MEMBRANE BOUND PROTEINS....

Introduction

- Serve as models for membrane structures.
- Explain the distinctive characteristics of membrane.
- mediate nearly all membrane functions, i.e
  - Carry out the dynamic activities.
  - Act as pumps.
  - Also serve as gates
  - Functions as receptors and enzymes
  - Helps in signal and energy transduction.

Distribution of membrane proteins

Distribution varies according to the;

- Cell type
- Type of the membrane
- Function of the membrane

Example

- Myelin (only 18% protein)
- Plasma membrane (50% protein)
- Mitochondrial inner membrane (75%)

Functions of Membrane Proteins

- **Transport:**
- A protein that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute.
- Some transport proteins hydrolyze ATP as an energy source to actively pump substances across the membrane.
- **Enzymatic activity:**
- A protein built into the membrane may be an enzyme with the active site exposed to substances in the adjacent solution.
- In some cases, several enzymes in a membrane are ordered as a team that carries out sequential steps of metabolic pathway**.**
- **Signal transduction:**
- A membrane protein may have a binding site with a specific shape that fills the shape of a chemical messenger such as hormone.

Cont…

- The external messenger (signal) may cause a conformational change in the protein that relays the message to the inside of the cell.

- **Intercellular joining:**

  Membrane proteins or adjacent cells may be hooked together in various kinds of junctions.

- **Cell-cell recognition:**

  Some glycoproteins (proteins with short chains of sugars) serve as identification tags that are specifically recognised by other cells.

- **Attachment to the cytoskeleton and extracellular matrix:**

- Microfilaments or other elements of the cytoskeleton may be bonded to membrane proteins, a function that helps maintain cell shape and fixes the location of certain membrane proteins.
- Proteins that adhere to the ECM can coordinate intracellular and extracellular changes.

Cont…..

- Biological proteins consist of a phospholipid bilayer and a variety of proteins that accomplish vital biological functions.
- Structural proteins are attached to microfilaments in the cytoskeleton which ensures stability of the cell.
- Cell adhesion molecules allow cells to identify each other and interact.
- Membrane enzymes produce a variety of substances essential for cell function.
- Membrane receptor proteins serve as connection between the cell's internal and external environments.
- Transport proteins play an important role in the maintenance of concentration of ions.

Types

Generally classified into two types according to ease of extraction.

1. **Integral or intrinsic proteins**:

- ✓ tightly bound to membrane - interact with interior (hydrophobic interactions)
- ✓ can be released only by disrupting the lipid bilayer and interfering with the hydrophobic interactions.
- ✓ require detergents (or organic solvents) for extraction from membranes .
- ✓ water-insoluble
- ✓ Some completely span membrane ("transmembrane proteins").
- ✓ Integral membrane proteins are peremanently attached to the membrane. So they can be defined as those proteins which require a detergent (such as SDS or trition X- 100) or some other polar solvent to be displaced.

- ✓ They can be classified according to their relationship with the bilayer.
- ✓ **Integral polytopic proetins**, also known as transmembrane proteins are proteins that are permenantly attached to the lipid membrane and span across the membrane.
- ✓ **Integral monotopic proteins** are proteins that are permenantly attached to the lipid membrane from only one side and do not span the membrane.

Peripheral proteins

- weakly associated with membrane at surface.
- bind to polar lipid heads and/or to integral membrane proteins.
- electrostatic interactions predominate (ionic bonds and/or hydrogen bonds)
- easily extractable from membranes by high salt concentrations (disrupting electrostatic interactions), or by EDTA (chelates Ca and Mg)
- usually water-soluble (globular).
- They are temporarily attached either to the lipid bilayer or to the integral proteins by a combination of hydrophobic, elctrostatic, and other non-covalent interactions.
- Peripheral proteins dissociate following treatment with a polar reagent such as solution with an elevated pH, or high salt concentrations.
- Integral and peripheral proteins may not be post translationally modified with added fatty acid chains which may be anchored in the lipid bilayer.

Lipid-anchored membrane proteins

- Proteins that are covalently linked to lipids
- Some lipid anchors can be reversibly attached to/detached from proteins.
- Example;
  - Prenyl groups such as farnesyl and geranylgeranyl
  - Fatty acyl groups such as myristoyl and palmitoyl
  - Lipid carbohydrate groups like glycosylphosphatidylinsitol.

Transmembrane Proteins

- Integral proteins Span the mambrane by arranging hydrophobic regions into secondary structures i.e α-helical or β barrel motifs.
- Can be either single pass (monopotic) or multiple pass (polytopic).

Glycophorin-A

- Glycoporin-A is a glycoprotein (integral membrane protein in erythrocytes by mass 60% carbohydrate and 40% protein).
- Has a single membrane α-helix.
- Has only 131 amino acid residues.
- These are rich in sialic acid which gives the red blood cells a very hydrophilic- charged coat. This enables them to circulate without adhering them to other cells or vessel walls.
- Most of the protein (N-terminal portion) on outside of cell, exposed to water mainly; hydrophilic residues.
- Extracellular part of the protein also receptor for influenza virus binding to cells.
- C-terminal portion on cytosolic side of membrane interacts with cytoskeletal proteins.

Bacteriorhodopsin

- 7 transmembrane α-helices.
- globular shape, most of protein embedded in the membrane
- 247 amino acid residues (26,000 MW)
- When oxygen is scarce, uses light energy to pump protons across membrane against a concentration gradient .
- generates and maintains [H+] gradient (pH gradient) across cell membrane.
- Resulting transmembrane proton gradient = "stored" potential energy - used by a different protein to drive ATP synthesis (ATP synthase).

Prostaglandin H_2 synthase

- Also called as cyclooxygenase (Cox)
- Main catalytic function is the conversion of arachidonic acid to prostaglandin H_2 (PG H_2)
- Monotpoic integral membrane proteins; bind to luminal leaflet of ER membrane and nuclear membrane.
- Implications in thrombosis, inflammation, neurological disorders and cancer.
- Great deal of attention as the target of non- steroidal anti-infalmmatory drugs (NSAIDs).

Porins

- Porins are beta proteins that cross a cellular membrane and act as a pore through which molecules can diffuse.
- Porins are large enough to allow passive diffusion, i.e they act as channels that are specific to different types of molecules.
- They are present in the outer membrane of gram negative bacteria and some gram positive bacteria.
- Porins typically control the diffusion of small metabolites like sugars, ions and amino acids.