no.5

Cytology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

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8.3 Membrane carbohydrates:

- Carbohydrates represent [2-10] % of the plasma membrane weight

- 90% of these carbohydrates are covalently linked to proteins → glycoprotein

- The remaining linked covalently to lipid → glycolipid

- All carbohydrates face away from cytosol (In the plasma membrane, carbohydrates are toward the ECM. While in cytoplasmic membranes, they are found toward the lumen)

- Glycosylation: the modification of proteins by adding carbohydrates to it.

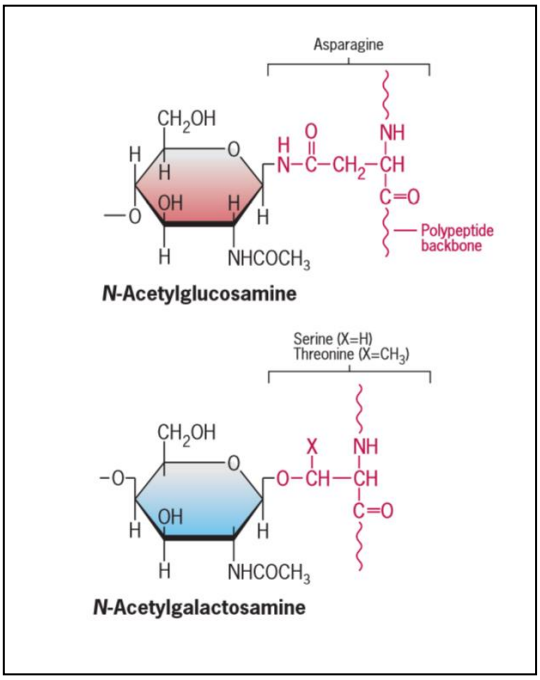
Glycosylation starts in rough ER, then continues in Golgi apparatus, then the glycoprotein fuses with the plasma membrane.

-The carbohydrates attached to the proteins are oligosaccharides: short (about 15 sugars per chain), branched, hydrophilic chains (because they are on the surface of a cell). These oligosaccharides give variety in composition and structure. Also the same protein can link to different oligosaccharides in different cells and tissues.

- Oligosaccharides can attach to different amino acids in 2 major linkages.

a) N-Acetylglucosamine: β glucose, the sugar attaches to asparagine, it links by N-glycosidic linkage with asparagine

b) N-Acetylgalactosamine: links with serine or threonine by O-glycosidic linkage.



- The importance of carbohydrates:

a) Mediating the interactions of a cell with its environment.

b) Sorting membrane proteins to different cellular compartments.

The glycolipids in RBCs determine the blood type (A, B, AB, O)

- The ABO modifications are found in many other tissues beside the blood, and the genetic variation in the AB gene is a strong predictor of risk of pancreatic cancer, heart disease, and viral infection.

- A: has an enzyme that adds adds N-Acetylgalactosamine to galactose

- B: has an enzyme that adds galactose

- AB: has these both enzymes

-O: lack of both enzymes

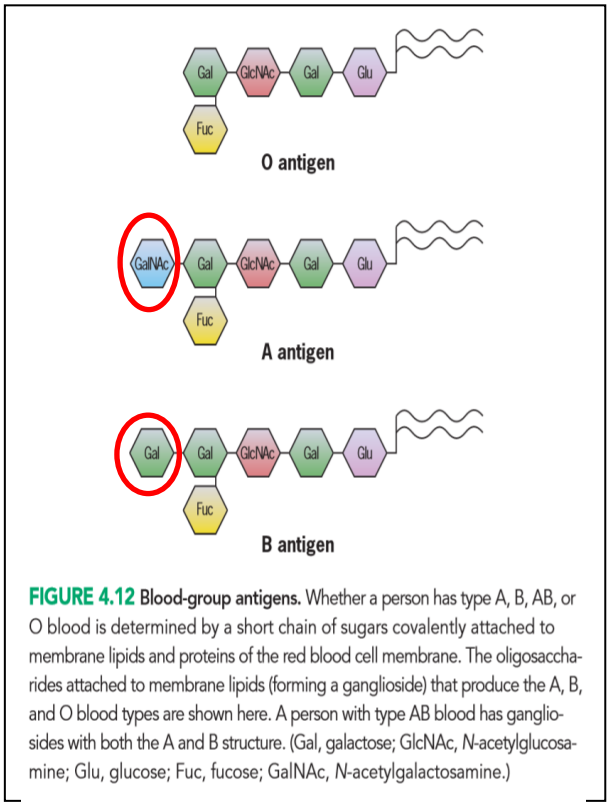


FIGURE 4.12 **Blood-group antigens.** Whether a person has type A, B, AB, or O blood is determined by a short chain of sugars covalently attached to membrane lipids and proteins of the red blood cell membrane. The oligosaccharides attached to membrane lipids (forming a ganglioside) that produce the A, B, and O blood types are shown here. A person with type AB blood has gangliosides with both the A and B structure. (Gal, galactose; GlcNAc, *N*-acetylglucosamine; Glu, glucose; Fuc, fucose; GalNAc, *N*-acetylgalactosamine.)

