Cell-surface sugar defects may trigger nerve damage in multiple sclerosis patients

September 20 2007

Defects on cell-surface sugars may promote the short-term inflammation and long-term neurodegeneration that occurs in the central nervous system of multiple sclerosis patients, according to University of California, Irvine researchers.

The findings also suggest that a dietary supplement similar to glucosamine may be useful as an oral therapy to correct these defects and to treat both the short-term and the long-term symptoms of the disease. Study results appear on the online version of the *Journal of Biological Chemistry*.

“The findings raise the possibility that these may both be treated by metabolic therapy,” said Dr. Michael Demetriou, an assistant professor of neurology, and microbiology and molecular genetics. “This is particularly important, as therapies are not currently available to treat neurodegeneration in MS.”

In tests on mice, Demetriou found that genetic deficiencies in a process called protein glycosylation led to a spontaneous disease very similar to MS, including paralysis associated with inflammatory damage to the protective myelin coating on nerve cells and degeneration of axons and neurons. Protein glycosylation refers to the addition of specific sugars to proteins; virtually all cell-surface and secreted proteins have complex sugars attached to them.

MS is a two-stage disease, with initial attacks of inflammatory

demyelination, which damages myelin, followed approximately 10 years later by a slow, progressive neurdegenerative phase marked by loss of axons and nerve cells.

The irreversible damage to the central nervous system induced by neurodegeneration in MS leads to long term disability, including paralysis, incoordination, dementia and pain, and is not targeted by currently available therapies.

Demetriou's findings provide the first genetic model of MS in which both inflammatory demyelination and neurodegeneration arise from defects in a single biological pathway.

In previous studies, Demetriou found that the dietary supplement N-acetylglucosamine (GlcNAc), which is similar but more effective than the widely available glucosamine, corrected defects in protein glycosylation in cells and inhibited inflammatory demyelination in mice. The new study opens the possibility that metabolic therapy with GlcNAc may also prevent neurodegeneration. Studies in humans are required to assess the potential of this therapy in MS.

Source: University of California - Irvine