Cell Biology (Day 4)

Membrane Proteins

Proteins account for half of the mass of plasma membrane.

→ integral & peripheral.

Integral membrane proteins → transmembrane proteins

→ amphipilic (hydrophobic regions of protein & Lb interact)

Transmembrane → single-pass
→ multipass
→ have covalently attached fatty acid chain that links them to cytosolic lipid monolayer.

→ Structurally,

- Single α helix
- multiple α helices
- rolled up β sheet (β barrel)

How are membrane proteins attached to membrane?

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① either, by covalent attachment of fatty acid chains to cytosolic monolayer

(2) anchored to cytosolic monolayer by amphiphilic α helix.

(3) can be entirely in cytosol, but attached to membrane through lipid chain or prenyl group.

(4) can also be attached by oligosaccharide linker, to phosphatidylinositol in the non-cytosolic monolayer.

Lipid Anchors

- how a membrane protein is attached depends on its function - only transmembrane proteins can function on both sides of the bilayer (e.g., cell surface receptors)

Transient attachment

- proteins that function only on one side of the membrane are associated exclusively with the monolayer or a protein domain on that side.

- attachement may be Transient

Myristoylation - a myristic acid chain is added to N-terminal AA of protein during synthesis on ribosome → helps it to anchor to membrane; often another lipid like palmitic acid is added for stronger anchoring. When signaling is removed, palmitic acid & myristic acid is removed, and protein returns to cytosol.

How do transmembrane proteins cross the membrane?

Either as α-helices or β-barrels

- Depending on function of cytosolic & non-cytosolic domains, asymmetry in membrane protein location.
- The parts that pass the lipid bilayer mostly have amino acids with non-polar side chains.
- Peptide bonds polar ⟹ form H-bonds in bilayer
  - to maximise,
    - α-helix for single-pass
    - β-sheet for multipass
- X-ray crystallography → allowing us to determine 3D str. of protein.
  - allows us to predict sequence of α-helix from hydropathy plots
- Chain-bending energetically costly due to loss of regular H-bonding interactions.
  - hence a polypeptide chains that enters bilayer is likely to pass entirely before changing directions.

However, multipass proteins ⟹ can contain sections that fold into the membrane from either side, without

contacting lipid layer, by virtue of protein-protein interactions with the transmembrane helices.

No need to minimise H-bonding ⇒ variety of 2° str & chain bending.

↳ crucial for aquaporins.

Many membrane proteins are glycosylated

- Golgi body & ER responsible, hence always found on non-cytosolic side
- most membrane proteins are glycosylated → hence membrane coated with carbohydrates

polysaccharide chains of integral membrane proteoglycans.

occur as oligosaccharide chains bound to glycoproteins & glycolipids

- cell coat / glycocalyx — can be visualised using ruthenium red, as well as by its affinity for lectins
  - protects cell against mechanical & chemical damage.
  - prevents unwanted protein-protein interactions
- chains of sugars (less than 15) → often branched

- lectins help in cell recognition processes

Membrane proteins can be solubilised & purified in detergents

- How?
  By - disrupting hydrophobic interactions & destroying the lipid bilayer.

  When mixed with membranes, hydrophobic end of detergent binds to hydrophobic region of protein, thereby displacing membrane lipids.
  Since the other end of the detergent is polar, this binding tends to bring proteins into the solution as detergent-protein complexes.

- SDS - strong, ionic detergent, that denatures proteins

Cortical Cytoskeleton

- cell restricts lateral movement of membrane proteins by tethering them to surface.
- RBC has a spectrin network cytoskeleton
- cortical region rich in actin filaments → attached to the plasma membrane.