CHEM 537

Carbohydrate Biochemistry, and Glycobiology

Part III: Glycobiology, Glycoproteins & Glycoconjugates

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Chapters 11 & 23: *Biochemistry*, Voet/Voet, 4th edition, 2011

Introduction to Glycobiology, Taylor/Drickhamer, 3rd edition, 2011

Glycobiology: Definitions and terminology

Glycobiology: studies of the structures and functions of sugars attached to proteins and lipids.

Glycoconjugates: formed when mono-, oligo- or polysaccharides are attached to proteins or lipids.

Glycoproteins and glycolipids: proteins and lipids to which carbohydrate is covalently attached; the mechanism of attachment is *enzyme-catalyzed* in vivo.

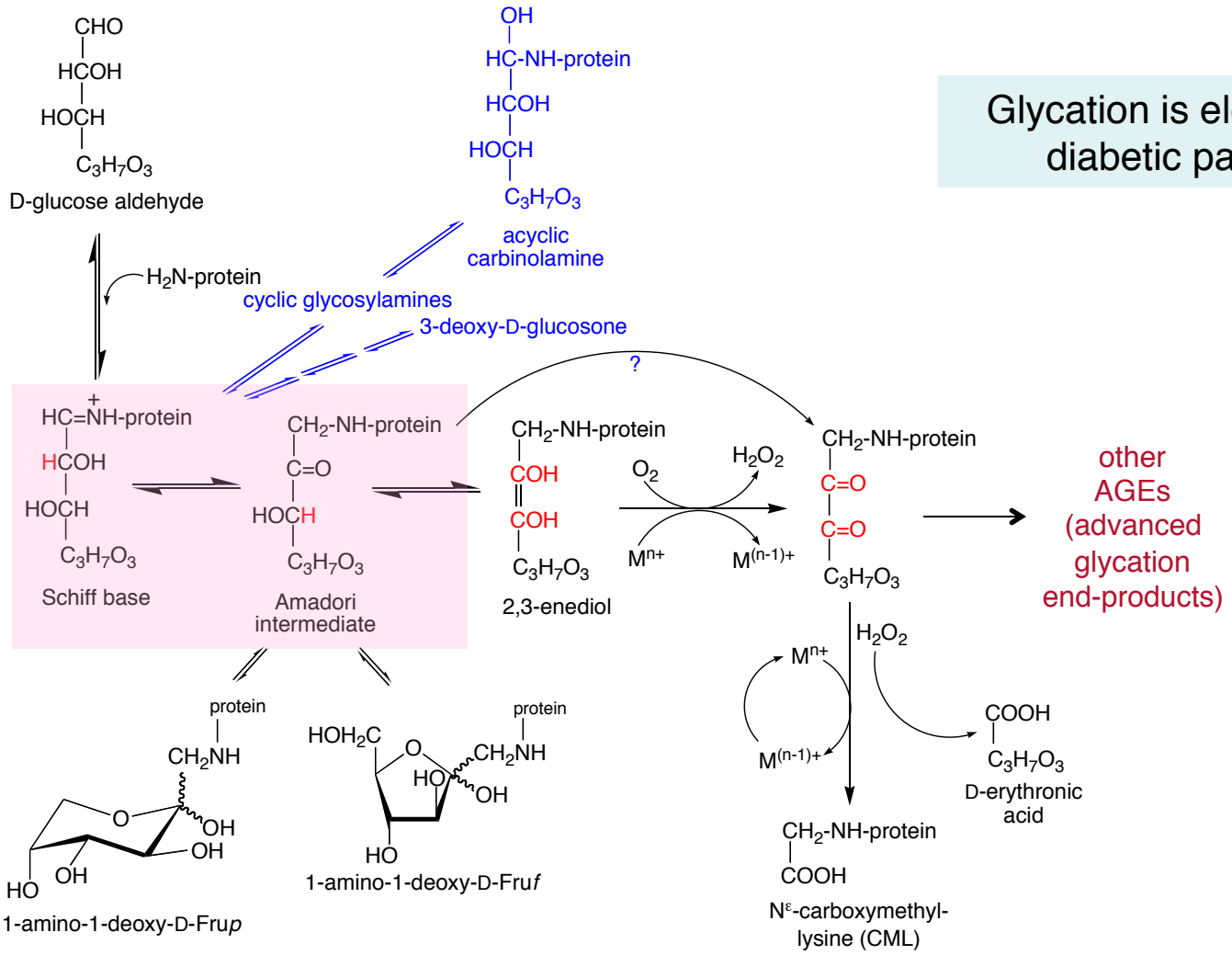
Glycan: the carbohydrate component of glycoproteins and glycolipids.

Glycosylation and glycation

Glycosylation: *enzyme-catalyzed* covalent modification of proteins and lipids; involves specific sugar donors such as nucleotide and dolichol sugars, and glycosyltransferases; glycosylated products have specific structures and biological functions.

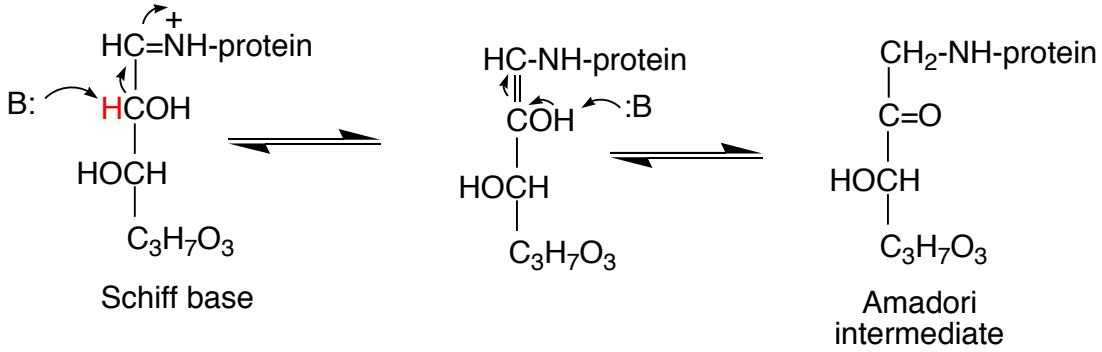
Glycation: chemical modification of proteins that occurs in vivo; spontaneous, *non-enzyme-catalyzed*; products are heterogeneous in structure and are often deleterious to the organism.

Protein glycation is not enzyme-catalyzed.

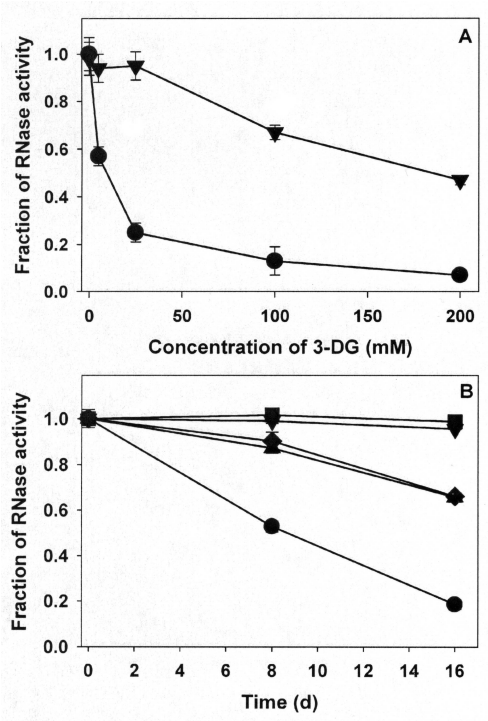


Glycation is elevated in diabetic patients.

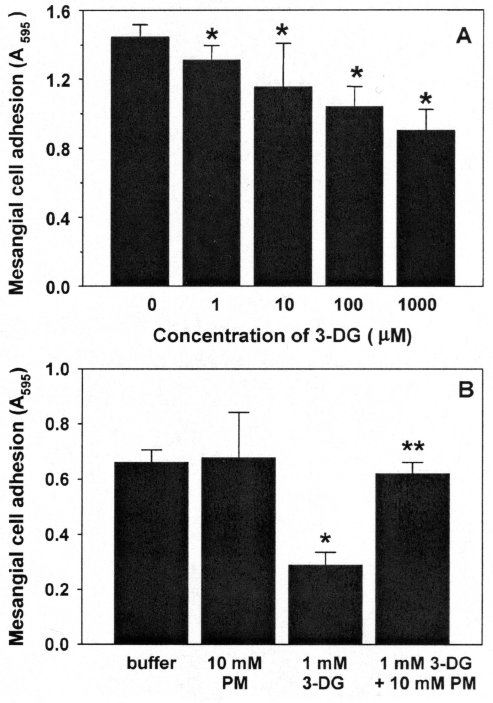
Mechanism of formation of the Amadori intermediate during protein glycation



Effect of glycation on protein structural integrity and function

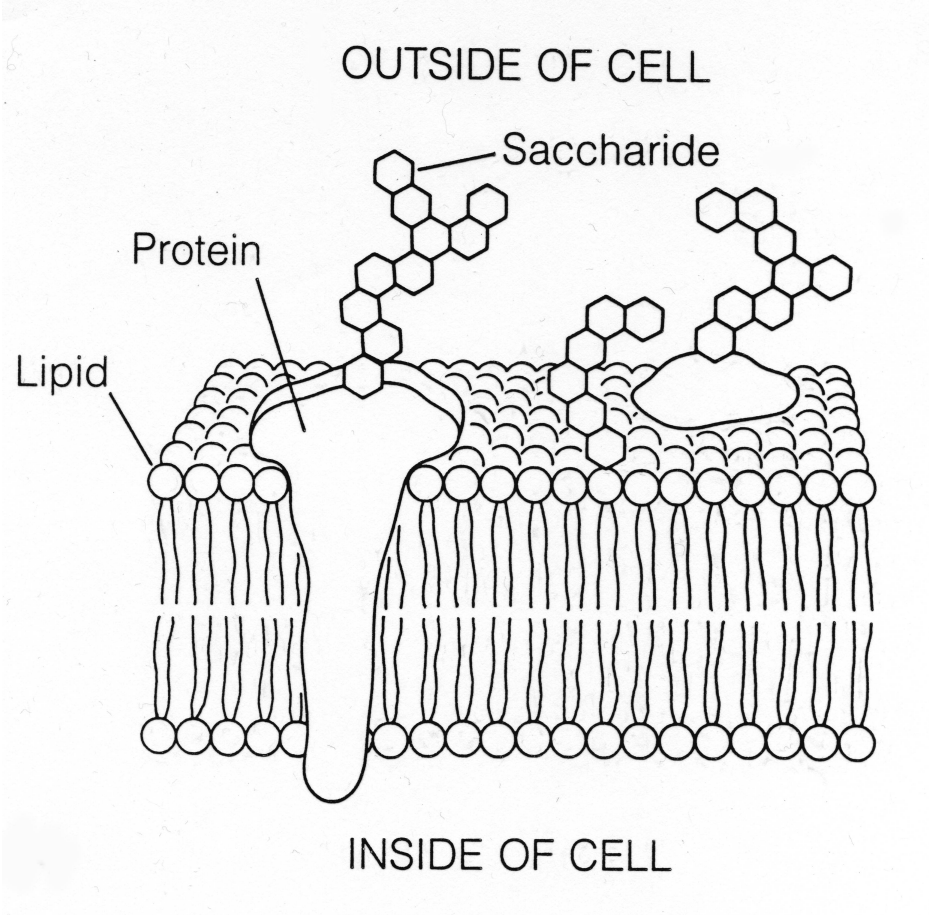


Inactivation of RNase by 3-deoxy-D-glucosone (3-DG)and protection by pyridoxamine (PM). (A) circles (-PM); triangles (+PM). (B) circles (+3-DG); squares (-3-DG); diamonds (+*N*-acetylarginine)



Inhibition of mesangial cell adhesion to 3DG-modified collagen IV and protective effect of PM

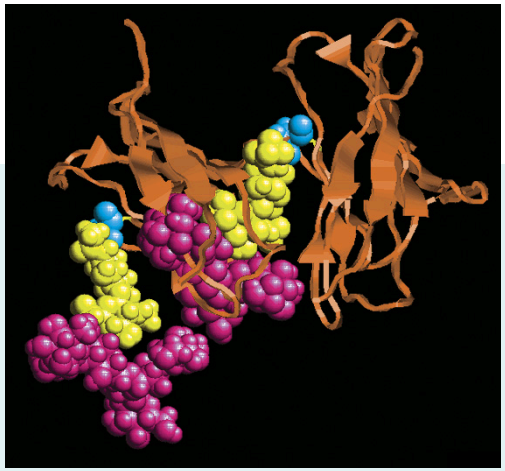
Chetyrkin *et al.*, *Biochemistry* **2008**, *47*, 997-1006



Glycoconjugates associated with plasma membranes (glycoproteins and glycolipids): asymmetric distribution of glycan on the extracellular side of the membrane.

The extracellular location allows specific glycan interactions with biomolecules, cells, viruses.

Glycoproteins



Glycosylation of proteins affects:

- thermodynamic stability
- biological half-life
- cellular localization
- biological activity

Protein glycosylation is under enzymatic control:

- glycosylation of a particular protein can differ by cell type, growth stage, metabolic activity, and substrate availability; resulting in different isoforms that differ by glycosylation only.
- glycosylation differences produce glycoforms characterized by their microheterogeneity (a conserved protein component but different glycan components)

Nearly all eukaryotic secreted and membrane-associated proteins are heavily glycosylated; glycosylation is the most common post-translational modification of proteins.

Two major forms of protein glycosylation: *N*-linked glycans and *O*-linked glycans

As a general rule, prokaryotes do not glycosylate proteins.

Some functions of protein glycosylation

Structural: *O*-glycosylation of mucins results in an open, extended structure.

Recognition: *N*- and *O*-glycosylation of membrane proteins promote cell identity and adhesion (leukocyte rolling, immune system recognition).

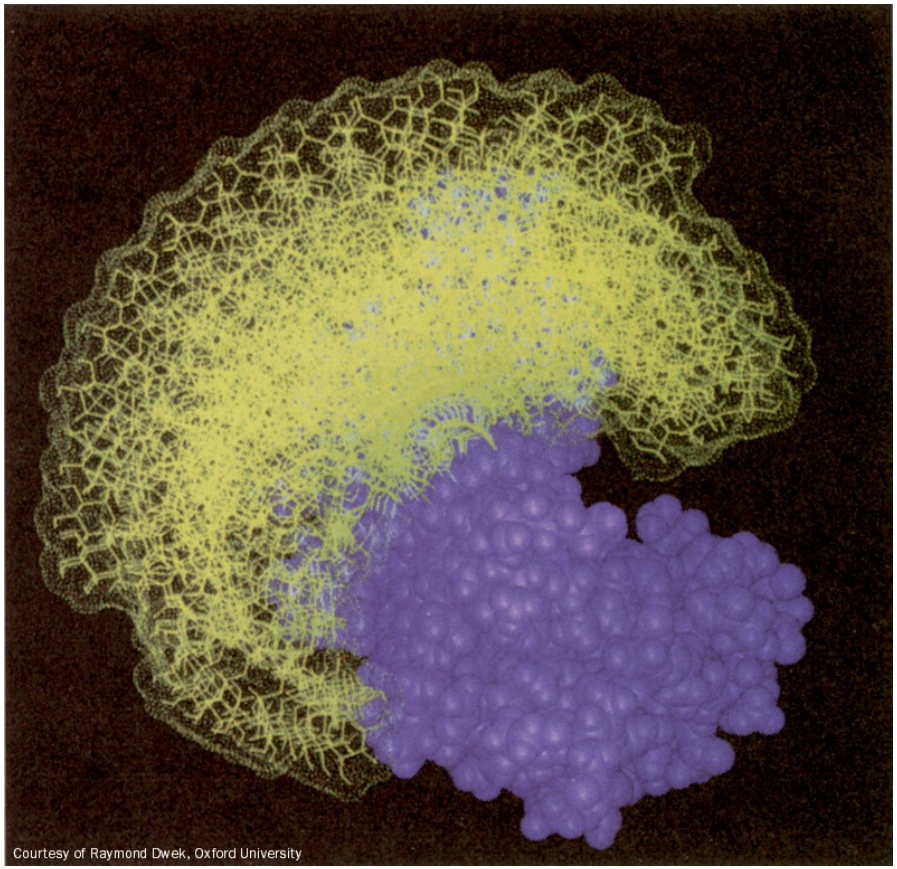
Protein degradation: Slow cleavage of *N*-linked glycans can serve as a timing device for initiating protein proteolysis.

Protein stability: *N*-linked glycans can increase protein stability by enhancing water activity around the protein, "magnifying" the influence of the hydrophobic effect.

Orientation in assemblies: protein glycosylation can affect their interactions to form larger assemblies (*e.g.,* membrane signaling complexes)

Glycoproteins and glycolipids on plasma membranes mediate cell identity, communication, adhesion and/or growth.

Most polysaccharides attached to proteins extend away from the protein's surface and probably do not affect protein structure significantly (we think).

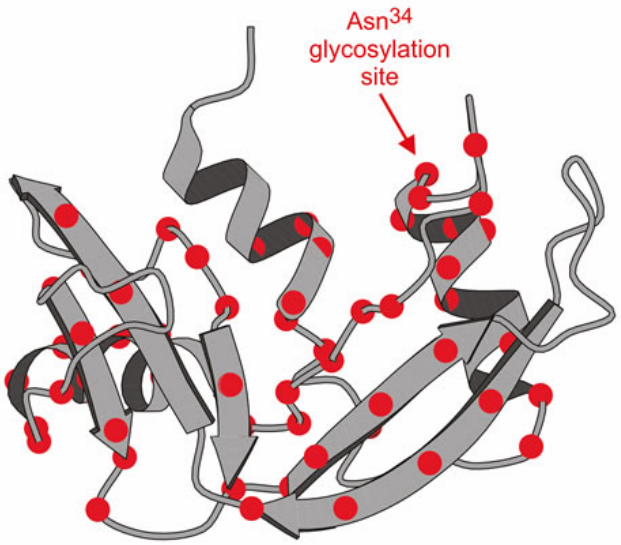


Model of oligosaccharide dynamics in bovine pancreatic RNase B. Note the extensive conformational space occupied by the carbohydrate component.

Digestive ribonuclease (RNase) is secreted from the pancreas into the intestine in unglycosylated (RNase A) and glycosylated (RNAse B) forms.

RNase B is an *N*-linked glycoprotein. It carries a single high-mannose oligosaccharide covalently attached to Asn 34. Glycoforms (microheterogeneity) vary in the number of attached Man residues (4-9).

The protein components of RNase A and RNase B have conserved structures.



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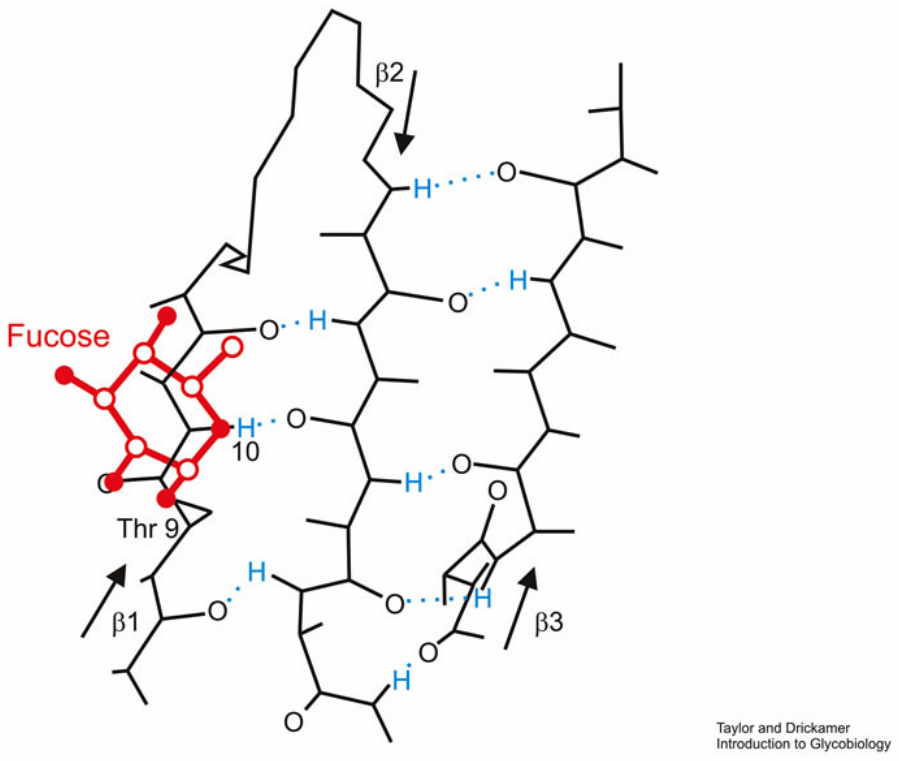
Exchange rates of backbone amide protons of RNase B (sites shown in red) are reduced in the glycosylated form of the protein, suggesting increased thermodynamic stability (rates of folding/unfolding differentially affected).

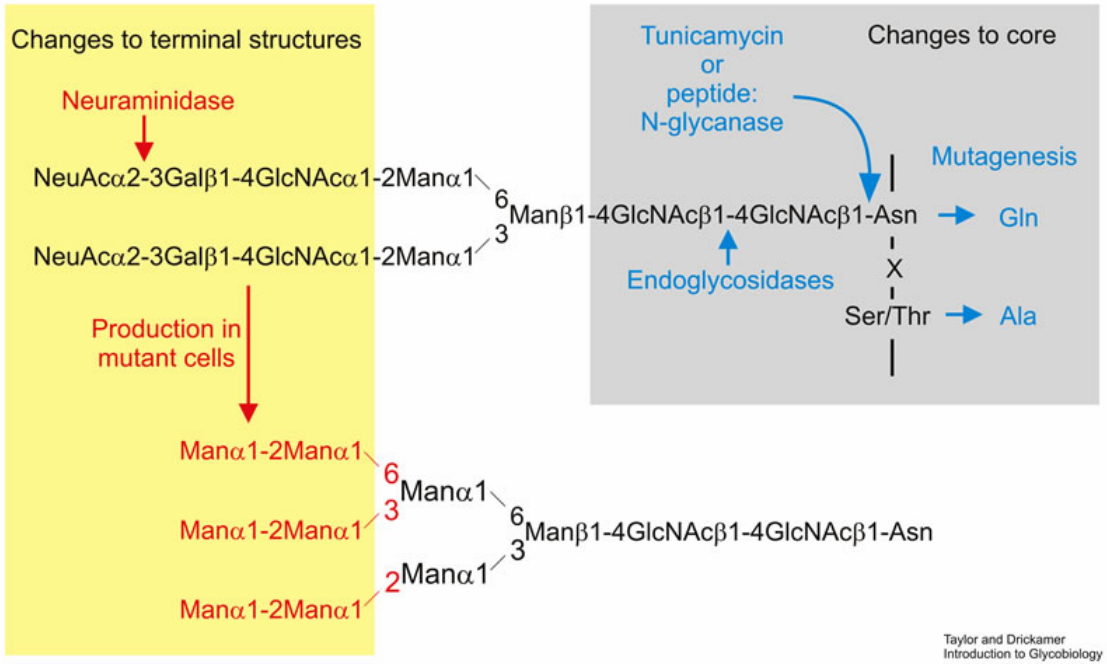
Crystal structure of RNase B not available (microheterogeneity problems), but glycosidase digestion studies suggest that the $GlcNAc_2$ portion of the oligosaccharide core closest to the attachment point interacts with the protein on either side of Asn 34, presumably causing the increased stability.



Insertion of a *single* fucose residue at Thr 9 (O-glycosylation) stabilizes PMP-C protease inhibitor, a 36-residue oligopeptide from locust.

The unfucosylated form of PMP-C exhibits a t_m value ~20° lower than fucosylated PMP-C. Rates of proton exchange with solvent in the three-stranded anti-parallel β-sheet core structure of PMP-C in the vicinity of the glycosylation site are reduced in the fucosylated form. The folded form is favored by fucosylated PMP-C,
whereas random coil is favored by unfucosylated PMP-C.

