Introduction to physiology
Cell Physiology

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Definition of physiology

- Physiology is the study of normal function of living organism. It includes many branches like viral physiology, bacterial physiology, cellular physiology, animal physiology & human physiology.

Human Physiology

- It is the branch of physiology which is concerned with

1. function of entire human body; from the subcellular component to organ& organ system.
2. How these functions are performed& how they are integrated.

Homeostasis

- All living organism composed of cells. Cells of body don’t only contain water, but also surrounded by water (intracellular& extracellular compartments).
- The extracellular fluid is the link between the external world& the cells. It carries the nutrient to the cells& eliminates their waste products. It circulates between any cells in the body& provides for them a homogenous environment.
- In other words, it is essential for survival of the cells. Disturbance of the extracellular fluid impairs functions of cells& result in a disease

- As the extracellular fluid is very important for the normal body functions, it is described as the **“internal environment**”.
- Homeostasis can be defined as maintenance of the normal constant.

Homeostasis

the tendency of biological systems to maintain relatively constant conditions in the internal environment while continuously interacting with and adjusting to changes originating within or outside the system. Homeostasis actually involves continuous motion, adaptation, and change in response to environmental factors.

Examples of homeostasis

1. Body temperature is kept within normal range
2. The osmotic pressure of the blood and hydrogen ion concentration (pH) is kept within strict limits,
3. Nutrients are supplied to cells as needed, and waste products removed before they accumulate and reach toxic levels of concentration.
4. These are a few examples of the thousands of homeostatic control systems within the body. Some operate within the cell and others operate within aggregate of cells (organs) to control the complex interrelationships among the various organs.

The cell structure

Cell membrane

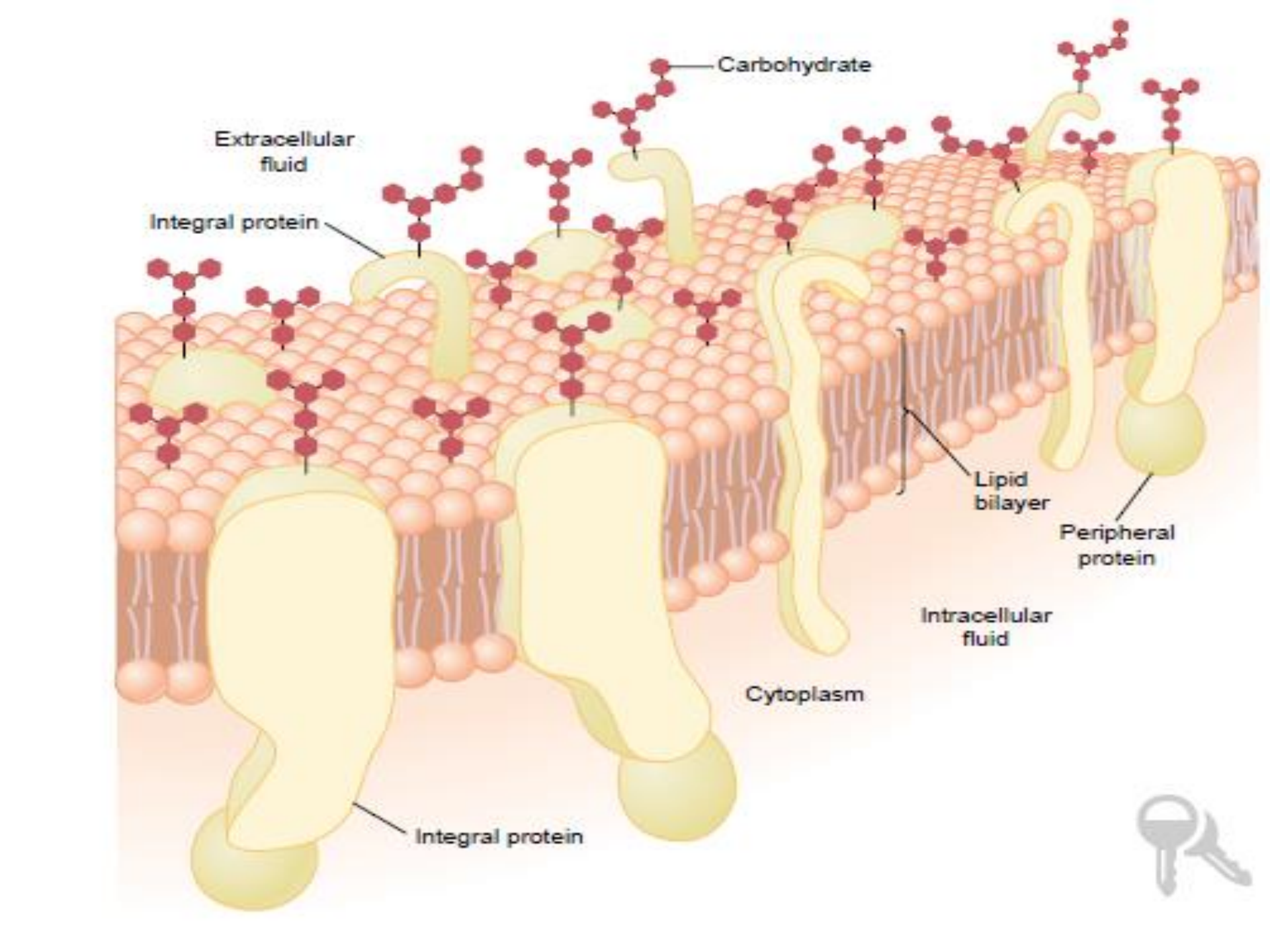
- It consist of phospholipid bilayer (25%) with proteins (about 50%); plus some cholesterol (13%),carbohydrate (3%)& other lipids.
- The phospholipid have hydrophilic part (phosphate) facing outside & hydrophobic part (fatty acid) facing inside i.e in the interior of membrane. Thickness =7.5nm (75 Angstrom)
- It is semipermeable membrane (allow passage of lipid soluble substance& prevent passage of water& water soluble ones).
- However, the protein channels& carriers in the membrane facilitate passage of many substances.

