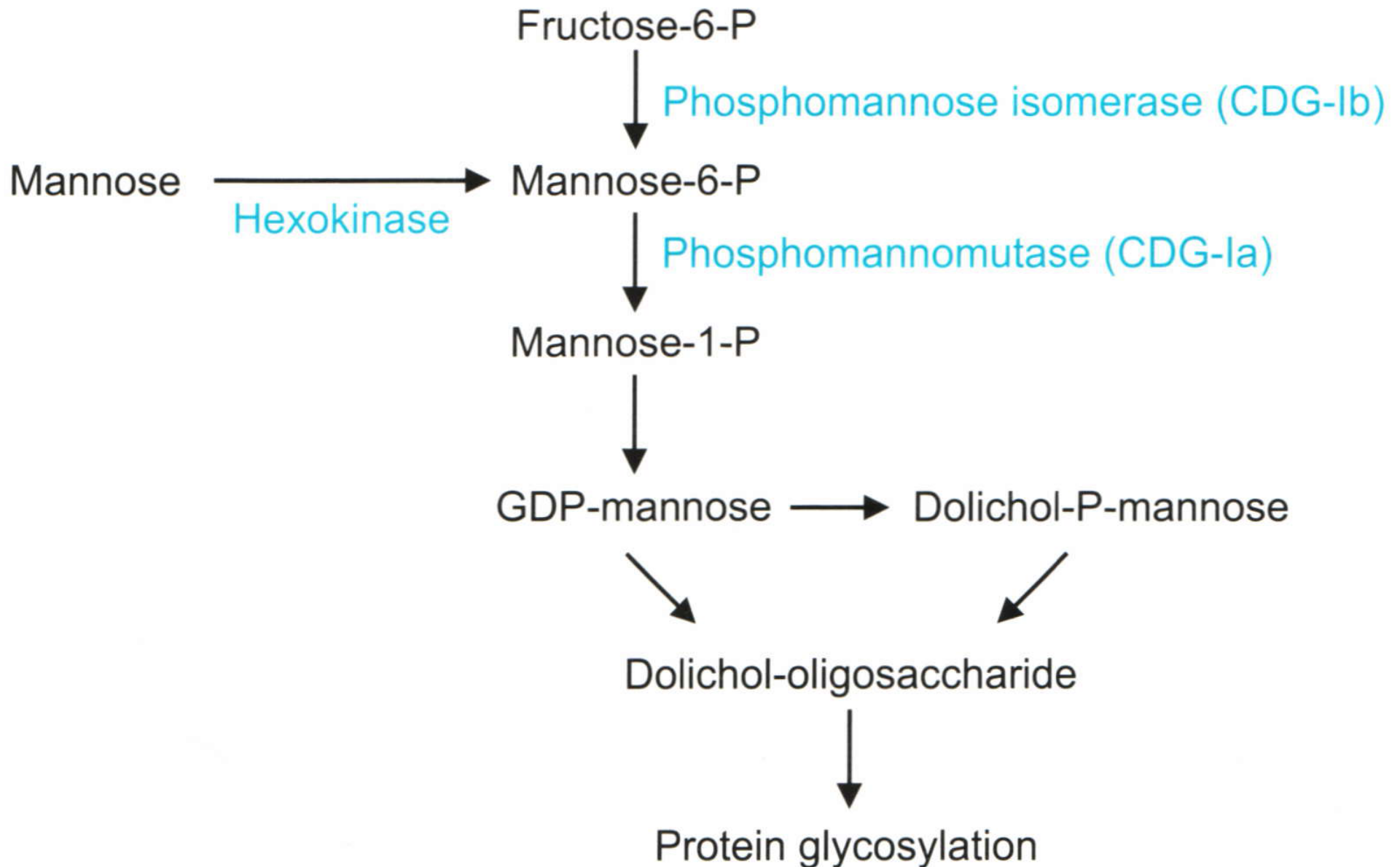


Incorporation of Mannose into Glycoproteins



Von Willebrand Factor Deficiency

Epithelial cells

Endothelial cells

Terminal sugars on
von Willebrand factor

Wild-type

GalNAc-transferase

von Willebrand factor

NeuAc α 2-3Gal β 1-4GlcNAc-

Misexpression

von Willebrand
disease

von Willebrand factor

+

GalNAc-transferase

NeuAc α 2-3Gal β 1-4GlcNAc-

GalNAc β 1

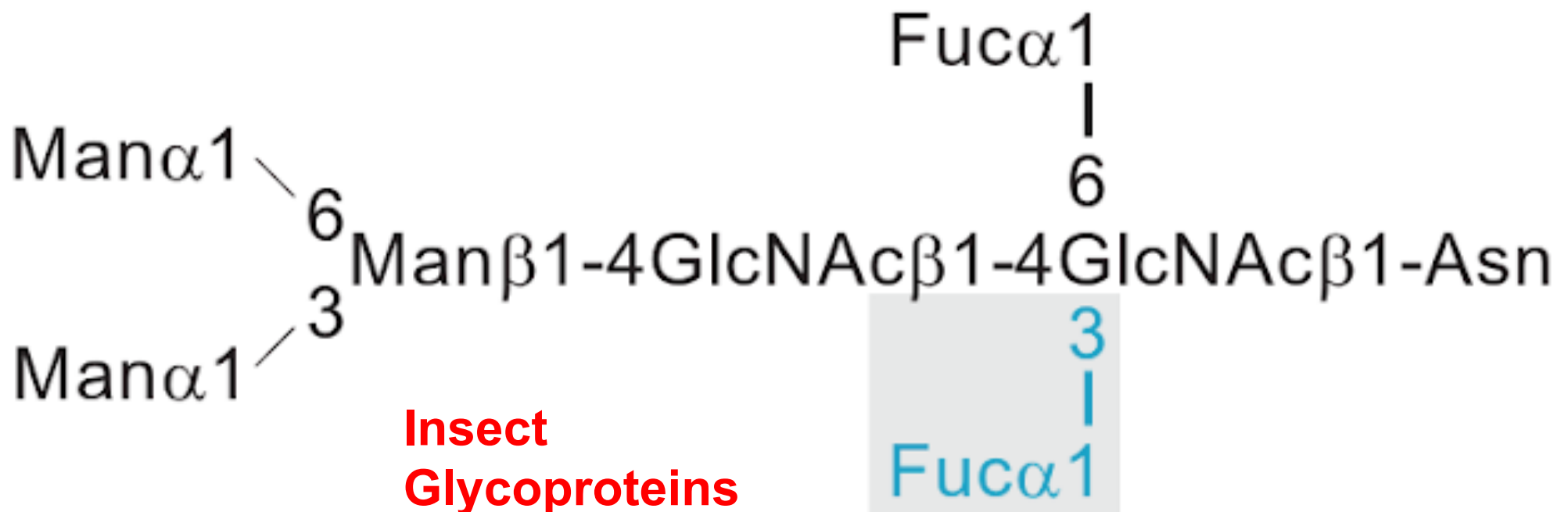
4

Antigenic Non-Human Carbohydrate Fragments

NeuAc α 2-3Gal β 1-4GlcNAc-

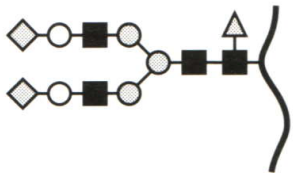
Gal α 1-3Gal β 1-4GlcNAc-

**Other
Primates**

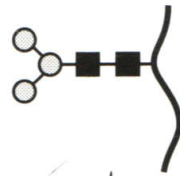


Expression of Recombinant N-Linked Glycoproteins

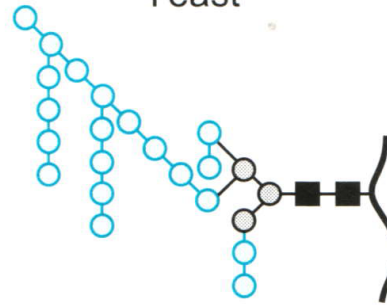
Mammalian cells
(CHO and BHK)



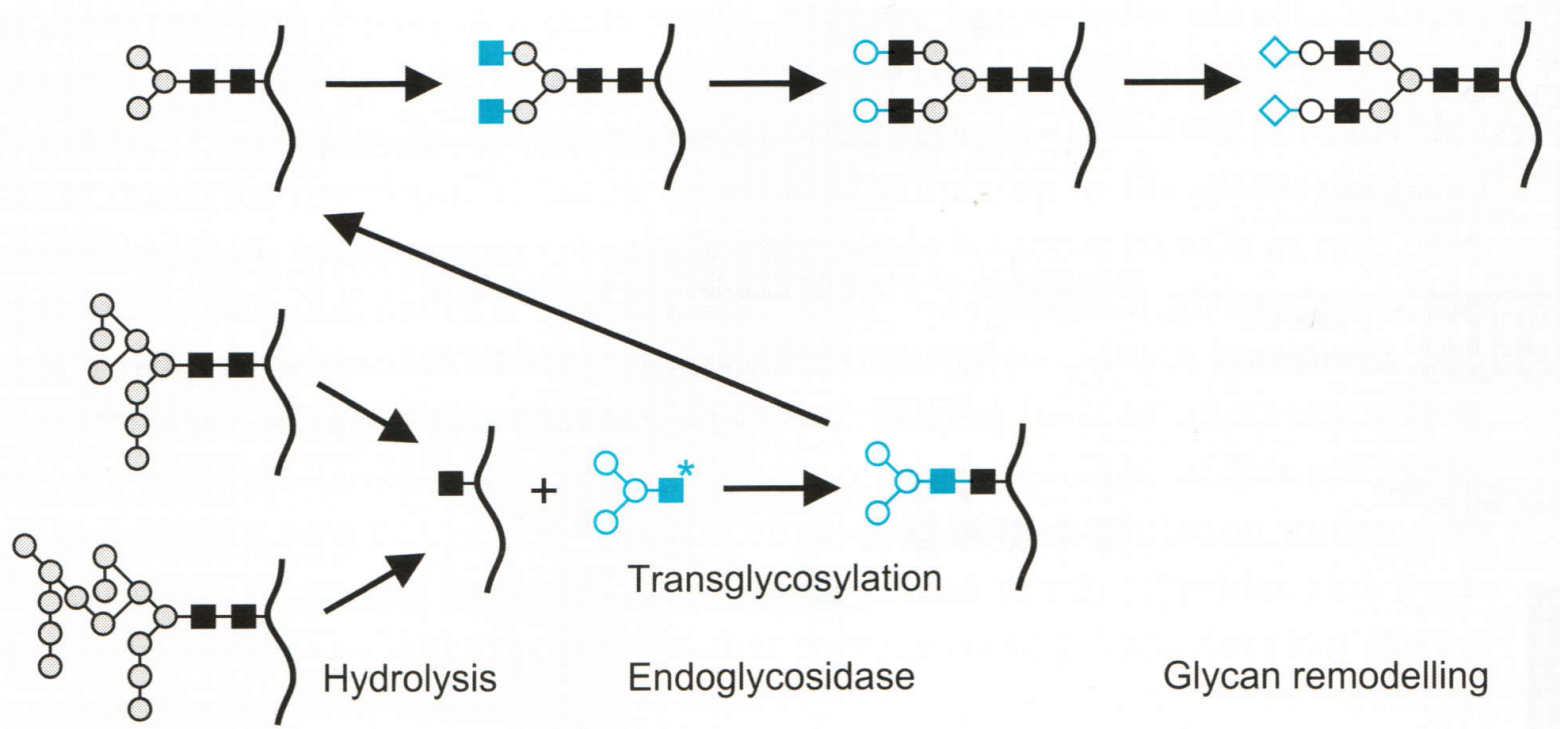
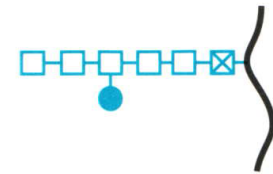
Insect cells



Yeast

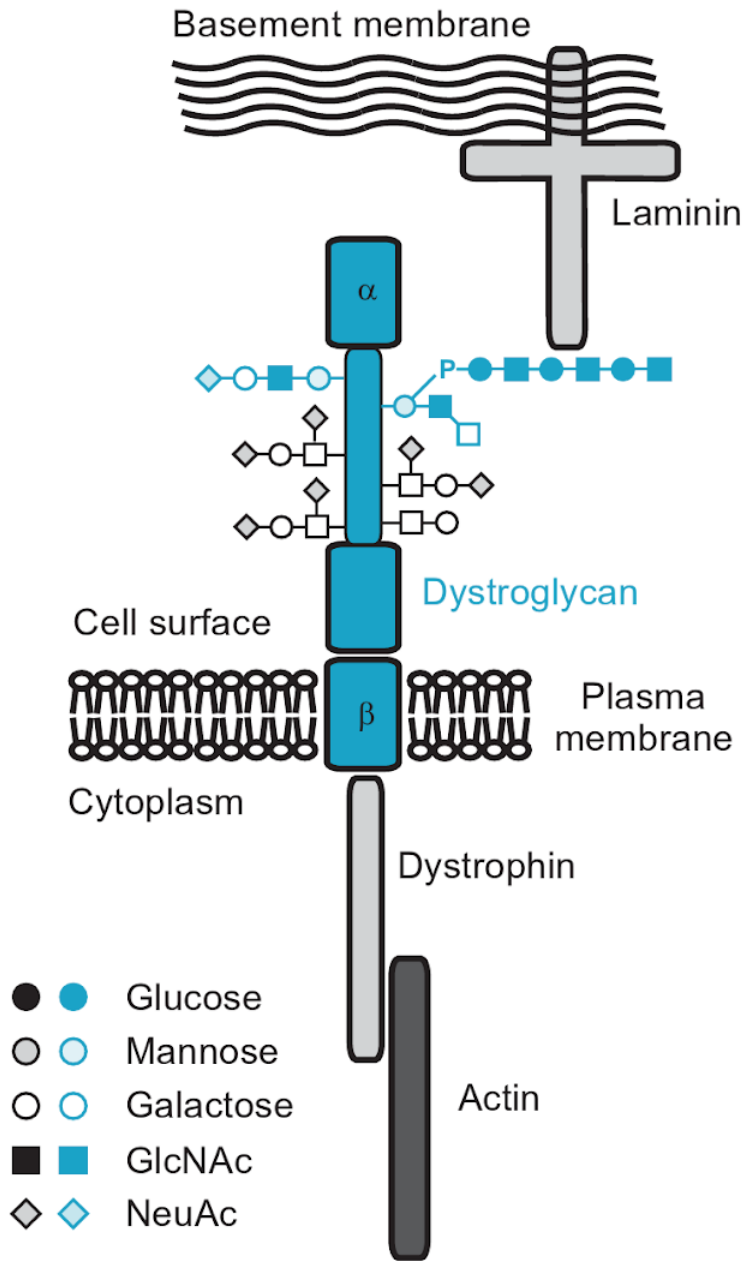


Bacteria



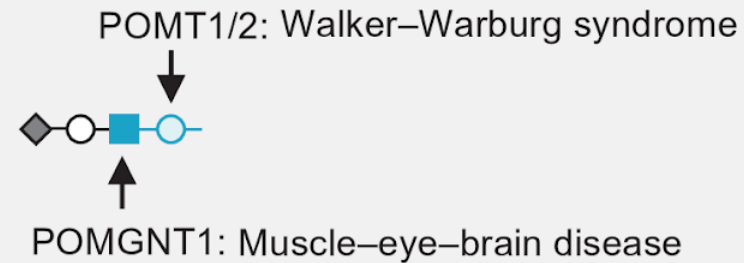
- ● Glucose
- ○ Mannose
- ○ Galactose
- ■ GlcNAc
- □ GalNAc
- ⊠ ⊠ Bacillosamine
- ◇ ◇ NeuAc
- △ △ Fucose

