Lecture 1: Cell Membranes

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Principles of Genetics and Molecular Biology

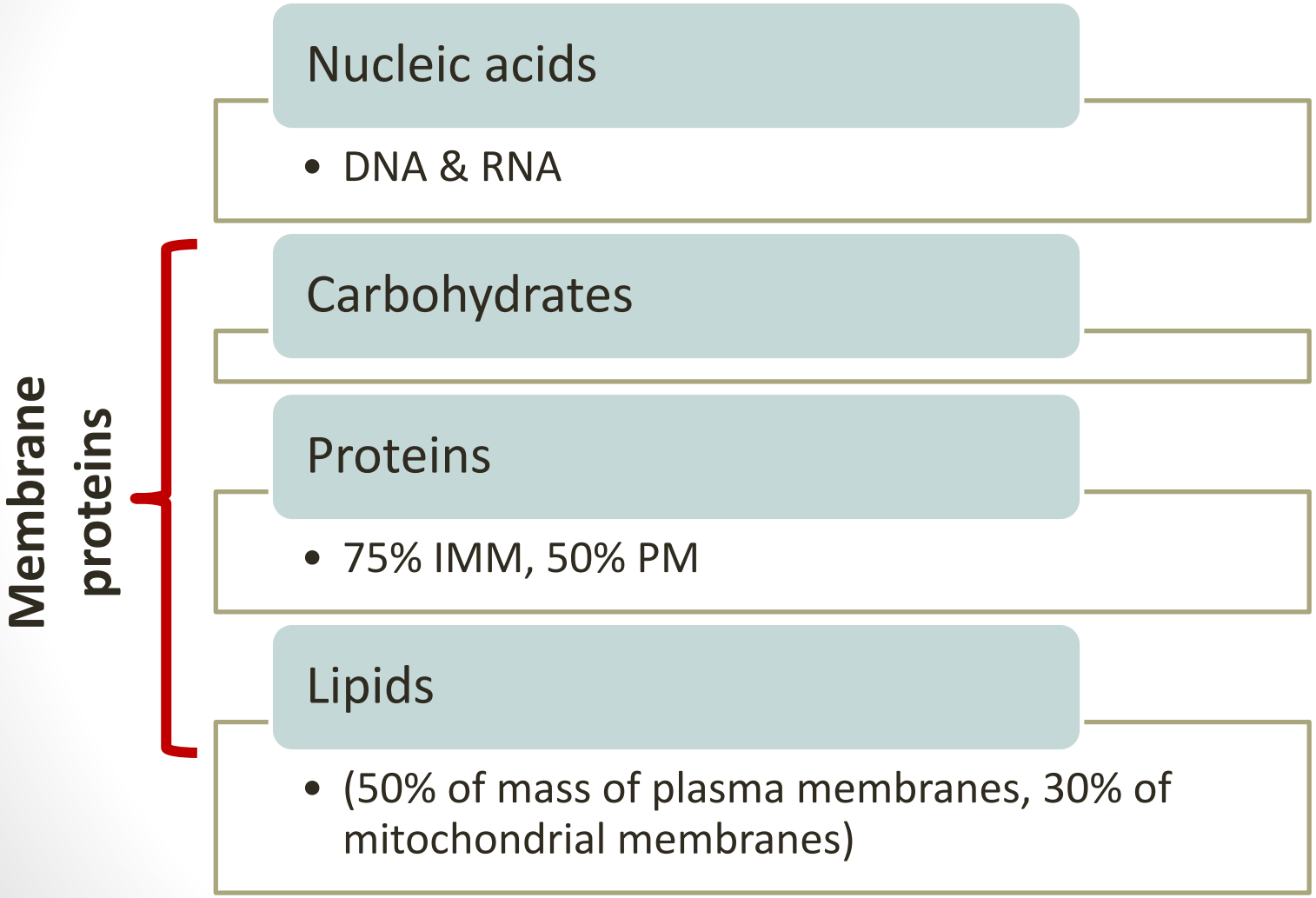
Organelles

TABLE 4-2 *Organelles*

Organelle	Function
Mitochondrion	transfers energy from organic compounds to ATP
Ribosome	organizes the synthesis of proteins
Endoplasmic reticulum (ER)	prepares proteins for export (rough ER); synthesizes steroids, regulates calcium levels, breaks down toxic substances (smooth ER)
Golgi apparatus	processes and packages substances produced by the cell
Lysosome	digests molecules, old organelles, and foreign substances
Microfilaments and microtubules	contribute to the support, movement, and division of cells
Cilia and flagella	propel cells through the environment; move materials over the cell surface
Nucleus	stores hereditary information in DNA; synthesizes RNA and ribosomes
Cell wall*	supports and protects the cell
Vacuole*	stores enzymes and waste products
Plastid*	stores food or pigments; one type (chloroplast) transfers energy from light to organic compounds

*Cell walls, large vacuoles, and plastids are found in the cells of plants and some other eukaryotes, but not in the cells of animals.

Major components of cells



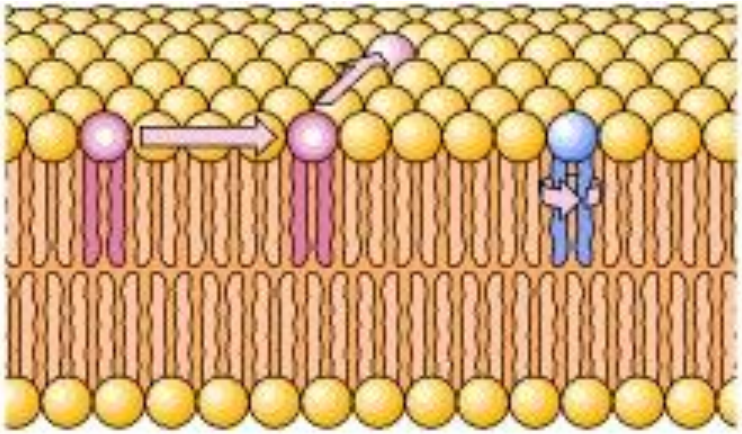
Composition of membranes

Table 8.18. Mass % Biochemical Composition of Cell and Organelle Membranes[531,939,996,997]

