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Glycobiology, glyco-conjugates and their applications

Glycobiology

The study of the structure and function of glycoconjugates

One of the most active and exciting areas of biochemistry and cell biology

Cells use specific oligosaccharides to encode important information about intracellular targeting of proteins, cell-cell interactions, cell differentiation and tissue development, and extracellular signals

Glycomics is the systematic characterization of all of carbohydrate components of a given cell or tissue, including those attached to proteins and to lipids

- In addition to their important roles as stored fuels (starch, glycogen, dextran) & as structural materials (cellulose, chitin, peptidoglycans), polysaccharides & oligosaccharides are information carriers.

- Some provide communication between cells & their extracellular surroundings

- Others label proteins for transport & localization in specific organelles, or for destruction (when the protein is malformed or superfluous)

- Others serve as recognition sites for extracellular signal molecules (growth factors, for example) or extracellular parasites (bacteria or viruses).

- On almost every eukaryotic cell, specific oligosaccharide chains attached to components of plasma membrane form a carbohydrate layer

- These glycocalyx, several nanometers thick, that serves as an information-rich surface that a cell shows to its surroundings.
- These oligosaccharides are central players in
    1. cell-cell recognition and adhesion
    2. cell migration during development
    3. blood clotting
    4. the immune response
    5. wound healing and other cellular processes.

- In most of these cases, the informational carbohydrate is covalently joined to a protein or a lipid to form a **glycoconjugate**, which is the biologically active molecule.

Proteoglycans

- **M**acromolecules of the cell surface or extracellular matrix
- In which one or more sulfated glycosaminoglycan chains are joined covalently to a membrane protein or a secreted protein.
- The glycosaminoglycan chain can bind to extracellular proteins through electrostatic interactions with the negatively charged groups on the polysaccharide.
- Proteoglycans are major components of all extracellular matrices