Aberrant α -Dystroglycan in Congenital Muscular Dystrophy

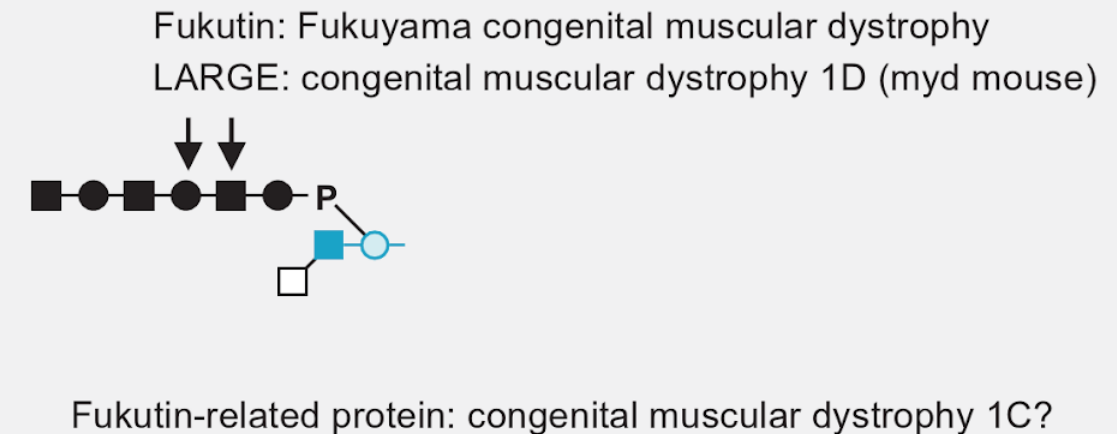


Dystrophy-associated glycosyltransferases

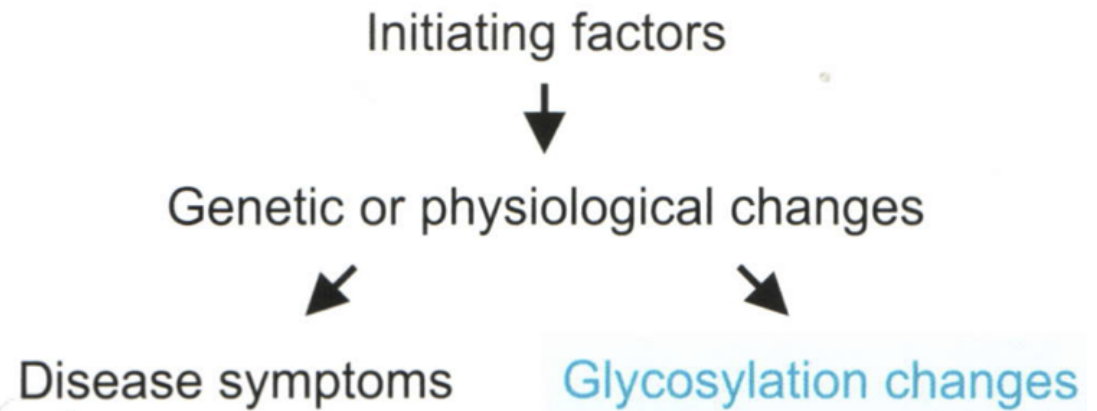
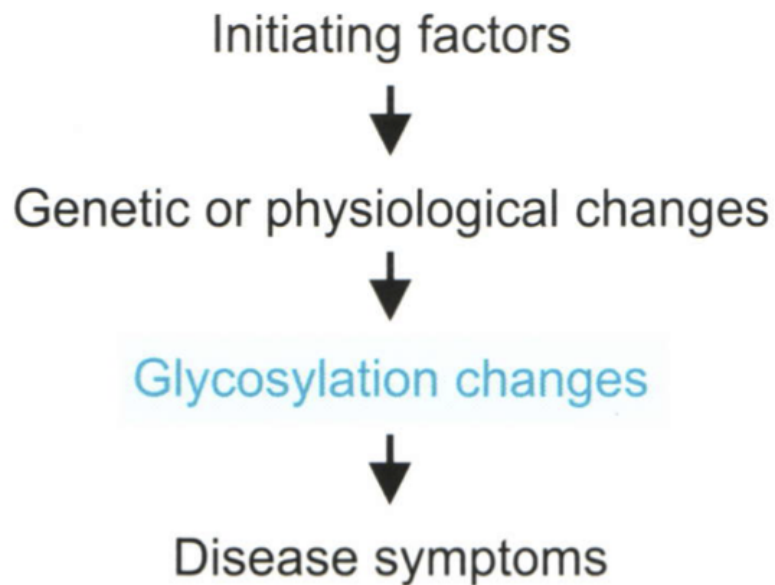
Synthesis of O-mannose core



Synthesis of phosphate-linked extensions

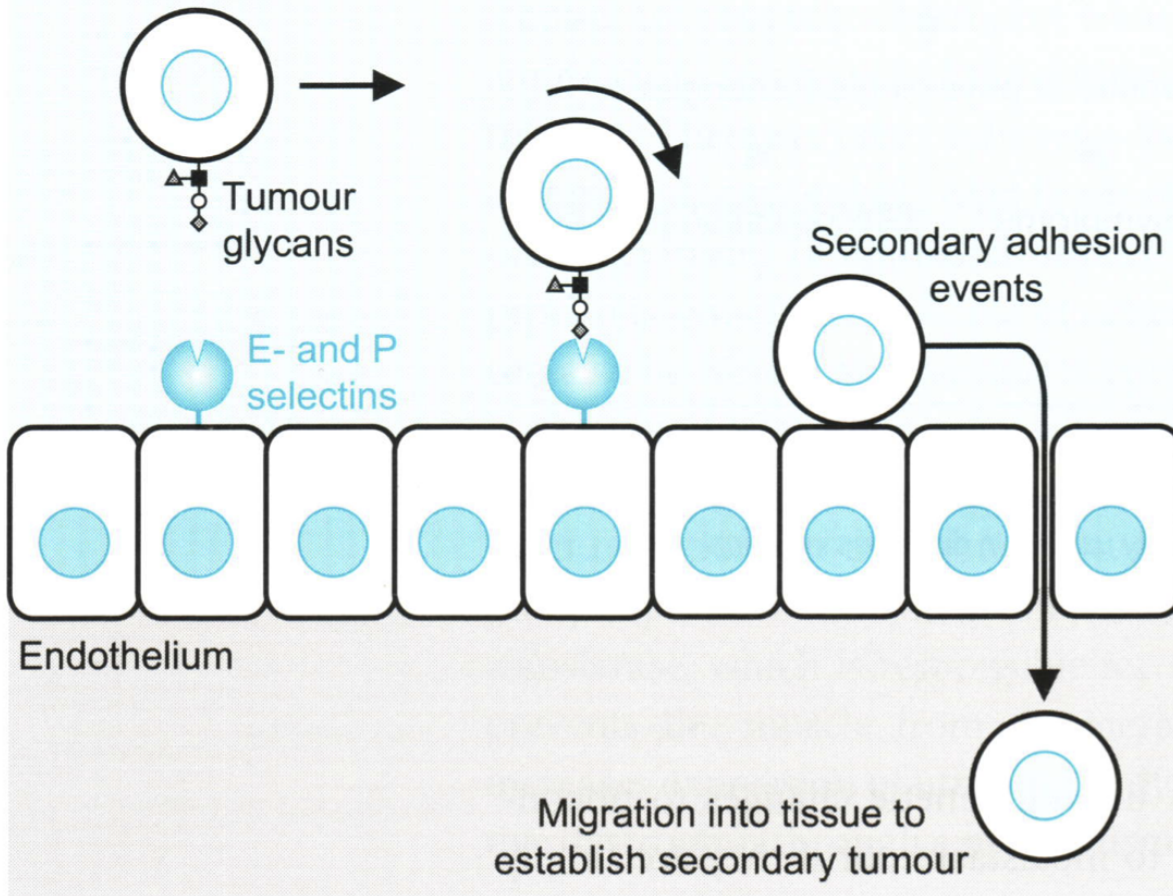


Glycosylation Changes in Cancer Development

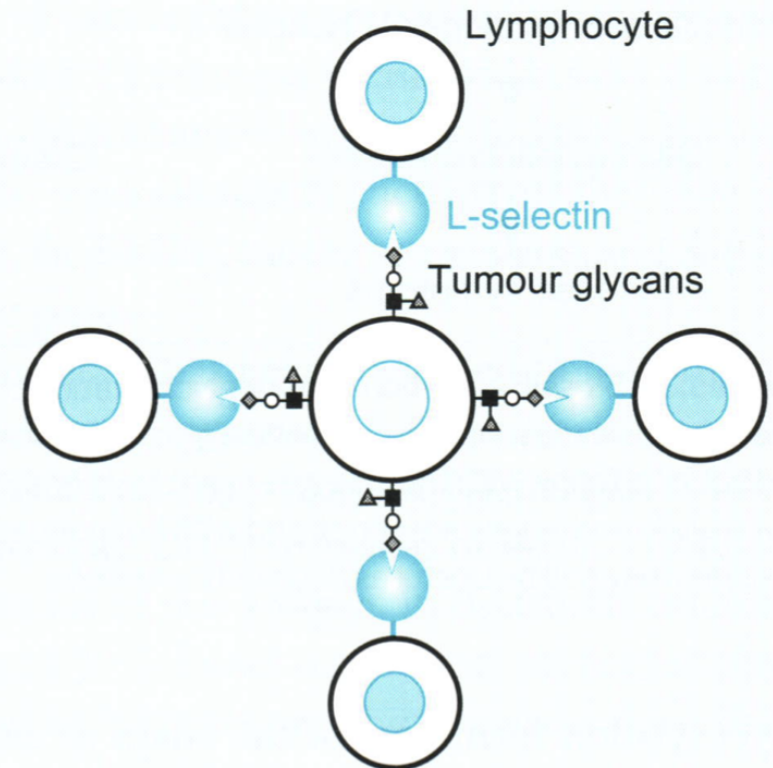


Role of Sialylated Glycans in Metastasis

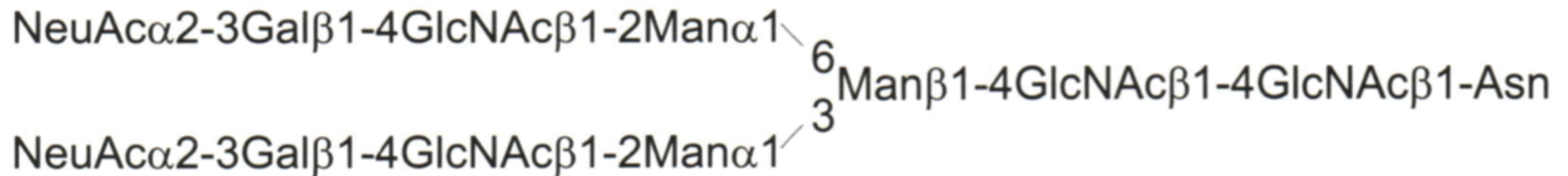
Model 1



Model 2

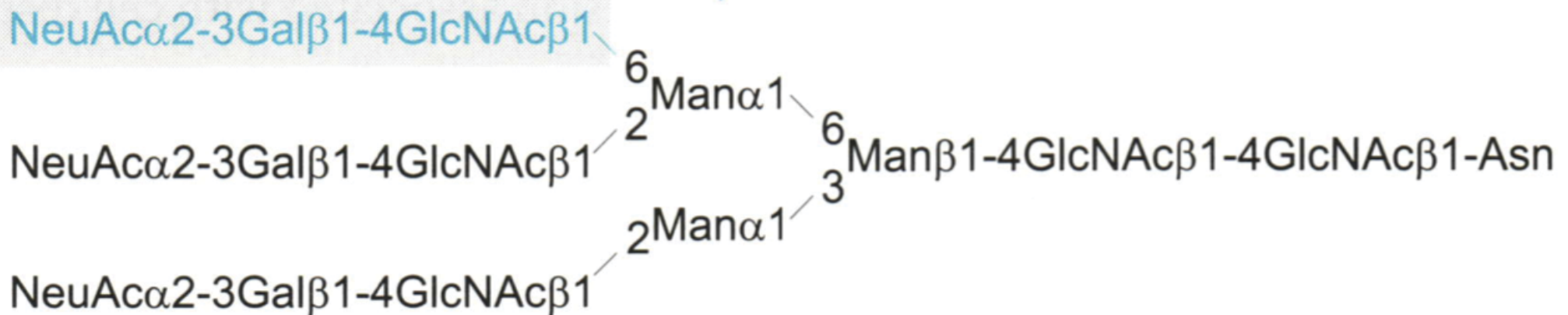


*Increased Glycan Branching in Tumor Cells
due to Increased GlcNAc-Transferase V
Activity Correlates with Metastatic Potential*

