

BIOC 385: M02.T06-Miesfeld

Assigned Reading: *Biochemistry* Chapter 16.2ab





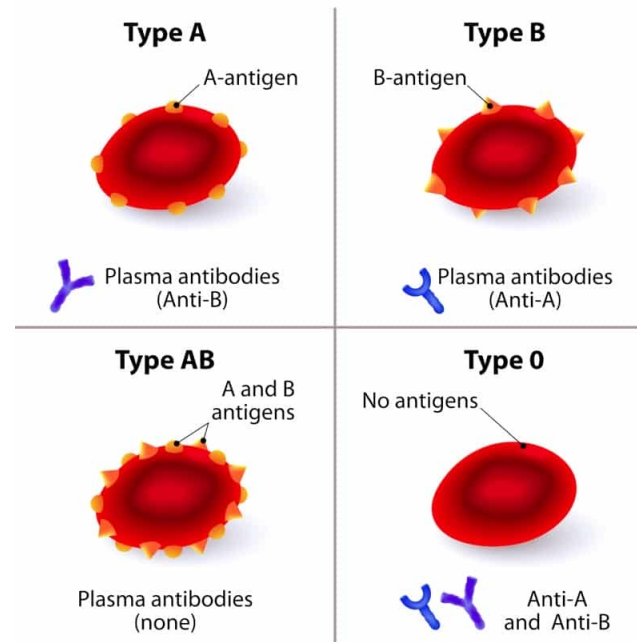
Glycoconjugates and ABO Human Blood Types



The Big Picture

- Glycoconjugates integrate carbohydrate chemistry with protein and lipid scaffolds, enabling structural integrity, signaling, and immune recognition.
- ABO blood groups illustrate how glycosyltransferase specificity at the molecular level dictates clinical transfusion compatibility.

