Materials and methods: The expression of IL-33 and its receptor ST2 on retinal pigment epithelial (RPE) cell line was examined by immunohistochemical staining. Next the severity of IRBP peptide induced-EAU was assessed in C57BL/6 mice treated with recombinant IL-33 or PBS. Cytokine secretion and production by the draining lymph nodes (DLNs) or spleen cells were measured at day 26 after immunization.
Results: We demonstrate that RPE cells expressed high levels of both IL-33 and ST2. Administration of IL-33 cytokine to EAU mice led to reduced disease severity. In line with the reduced inflammation in the retina of IL-33 treated mice, the percentage of IFN-γ+ or IL-17+ cells in the DLNs and spleen was markedly lower, while IL-5+ or IL-4+ cell percentage was increased. Furthermore, antigen specific production of IFN-γ, IL-17 and IL-6 by the DLN cells from IL-33 treated mice was also significantly reduced.
Conclusions: Our results suggest that IL-33 may play a protective role in the development of EAU possibly via its known role in promoting the function of alternatively activated macrophages.

P1148

Is Parkinson's disease the result of autoimmunity arising from Influenza A infection of the brain?

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Purpose/Objective: The mechanism of dopaminergic neuronal cell death remains a mystery in Parkinson's disease. Compelling epidemiological evidence links Parkinson's disease with Influenza A infection, with 5 million people developing the Parkinson's associated disease Encephalitis lethargica following the 1918 influenza pandemic. However, as Influenza induces an acute infection, where as Parkinson's disease is a chronic condition, and in the majority of cases the virus is absent from the lesion, this suggests that the virus has an indirect mode of action. An autoimmune reaction may thus be the effector mechanism linking the infection to neurological disease. Using a murine model we set out to investigate the relationship between influenza A and Parkinson's disease, and in particular, investigate the hypothesis that autoimmunity arising from infection results in dopaminergic neuronal death in the substantia nigra.
Materials and methods: A murine model was established with intranasal delivery of the neurotropic H1N1 A/WSN/33 Influenza strain. Following infection, brains were harvested and examined for the presence of the virus, T cell infiltrate and dopaminergic neuronal loss by immunohistochemistry and flow cytometry. Murine behaviour was also examined for Parkinsonian symptoms. A potential autoantigen, alpha synuclein; a protein central to the pathology in Parkinson's disease, was also examined. Mice were primed against alpha synuclein in CFA and T cell behaviour examined.
Results: Preliminary data using our murine model has shown that the Influenza virus was detected in the midbrain as late as 21 days post infection. T cell subsets were also detected in the brain following infection. In addition to this, we were able to generate alpha synuclein reactive T cells, and these cells were able to traffic to the brain.
Conclusions: Identifying autoimmune mediated dopaminergic neuronal loss would radically change therapeutic approaches and may thus provide new targets to prevent the disease or preserve the quality of life of the patients. We thus need to further examine the aberrant immune response in Parkinson's disease.

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Is there a functional role for KCNMA1 in the multiple sclerosis?

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Purpose/Objective: A more detailed insight into disease mechanisms of multiple sclerosis (MS) is crucial for the development of new and more effective therapies. MS is a chronic inflammatory autoimmune disease of the central nervous system. The aim of this study is to identify novel disease associated proteins that are functionally involved in the MS brain pathology.
Materials and methods: In a previous proteomics study, brainstem proteins were obtained from Lewis rats with MBP induced acute experimental autoimmune encephalomyelitis (EAE), a well characterized disease model of MS. Samples were collected at different time points: just before onset of symptoms, at the top of the disease and following recovery. To analyze changes in the brainstem proteome during the disease course, a quantitative proteomics study was performed using two-dimensional difference in-gel electrophoresis (2D-DIGE) followed by mass spectrometry.
Results: We identified 75 proteins with a significant abundance difference between the different disease stages. Regulated proteins were mapped to existing biological networks by Ingenuity Pathway Analysis (IPA). Post-synaptic density protein 95 (DLG4), a key player in neuronal signalling and calcium-activated potassium channel alpha 1 (KCNMA1), involved in neurotransmitter release, are 2 putative regulators connecting 64% of the proteins identified. The involvement of KCNMA1 in macrophage functionality was studied *in vitro* by using a specific functional blocker for KCNMA1, paxillin. We show that blocking of KCNMA1 altered myelin phagocytosis and proinflammatory cytokine release, disease mechanisms which are highly involved in EAE and MS pathology. We are currently investigating possible influences of this blocker on functionality of other disease relevant cells and processes using *in vitro* and *in vivo* models.
Conclusions: This study will elucidate to what extent modulation via this ion channel affects disease processes in the context of EAE/MS.

P1150

Mast cells protect from post-traumatic spinal cord inflammation in mice by degrading inflammation-associated cytokines via mouse mast cell protease 4

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Purpose/Objective: It becomes increasingly clear that mast cells (MCs) are not only key players in allergic diseases (e.g. asthma), but seem to play a complex role in neuroinflammatory diseases such as multiple sclerosis and stroke. However, their role during and after mechanical CNS trauma is not clear. In the present study, we have investigated the effects of MC-deficiency on the histological and clinical outcome after spinal cord injury (SCI) in mice.
Materials and methods: MC-deficient W-sash c-kit mutant knockout mice ($kit^{W\text{-}sh/W\text{-}sh}$), mMCP-4 deficient ($mMCP4^{-/-}$) mice and control mice underwent spinal cord hemisection at thoracic level T8 resulting in a complete transection of the dorsomedial and ventral corticospinal tract. Functional recovery in SCI mice was tested with the Basso Mouse Scale. Spinal cord sections were analyzed by immunofluorescence. RT-PCR and Western blotting were used to analyze cytokine/chemokine mRNA and protein levels. In degradation assays murine recombinant