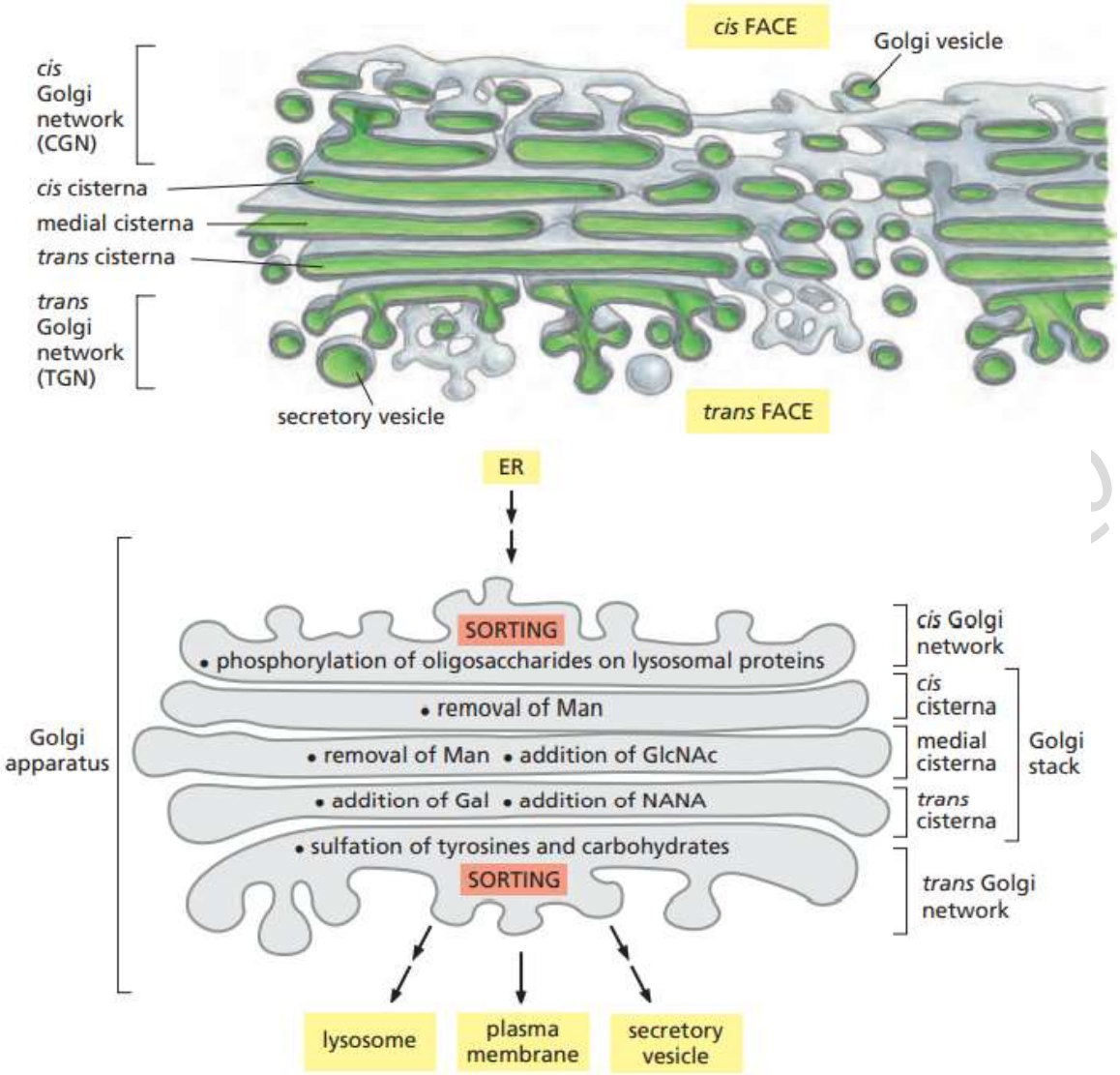
The Golgi Complex

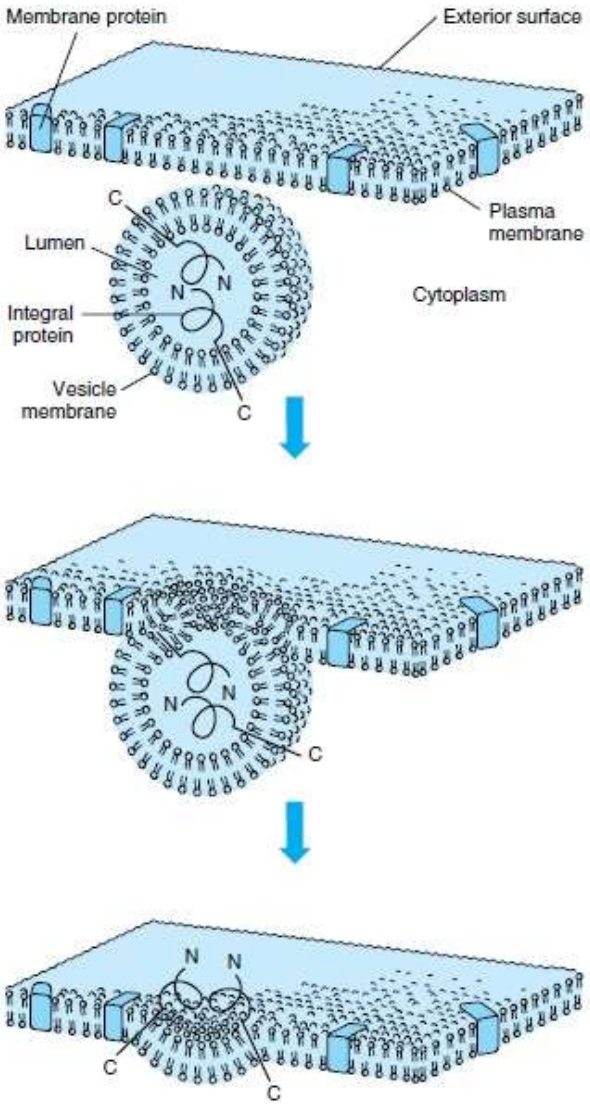
- Golgi complex composed of a series of flattened membrane vesicles or sacs (cisternae), surrounded by a number of more or less spherical membrane-limited vesicles.
- After proteins to be secreted and membrane proteins are modified in the Golgi complex, they are transported out of the complex by a second set of vesicles, which seem to bud from the trans side of the Golgi complex.
- Some modifications involve cleavage of oligosaccharide side chains followed by attachment of different sugar moieties in place of the side chain. Other modifications may involve the addition of fatty acids or phosphate groups (phosphorylation) or the removal of monosaccharides.
- The removal of mannose moieties occurs primarily in the cis and medial cisternae, whereas the addition of galactose or sulfate occurs primarily in the trans cisternae. In the final stage of transport through the Golgi apparatus, modified proteins and lipids are sorted in the trans Golgi network and are packaged into vesicles at the trans face. These vesicles then deliver the molecules to their target destinations, such as lysosomes or the cell membrane.
- In addition, within the vesicles are proteases that cut many secretory proteins at specific amino acid positions. This often results in activation of the secretory protein.



Man, mannose; GlcNAc, N-acetylglucosamine; Gal, galactose; NANA, N-acetylneuraminic acid (sialic acid).