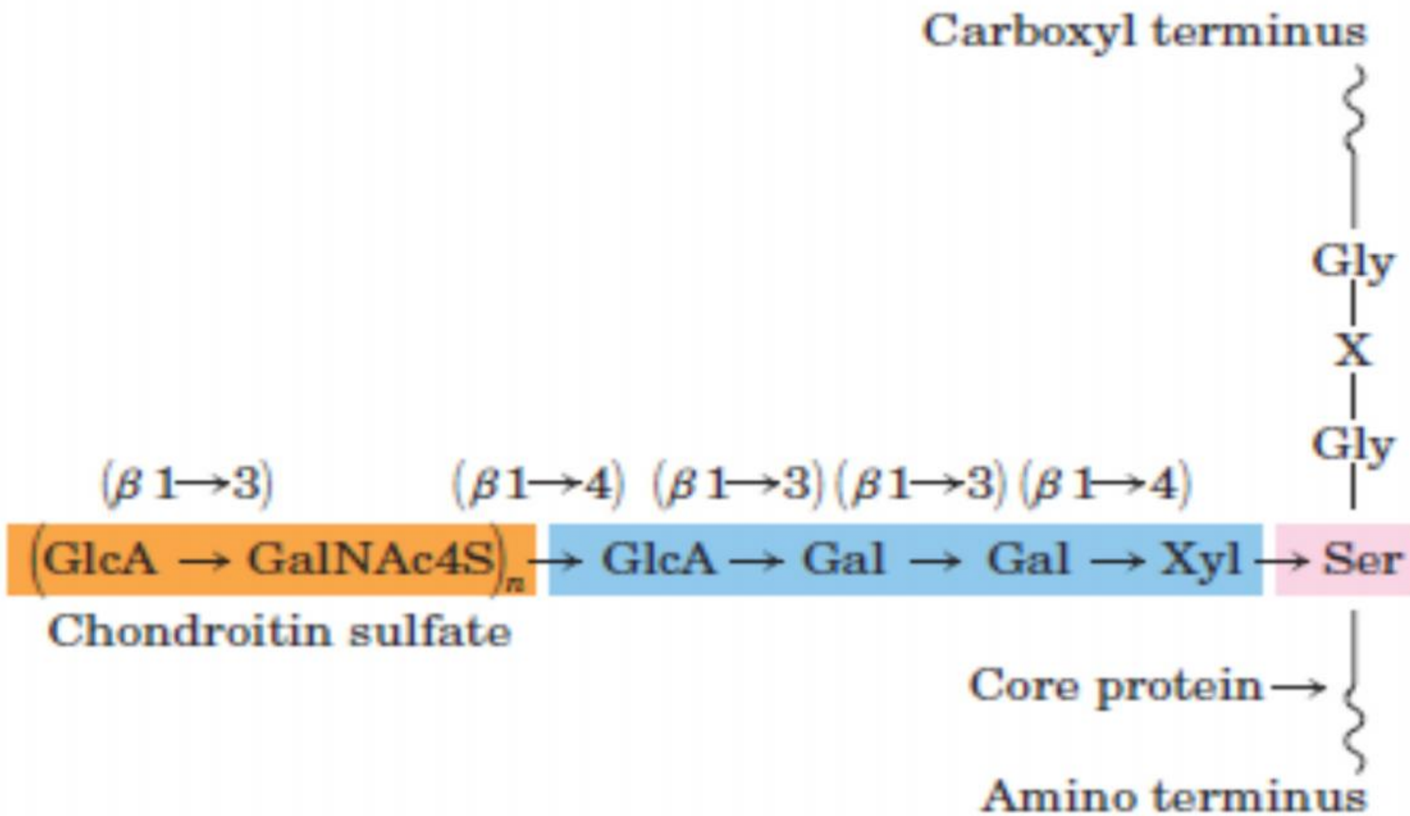


FIGURE 7–24 Proteoglycan structure, showing the tetrasaccharide bridge. A typical tetrasaccharide linker (blue) connects a glycosaminoglycan—in this case chondroitin 4-sulfate (orange)—to a Ser residue (pink) in the core protein. The xylose residue at the reducing end of the linker is joined by its anomeric carbon to the hydroxyl of the Ser residue.

Glycoproteins

- One or several oligosaccharides of varying complexity joined covalently to a protein.
- Found on
    1. outer face of plasma membrane (as part of glycocalyx)
    2. extracellular matrix
    3. blood.

- Inside cells found in specific organelles such as Golgi complexes, secretory granules, and lysosomes
- Oligosaccharide portions - very heterogeneous and rich in information, forming highly specific sites for recognition and high affinity binding by carbohydrate-binding proteins called lectins.
- Some cytosolic and nuclear proteins can be glycosylated as well.