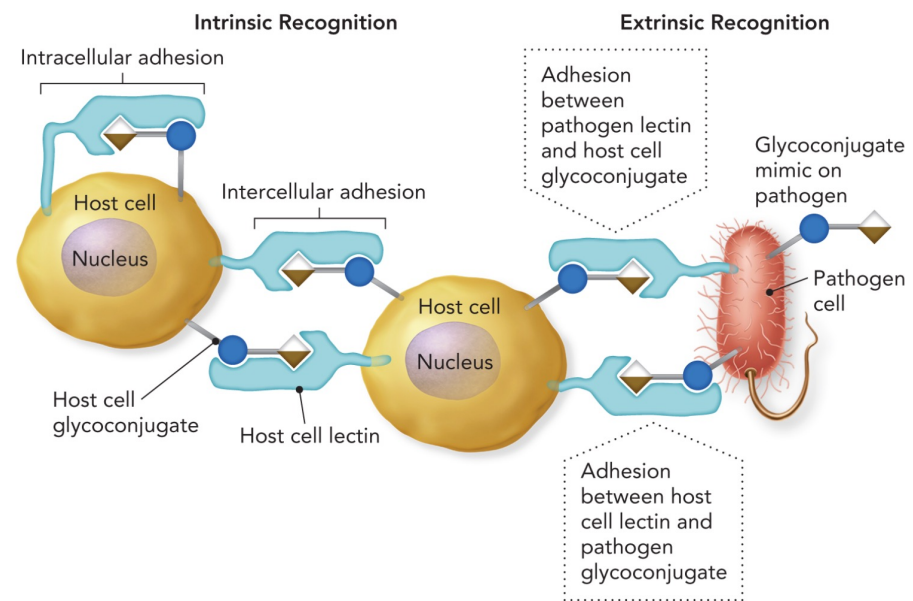
ABO blood group



<https://www.bbguy.org/2018/08/01/abo/>

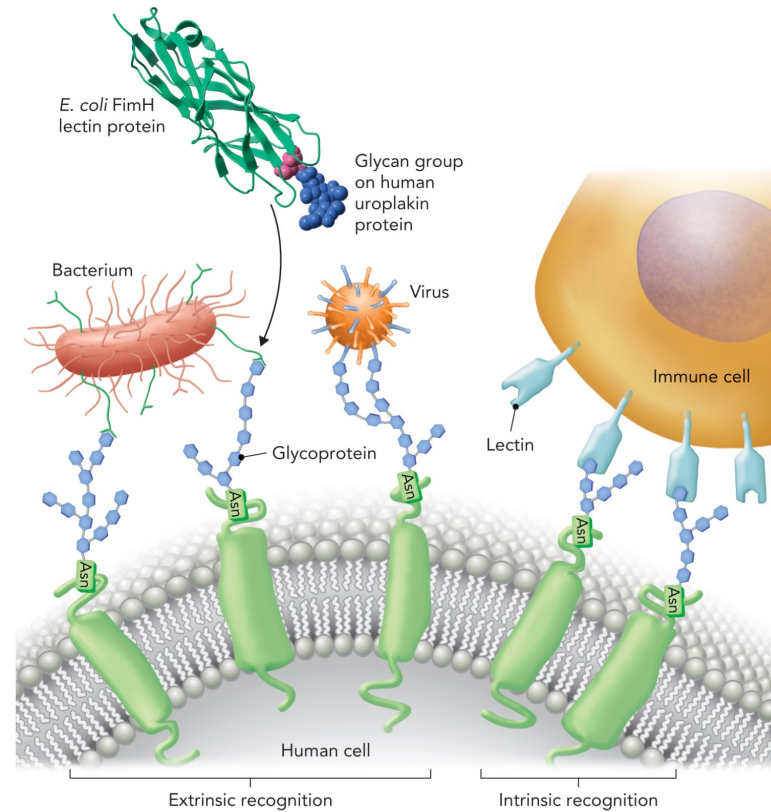
Intrinsic and Extrinsic Glycan Recognition

- Intrinsic glycan–lectin interactions mediate host immune cell recognition and adhesion within tissues; lectins are proteins.
- Extrinsic recognition occurs between host glycans and pathogen lectins, influencing infection and immune defense.



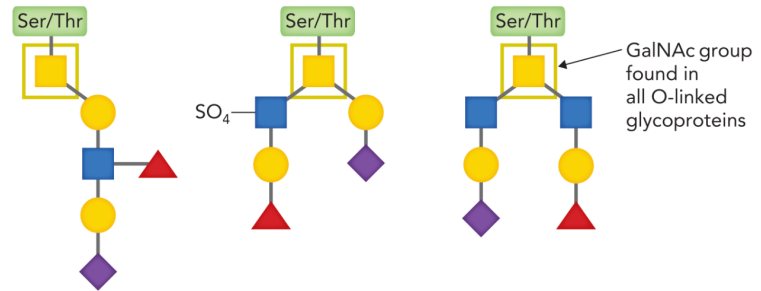
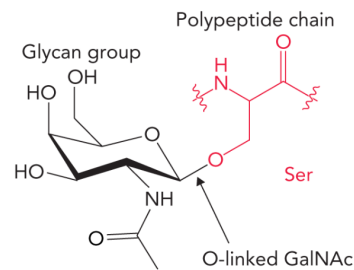
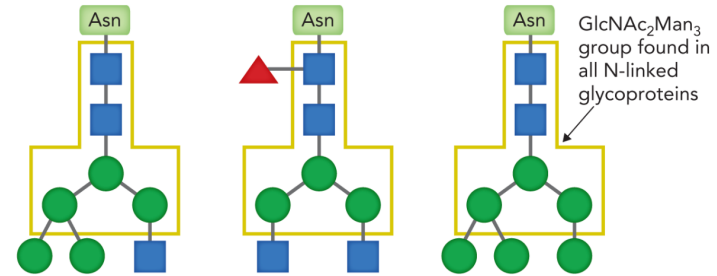
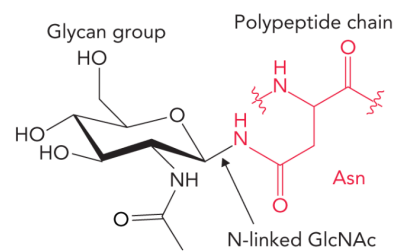
Glycoproteins Located on the Cell Surface

- An example of an extrinsic glycoconjugate interaction is the binding of the *E. coli* FimH lectin protein to the mannose glycan on the human uroplakin protein on the surface of human bladder cells.
- Because this binding interaction can lead to urinary tract infections, drugs are being developed that mimic glycan groups on human bladder cells and can function as inhibitors of bacterial cell adhesion.



