

Chapter 2

Cytology

2.1. Introduction

The cell is the basic unit of life. In all vertebrates the cell is eucaryotic, having a distinct nucleus. A cell could be considered to be a mass of protoplasm surrounded by a cell membrane. The protoplasm can be divided into: Cytoplasm - which lays between the cell membrane and the nucleus. Nucleoplasm - which lays within the nuclear membrane.

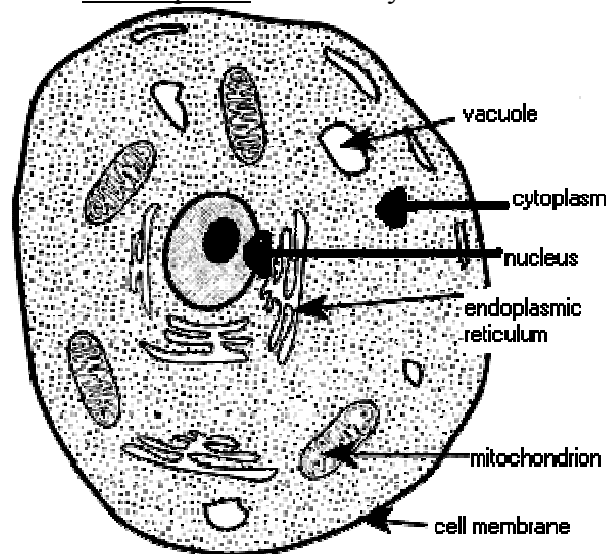


Fig.2.1. The Structure of an Animal Cell

2.2. The Cell Membrane

The cell membrane is also known as the plasmallema or plasma membrane. The cell membrane separates the cell from the external environment allowing it to maintain its own internal environment. This is essential for the cell to conduct metabolism and to maintain homeostasis. It is semipermeable in nature allowing some things, but not all things, to cross.

1.2.1 The Structure of the Cell Membrane

(a) Lipid Bilayer

The structure of the cell membrane is explained by The Fluid Mosaic Model which describes it as a phospholipid bilayer interdigitated by proteins and other lipids. The Phospholipid Bilayer forms the "backbone" of the cell membrane. The phospholipid bilayer is the result of the amphipathic nature of the phospholipid molecule. The phospholipid molecule has a hydrophilic (polar) "head" and a hydrophobic (nonpolar) "tail". The "heads" orientate toward the aqueous external and internal environments. As a result the "tails" are positioned in a nonaqueous region between the two layers of "heads". The amphipathic nature of the phospholipid molecule will cause the cell membrane to spontaneously form and to spontaneously repair itself. The hydrophobic tail is attached to the hydrophilic head of the phospholipid molecule by a single covalent

bond. This single covalent bond allows the tails to rotate and accounts for the "fluidity" of the Fluid Mosaic Model. Lipids other than phospholipids also interdigitate the cell membrane. Triglycerides serve a variety of purposes. Cholesterol stabilize the degree of fluidity to the cell membrane.