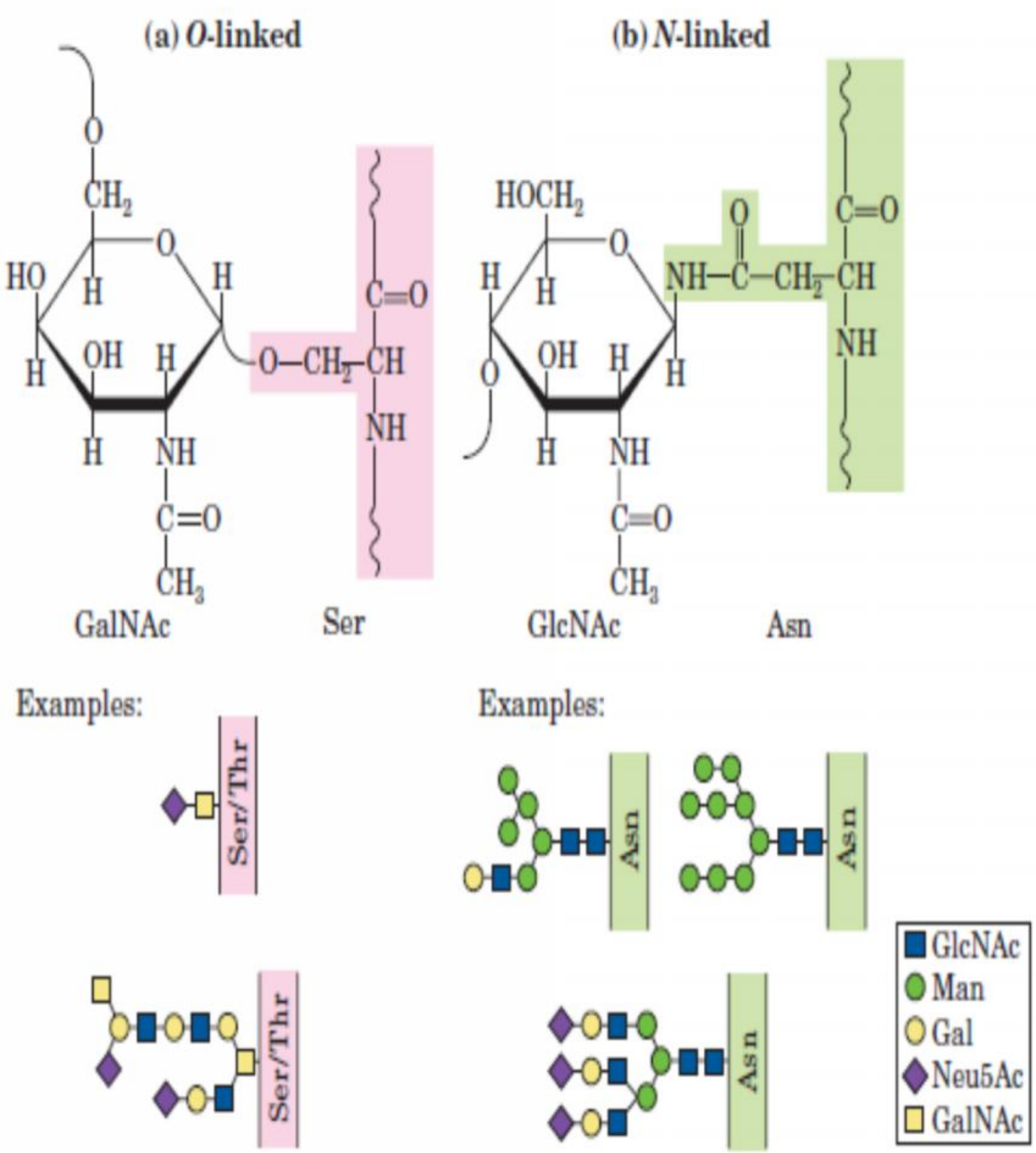
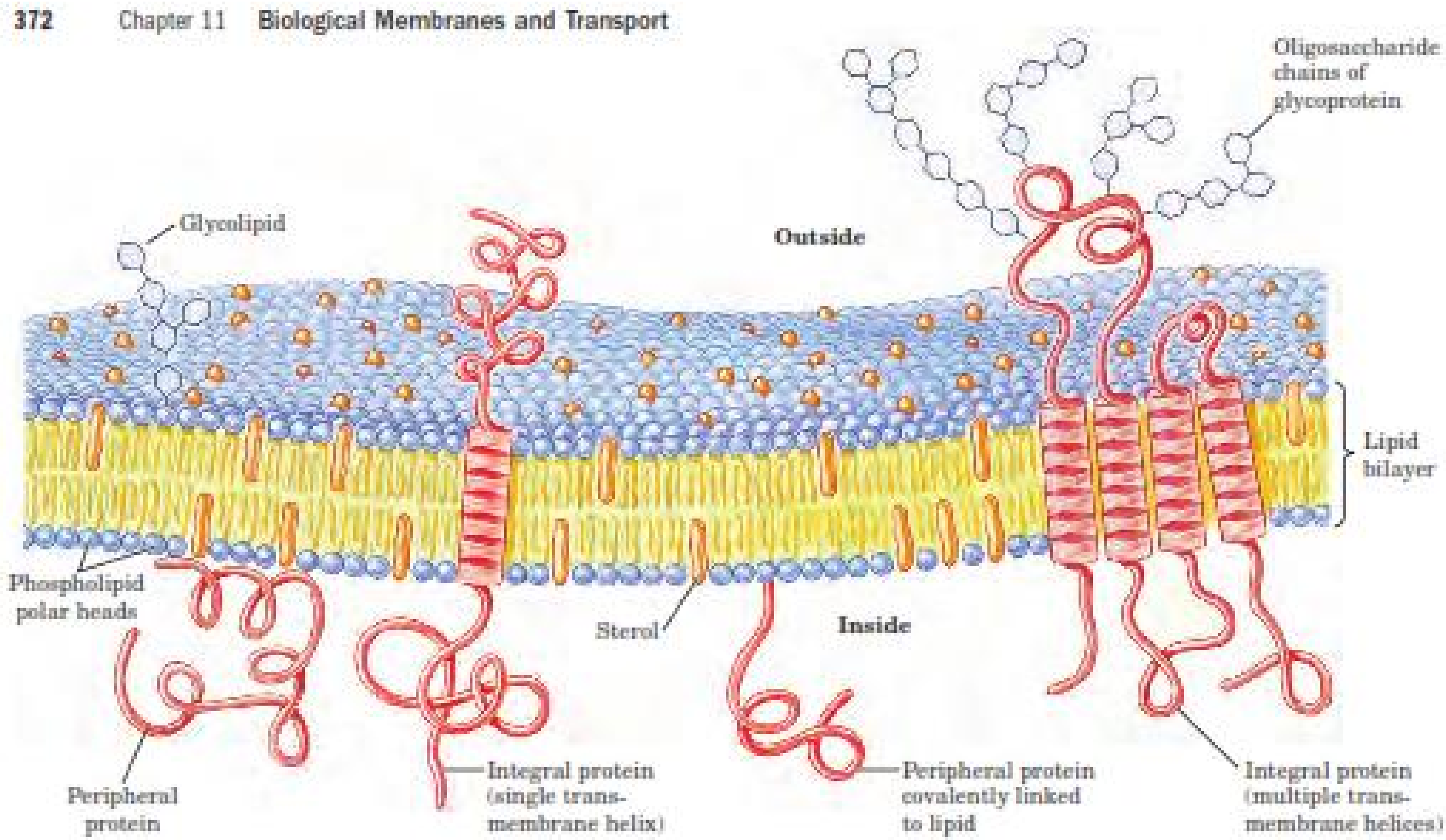