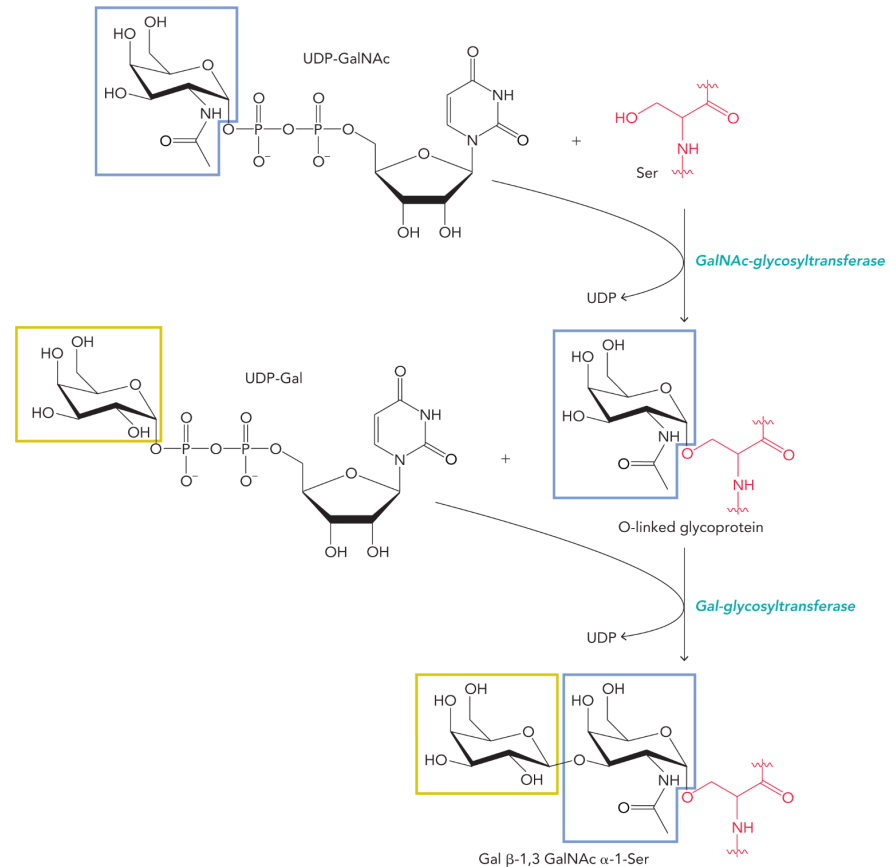
N-Linked and O-linked Protein Glycosylation

- N-linked glycans attach via GlcNAc to asparagine in Asn-X-Ser/Thr motifs, sharing a $\text{GlcNAc}_2\text{Man}_3$ core.
- O-linked glycans attach via GalNAc to serine or threonine and extend with Gal or GlcNAc; mucins protect epithelial barriers.