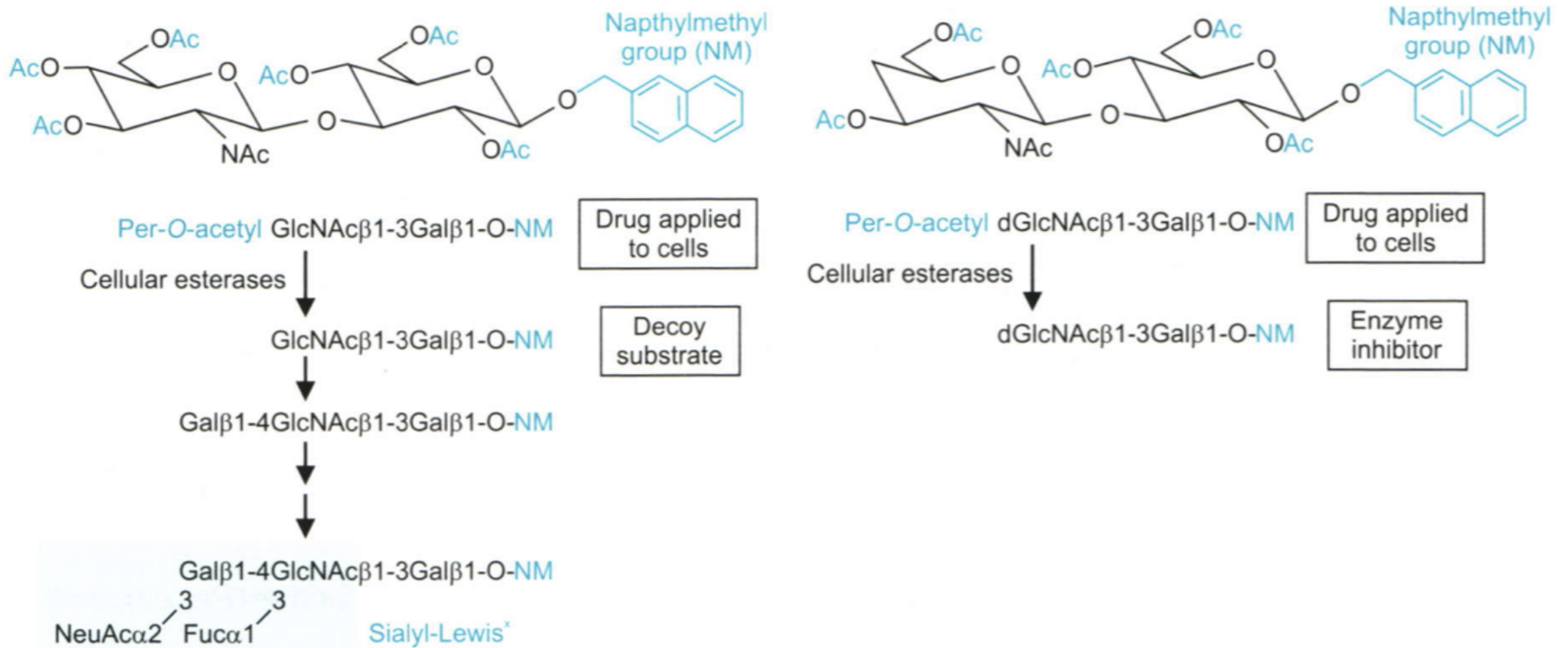


Branching of 1,6 arm

GlcNAc-transferase V

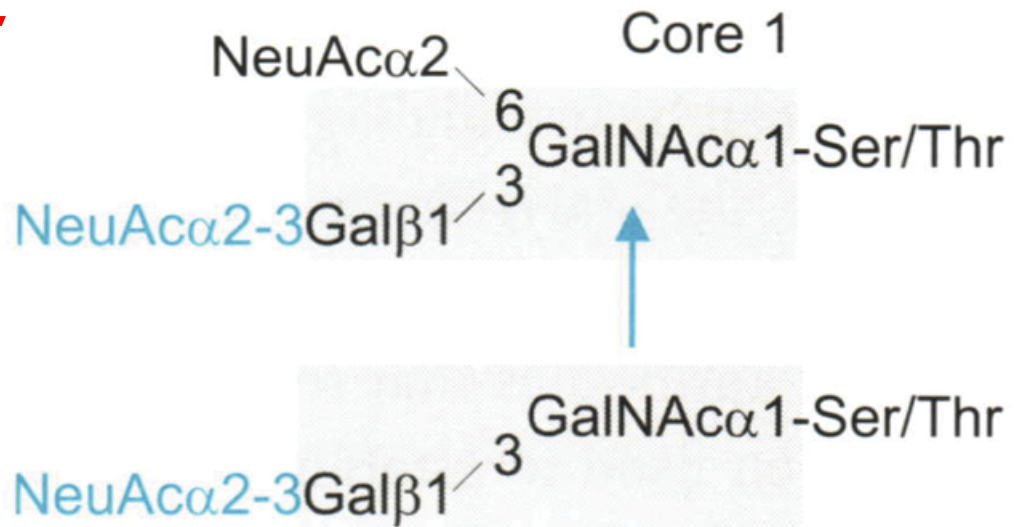


Therapeutics to Block Selectin-Glycan Interactions

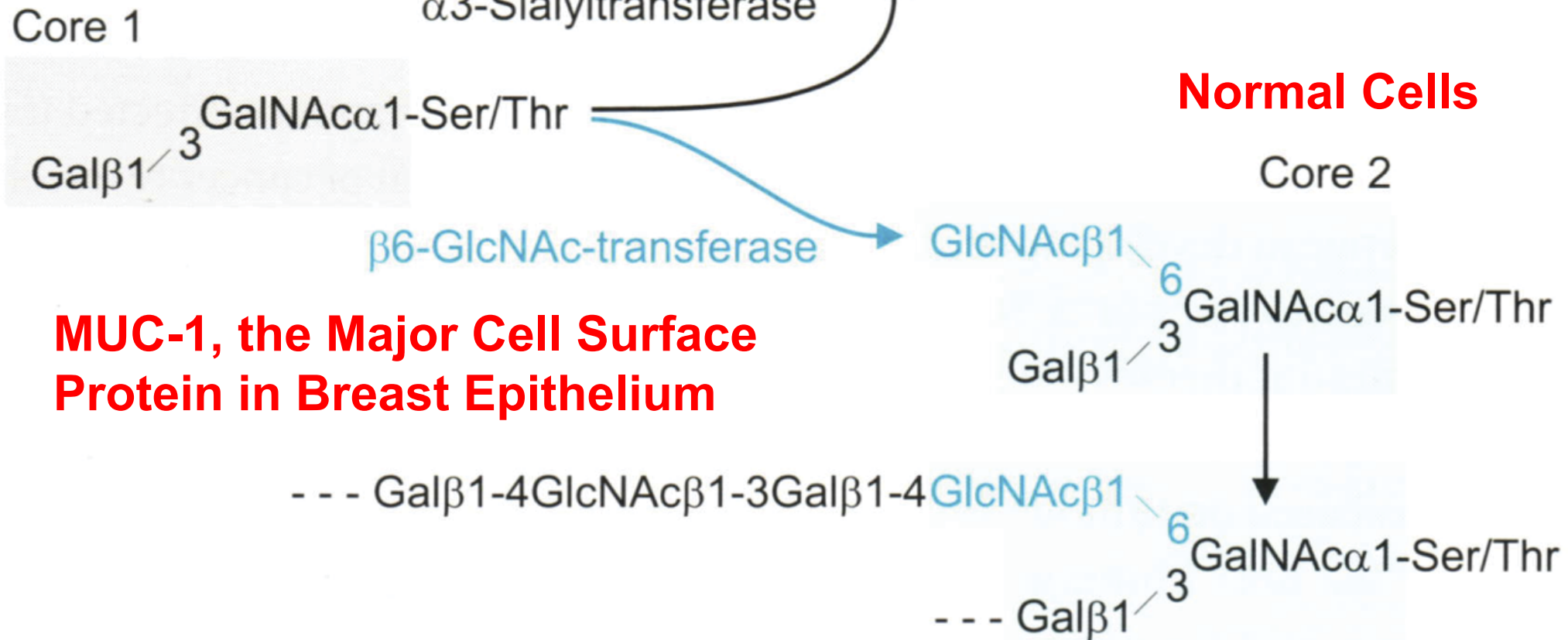


Competition between Sialyl- & GlcNAc-Transferases May Lead to New Cancer Immunotherapies

