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Sialylated autoantigen-reactive IgG antibodies attenuate disease development in mouse models of lupus nephritis and rheumatoid arthritis

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Pro- and anti-inflammatory effector functions of IgG antibodies (Abs) depend on their subclass and Fc glycosylation pattern. Accumulation of non-galactosylated (agalactosylated; G0) IgG Abs in the serum of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients reflects severity of the diseases. In contrast, sialylated IgG Abs are responsible for anti-inflammatory effects of the intravenous immunoglobulin (IVIG; pooled human serum IgG from healthy donors), administered in high doses (2 g/kg) to treat autoimmune patients. However, whether low amounts of sialylated autoantigen-reactive IgG Abs can also inhibit autoimmune diseases has been hardly investigated. Here, we explored whether sialylated autoantigen-reactive IgG Abs can inhibit autoimmune pathology in two mouse models (Bartsch et al., Front. Immunol. 2018; 9:1183). We found that sialylated IgG autoantibodies fail to induce inflammation and lupus nephritis in a B cell receptor (BCR) transgenic lupus model, but instead are associated with lower frequencies of pathogenic Th1, Th17 and B cell responses. In accordance, the transfer of small amounts of immune complexes containing sialylated IgG Abs was sufficient to attenuate the development of nephritis. We further showed that administration of sialylated collagen type II (Col II)-specific IgG Abs attenuated the disease symptoms in a model of Col II-induced arthritis and reduced pathogenic Th17 cell and autoantigen-specific IgG Ab responses. We conclude that sialylated autoantigen-specific IgG Abs may represent a promising tool for treating pathogenic T and B cell immune responses in autoimmune diseases.