IgG glycan hydrolysis by EndoS inhibits experimental autoimmune encephalomyelitis.

Abstract:
Studies in experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis, have shown that B cells markedly influence the course of the disease, although whether their effects are protective or pathological is a matter of debate. EndoS hydrolysis of the IgG glycan has profound effects on IgG effector functions, such as complement activation and Fc receptor binding, suggesting that the enzyme could be used as an immunomodulatory therapeutic agent against IgG-mediated diseases. We demonstrate here that EndoS has a protective effect in myelin oligodendrocyte glycoprotein peptide amino acid 35-55 (MOG(35-55))-induced EAE, a chronic neuroinflammatory demyelinating disorder of the central nervous system (CNS) in which humoral immune responses are thought to play only a minor role. EndoS treatment in chronic MOG(35-55)-EAE did not impair encephalitogenic T cell priming and recruitment into the CNS of mice, consistent with a primary role of EndoS in controlling IgG effector functions. In contrast, reduced EAE severity coincided with poor serum complement activation and deposition within the spinal cord, suggesting that EndoS treatment impairs B cell effector function. These results identify EndoS as a potential therapeutic agent against antibody-mediated CNS autoimmune disorders.