

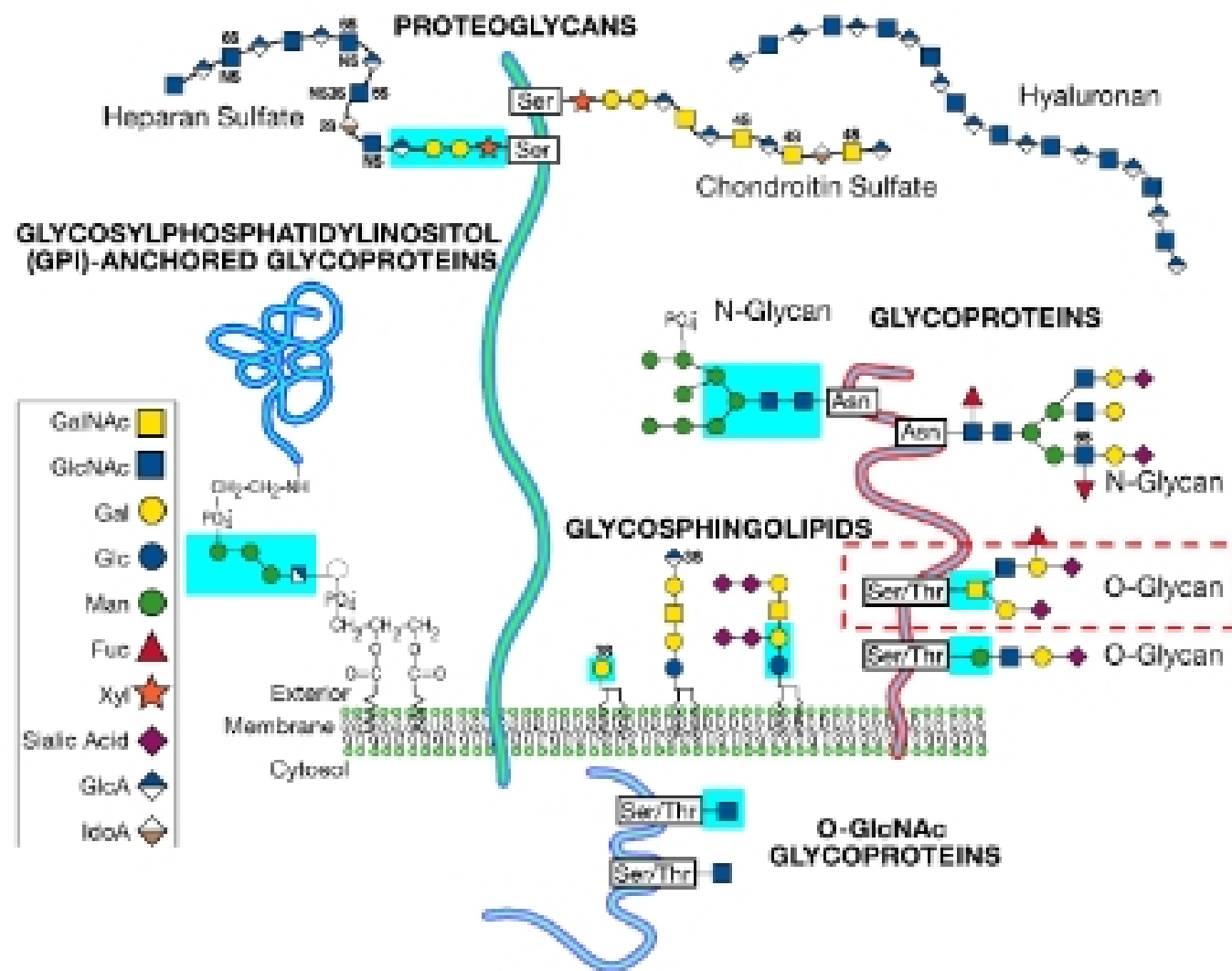
O-GalNAc Glycans

➤ **Dr. Lianchun Wang**

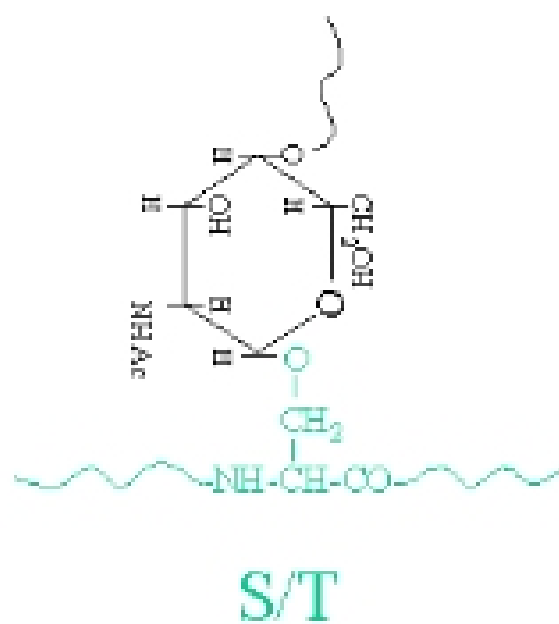
Outline

- **O-GalNAc Glycans**
- **Mucin Glycoproteins**
- **Function of Mucin Glycoproteins**
- **O-GalNAc Glycan Structures and Tissue Distribution**
- **Modification of O-GalNAc Glycans**
- **O-GalNAc Glycan Analysis**
- **O-GalNAc Glycan Biosynthesis**
- **Functions of O-GalNAc Glycans**