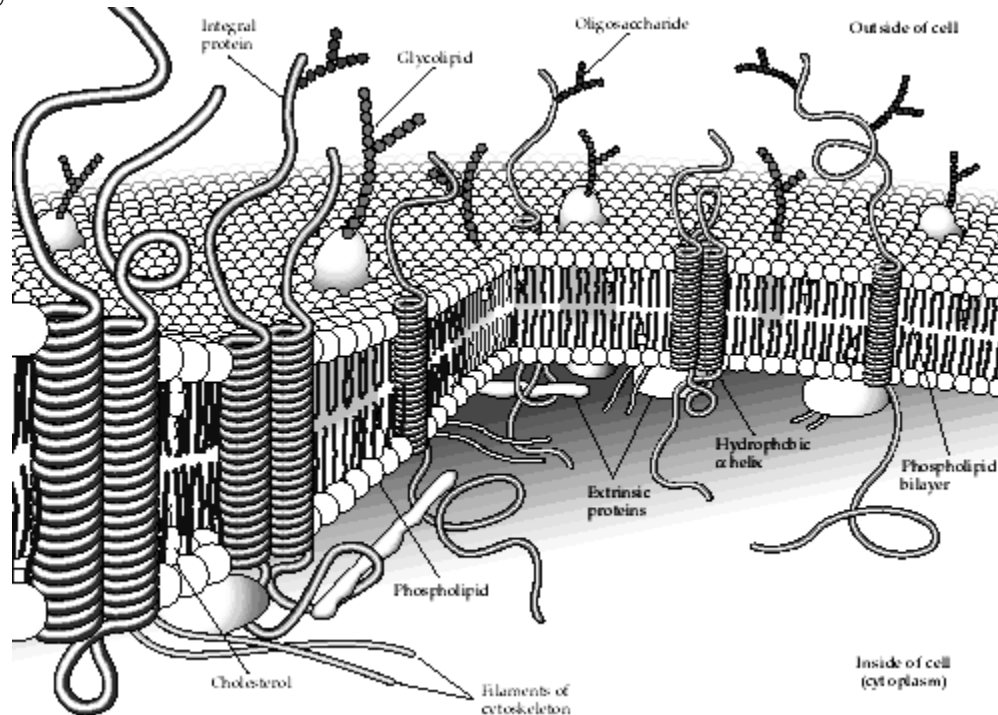


Fig.2.2. The Structure of the Cell Membrane

b) Membrane Proteins

Membrane proteins are the proteins of the cell membrane and comprise approximately 50% of the plasmalemma. Membrane proteins serve a wide array of functions such as: recognition, identification, and the transportation of substances across the cell membrane. The membrane proteins are divided into two classes based upon the extent to which they penetrate the phospholipid bilayer.

1] Peripheral Proteins - are the class of membrane proteins which DO NOT extend into the hydrophobic/tail portion of the phospholipid bilayer. They are not embedded in the cell membrane.

2] Integral Proteins - are the class of membrane proteins which DO extend into the hydrophobic/tail portion of the phospholipid bilayer. They are embedded in the cell membrane. Some integral proteins will extend through the entire bilayer. This subclass of integral proteins is called the Transmembrane Proteins. Ex; the sodium-potassium pump

c) Carbohydrates

Carbohydrates are also associated with the cell membrane. Typically they are linked to proteins or lipids forming glycoproteins or glycolipids respectively. Most are located on the external surface (the E face) of the plasmalemma. Often the membrane sugars serve as specific receptor sites. Ex; for hormones

2.2.2. Structural Specializations of the Cell Membrane:

Intercellular Junctions

a) Gap Junctions

Gap junctions are also known as; nexus, communicating junctions, or macula communicans. These junctions also consist of a "passageway" for intercellular communication and allow for the flow of chemical substances. This is especially true for ions. The two adjacent cell membranes are within 2nm of each other. This 2 nm gap is bridged by proteinaceous structures called connexons.

b) Desmosomes

Desmosomes are also known as zona adherens. Desmosomes are junctions holding two adjacent cells together. Each membrane has a protein unit, a desmosome, on its inner or P face. Radiating between these two desmosomes are proteinaceous filaments (made up of actin) that serve to hold the two cells together. The desmosomes are the anchor for these connecting filaments. There is a small gap of 5nm between the two cells at the point of the desmosomal junction.

c) Tight Junctions

Tight Junctions are also known as zona occludens. Like desmosomes, tight junctions serve to hold two cells together. They differ dramatically, however, in structure. The tight junction is a point where the two adjacent cell membranes actually fuse together becoming, in effect, one membrane at that point. This is due to the amphipathic nature of the phospholipid molecule. As a result, there is no space between the two opposing cells at the tight junction.