Breast Cancer

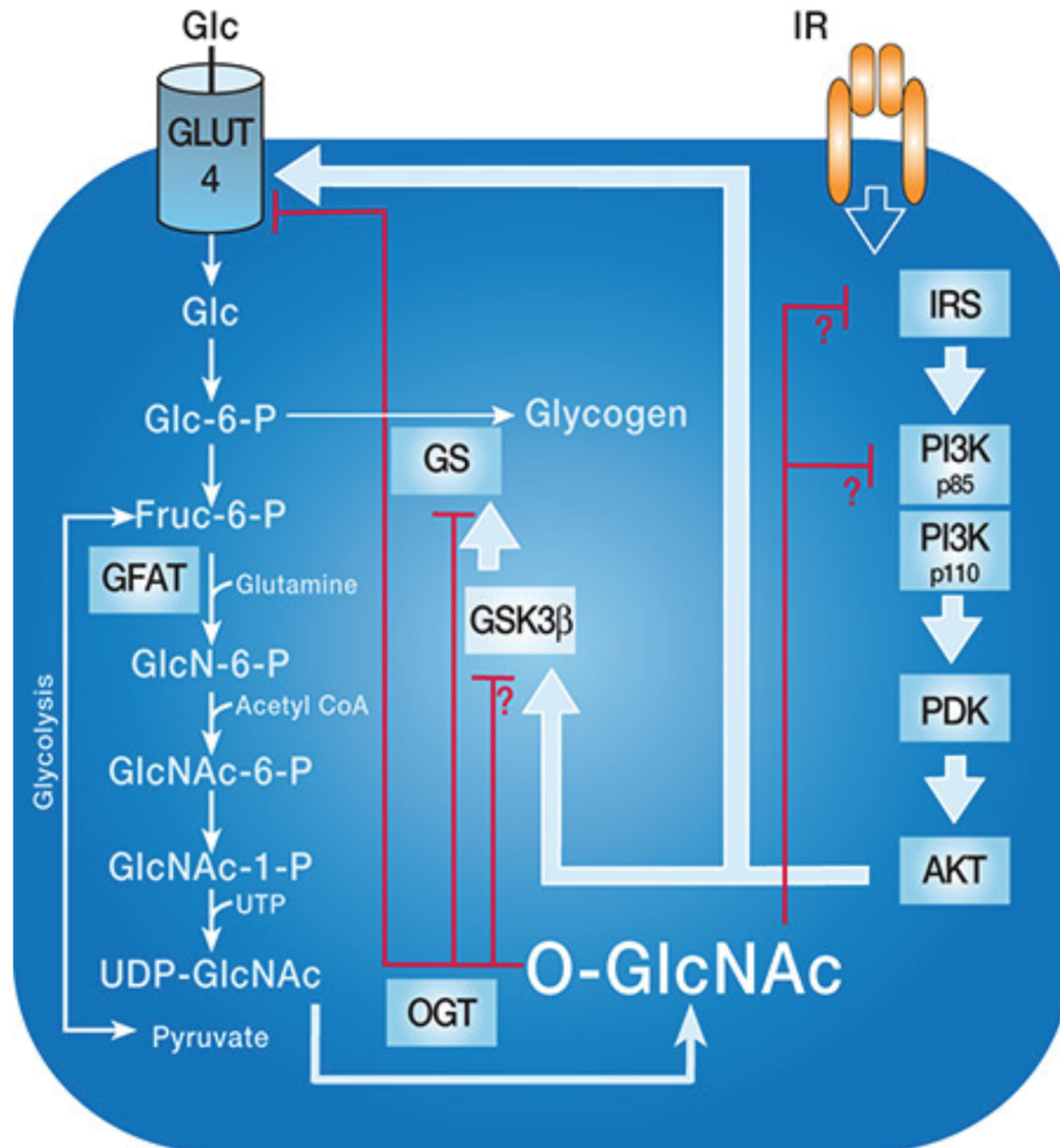


Normal Cells

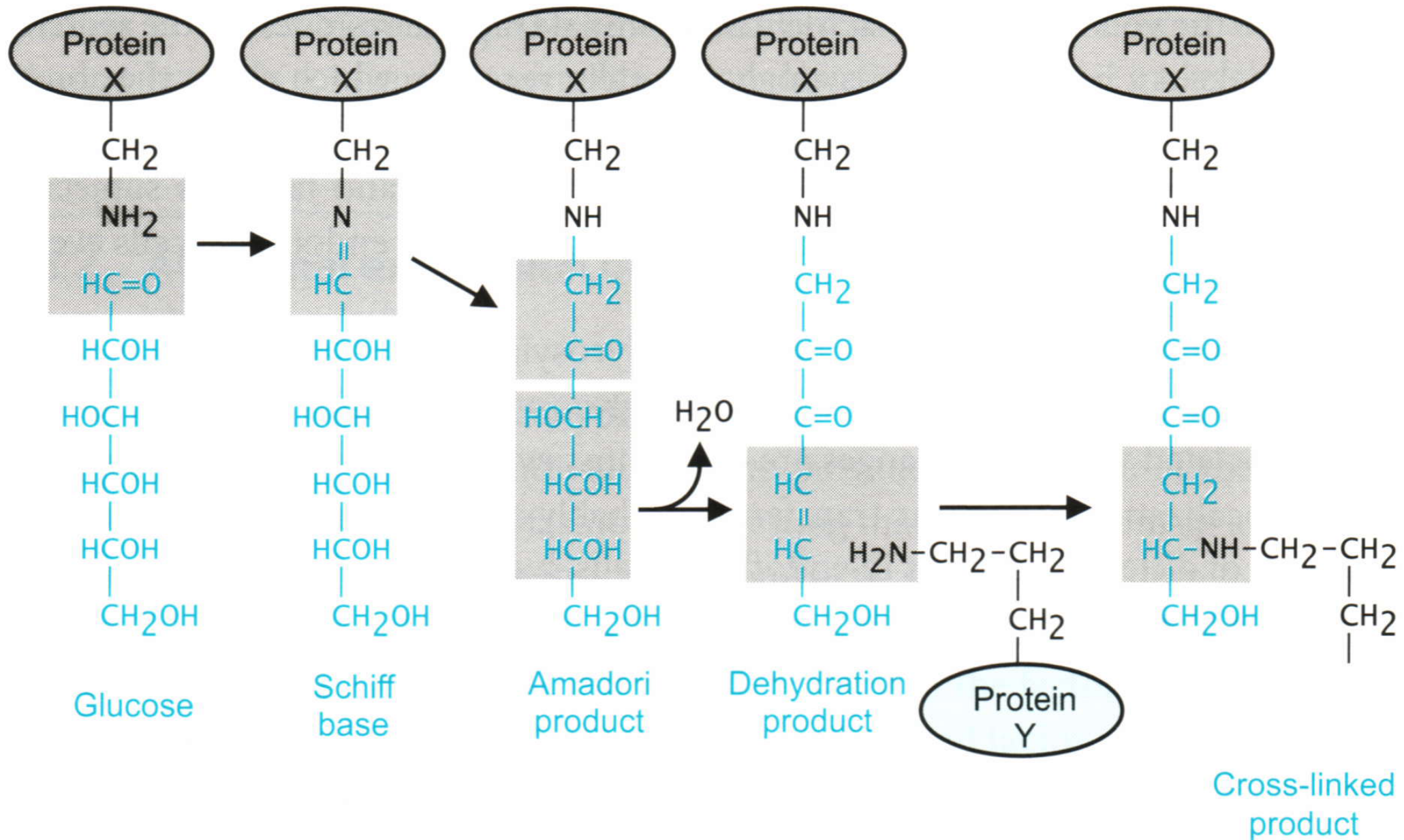


MUC-1, the Major Cell Surface Protein in Breast Epithelium

Elevated O-GlcNAc Blocks Insulin Signalling

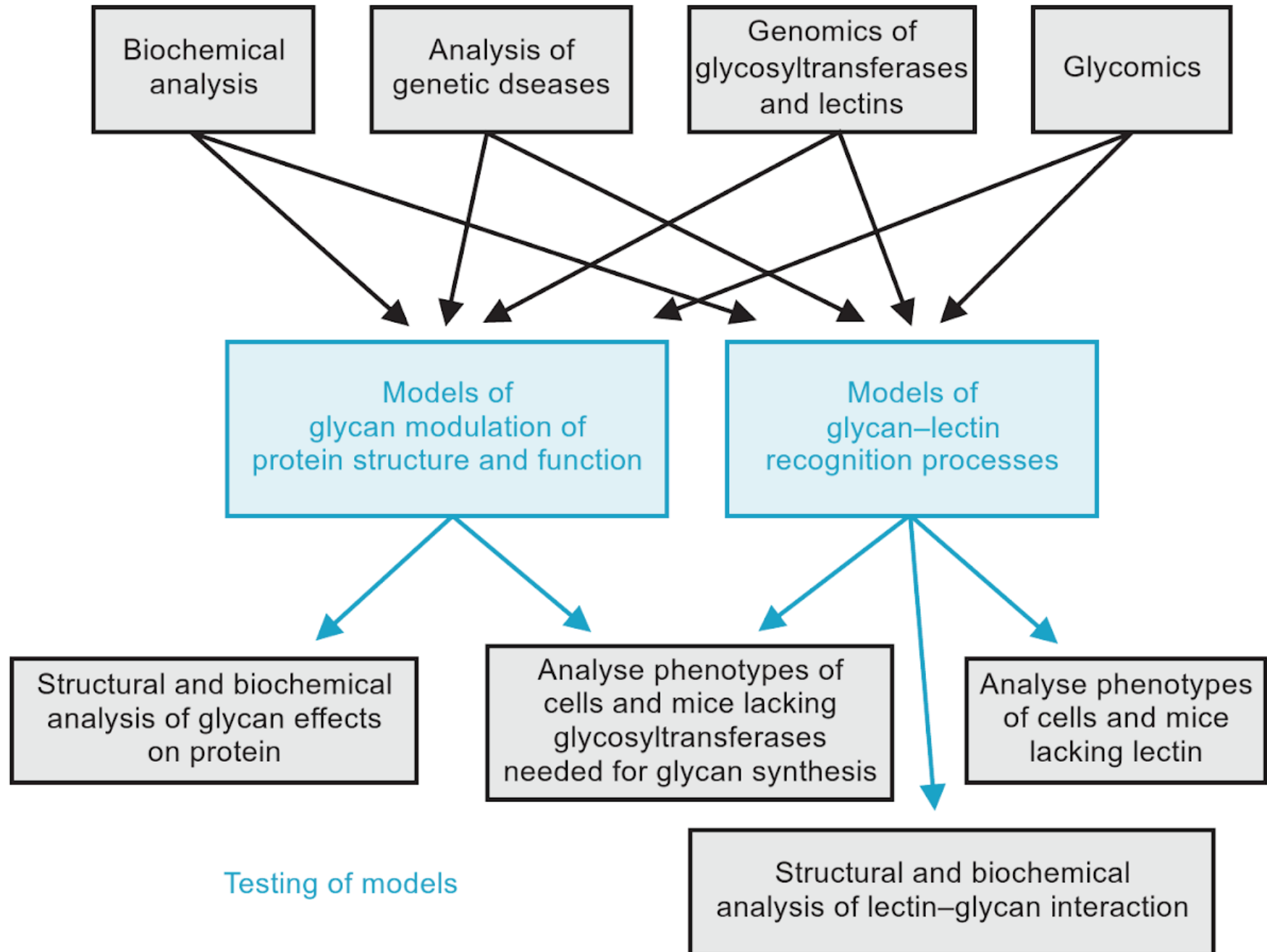


Chemical Glycation of Proteins in Diabetes



Approaches to Understanding Glycans & Lectins

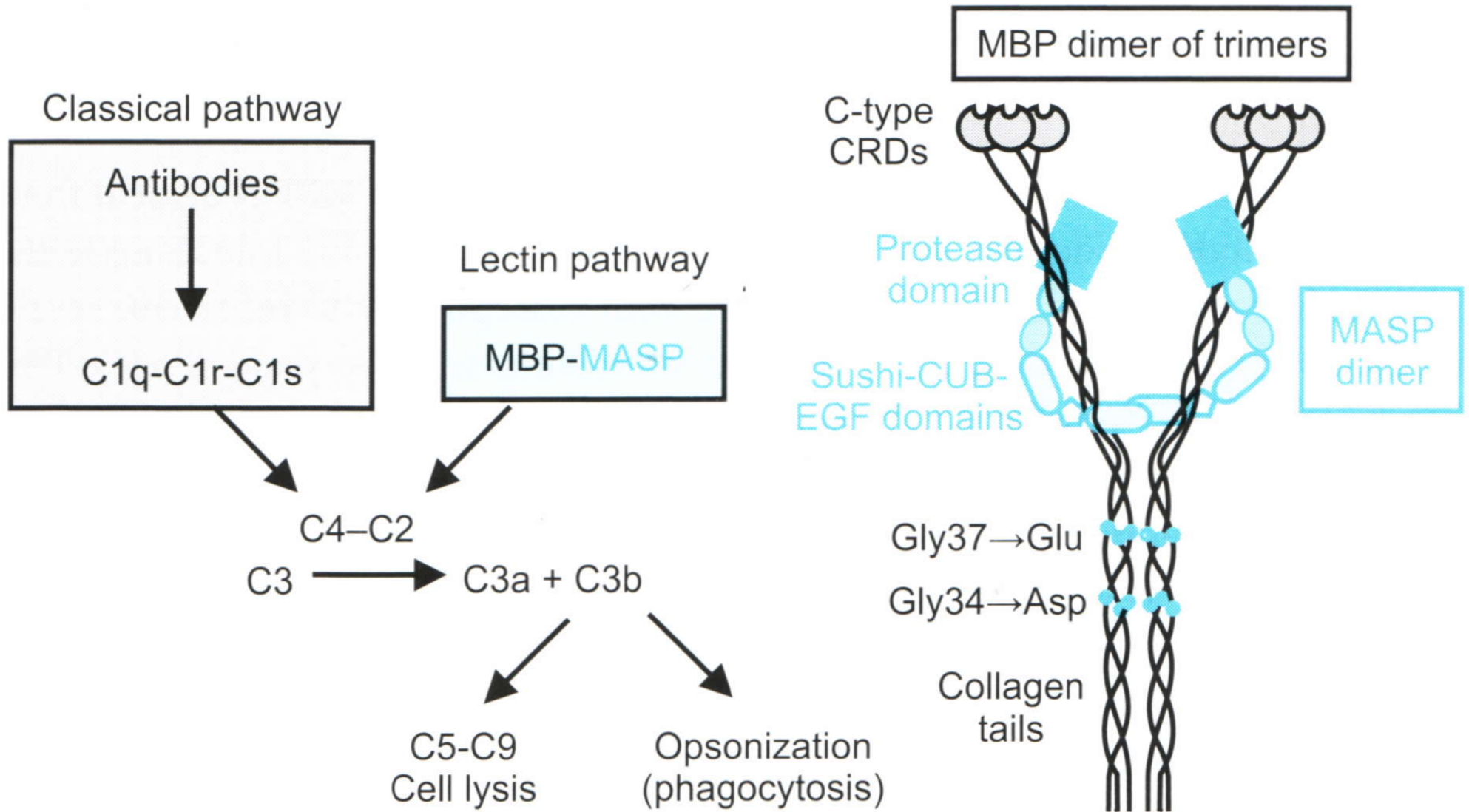
Generation of models



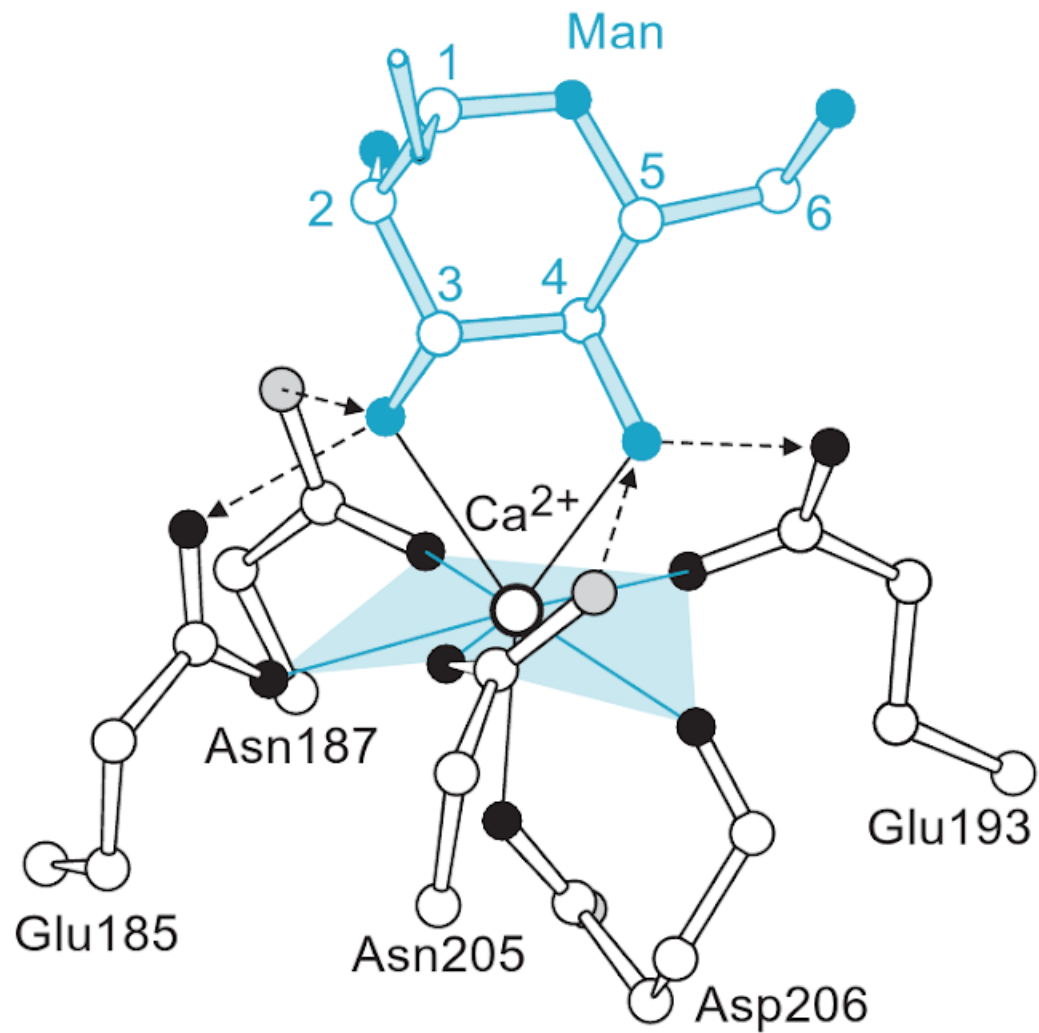
Carbohydrate Recognition Domains (CRDs)

Type	Structure	Typical ligands	Examples of functions
Calnexin	β -sandwich	Glc_1Man_8	Protein sorting in the endoplasmic reticulum
M-type	α -helical barrel	Man_8	Endoplasmic reticulum-associated protein degradation
L-type	β -sandwich	Man_{5-9}	Protein sorting in the endoplasmic reticulum
P-type	Unique β -rich structure	Man 6-phosphate	Protein sorting post-Golgi
C-type	Unique mixed α/β structure	Various	Cell adhesion (selectins) Glycoprotein clearance Innate immunity (collectins)
Galectins	β -sandwich	b-galactosides	Glycan cross-linking at the cell surface
I-type	Immunoglobulin superfamily	Sialic acid	Cell adhesion (siglecs)
R-type	β -trefoil	Various	Enzyme targeting Glycoprotein hormone turnover

Mannose Binding Protein in Innate Immunity



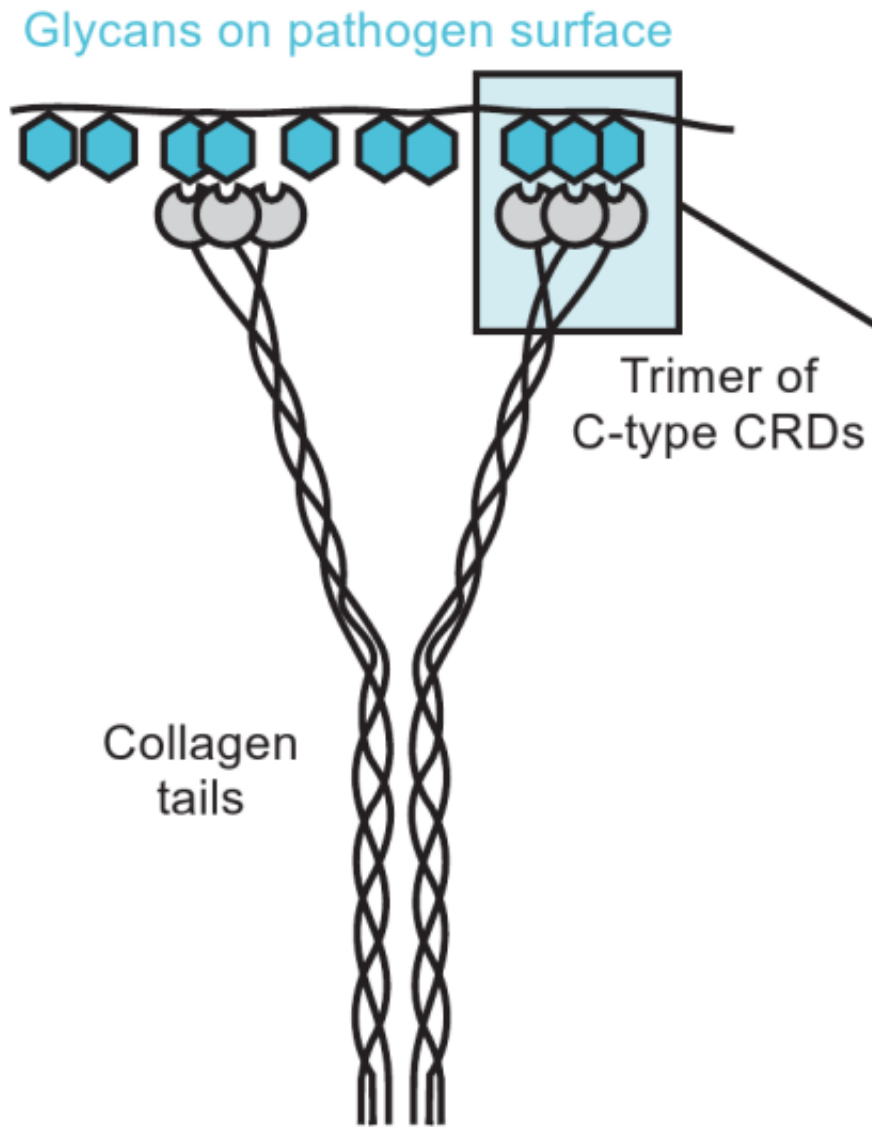
MBP with Bound Oligosaccharide



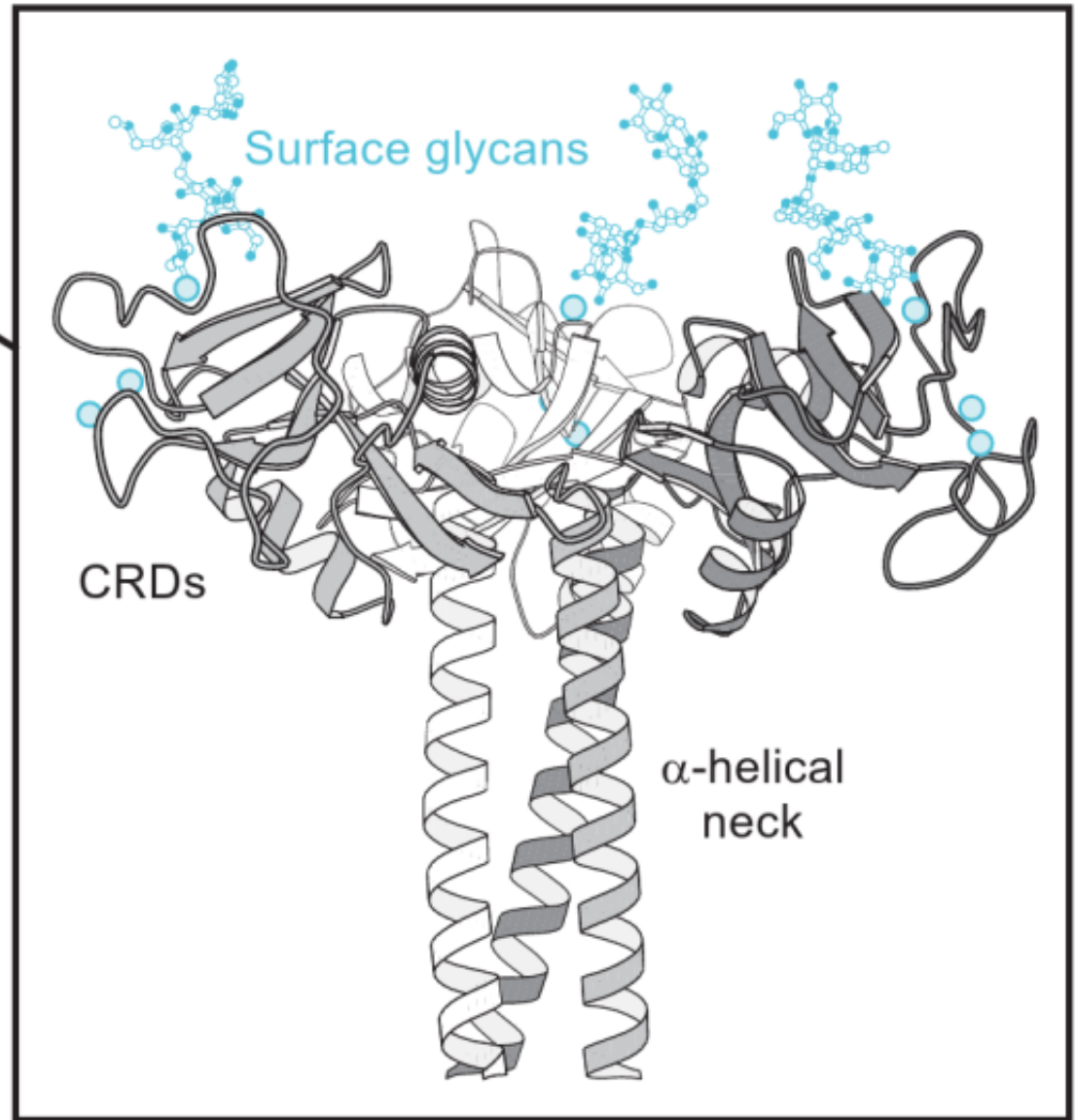
○ ○ C ● ● O ● ● N O Ca²⁺

PDB: 2MSB

Structure of Mannose Binding Proteins (MBPs)

