

# Protein Modification

Based on H3 Biology (2025)

ZHAO WENYING

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## 1 Glycoproteins

The structure of a glycoprotein is that of an oligosaccharide covalently bonded with a protein. The process by which this occurs is glycosylation, which typically occurs in the endoplasmic reticulum and golgi apparatus.

### Key CD Markers in humans

Glycoproteins play a major role in bodily cells, especially in the immune system e.g. Leukocytes. On leukocytes, they function as CD markers (Clusters of differentiation markers), CD45 being a universal marker for all white blood cells. A positive indicator for CD45 confirms a cell's identity as a leukocyte.

#### 1. Lymphocytes (Agranulocytes)

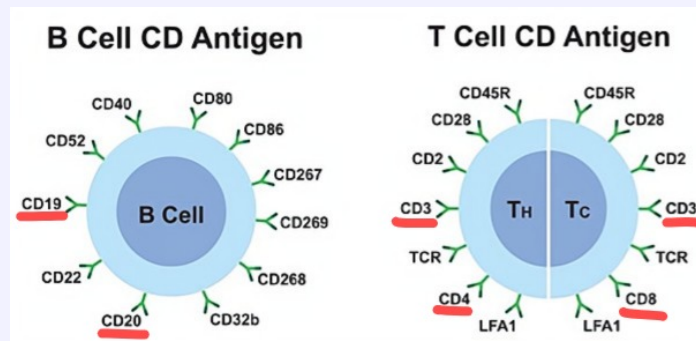
##### (a) T cells

- CD3 – Universal biomarker for T cells, binds with TCR complex for intracellular signalling
- CD4 – Helper T cells express  $CD4^+$ , coreceptor for antigen recognition
- CD8 – Cytotoxic T cells express  $CD8^+$ , activates T cell to release destructive enzymes and increase sensitivity to foreign antigens

The CD 3 4 8 count test supports the diagnosis of HIV and AIDS.

##### (b) B cells

- CD19 – Important coreceptor on B-cell surface
- CD20 – Acts as calcium-ion channel on plasma membrane, expressed ONLY from late pre-B stage until mature B



## (c) Natural Killer (NK) cells

- CD56 – Homophilic adhesion molecule, binding to cells sharing CD56, expression density defines NK cell sub-populations

## 2. Monocytes (Agranulocytes)

- CD14 – Bind to Lipopolysaccharide (LPS)—(toxic molecule found on *Gram*<sup>−</sup>) and transfers it to a neighbouring receptor, triggering release of inflammatory cytokines
- CD16 – Used alongside CD14 to split monocytes into functional subgroups (Classical, Intermediate, and Non-classical), triggers phagocytosis/release of toxins

## 3. Granulocytes

## (a) Neutrophils

- CD16 – Definitive marker for mature neutrophils, triggers phagocytosis after antibody is detected
- CD15 – Rolling adhesion, targets inflammation by rolling along blood vessel wall

## (b) Eosinophils

- CD193 – Chemotaxis, senses gradient of eotaxins (secreted by damaged tissues) and physically steers eosinophil to site
- CD49d – Tissue entry, adhesion to tissue to move to site

## (c) Basophils

- CD123 – Part of subunit telling basophil to maintain life
- FCER 1 (Fc Epsilon Receptor 1a) – Allergic reaction alpha subunit of IgE, when allergen cross-links with IgE, triggers release of histamine into blood

Go to the BD CD Marker Handbook for more information.

| Cluster of differentiation | Characteristic marker                           |
|----------------------------|-------------------------------------------------|
| <b>CD45</b>                | Every white cell                                |
| <b>CD14</b>                | Monocytes                                       |
| <b>CD16</b>                | Macrophages                                     |
| <b>CD33</b>                | Colony Forming Unit- Monocytes                  |
| <b>CD34</b>                | Colony Forming Unit- Granulocytes and Monocytes |
| <b>CD209</b>               | Dendritic cells                                 |

CD: Cluster of Differentiation.

