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.

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WFN15-0930
Demyelinating Disorders 2
Association between soluble L-selectin and anti- JCV antibodies in natalizumabtreated relapsing-remitting MS patients

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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.

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Demyelinating Disorders 2
Helicobacter pylori infection reduces disease severity in an experimental model of multiple sclerosis

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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.

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Demyelinating Disorders 2
Absence of the anti-oxidant transcription factor Nrf2 exacerbates optic neuritis in a mouse model of multiple sclerosis

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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.

Objective: It has been previously demonstrated that mice deficient for the master anti-oxidant transcription factor Nrf2 are more susceptible to the motor deficits and spinal cord pathology induced by EAE. The goal of this study was to determine if Nrf2-deficient mice also exhibited exacerbated visual pathology in EAE.
Materials and Methods: EAE was induced in 8-week-old wildtype (WT) and Nrf2 knockout (KO) mice via immunization against MOG antigen. Visual acuity via optokinetic tracking (OKT) and motor deficits were assessed daily. Mice were harvested 21 days post-immunization. Retinas were flatmounted, immunostained, and RGCs were counted. ONs were paraffin-embedded and stained with H&E or immune cell-specific antibodies.
Results: Nrf2 KO mice exhibited more severe motor deficits, OKT decreases, RGC loss, and ON inflammation in response to EAE. This was not due to global differences in immune system development relative to WT mice.
Conclusion: Nrf2 plays a neuroprotective role in EAE-associated optic neuritis and may be an optimal therapeutic target to prevent RGC degeneration that leads to permanent visual impairment in MS patients.

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