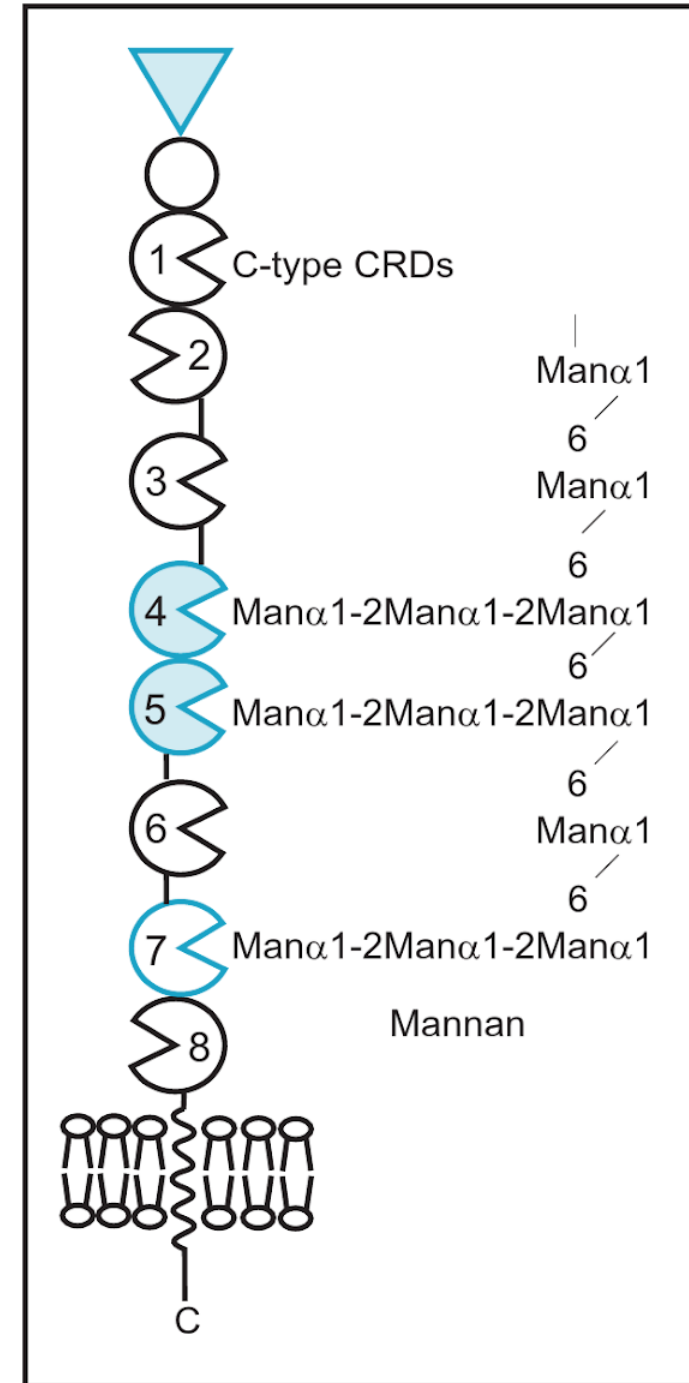
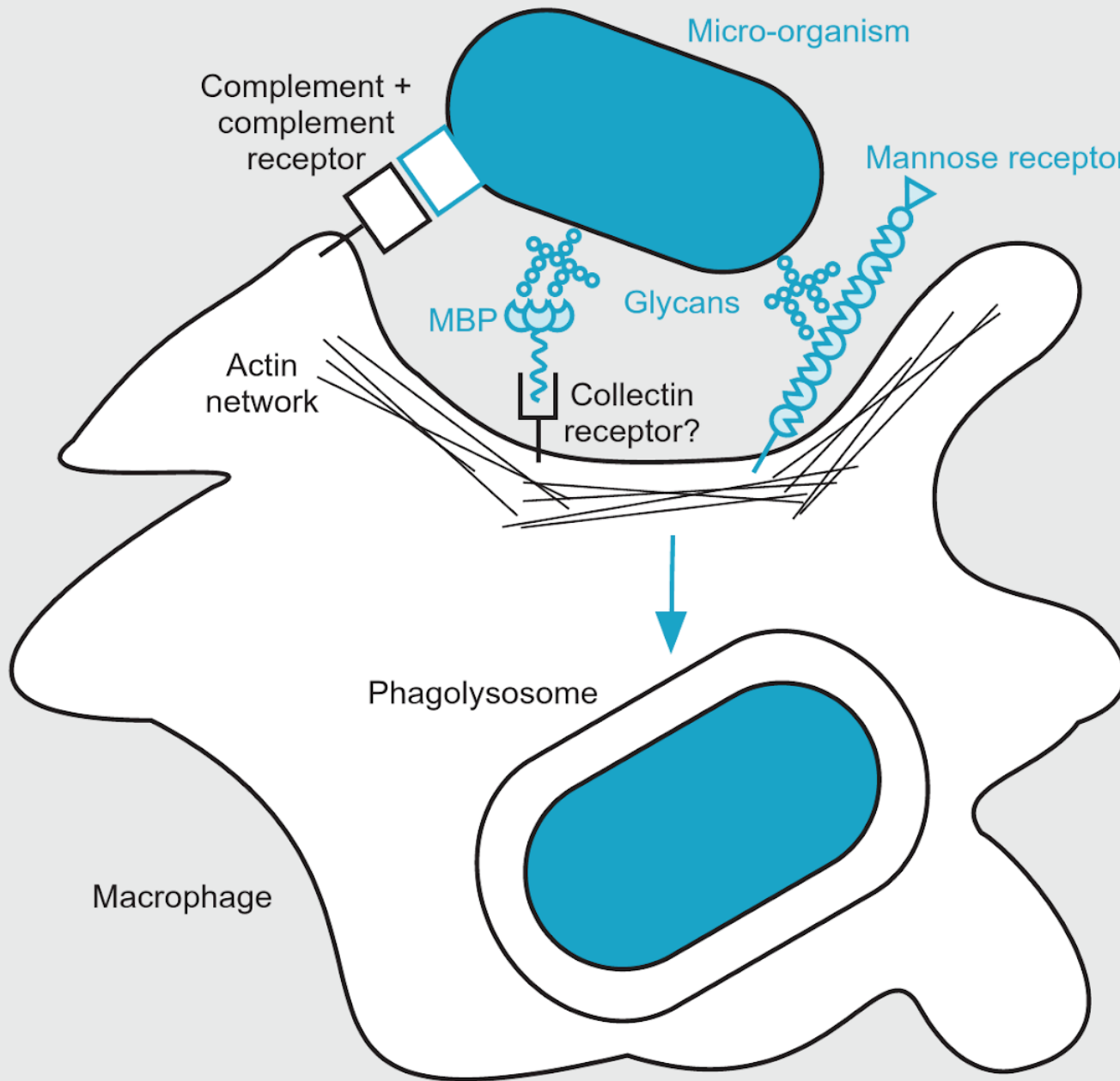


Binding at Cell Surface

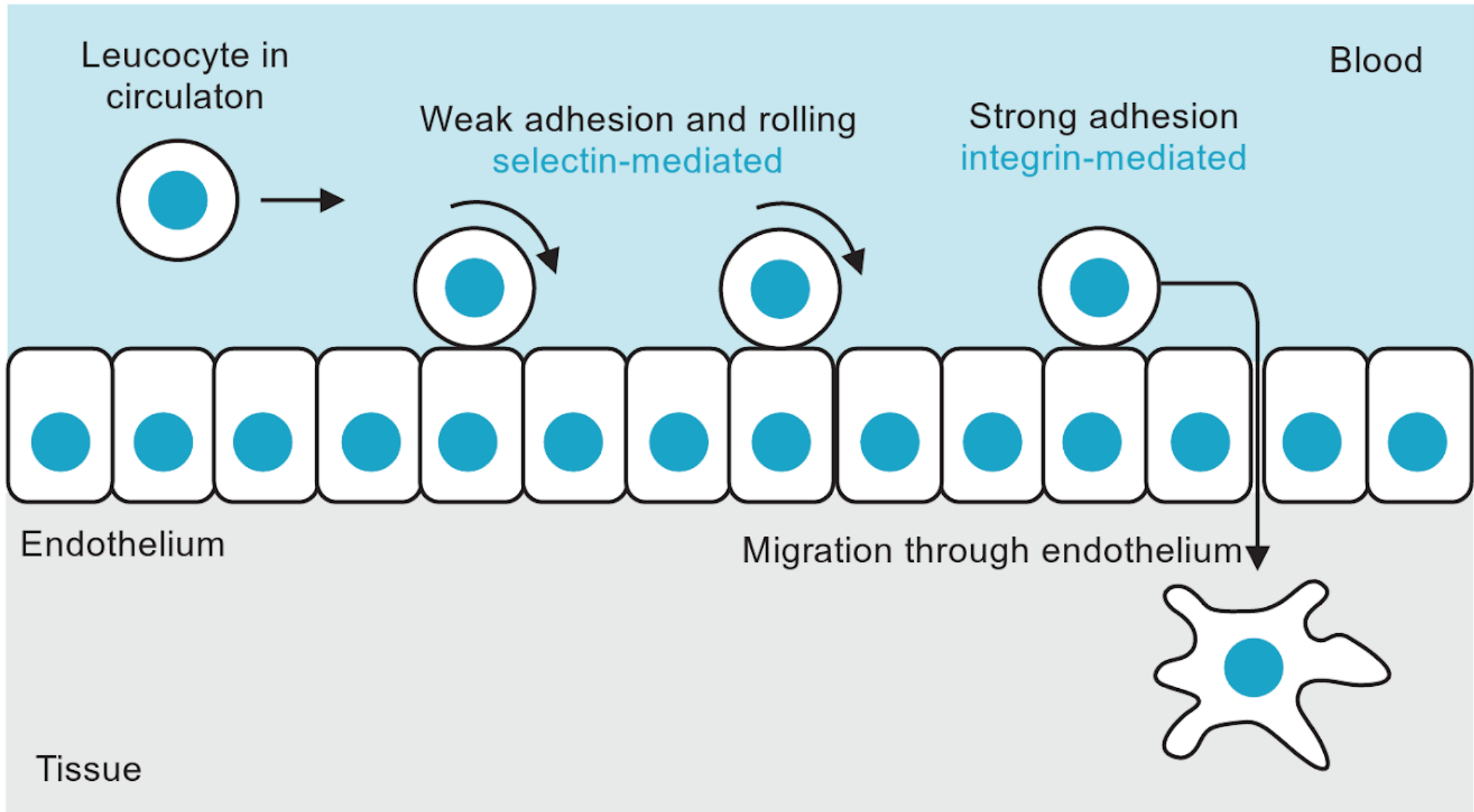


Trimeric CRD Cluster

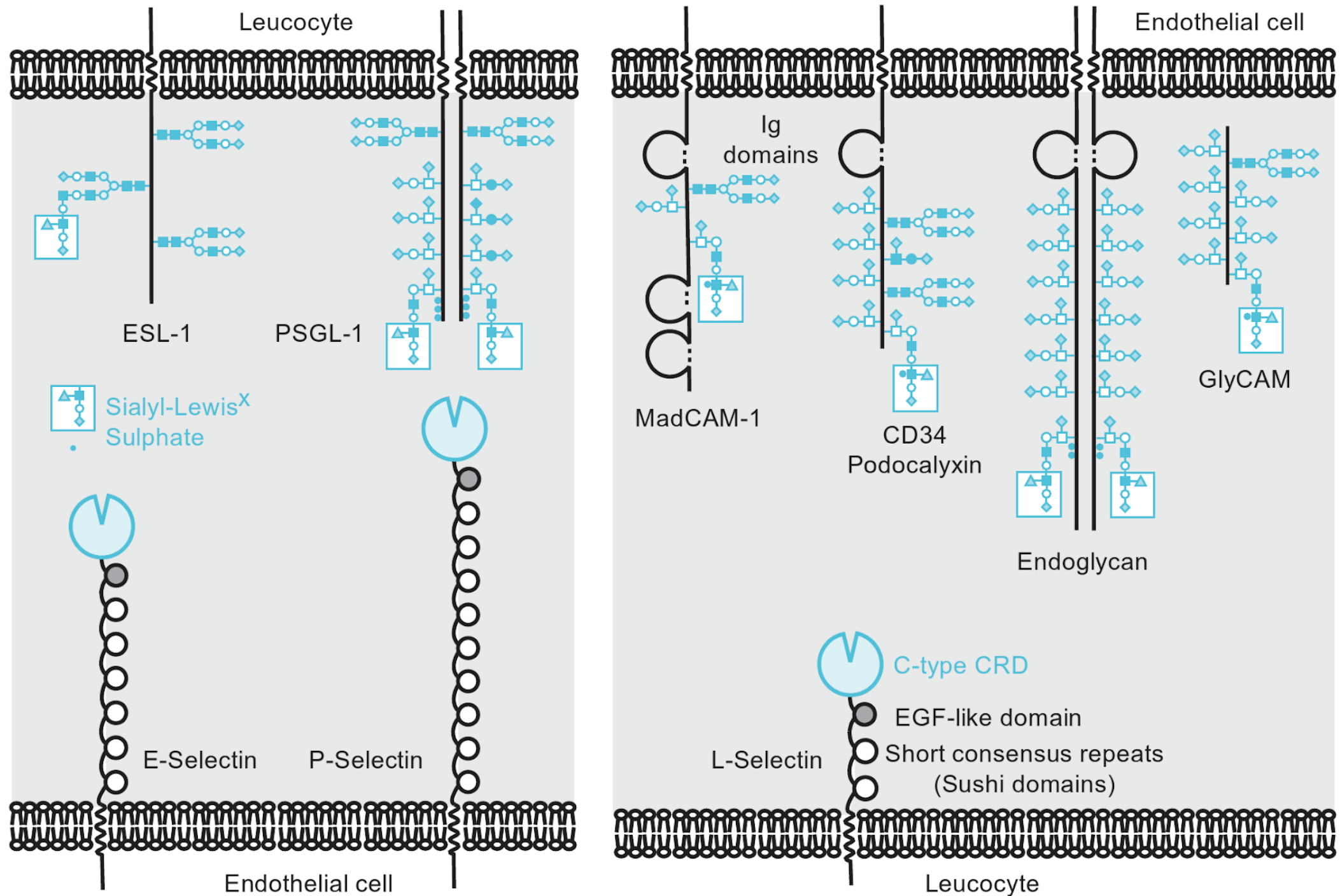
Receptor Mediated Phagocytosis by Macrophages