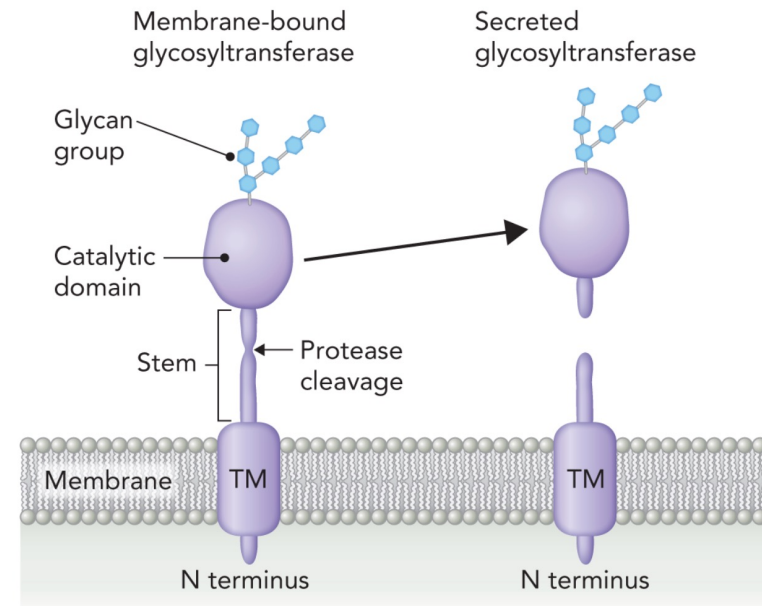
Glycosyltransferase Enzymes Are Sequential

- Glycosyltransferase enzymes act stepwise, e.g., one enzyme transfers GalNAc from UDP-GalNAc to Ser and another glycosyltransferase adds Gal from UDP-Gal.
- This ordered sequence ensures precise elaboration of glycan cores into functional structures.



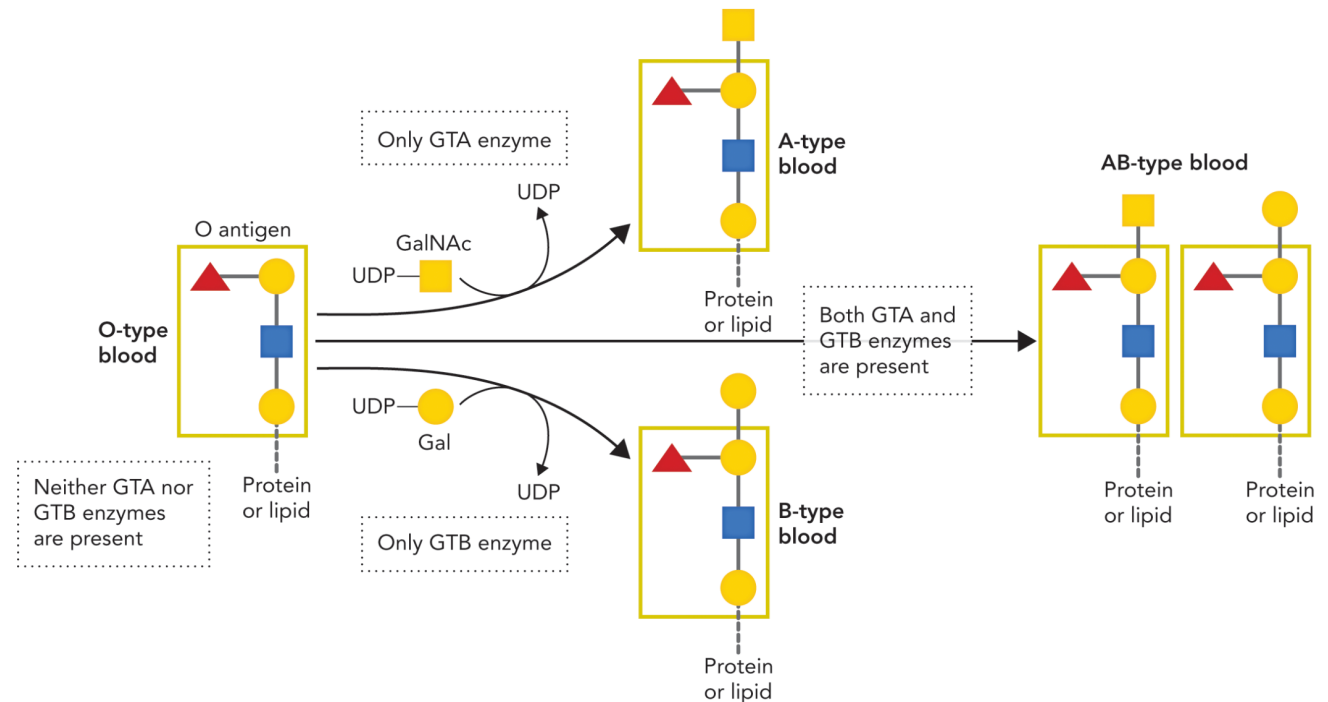
Glycosyltransferases are Membrane Proteins

- Glycosyltransferase enzymes contain N-terminal transmembrane domains targeting them to ER and Golgi membranes.
- Some are cleaved and secreted, expanding their functional range beyond the membrane.



