

Glycosylation

N-linked

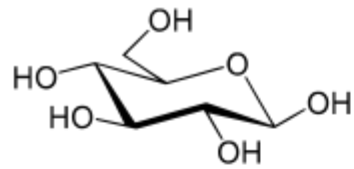
O-linked

C-linked

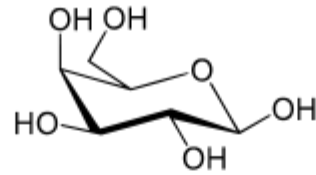
Glycosylation

- Glycosylation is a form of co-translational and post-translational modification. Glycans serve a variety of structural and functional roles in membrane and secreted proteins.
- The majority of proteins synthesized in the rough ER undergo glycosylation. It is an enzyme-directed site-specific process.
- Types:
 - N*-linked glycans attached to a nitrogen of asparagine.
 - O*-linked glycans attached to the hydroxyl oxygen of serine, threonine, tyrosine, hydroxylysine.
 - C*-linked glycans attached to a carbone of tryptophane.

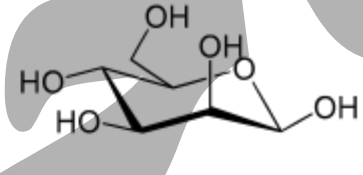
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- O-linked glycosylation involves the posttranslational transfer of an oligosaccharide to a serine or threonine residue.
 - N-linked glycosylation is a cotranslational process involving the transfer of the precursor oligosaccharide to asparagine residues in the protein chain.



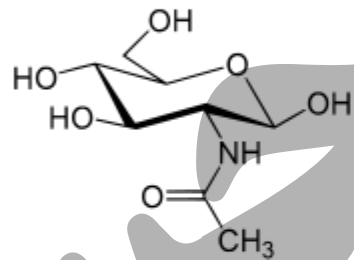
β -D-Glc



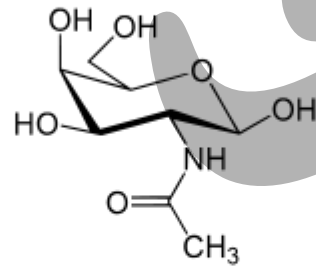
β -D-Gal



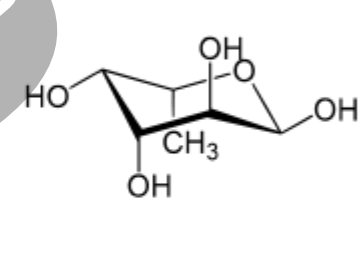
β -D-Man



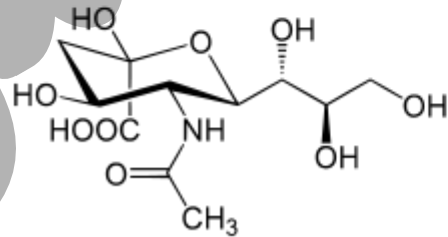
β -D-GlcNAc



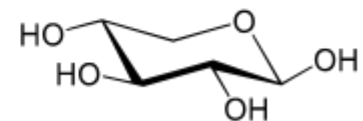
β -D-GalNAc



α -L-Fuc



α -D-Neu5Ac



β -D-Xyl

Purpose

- Correctly protein folding
- Stability of some secreted glycoproteins
- cell-cell adhesion

glycoproteins

- One example of glycoproteins found in the body is mucins, which are secreted in the mucus of the respiratory and digestive tracts. The sugars attached to mucins give them considerable water-holding capacity and also make them resistant to proteolysis by digestive enzymes.
- glycoproteins in the immune system are:
molecules such as antibodies (immunoglobulins), which interact directly with antigens.
molecules of the major histocompatibility complex (or MHC), which are expressed on the surface of cells and interact with T cells.