Experimental methods to modify protein glycosylation patterns

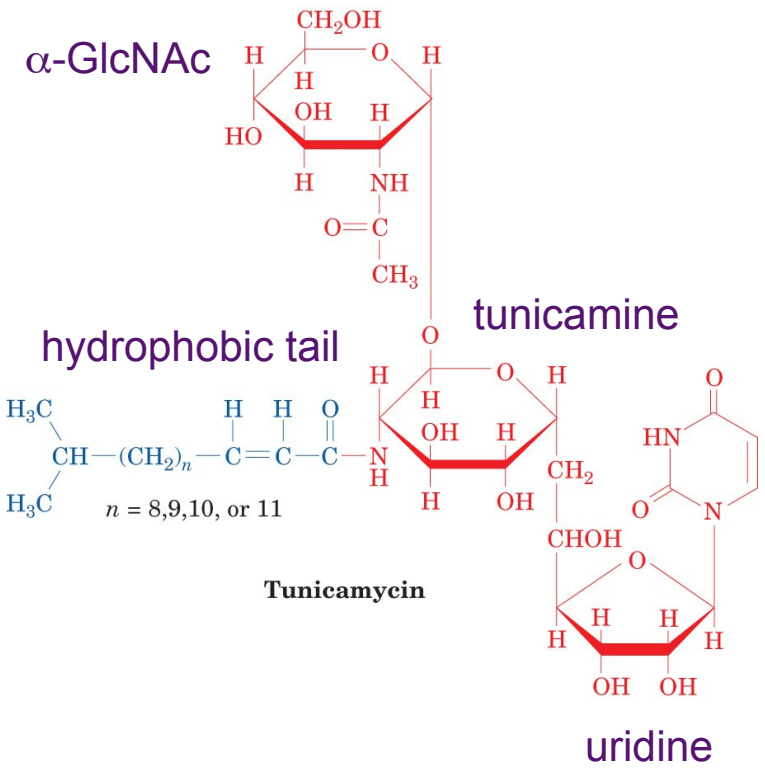


Peptide *N*-glycanase (PNGase): Cleaves at the GlcNAc-Asn attachment point, liberating the full *N*-glycan in vitro.

Tunicamycin: a small molecule inhibitor of the initial step of protein *N*-glycosylation (dolichol-P stage); prevents *N*-glycosylation in vivo. Mutagenesis can achieve the same effect, although the protein is modified.

Endo- and exo-glycosidases trim existing oligosaccharides in vitro.

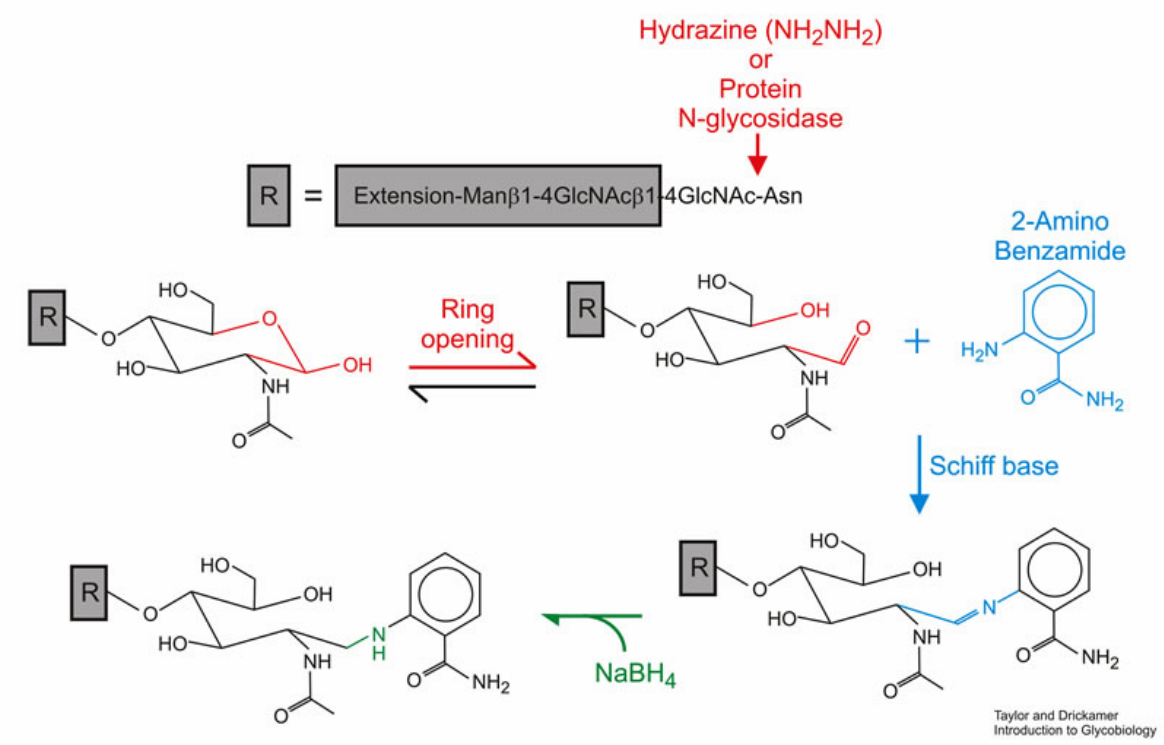
Protein expression in different organisms/cells can modify glycosylation patterns in vivo.



In eukaryotes, tunicamycin inhibits the GPT translocase involved in the biosynthesis of GlcNAc-linked dolichol pyrophosphate (an early event in protein *N*-glycosylation). Tunicamycin is thus widely used to inhibit glycoprotein translocation and processing.

Tunicamycins are natural products isolated from *Streptomyces*. They vary in the structure of the fatty acid hydrophobic tail.

Xu *et al. Biochemistry* **2004**, *43*, 13248-13255



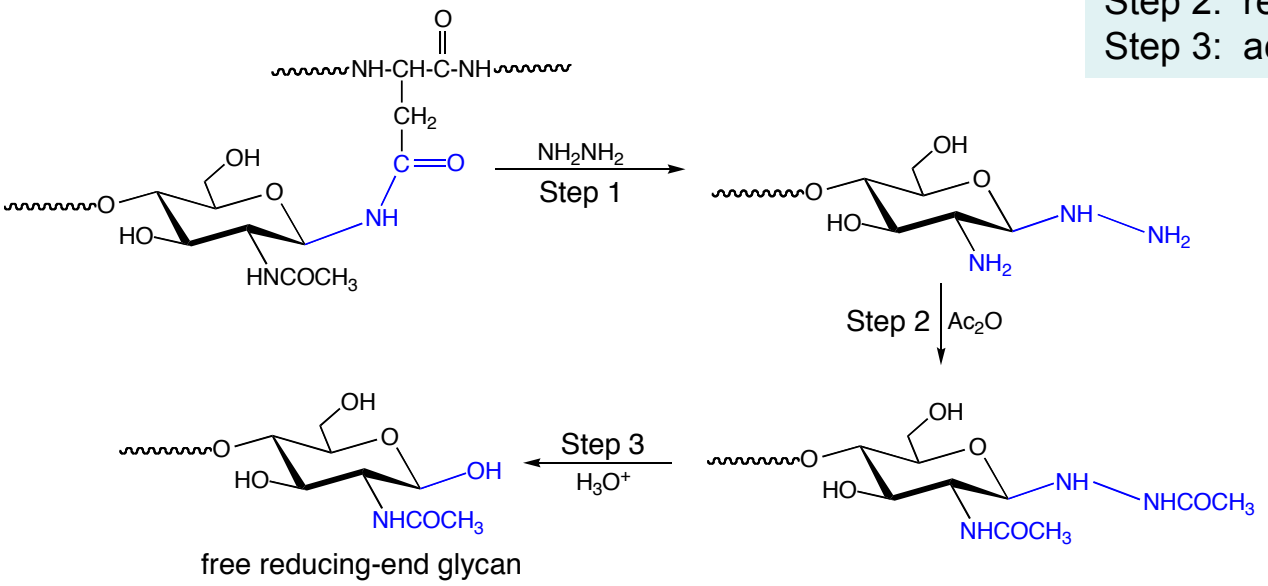
Use of hydrazine or PNGase to release an intact *N*-glycan from a glycoprotein, and subsequent tagging of the released oligosaccharide at the reducing end with a fluorescent probe to facilitate its analysis by HPLC.

Mechanism of hydrazine-mediated cleavage of an *N*-glycan from a glycoprotein

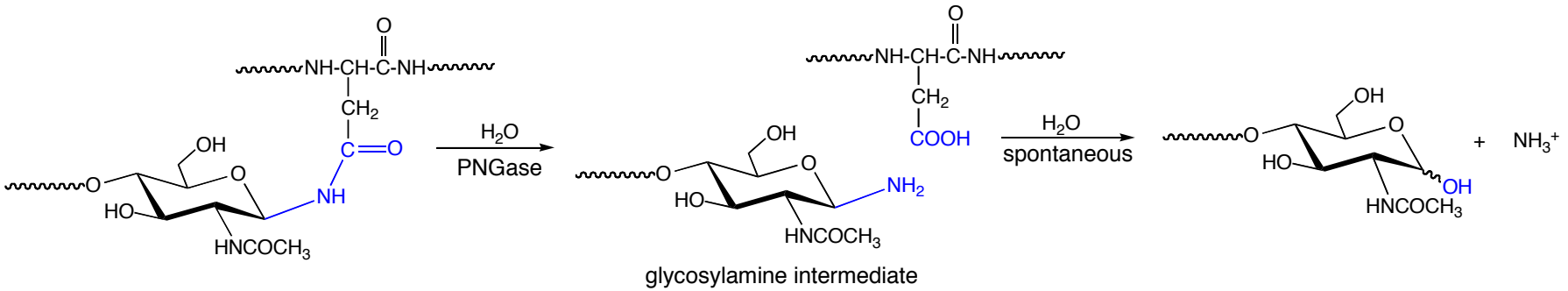
The precise mechanism by which hydrazine cleaves the *N*-glycoside linkage of N-glycans is not completely understood.

A proposed reaction scheme:

Step 1: hydrazinolysis
Step 2: re-*N*-acetylation
Step 3: acetohydrazone cleavage



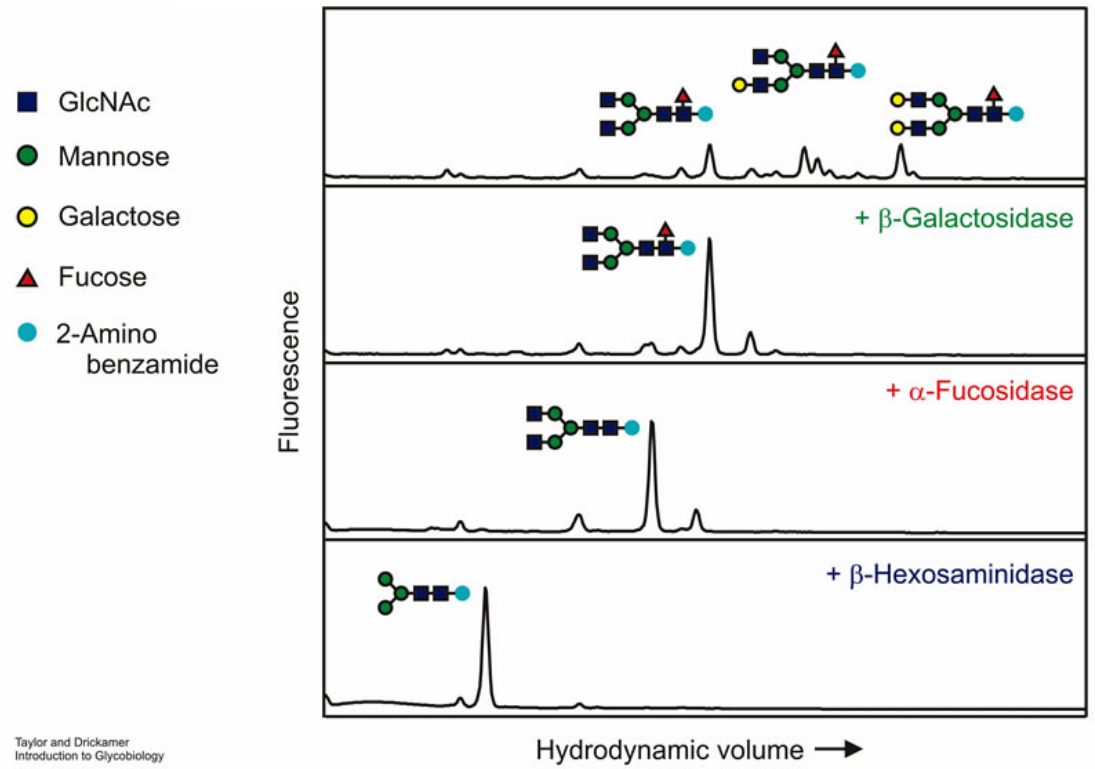
Hydrolysis of the *N*-glycoside bond of *N*-glycans by peptide *N*-glycanase



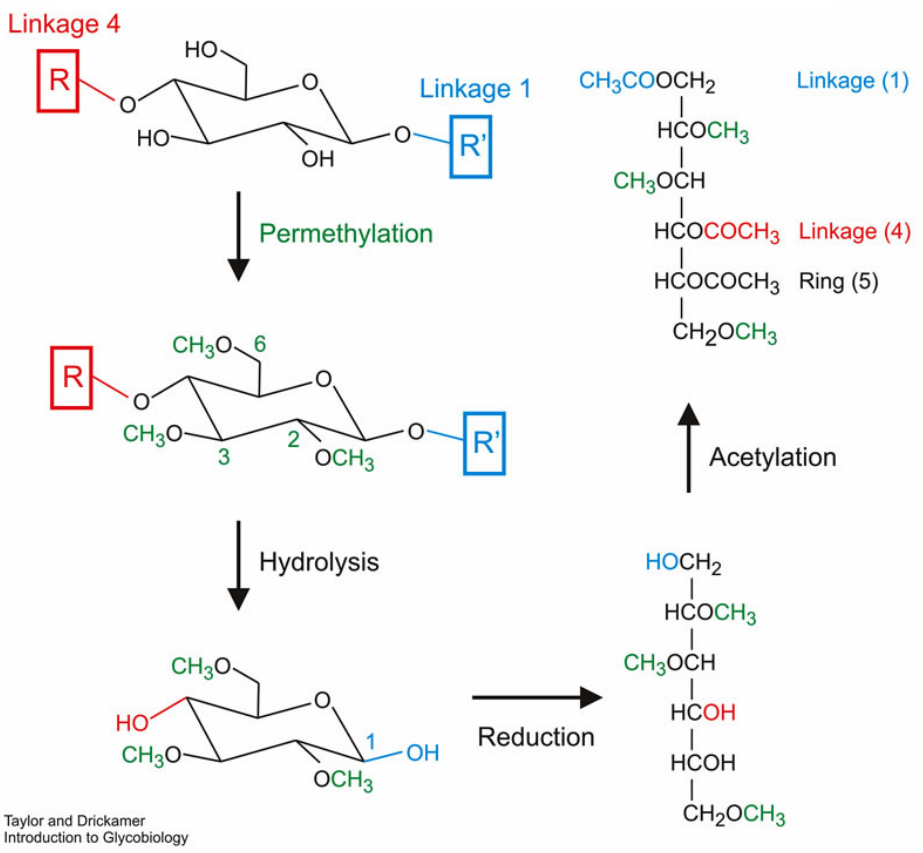
glycosylamine intermediate

Results in release of the intact *N*-glycan from the protein; *N*-glycan has free reducing end available for derivatization

Fi



Structural characterization of an end-labeled oligosaccharide by HPLC, assisted by the sequential use of specific exoglycosidases.



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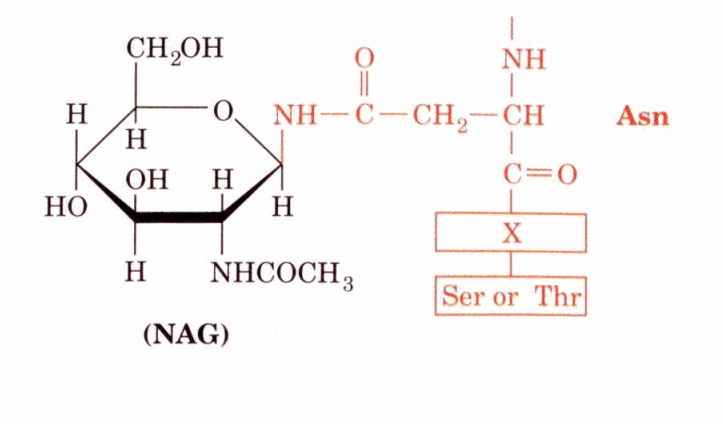
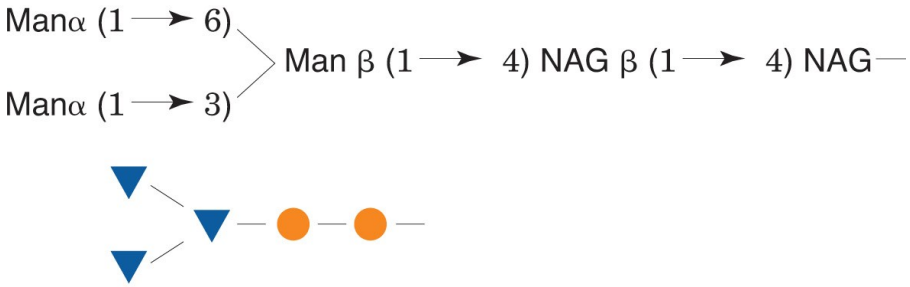
Permethylation (linkage) analysis of an oligo- or polysaccharide by chemical derivatization: formation of methyl ethers, followed by hydrolysis, reduction, and peracetylation. The resulting monomeric products are volatile, allowing analysis by gas-liquid chromatography (GLC) using appropriate alditol standards.

Reduction to alditols simplifies the analysis by eliminating anomeric mixtures, but information on linkage stereochemistry is lost.

N-Linked Glycoproteins and *N*-Glycans

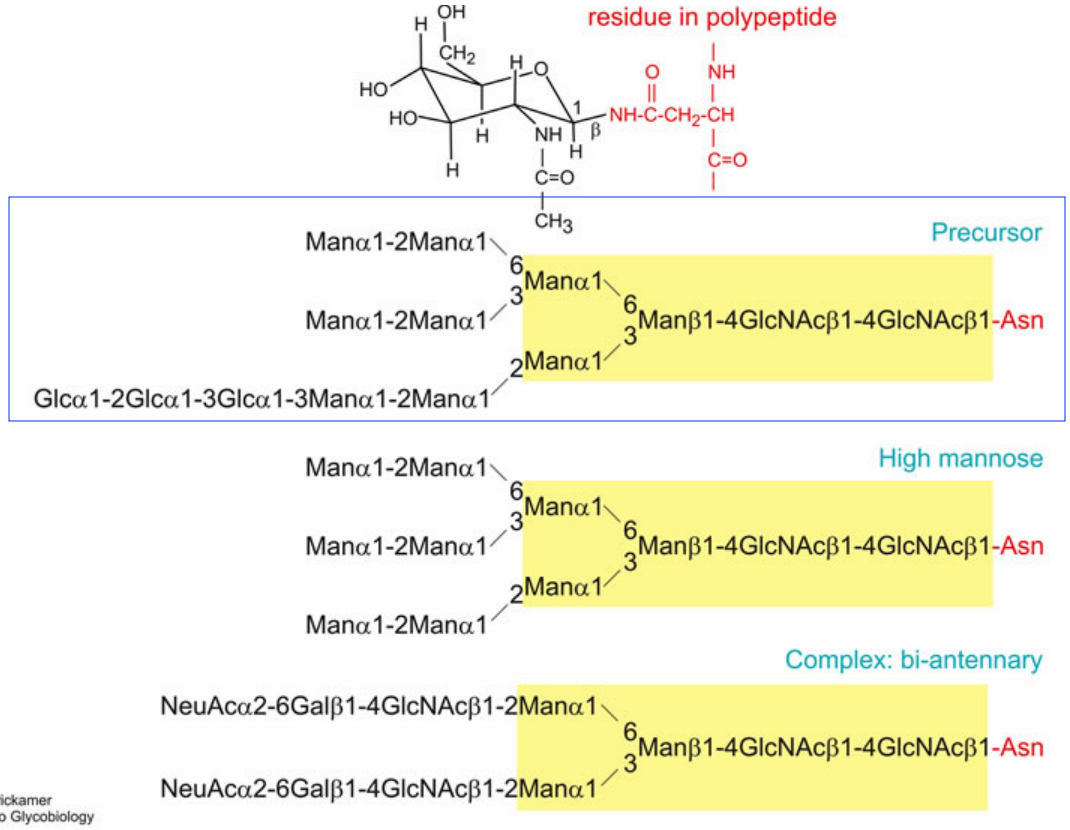
N-Glycosylation involves a consensus sequence:
GlcNAc is β-linked to the amide nitrogen of an Asn sidechain
consensus tripeptide sequence = Asn-X-Ser or Thr (X ≠ Pro / Asp)





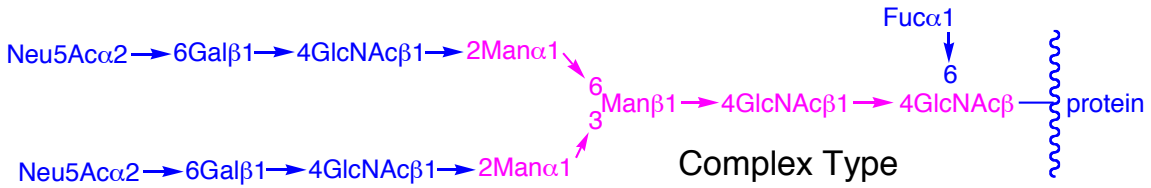
N-linked glycans contain a common pentasaccharide core: $(Man)_3$ $(GlcNAc)_2$

● = NAG, ▼ = Mannose, ▲ = Galactose,
■ = *N*-Acetylneuraminic acid, ◆ = Fucose

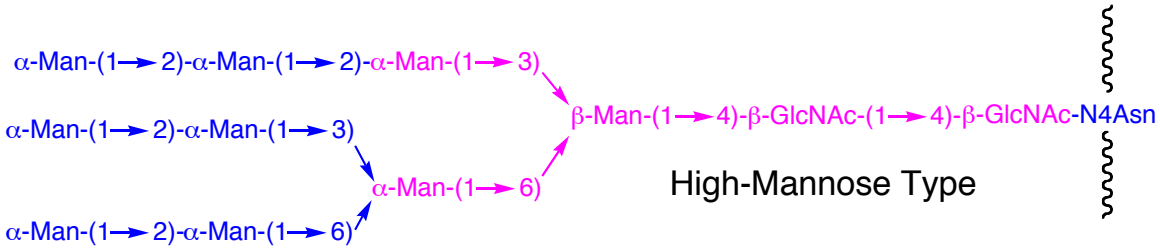


The $GlcNAc_2Man_3$ "core" pentasaccharide is common to all *N*-linked glycans. The two Man branch points in this core pentasaccharide give rise to the 1,3 and 1,6 arms of the oligosaccharide. The $GlcNAc_2Man_9Glc_3$ oligosaccharide is the biological precursor in the construction of all *N*-linked glycans in vivo.