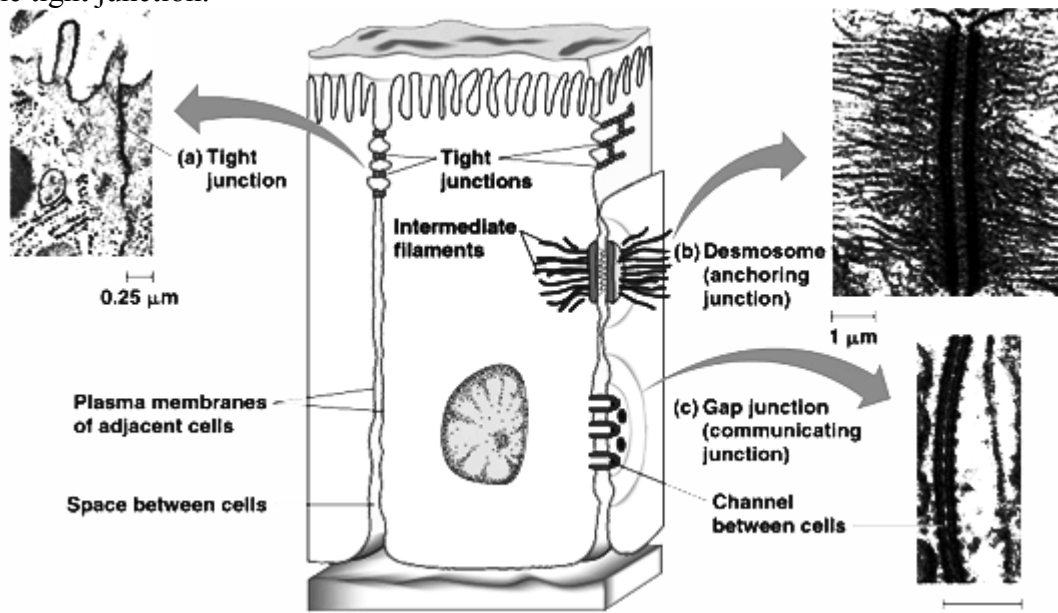


Fig.2.3. Intercellular Junctions

2.2.3. The Function of the Cell Membrane

Although the cell membrane serves as a barrier between the cell's external and internal environments it is not totally impermeable. Instead the cell membrane is semipermeable. Semipermeability means that the cell membrane allows certain substances, but not all substances, to cross.

a) Passive Transport

Passive Transport is the movement of molecules across the cell membrane without the use of cellular energy. Instead the energy of movement comes from the kinetic energy of

the molecules themselves.

i] **Diffusion** - is the net movement of molecules from an area of high concentration to an area of low concentration. There are two types:

ii] **Osmosis** - is the diffusion of solvent molecules (usually water).

iii] **Dialysis** - is the diffusion of solute molecules.

iv] **Facilitated Diffusion** - is diffusion requiring the cell membrane to be made permeable to the diffusing molecules due to the action of a carrier protein.

These special membrane proteins will temporarily bind to the diffusing molecule to accelerate it's movement into/out of the cell. Often the carrier protein changes the charge of the molecule so it can then travel along the osmotic gradient. These carrier proteins will be specific for specific molecules.

b) Active Transport

Active transport requires the expenditure of cellular energy. This is often due to the fact that the movement of the molecules is against the concentration gradient. In some cases ATP may also be required since the molecule would normally be unable to cross the cell membrane. Ex; the sodium-potassium pump

c) The Transport of Large Molecules Across the Cell Membrane

i] **Exocytosis** - is the movement of large molecules out of the cell. Often these large molecules are secretory products or waste products.

The substance is enclosed in an vesicle, within the cytoplasm, and moved to the cell membrane. The vesicle will fuse to the cell membrane, due to the amphipathic nature of the phospholipid molecule, which releases the substance into the external environment.

ii] **Endocytosis** - is the movement of large molecules into the cell. There are three strategies of endocytosis used by cells:

iii] **Phagocytosis** ("cell eating"): Out foldings of the cell membrane surround and engulf the "food substance". The food is now surrounded by a vesicle which pinches off from the cell membrane. This vesicle will move deeper into the cytosol where it will become surrounded by enzyme filled vesicles, lysosomes, which will digest the food. Ex' A neutrophil consuming a bacterium

iv] **Pinocytosis** ("cell drinking"): The mechanism of pinocytosis is similar to that of phagocytosis except that the object to be brought into the cell is already in solution. So lysosomes are not required. Instead the molecules can simply diffuse out of the vesicle into the cytosol.

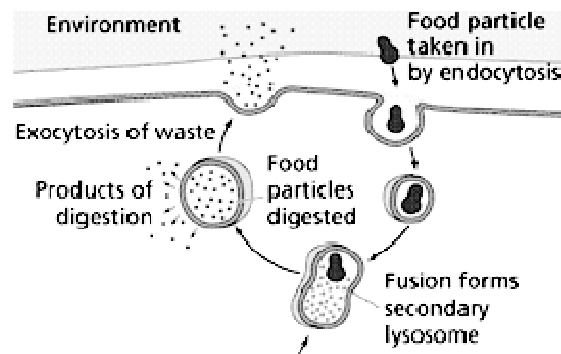


Fig.2.4. Endocytosis and Exocytosis

v] Receptor Mediated Endocytosis

Receptor mediated endocytosis is very similar to phagocytosis except that it requires special receptor proteins on the cell membrane to recognize the substance to be brought into the cell. The vesicles which form will be covered with these receptor proteins and so are called "whiskered" or "coated" vesicles. These receptor proteins are lost from the vesicle and return to the cell membrane prior to the lysosome mediated degradation of the object.

