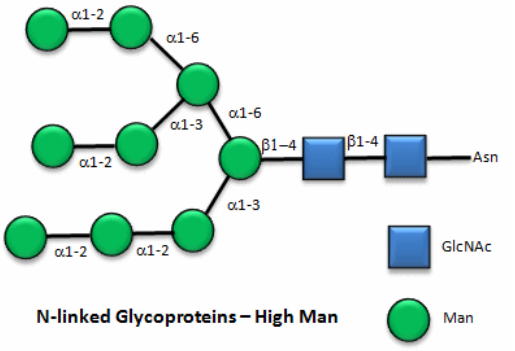
24.11: CELL SURFACE CARBOHYDRATES AND INFLUENZA VIRUSES

Objectives

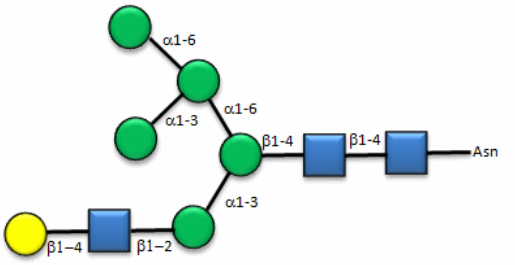
You may omit Section 25.11.

Carbohydrates are covalently attached to many different biomolecules, including lipids, to form glycolipids, and proteins, to form glycoproteins. Glycoproteins and glycolipids are often found in biological membranes, to which they are anchored by through nonpolar interactions. A special kind of glycoprotein, a proteoglycan, actually has more carbohydrate mass than protein. What is the function of these carbohydrates? Two are apparent. First, glycosylation of proteins helps protect the protein from degradation by enzyme catalysts within the body. However, there main functions arises from the fact that covalently attached carbohydrates that "decorate" the surface of glycoproteins or glycolipids provide new binding site interactions that allow interactions with other biomolecules. Hence glycosylation allows for cell:cell, cell:protein, or protein:protein interactions. Unfortunately, bacteria and viruses often recognize glycosylated molecules on cell membranes, allowing for their import into the cell.

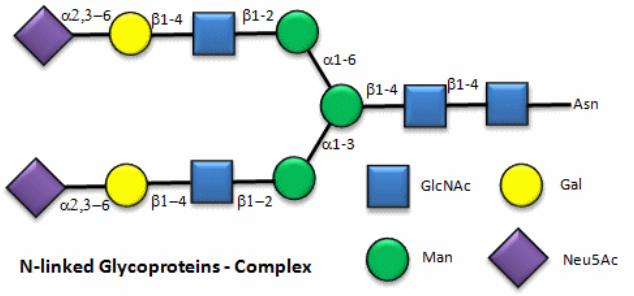
Here are some "cartoon" examples of carbohydrates covalently linked to the amino acid asparagine (Asn) on a glycoprotein.



N-linked Glycoproteins – High Man



N-linked Glycoproteins – Mixed (Hybrid)

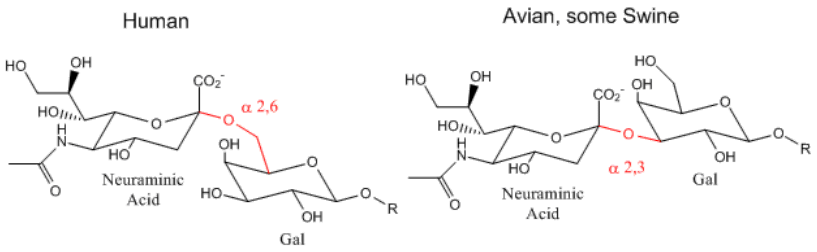


N-linked Glycoproteins - Complex

Here are some examples of biomolecular interactions promoted by IMFs involving carbohydrates.

Influenza Virus binding to Cell Surface Glycoproteins with Neu5Ac - A protein on the surface of influenza virus, hemagluttinin, bind to sialic acid (Sia), which is covalently attached to many cell membrane glycoproteins on host cells. The sialic acid is usually connected through an alpha (2,3) or alpha (2,6) link to galactose on N-linked glycoproteins. The subtypes found in avian (and equine) influenza isolates bind preferentially to Sia (alpha 2,3) Gal which predominates in avian GI tract where viruses replicate. Human virus of H1, H2, and H3 subtype (cause of the 1918, 1957, and 1968 pandemics) recognize Sia (alpha 2,6) Gal, the major form in human respiratory tract. The swine influenza HA bind to Sia (alpha 2,6) Gal and some Sia (alpha 2,3)both of which found in swine.

Binding Site for Influenza Hemagluttinin Protein



- Jmol model of viral hemagluttinin bound to antiviral drugs and sialic (neuraminic acid) from Proteopedia

Leukocyte: Cell Wall binding - During inflammation, circulating leukocytes (a type of white blood cell) tether and roll on the walls of blood vessels where they become active. E-, L- and P-selectin proteins are the primary proteins responsible for the tethering and rolling of these leukocytes. P-selectin binds, in part, to a tetrasaccharide, sialyl-Lewisx (SLEX) on the cell surface.. The interaction between P-selectin and the cell mediates the initial binding/rolling of the leukocyte on the vessel wall.

- Jmol model of P-selectin binding to tetrasaccharide

CONTRIBUTORS AND ATTRIBUTIONS

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