The cell membrane and receptors

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Abstract

The plasma membrane forms the interface between the cell and its environment. It is composed essentially of a phospholipid matrix and many different types of protein molecules which may be embedded within the matrix (integral proteins) or more loosely associated with the cytoplasmic 'face' of the membrane (peripheral proteins). The passage of essential ions and molecules across the membrane is controlled by integral proteins acting as channels or transporters. Intercellular communication is mediated by protein receptors, which are activated by signalling molecules such as hormones and neurotransmitters. Physical contact between the cell and its environment (and between cells) is mediated by membrane adhesion proteins. The plasma membrane is a highly dynamic structure in terms of molecular composition and topological configuration. The linkage of the internal cytoskeleton to the plasma membrane (via peripheral and integral proteins) expedites cellular shape changes or amoeboid motion of some types of cell. The process of endocytosis enables the cell to internalize small volumes of extracellular fluid (pinocytosis) by invagination and formation of intracellular vesicles or to engulf entire cells by phagocytosis. Secretion of molecules, such as hormones, is accomplished by fusion of intracellular vesicles with the plasma membrane. This mechanism of exocytosis is mediated by another type of protein: the SNARE proteins.

Keywords Endocytosis; exocytosis; ion channels; phospholipids; transporters

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Learning objectives

After reading this article, you should be able to describe:

- the basic arrangement of phospholipids to form the cell membrane, and factors that influence the fluidity of this structure
- the role of proteins (structural and forming channels, receptors, enzymes and carriers), glycoproteins and glycolipids
- different types of channel (including voltage-gated and ligand-gated channels) and roles of carrier proteins
- ways in which ligands binding to the cell surface can trigger changes within the cell
- links between the cell membrane and the cytoskeleton, and their role in cell movement
- the processes of endocytosis and exocytosis and the roles of SNARE proteins

The cell membrane (plasma membrane, plasmalemma) of animal cells is a fundamental cellular component, providing a barrier between the external environment and the intracellular cytoplasm. However, it is far from acting merely as a passive barrier. The plasma membrane acts as a 'gatekeeper', controlling the movement of important ions and molecules into and out of the cell. It is the interface between the cell and its environment, and is the initial site of action of a plethora of signalling molecules. The plasma membrane establishes physical contact between the cell and adjacent structures (usually other cells within a tissue) and is responsible for mediating intercellular communication. Furthermore, the plasma membrane is a dynamic structure; intimate connections to the internal cytoskeleton allow some cells to engulf and internalize small volumes of the extracellular medium (or even move in an amoeboid manner). Intracellular vesicles can fuse with the plasma membrane to mediate the secretion of important cellular contents, such as hormones or neurotransmitters. These properties of the plasma membrane have become highly modified in many cells (e.g. nervous system function depends on the specialized properties of neurones, which possess electrically excitable membranes and specialized intercellular contact points). In this article the basic structure and functions of the plasma membrane, together with its main physiological specializations, are reviewed.

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Structure

The basic matrix of the plasma membrane consists essentially of two sheets (a bilayer) of phospholipid molecules (Figure 1). The phospholipids are amphoteric molecules (i.e. one end of the molecule is hydrophilic or water soluble and the other end is hydrophobic or water insoluble). Therefore, in an aqueous environment, the two sheets adopt a phospholipid bilayer, with the hydrophobic ends of the molecules on the inside of the bilayer and the hydrophilic ends on the outside. Within this 'sea' of phospholipids are embedded many different types of protein molecules, which have many specialist functions. This is the basic 'fluid-mosaic' model of the plasma membrane formulated in the 1960s and early 1970s. Most plasma membranes are 6–10 nm thick, and are approximately 50% lipid and 50% protein by weight. In addition to the different types of phospholipids and proteins, other molecules may be present in the plasma membrane according to tissue location: for example, cholesterol and small amounts of carbohydrates (attached to proteins to form glycoproteins or to lipids to form glycolipids). The carbohydrate moieties of the glycoproteins and glycolipids are situated on the extracellular face of the membrane, forming a coat (glycocalyx). The glycocalyx provides a protective covering for the cell, and many of the sugar moieties act as cellular markers, mediating cell–cell interactions.

Membrane lipids

The fluidity of the plasma membrane is largely determined by the nature of lipids constituting the basic matrix. The fluidity of the