2.2.4. The Organelles

a) The Nucleus

The nucleus is typically the most prominent organelle in a vertebrate cell. It averages 5 um in diameter. It is typically spherical in shape. Typically vertebrate cells are uninucleated but there are some exceptions: Ex; Erythrocytes and thrombocytes are anucleated. Ex; Skeletal muscle cells are multinucleated. The nucleus is surrounded by a double membrane structure called the Nuclear Envelope (aka; Nuclear Membrane, Nucllemma). This nuclear envelope is even more selectively permeable than is the cell membrane. It does allow some substances to pass through by means of openings called Nuclear Pores. The nucleus contains the bulk of a cell's genetic information. This genetic material consists of DNA, RNA, and histone proteins. The term that is used to describe this genetic material is based on it's degree of condensation: Chromosomes are the most condensed form of this genetic material and is observed prior to and during cell division. Chromatin is a relatively less condensed form of the genetic material and is it's normally occurring state. There are in two forms: Euchromatin - extended, or not very condensed chromatin. It does not stain well. Heterochromatin - very condensed chromatin. It does stain well. Transcription will produce a copy of a particular genetic code on a chromatin strand. This copy is the mRNA molecule and it will exit the nucleus into the cytoplasm.

iii) The Nucleolus - a nonmembranous intranuclear organelle of the nucleus responsible for the synthesis of rRNA and, thusly, of ribosomes.

b) The Ribosome

Ribosomes are small organelles being made up of two subunits. These two subunits are composed of rRNA and protein. The two subunits come together only in the presence of an mRNA molecule. They are responsible for translation, the conversion of the genetic code, held on the mRNA, into a protein/peptide. Ribosomes can exist either freely in the cytoplasm or attached to another class of organelle, the endoplasmic reticulum.

c) The Endoplasmic Reticulum (ER)

The ER is a maze of parallel internal membranes that serves to connect the nucleus to other structures in the cell and to the cell membrane. The ER allows for compartmentalization within the cell. It forms chambers called Cisternae for particular chemical reactions. The ER, and it's cisternae, contain a variety of enzymes to facilitate a variety of chemical reactions. The ER is divided into two types based upon the presence or absence of attached ribosomes:

i] Rough Endoplasmic Reticulum (RER)

This ER is studded with numerous ribosomes giving it a "roughened" appearance. These ribosomes covey certain peptides, produced by translation, into the RER for the continuation of protein synthesis. RER is also involved in transport.

ii] Smooth Endoplasmic Reticulum (SER)

This form of ER lacks ribosomes on its surface. SER functions include:

- i} the primary site of phospholipid, sterol, and triglyceride metabolism
- ii} transport
- iii} the detoxification of certain harmful substances Ex; SER is quite abundant in hepatocytes

d) The Golgi Organelle

The Golgi organelle is also known as: Golgi apparatus, Golgi complex, or Golgi. It was first described in 1898 by Camillo Golgi. The Golgi organelle is a stack of membranes that packages the products of the cell. Actually, the Golgi is a stack of smooth membraned cisternae which receive proteins from RER for required posttranslational modifications.

These modifications include:

1. The addition of carbohydrate groups to certain proteins to form glycoproteins
2. The addition of fatty acid chains to certain proteins to form glyceroproteins
3. The packaging of the protein products into vesicles (aka; sacs).

Vesicles are spheroids of membrane containing some substance. The modification and destination of these protein products is determined by their amino acid sequence, which is determined by the genetic code. The protein is carried in transport vesicles and approaches the Golgi, from the RER, at the cis side of the organelle. The protein is processed, packaged, and released from the Golgi at its trans side.

e) The Lysosome

Lysosomes are specialized vesicles containing digestive enzymes. There are a wide variety of enzymes found in lysosomes designed to work on different substrates such as: fats, carbohydrates, proteins, and nucleic acids. Presently over 40 different enzymes have been identified in the lysosomes of human cells. Most of these enzymes work best at a pH of 5. These enzymes are responsible for lysosome functions within the cell: the digestion of food substances, the digestion of foreign invaders, the digestion of the cell's own organelles to release energy during periods of "starvation" and the digestion of the cell itself when it dies which gives lysosomes the nickname "suicide sacs".

f) The Microbody

Microbodies are another special group of vesicles containing a variety of enzymes for a variety of metabolic reactions. The most common type of microbody in mammalian cells is the peroxysome. Peroxysomes are used in the break down of fats and may also serve to detoxify substances in the liver and kidneys. Peroxysomes get their name from an intermediate product of this break down, peroxide. The peroxide is further broken down by the microbody.