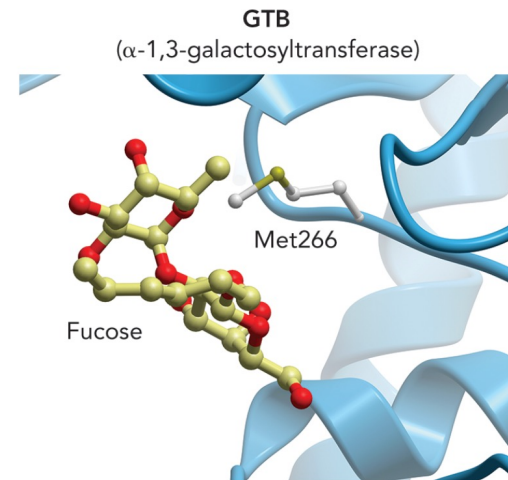
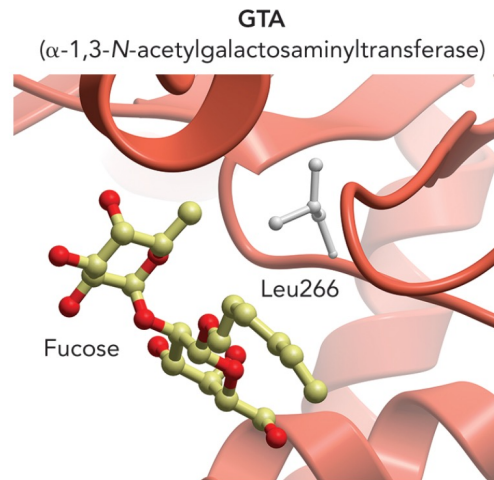
Glycans Account for Human ABO Blood Types

- All ABO glycans share the O antigen core (N-acetyllactosamine) present at $\sim 2 \times 10^6$ molecules per RBC.
- Addition of GalNAc yields A-type, Gal yields B-type, Gal and GalNAc yields AB type, and absence of both Gal and GalNAc yields O-type.



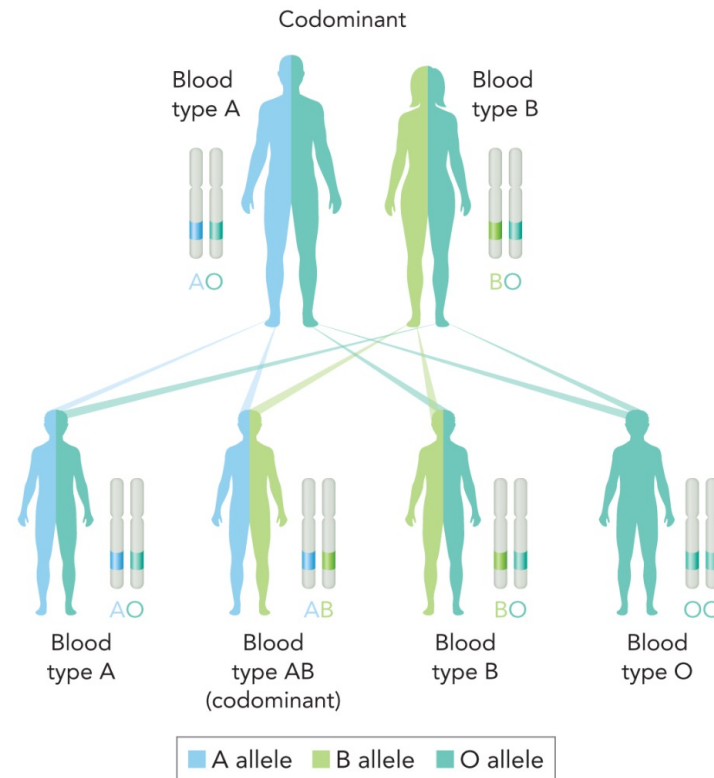
Active Site Specificity of GTA and GTB Enzymes