Common Classes of Animal Glycans



O-GalNAc Glycans



- O-glycosylation is a common covalent modification of serine and threonine residues of mammalian glycoproteins.
- O-GalNAc glycans are covalently α -linked via an N-acetylgalactosamine (GalNAc) moiety to the -OH of serine or threonine by an O-glycosidic bond
- Core structure: α -linked N-GalNAc residue linked to serine or threonine. The further addition of Gal, GlcNAc or GalNAc defines Cores 1-8.
- O-GalNAc glycans are antigenic
- Modification of O-GalNAc glycans: O-acetylation of sialic acid and O-sulfation of galactose and N-acetylglucosamine, leading to structural heterogeneity.
- Other O-glycans: α -linked O-fucose, β -linked O-xylose, α -linked O-mannose, β -linked O-GlcNAc, α - or β -linked O-galactose, and α - or β -linked O-glucose glycans
- Shield the epithelial surfaces against physical and chemical damage and protect against infection by pathogens

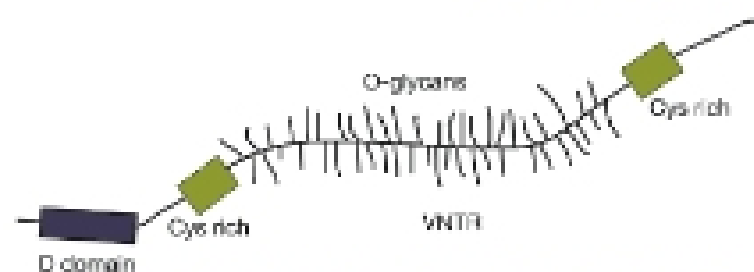
O-GalNAc Glycans

Structures of O-glycan cores and antigenic epitopes found in mucins

O-Glycan	Structure
Core	
Tn antigen	GalNAcSer/Thr
Sialyl-Tn antigen	Siaα2-6GalNAcSer/Thr
Core 1 or T antigen	Galβ1-3GalNAcSer/Thr
Core 2	GlcNAcβ1-6(Galβ1-3)GalNAcSer/Thr
Core 3	GlcNAcβ1-3GalNAcSer/Thr
Core 4	GlcNAcβ1-6(GlcNAcβ1-3)GalNAcSer/Thr
Core 5	GalNAcα1-3GalNAcSer/Thr
Core 6	GlcNAcβ1-6GalNAcSer/Thr
Core 7	GalNAcα1-6GalNAcSer/Thr
Core 8	Galα1-3GalNAcSer/Thr
Epitope	
Blood groups O, H	Fucα1-2Gal-
Blood group A	GalNAcα1-3(Fucα1-2)Gal-
Blood group B	Galα1-3(Fucα1-2)Gal-
Linear B	Galα1-3Gal-
Blood group I	Galβ1-4GlcNAcβ1-3Gal-
Blood group I	Galβ1-4GlcNAcβ1-6(Galβ1-4GlcNAcβ1-3)Gal-
Blood group Sd(a), Cad	GalNAcβ1-4(Siaα2-3)Gal-
Blood group Lewis ^x	Galβ1-3(Fucα1-4)GlcNAc-
Blood group Lewis ^y	Galβ1-4(Fucα1-3)GlcNAc-
Blood group sialyl-Lewis ^x	Siaα2-3Galβ1-4(Fucα1-3)GlcNAc-
Blood group Lewis ^y	Fucα1-2Galβ1-4(Fucα1-3)GlcNAc-

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Mucin Glycoproteins



- **Mucin:** Large glycoprotein with a high content of serine, threonine, and proline residues and numerous O-GalNAc-linked saccharides, often occurring in clusters on the polypeptide.
- In mucous secretions and as transmembrane glycoproteins.

- **Gel-forming mucins:** large, mainly produced in the goblet or mucous cells of the tracheobronchial, gastrointestinal, and genitourinary tracts.
- In goblet cells, mucins are stored intracellularly in mucin granules and can be quickly secreted upon external stimuli.
- **Hallmark:** Repeated peptide stretches [Variable number of tandem repeat (VNTR)]
 - Rich in serine and/or threonine
 - Abundant O-GalNAc glycans
 - “bottle brush” conformation
 - Rich in proline that facilitates O-GalNAc glycosylation
- Secreted mucins have cysteine-rich regions and cystine knots that are responsible for their polymerization and the formation of extremely large molecules of several million daltons.
- Cell-surface mucins contain an extracellular domain with a central VNTR region that carries O-GalNAc glycan chains, a single transmembrane domain, and a small cytoplasmic tail at the carboxyl terminus.
- About 20 mucin genes, express in tissue-specific fashion and vary in the number and composition of the peptide repeats in their VNTR regions. Within the same mucin, the repeats usually vary in their amino acid sequences.
- The expression of mucin genes is regulated by a large number of cytokines and growth factors, differentiation factors, and bacterial products.