Leucocyte Interaction with Endothelial Cells

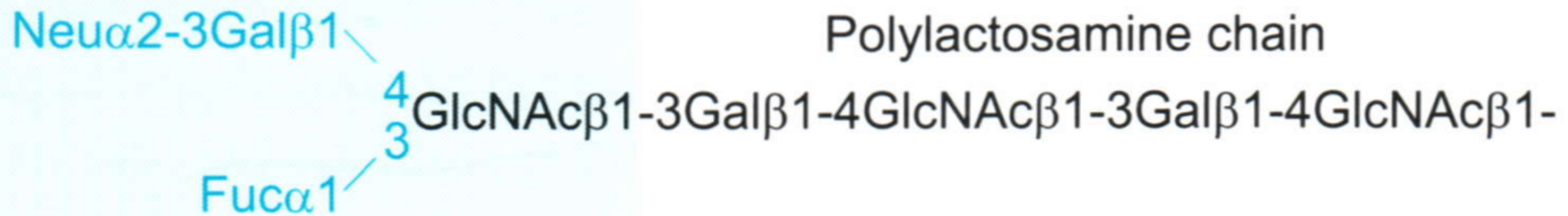


Selectins and Some Glycoprotein Ligands



Structures of Lewis^x Ligands for Selectins

Sialyl-Lewis^x



Sialyl-Lewis^a



6-Sulphosialyl-Lewis^x

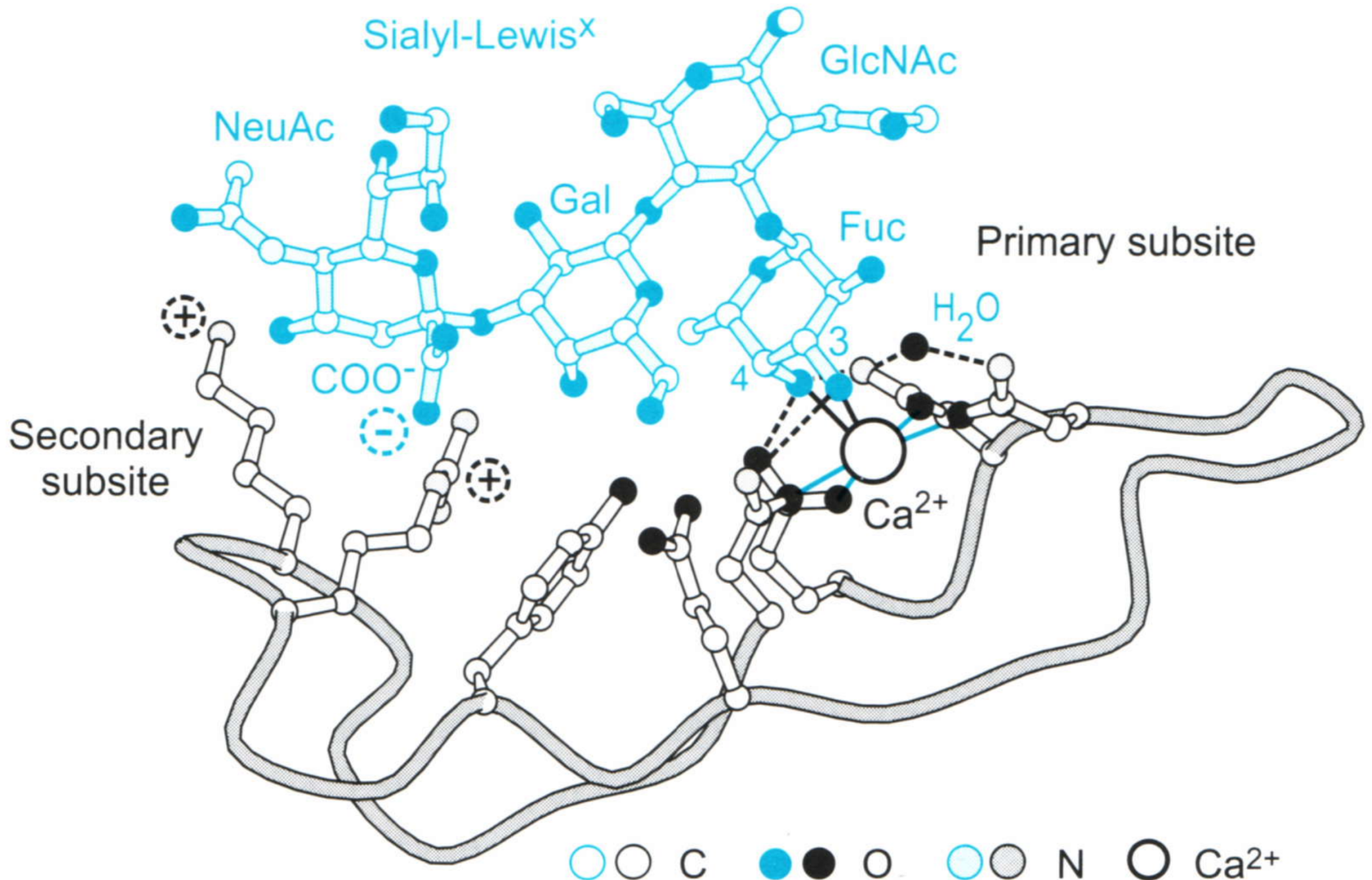


N-terminus of PSGL-1

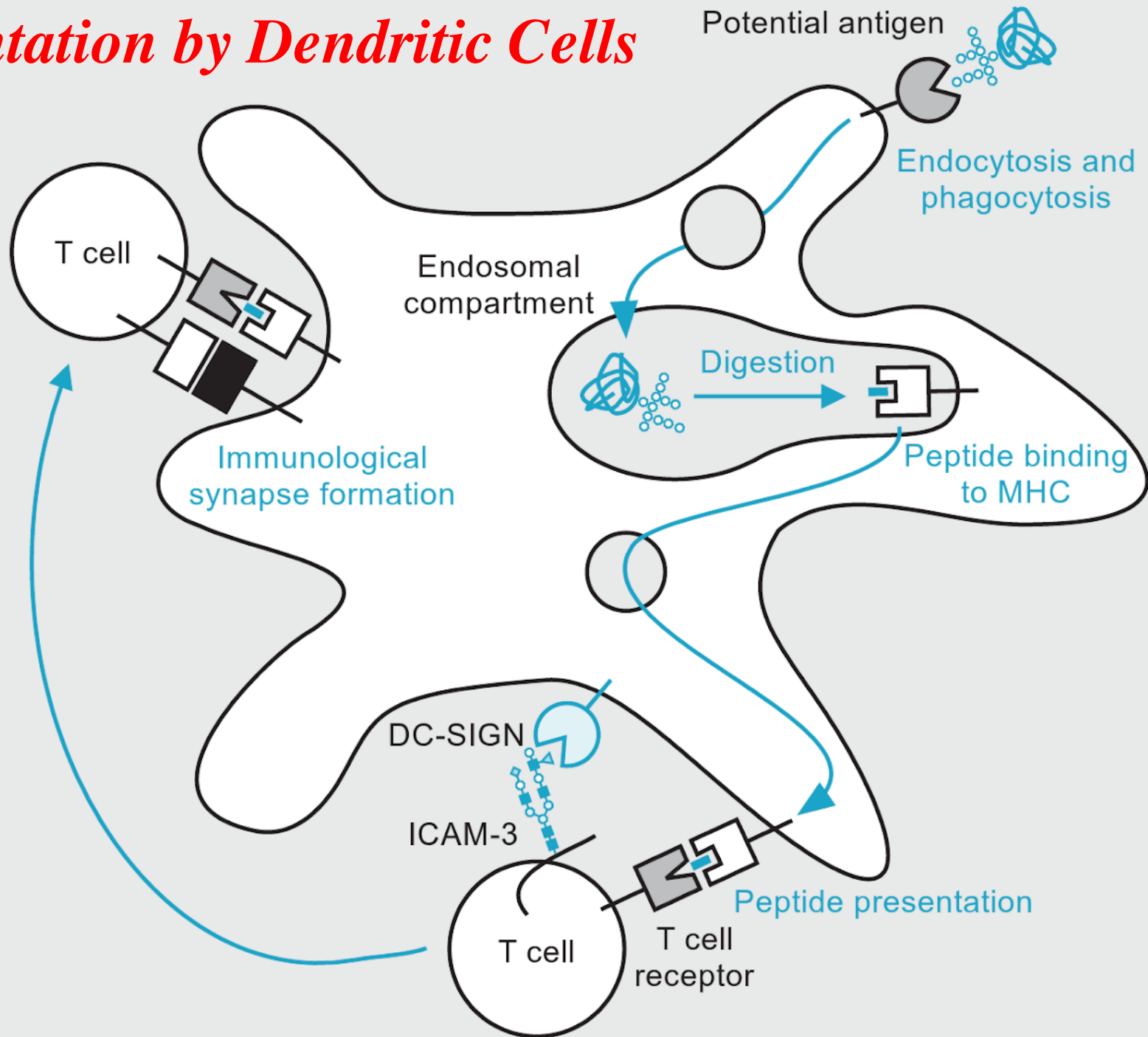


Glycan-bearing
 sialyl-Lewis^x
 structure

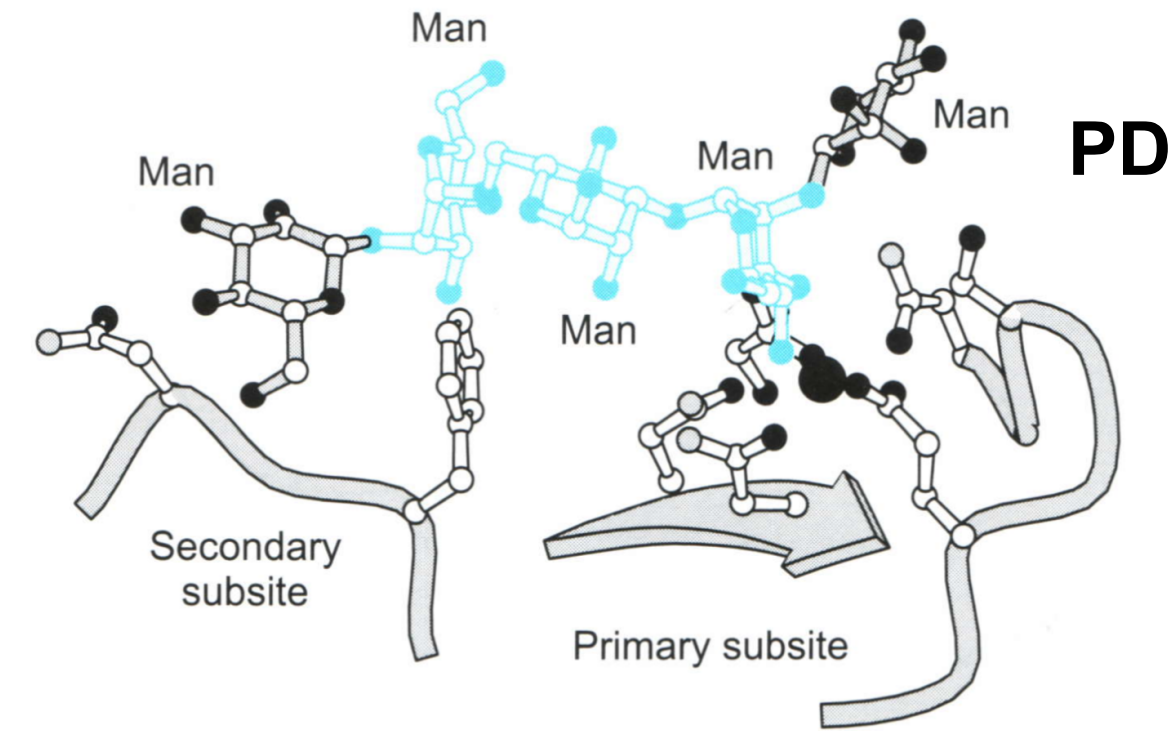
Extended Binding Site in E-Selectin CRD



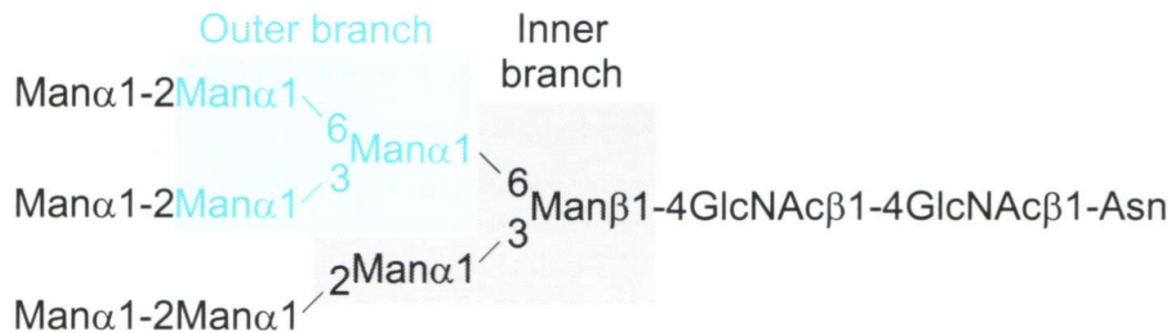
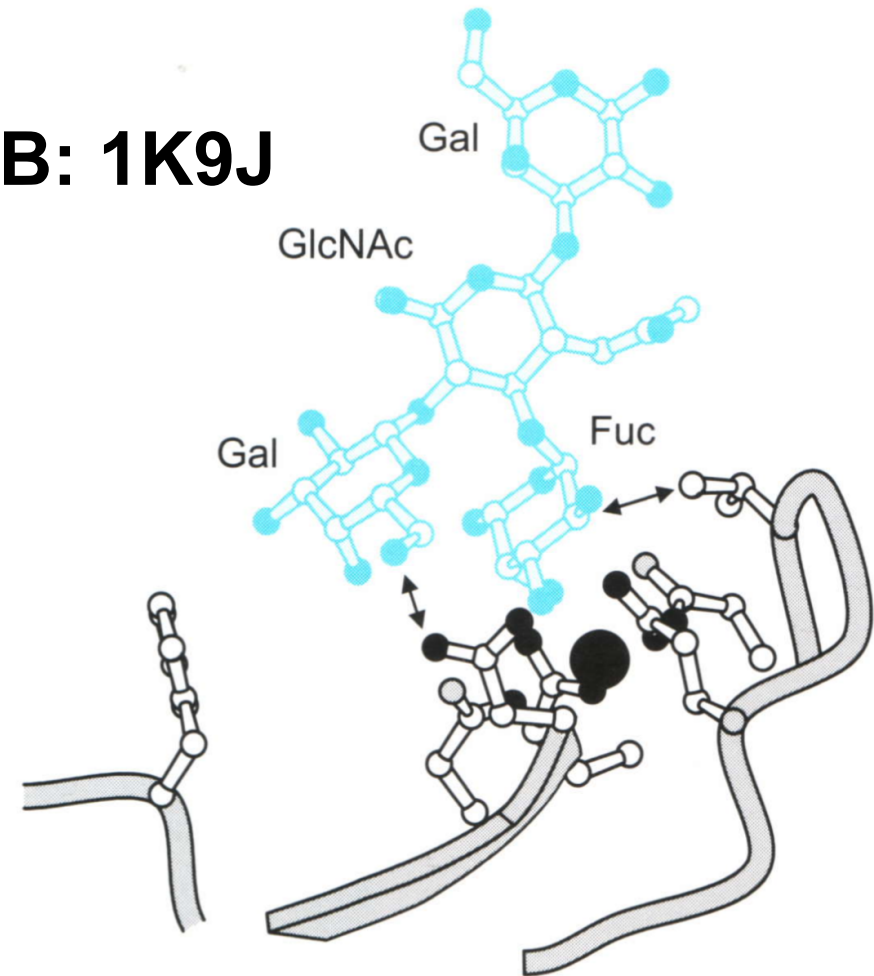
C-Type Lectins in Antigenic Presentation by Dendritic Cells



