Project Summary: Many ion channels are expressed on glia cells and neurons and thus are potential targets of autoimmune responses in multiple sclerosis (MS). We identified an antibody response to the inward rectifying potassium channel KIR4.1 in a subset of patients with MS. However, KIR4.1 undergoes extensive pre- and posttranslational modifications that influence antibody binding and thus antigenicity.

In the second funding period, our aim is to determine whether KIR4.1 specific T and B cells are found in the CNS compartment and how tissue specific modifications of KIR4.1 affect antigenicity. We will dissect the T- and B-cell receptor repertoire in CSF by next generation sequencing and relate the sequences to KIR4.1-specific T and B cells. We will determine the nature of tissue specific KIR4.1 modifications and investigate the impact on adaptive immune responses in MS.

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