DAREMUS
Dansk Selskab for Forskning i Multipel Sklerose

Abstract form: Max 350 ord (punkt 3 – 6) på max én A4 side

Ønsker deltagelse i foredragskonkurrencen (4 abstracts udvælges): JA (x) ; NEJ ( )

Navn Vian Wais **Institution** IMM, SDU **Alder** 34 (hvis deltagelse i konkurrence)

Følgende struktur bedes fulgt:

1) Titel

The role of CNS-endogenous NOD2 and TLR9 in MS-like disease in mice

2) Forfattere

Vian Wais, Reza Khorooshi, Gill Webster, Stefan Lienenklaus and Trevor Owens

3) Hypotese

Administration of MIS416 into the cerebrospinal fluid via the cisterna magna of mice induces Type I interferons (IFNs) within the central nervous system (CNS) and plays a protective role in experimental autoimmune encephalomyelitis (EAE).

4) Metoder

To examine the Type I IFN induction in the CNS, I will inject MIS416, a microparticle consisting of ligands to Toll-like receptors 9 (TLR9) and Nucleotide-binding oligomerization domain 2 (NOD2), directly into the cerebrospinal fluid of reporter mice. Interferon-β (IFNβ) induction in the CNS will be investigated in reporter mice that express luciferase under the control of IFNβ promoter, by in vivo imaging. The cellular sources will be investigated in IFNβ -yellow fluorescence protein- reporter mice, by immunohistochemistry. I will sort microglia and astrocytes cells to investigate type I IFN expression using quantitative real-time PCR. Furthermore, the role of intrathecally administered MIS416 and TLR9 ligand on EAE will be determined.

5) Resultater

We have recently shown microglia as a major source of Type I IFN in response to a TLR3 ligand. We expect in this study, that microglia respond to MIS416 and TLR9 ligands and produce Type I IFN, which will protect mice against EAE. Our preliminary results show intrathecally administered MIS416 induce IFN-β in the CNS of reporter mice.

6) Diskussion

Type I IFNs, including IFN-β, play a central role in regulation of inflammation. IFN-β is used as a therapeutic for multiple sclerosis (MS), an inflammatory demyelinating disease in CNS. IFN-β belongs to Type I IFN family and is induced by ligation of innate immune receptors including TLRs and NOD2. MIS416 is a microparticle consisting of ligands to TLR9 and NOD2, and was found to induce IFN-γ when administered intravenously but the association with IFN-β has not yet been investigated in the CNS. With this study we want to investigate Type I IFN signalling in CNS.

Deadline for indsendelse af abstract til: Henrik.Boye.Jensen@rsyd.dk SENEST 15. februar 2016.