Purpose of protein glycosylation

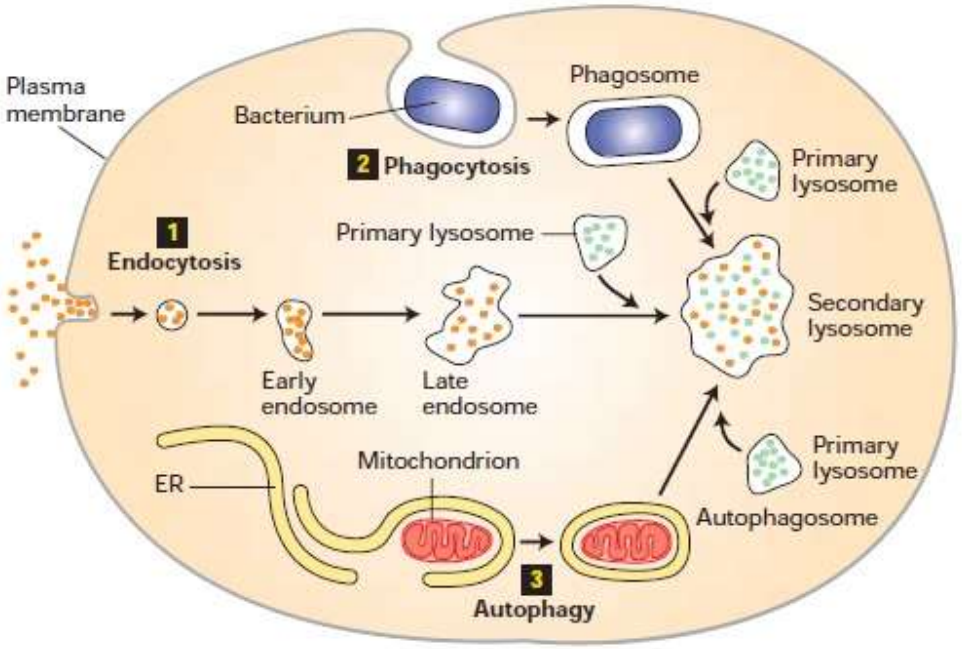
- Unlike nucleic acids and proteins, which are copied from a template in a repeated series of identical steps, complex carbohydrates require a different enzyme at each step, each product being recognized as the exclusive substrate for the next enzyme in the series.
- N-linked glycosylation promotes protein folding in two ways. First, it has a direct role in making folding intermediates more soluble, thereby preventing their aggregation. Second, the sequential modifications of the N-linked oligosaccharide establish a "glyco-code" that marks the progression of protein folding and mediates the binding of the protein to chaperones.
- The presence of oligosaccharides tends to make a glycoprotein more resistant to digestion by proteolytic enzymes.
- The mucus coat of lung and intestinal cells protects against many pathogens. The presence of oligosaccharides may modify a protein's antigenic and functional properties, making glycosylation an important factor in the production of proteins for pharmaceutical purposes.
- Modification changes the specificity of glycoproteins for the cell-surface signal proteins that activate it.