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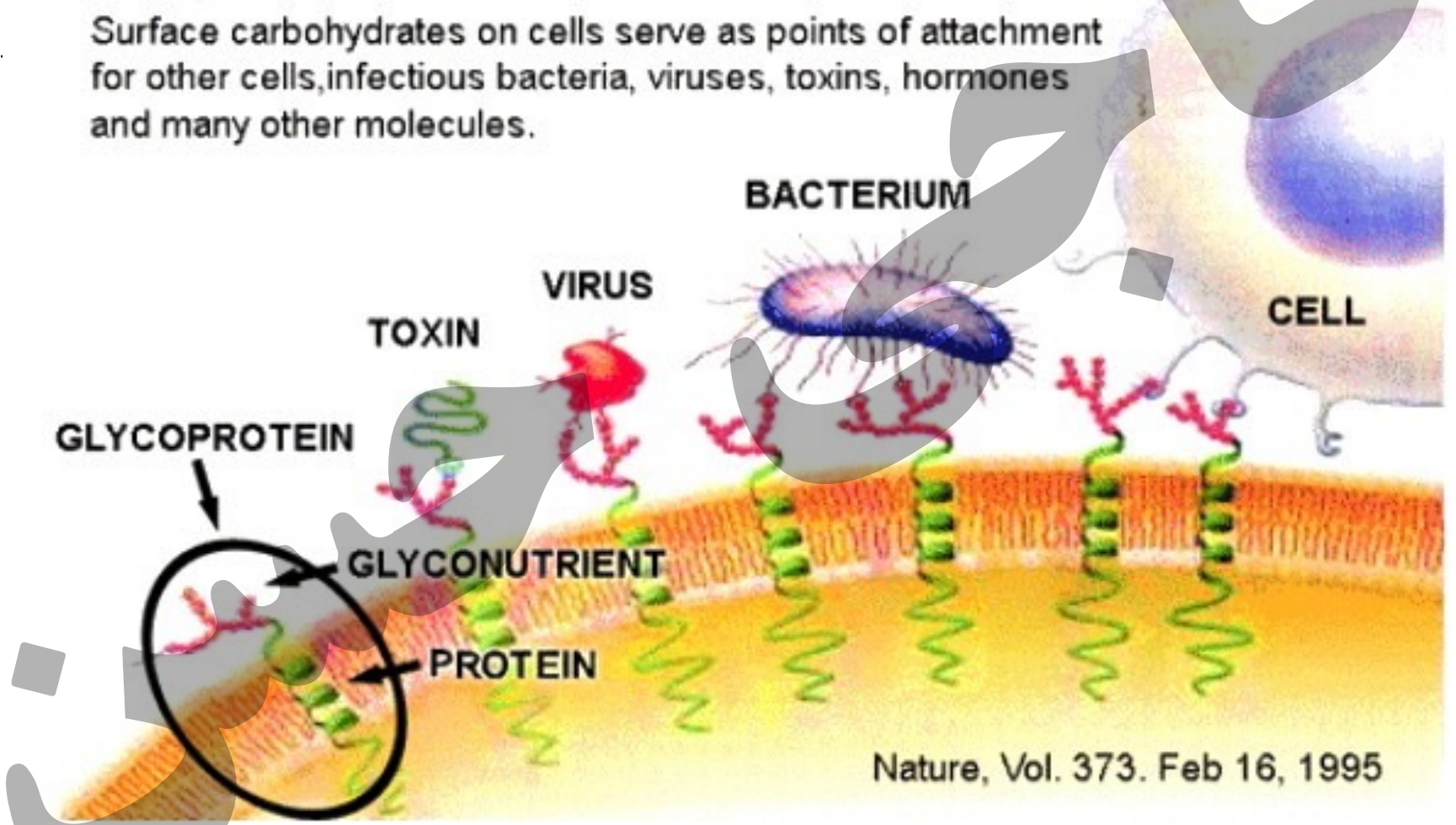
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Glycoprotein Cell Receptors

Surface carbohydrates on cells serve as points of attachment for other cells, infectious bacteria, viruses, toxins, hormones and many other molecules.



Nature, Vol. 373. Feb 16, 1995

proteoglycans

- Proteoglycans are a major component of the animal extracellular matrix.
- The basic proteoglycan unit consists of a "core protein" with one or more covalently attached glycosaminoglycan (GAG) chain(s).
- The chains are long, linear carbohydrate polymers that are negatively charged under physiological conditions.

