

## **Elevated cerebrospinal fluid fetuin-a levels are a marker of disease activity in multiple sclerosis**

**J. DINZEY, N. DONELAN, Q.-J. YAN, M. RAMMAL, S. A. SADIQ**

Multiple Sclerosis Research Center of New York

### *Abstract:*

Previously, cerebrospinal fluid (CSF) proteomic analysis revealed elevation of Fetuin-A (Alpha2-Hermans-Schmid glycoprotein) in patients with multiple sclerosis (MS). Because Fetuin-A is known to activate matrix metalloproteinases which are implicated in increasing blood-brain barrier permeability in MS, we investigated whether central nervous system (CNS) Fetuin-A levels correlated with disease activity in MS. CSF Fetuin-A levels were analyzed by ELISA in 50 patients with active MS and 50 patients with inactive disease. Disease activity was determined clinically and by brain MRI. The presence of Fetuin-A protein was also compared by immunostaining in 10 normal and 22 MS human brain sections. For MS brains, the distribution of Fetuin-A protein was assessed in demyelinated plaques as well as in normal-appearing white and grey matter. In addition, Fetuin-A expression levels in 10 normal and 10 MS brains were measured by quantitative PCR. CSF levels of Fetuin-A in patients with active disease was significantly elevated in comparison to patients with stable disease [mean 1655 ug/mL versus mean 1154 ug/mL respectively,  $p < 0.0001$ ]. By immunohistochemistry, Fetuin-A levels were markedly elevated in all active MS plaques in comparison to other brain regions in the same brain and also by comparison to staining in control brains. In non-plaque areas, the most notable immunostaining for Fetuin-A was seen in the Purkinje cells of the cerebellum in MS brains, a finding not seen in normal brains. Results from quantitative PCR showed that Fetuin-A expression levels was significantly higher in MS brains than in normal brains [ $p < 0.01$ ]. These results show that CNS Fetuin-A levels correlate with disease activity in MS. Further investigation will determine the underlying mechanisms of our observations and whether CSF Fetuin-A levels can be used clinically as a marker of disease activity and therapeutic efficacy.