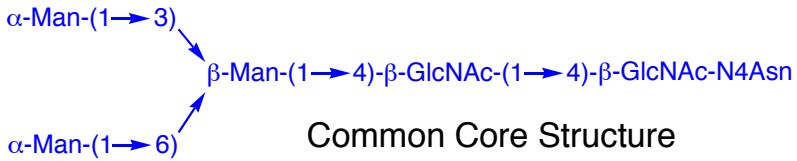
Major classes of *N*-glycans of human glycoproteins



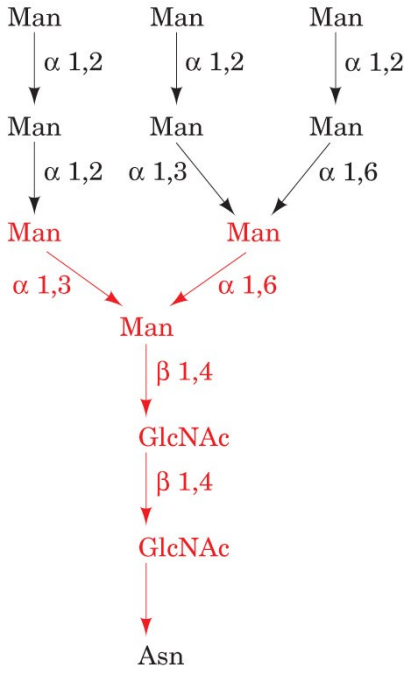
biantennary



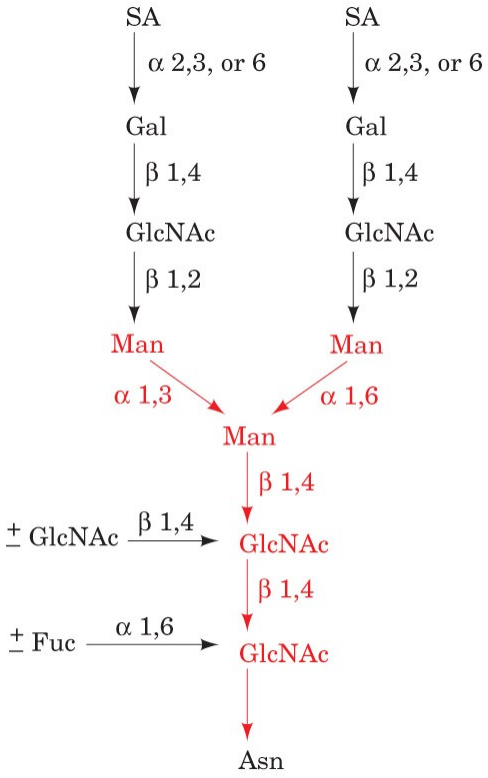
triantennary



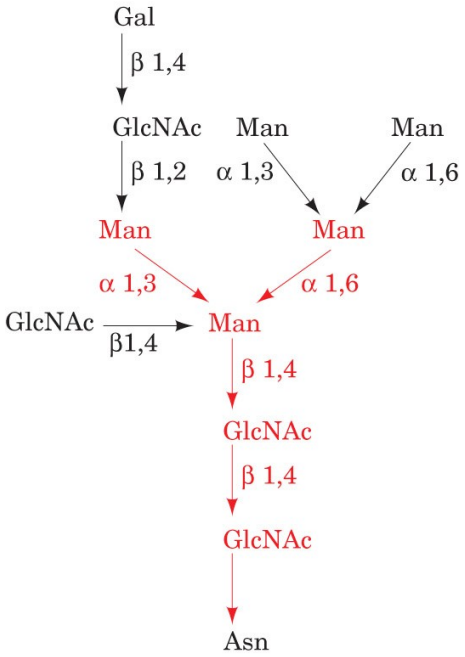
Three main classes of *N*-glycans



High mannose

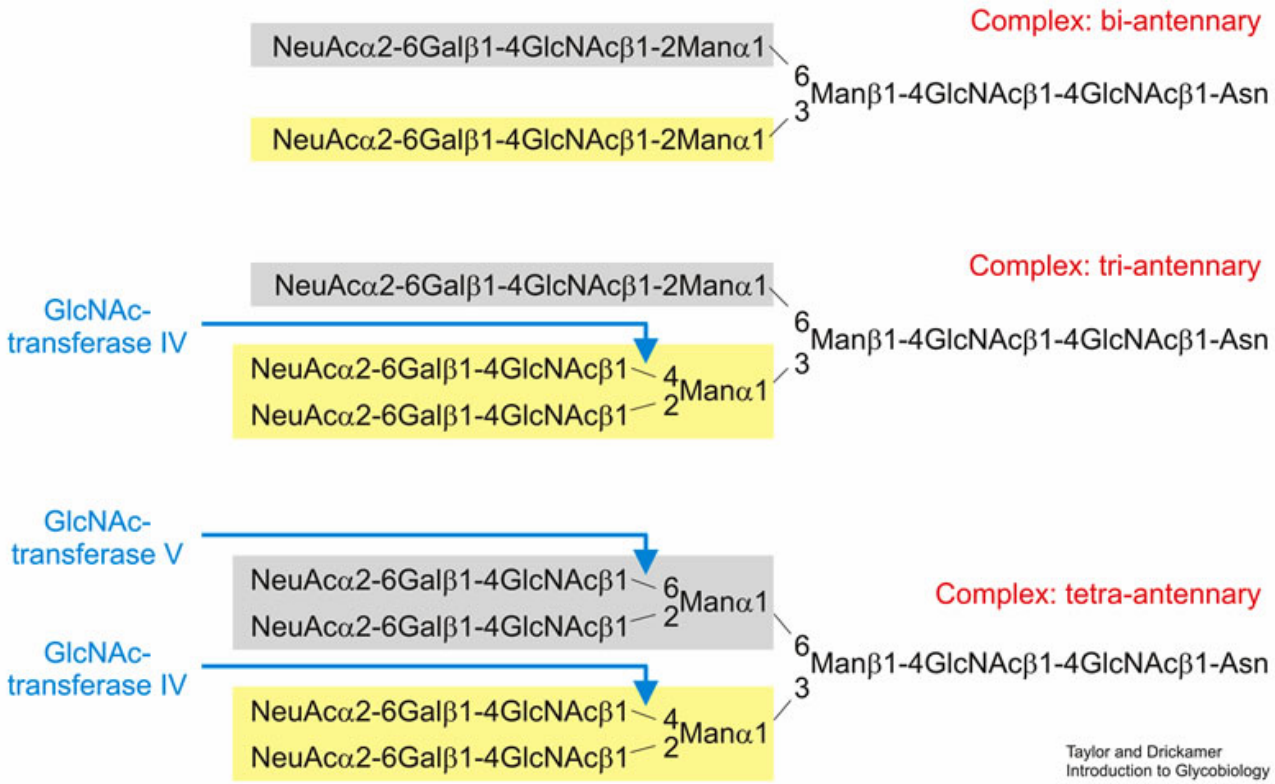


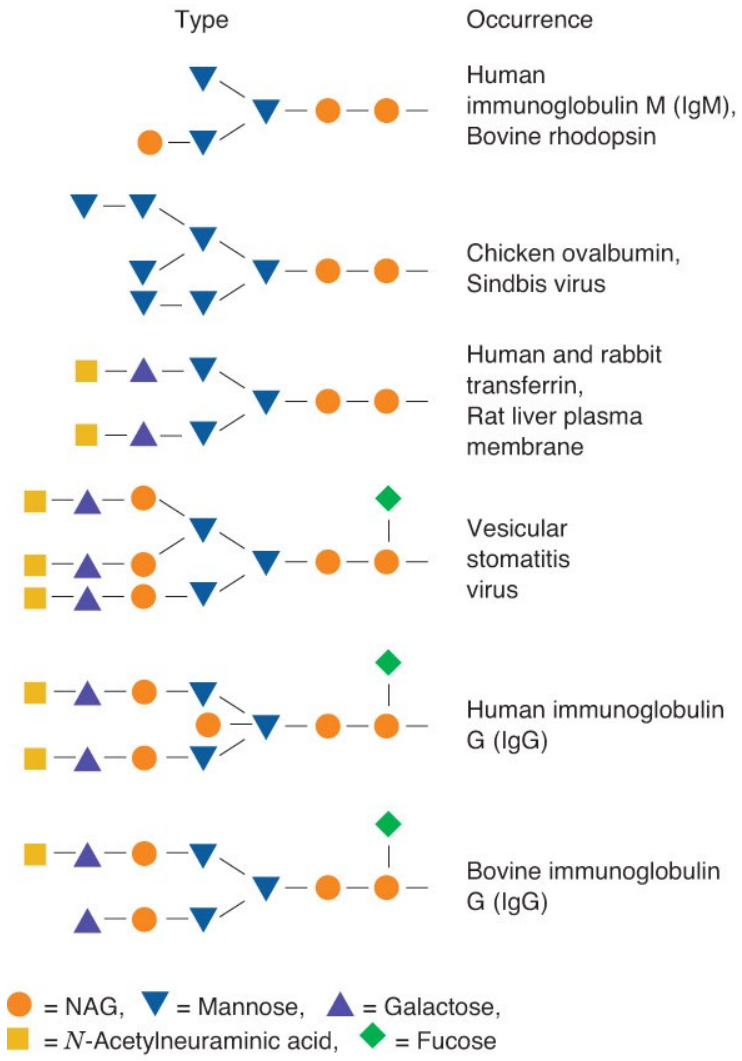
Complex



Hybrid

Figure 3.7 Some of the common complex N-linked glycans





Some examples of *N*-linked glycans on glycoproteins

N-Linked glycans tend to be very heterogeneous structurally.

Figure 3.8 Variations on N-linked glycan structures

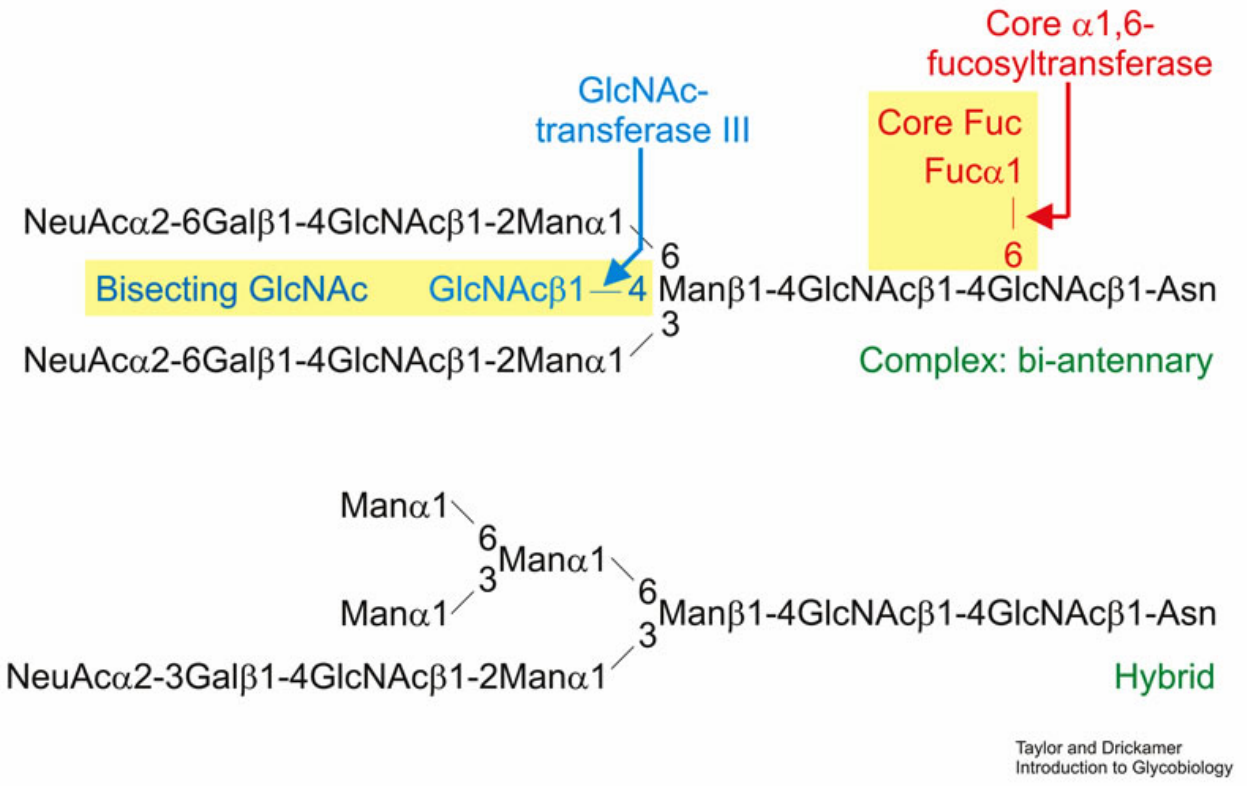


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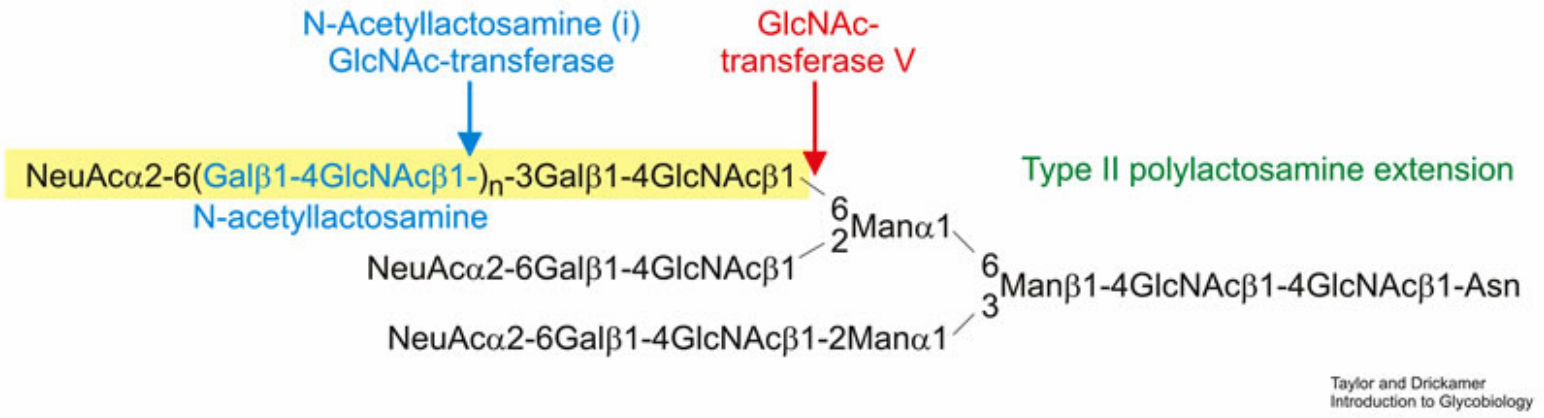
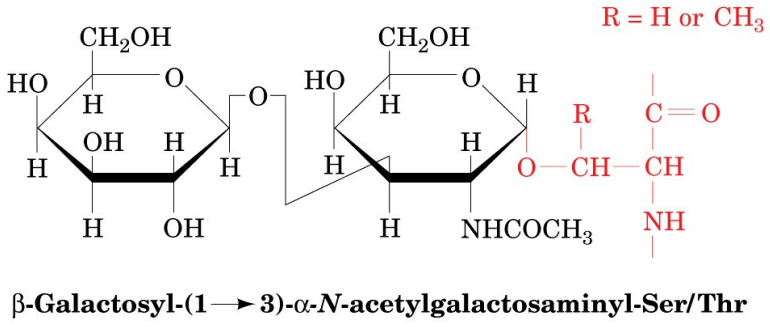
Figure 3.9 One possible form of an N-linked glycan with a polylactosamine extension



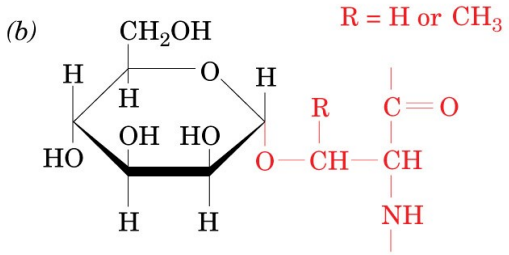
O-Linked Glycoproteins and *O*-Glycans

O-Glycosylation

β-D-Galactopyranosyl-(1,3)-*N*-acetyl-D-galactosamine α-linked to the side-chain OH group of either Ser or Thr.



β-Galactosyl-(1→3)-α-*N*-acetylgalactosaminyl-Ser/Thr



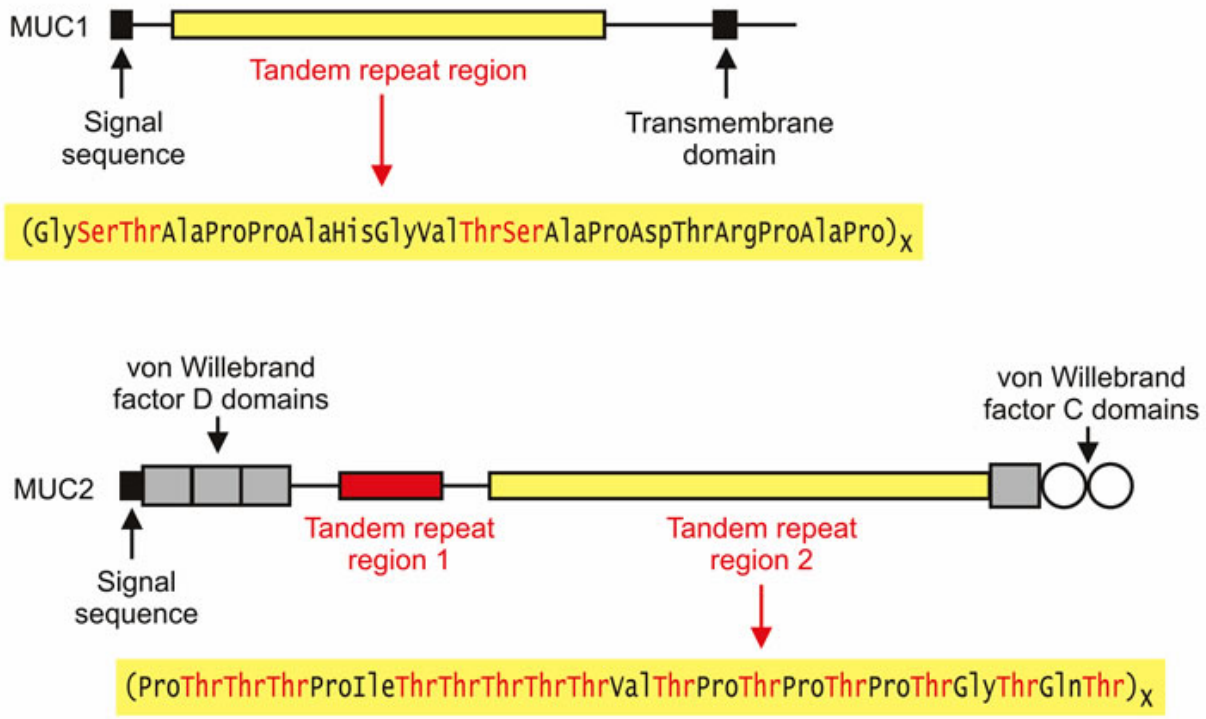
α-Mannosyl-Ser/Thr

O-Linked glycosylation is often structural (*e.g.*,in the proteoglycans and the mucins). Heavy *O*-glycosylation forces the protein to adopt an extended conformation.

Mucins are large, heavily *O*-glycosylated proteins.

The primary purpose of many mucins is to retain water at surfaces that are exposed to the environment but are not sealed by moisture-impermeable layers (e.g., digestive tract, genital tract, respiratory system). They serve as lubricants and protect from invasion by microorganisms.

The polypeptide component: up to 10,000 aa; membrane-bound or secreted; contain tandem repeats of simple aa sequences rich in Ser and Thr; tandem repeats differ in sequence between mucin types; *O*- and *N*-glycosylation can occur outside the region of tandem repeats.



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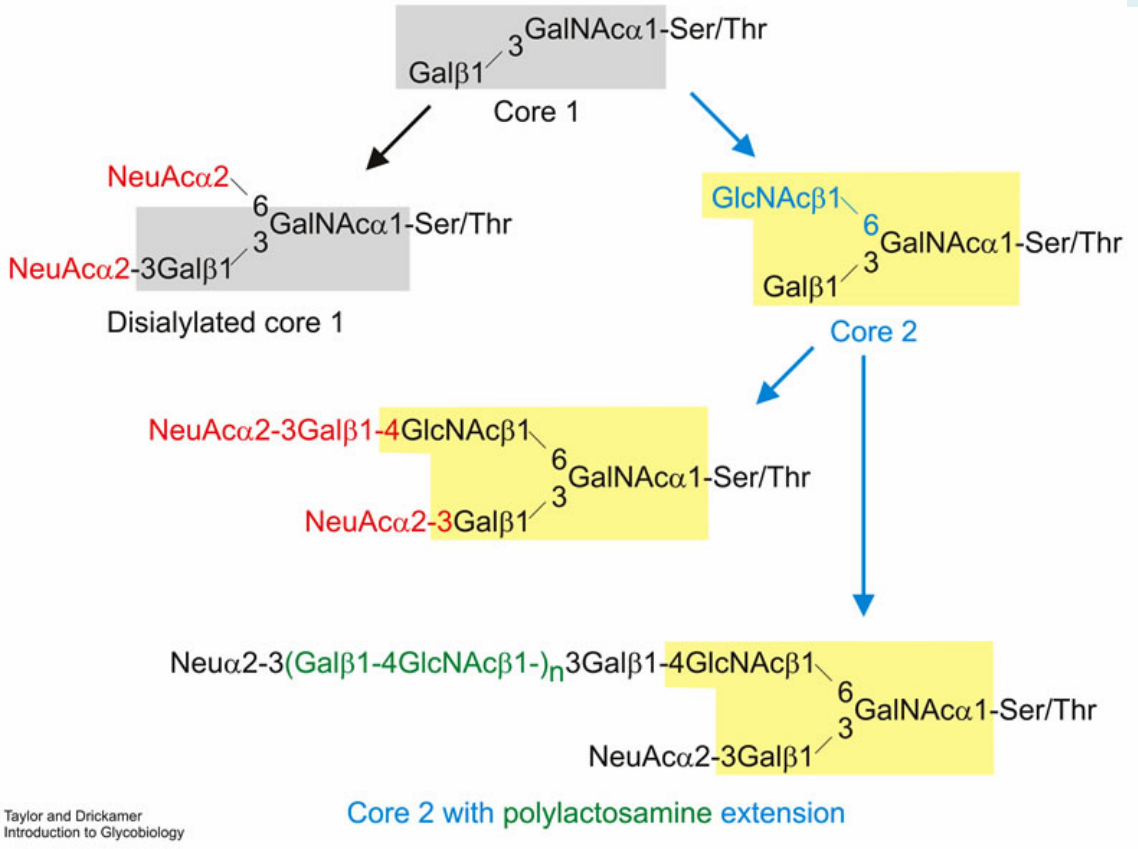
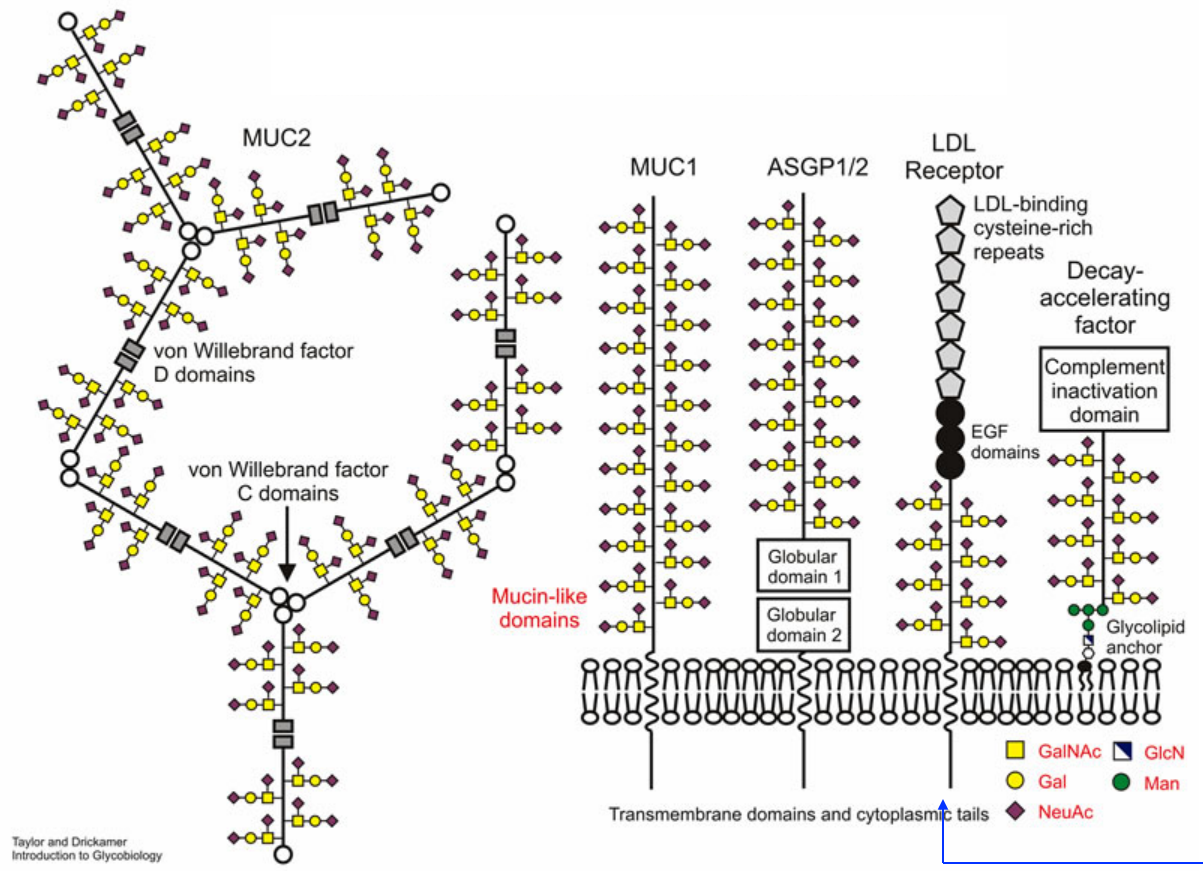
Organization of two mucins MUC1 and MUC2 showing examples of tandem repeat sequences

Mucin O-glycosylation patterns



Core 1 and Core 2 structures attached to Ser and Thr side-chains through α-GalNAc residues. This mucin-type *O*-linked glycosylation is observed in mucins and in other glycoproteins.