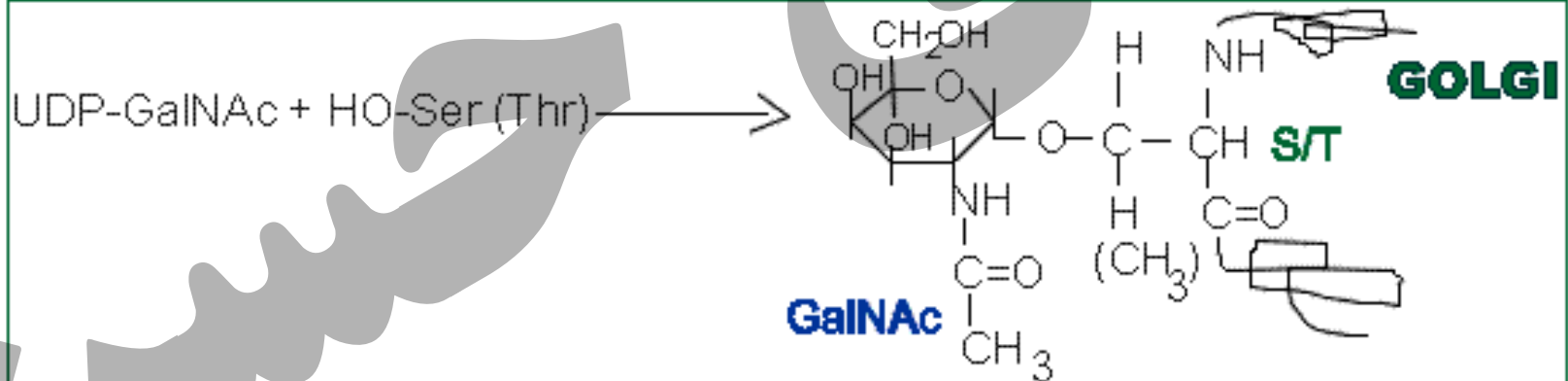
O-linked glycosylation

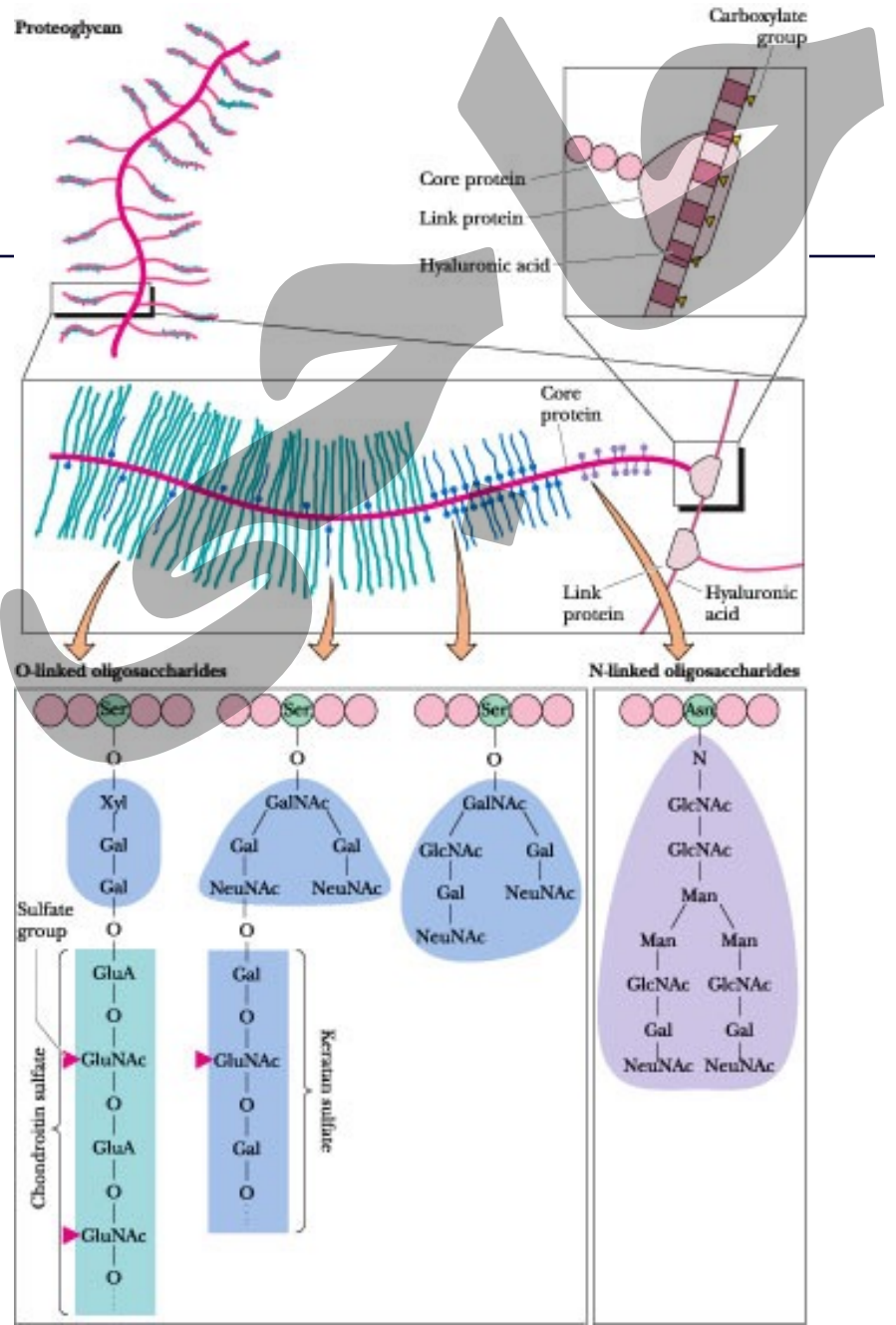
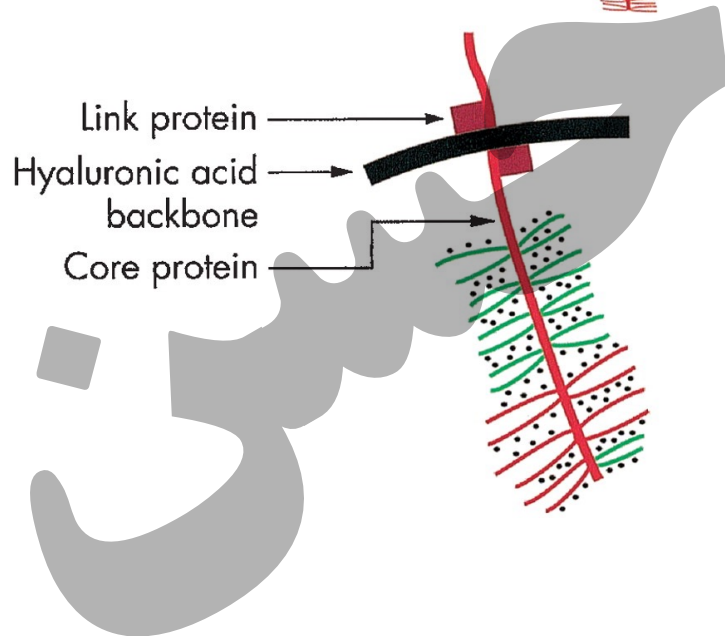
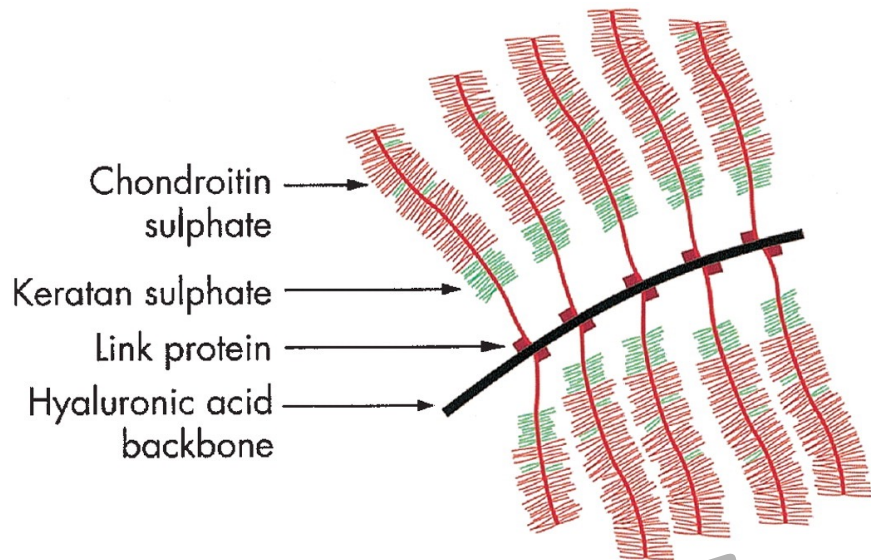
- This is the addition of **N-acetyl-galactosamine** to serine or threonine residues by the enzyme *UDP-N-acetyl-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase*, followed by other carbohydrates (such as galactose and sialic acid).
- proteoglycans (are a major component of the animal extracellular matrix)