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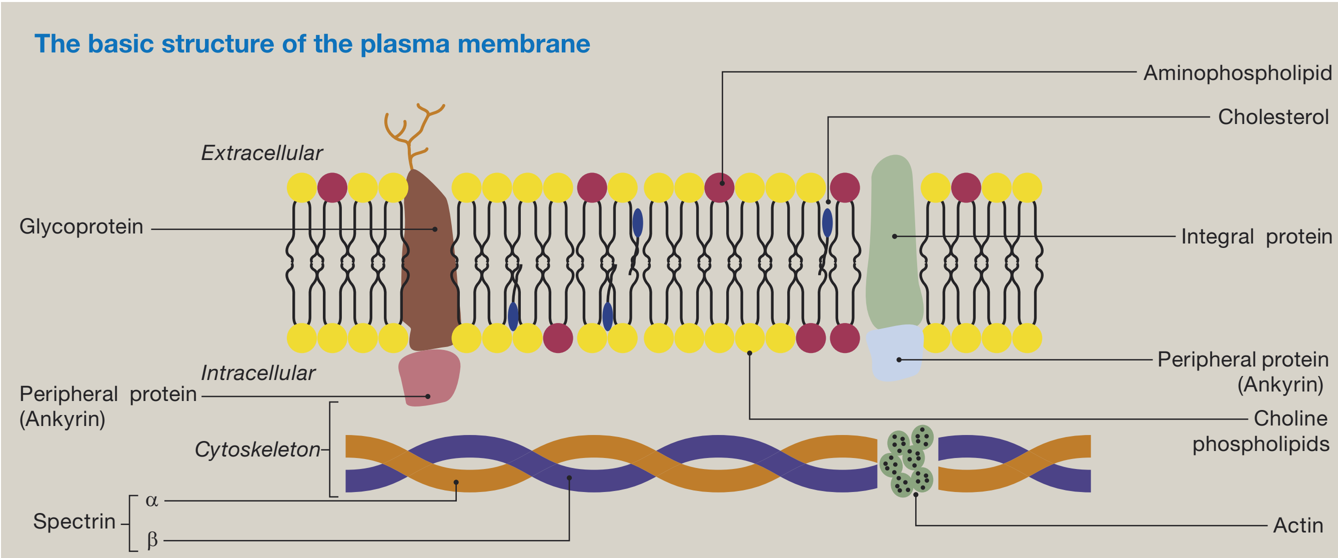

Figure 1

phospholipid bilayer is of critical importance in membrane function because this, in turn, can influence the functions of the various proteins embedded in the matrix. The phospholipid bilayer largely determines the general passive permeability properties of the cell membrane, allowing water and small lipophilic molecules to pass through, but acting as a barrier to ions and hydrophilic molecules. Phospholipids make up the bulk of the membrane lipids (e.g. phosphatidylcholines, sphingomyelins). The steroid, cholesterol, is also a major component of membrane lipids, functioning generally to regulate the fluidity of the membrane bilayer. Glycolipids are also usually present and are oriented such that the carbohydrate moieties of the molecules protrude from the external surface of the membrane to function as receptors or antigens. The action of cholera toxin is mediated by a ganglioside glycolipid to which the toxin binds; and the antigens determining the human A or B blood groupings are the carbohydrate moieties of gangliosides in the erythrocyte membrane.

Receptor proteins embedded in the membrane seem to be sequestered within specialized regions of the phospholipid matrix known as 'microdomains' or 'lipid rafts'. These regions are rich in cholesterol and sphingolipids and differ in physicochemical properties from the rest of the matrix in several ways (e.g. they are relatively detergent-resistant and are less fluid than the general matrix). The presence of excess cholesterol (which occurs during atherosclerosis) alters the properties of these rafts which, in turn, can disrupt the function of proteins embedded within them (e.g. the function of ion channels can be disrupted, leading to hindered calcium transport in vascular smooth muscle cells).

Membrane proteins

The numerous types of protein molecule associated with the plasma membrane can be broadly classified as extrinsic (peripheral) or intrinsic (integral). Intrinsic proteins include receptors that span the width of the membrane; extrinsic proteins include various enzymes involved in mediating the intracellular effects of receptor activation by signalling molecules. Functionally, the membrane proteins can be divided into several distinct groups:

- **receptors** – respond to the binding of specific signalling molecules
- **ion channels** – permit the passage of specific ions
- **transporters** – carry important ions or molecules across the membrane, sometimes against a concentration gradient
- **others** – the true complexity of membrane structure cannot be described in this short review, necessitating this category of 'other proteins', which includes many critically important (and incompletely characterized) molecules involved in membrane dynamics (e.g. SNARE proteins, 'band 3' proteins and glycophorin).

Some proteins do not fit neatly into a single category; for example, some receptors are actually ion channels that open when the signalling molecule binds (so-called 'ligand-gated ion channels') such as the nicotinic acetylcholine receptor mediating the contraction of skeletal muscle. There are also other membrane-associated proteins that perform specialist functions, such as SNARE proteins that mediate the fusion of intracellular vesicle membranes with the plasma membrane to permit secretion of cellular metabolites or release of neurotransmitters. There are also integral proteins that provide 'anchoring points' for the cytoskeleton to enable topological changes of the plasma membrane or amoeboid movement of the entire cell.

It is essential for each cell to possess an encompassing plasma membrane to separate the highly complex intracellular metabolic 'machinery' from the external environment; however, this poses a problem for the cell in terms of the transfer of important hydrophilic ions and molecules into and out of the cytoplasm. This problem is solved by the presence in the membrane of ion channels and transporter proteins. Ion channels are subdivided into three broad groups on the basis of the 'gating' (mechanism of opening) of the channel: (1) those that are always open – so-called 'leak' channels; (2) those that are opened ('gated') by

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