Extended Binding Sites in DC-SIGN



PDB: 1K9J

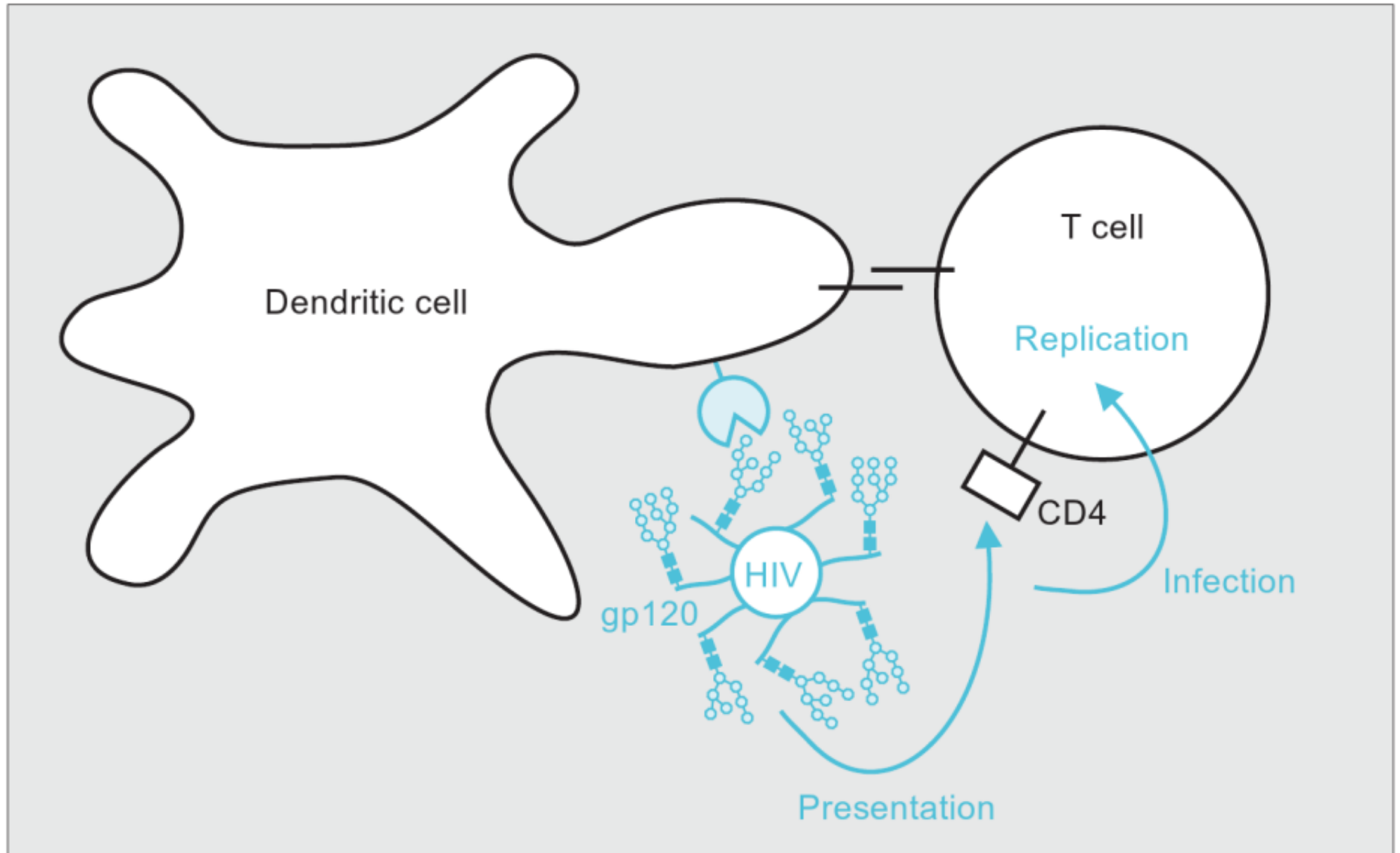


○ ○ C ● ○ ○ N ● Ca²⁺

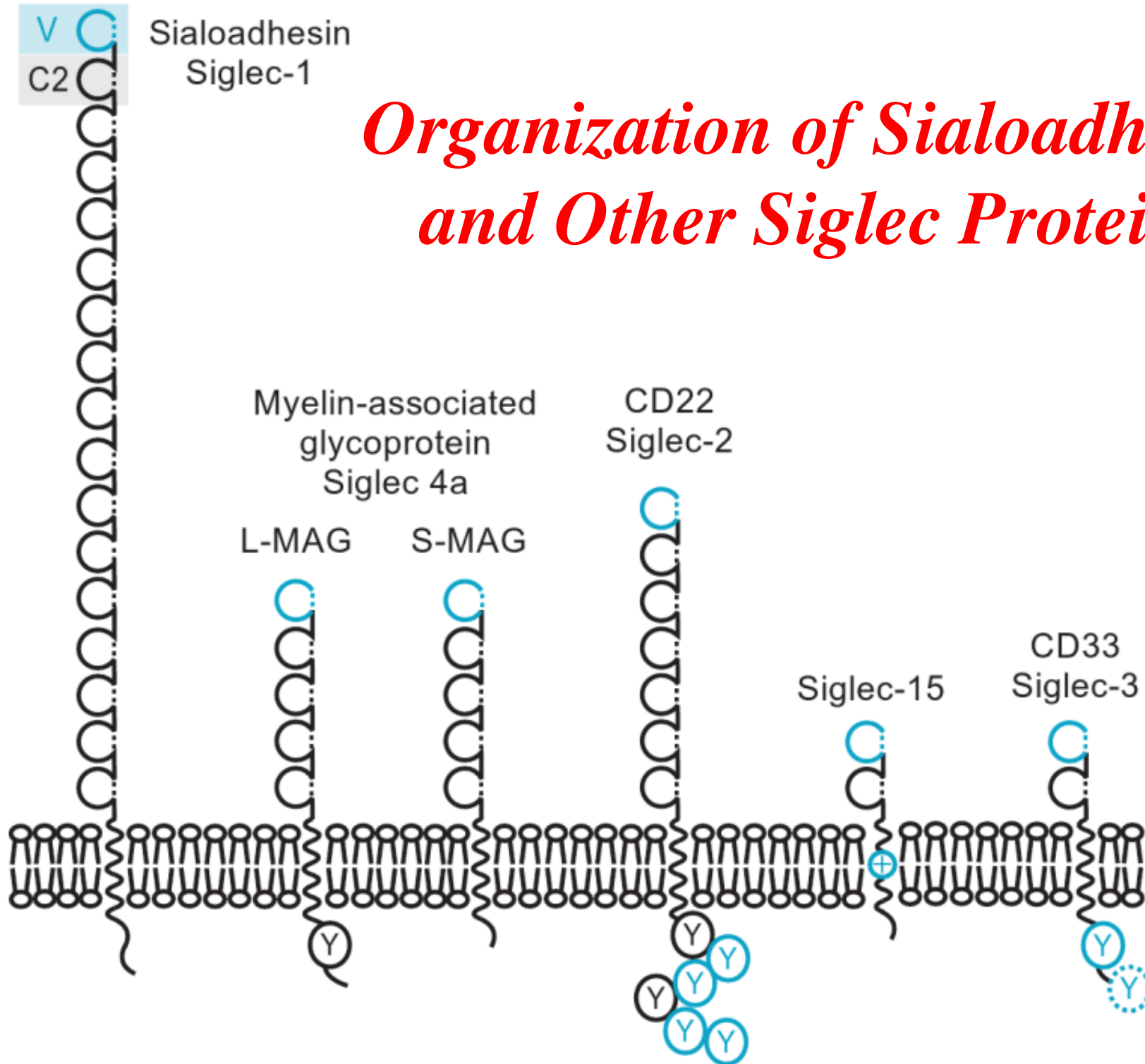
Branched Trimannose

Terminal Fucose

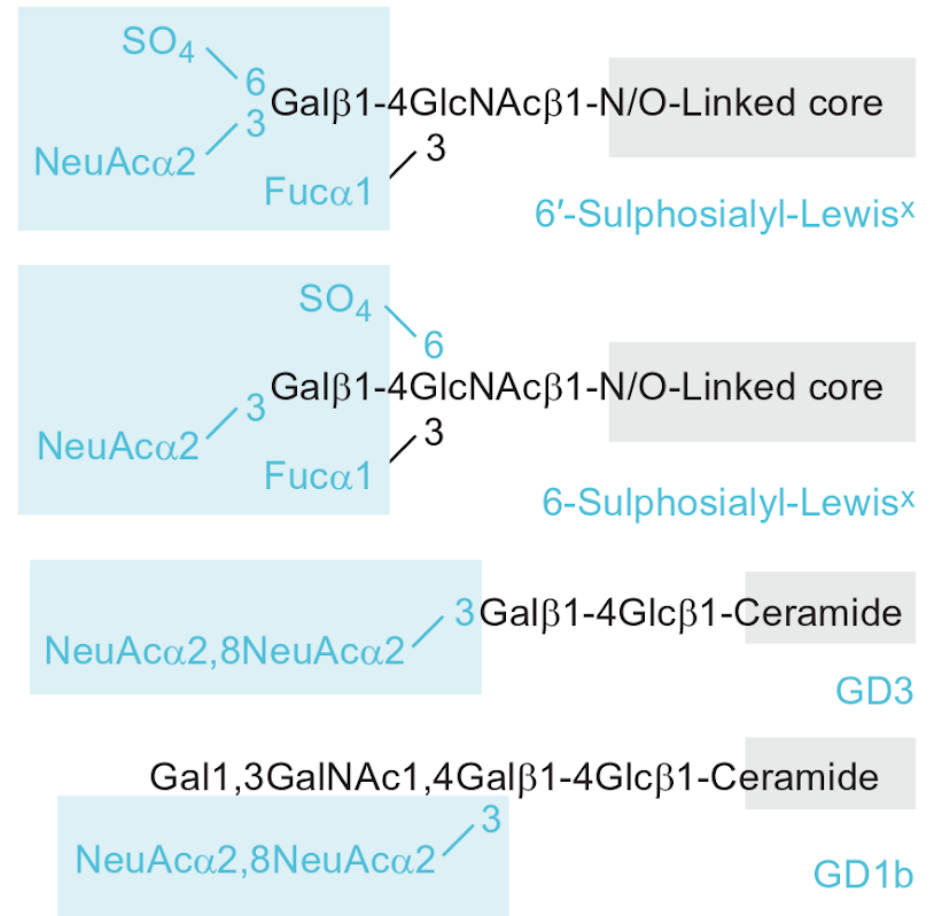
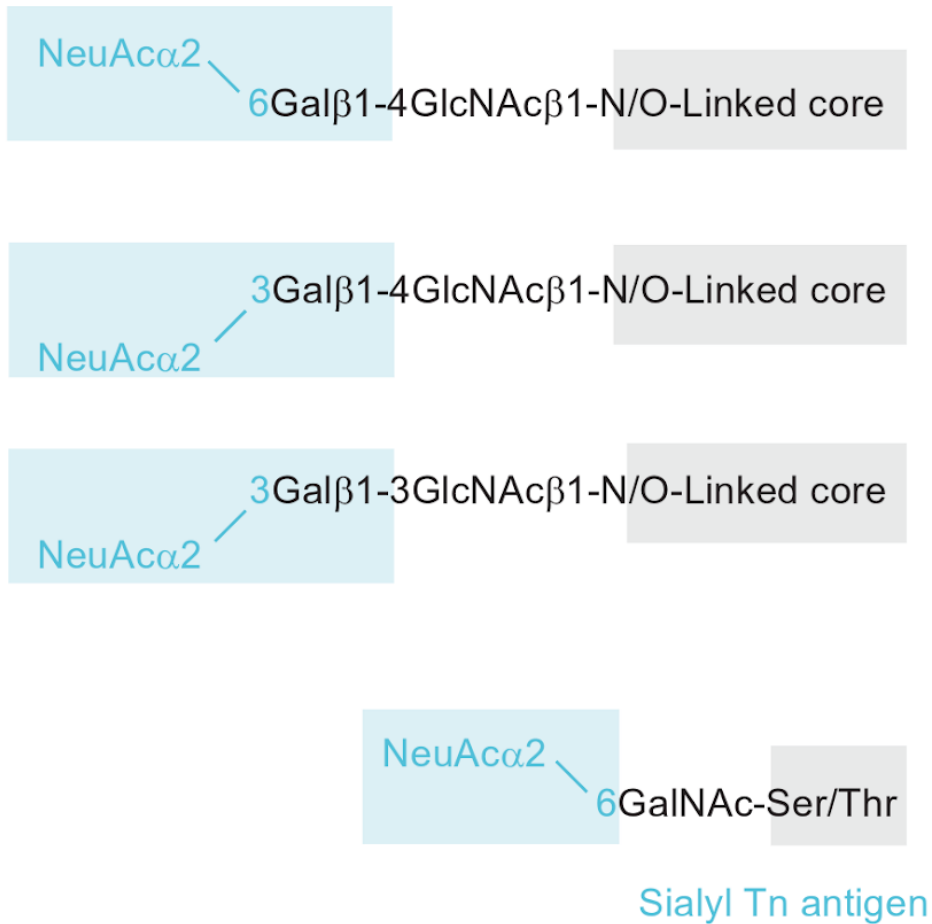
DC-SIGN Enhances T-Cell Infection by HIV



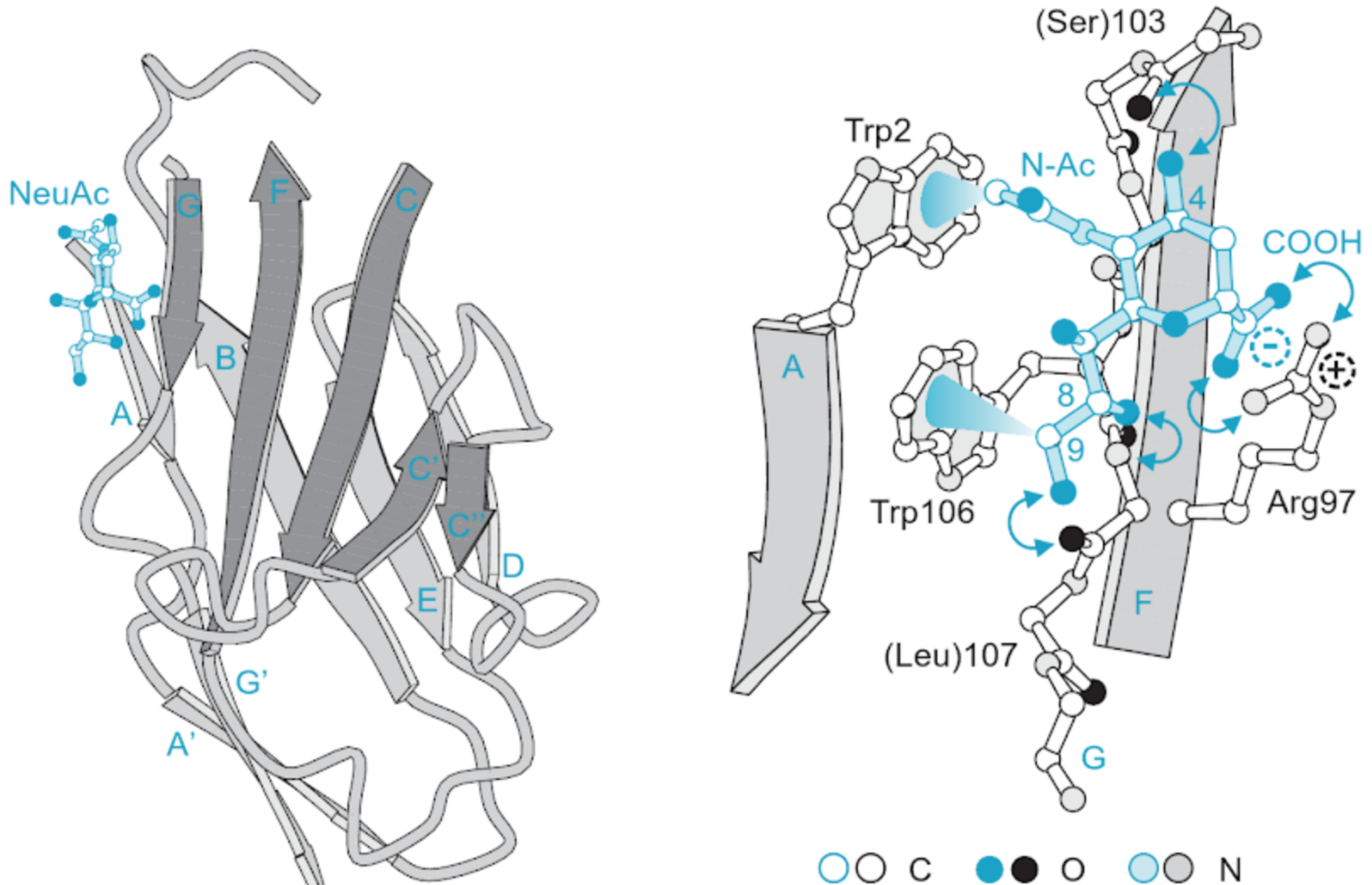
Organization of Sialoadhesin and Other Siglec Proteins