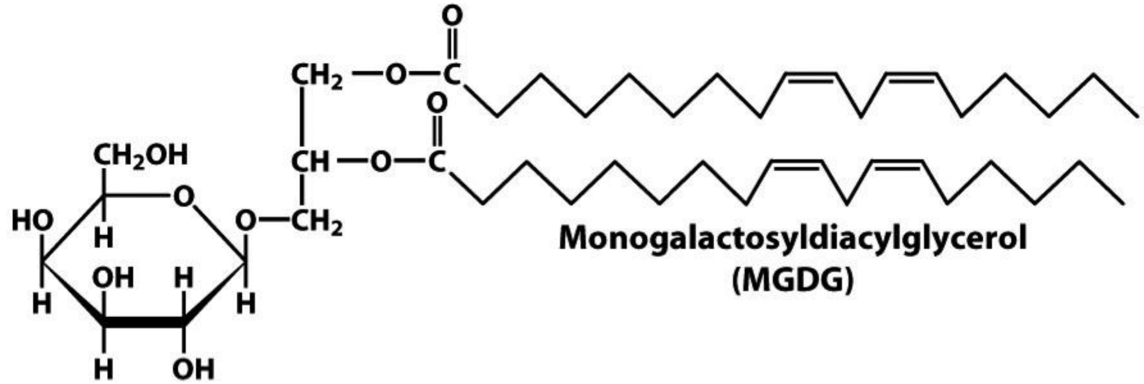
FIGURE 7–29 Oligosaccharide linkages in glycoproteins. (a) *O*-linked oligosaccharides have a glycosidic bond to the hydroxyl group of Ser or Thr residues (pink), illustrated here with GalNAc as the sugar at the reducing end of the oligosaccharide. One simple chain and one complex chain are shown. **(b)** *N*-linked oligosaccharides have an *N*-glycosyl bond to the amide nitrogen of an Asn residue (green), illustrated here with GlcNAc as the terminal sugar. Three common types of oligosaccharide chains that are *N*-linked in glycoproteins are shown. A complete description of oligosaccharide structure requires specification of the position and stereochemistry (α or β) of each glycosidic linkage.

