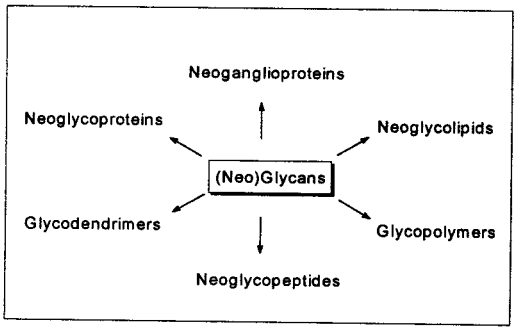
TOPICS

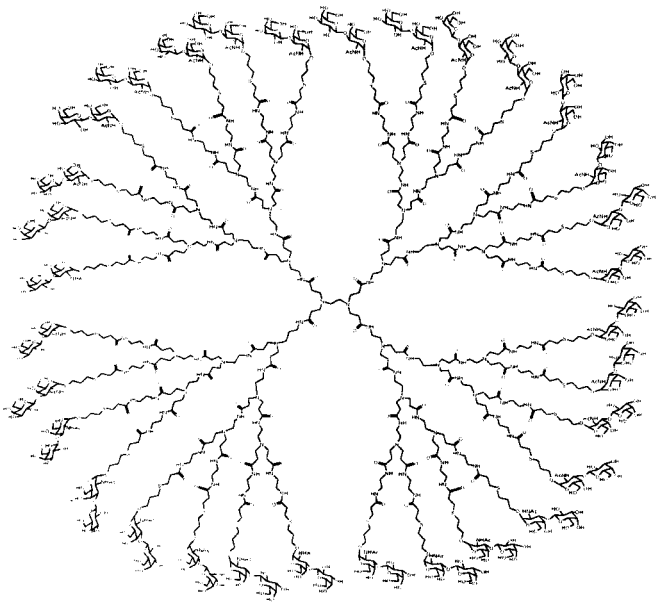
Neoglycoconjugates: Chemistry and Biology

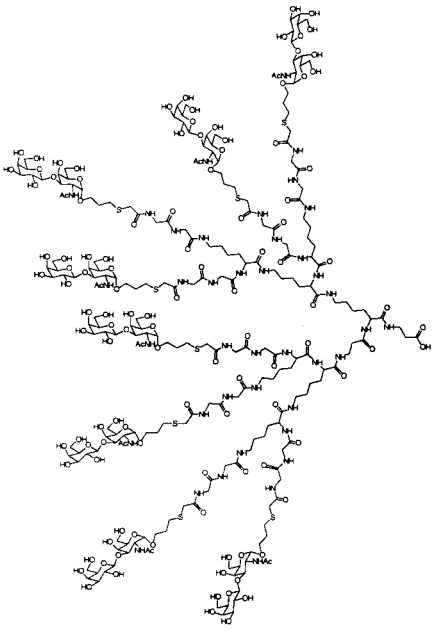
Cell surface carbohydrates are mainly composed of glycolipids, glycoproteins, proteoglycans and capsular polysaccharides and these glycoconjugates are externally expressed. This makes carbohydrates frontline mediators in inter-/intracellular events. Due to the major components of cell and tissues, they are involved in key recognition interactions with receptor proteins such as hormones, enzymes, toxins, lectins, antibodies and viruses invoking numerous biological functions, cell growth, regulation and differentiation, cancer metastasis, inflammation and microviral processes.

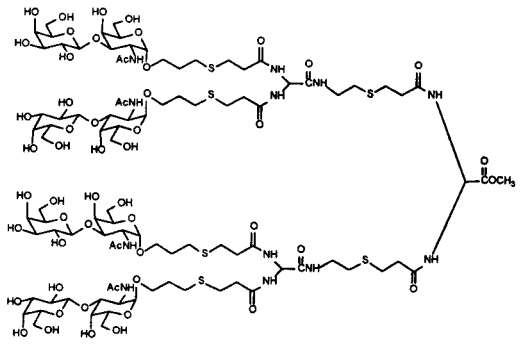


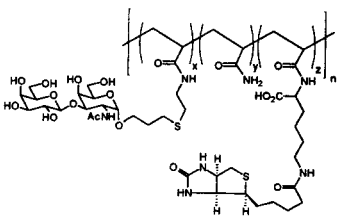
As most cell surface carbohydrate-protein interactions are in the low millimolar ranges for individual carbohydrate epitope, it is advantageous to get access to conjugates (clusters) having affinities in the nanomolar or lower. This is called as "multivalent effect". Most of critical biological processes such as antibody-antigen interactions and cell-cell recognition processes involve multivalency. Numerous examples of neoglycoconjugates having tremendously increased affinities (avidities) toward their corresponding receptors have been observed. As shown in the figure, there are several types of conjugates depending on what kind of carriers they have. It might be polyamino acids, lipids, enzymes, organic/inorganic particles, high molecular weight of organic compounds (linear polymers or dendrimers) and drugs. Especially, macromolecular scaffolds use as a basis for the design of multivalent ligands range from large polymers to oligomeric to dendrimers to small clusters. Even though many bio-organic and glycobiologists try to understand the mechanism of multivalency, the source of the enhancements remains uncertain. Some researchers believe that multivalent binding processes are similar to intramolecular chelation process. Other scientist proposed that multivalent binding is originated from an aggregation or precipitation process between two concepts, there are still some controversy to explain multiple binding effect. Rather intramolecular chelation process is independent of ligand concentration and the multivalent effect can be achieved at low concentration, the other concept is strongly dependent on concentration. This is the hottest issue to understand what is going on. Now it is well known that these conjugates are antigenic and applied as inhibitors for viral infection of cell and shiga-like toxin and enterotoxin, for example. In addition, sialic acid (or mannose) containing glycopolythiophene assemblies have been developed as sensory devices to detect influenza virus (*E. coli*). T(Thomson-Friedenrich)-antigen has been known cancer related antigen, especially in breast cancer, as a tumor marker. T-antigen containing glycoprotein was employed to immunize mouse to generate mouse monoclonal antibody FAA-J11(IgG3). In this particular example, the conjugate is immunogenic and has a potential to prevent cancer cell metastasis.

Biologically active glycoconjugates are able to be applied in the medicinal and immunochemical fields as step1) diagnostic purposes, step 2) drug discovery and step 3) vaccine development. One more thing that we have to know is that chemically well designed conjugates may give a chance pairing of receptors like cell-cell pairing that could generate communication signal in the biological systems. One scientist says "When you make a vaccine, you are making ligands that act as effectors because you are trying to give rise to a particular cellular signal-the signal to produce antibodies".









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