Glycan remodeling regulates germinal centre B cell response through CD22

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Abstract

Germinal centres (GCs) are specialized sites within the secondary lymphoid organs where B-cells undergo iterative clonal expansion and diversification of their immunoglobulin genes through somatic hypermutation. High affinity clones arising from these cellular events are then selected to differentiate into memory B cells and antibody-secreting plasma cells. Precise detection of GC B cells relies on distinct changes on their surface carbohydrates, known as glycans. One striking modification relates to the monosaccharide sialic acid, which leads to the emergence of glycan epitope detected by the GL7 antibody. As a consequence of this alteration, GC B cells lose the preferred ligand for CD22, a member of the sialic acid-binding immunoglobulin-type lectins and an inhibitory co-receptor of the B-cell antigen receptor. To assess the functional role of downregulated CD22 ligands in the GC, we develop a mouse model that constitutively express ligands for CD22 on GC B cells. Using this model, we determine that glycan remodeling is critical for the GC B-cell responses, by modulating BCR activation, GC B-Tfh interaction, and maturation of antibodies. We also demonstrate that the function of these altered glycans is dependent on CD22, highlighting that coordinated loss of preferred ligands acts to modulates CD22 activity in the GC B cells. Overall, our study reveals that downregulation of CD22 ligands maintains B cell competitiveness in the GC.