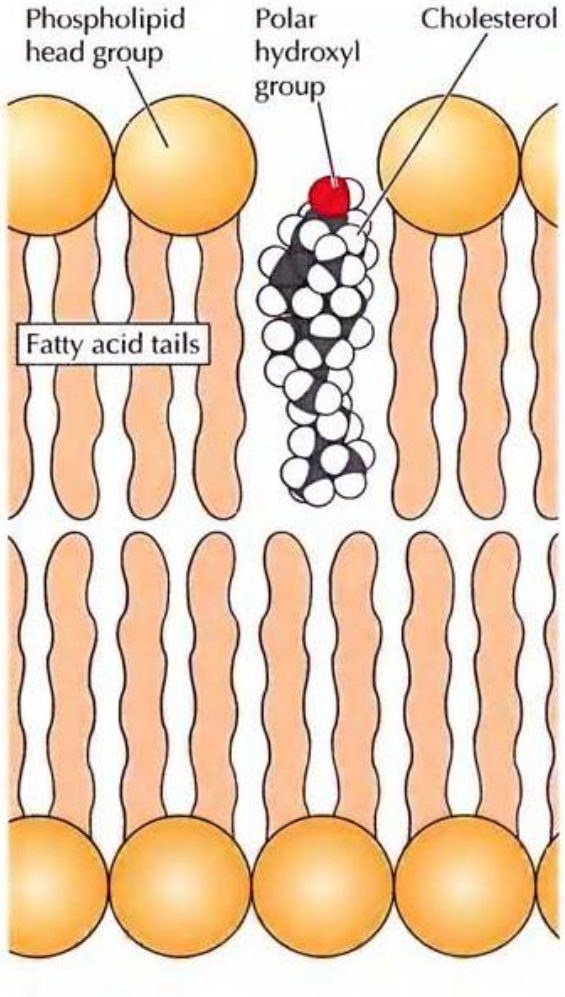
Type of Membrane Molecule	Liver Cell Plasma Membrane	Red Cell Plasma Membrane	Myelin Sheath	Mitochondrion Inner/Outer Membranes	Endoplasmic Reticulum Membrane	*E.coli* (Bacterial Membrane)
Lipid	--	40%	~81%	~24%/~48%	--	--
Protein	~50%	52%	~19%	~76%/~52%	~50%	~50%
Carbohydrate	--	8%	--	--	--	--
Lipid Class:						
Cholesterol	17%	23%	22%	3%	6%	0%
Phospholipids						
Phosphatidylethanolamine	7%	18%	15%	35%	17%	70%
Phosphatidylserine	4%	7%	9%	2%	5%	trace
Phosphatidylcholine	24%	17%	10%	39%	40%	0%
Sphingomyelin	19%	18%	8%	0%	5%	0%
Glycolipids	7%	3%	28%	trace	trace	0%
Other lipids	22%	13%	8%	21%	27%	30%

- **No entry after I am in.**
- **No section change**
- **No empty seats in the front**
- **Side chats = OUT**

Composition and properties of membranes



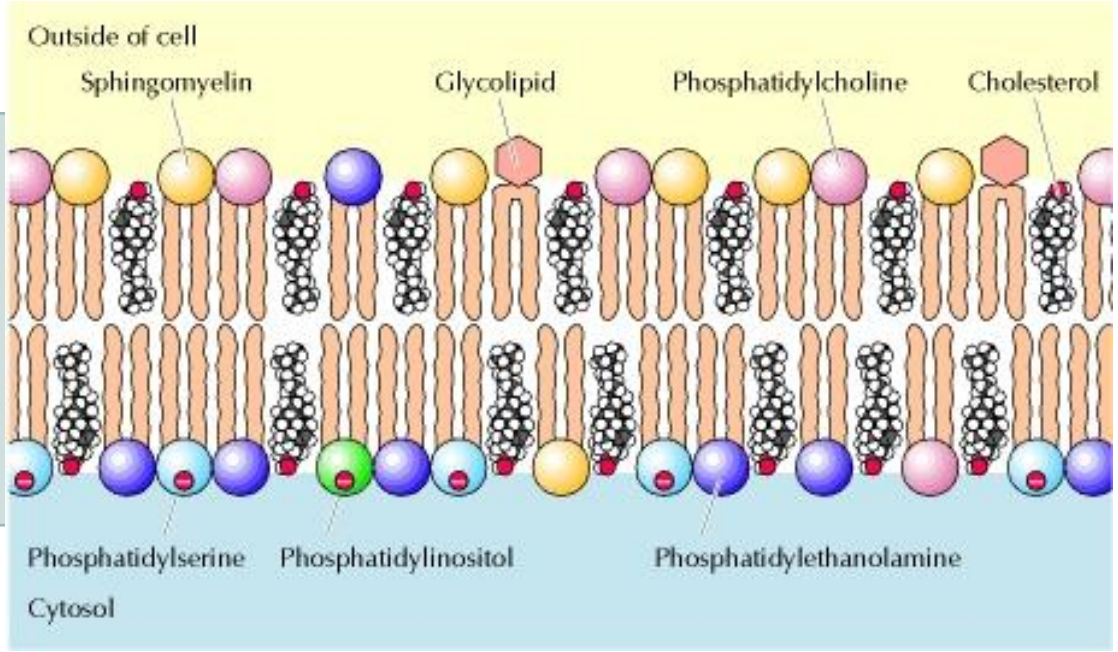
Phospholipids can rotate and move laterally within a layer



Cholesterol is an essential component of animal plasma membrane.
It is not present in bacteria and plant cells, but the latter cells contain sterols.

