Role of sulfated-glycans in immune responses

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Mucosal lymphoid tissues such as Peyer's patches, tonsil, and NALT (Nasal-associated lymphoid tissues) function as a first line of immunological defense against invading pathogens. NALT contains various types of lymphoid cells that are required for the induction and regulation of mucosal immune responses to antigens delivered from the nasal cavity. However, molecular mechanisms underlying lymphocyte recruitment to NALT are still elusive. Immunohistochemical studies revealed that high endothelial venule (HEV) in NALT strongly expresses peripheral lymph node addressin (PNAd) bearing mucin-like domains that functions as scaffolding for sulfated *O*-glycans. In this study, we investigated the role of PNAd in lymphocyte recruitment to NALT using gene-targeting mice deficient in two sulfotransferases, GlcNAc6ST-1 and GlcNAc6ST-2, that are involved in PNAd biosynthesis. NALT HEV in the double null (DKO) mice were devoid of immunoreactivity against MECA-79 monoclonal antibody which specifically recognizes PNAd, indicating that the two sulfotransferases are essential for PNAd biosynthesis in NALT HEV. Short-term homing assay indicated that lymphocyte recruitment to NALT was significantly decreased by approximately 80% in DKO mice. Moreover, number of lymphocytes in NALT was reduced in DKO mice compare with wild-type mice. These results demonstrate that PNAd plays an essential role in lymphocyte recruitment to NALT and nasal immune responses, suggesting a novel therapeutic approach to modulate allergic reactions using sulfated-glycans such as fucoidan from *Fucus vesiculosus* by targeting PNAd-mediated lymphocyte recruitment.