

The future treatment of nmo is immune tolerance, not immune suppression: yes

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The time is ripe to explore immune tolerance treatments for NMOSD. First, the autoantigen, AQP4, has been definitively identified as has an immunodominant peptide to which T cells respond, an essential step to facilitating immune tolerance therapeutics. Second, as a consequence of improved understanding of T cell activation and T-B cell interactions, potential therapeutic strategies have been identified. Thirdly, technical advances in immunology and genomics render success achievable. Potential approaches to immune tolerance include: Vaccination to the inciting antigen to induce anergy; Vaccination to autoreactive idiotype-restricted T cells; Vaccination with dendritic cells, possibly modified by immunosuppressive agents, cytokines or antisense oligonucleotides targeting key costimulatory molecules, such as CD40, CD80 or CD86.; Transfer of T regulatory cells engineered to be AQP4 antigen specific by transducing AQP4 antibody with an appropriated signaling domain; Transfer or enhancement of B regulatory cells, by a variety of methods There can be no doubt that this approach is in its infancy, and no dramatic examples of clinical success can be claimed that would leave no doubt of the ultimate success of this “brave new world” of immune tolerance. But there is little doubt that this approach is the future and immune suppression with the need for indefinite treatment, partial efficacy and toxicity (infection, cancer and other autoimmune diseases) is less than desirable. The future is clearly restoring immune tolerance, repairing what is wrong, and working with the immune system as a partner and not fighting the immune system as an enemy.