Composition and properties of plasma membranes

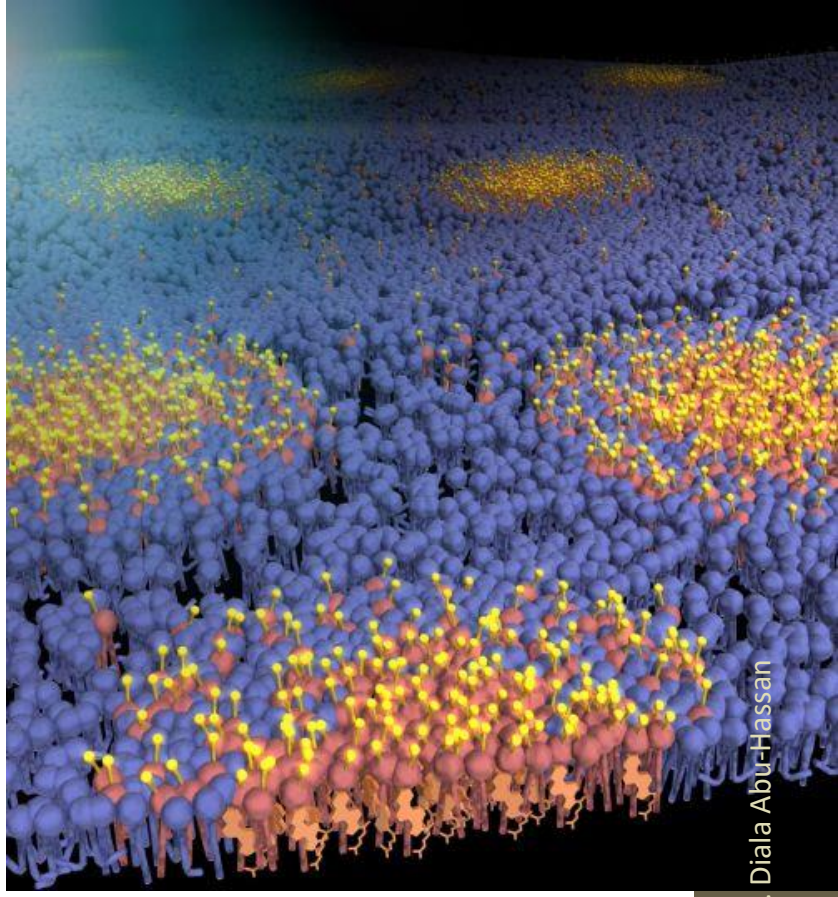
Asymmetric distribution of phospholipids between the two leaflets of the membrane bilayer.

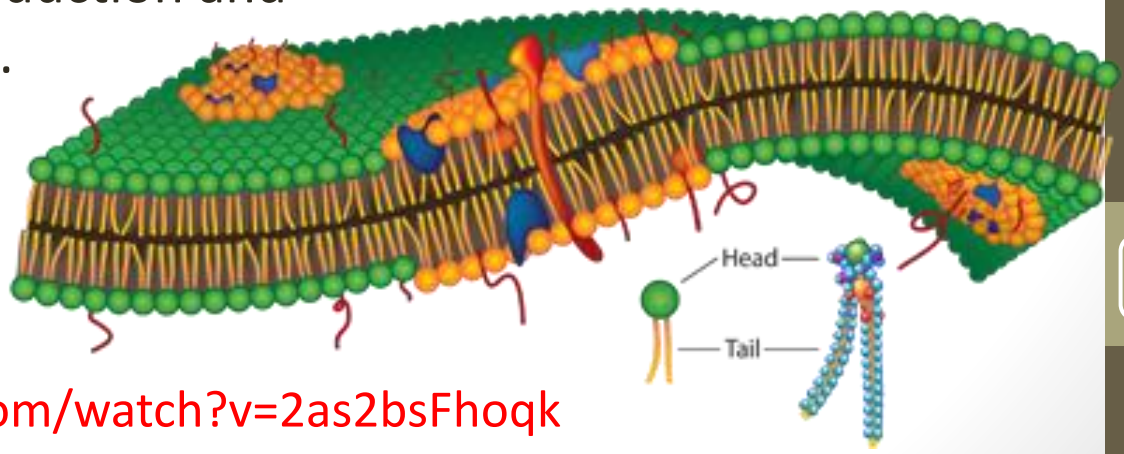


- The outer leaflet: Ⓟcholine, sphingomyelin, glycolipids
- The inner leaflet:Ⓟethanolamine, Ⓟserine, Ⓟinositol (minor)
- Ⓟinositol has a role in cell signaling, cell junctions and endocytosis.
- The head groups of both Ⓟserine and Ⓟinositol are negatively charged, thus, the cytosolic face of the plasma membrane has a net negative charge.

Lipid rafts

- Semisolid clusters (10-200 nm) of cholesterol and sphingolipids (sphingomyelin and glycolipids).
- Sphingolipids provide a more ordered lipid structure than phospholipids.
- Are enriched in glycosylphosphatidylinositol (GPI)-anchored proteins, and proteins involved in signal transduction and intracellular trafficking.