1.4 The structure and functions of membrane proteins

Proteins in the plasma membrane differ depending on: the organelles in the cell, and the cell type.

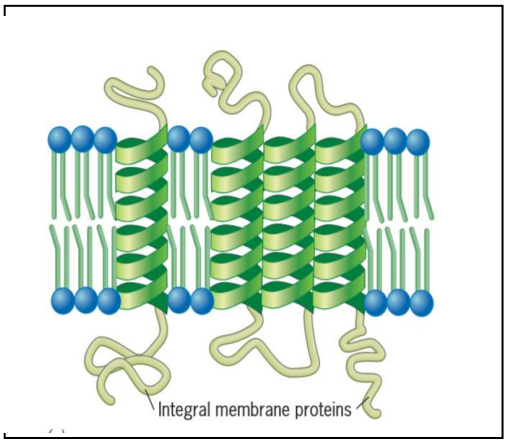
A membrane may contain hundreds of different proteins.

Also, proteins differ among the sides of the same membrane, this asymmetry is referred to "sidedness".

e.g. proteins that interact with other cells (exposed to ECM) are different from those interact with the cytosol.

Proteins are classified according to intimacy to their relationship to the lipid bilayer to:

1) Integral membrane proteins: penetrating the lipid bilayer.



- Transmembrane proteins: proteins that pass entirel through the lipid bilayer, having domains that protrude from the both extracellular and cytoplasmic sides of the membrane.

Proteins are: i) one membrane spanning segment

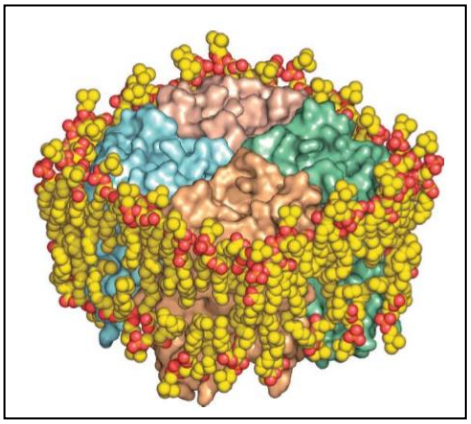
ii) multispanning

** [25-30] % of membrane proteins are integral and roughly 60% of all current drug targets.

Integral proteins serve as:

i) Receptors that bind specific substances at the membrane surface.
ii) Channels or transporters involved in the movement of ions and solutes across the membrane.
iii) Agents that transfer electrons during the processes of photosynthesis and respiration.

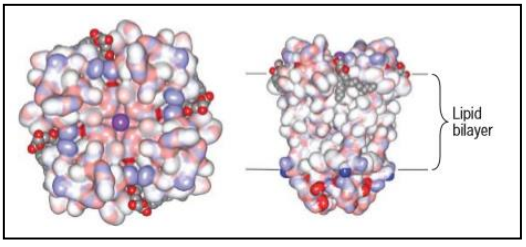
** Proteins are amphipathic; having hydrophobic regions that interact with fatty acyl chains of lipids by Van Der Waals force, which seals the protein into the lipid of the membrane.



Aquaporin protein, it has four subunits, and surrounded by lipid molecules. In this case, these lipid molecules are not likely to play a role in the function of aquaporin because the protein retains its function as a water channel in

- most of the lipid molecules that make contact with a transmembrane domain, , are simply passive bystanders and are rapidly exchanged with other lipid molecules in the bilayer.

-Certain sites on the surface of many membrane proteins do form important functional interactions with specific lipid molecules. E.g. KcsA K + channel, the channel does not open normally in a bilayer that lacks binding to anionic lipids in the crevice at the interfaces between the subunits. (the figure is shown below).



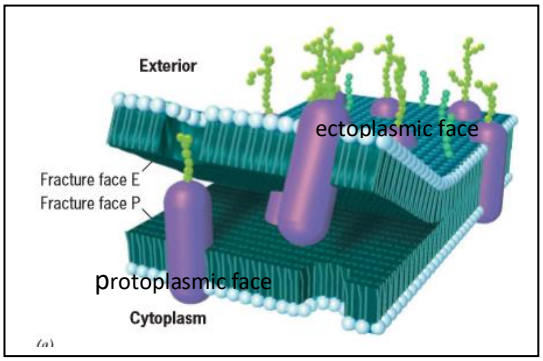
- Proteins also can have portions (hydrophilic) that project into cytoplasm or ECM, these portions tend to be more like globular protein.

-In some membrane proteins, the transmembrane domains are essentially devoid of water molecules, whereas others allow the aqueous solvent to penetrate deep into the protein's membrane-embedded regions.

**Several large families of membrane proteins contain an interior channel that provides an aqueous passageway through the lipid bilayer.

NOTE : integral proteins need not be fixed structures but may be able to move laterally within the membrane .