Glycolipids

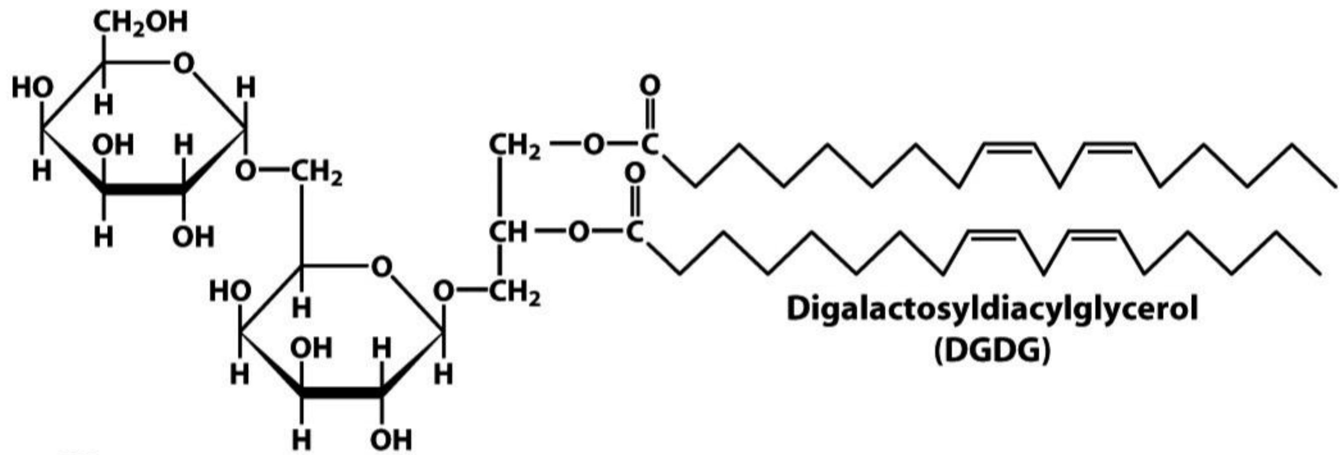
- membrane sphingolipids in which hydrophilic head groups are oligosaccharides.
- Oligosaccharides act as specific sites for recognition by lectins.
- The brain and neurons are rich in glycolipids, which help in nerve conduction and myelin formation.
- Glycolipids also play a role in signal transduction in cells.

Biological membranes

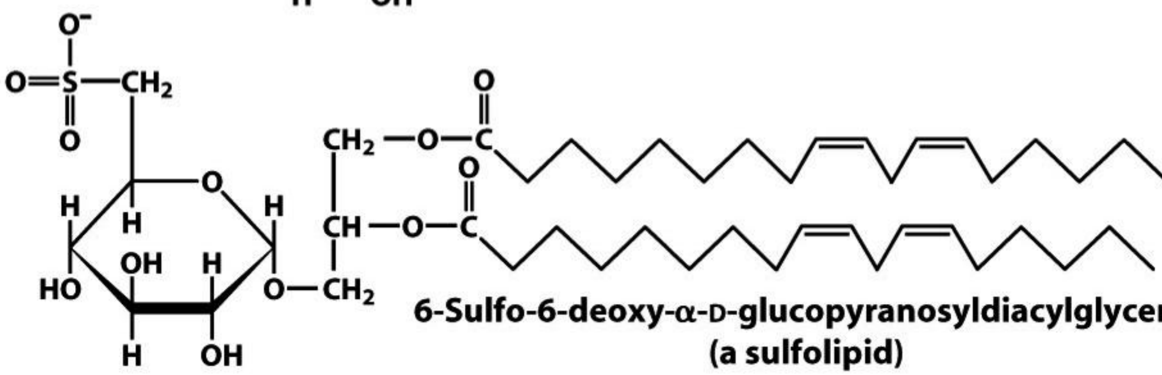




Monogalactosyldiacylglycerol (MGDG)



Digalactosyldiacylglycerol (DGDG)