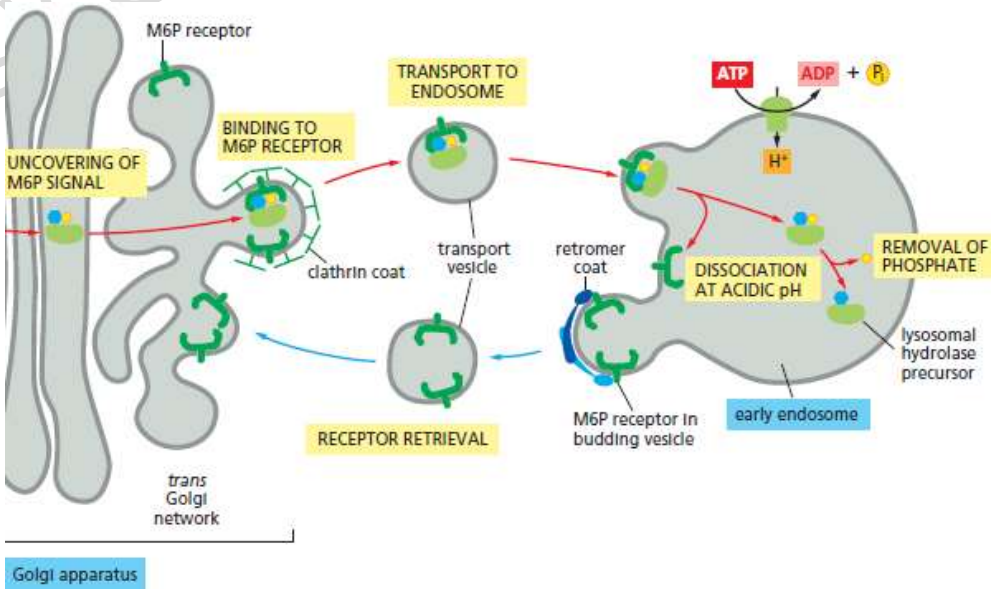
- Transport vesicles destined for the plasma membrane normally leave the TGN in a steady stream, thus membrane proteins and the lipids in the vesicles provide new components for the cell's plasma membrane, while the soluble proteins inside the vesicles are secreted to the extracellular space.
- The fusion of the vesicles with the plasma membrane is called exocytosis. This is the route, for example, by which cells secrete most of the proteoglycans and glycoproteins of the *extracellular matrix.*
- Secretory vesicles have unique proteins in their membrane, some of which might serve as receptors for aggregated protein in the TGN.
- Once loaded, a secretory vesicle has to reach the site of secretion, which in some cells is far away from the TGN. Microtubules can guide transport vesicles to the cell surface for **constitutive** exocytosis.
- Whereas transport vesicles containing materials for constitutive release fuse with the plasma membrane once they arrive there, secretory vesicles in the **regulated** pathway wait at the membrane until the cell receives a signal to secrete, and they then fuse.

Lysosomes

- Found exclusively in animal cells, lysosomes are responsible for degrading certain components that have become obsolete for the cell or organism.
- The process by which an aged organelle is degraded in a lysosome is called *autophagy* ("eating oneself").
- Lysosomes contain a group of enzymes that degrade polymers into their monomeric subunits.
- All the lysosomal enzymes work most efficiently at acid pH values and collectively are termed *acid hydrolases.*
- Transport proteins in the lysosomal membrane work together to pump H^+ and Cl^- ions (HCl) from the cytosol across the membrane, thereby acidifying the lumen.



- The heterogeneous morphology of lysosomes contrasts with the relatively uniform structures of many other cell organelles.
- Most of the lysosome membrane proteins are highly glycosylated, which helps to protect them from the lysosome proteases in the lumen. Transport proteins in the lysosome membrane carry the final products of the digestion of macromolecules—such as amino acids, sugars, and nucleotides—to the cytosol, where the cell can either reuse or excrete them.
- Vesicular pathway delivers lysosomal hydrolases from the TGN to lysosomes. The enzymes are first delivered to endosomes in transport vesicles that bud from the TGN, before they move on to endolysosomes and lysosomes.
- In animal cells lysosomal hydrolases carry a unique marker in the form of *mannose 6-phosphate* (*M6P*) groups, which are added exclusively to the *N*-linked oligosaccharides of these soluble lysosomal enzymes as they pass through the lumen of the *cis* Golgi network.
- Transmembrane M6P receptor proteins, which are present in the TGN, recognize the M6P groups and bind to the lysosomal hydrolases on the lumenal side of the membrane and to adaptor protein in assembling clathrin coats on the cytosolic side and deliver the contents to early endosomes.
- *Lysosomal secretion* of undigested content enables all cells to eliminate indigestible debris. Some cell types, contain specialized lysosomes that have acquired the necessary machinery for fusion with the plasma membrane. *Melanocytes* in the skin, for example, produce and store pigments in their lysosomes. In some genetic disorders, defects in melanosome exocytosis block this transfer process, leading to forms of hypopigmentation (albinism).



Reference and further reading

- Molecular Cell Biology. Lodish et al. W. H. Freeman and Company.
- Molecular Biology of the cell. Alberts et al. Garland Science, Taylor & Francis Group.
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- The Cell: A Molecular Approach. Cooper et al. Sinauer Associates Inc.