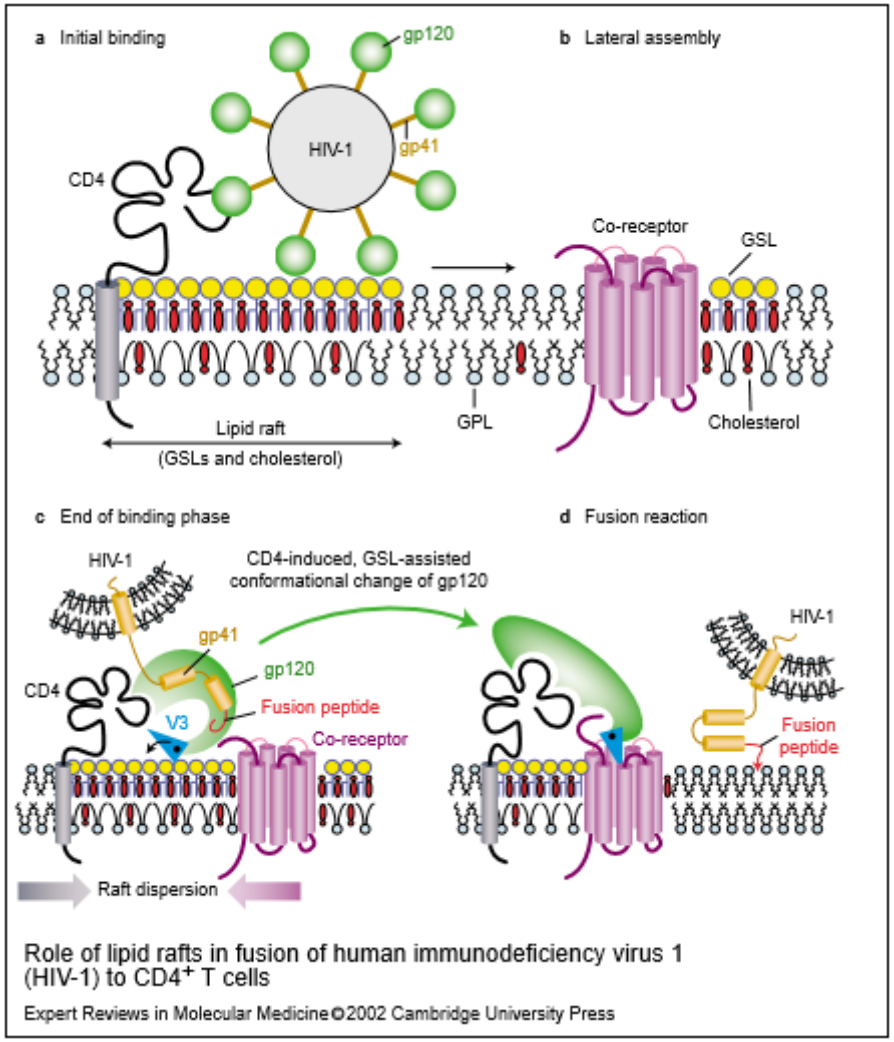




https://www.youtube.com/watch?v=2as2bsFhoqk

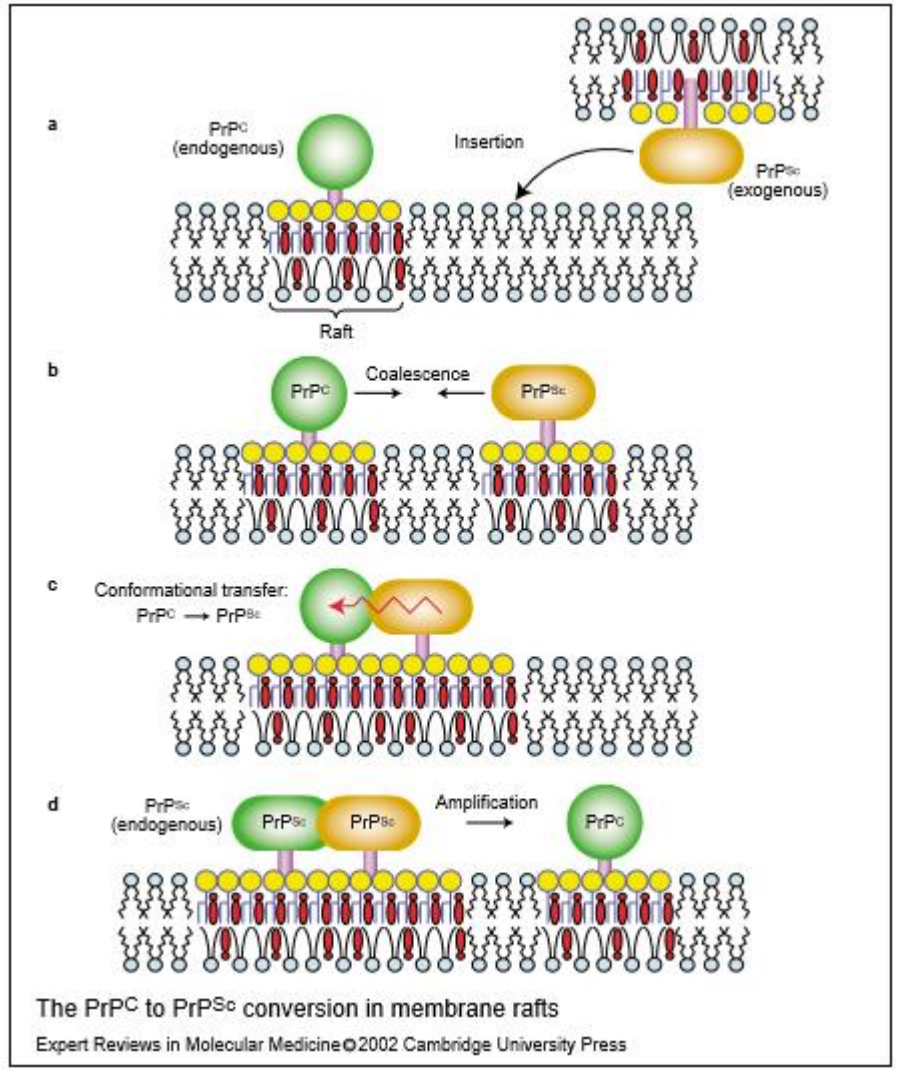
Application: Lipid rafts and viral infections

1. HIV virus
   - Budding may occur from lipid rafts
   - Viral fusion to $CD4^+$ T cells
2. Influenza virus
   - Raft-associated glycoproteins in envelope



Role of lipid rafts in fusion of human immunodeficiency virus 1 (HIV-1) to $CD4^+$ T cells