<sup>a</sup>Image references: <https://www.creative-diagnostics.com/functions-of-human-cd-markers.htm>

Kyventidis, A. & Tzimagiorgis, Georgios & Didangelos, Triantafyllos. (2015). Peripheral blood can differentiate into efficient insulin-producing cells in vitro. Hippokratia. 19. 344-351.

## Structure

Glycoproteins can be categorised by how the sugar chain is linked to the protein, giving rise to 2 main groups, N-link and O-link. We will talk more about this in the next section.

1. General Structure As mentioned before, there are 10 possible monosaccharides in glycans which can be linked to a peptide chain,

- Glucose (Glc)
- Fucose (Fuc)
- Xylose (Xyl)
- Mannose (Man)
- Galactose (Gal)
- N-acetylglucosamine (GlcNAc)
- Glucuronic acid (GlcA)
- Iduronic acid (IdoA)
- N-actylgalactosamine (GalNAc)
- Sialic acid – A key dependency in glycoprotein half-life
- 5-N-actylneruraminic acid (Neu5Ac)

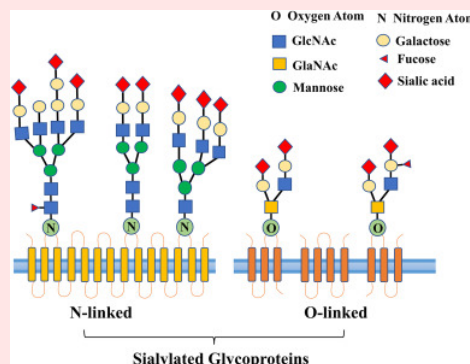
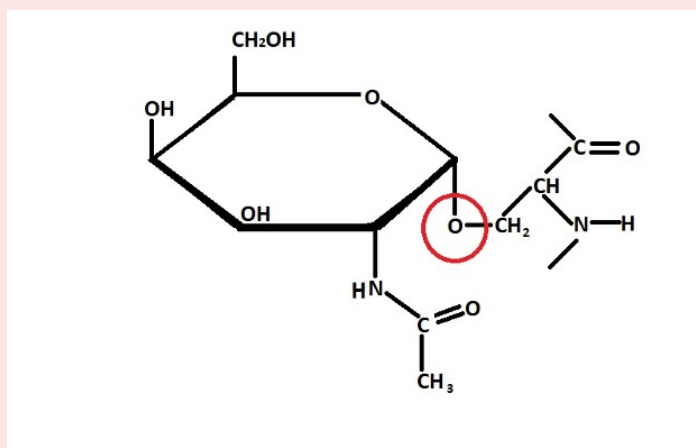


Image source:

<https://www.sciencedirect.com/science/article/abs/pii/S0008621522000994>

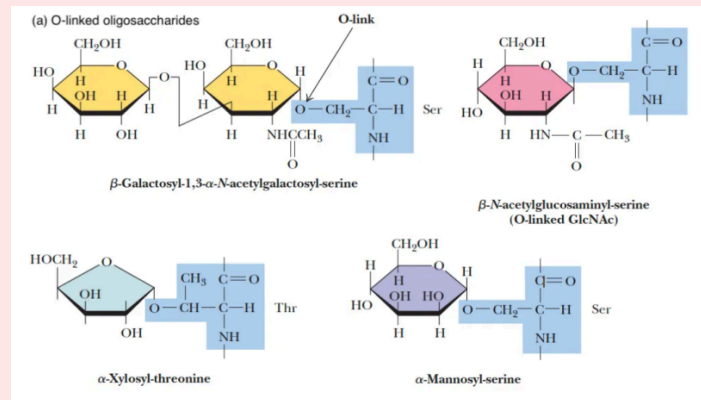
A glycan chain can be made of 2 to 15 monosaccharide units, which connect to the protein via specific amino side chains.

