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Grant title: Pathological role of HEV-specific sulfated glycans revealed by anti-glycan mAbs

Abstract

The addition of sulfate groups to the *N*- and *O*-glycans is catalyzed by sulfotransferases, which transfer a sulfate group from 3'-phosphoadenosine 5'-phosphosulfate (PAPS) to a specific position on the acceptor oligosaccharide. The *N*-acetylglucosamine-6-*O*-sulfotransferases (GlcNAc6STs) catalyze the 6-*O*-sulfation of *N*-acetylglucosamine (GlcNAc) on the acceptor glycans. So far, five GlcNAc6STs in humans and four in mice have been identified. Two of these, GlcNAc6ST-1 and



GlcNAc6ST-2 (also called HEC-GlcNAc6ST or L-selectin ligand sulfotransferase (LSST)), are involved in the biosynthesis of sulfated glycans in high endothelial venules (HEVs) in peripheral lymph nodes (PLN) that function as major ligand for lymphocyte homing receptor, L-selectin.

Lymphocyte homing to the secondary lymphoid organs is pivotal for proper immune responses. Studies using sulfotransferase GlcNAc6ST-1/2 doubly-deficient (DKO) mice showed that sulfated glycans synthesized by these sulfotransferases play critical roles in lymphocyte homing to the PLNs and immune responses against foreign antigens. We previously generated an anti-sulfated glycan monoclonal antibody S2 which specifically recognizes such sulfated glycans expressed on HEV in PLN as well as nasal-associated lymphoid tissues (NALT) by immunizing GlcNAc6ST-1/2 DKO mice with CHO-K1 cells stably expressing the missing sulfotransferases. In this study, we found that S2 administration inhibited lymphocyte recruitment to NALT and allergic rhinitis induced by intranasal administration of OVA. S2 administration to OVA-immunized mice resulted in the reduction of OVA-specific serum IgE, and counts of sneezes and nose scratches after nasal immunization. Total cell numbers in NALT and expression of Th2-related cytokines such as IL-5 and IL-13 were also diminished after S2 administration. Taken together, these results suggest that S2 would serve as a novel therapeutic agent useful for the treatment of allergic rhinitis.