Application: Lipid rafts & diseases



The PrP^{C} to PrP^{Sc} conversion in membrane rafts

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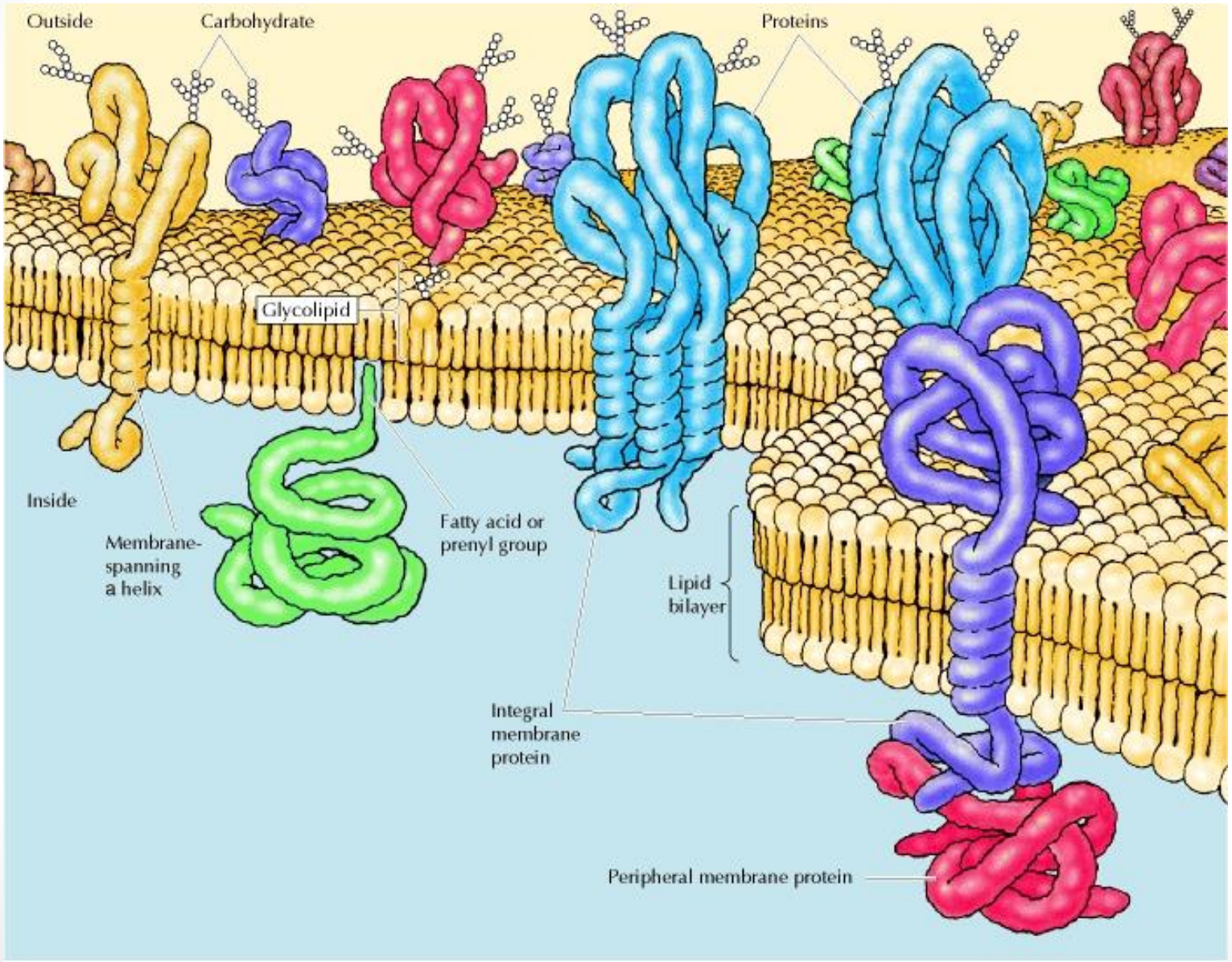
3. Prion disorder

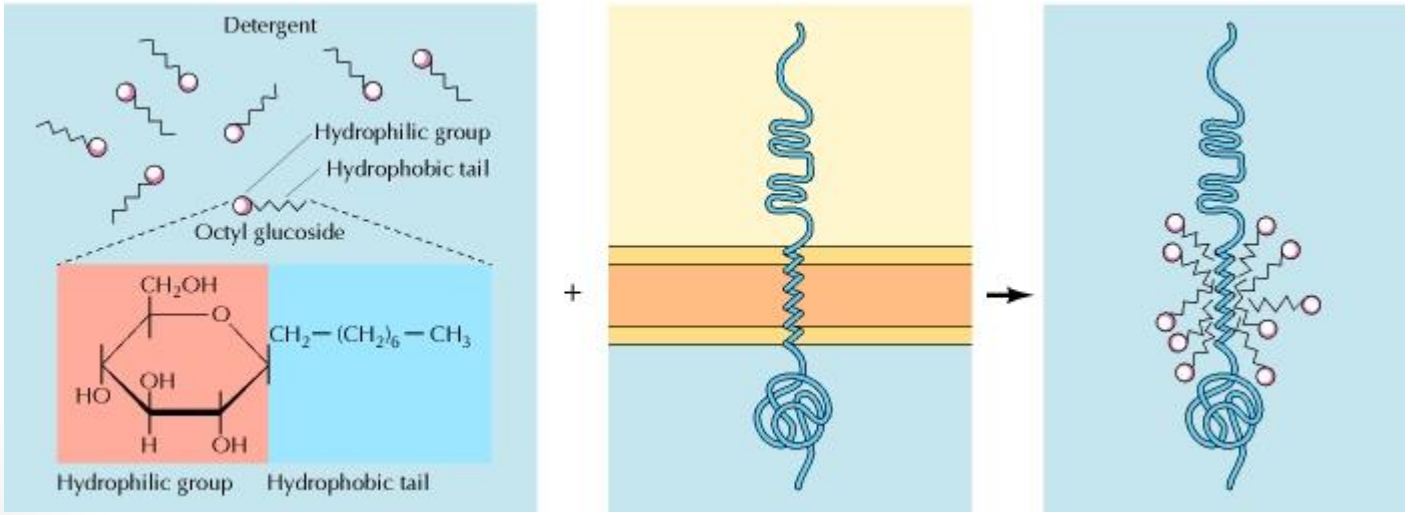
- Normal prion protein (PrPc) is converted to abnormal proteins (PrPsc) in lipid rafts .

