacks by inhibiting energy production in these nerve fiber cells, ultimately causing them to degenerate and die. Study results appear in the Oct. 15 issue of the *Journal of Immunology*.

B-cell-axon activity is an emerging area of MS research, one that is changing how scientists and clinicians can look at this disease. In this study, Dr. Yufen Qin and fellow researchers from UC Irvine's School of Medicine analyzed spinal fluid and tissue samples from MS patients to identify substances that stimulate a B-cell immune response. They noted an increased level of B-cell antibodies on lesions and in spinal fluid bound to two specific enzymes -- GAPDH and TPI.

These two enzymes are essential for efficient energy production. The researchers believe that the binding of these antibodies to these enzymes -- GAPDH, in particular -- may lower the amounts of ATP -- the chemical fuel for cells -- available in cells, which eventually can lead to axon cell degeneration and death. In addition to the energy-production function, GAPDH is involved with a number of genetic activities, such as RNA translocation, DNA replication and DNA repair.

Other recent studies have shown that binding of inhibitors to GAPDH and TPI causes decreased ATP production in neurons, followed by progressive neuronal degeneration and death. Moreover, patients with TPI deficiency can develop progressive neurological disorders.

"This research is exciting and potentially important for future treatments because it identifies new antibodies associated with MS that can be targeted with emerging therapies," said Qin, an assistant professor of neurology. "Significantly, these are the first antibodies to be identified with axon activity, which is a new area researchers are exploring in the pathology of MS."

MS is a chronic central nervous system disease that can cause blurred vision, poor coordination, slurred speech, numbness, acute fatigue and, in its most extreme form, blindness and paralysis. Some 400,000 Americans have this disease. Its causes are unknown, and symptoms are unpredictable and vary greatly in severity.

Much MS research is focused on an autoimmune process in which T-cells attack and damage myelin, the fatty insulating tissue of axons. These T-cells do not attack axons themselves; the process of demyelination interrupts electrical impulses that run through these nerve fibers, thus causing MS symptoms. Demyelination has been considered the central feature of MS.

Recently, however, Qin has been among a group of researchers who have discovered that B-cells too are involved with the autoimmune response to MS. Instead of targeting myelin, these B-cells attack axons directly. Axons are the long, slender fibers of a neuron that serve as the primary transmission lines of the nervous system, and as bundles they help make up nerves.

Research at UCI and elsewhere has shown that myelin grows back if the

T-cell autoimmune response is turned off, and drugs exist or are in development to block demyelination. Axons, in turn, repair very slowly, which implies that B-cell attacks on axons may have a significant impact on the chronic central nervous system damage caused by MS.

"Since this area of research is in its early stage, it's important to understand the process by which these B-cell responses happen," Qin said. "Hopefully, by identifying these two crucial enzymes, it will lead to a greater understanding of MS and lead to more effective treatments for people who live with this disease."

Source: University of California - Irvine