Some cell surface proteins have mucin-like domains.

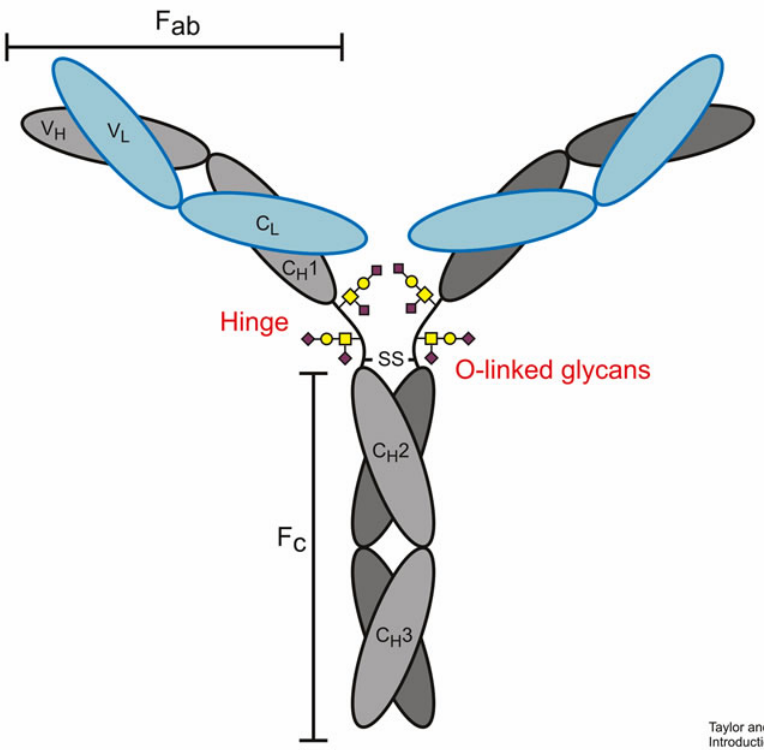


Comparison of secretory mucin MUC2, membrane mucins MUC1 and ASGP, and other membrane proteins containing mucin-like domains

Transmembrane proteins containing both mucin-like and globular domains: mucin-like domains are often located between the membrane anchor and the globular domains and serve to project the latter away from the membrane surface

Many soluble and cell-surface glycoproteins contain small clusters of *O*-linked sugars.

Figure 4.4 Small clusters of O-linked glycans in the hinge region of IgA



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The presence of oligosaccharide in IgA may determine the conformation of the hinge region and may be responsible for its resistance to proteolysis.

Biosynthetic machinery for protein *O*-glycosylation

Comparisons to protein *N*-glycosylation

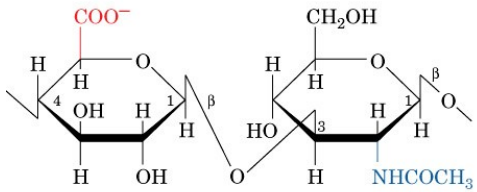
- Protein *O*-glycosylation involves glycosyltransferases analogous to those involved in protein *N*-glycosylation.

- Saccharide residues are added one at a time, starting from the initial GalNAc attached to Ser or Thr (there is no preformed core or *en bloc* transfer). There are numerous GalNAc transferases that attach the initial GalNAc to protein, each apparently displaying a unique specificity.

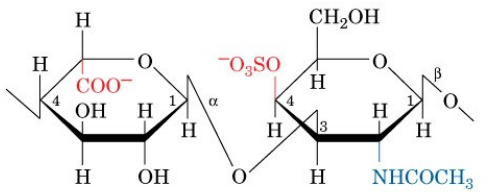
- There are no simple target (consensus) sequences for *O*-glycosylation.

- *O*-Glycosylation occurs post-translationally in the Golgi.

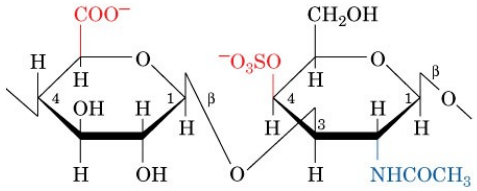
Proteoglycans



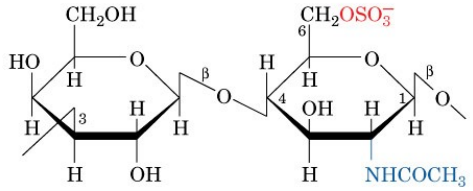
Hyaluronate



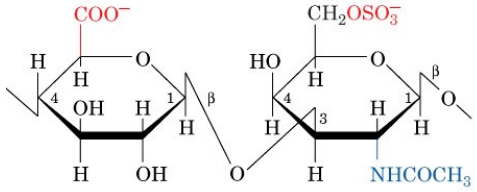
Dermatan sulfate



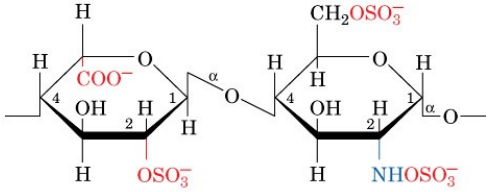
Chondroitin-4-sulfate



Keratan sulfate



Chondroitin-6-sulfate

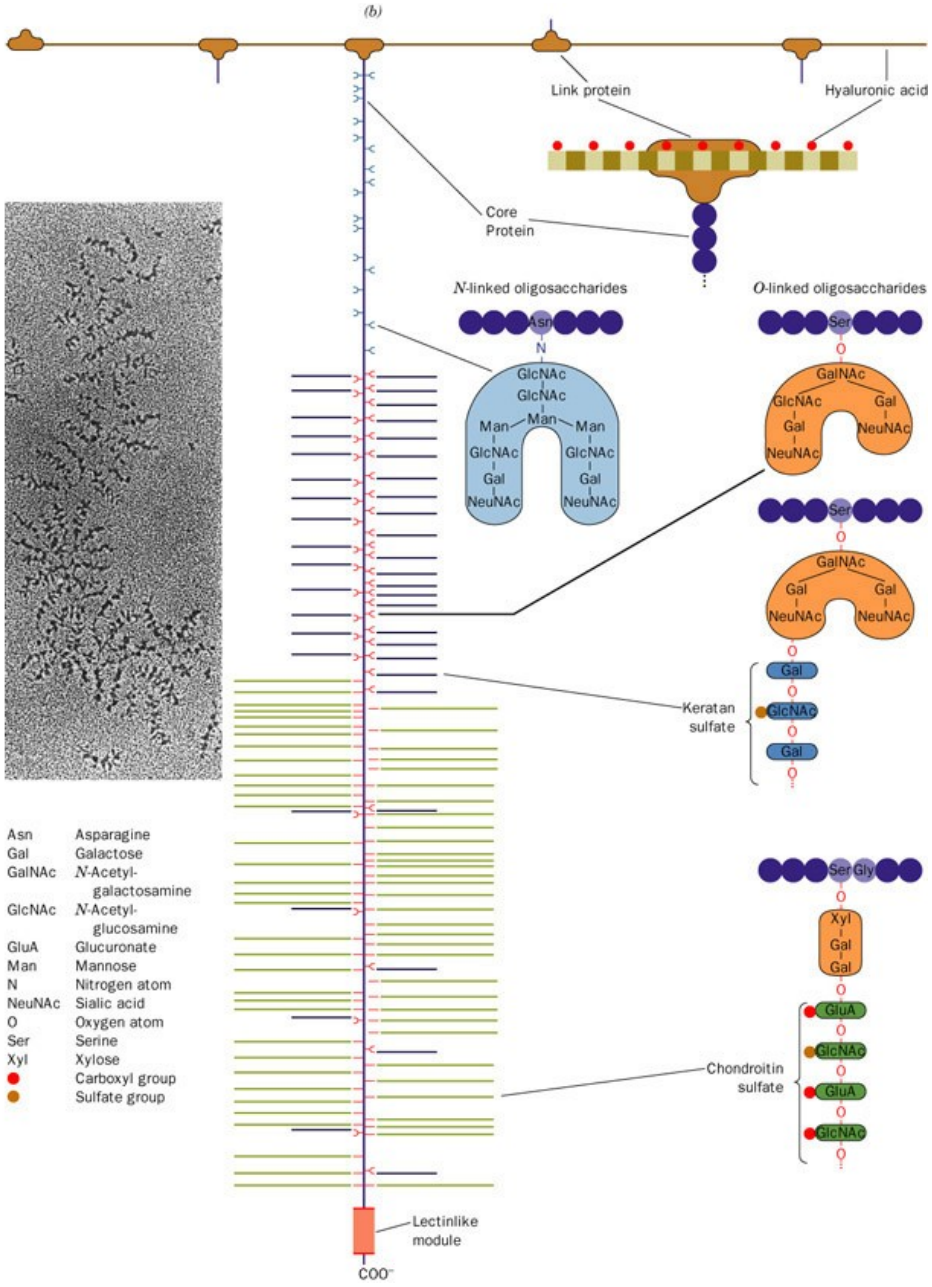


Heparin

The second major class of heavily *O*-glycosylated proteins are *proteoglycans* that give strength to the extracellular matrix.

In comparison to the *O*-glycans of mucins, the *O*-glycans of proteoglycans may have up to 100 residues; these are largely linear chains of alternating residues (termed glycosaminoglycans)

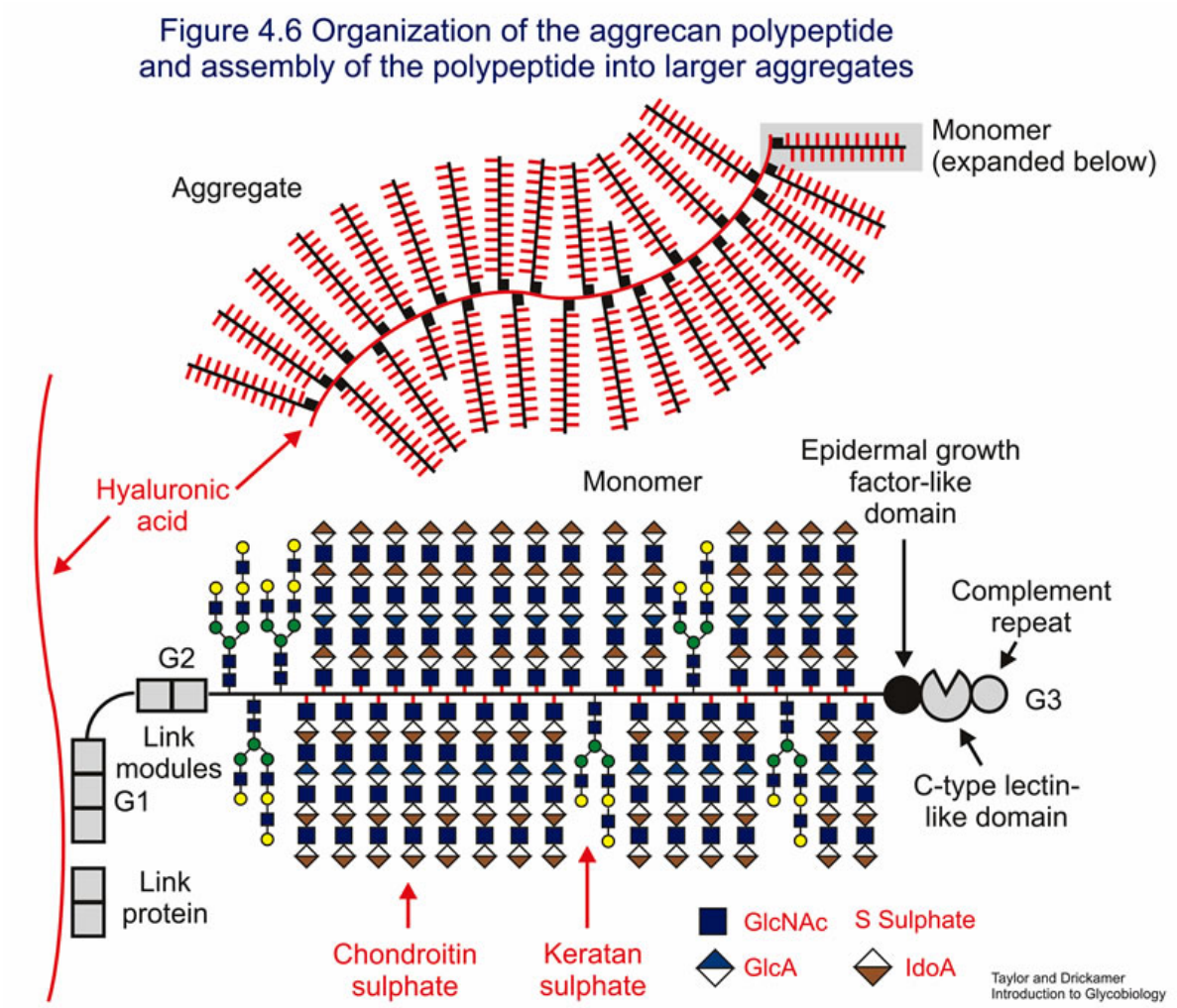
Disaccharide repeating units of the common glycosaminoglycans found in proteoglycans of connective tissue, cartilage, cornea, etc.



Proteoglycan structure

Electron micrograph showing a central strand of hyaluronic acid, and a bottlebrush model

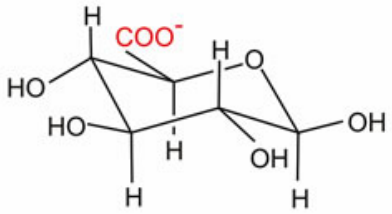
of the proteoglycan, aggrecan.



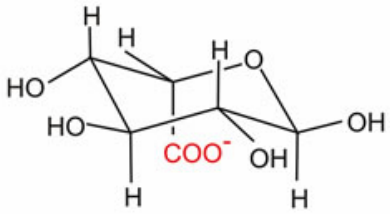
Proteoglycan structure

Figure 4.5 Glycosaminoglycan structures and typical sites of expression

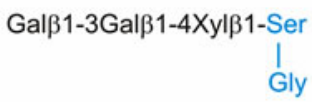
Glycosaminoglycan	A unit	B unit	Protein Core	Linkage	Tissues
Hyaluronic acid	GlcA	GlcNAc	No	None	Connective tissues Skin Cartilage Synovial fluid
Chondroitin sulphate	GlcA	GalNAc	Yes	O-Xylose	Cartilage Cornea Bone Skin Arteries
Dermatan sulphate	GlcA/IdoA	GalNAc	Yes	O-Xylose	Skin Blood vessels Heart valves
Heparan sulphate	GlcA/IdoA	GlcNAc	Yes	O-Xylose	Lung Arteries Cell surfaces
Keratan sulphate	Gal	GlcNAc	Yes	N-GlcNAc	Cartilage Cornea



D-Glucuronic acid
(GlcA)



L-Iduronic acid
(IdoA)



O-Xylose linkage region

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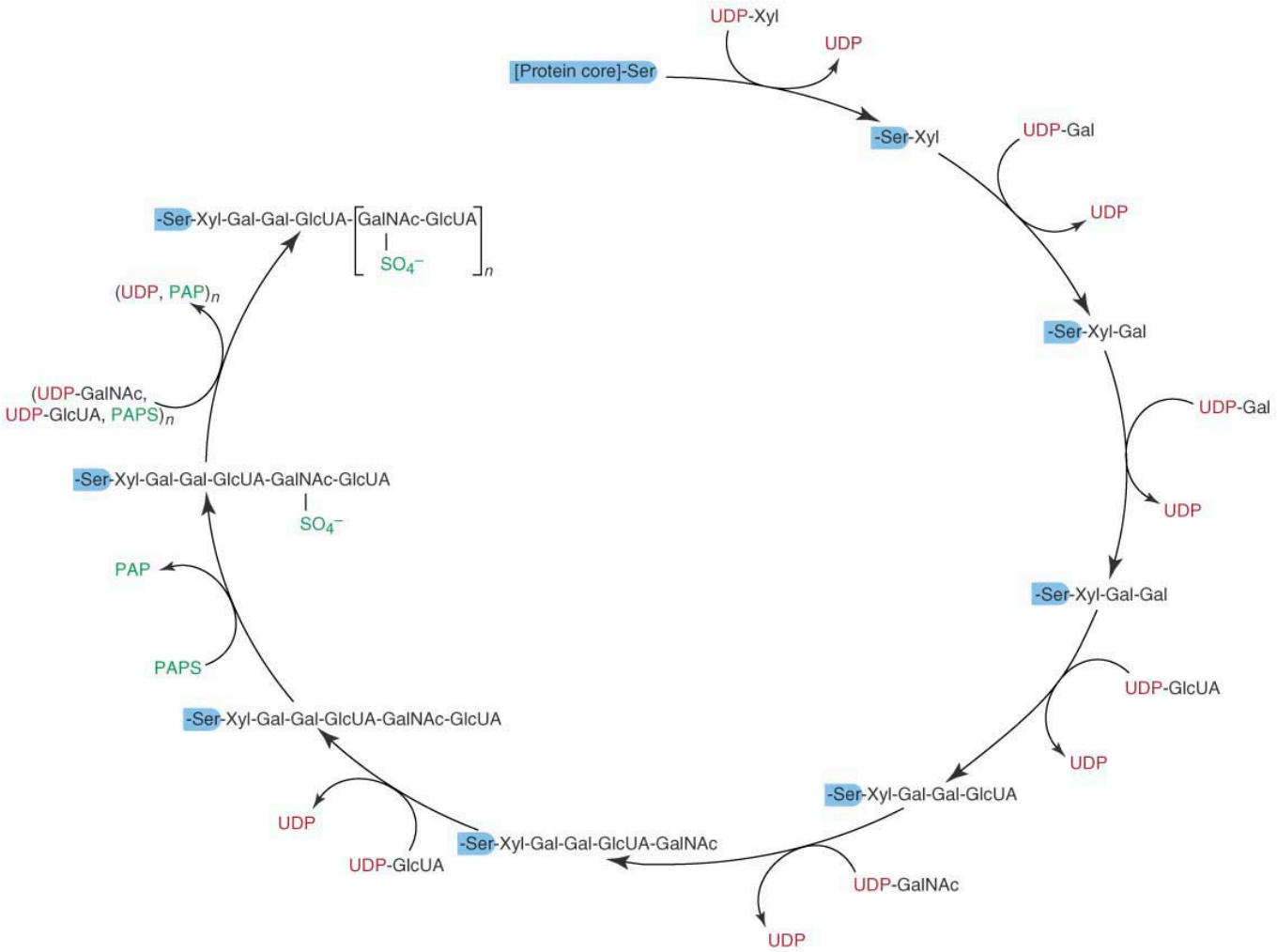
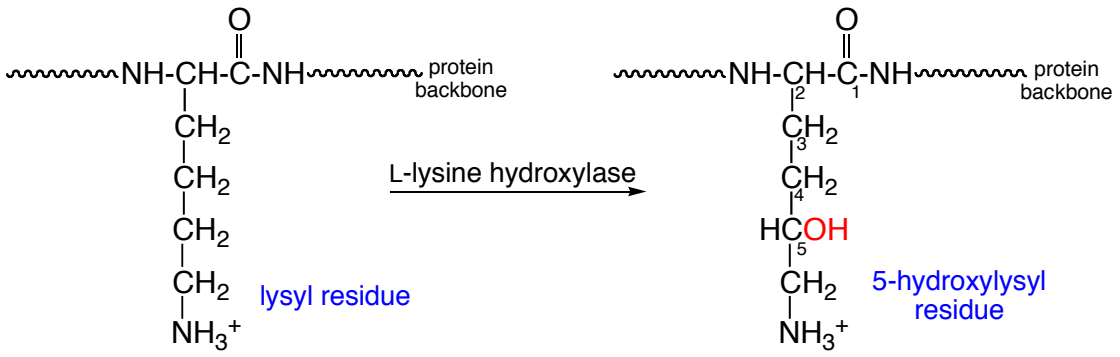
Introduction to Glycobiology

Biosynthetic pathway for the synthesis of chondroitin sulfate proteoglycan

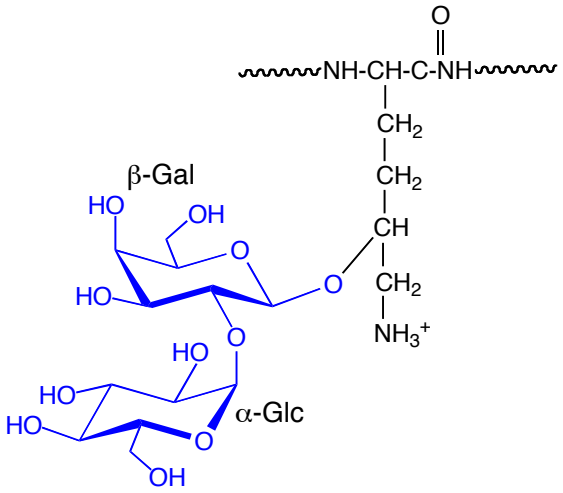


Biosynthetic route for the construction of a protein-bound chrondroitin sulfate polysaccharide chain, showing sequential multiple additions of saccharide units

Enzyme-catalyzed hydroxylation of collagen lysine residues in vivo (a post-translational modification)

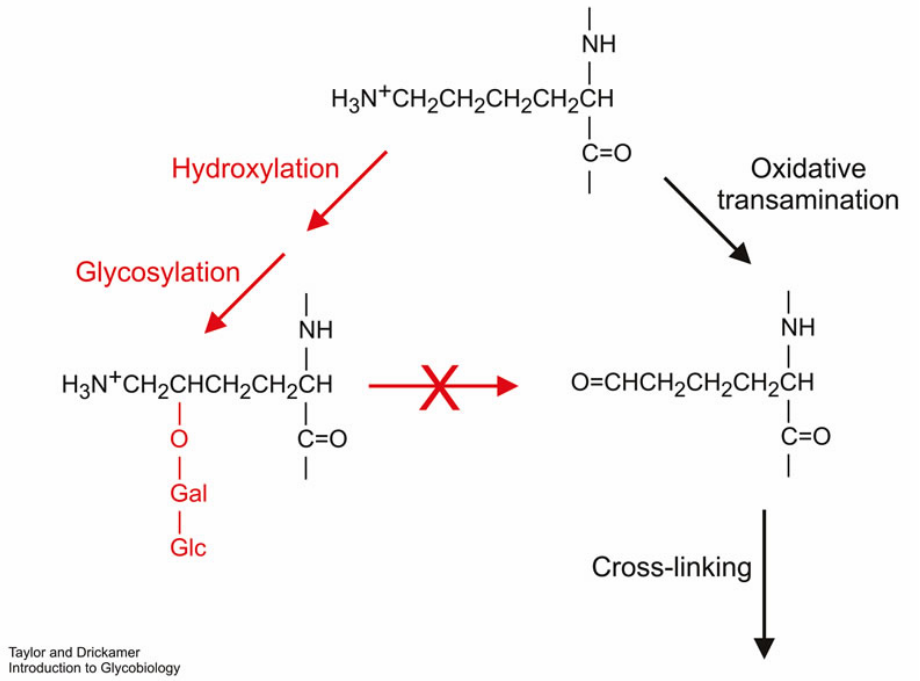


Hydroxylysine (Hyl) residues of collagen are involved in (a) crosslinking of collagen fibrils and (b) glycosylation of collagen.



