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NAAC ACCREDITED 'A' GRADE



Topic:Red Cell Membrane Structure

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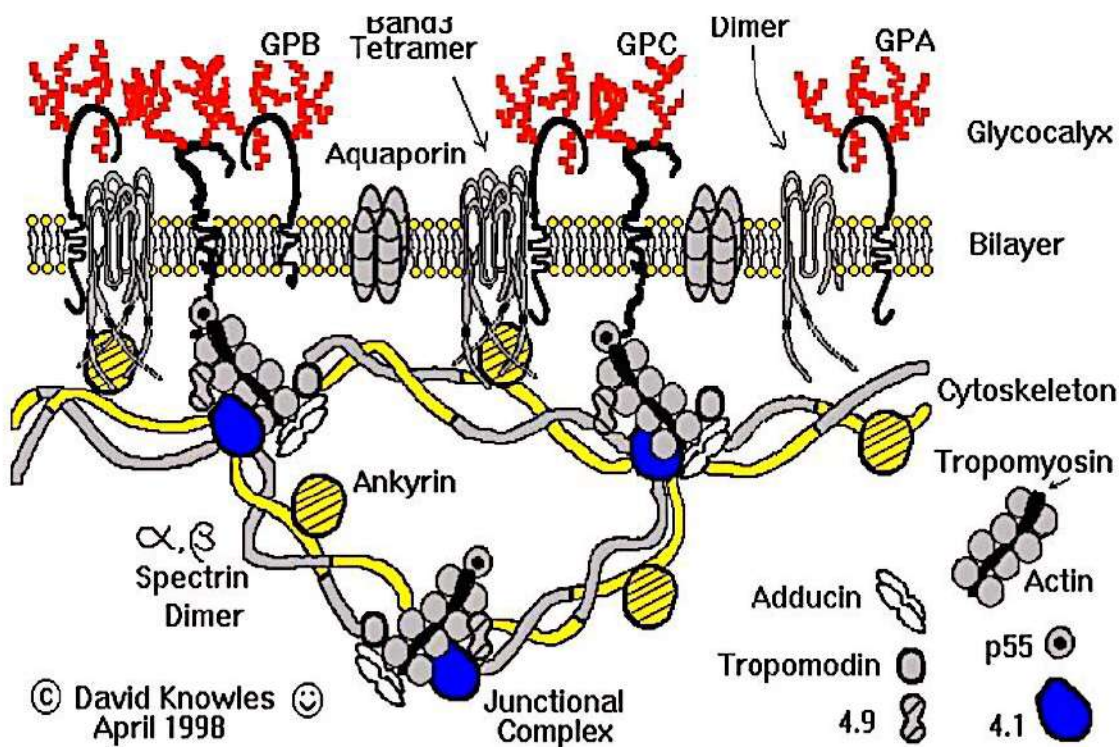
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RED CELL MEMBRANE STRUCTURE



The red blood cell membrane consists three basic components: a lipid bilayer, transmembrane (integral) proteins and a cytoskeletal network:

Lipid Bilayer

The lipid bilayer is a semipermeable, incompressible, two dimensional liquid crystal which is asymmetric in composition and separates the cytoplasm, within the cell, from the extracellular medium. Phosphatidylcholine (PC), sphingomyelin and the sterol cholesterol are the dominant extra leaflet components while phosphatidylserine (PS) and phosphatidylethanolamine (PE) are the dominant inner leaflet components. Interestingly enough there are proteins in the bilayer called flippases which maintain the correct lipid asymmetry.