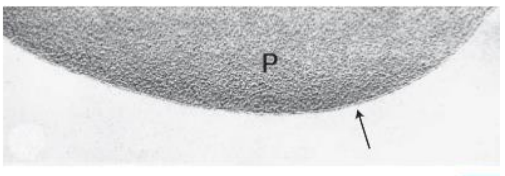
- Freeze fracture replication: A technique used to derive the concept that proteins penetrate through membranes.



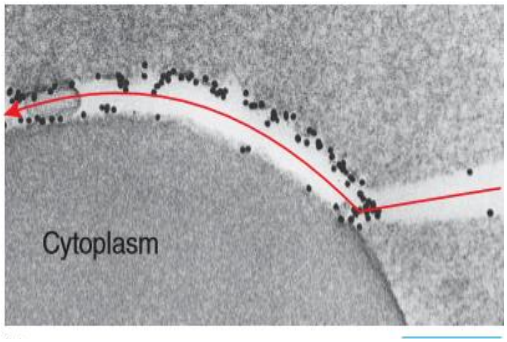
The procedure is:

a) A tissue is frozen solid and then struck with a knife blade.

b) The path of fraction leads through the middle of the lipid bilayer and proteins segregate with one of the two halves of the bilayer.



The P fracture face is seen to be covered with particles approximately 8 nm in diameter



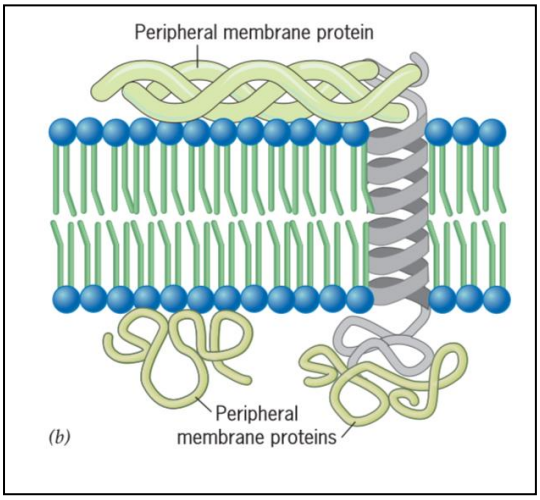
After freezing and fracturing the cell, it was thawed, fixed, and labeled with a marker for the carbohydrate groups on glycophorin. Glycophorin molecules were segregated with the outer half.

2) Peripheral membrane proteins:

- Peripheral proteins are hold with the membrane by hydrophilic interactions (electrostatic bonds).

-In actual fact, the distinction between integral and peripheral proteins is blurred because many integral membrane proteins consist of several polypeptides, some that penetrate the lipid bilayer and others that remain on the periphery.

- Peripheral proteins located on the outer or inner surface of the membrane.

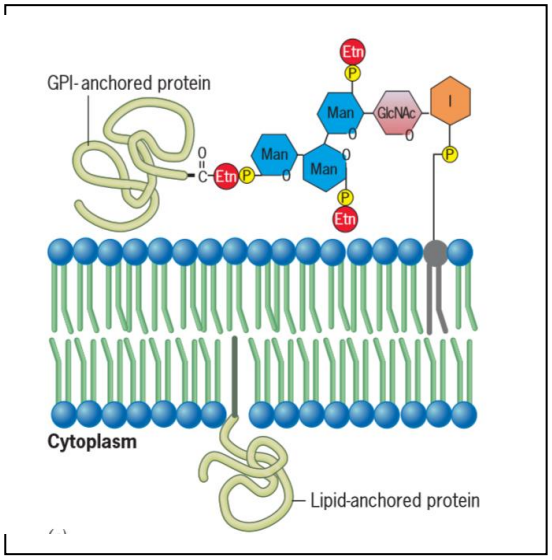


The internal (cytosolic) surface of the plasma membrane: forming fibrillar network that acts as a membrane "skeleton" .These proteins provide mechanical support for the membrane and function as an anchor for integral membrane proteins, also they can function as enzymes or factors that transmit transmembrane signals.

** Peripheral proteins are non-covalently bonded giving a dynamic relationship with the membrane.

3) Lipid-Anchored Membrane Proteins:

These are proteins located either on the cytoplasmic surface of the membrane, or the extracellular surface. They are covalently bonded to a lipid molecule of the membrane.



a) GPI-anchored proteins: proteins bound to the membrane by a small, complex oligosaccharide linked to a molecule of phosphatidylinositol that is embedded in the outer leaflet of the lipid bilayer.

How was it discovered? Certain membrane proteins could be released by a phospholipase that specifically recognized and cleaved inositol-containing phospholipids.

** It functions as receptors, enzymes, and cell-adhesion proteins.

** A rare type of anemia, paroxysmal nocturnal hemoglobinuria, results from a deficiency in GPI synthesis that makes red blood cells susceptible to lysis.

b) In the cytoplasmic side of the plasma membrane, proteins are anchored to the membrane by one or more long hydrocarbon chains embedded in the inner leaflet of the lipid bilayer.

** Src and Ras (anchored proteins on the cytoplasmic surface) have been implicated in the transformation of a normal cell to a malignant stat.

Book reference p[319-323]

THE END