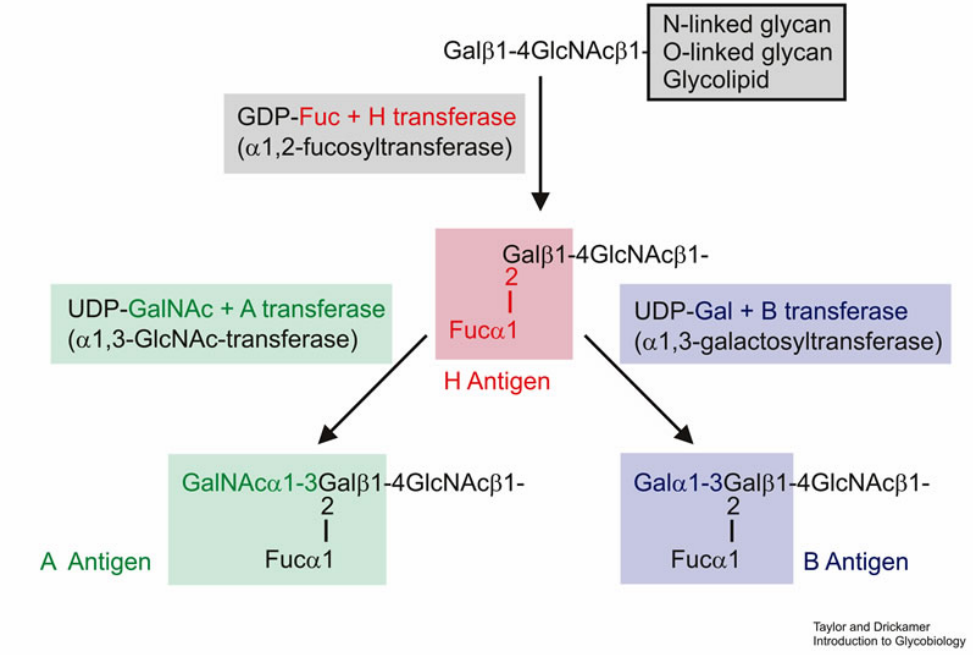
Collagen glycosylation at Hyl residue by the disaccharide, α-Glc-(1→2)-β-Gal.

Figure 4.8 Alternative modifications of lysine residues in collagen



Taylor and Drickamer
Introduction to Glycobiology

Glycosylation of hydroxylysine residues in collagen regulates crosslinking.



The ABO blood-group substances found on the outer surface of erythrocyte plasma membranes.

A-individuals: develop antibodies against the B structure.

B-individuals: develop antibodies against the A structure.

O-individuals: develop antibodies against both A and B structures (universal RBC donor; have H-antigen)

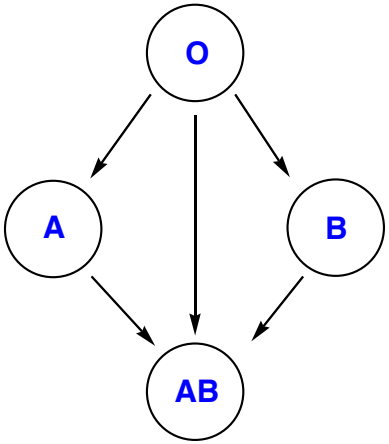
AB-individuals: develop antibodies against neither A nor B structures (universal RBC recipient)

Transfused *cells* must not express glycans to which the recipient has antibodies.

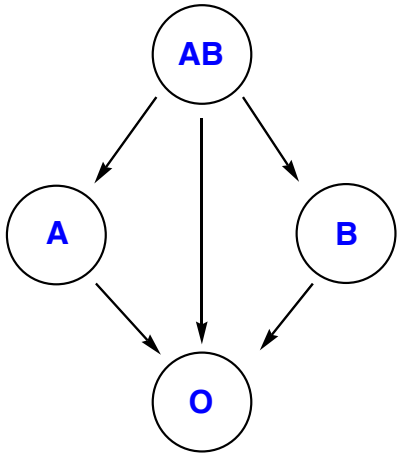
Note: A rare blood type (Bombay): Have h antigen (H-antigen without the fucose)

Summary

- Individuals with type A RBC: have type A antigens; carry anti-B antibodies in their serum *(can accept RBC from A- and O-type donors)*
- Individuals with type B RBC: have type B antigens; carry anti-A antibodies in their serum *(can accept RBC from B- and O-type donors)*
- Individuals with type AB RBC: have type A and type B antigens; carry neither anti-A nor anti-B antibodies in their serum (universal recipient) *(can accept RBC from AB, A, B and O donors)*
- Individuals with type O RBC: have neither type A nor type B antigens; carry both anti-A and anti-B antibodies in their serum (have type H antigen) (universal donor) *(can accept RBC only from O donors)*

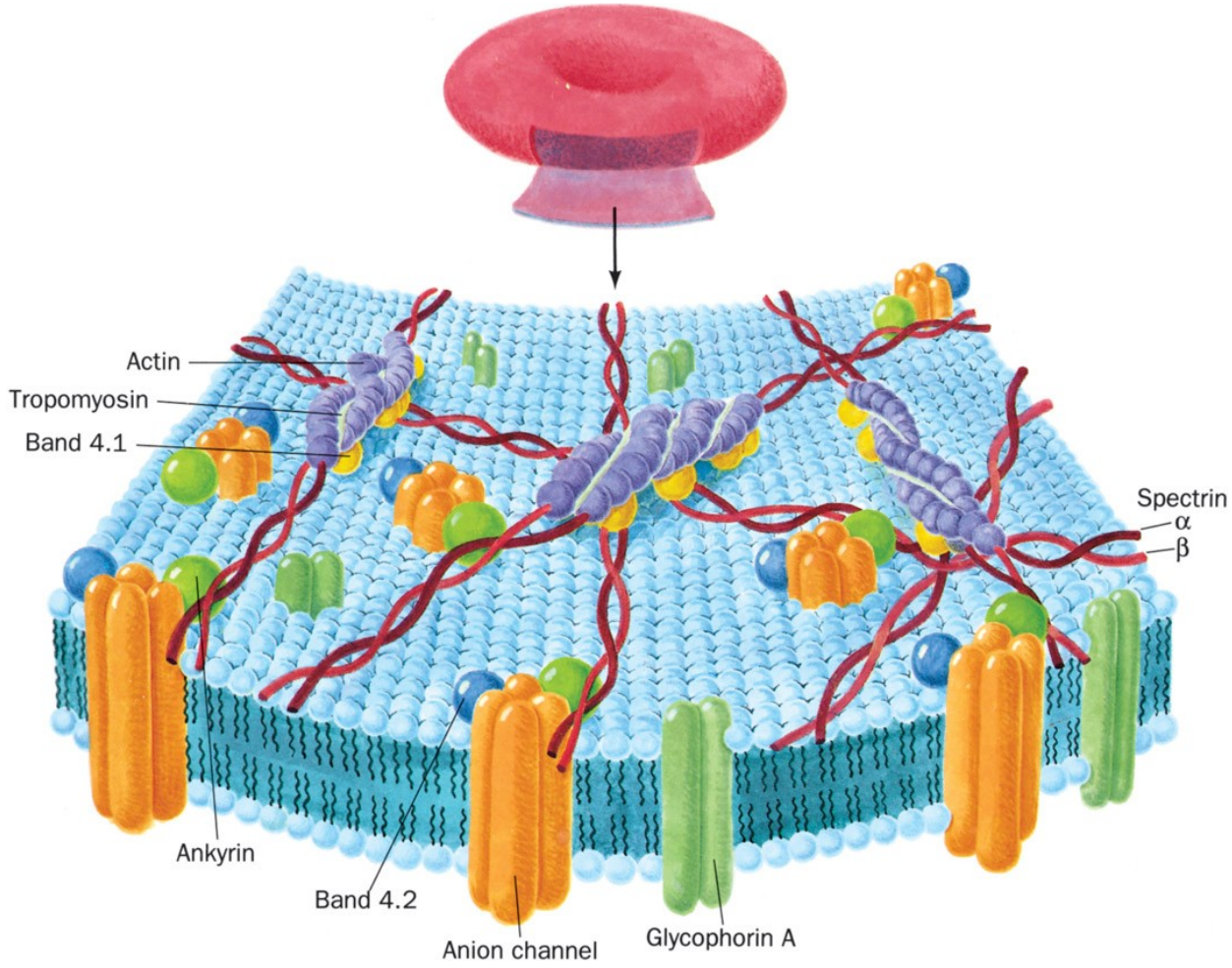


RBC compatibility chart (in addition to donation to the same blood group)

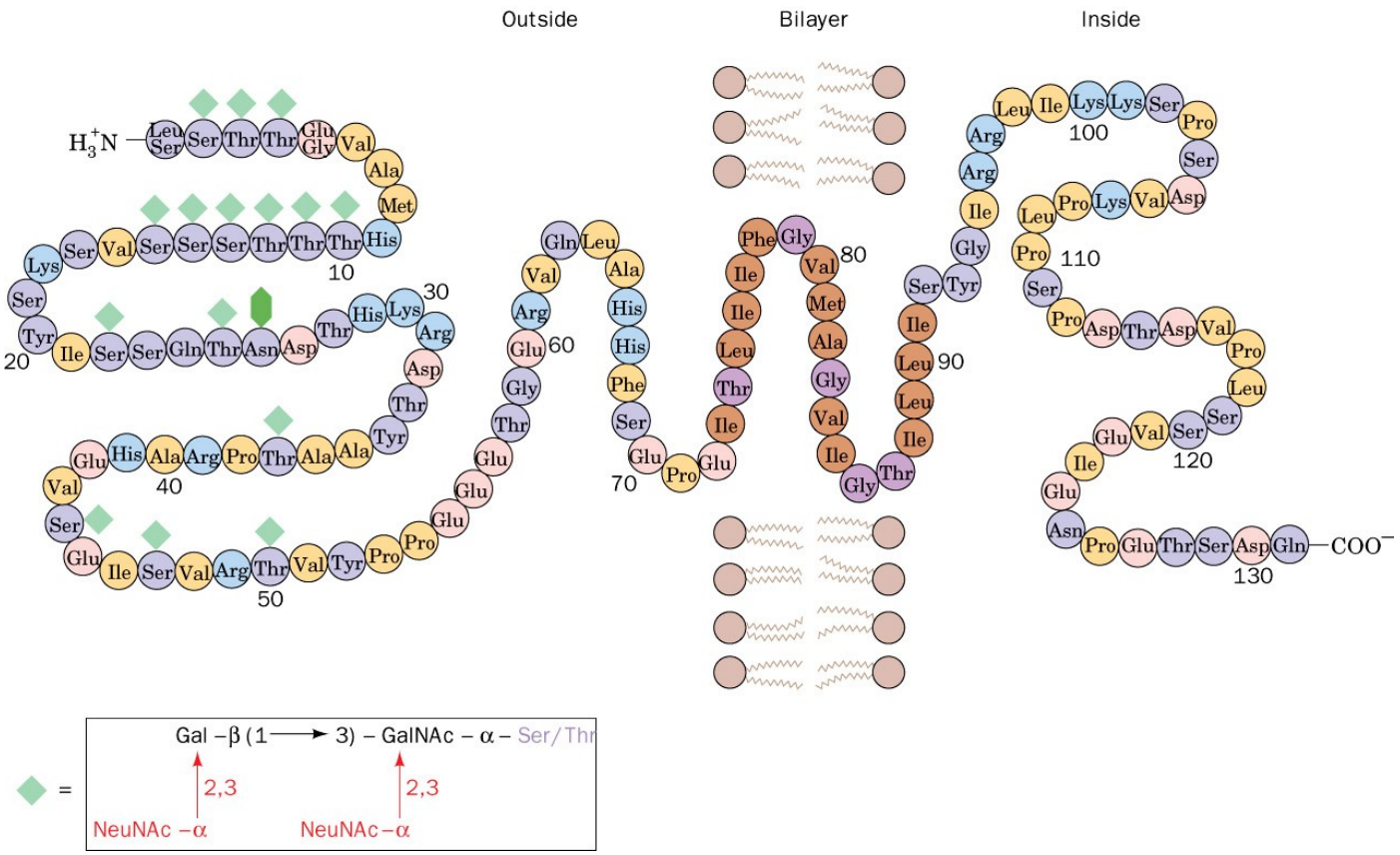


Plasma compatibility chart (in addition to donation to the same blood group)

[treatment ignores RhD +/- antigens]



Model of the human erythrocyte cytoskeleton



Amino acid sequence, membrane location, and predominant *O*-linked oligosaccharide of human erythrocyte glycoprotein, glycophorin A

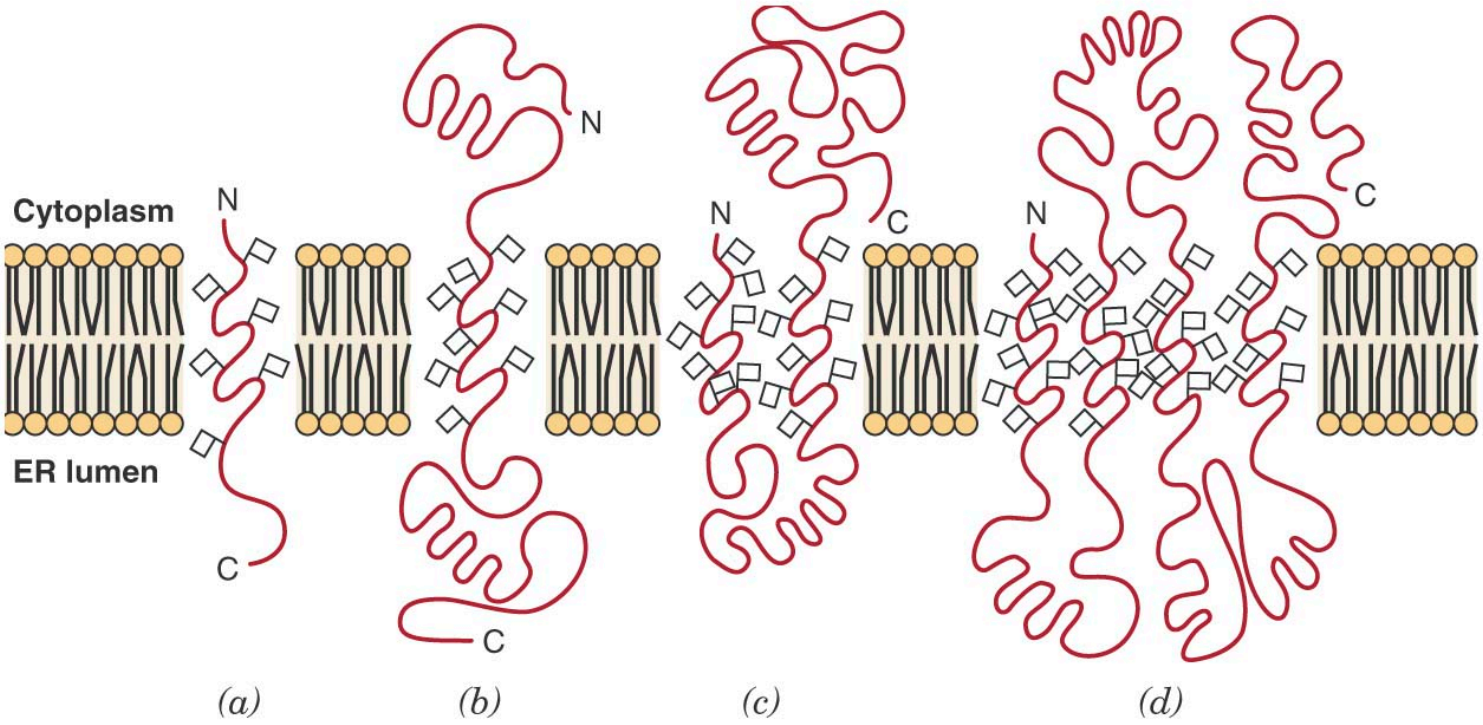


Figure 6.18. Topology of proteins at membranes of endoplasmic reticulum.

Biosynthesis of *N*-linked glycoproteins: Three stages

1. Formation of a lipid-linked precursor (parent) oligosaccharide ($Glc_3Man_9GlcNAc_2$)
2. *En bloc* transfer of the parent oligosaccharide to the polypeptide
3. Processing of the parent oligosaccharide; involves removal of some of the original saccharide residues (trimming by exoglycosidases) followed by addition of new saccharides (by glycosyltransferases) to the non-reducing termini of the glycan
4. The overall process occurs intracellularly in spacially differentiated steps.

The spacially-differentiated steps in *N*-linked glycoprotein biosynthesis

- **Rough ER**: lipid-linked precursor biosynthesis; *en bloc* transfer to protein; initial trimming reactions
- **Golgi apparatus** (*cis*, medial, *trans*): subsequent processing steps

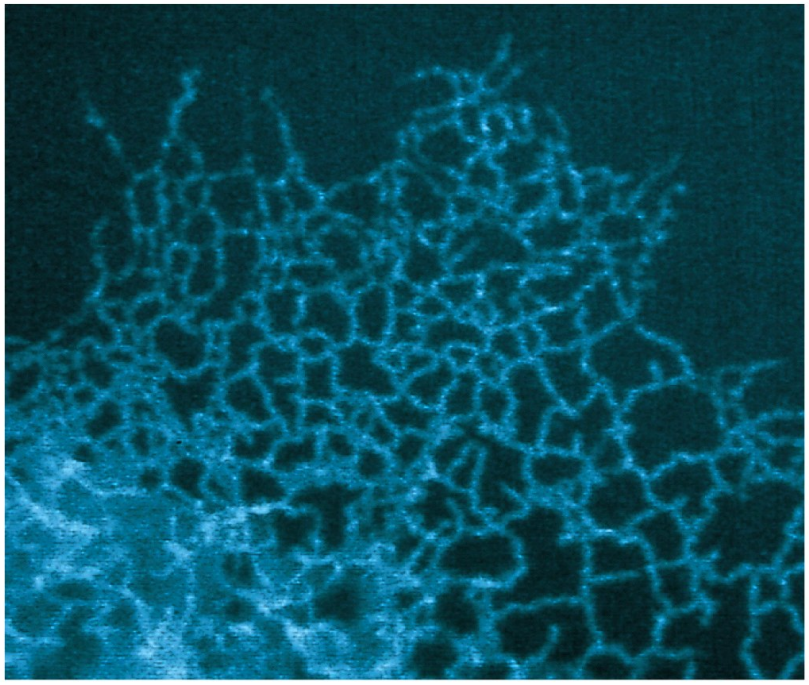


Figure 12-34a Molecular Biology of the Cell 5/e (© Garland Science 2008)

Part of the ER network in a mammalian cell, stained with an antibody that binds to a protein retained in the ER; the ER extends throughout the cytosol.

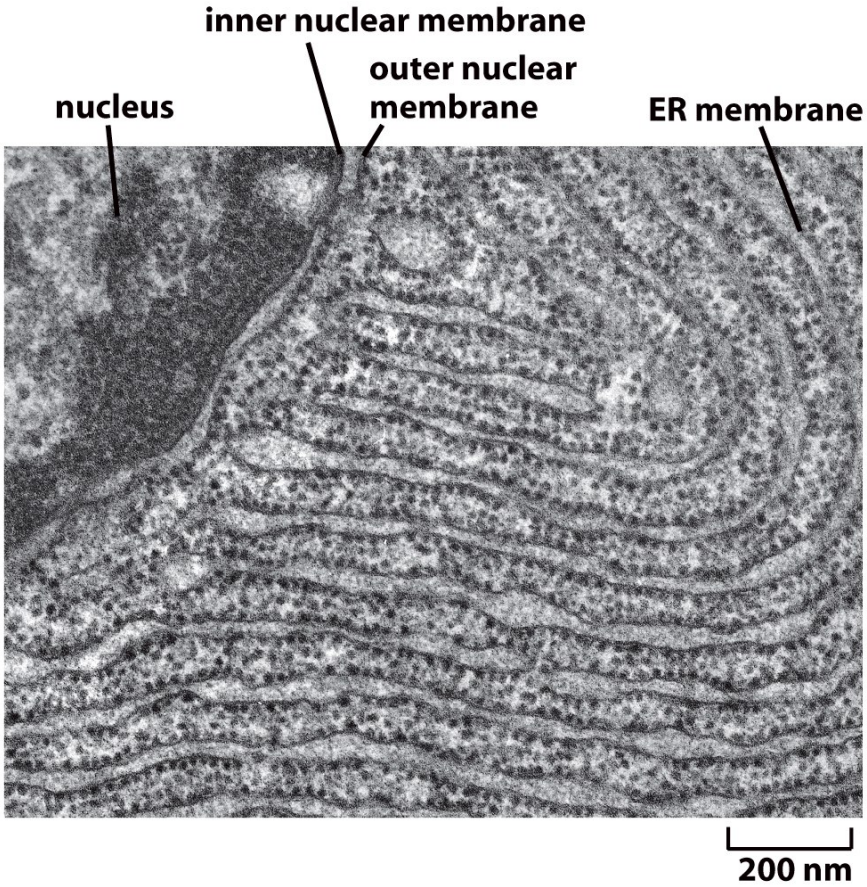


Figure 12-36a Molecular Biology of the Cell 5/e (© Garland Science 2008)

An electron micrograph of rough ER in a pancreatic cell that makes and secretes large amounts of digestive enzymes each day. The outer nuclear membrane is continuous with the ER and is also studded with ribosomes.

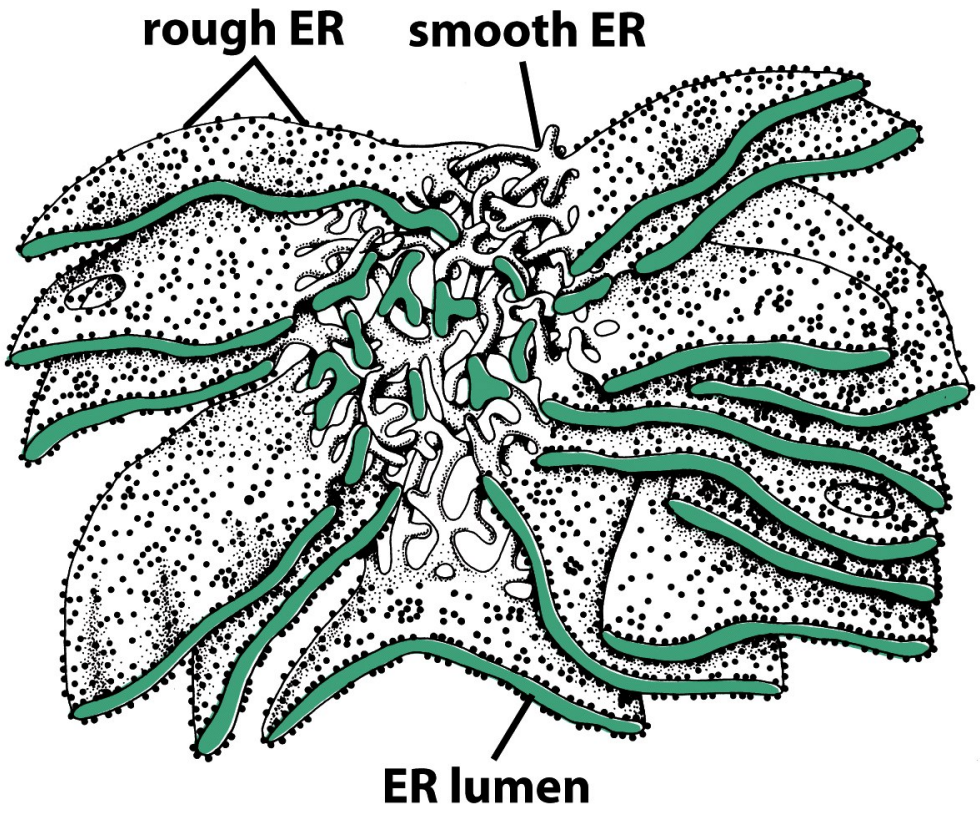


Figure 12-36c Molecular Biology of the Cell 5/e (© Garland Science 2008)

The RER forms oriented stacks of flattened cisternae, each having a lumenal space 20-30 nm wide. The SER is connected to these cisternae and forms a fine network of tubules 30-60 nm in diameter.