- The enzyme α -1,3-*N*-acetylgalactosaminyltransferase (GTA) attaches a GalNAc sugar moiety to the O antigen, whereas α -1,3-galactosyltransferase (GTB) attaches a Gal sugar moiety.
- The GTA and GTB enzymes differ by only four amino acids; residue 266 is either Leu (GTA) or Met (GTB).



ABO Inheritance is a Codominant Trait

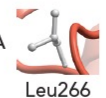
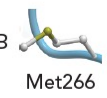
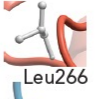
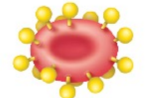
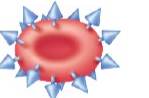
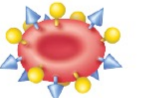




- ABO blood type follows codominant inheritance: GTA and GTB together yield AB phenotype.
- A × B parental crosses yield A, B, AB, or O progeny with 25% probability each, integrating genetics with biochemistry.



Molecular Basis for Blood Transfusions

- Red blood cells (RBCs) and plasma are carefully matched in blood transfusions to avoid RBC lysis and blood clotting; RBC preparations lack antibodies and plasma preparations lack RBCs.
- **Whole blood**: unseparated cells, **plasma**: liquid in blood w/o cells, **serum**: clotted plasma to remove fibrinogen, **RBCs**: packed red blood cells only.
- Individuals who have O-type blood are considered universal RBC donors, whereas individuals with AB-type blood are considered universal plasma donors.

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	Type A	Type B	Type AB	Type O
Glycosyl-transferase	GTA  Leu266	GTB  Met266	GTA  Leu266 GTB  Met266	Does not contain functional GTA and GTB enzymes
RBCs	Antigen A 	Antigen B 	Antigens A and B 	Neither antigen A nor B 
Can <i>donate</i> RBCs to:	Types A, AB	Types B, AB	Type AB only	Types O, A, B, AB <div style="border: 1px dashed black; padding: 2px;">Type O is the universal RBC donor</div>
Can <i>receive</i> RBCs from:	Types A, O	Types B, O	Types A, B, AB, O	Type O
Plasma	Anti-B antibodies 	Anti-A antibodies 	Neither anti-A nor anti-B antibodies	Both anti-A and anti-B antibodies 
Can <i>donate</i> plasma to:	Types A, O	Types B, O	Types A, B, AB, O <div style="border: 1px dashed black; padding: 2px;">Type AB is the universal plasma donor</div>	Type O
Can <i>receive</i> plasma from:	Types A, AB	Types B, AB	Types AB only	Types A, B, AB, O



Key Concepts to Guide Your Learning

- Lectins are glycan binding proteins that mediate : (1) *intrinsic* glycoconjugate binding between glycans and lectins, and (2) *extrinsic* glycoconjugate binding between glycans and lectins on human cells and pathogen cells.
- Glycan attachments to glycoproteins are either the amide nitrogen atom of asparagine, leading to the generation of N-linked oligosaccharides, or the oxygen atom of serine or threonine residues, resulting in O-linked oligosaccharides.
- The GTA (A-type blood) and GTB (B-type blood) glycosyltransferase enzyme variants differ by only a few amino acids, yet they account for the differential addition of GalNAc or Gal to the O-antigen blood group glycan on erythrocytes.
- Individuals with O-type blood are considered universal RBC donors because their RBCs do not contain either the A-type or B-type glycoconjugates, whereas AB individuals are considered universal plasma donors because their plasma does not contain antibodies that recognize either A-type or B-type glycoconjugates.