Membrane proteins



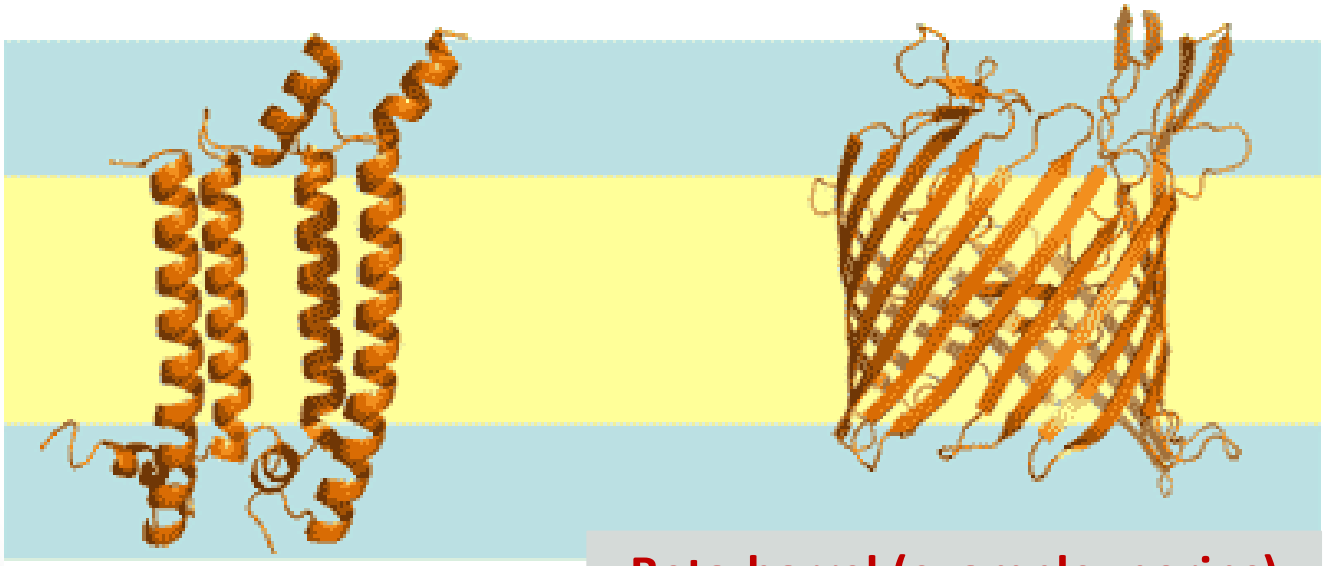
Integral membrane proteins

- Portions of integral membrane proteins are inserted into the lipid bilayer.
- They are dissociated by reagents of small amphipathic molecules.
  - The hydrophobic portions of detergents disrupt hydrophobic interactions.
  - The hydrophilic part makes the detergent-protein complexes soluble in aqueous solutions.



α-helices vs. β-sheets

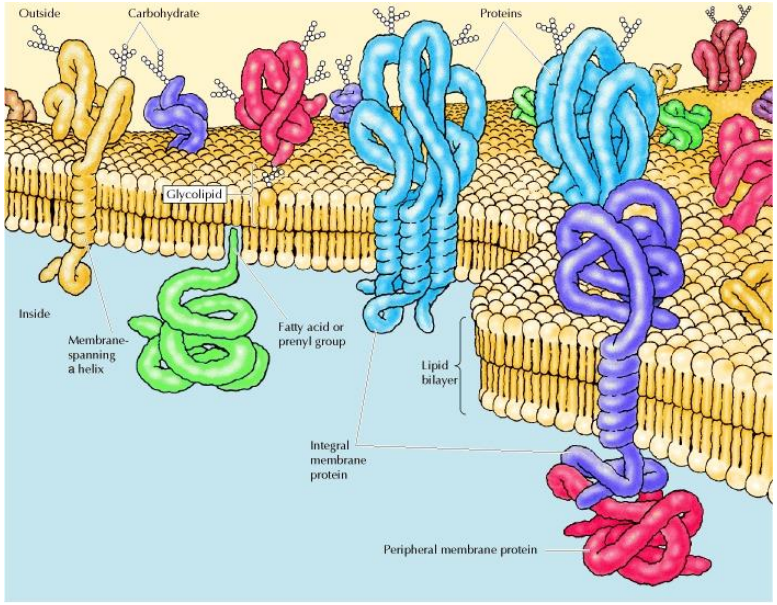
- The membrane-spanning portions of transmembrane proteins are usually α-helices of 20-25 hydrophobic amino acids.
- They are usually glycosylated with the oligosaccharides exposed on the outer surface of the cell.



Beta-barrel (example: porins)

