Project summary: Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disease of the CNS. Many findings suggest an autoimmune pathogenesis of MS; however, the target of the immune response is as yet unknown. To identify MS specific autoantibodies, we screened serum IgG from MS patients for binding to brain tissue. In a subgroup of patients, specific IgG binding to glial cells was observed. Using a proteomic approach focusing on membrane proteins, the inward rectifying potassium channel KIR4.1 was identified as the target of the serum autoantibodies. A multi-faceted validation strategy was used to confirm KIR4.1 as a target of the autoantibody response in MS and demonstrate its potential pathogenicity in vivo. Serum antibodies to KIR4.1 were detected in 50% of patients but not in healthy donors or patients with other neurological diseases. Transfer experiments with KIR4.1 antibody containing sera suggest that the anti-KIR4.1 antibody leads to a profound loss of KIR4.1 expression and activation of the complement cascade at sites of KIR4.1 expression in the cerebellum. These findings suggest that KIR4.1 is a relevant target of the autoimmune response in MS and may play an important role in the pathogenesis of the disease. The aim of this project is to further investigate the nature of the antibody response to KIR4.1 in MS. We will determine (a) the HLA and genetic background, (b) lesion pathology, (c) the specificity of the antibody response, (d) the underlying T cell immunity to KIR4.1 in MS patients and (e) the encephalitogenicity of KIR4.1 in mice. The results of the studies will provide additional support for the role of KIR4.1 in MS.

Principal investigator:

Prof. Dr Bernhard Hemmer
Technische Universität, Klinikum rechts der Isar
Klinik und Poliklinik für Neurologie
Ismaninger Str. 22
81675 München
Tel: + 49 89 4140-4601
Fax: + 49 89 4140-7681
Email: hemmer@lrz.tu-muenchen.de