BIOSYNTHESIS OF O-LINKED OLIGOSACCHARIDES

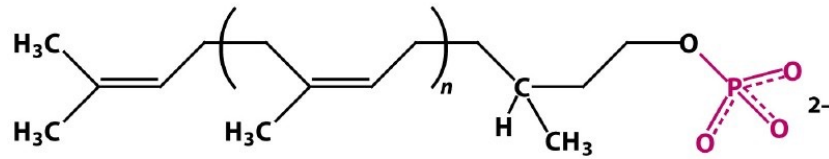
CYTOSOL





N-linked glycosylation

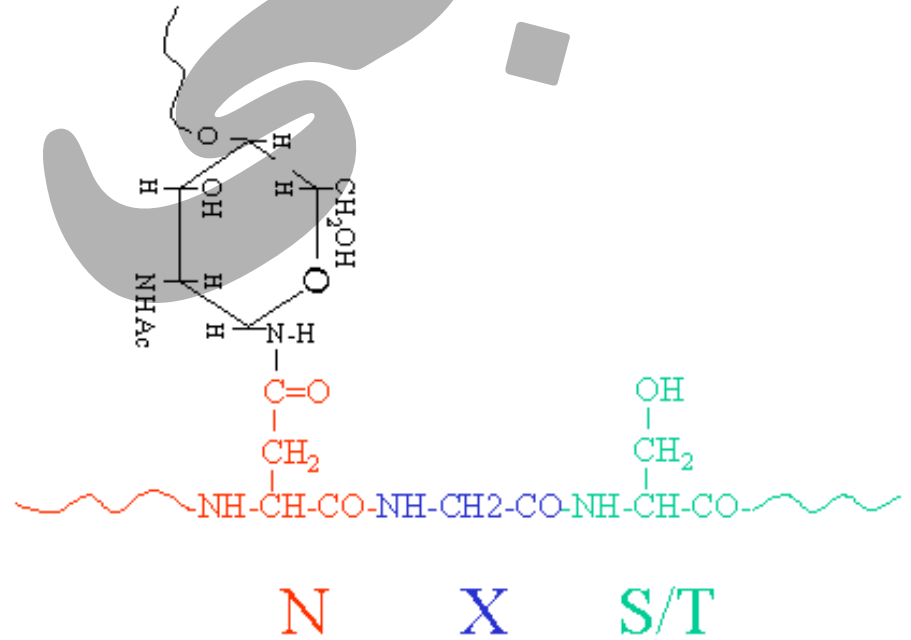
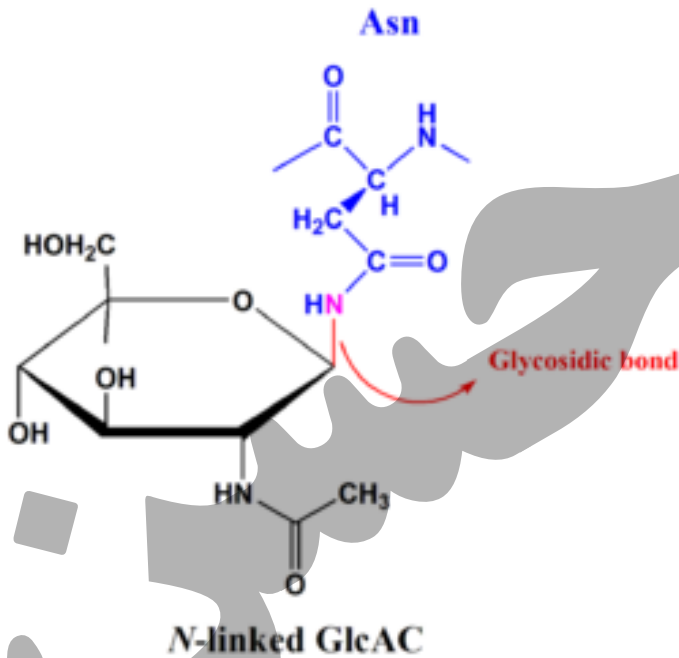
- **N-linked glycosylation** is important for the folding of some eukaryotic proteins. The *N*-linked glycosylation process occurs in eukaryotes and widely in archaea, but very rarely in bacteria.
- In Eukaryotes, most *N*-linked oligosaccharides begin with addition of a 14-sugar precursor to an asparagine in the polypeptide chain of the target protein. The structure of this precursor is common to most eukaryotes, and contains 3 glucose, 9 mannose, and 2 *N*-acetylglucosamine molecules.
- carrier molecule: dolichol