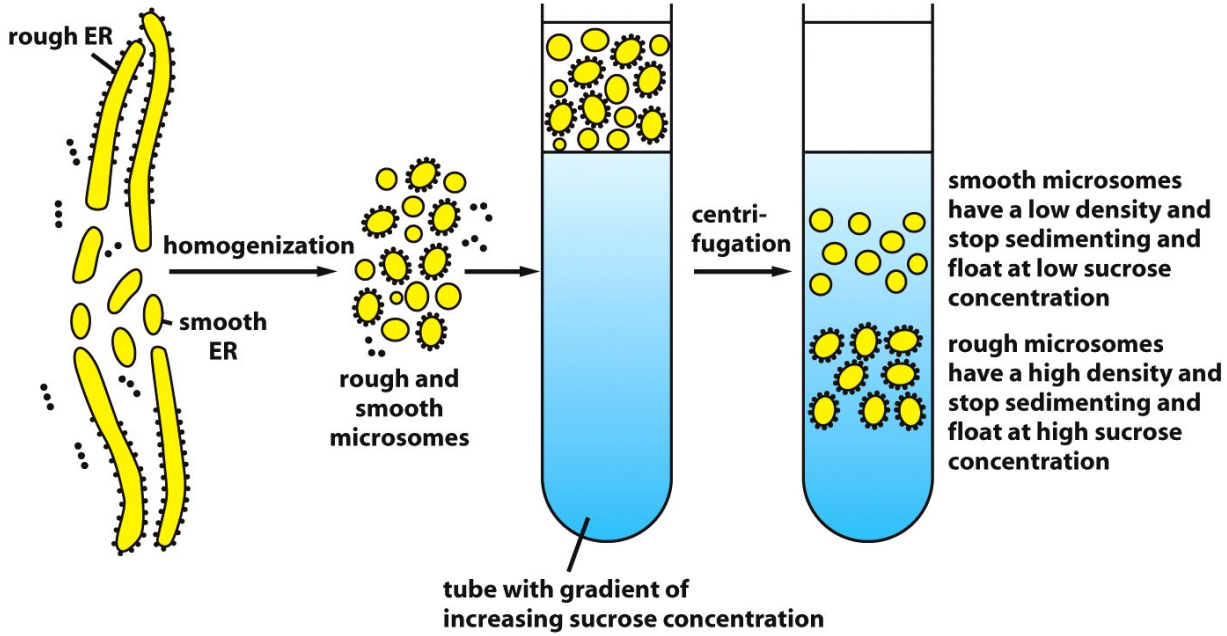


Figure 12-37b Molecular Biology of the Cell 5/e (© Garland Science 2008)

Isolation of purified rough and smooth microsomes from the ER

When sedimented to equilibrium through a sucrose gradient, the two types of microsomes (closed vesicles 100-200 nm in diameter) separate from each other on the basis of their different densities.

Microsomes represent small authentic versions of the ER, still capable of protein translocation, protein glycosylation, Ca^{2+} uptake and release, and lipid synthesis. Ribosomes are always found on the outside surface of microsomes, so the interior of microsomes is biochemically equivalent to the ER lumenal space.

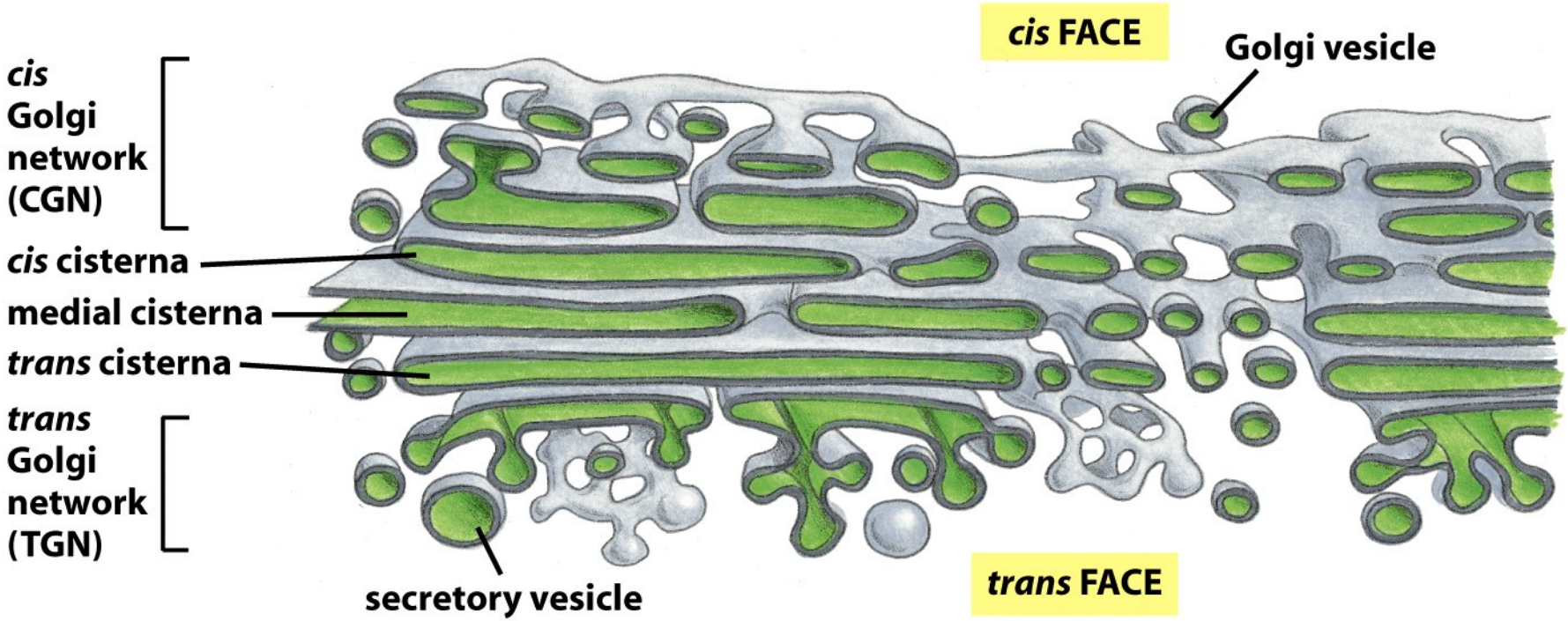
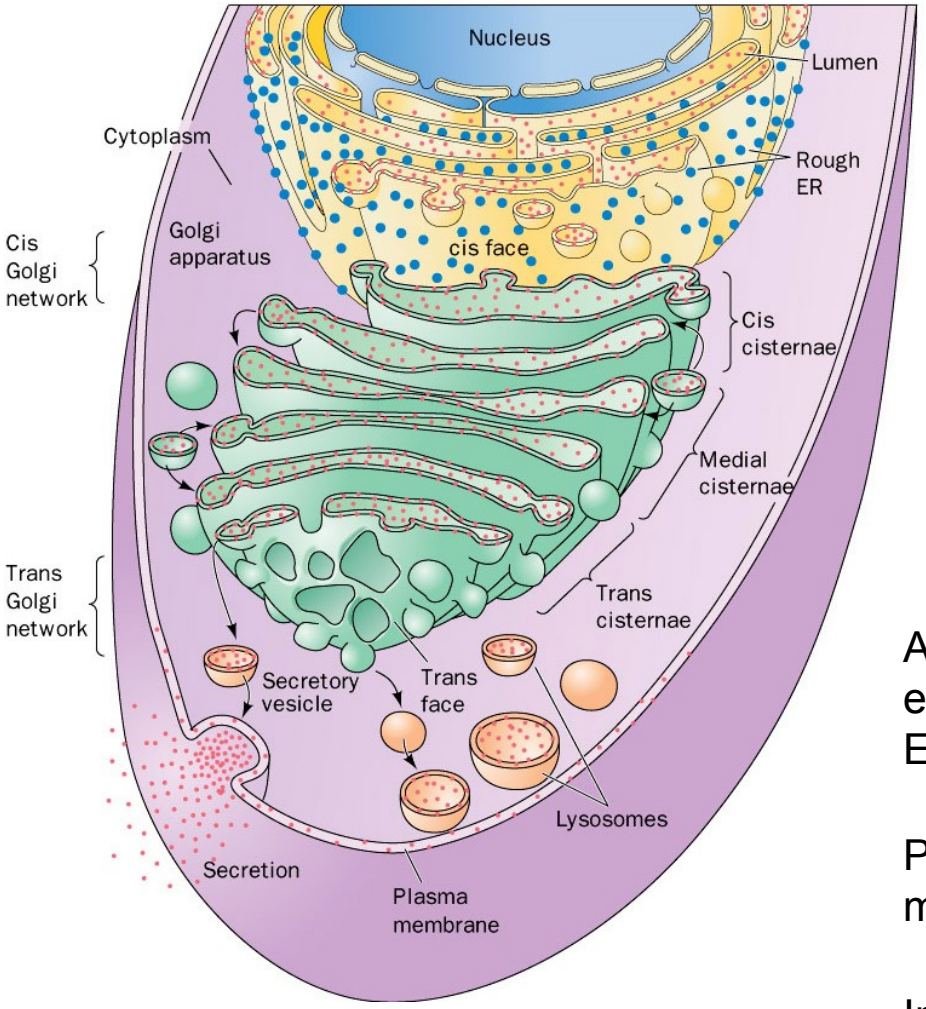


Figure 13-25a Molecular Biology of the Cell 5/e (© Garland Science 2008)

3D reconstruction from EMs of the Golgi apparatus in a secretory animal cell

The *cis* face is closest to the ER.



Posttranslational processing of proteins

Proteins destined for secretion, insertion into plasma membrane, or transport to lysosomes

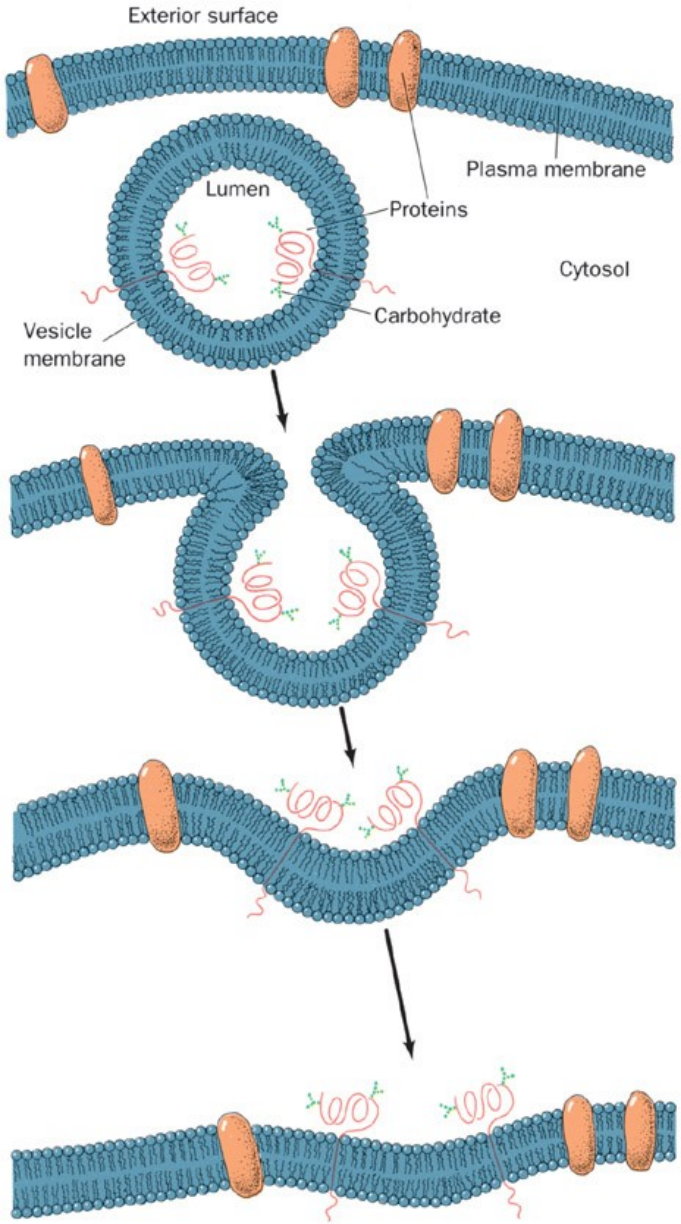
Synthesized by RER-associated ribosomes

During synthesis, proteins are either injected into the lumen or inserted into its membrane

After initial processing in the ER, proteins are encapsulated into vesicles that bud from the ER and fuse with the *cis* Golgi network.

Progressive processing occurs in the *cis*, medial and *trans* cisternae of the Golgi.

In the *trans* Golgi, completed glycoproteins are sorted for delivery to plasma membrane, secretory vesicles or lysosomes; transported by other vesicles.



The fusion of a vesicle with the plasma membrane preserves the orientation of the integral proteins embedded in the vesicle bilayer.

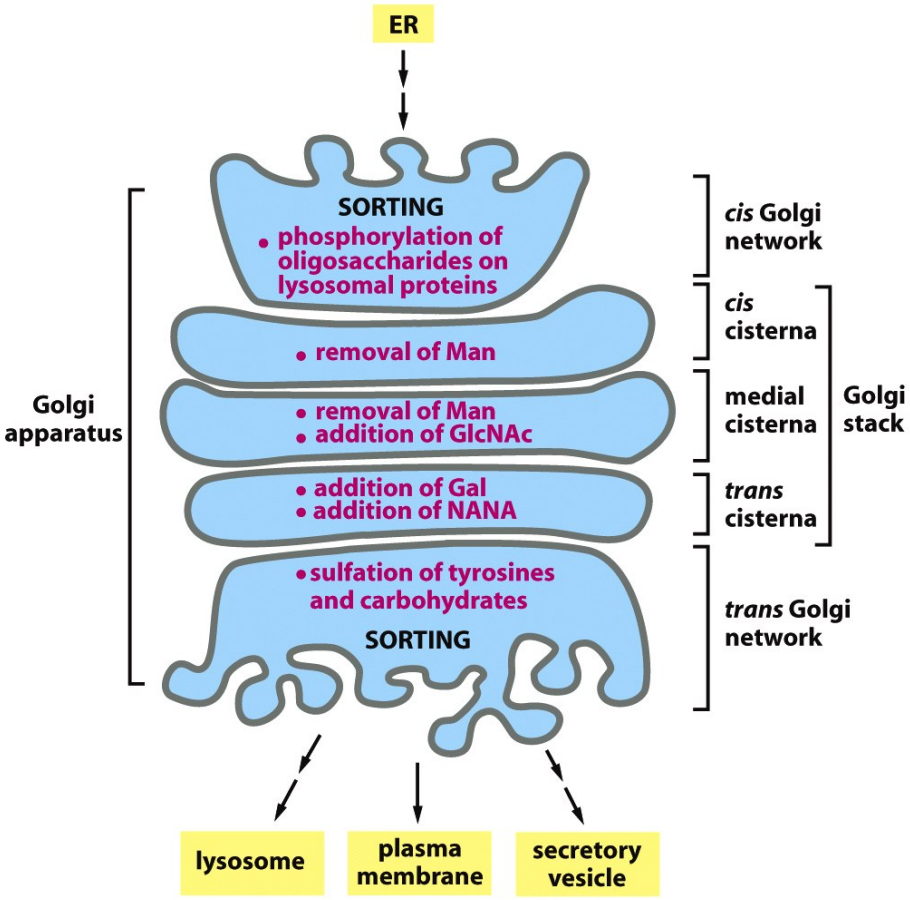


Figure 13-28 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Oligosaccharide processing in Golgi compartments

Processing enzymes are not spacially restricted to a particular cisternae; instead, their distribution is graded across the stack, such that early-acting enzymes are present mostly in the *cis* Golgi cisternae and later-acting enzymes are mostly present in the *trans* Golgi cisternae.

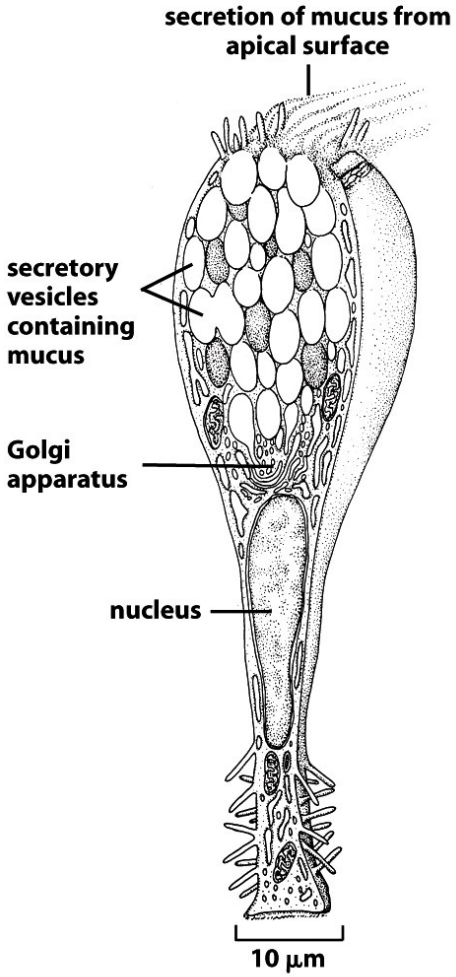
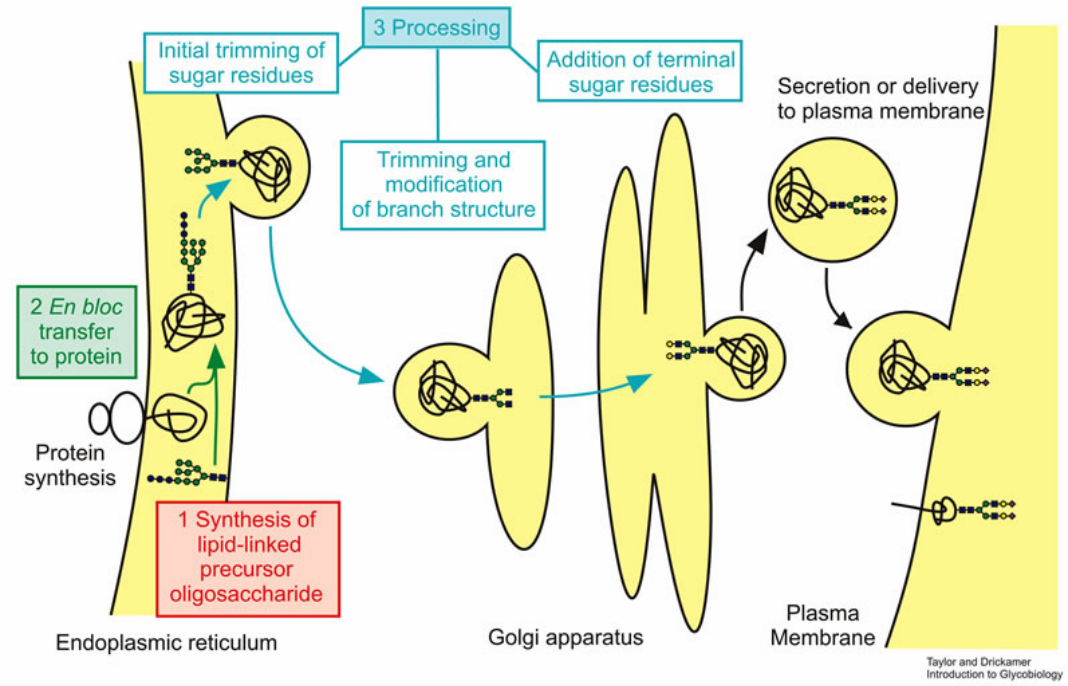


Figure 13-29 Molecular Biology of the Cell 5/e (© Garland Science 2008)

A goblet cell of the small intestine

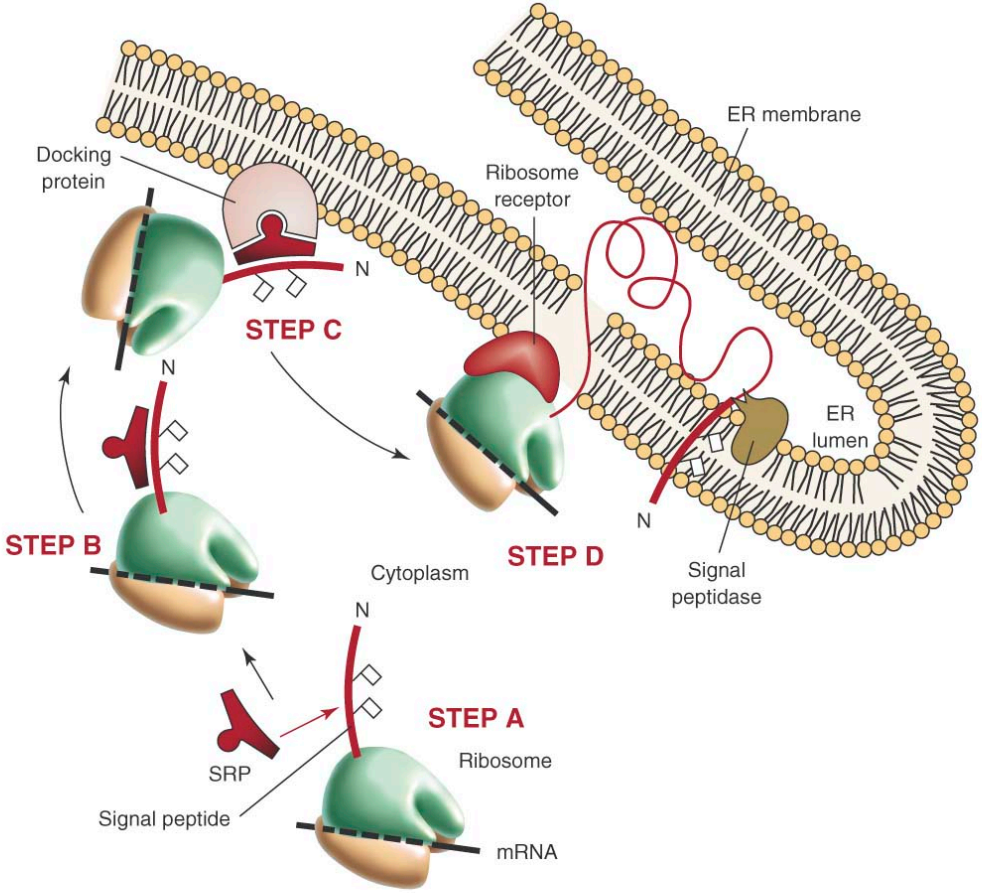
Secretes mucus, which is a mixture of glycoproteins and proteoglycans synthesized in the ER and Golgi. A highly polarized cell: its apical domain faces the lumen of the gut and its basolateral domain faces the basal lamina. The Golgi apparatus is polarized to facilitate the discharge of mucus by exocytosis at the apical domain of the plasma membrane.

Initial attachment of an *N*-glycan to a protein is a co-translational event that occurs in the ER.



An overview of the pathway for glycoprotein biosynthesis and its intracellular location. Early stages involve glycan assembly on a glycolipid and subsequent transfer to nascent protein in the ER. Subsequent processing by glycosidases and glycosyltransferases occurs in the ER and Golgi apparatus.

The secretory pathway: signal peptide recognition



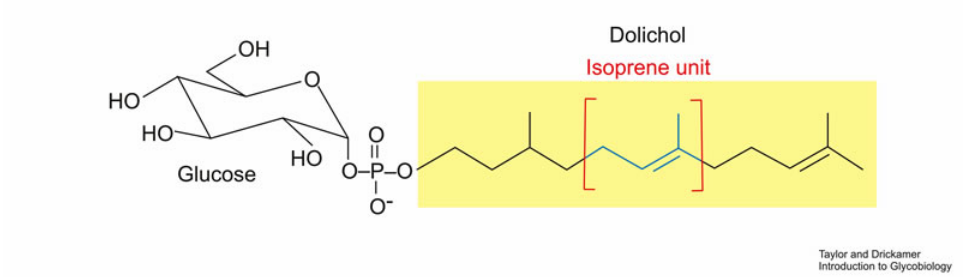
Step A: A hydrophobic signal peptide emerges from a free ribosome in the cytosol.

Step B: Signal recognition particle (SRP) binds the signal peptide and elongation is temporarily halted.