Transmembrane Proteins

Transmembrane proteins are solutes in a two dimensional fluid, the bilayer, and thus have varying degrees of lateral mobility in the plane of the membrane. They have a transbilayer domain and either or both an extrafacial domain, which contributes to the glycocalyx and a cytoplasmic domain. The major transmembrane proteins are glycoproteins, band 3 and glygophorin. Band 3 is a multispanning ion transport channel and exists in a dimer / tetramer equilibrium. It is structurally important because band 3 tetramers, rather than dimers, tether the bilayer to the skeleton via an interaction between its cytoplasmic domain and ankyrin which is associated with spectrin. Glycophorins have a single spanning alpha helix and are a general class of proteins which contribute the major portion of glycosylation (sugar) at the extracellular domain. Glycophorin C (GPC) is another bilayer / skeleton tethering point via its interaction with protein 4.1 within the junctional complex. Glycophorin A (GPA) is partially associated with band 3. There are a host of other transmembrane proteins. Aquaporin, as the name suggests, is a water channel protein existing as a homotetramer. Rh is a protein complex thought to associate with band 3. One class of proteins, which are not strictly transbilayer, are Glycosylphosphatidylinositol (GPI)-linked proteins. GPI is a lipid analog which links an extrafacial protein, for example, CD59.

The Cytoskeleton

The cytoskeleton is an irregular hexagonal lattice of polymeric spectrin molecules which are tied together by actin, 4.1 and other numerous proteins at nodes called junctional complexes. The skeleton makes a two dimensional network which is very flexible, compressible with obvious structural importance.

Questions with probable Answers

1. What is the structure of the membrane skeleton, and what role does it play in supporting red cells?

A. The proteins responsible for imparting the membrane skeleton are tethered to the cytoplasmic surface of the membrane, and are responsible for the elasticity and stability of the red cell membrane. The key proteins that make up the membrane skeleton are spectrin, actin, protein 4.1, pallidin, and ankyrin, although many other proteins are involved. Spectrin alpha and beta subunits are entwined to form dimers, and dimers associate head to head to form tetramers; spectrin tetramers form hexagonal units that form a mesh-like structure. Spectrin tetramers are bound together by junctional complexes comprising actin, protein 4.1, and other proteins. The skeleton is coupled to the lipid membrane by ankyrin, which binds to band 3, strengthened by band 4.2. Proteins forming horizontal and vertical interactions maintain the integrity and shape of the red cell. The vertical interactions (including spectrin-ankyrin-band 3 interactions, spectrin-protein 4.1R-junctional complex linkages, and interactions between skeletal proteins and negatively charged proteins of the inner component of the lipid bilayer) stabilize the lipid membrane, and the horizontal interactions (involving the spectrin heterodimer associations) support the structural integrity of the red cell, including after exposure to shearing.

The integral proteins, which are embedded in and span the lipid membrane, have necessary functions for red cell and membrane homeostasis and also interact with the skeleton to tether it to the lipid membrane. Band 3, an anion exchanger, plays a critical role in maintaining red cell hydration; however, it also tethers the red cell skeleton to the lipid membrane via interactions with ankyrin, protein 4.2, 4.1 and other proteins. Glycophorins (A, B, C, and D) are glycoproteins rich in sialic acid that impart a net negative charge to the cell surface, preventing excessive cell-cell and cell-endothelium interactions. The glycophorins appear to serve as a receptor for, and be important in, plasmodium invasion of red cells. Other integral membrane proteins include a range of ion, water, and gas transport channels, and proteins for which the function has not yet been fully elucidated.

2. What are the functions of the red cell membrane?

A. One function is to maintain structure and contain the contents of the red cell—chiefly, hemoglobin. Far from being just a casing, however, the red cell membrane plays a critical role in maintaining cellular functions in the only non-nucleated cell in the body (the cellular organelles are lost during red cell maturation). Thus, the red cell membrane accomplishes vital tasks in the transport of salts and nutrients.

3. What are the properties of the red cell membrane that allow it to carry out these functions?

A. The red cell membrane achieves its key structural properties by being deformable but stable, and by having a unique biconcave shape with a high surface area to volume ratio. It achieves its transport role through the range of proteins that span it and are embedded in it, although transport through passive diffusion also occurs.