2. O-linked Glycoproteins

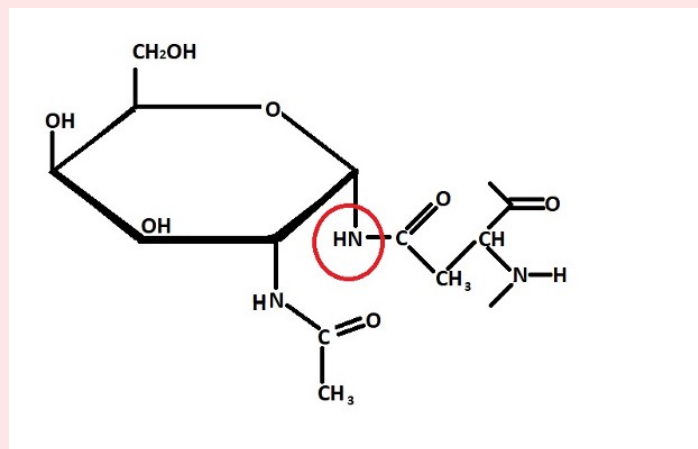


- Sugars bind to -OH group of Serine (Ser) or Threonine (Thr) residues via the O-glycosidic bond

- Common in mucins to provide a protective, gel-like barrier in the respiratory and gastrointestinal tracts
- e.g. Mucins, Blood antigens, Collagen



### 3. N-linked Glycoproteins



- Oligosaccharide attaches to the -NH<sub>2</sub> group of Asparagine (Asn) residues
- e.g. Immunoglobins/Antigens (IgA, IgG, IgM), Receptors, Thyroglobulin

Table 1: Comparison between N-linked and O-linked glycoproteins

|                       | N-linked                                           | O-linked                               |
|-----------------------|----------------------------------------------------|----------------------------------------|
| Site of glycosylation | Initiated in ER, modified in golgi                 | Strictly occurs in the Golgi apparatus |
| Attachment Site       | Asparagine (Asn)                                   | Serine (Ser) or Threonine (Thr)        |
| Chain Complexity      | highly branched, structurally complex              | shorter, simpler, and more linear      |
| Primary Function      | Protein folding, quality control, cell recognition |                                        |

### More about Mucin

Mucins are around 80% O-linked glycoprotein, and one of the most commonly found O-linked glycoproteins. Mucins are proteins that rely on these O-linked glycans to function, with carbohydrate chains covalently attached to the hydroxyl group of serine and threonine amino acids.

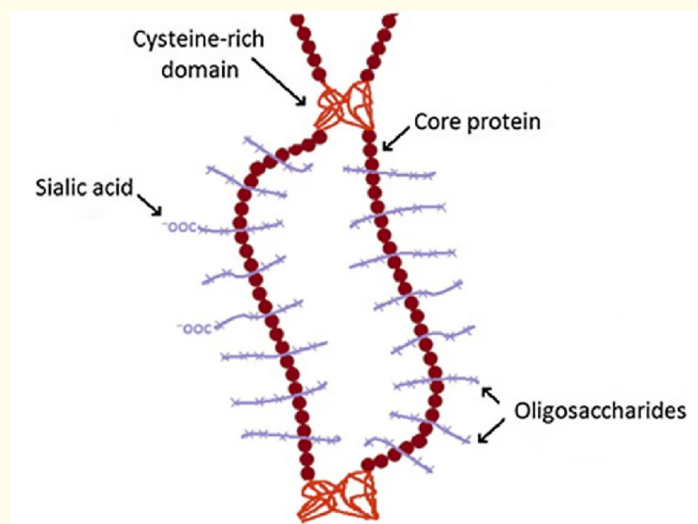


Image from

[https://www.researchgate.net/figure/Schematic-structure-of-mucin-glycoproteins\\_fig1\\_331739004](https://www.researchgate.net/figure/Schematic-structure-of-mucin-glycoproteins_fig1_331739004)