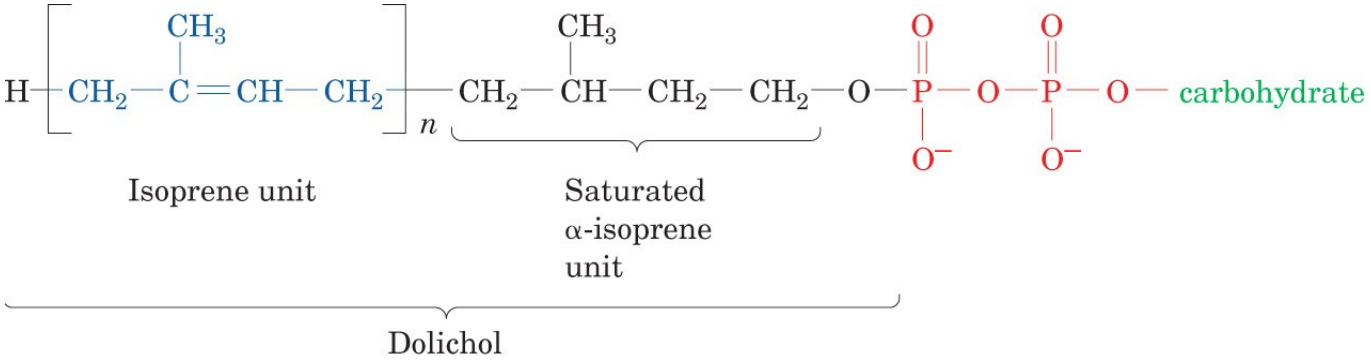
Step C: The ribosome moves to the ER membrane where a docking protein binds the SRP.

Step D: The ribosome is transferred to a translocon, elongation is resumed, and newly synthesized protein is extruded through the membrane into the ER lumen.

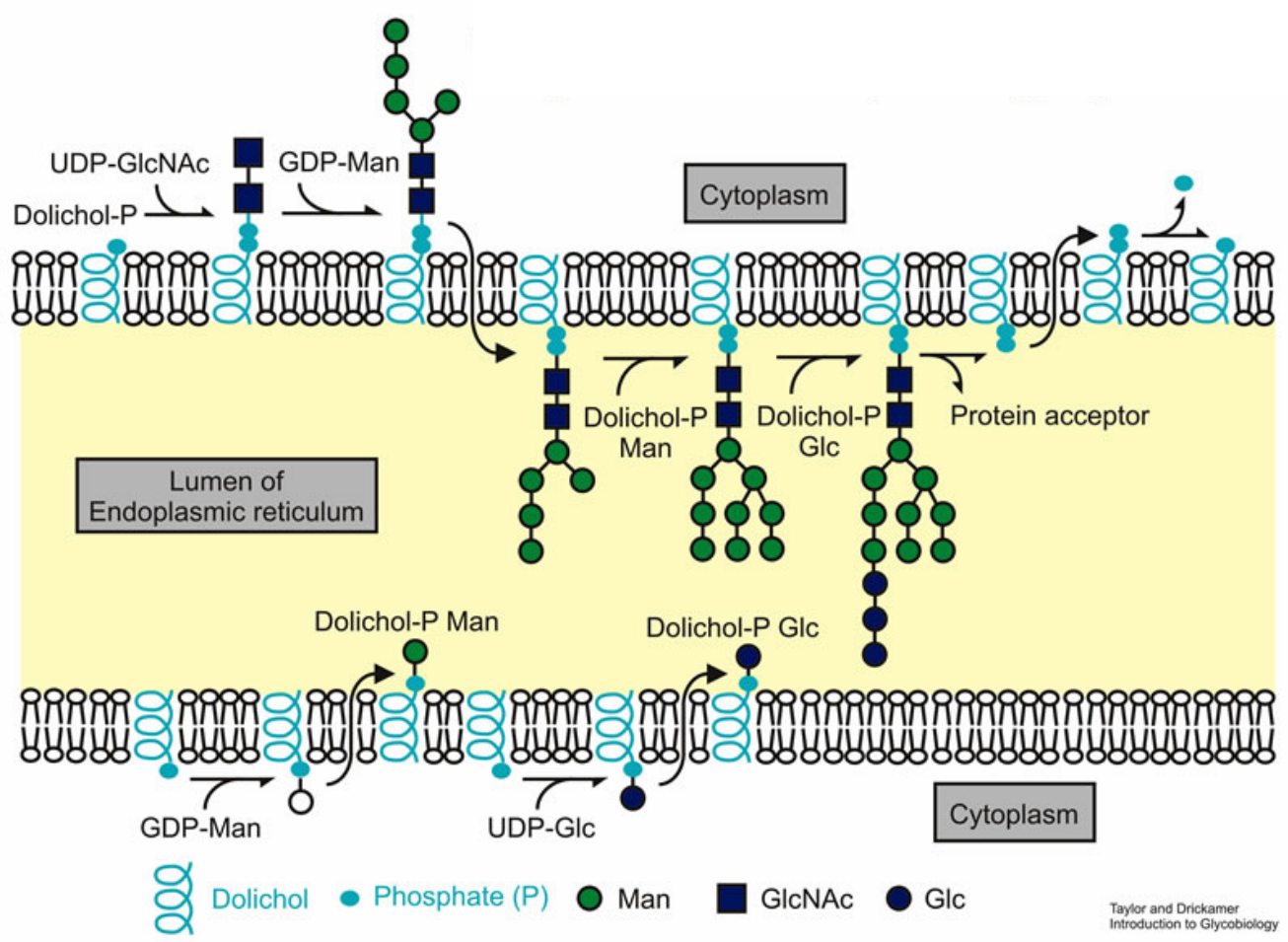
Dolichol derivatives serve as donors and carriers in the co-translational attachment of the parent *N*-glycan to nascent polypeptide on the luminal side of the ER membrane. Two kinds of glycosylated dolichols are involved: dolichol monophosphosugars and dolichol bisphosphosugars.



The long poly-isoprene tail, although far longer than the fatty acid tails of membrane phospholipids, is capable of lipid bilayer insertion, possibly in a helical or folded conformation.



Generation of the dolichol-linked oligosaccharide donor (14-mer) for protein *N*-glycosylation: ER reactions



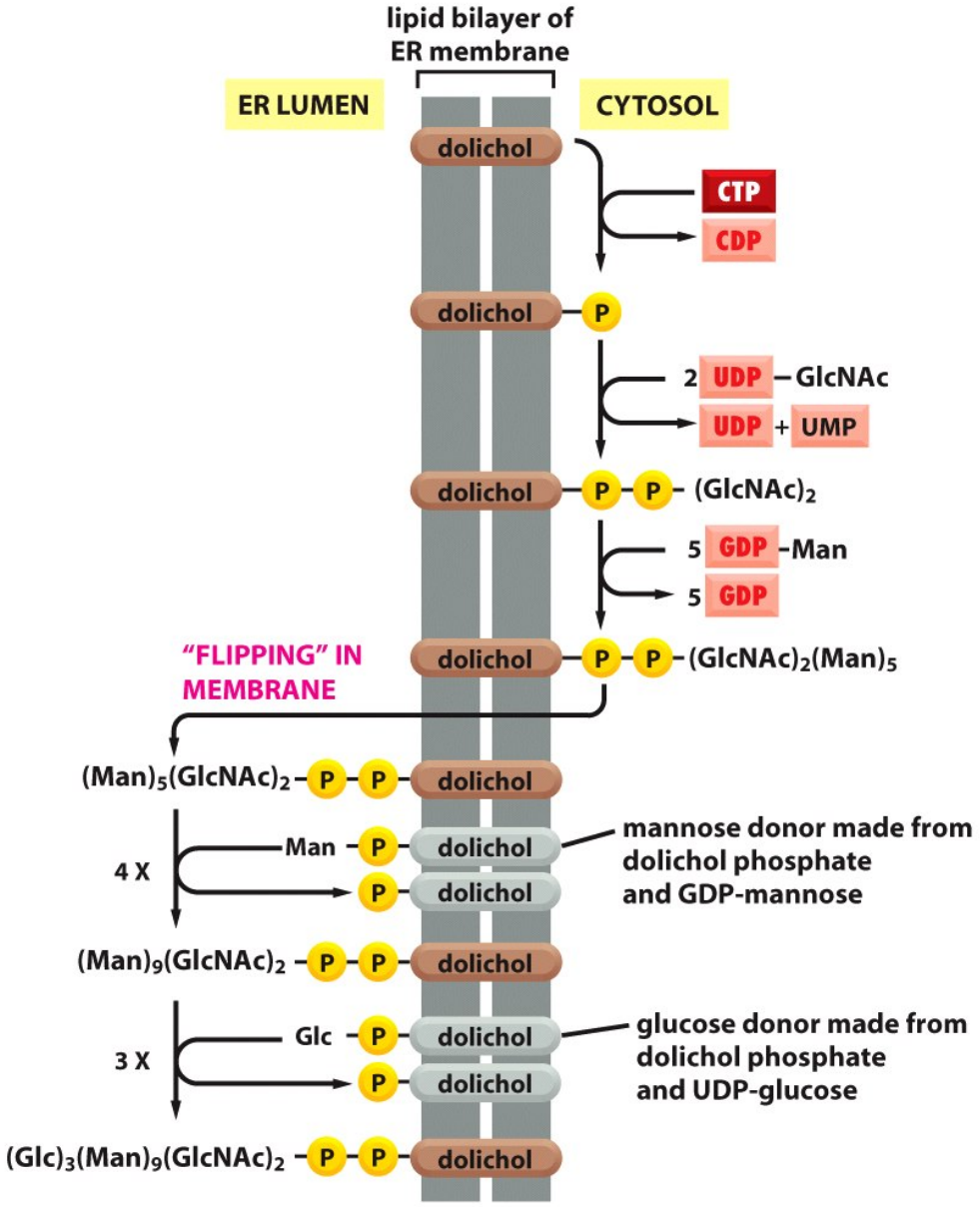
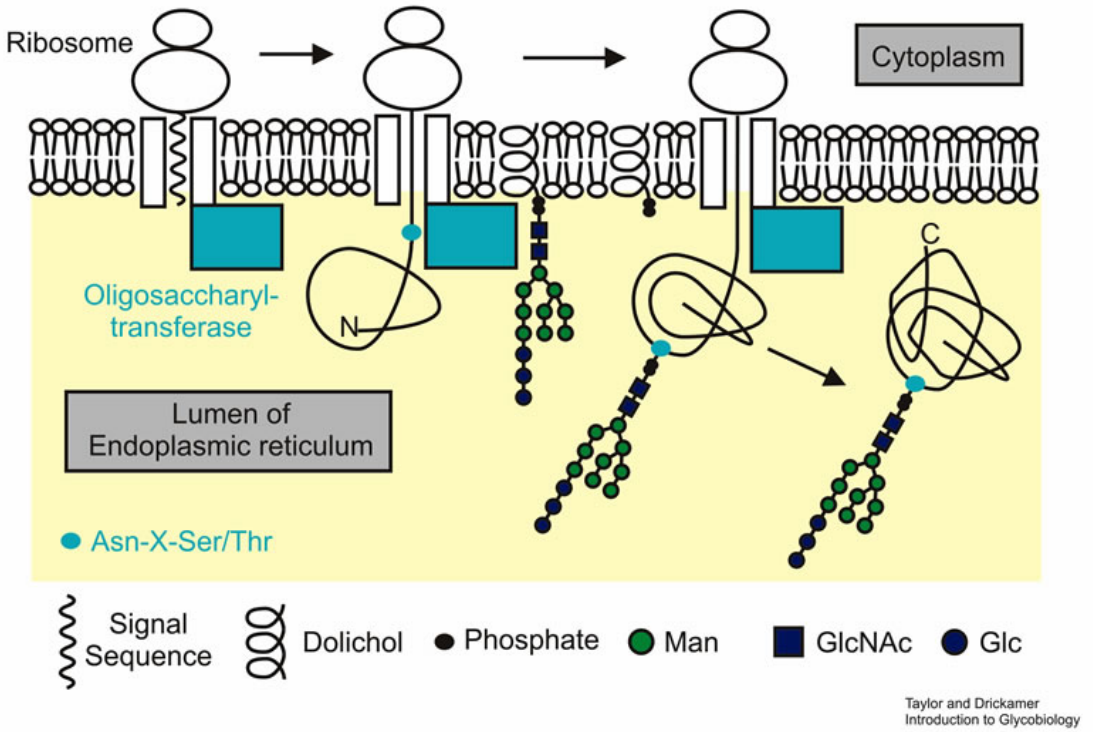


Figure 12-52 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Another representation of the biosynthesis of dolichol-(14-mer) donor oligosaccharide in the ER

En bloc transfer of the precursor oligosaccharide (14-mer:$GlcNAc_2Man_9Glc_3$) is catalyzed by oligosaccharyl transferase (OST).

Consensus sequence: Asn-Xaa-Ser or Asn-Xaa-Thr, where Xaa can be any amino acid except Pro or Asp



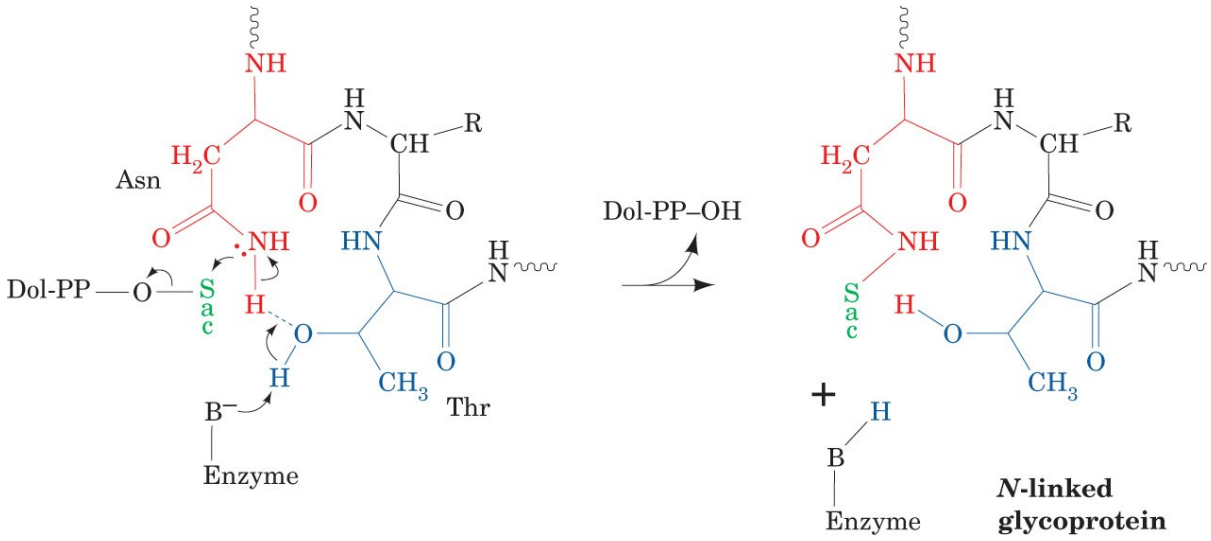
Co-translational addition of *N*-linked glycan to a nascent polypeptide

OST is associated with the channel through which the polypeptide is translocated to the ER lumen, so glycosylation occurs while the polypeptide is still unfolded.

N-Linked glycans are found at the surfaces of glycoproteins (not buried). Since transfer is co-translational involving presumably unfolded or partially folded protein, the mechanism for discrimination between consensus sites is unclear (*i.e.,* some consensus sequences are buried and unglycosylated).

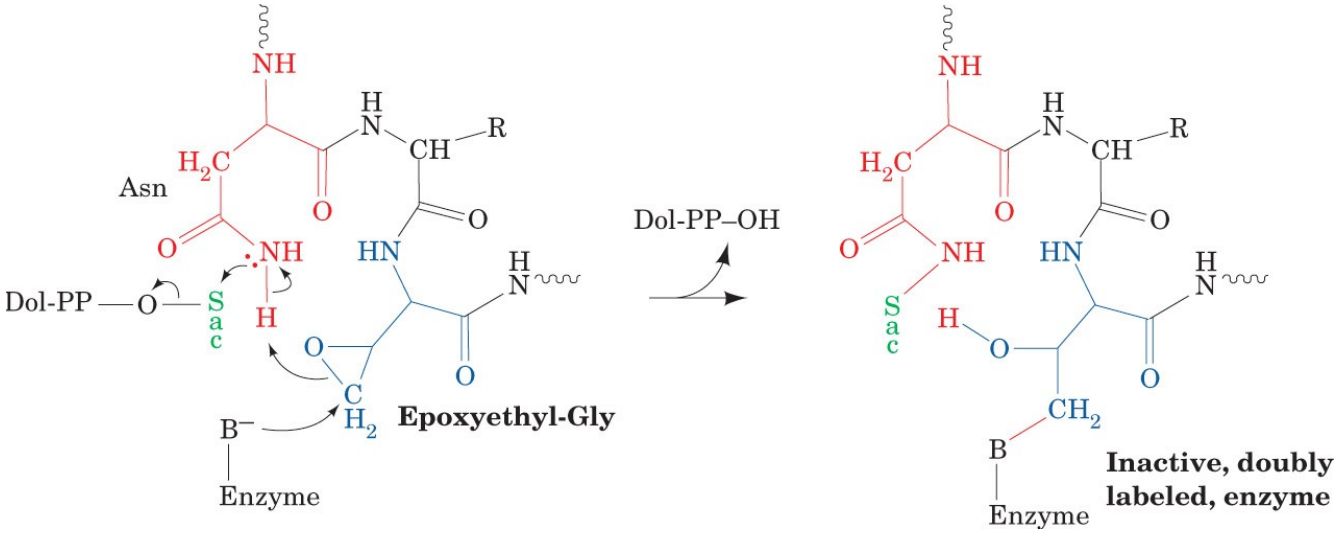
Mechanism of the oligosaccharyl transferase (OST) reaction

Chemical rationale for the Asn-X-Ser/Thr consensus sequence

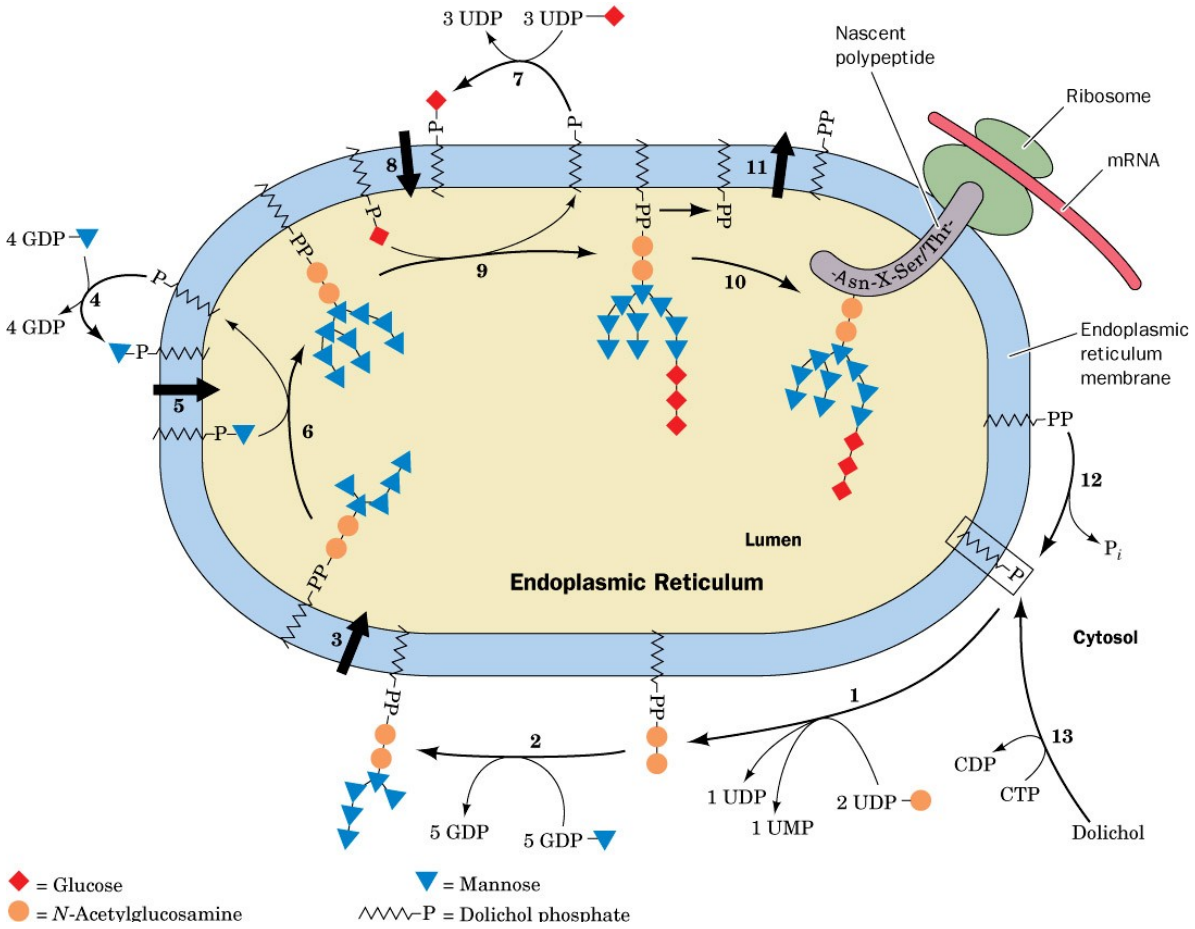


The Asn-X-Thr component of a hexapeptide model substrate forms a ring that is closed by an H-bond between the Asn side-chain amide hydrogens and the Thr hydroxyl group. A basic residue in the OST active site facilitates nucleophilic displacement of dolichol-PP from the oligosaccharide (Sac) by the Asn amide nitrogen, forming the *N*-glycosidic linkage.

