

## T Cell Epitope Mapping of AQP4 and MOG in patients with NMOSD

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**Background:** T-cells, especially CD4<sup>+</sup> T-cells, are key players in the pathogenesis of autoimmune diseases. Autoantibodies targeting the aquaporin-4 (AQP4)-water-channel-protein and the myelin-oligodendrocyte-glycoprotein (MOG) are associated with a broad spectrum of human CNS demyelinating diseases including neuromyelitis optica spectrum disorders (NMOSD) and acute disseminated encephalomyelitis (ADEM). Whereas the role of AQP4-specific T-cells has already been analysed in some studies, little is known about MOG-specific T-cells in these diseases.

**Aims and Methods:** We therefore aimed to identify the immunodominant T-cell epitopes of AQP4 and MOG in patients with NMOSD using the CFSE-proliferation assay. For this, peripheral blood mononuclear cells (PBMCs) of eight AQP4-antibody and four MOG-antibody positive NMOSD patients, one MOG-antibody positive ADEM patient and ten healthy controls were stimulated with eight AQP4 and nine MOG peptides. After eleven days, the proliferation of T-cells was analysed via the dilution of the CFSE-staining using flow cytometry. Furthermore, we aimed to examine the functional phenotype of autoreactive T-cells and therefore evaluated cytokine secretion (granulocyte-macrophage-colony-stimulating factor (GM-CSF), interferon(IFN)- $\gamma$ , interleukin(IL)-4, IL-6, IL-17A) using ELISA and cytokine production (IFN- $\gamma$ , IL-4, IL-6, IL-17A) using flow-cytometry-based intracellular staining. In addition, a HLA genotyping of all participants was performed.

**Results:** We detected higher peptide specific T-cell proliferation in response to AQP4 peptides in all NMOSD patients when compared to healthy controls. A T-cell response to MOG peptides, preferably to peptides corresponding to the extracellular immunodominant immunoglobulin-domain, was found in NMOSD patients as well as in healthy controls. The cytokine secretion was either not detectable or not specific. However, cytokine production of IFN- $\gamma$  was observed.

**Conclusion:** To conclude, our study indicates a specific T-cell response to AQP4, but not to MOG, in patients with NMOSD. We hope that our results will be helpful for the development of new individualised immune-tolerance therapies.

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