$n = 15-19$


Dolichol phosphate


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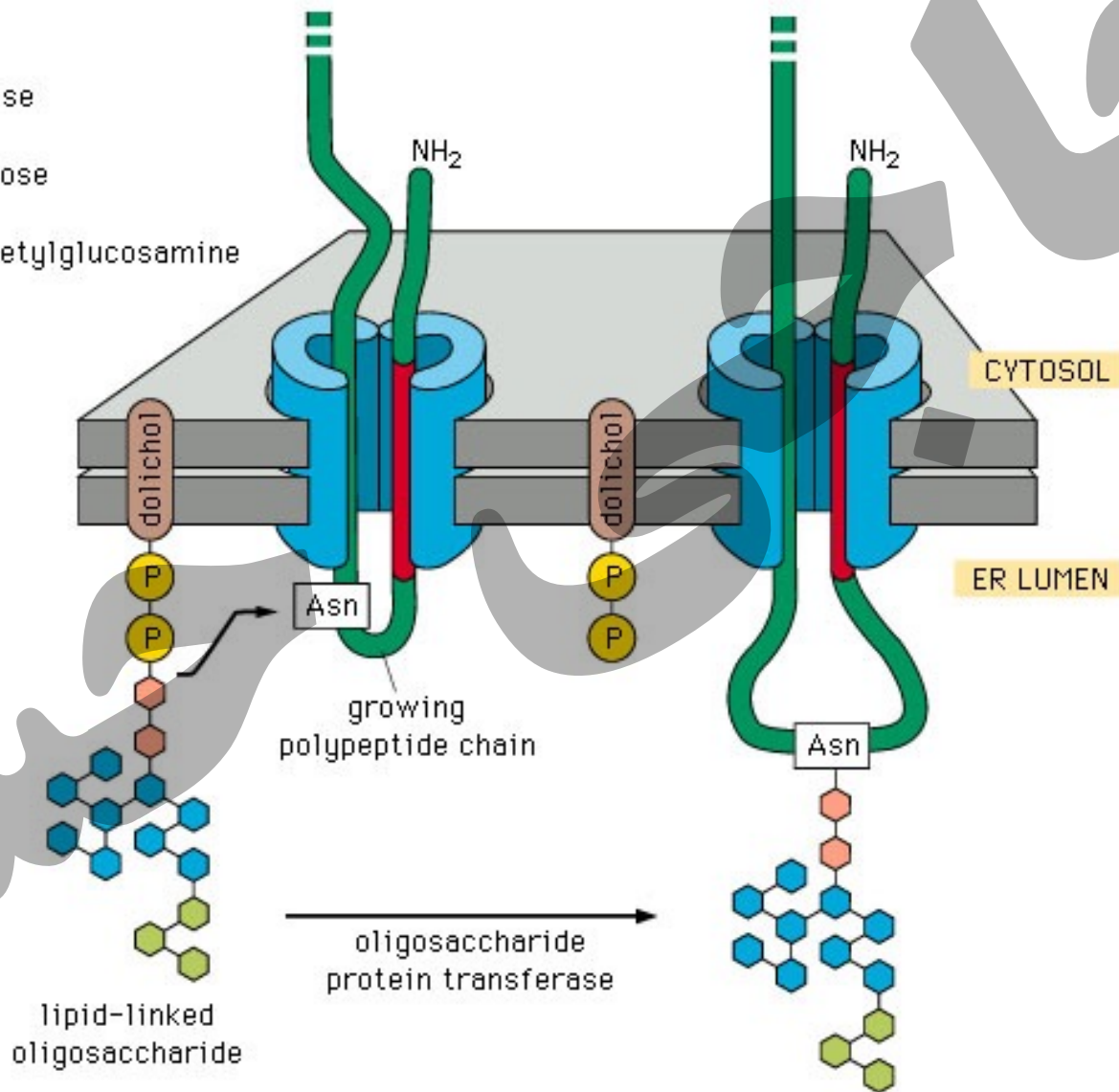
X could be any amino acid except Pro

KEY:

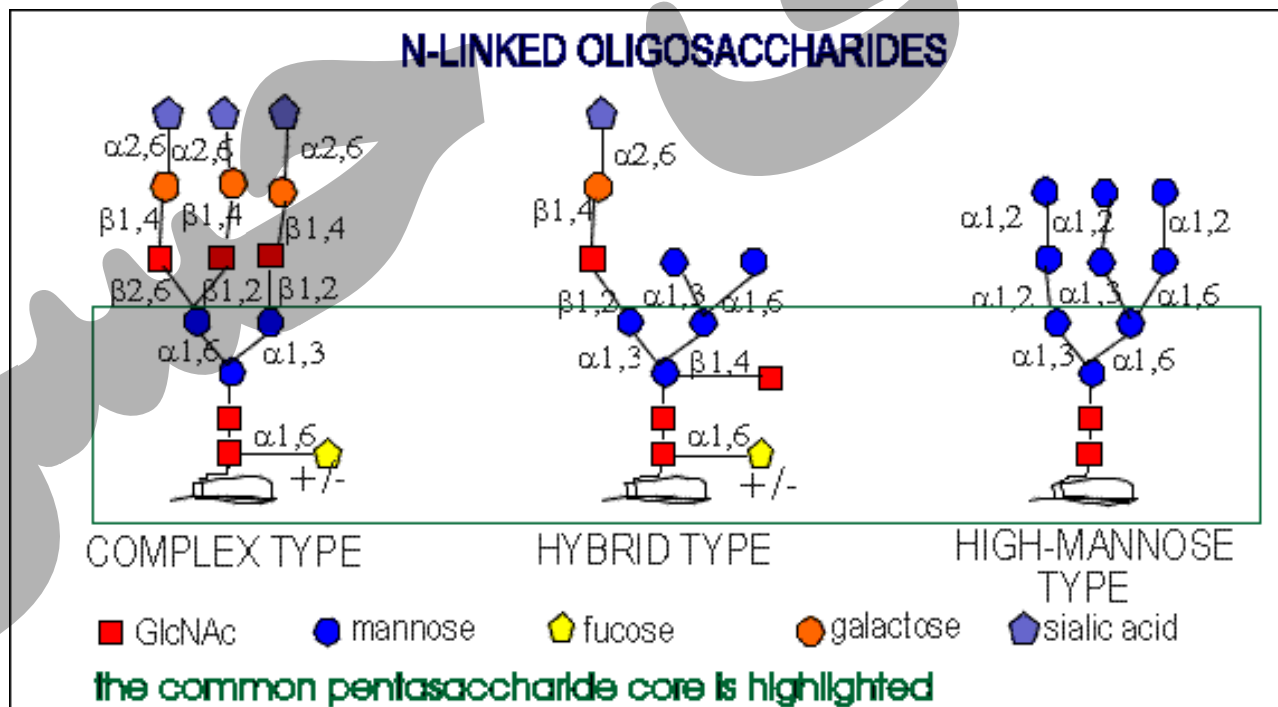
 = glucose

 = mannose

 = *N*-acetylglucosamine



- There are three major classes of *N*-linked saccharides resulting from this core: high-mannose oligosaccharides, complex oligosaccharides and hybrid oligosaccharides.



