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Titel des Beitrags: Functional characterization of aquaporin-4 specific T cells: towards a model for neuromyelitis optica.

Abstract: Antibodies to the water channel protein aquaporin-4 (AQP4), which is expressed in astrocytic endfeet at the blood brain barrier, have been identified in the serum of Neuromyelitis optica (NMO) patients and are believed to induce damage to astrocytes. However, AQP4 specific T helper cell responses that are required for the generation of anti-AQP4 antibodies and most likely also for the formation of intraparenchymal CNS lesions have not been characterized. Using overlapping 15-meric peptides of AQP4, we identified the immunogenic T cell epitopes of AQP4 that are restricted to murine major histocompatibility complex (MHC) I-A(b). The N-terminal region of AQP4 was highly immunogenic. More precisely, the intracellular epitope AQP4(22-36) was detected as major immunogenic determinant. AQP4(82-108) (located in the second transmembrane domain), AQP4(139-153) (located in the second extracellular loop), AQP4(211-225) (located in the fifth transmembrane domain), AQP4(235-249) (located in the sixth transmembrane domain), as well as AQP4(289-306) in the intracellular C-terminal region were also immunogenic epitopes. AQP4(22-36) and AQP4(289-303) specific T cells were present in the natural T cell repertoire of wild type C57BL/6 mice and T cell lines were raised. However, active immunization with these AQP4
peptides did not induce signs of spinal cord disease. Rather, sensitization with AQP4 peptides resulted in production of IFN-?, but also IL-5 and IL-10 by antigen-specific T cells. Consistent with this cytokine profile, the AQP4 specific antibody response upon immunization with full length AQP4 included IgG1 and IgG2, which are associated with a mixed Th2/Th1 T cell response. AQP4 is able to induce an autoreactive T cell response. The identification of I-A(b) restricted AQP4 specific T cell epitopes will allow us to investigate how AQP4 specific autoimmune reactions are regulated and to establish faithful mouse models of NMO that include both cellular and humoral responses against AQP4.

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