g) The Mitochondrion

The mitochondrion is a double membraned capsule-shaped organelle where the chemical energy present in food is converted into ATP. It is the site of the Krebs's cycle and oxidative phosphorylation stages of aerobic respiration. Since they are energy producing organelles, mitochondria are most numerous in the most active cells (ex; spermatozoa). Mitochondria contain their own DNA, called mitochondrial DNA, which is maternally inherited. The mitochondrion has an outer and an inner mitochondrial membrane. Between these two membranes is the intermembrane space. The inner mitochondrial

membrane encloses a second space called the matrix. The inner mitochondrial membrane is actually larger than is the outer mitochondrial membrane and so is arranged into folds projecting into the matrix called cristae. The greater size of the inner mitochondrial membrane is to afford more surface area for oxidative phosphorylation.

h) The Cytoskeleton

The shape of the cell, its mobility, and the mobility and location of its organelles is due to a complex matrix of protein filaments forming a framework called the "cytoskeleton". There are three classes of cytoskeletal components based on structure and diameter size:

i) Microfilaments

Microfilaments are the smallest of the three classes being 7 nm in diameter. They are solid protein fibers composed of globular protein subunits. One example is actin. Functions of microfilaments are: When associated with the microtubule myosin contractile structures are formed. When cross linked to other proteins it forms a meshwork that gives support to many other cellular structures. Ex; stress fibers in c.t. cells.

ii) Intermediate Filaments (aka; Tonofilaments)

Tonofilaments are intermediate in size ranging between 8 to 10 nm in diameter. Intermediate filaments are formed from fibrous proteins (i.e.; keratin) and so are the more stable of the three classes.

a) As a result, they serve to help strengthen the cytoskeleton.

b) They are also solid rods of protein.

c) Microtubules

Microtubules are the largest of the three classes being ~ 25 nm in diameter. Microtubules are hollow, tube-like structures composed of globular proteins called globulins. The globulin proteins come in two forms alpha and beta and arranged into pairs or dimers. Each dimer has one alpha and one beta globulin. Microtubules grow by the addition of dimers. To function microtubules need an anchoring point called the Microtubule Organizing Center or Centrosome in nondividing cells. A microtubule organizing center consists of a pair of centrioles organized at right angles to one another. A centriole consists of 9 groups of 3 microtubules arranged to form a hollow tube. The centriole may also function in microtubule assembly.

iii) Cilia and Flagella

Cilia and flagella may initially look different but are structurally quite similar. They are microtubular structures used in locomotion by the cell. Cilia are numerous and short. Flagella are few (often singular) and long. Cilia and flagella both consist of a slender stalk surrounded by an extension of the cell membrane. The "stalk" consists of a group of microtubules arranged in a 9 + 2 conformation called the Axoneme. This is 9 pairs of microtubules arranged in a ring around a central pair of microtubules. The microtubules have extensions called dynein arms which allow them to slide past one another by a ratcheting motion of the arms. This produces the movement of a cilium or flagellum. At the base of the cilia or flagella is a Basal Body. The basal body is organized like a centriole. It serves as an anchor for the cilium or flagellum.

iv) Cytoplasmic Inclusions

Unlike organelles, cytoplasmic inclusions are variably present in cells. They occur only in specific cell types or in association with a specific stage of functional activity.

Types of Cytoplasmic Inclusions are

1) Pigments

a] Melanin: Melanin is contained in membrane-limited granules called Melanosomes. Melanosomes are only found in certain cells such as the melanocytes of the epidermis. Melanin determines skin, hair, and eye color and shields the body from ultraviolet radiation.

b] Lipofuscin: Lipofuscin is a golden-brown pigment which is an end product of lysosomal activity. Lipofuscin accumulates as a cell ages. Since it is derived from lysosomes, lipofuscin is contained in membranous vesicles.

c] Hemosiderin: Hemosiderin is another golden-brown pigment. It gets its color due to its high iron content. The high iron content is due to the fact that hemosiderin is a product of the breakdown of erythrocyte.

2) Lipids

Oil droplets within the cytosol can serve a variety of functions such as: energy stores, sources of lipid for membrane turnover and flotation devices in unicellular organisms.

3) Glycogen

Glycogen serves as the storage form of glucose in cells. Cells reproduce by means of Mitosis. Mitosis only a short portion of the cell cycle.