Significance and Functions of Carbohydrates

Bacterial Cell Walls

The cell walls of Gram-positive bacteria consist of a polysaccharide-peptide complex called the **peptidoglycan**. Long polysaccharide chains composed of alternating N-acetylglucosamine and N-acetylmuramic acid form the backbone of the cell wall. Attached to the lactate side chain of the muramic acid is a tetrapeptide - (L-Ala)-(D-Glu)-(L-Lys)-(D-Ala). Note the presence of D-amino acids. The polysaccharide chains are joined together via pentaglycines. Teichoic acids made up of repeating units of glycerol or ribitol phosphate are also a part of the cell wall.
Cell walls of Gram-negative bacteria are much more complex. Sandwiched between an inner and outer membrane is a layer of peptidoglycan. The outer membrane is coated with lipopolysaccharide, consisting of a lipid group joined to a highly complex polysaccharide. Repeating carbohydrate structures make thousands of different antigenic groups, with the antigenic determinant known as the O-antigen.

**Glycolipids and lysosomal storage diseases**

1. Multiple carbohydrate structures bound to sphingosine.
2. Widely distributed on outer surface of cells.
3. Tay-Sachs disease results from loss of hexosaminidase A.

- The structure of the glycolipid that builds up in the brain in Tay-Sachs disease and leads to an irreversible neurological degeneration that is always fatal.

**Glycosaminoglycans and Proteoglycans in Extracellular Matrices and Connective Tissues.**

- Complex polysaccharide complexes of varying sizes, up to several million daltons (+/- proteins).
- Part of membrane complexes or the extracellular matrix.
- Some classes on cells bind growth factors, and may be a kind of antennae to collect and store these factors.
- In connective tissues the very hygroscopic complexes bind water and serve to cushion joints. Cartilage is flexible and resilient because of the glycosaminoglycan part of proteoglycans.
Examples of some of the repeating disaccharides of glycosaminoglycans. Notice that long polymers would be extended, with multiple negative charges.

**Heparin**, an example of structure containing acidic repeating disaccharide units. Heparin forms extended structures due to the charge repulsion of its sulfate groups.
Hurler’s syndrome is one example of a lysosomal storage disease, caused by loss of a degradative enzyme. In this case the enzyme α-L-iduronidase, which hydrolyzes glycosidic bonds involving L-iduronic acid, is deficient.

**Glycoproteins**

O-linked sugars in glycoproteins

N-acetylglactosamine attaches to the protein via a Ser or Thr in **O-linked glycoproteins**.
Among the O-linked glycans are the blood group substances.

- **Functions**
  - Mucins contain large numbers of O-linked saccharides, and protect mucous membranes in the respiratory and GI tracts.
  - Carbohydrate gives an extended conformation to the protein, leading to high viscosity and extensive networks.
  - Some membrane receptors contain domains that are very rich in O-linked saccharides. The extended conformations of such regions have been postulated to hold the ligand-binding domain of some receptors out away from the carbohydrate complexes (glycocalyx layer) right at the cell surface.
The LDL receptor contains a carbohydrate rich domain that may orient the receptor above the cell glycocalyx, increasing the chance of binding the LDL particle.

- N-linked sugars in glycoproteins.
  - In glycoproteins, carbohydrate chains are attached to the protein.
  - In N-linked glycoproteins N-acetylglucosamine attaches to the protein via the amide N of an Asn.
  - N-linked glycoproteins can have complex oligosaccharide chains (glyprot).
  - The carbohydrate moiety in glycoproteins has high mobility.
  - In antibodies, carbohydrates chains serve a structural role, holding the two heavy chains together (Igg).
Examples of N-linked saccharide structures

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<tr>
<th>Glc Mannose</th>
<th>Hybrid</th>
<th>Complex Type</th>
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- Glucose and mannose containing oligosaccharides are added during translation in the endoplasmic reticulum (ER). Trimming removes terminal glucose and mannose residues. Glycoproteins that fold incorrectly may have glucose added back; a signal keeps the protein in the ER so that chaperones can complete proper folding.
- If the protein has a high mannose oligosaccharide, addition of phosphate to mannose is a signal to target the protein to lysosomes.
- Modification of oligosaccharides occurs in the cis, medial, and trans Golgi regions.
- Protozoans including yeast lack the ability to add GlcNAc to the mannose core for synthesis of complex oligosaccharides. The enzyme, GlcNAc TI (Glucosaminyl transferase I) that adds the first GlcNAc appears to separate metazoans from unicellular protozoans. This observation is interpreted to mean that the cellular interactions for multicellular organisms require complex oligosaccharides. (Ref: Dennis et al. Bioessays 21, 412 (99)).
- Knock-out mice are being used to study the functions of the sugars. Loss of the GlcNAc TI is lethal early in development.
- Oligosaccharides on glycoproteins are very heterogeneous, with multiple oligosaccharide structures found at a single glycosylation site on different molecules.
- Loss of terminal sialic acid of complex oligosaccharides of "old" circulating glycoproteins by action of enzymes in blood vessel walls causes binding/recognition by liver asialoglycoprotein receptor, leading to removal (endocytosis) and degradation by lysosomes.
Lectins and cell adhesion proteins

- Proteins that specifically bind to carbohydrates.
- Originally discovered in plants, but are important parts of the biology of all multi-cellular organisms.
- Animal lectins include the selectins, carbohydrate binding proteins on leukocytes and endothelial cells of vascular tissue. Expressed in response to signals from pathogens, these cause leukocytes and neutrophils to adhere to the vascular wall, and move into infected tissues.