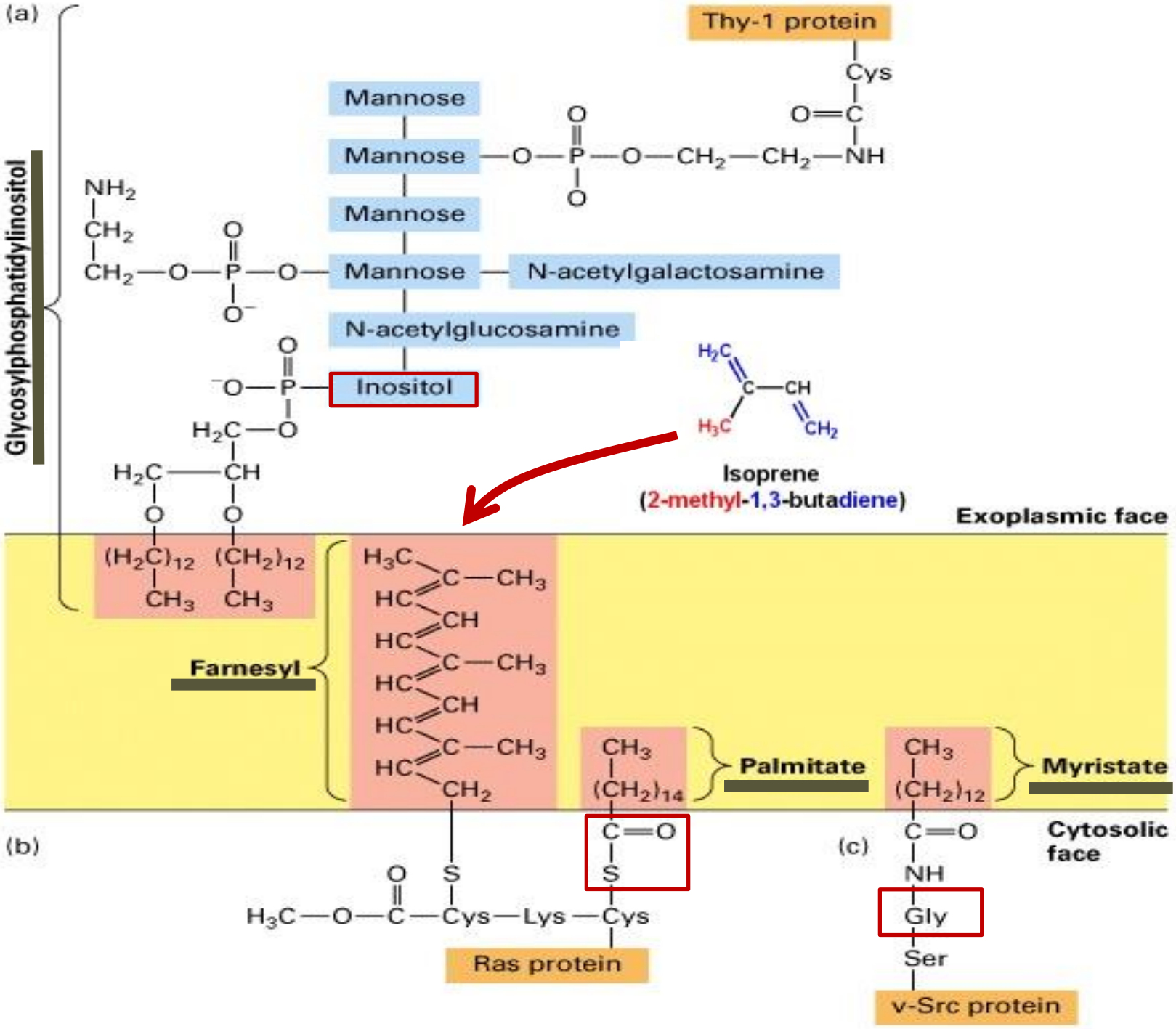
Peripheral membrane proteins

- Are proteins that dissociate from the membrane following treatments with polar solutions of extreme pH or high salt concentration
- They do not disrupt the phospholipid bilayer.
- Once dissociated, they are soluble in aqueous buffers.
- Are indirectly associated with membranes through protein-protein interactions, mainly ionic bonds.



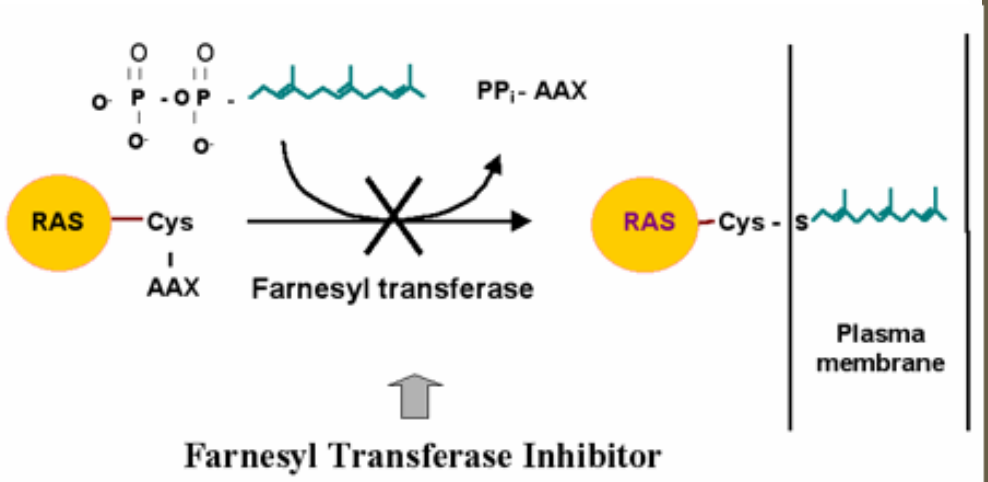
Lipid-anchored membrane proteins

- Proteins are anchored to the inner or outer leaflets of the membrane.
- Types of anchors:
  a) Myristoylation
     - Myristoyl group is attached the N-terminus
  b) Palmitoylation
     - Palmitate is added to –SH group of the side chains of internal cysteine residues.
  c) Prenylation
     - It refers to linking of "isoprene"-based groups
     - Prenyl group is attached to –SH group of cysteine near C-terminus of proteins
  d) Glycosyl phosphatidylinositol (GPI) anchors on the **outer** surface
     - The carbohydrate bridges the protein with the fatty acid chains of the phospholipid (usually ethanolamine)
     - GPI anchors are added to the C-terminus of a protein in the ER


(a)
Thy-1 protein
Cys
Mannose
Mannose
Mannose
Mannose
N-acetylgalactosamine
N-acetylglucosamine
Inositol
Glycosylphosphatidylinositol
Isoprene
(2-methyl-1,3-butadiene)
Exoplasmic face
Farnesyl
Palmitate
Myristate
Cytosolic face
(b)
Ras protein
(c)
Gly
Ser
v-Src protein

Application: farnesylation inhibitors and disease treatment

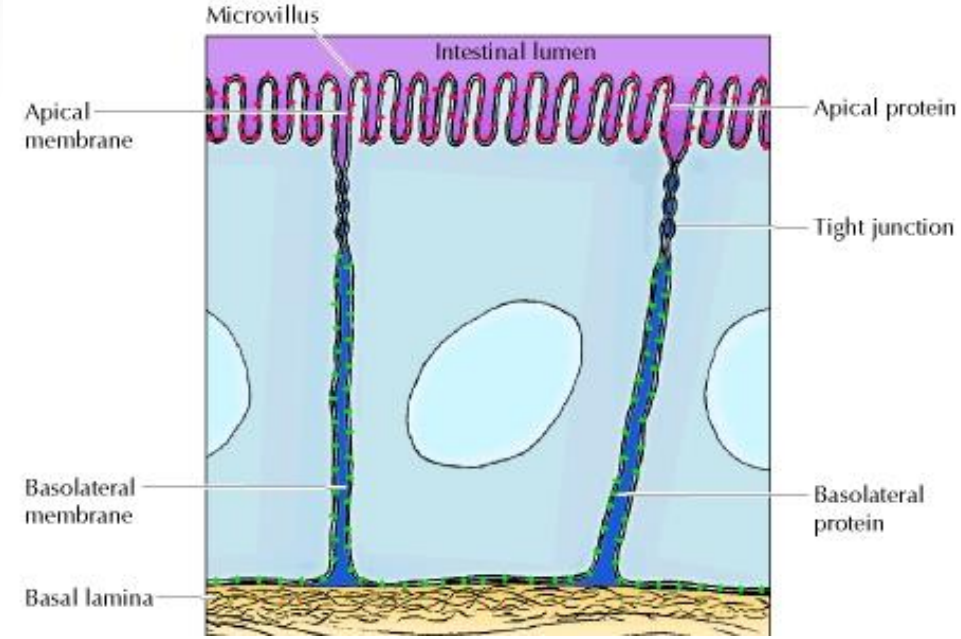
- Ras is an oncogene that needs farnesylation for its function and oncogenic activity.
- Farnesyl transferase inhibitors (FITs) have anti-tumor activity in preclinical cell culture and mouse models, but they failed in human clinical trials because:
  - FTIs did not block prenylation of other Ras isoforms (N-Ras and K-Ras) and their tumorigenic activity.
  - Other farnesylated proteins have important roles in cell including growth regulation.