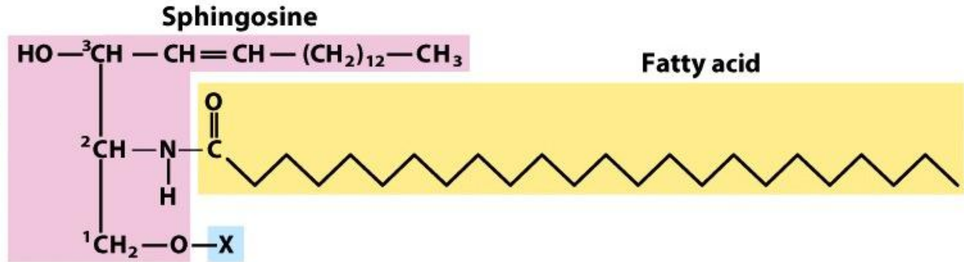


6-Sulfo-6-deoxy-α-D-glucopyranosyldiacylglycerol (a sulfolipid)

Figure 10-11

Lehninger Principles of Biochemistry, Fifth Edition

Sphingolipid (general structure)



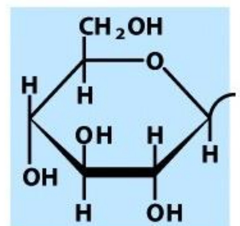
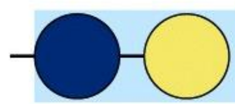
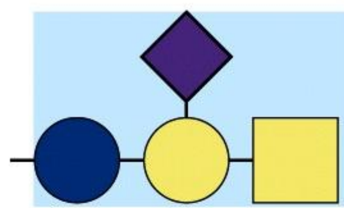
Name of sphingolipid	Name of X—O	Formula of X
Ceramide	—	$—H$
Sphingomyelin	Phosphocholine	$—\overset{O}{\overset{\Vert}{\underset{O^-}{\underset{\vert}{P}}}}—O—CH_2—CH_2—\overset{+}{N}(CH_3)_3$
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Figure 10-13