Irreversible inactivation of OST by a hexapeptide containing Asn-Gly-epoxyethylGly

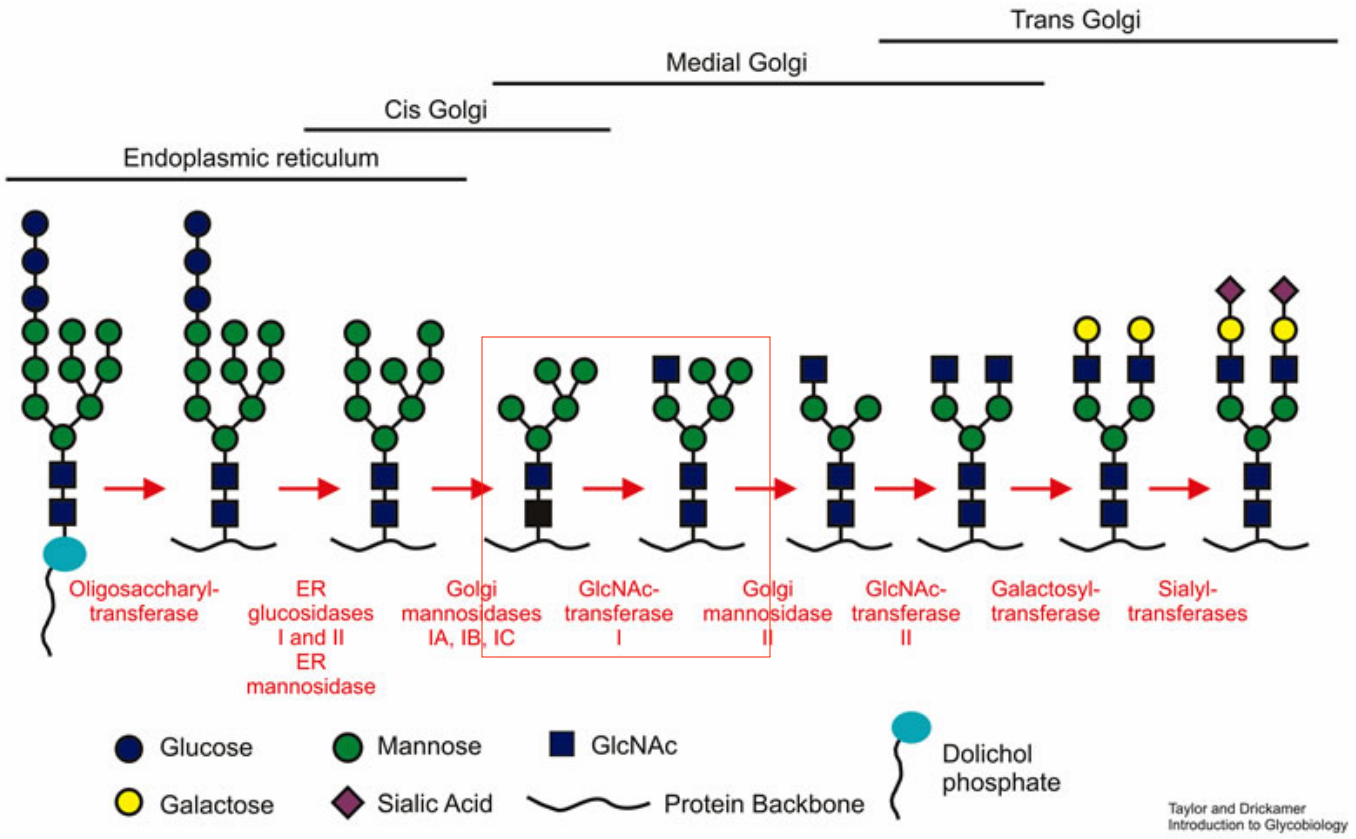


Pathway of dolichol-PP-oligosaccharide synthesis



A summary

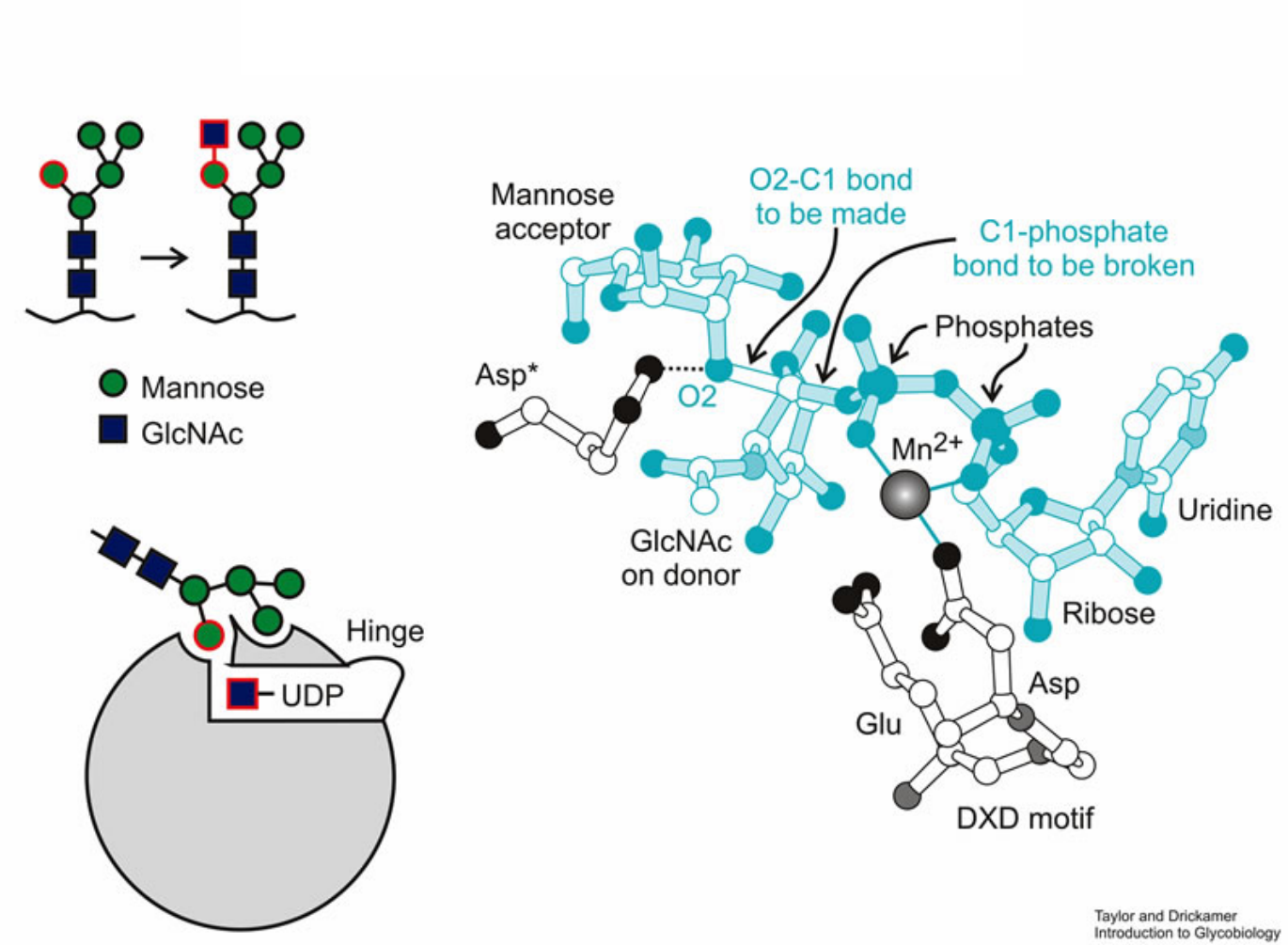
Processing: High-mannose glycan to complex glycan



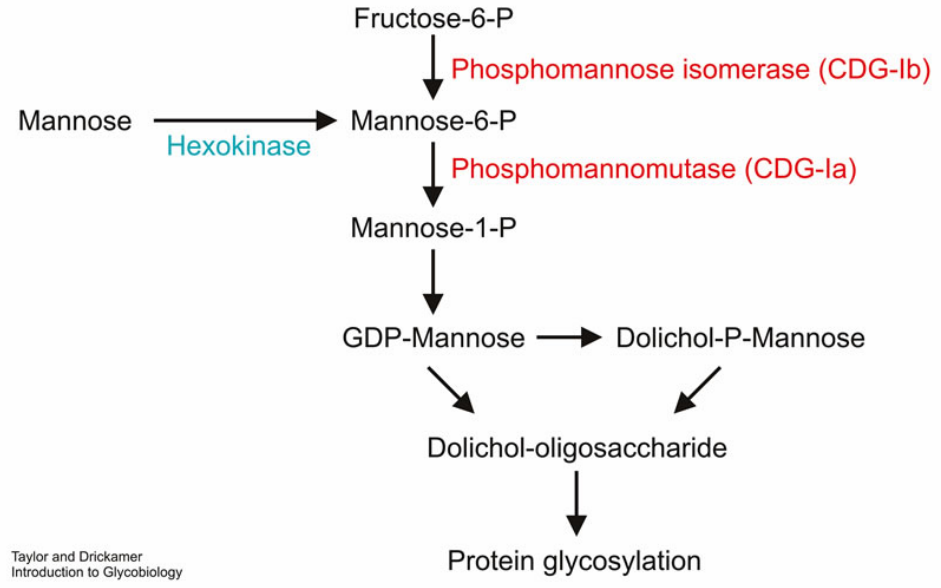
The GlcNAc transferases of the medial Golgi

- **GlcNAc transferase I**: adds a GlcNAc residue to the 1,3-arm of the trimmed *N*-glycan core
- **GlcNAc transferase II**: adds a GlcNAc residue to the 1,6-arm of the maturing *N*-glycan

Mechanism of GlcNAc transferase I



Diseases caused by aberrant glycosylation



Congenital disorders of glycosylation (CDGs): Rare

Results in hypoglycosylation: Leads to developmental defects, loss of muscle tone; defects in cell surface and matrix glycoproteins

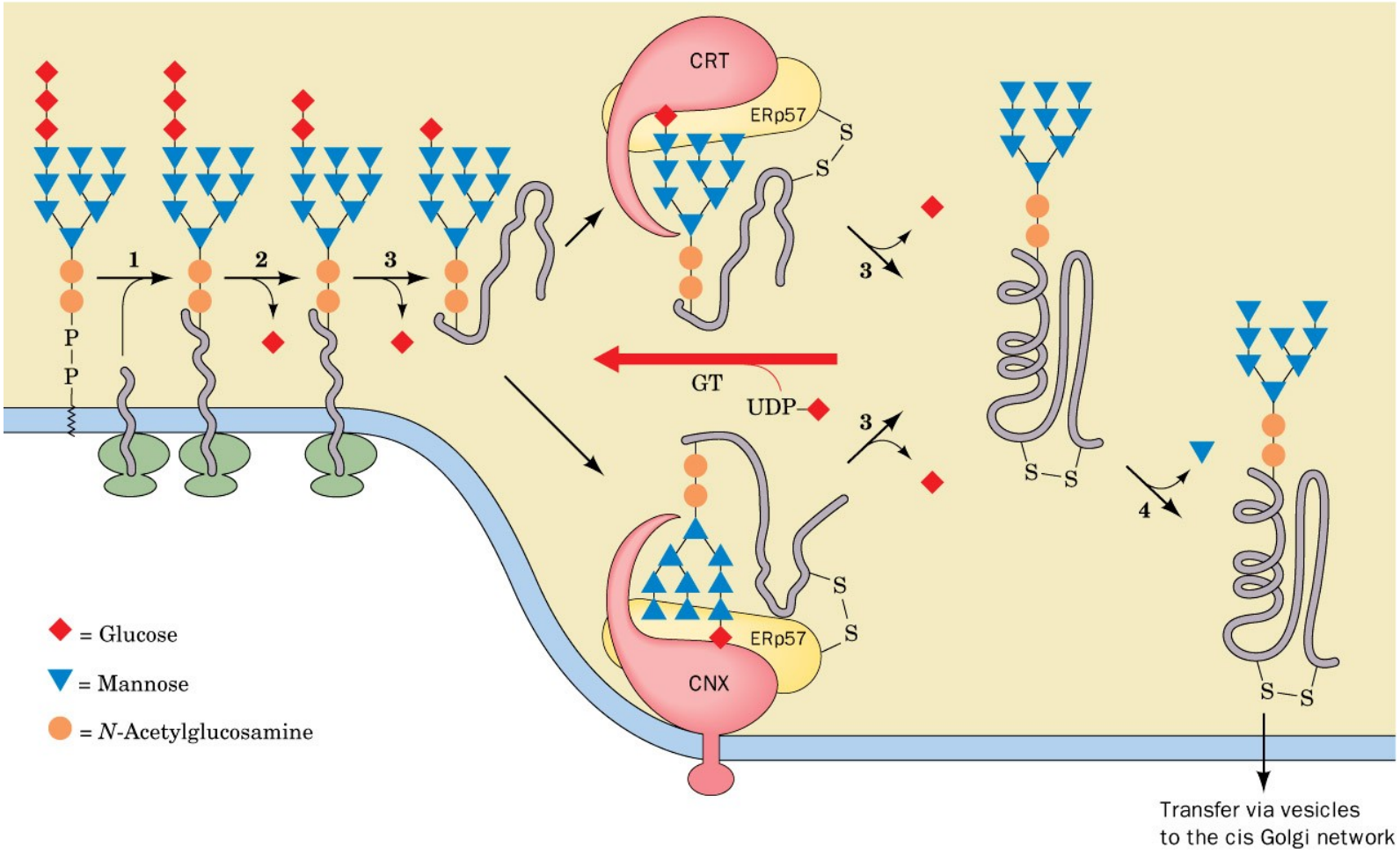
END

Diseases associated with aberrant glycosylation

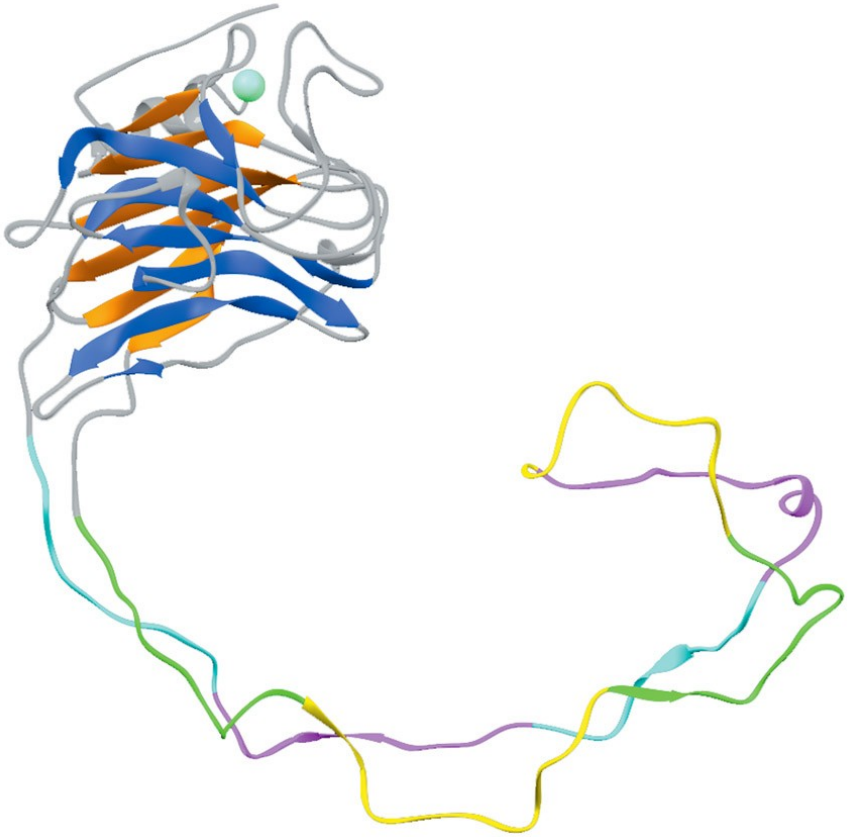
Diseases facilitated by glycosylation

Glycomics

The calnexin/calreticulin cycle for glycoprotein folding in the endoplasmic reticulum



X-Ray structure of the luminal portion of canine calnexin



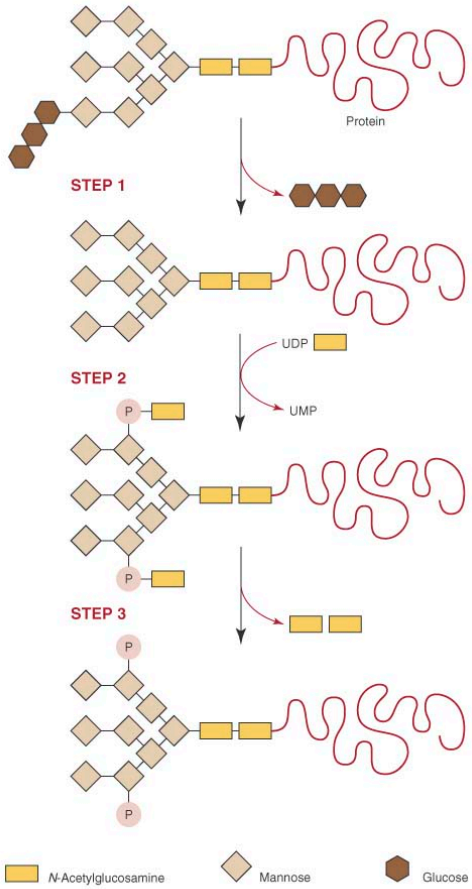


Figure 6.17. Targeting of enzymes to lysosomes. Adapted from Kornfeld, R. and Kornfeld, S. *Annu. Rev. Biochem.* 54:631, 1985.

Some modes of saccharide recognition by proteins and nucleic acids

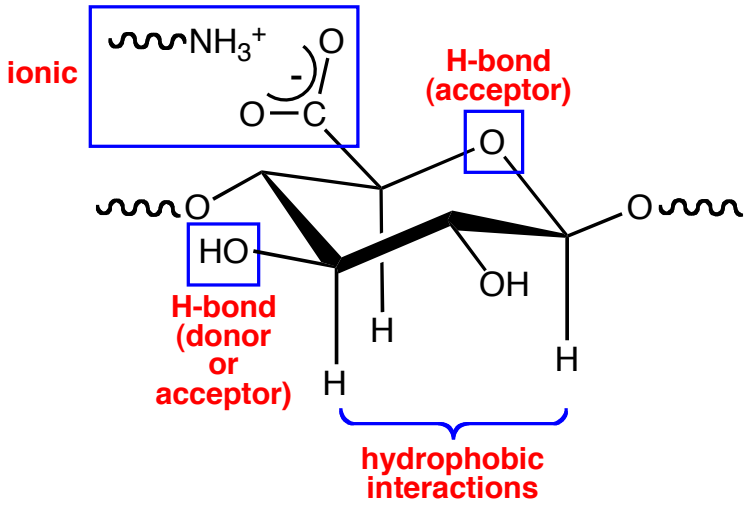


Figure 10.8 Overall structure of bacterial pilus showing subunit arrangement and the structure of the receptor-binding domain of the PapG subunit bound to a glycolipid head group oligosaccharide

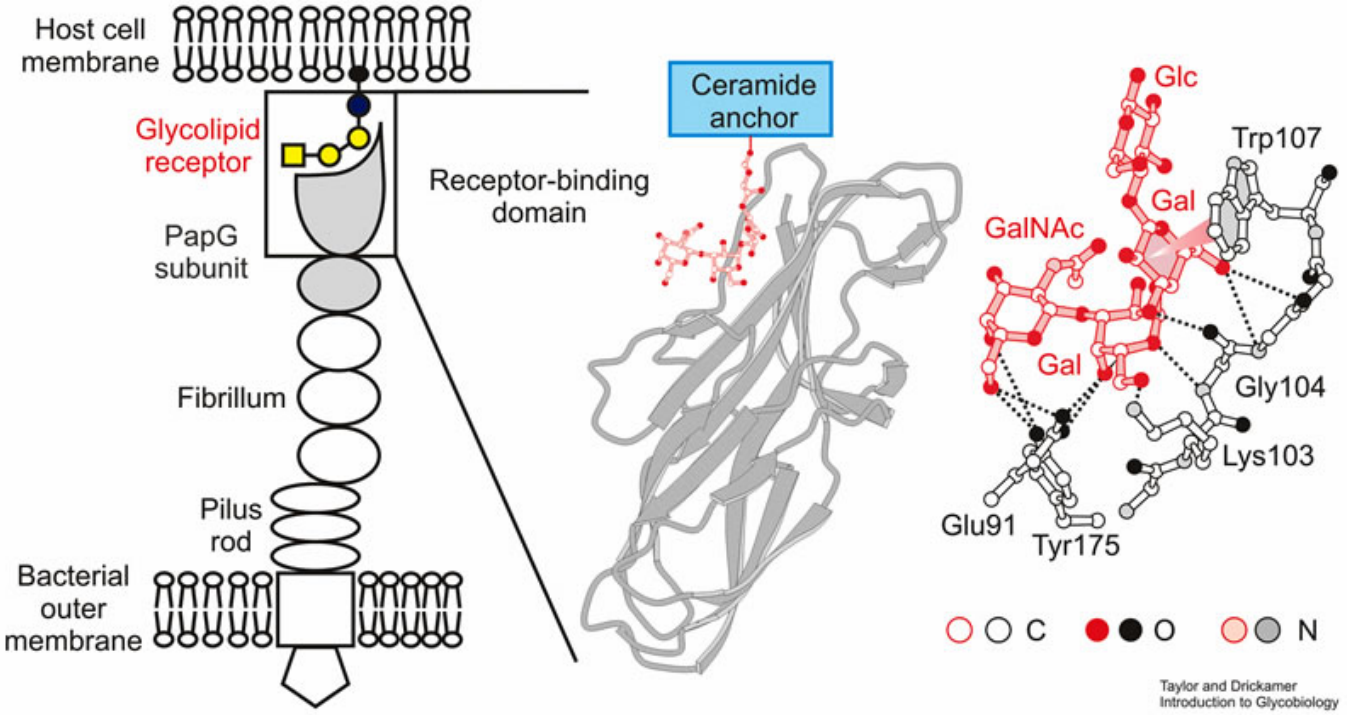


Figure 8.18 Galβ1,4GlcNAc binding site in galectin 1

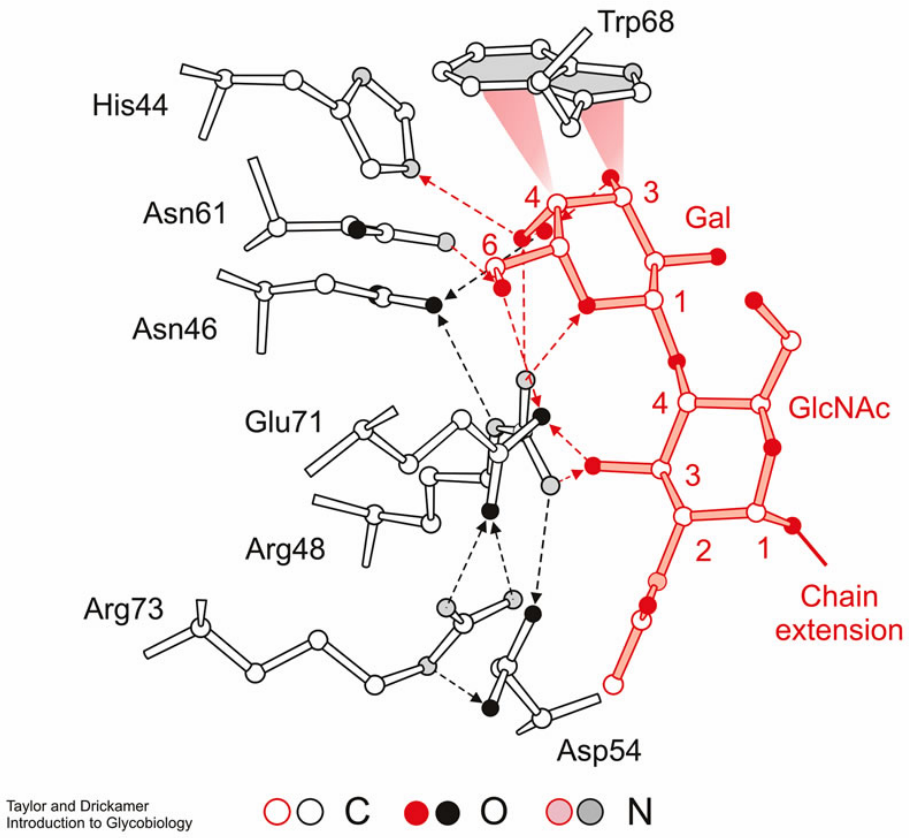


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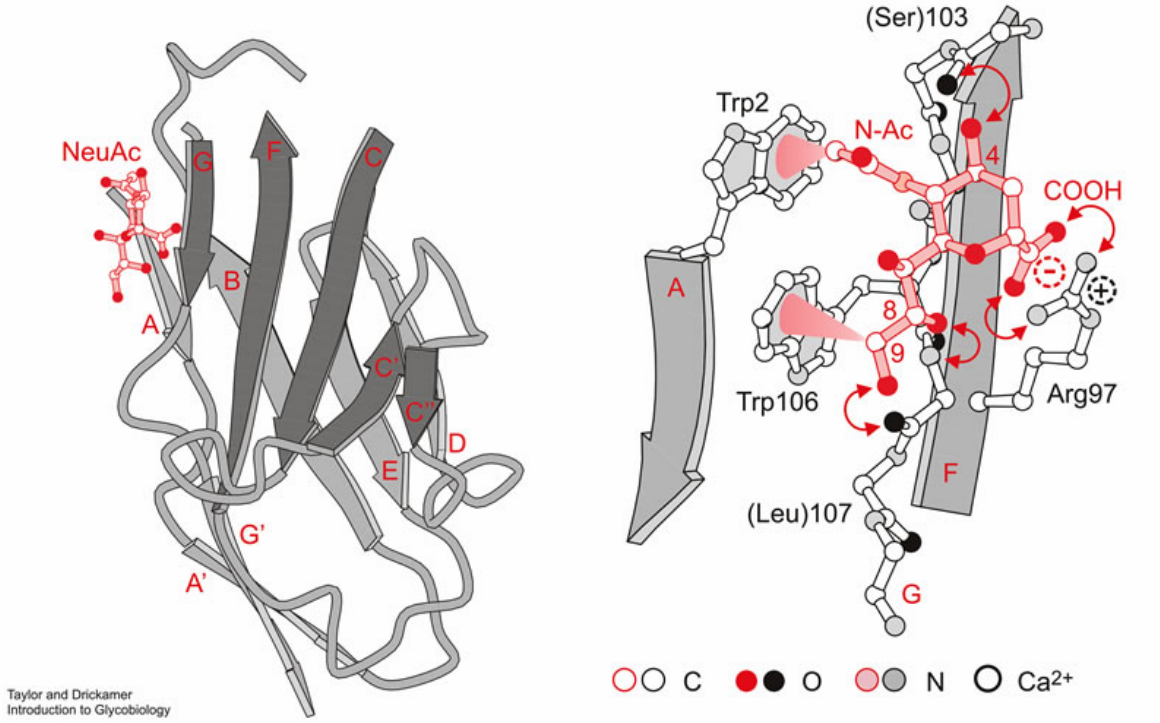
Figure 8.15 Overall fold and monosaccharide-binding site of the CRD from sialoadhesin



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