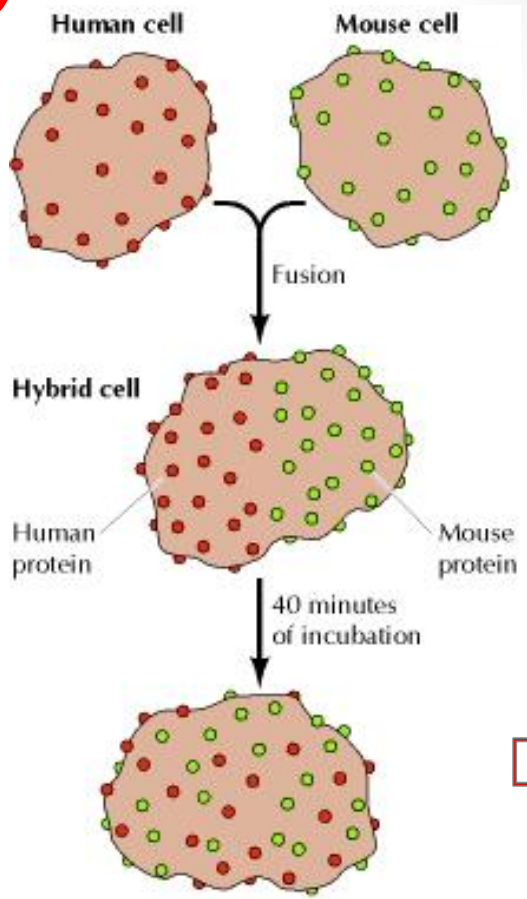


-FTIs are considered for the treatment of other diseases such as Hutchinson-Gilford Progeria Syndrome (AKA progeria), caused by mutated farnesylated lamin A protein.
-FITs can be used in the treatment of malaria.

Protein mobility

Both proteins and lipids diffuse laterally through the membrane.



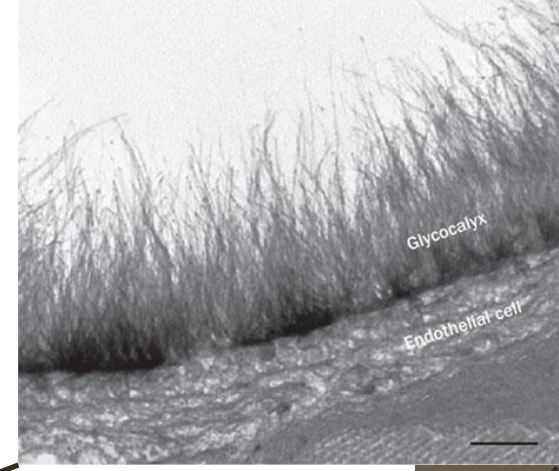


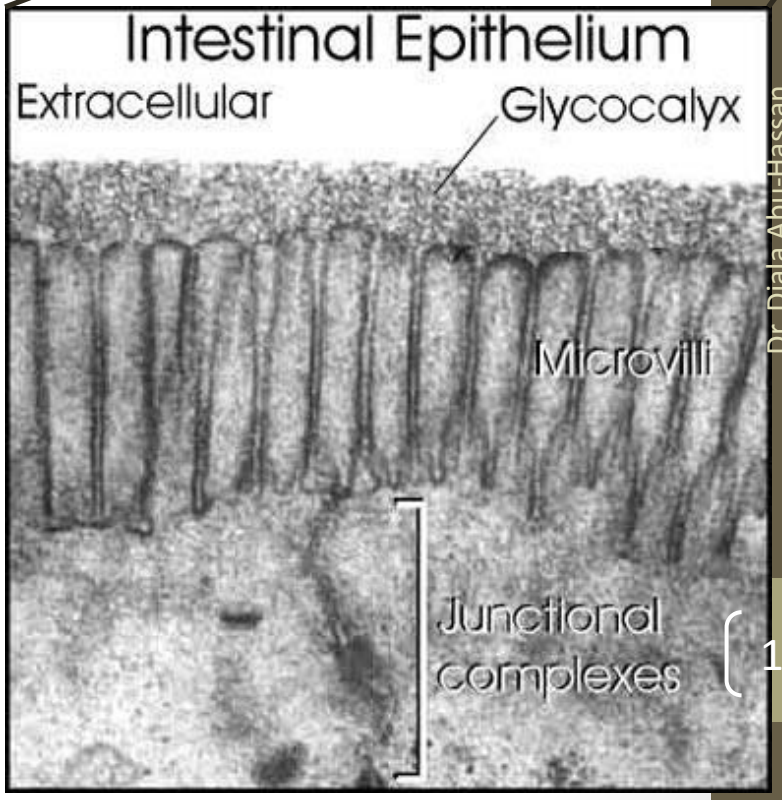
The mobility of membrane proteins is restricted by

- **Association with the cytoskeleton, ECM proteins, proteins on the surface of adjacent cells)**
- **Specific membrane domains such as tight junctions, that maintain the spatial distribution of apical and basolateral proteins**
- **Lipid composition (lipid rafts rich in GPI anchored-proteins) restrict protein mobility.**

Glycocalyx

- A carbohydrate coat that covers the surface of the cell.
- Is formed by the oligosaccharides of glycolipids and transmembrane glycoproteins.





Functions:

- **Cell-cell interactions (leukocytes)**
- **Protection of cell surface from ionic and mechanical stress**
- **Acts as a barrier for microorganisms**