Lehninger Principles of Biochemistry, Fifth Edition

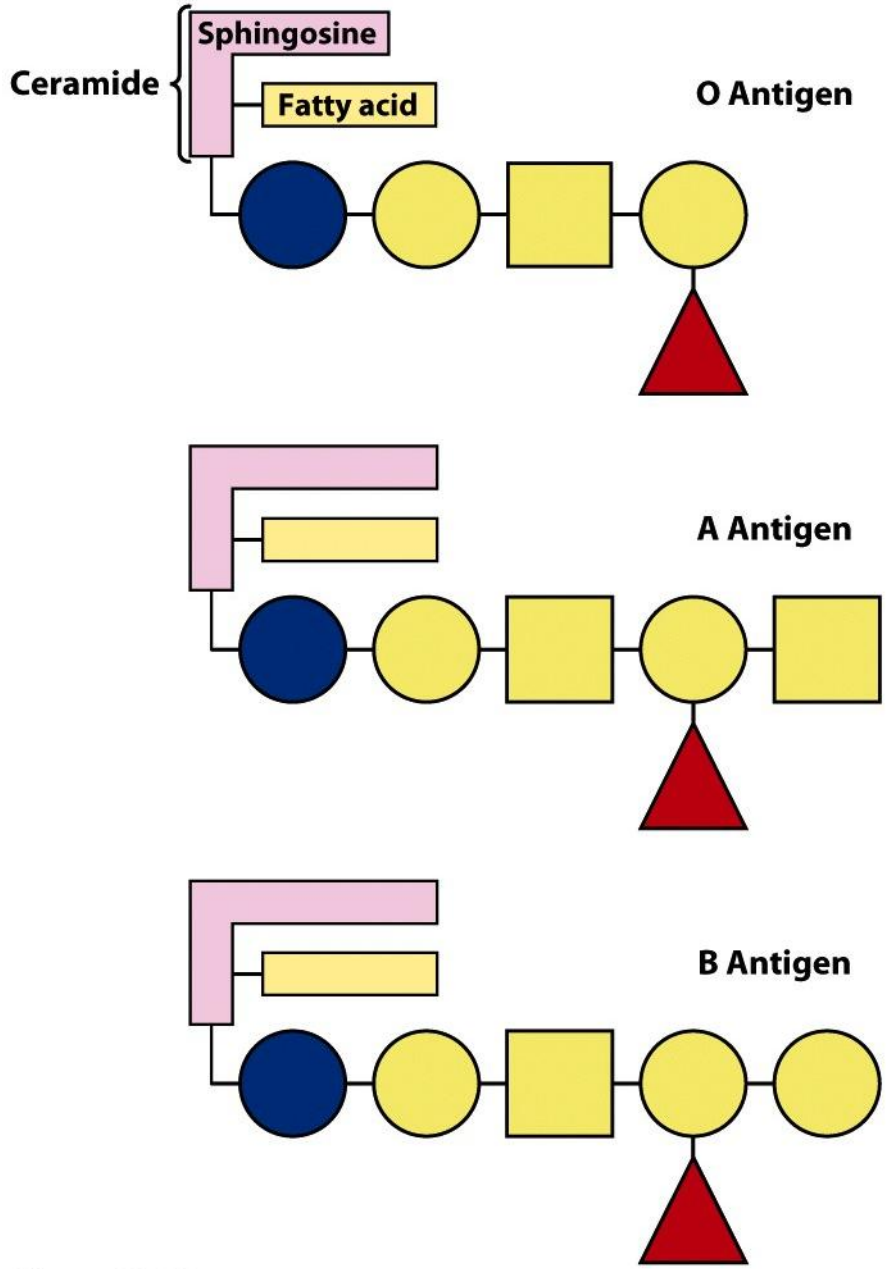


Figure 10-15
Lehninger Principles of Biochemistry, Fifth Edition

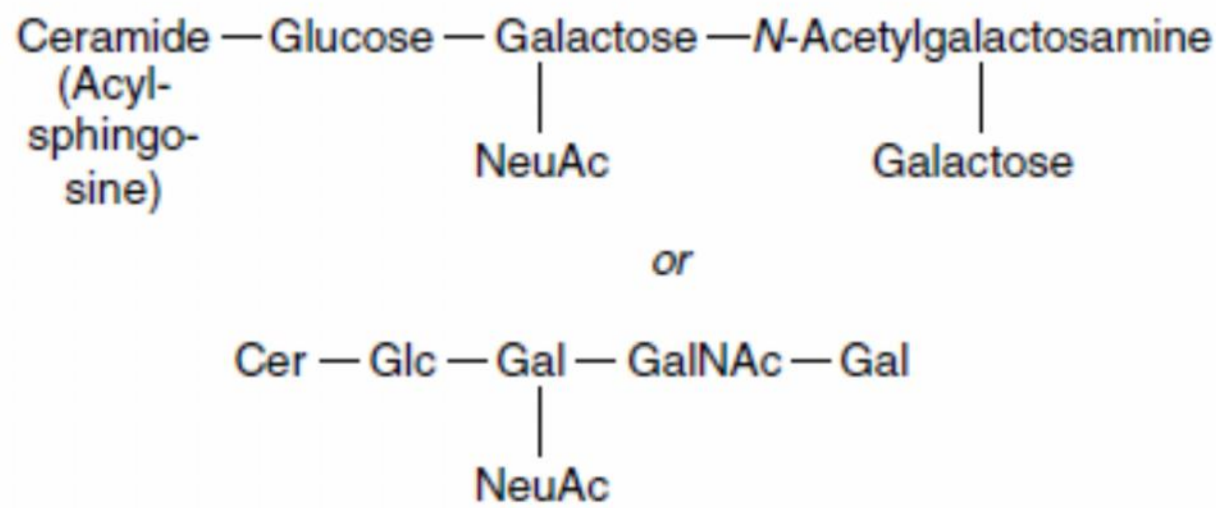
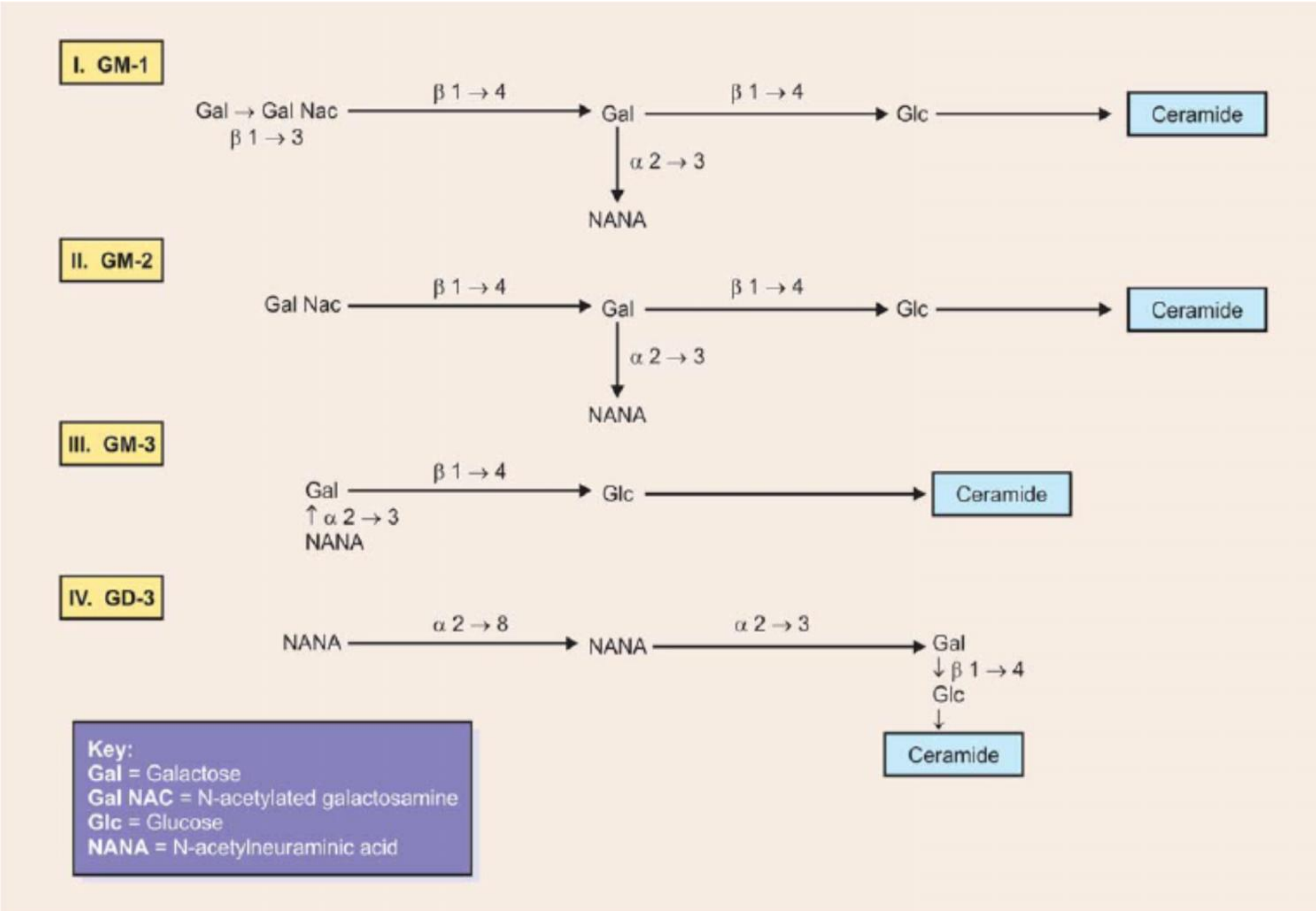


Figure 14–13. G_{M1} ganglioside, a monosialoganglioside, the receptor in human intestine for cholera toxin.


I. GM-1
Gal → Gal Nac
β 1 → 3
β 1 → 4
Gal
α 2 → 3
NANA
β 1 → 4
Glc
Ceramide
II. GM-2
Gal Nac
β 1 → 4
Gal
α 2 → 3
NANA
β 1 → 4
Glc
Ceramide
III. GM-3
Gal
↑ α 2 → 3
NANA
β 1 → 4
Glc
Ceramide
IV. GD-3
NANA
α 2 → 8
NANA
α 2 → 3
Gal
↓ β 1 → 4
Glc
↓
Ceramide
Key:
Gal = Galactose
Gal NAC = N-acetylated galactosamine
Glc = Glucose
NANA = N-acetylneuraminic acid