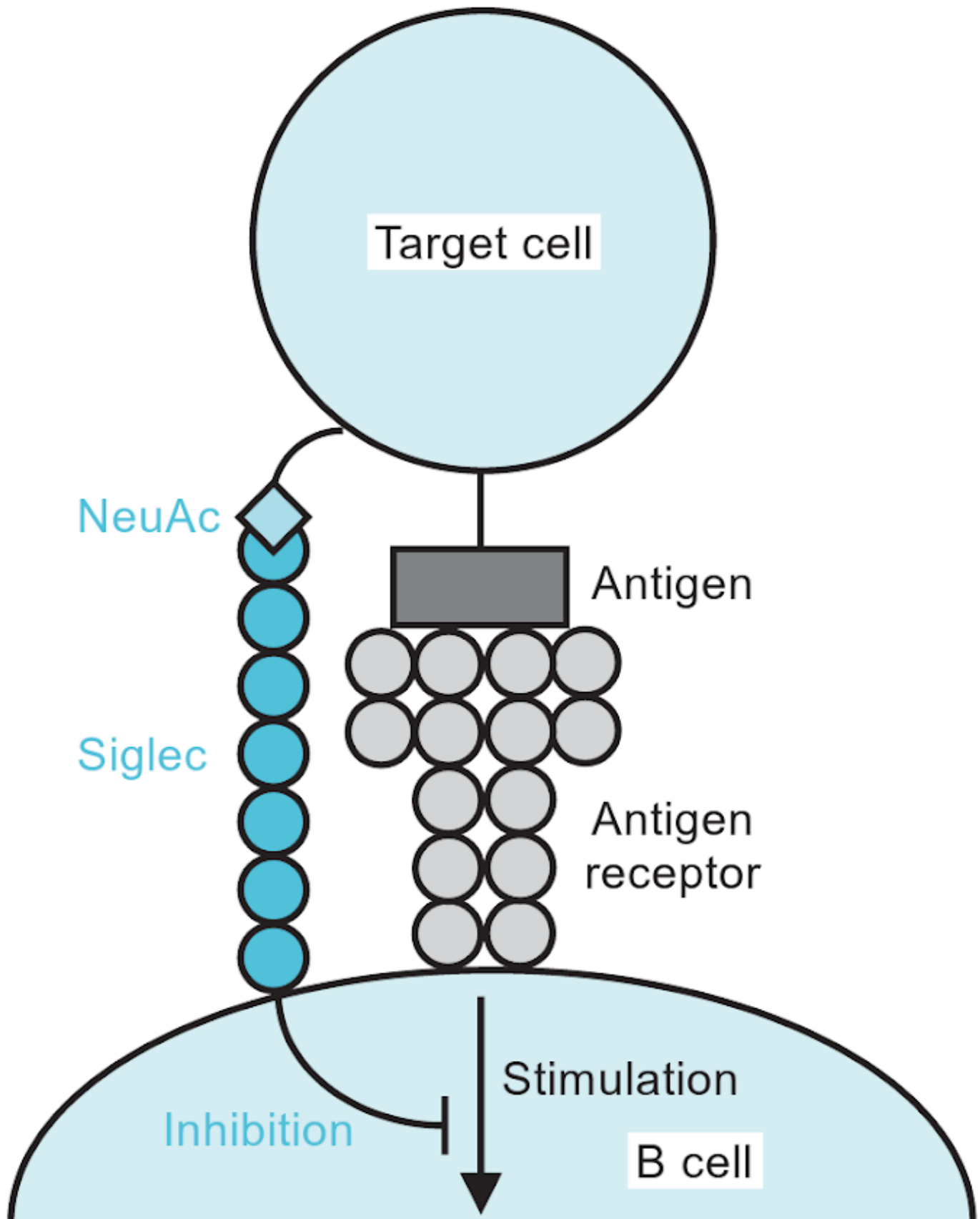
Sialic Acid-Containing Siglec Ligands

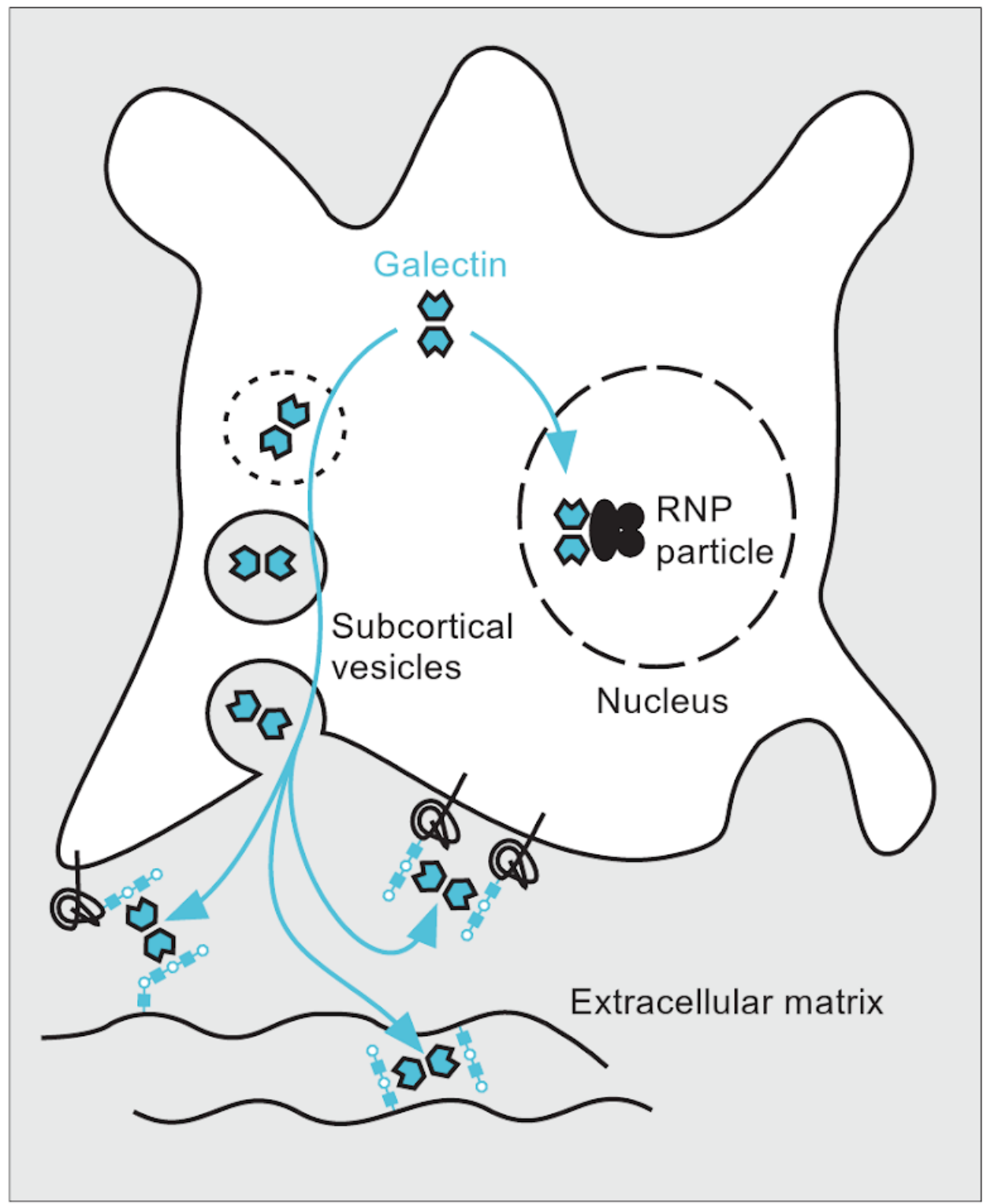
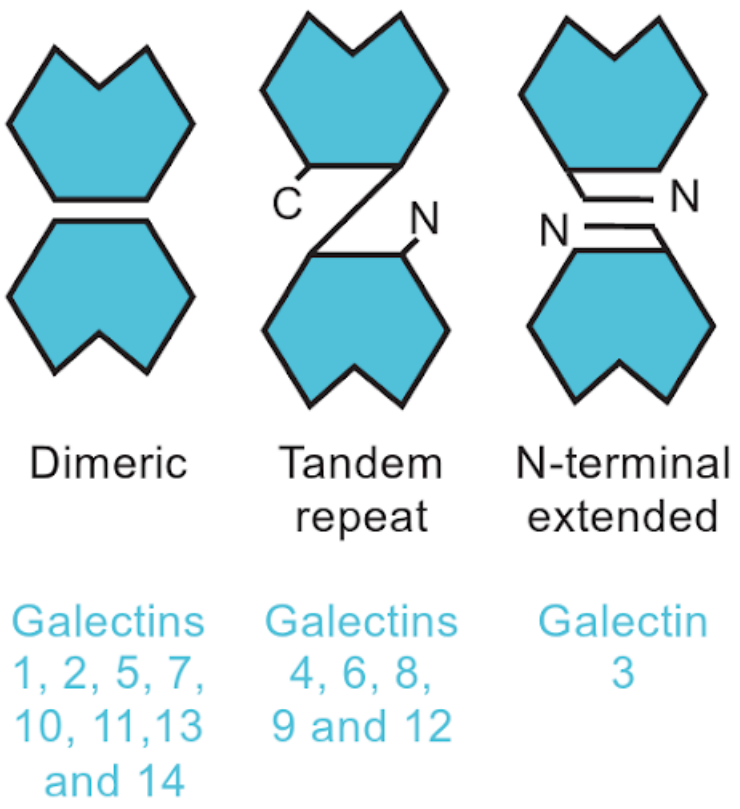


Overall Fold & Binding in Sialoadhesin CRD

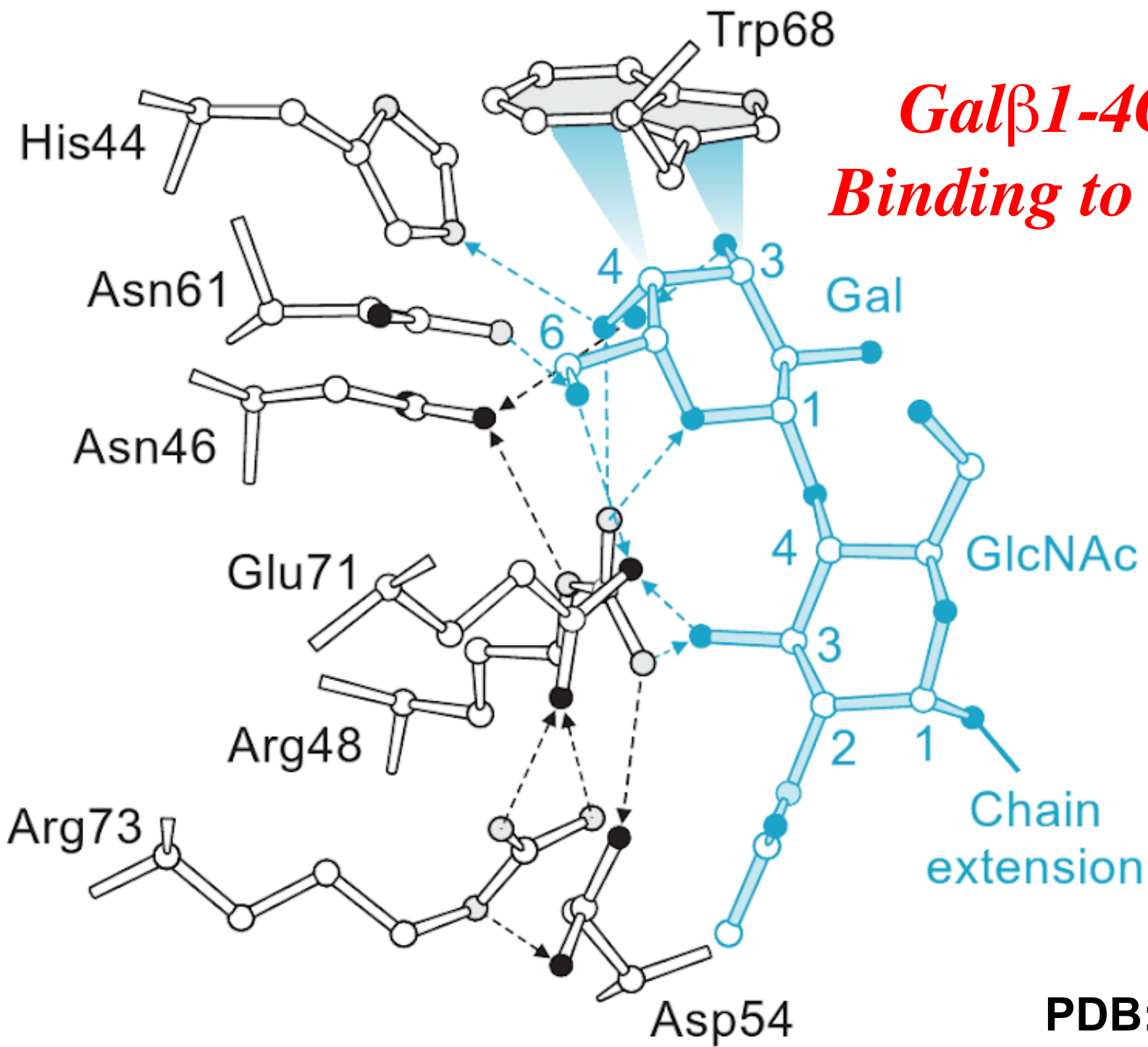


CD22 Inhibits Reactivity with Sialic Acid-Bearing Cells





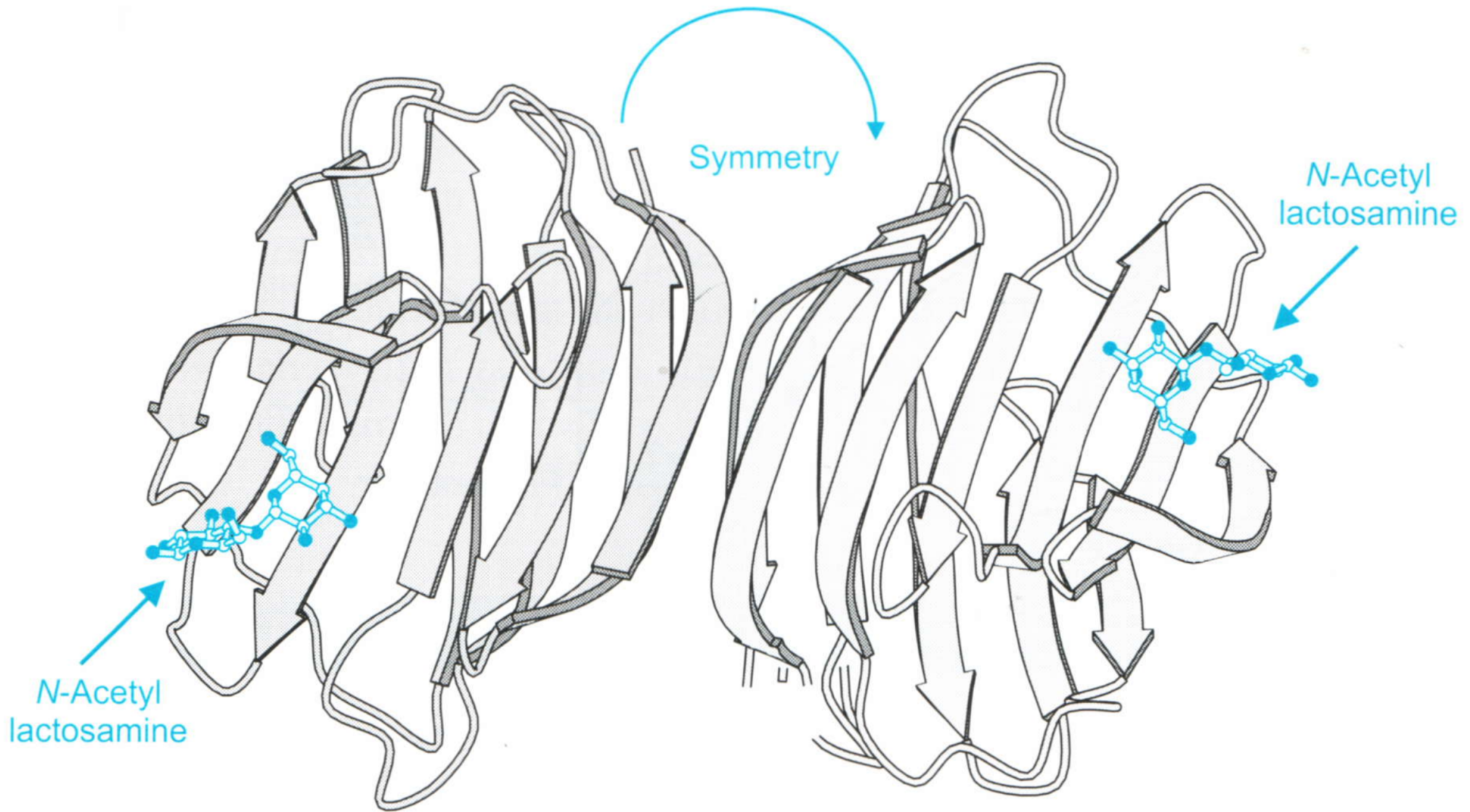
*Galβ1-4GlcNAc
Binding to Galectin 1*



PDB: 1HLC

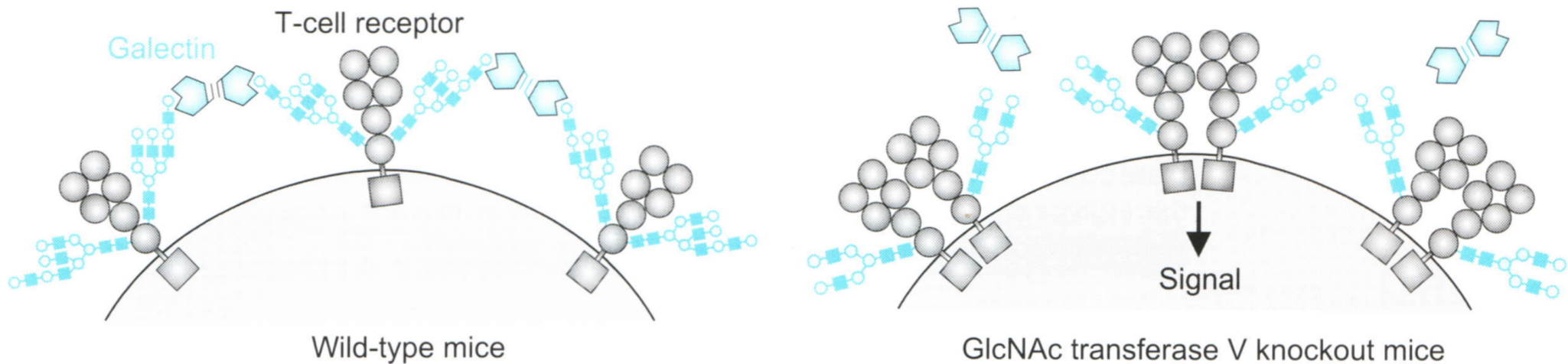
○ ○ C ● ● O ● ● N

Structure of the Galectin Dimer with Bound Disaccharides that Bridge between Glycans



PDB: 1HLC

T-Cell Receptor Activation & Galectin 3



Cross Linking of Glycans by Galectin 3 keeps T-cell Receptor molecules spaced apart. Thus, the receptors cannot cluster as they normally would, and activation of the lymphocyte is suppressed.

Function of Galectins in Apoptosis of T-Cells

