

# **NMO-IgG is sufficient to cause the pathology of an NMO lesion without participation of T cells**

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Neuromyelitis optica (NMO) is a demyelinating inflammatory disorder of the central nervous system (CNS) that is clinically and pathologically defined as the co-occurrence of optic neuritis and myelitis. Aquaporin (AQP)4 is considered a potential autoantigen in patients with NMO after an autoantibody, designated NMO-IgG, that binds to human (h) AQP4 was detected in the serum of the vast majority of patients with NMO. The presence of the NMO-IgG has led many neurologist and neuroimmunologists to believe that NMO may be a primarily B cell-mediated disease.

However, there is evidence to suggest a cellular immune response in NMO during disease initiation or perpetuation. HLA haplotype analyses of patients with NMO suggest a positive association with *HLA-DRB1\* 03:01* (DR17), a gene that codes for a major histocompatibility class (MHC) II molecule that presents linear antigens to CD4<sup>+</sup> T cells. Also, NMO-IgG is undetectable in a substantial number of patients with NMO. A NMO-IgG, antibody isotype switch from IgM to IgG could not occur without CD4<sup>+</sup> T cell involvement, which are abundantly present in NMO lesions. B cell-depleting therapies are not consistently beneficial in patients with NMO. Finally, transfer of AQP4-reactive T cells into wild-type mice and rats results in neurological deficits and CNS inflammation.