

filtration was performed by in-house developed strategy between the subjects. SNPs and Indels were filtered to look for pathogenic mutations using public databases. In family, we filtered unique variants in the probands and unique shared sequence variants present in carrier parent and proband grandparent. Variants were confirmed by Sanger sequencing using specific designed primers.

Result: The exome sequence resulted in identification of 10,257 variants among 11 unaffected and seven affected family members of our familial MS based on the human reference genome (hg19), of which 1268 variants were found uniquely novels 35 variants were shared between affected members and predicted to have a deleterious or damaging effect. Mutation were confirmed by Sanger sequencing

Conclusion: We predicted involvement of 10 newly candidate genes from 35 new variants in Familial MS. Further studies are required on large cohort scale of familial and sporadic MS.

doi:10.1016/j.jns.2015.08.130

47

WFN15-0930

Demyelinating Disorders 2

Association between soluble L-selectin and anti-JCV antibodies in natalizumab-treated relapsing-remitting MS patients

P. Basnyat^a, S. Hagman^a, M. Kolasa^a, K. Koivisto^b, A. Verkkoniemi-Ahola^c, L. Airas^d, I. Elovaara^e. ^aMedical School, University of Tampere, Tampere, Finland; ^bDepartment of Neurology, Seinäjoki Central Hospital, Seinäjoki, Finland; ^cDepartment of Clinical Neurosciences, Helsinki University Central Hospital, Helsinki, Finland; ^dDepartment of Clinical Neurosciences, Turku University Hospital, Turku, Finland; ^eDepartment of Neurology, Tampere University Hospital, Tampere, Finland

Background: Long-term treatment of Natalizumab in relapsing-remitting MS (RRMS) patients is associated with the risk of developing progressive multifocal leukoencephalopathy (PML), a JC virus (JCV)-mediated disease of the CNS. Measurement of anti-JCV antibodies in natalizumab-treated MS patients is used for the estimation of patient's risk for PML and lower percentage of L-selectin CD4 + T cells has been suggested as a biomarker for individual PML risk assessment.

Objective: L-selectin is also present as functionally active soluble form in the blood upon shedding from the cell surface of activated T cells. Therefore, our aim was to examine whether the levels of soluble L-selectin (sL-selectin) can predict the risk of PML in natalizumab-treated RRMS patients.

Methods: The levels of sL-selectin and anti-JCV antibody indices in sera were measured from a total of 99 subjects of whom 44 RRMS patients were treated with natalizumab, 30 patients with IFN-β and 25 subjects were healthy controls.

Results: The significant correlation was found between the levels of sL-selectin and JCV-antibody indices in the natalizumab-treated patients ($r = 0.402$; $p = 0.007$; $n = 44$), but not in those treated with IFN-β. This correlation became even stronger in JCV-seropositive patients treated with natalizumab longer than 18 months therapy ($r = 0.529$; $p = 0.043$; $n = 15$). Moreover, significantly higher level of sL-selectin was detected in the high-risk group (JCV antibody index >1.5) compared to that with low risk group (JCV antibody index ≤1.5) for developing PML.

Conclusion: Our data suggest that the measurement of sL-selectin should be evaluated further as a potential biomarker for predicting the risk of developing PML.

doi:10.1016/j.jns.2015.08.131

48

WFN15-1009

Demyelinating Disorders 2

Helicobacter pylori infection reduces disease severity in an experimental model of multiple sclerosis

B. Gran^a, J. Crooks^a, K. Cook^b, K. Hussein^c, K. O'Brien^a, M. Braitch^a, H. Kareem^a, C.S. Constantinescu^a, K. Robinson^d. ^aDivision of Clinical Neuroscience, University of Nottingham, Nottingham, United Kingdom; ^bDepartment of Clinical Oncology, Scancell, Nottingham, United Kingdom; ^cAcademic Unit of Cancer Sciences, University of Southampton, Southampton, United Kingdom; ^dNottingham Digestive Disease Centre, University of Nottingham, Nottingham, United Kingdom

Background: Infection with *Helicobacter pylori* may reduce the risk of developing inflammatory diseases. The infection is also less common amongst patients with multiple sclerosis (MS), an inflammatory demyelinating disease of the central nervous system. However, there is no direct evidence that *H. pylori* is protective.

Objective: We aimed to investigate the impact of *H. pylori* infection on experimental autoimmune encephalomyelitis (EAE), an animal model for MS.

Design/methods: Groups of C57BL/6 mice were infected with *H. pylori*, or given the diluent alone as a placebo, prior to induction of EAE with myelin oligodendrocyte glycoprotein (MOG) peptide in CFA. Clinical scores were assessed and at termination of the experiment, tissues were harvested. CD4 + T-cell subsets were quantified by flow cytometry, and T-cell proliferation assays were performed.

Results: *H. pylori* infection significantly reduced the severity of EAE clinical scores and the proliferation of MOG peptide-specific T-cells in infected mice. There was a 4-fold reduction in the frequency of CD4 + cells in the CNS. CD4 + populations in both the CNS and the spleens of infected mice also contained greatly reduced proportions of IFNγ+, IL-17+, T-bet+, and RORγt+ cells. The frequencies of Foxp3+ cells were equivalent. There were no differences in the frequency of splenic CD4+ cells expressing markers of apoptosis between infected and uninfected animals.

Conclusions: *H. pylori* infection exerted some protection against EAE in mice, inhibiting both Th1 and Th17 responses. We provide experimental evidence to suggest that *H. pylori* may provide protection against immune-mediated diseases such as MS.

doi:10.1016/j.jns.2015.08.132

49

WFN15-1039

Demyelinating Disorders 2

Absence of the anti-oxidant transcription factor Nrf2 exacerbates optic neuritis in a mouse model of multiple sclerosis

C. Larabee^a, B. Axtell^b, A. Agasing^b, S. Desai^c, S. Plafker^c. ^aOklahoma Center for Neuroscience, University of Oklahoma Health Sciences Center, Oklahoma City, USA; ^bClinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, USA; ^cFree Radical Biology & Aging, Oklahoma Medical Research Foundation, Oklahoma City, USA

Background: Optic neuritis is experienced by a majority of multiple sclerosis (MS) patients and is typically characterized by episodes of acute, monocular vision loss. These inflammatory episodes can lead to damage or degeneration of the retinal ganglion cells (RGCs) comprising the optic nerve (ON). Experimental autoimmune encephalomyelitis (EAE) is a well-established model of MS in which mice are immunized to produce a neuro-autoimmunity that recapitulates the cardinal hallmarks of the human disease, namely, increased oxidative stress, demyelination, and neurodegeneration.