- GlcNAc
- Mannose
- GalNAc
- Galactose
- ▲ Fucose
- ◆ Sialic Acid

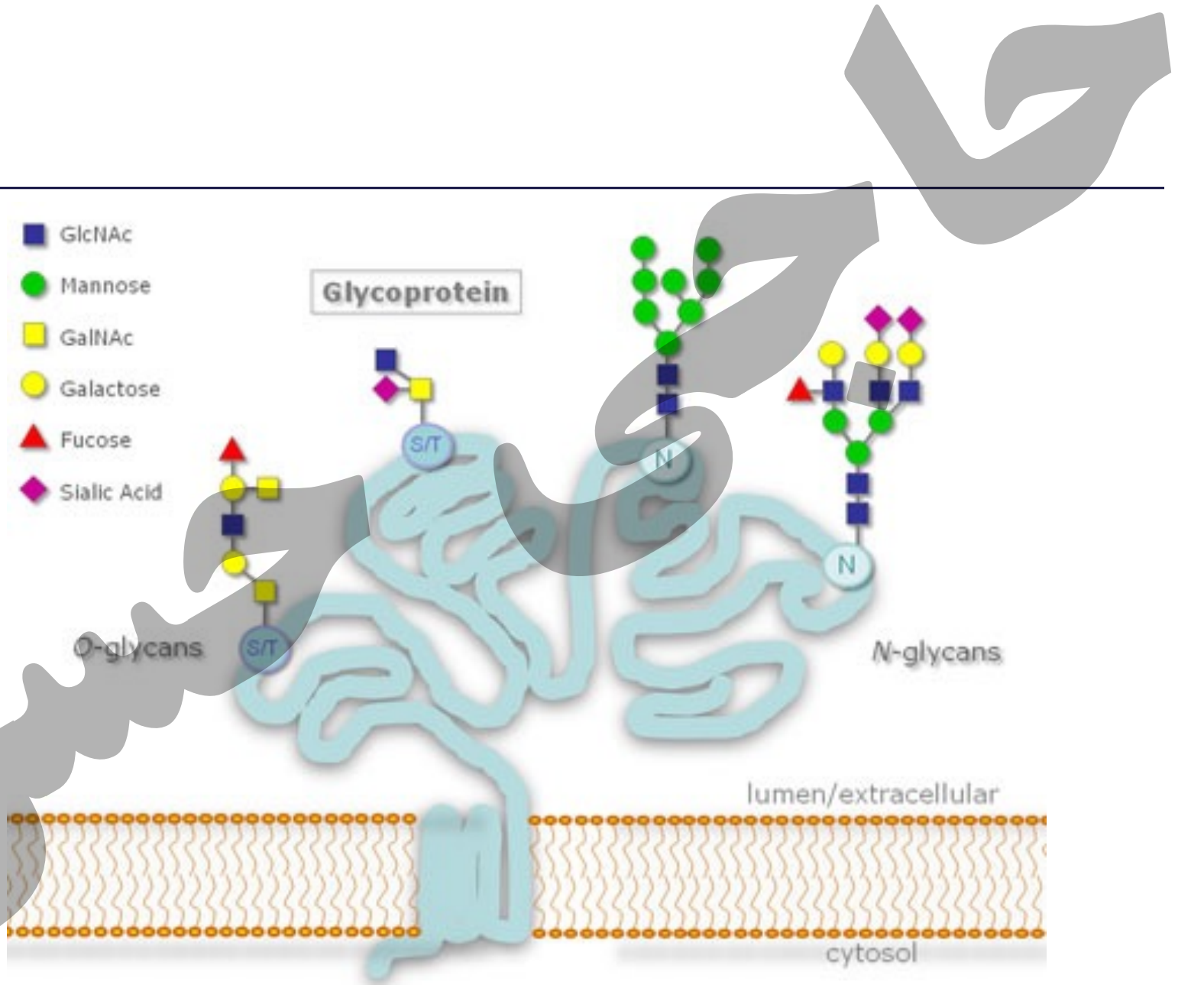
Glycoprotein

O-glycans

N-glycans

lumen/extracellular

cytosol





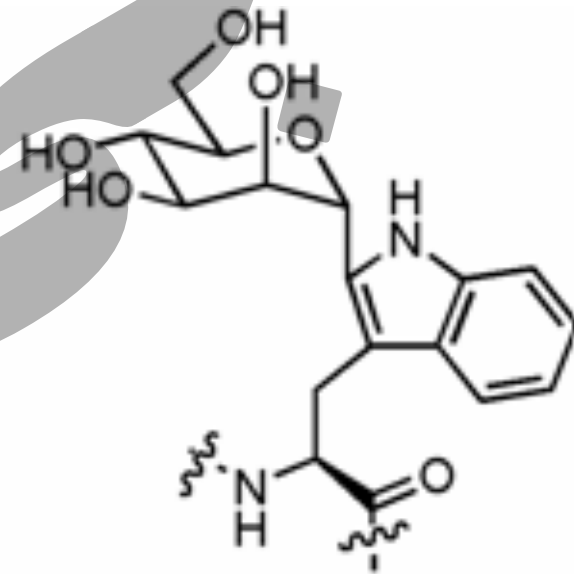
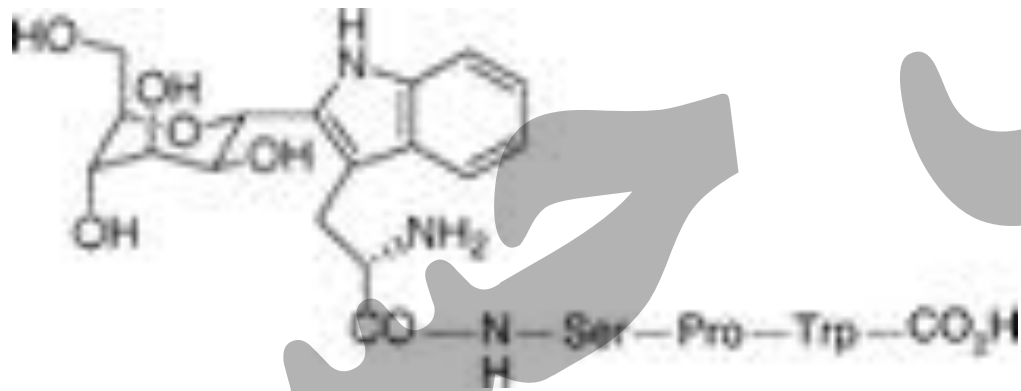
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C-mannosylated Trp