Sialic acids as determinants of self

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Sialic acids are found as terminal sugars on glycans of glycoproteins and glycolipids of all mammalian cells. The 'sialoglycome' represents a highly diverse set of structures that varies from cell to cell, presenting a prominent molecular signature to the extracellular environment, mediating recognition by pathogens and neighboring cells. Influenza virus is an exemplary pathogen that recognizes sialosides as receptors for initial binding to and infection of airway epithelium. It is now clear that avian and human viruses recognize different sialoside receptors, representing a species barrier for transmission of avian viruses in human hosts. Avian viruses that acquire specificity for human type receptors are considered to have increased pandemic risk. We seek to identify the glycans that comprise the molecular signature recognized by human influenza virus, to better understand the nature of the barrier for new pandemic viruses from animal populations. The mammalian immune system has also evolved a family of receptors called siglecs that aid immune cells in distinguishing between self and non-self. Our work on the B cell siglec, CD22 (Siglec-2) has shown that it helps prevent activation of B cells to membrane self-antigens. Ligands on antigen expressing cells recruit CD22, preventing upregulation of B cells that recognize the antigen, resulting in suppression of B cell activation, and eventually apoptosis of the cell, eliminating it from the B cell repertoire. This function of CD22 can be exploited to induce antigen specific tolerance in an animal administering liposomal nanoparticles displaying both the desired antigen and a high affinity ligand of CD22, resulting in selective deletion of B cells that recognize the antigen. (Supported by NIH grants: AI51043, AI099141, AI099274, HL107151)