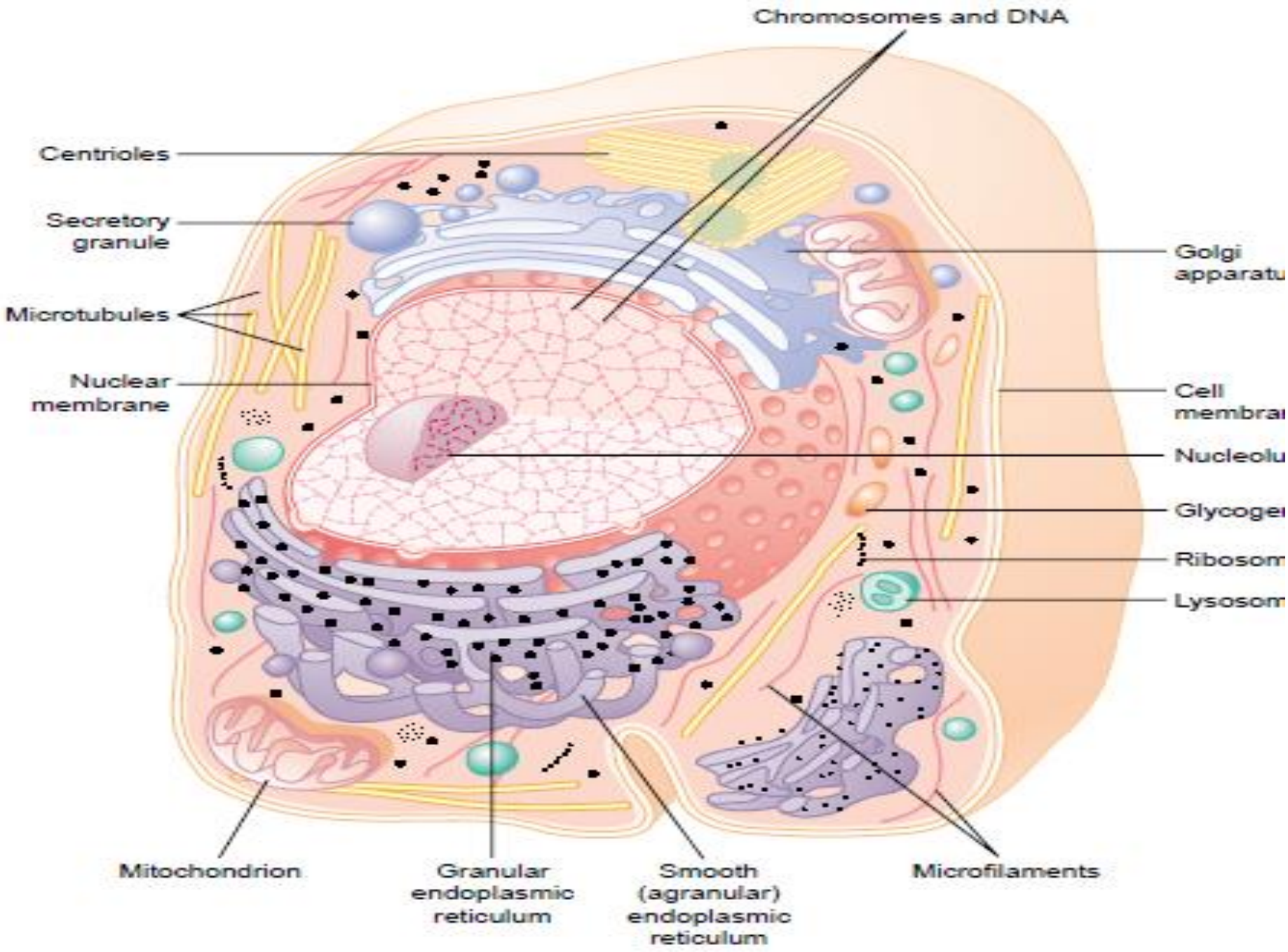
Cell membrane contains 2 types of protein:

1)Peripheral proteins

2)Integral proteins

- Peripheral proteins attached to one side of the cell membrane (usually the inner surface).
- Integral proteins: extend throughout the cell membrane.


Carbohydrate
Extracellular fluid
Integral protein
Lipid bilayer
Peripheral protein
Intracellular fluid
Cytoplasm
Integral protein


Chromosomes and DNA
Centrioles
Secretory granule
Microtubules
Nuclear membrane
Golgi apparatu
Cell membra
Nucleolu
Glycoge
Ribosom
Lysosom
Mitochondrion
Granular endoplasmic reticulum
Smooth (agranular) endoplasmic reticulum
Microfilaments

Function of protein in the cell membrane:

1) Offer **structural support** to the membrane (cytoskeleton).
2) Act as an **adhesion molecules** (connect cells together).
3) Act as an **enzymes** (catalyze chemical reactions on the cell membrane).
4) Act as **antigens** (usually glycoproteins like the blood group antigens on the surface of RBCs &the HLA Ags (human leukocyte Ags) on the surface of all nucleated cells. HLA Ags also called MHC Ags. They are encoded by group of genes in the short arm (p arm) of chromosome 6. They include different classes (e.g. I, II& III).

MHC mean major histocompatibility complex. HLA Ags are unique for each person; that is why they are used by the immune system to distinguish self-cells or Ags from non-self-cells or Ags.

HLA or what is also named MHC are considered in selection of a donor in organ transplantation.

5) Act as **ion channels** for the movement of water and ions across the cell membrane *(osmosis & simple diffusion)*.

6) Act as **carriers** for passive transport of certain substance across the cell membrane *(facilitated diffusion).*

7) Act as **pumps** for active transport of certain substance across the cell membrane *(active transport).*

8) Act as **receptor** for hormones & neurotransmitter.

Remember that:

- *Peripheral proteins act as enzymes whereas the integral proteins carry out other functions*
- Carbohydrates on the surface of cell membrane are either attached to protein (forming glycoprotein) or lipids (forming glycolipids).

The nucleus

- Contain chromatin (DNA) which condenses to form chromosomes before cell division. The DNA replicates during cell division to carry genetic material from the mother cells to the daughter cells.
- The nucleus also contains one or more nucleoli rich in ribosomal RNA

RNA

The chemical structure of **RNA** is very similar to that of **DNA**, but differs in three main ways:

1. Unlike double-stranded DNA, RNA is a single-stranded molecule and has a much shorter chain of nucleotides. However, RNA can be double helixes, as in tRNA (transfer RNA)
2. While DNA contains deoxyribose, RNA contains ribose (in deoxyribose there is no hydroxyl group attached to the pentose ring in the 2' position). These hydroxyl groups make RNA less stable than DNA because it is more prone to hydrolysis.
3. The complementary base to adenine in DNA is thymine, whereas in RNA, it is uracil, which is an unmethylated form of thymine.

Types of RNA

1. **Messenger RNA (mRNA)** is the RNA that carries information from DNA to the ribosome, the sites of protein synthesis (**translation**) in the cell. The coding sequence of the mRNA determines the amino acid sequence in the protein that is produced.
2. **Transfer RNA (tRNA)** is a small RNA chain of about 80 nucleotides that transfers a specific amino acid to the ribosomes in the rough endoplasmic reticulum for protein synthesis during translation.
3. **Ribosomal RNA (rRNA)** links amino acids together to form proteins

Remembers

- Adenine and guanine are purines, cytosine and uracil are pyrimidines.
- Synthesis of RNA is usually catalyzed by an enzyme—RNA polymerase—using DNA as a template, a process known as transcription.
- The proteins which is synthesized may act with in the cell or may be packed within vesicles (in the Golgi apparatus for secretion to outside).

The endoplasmic reticulum (EPR)

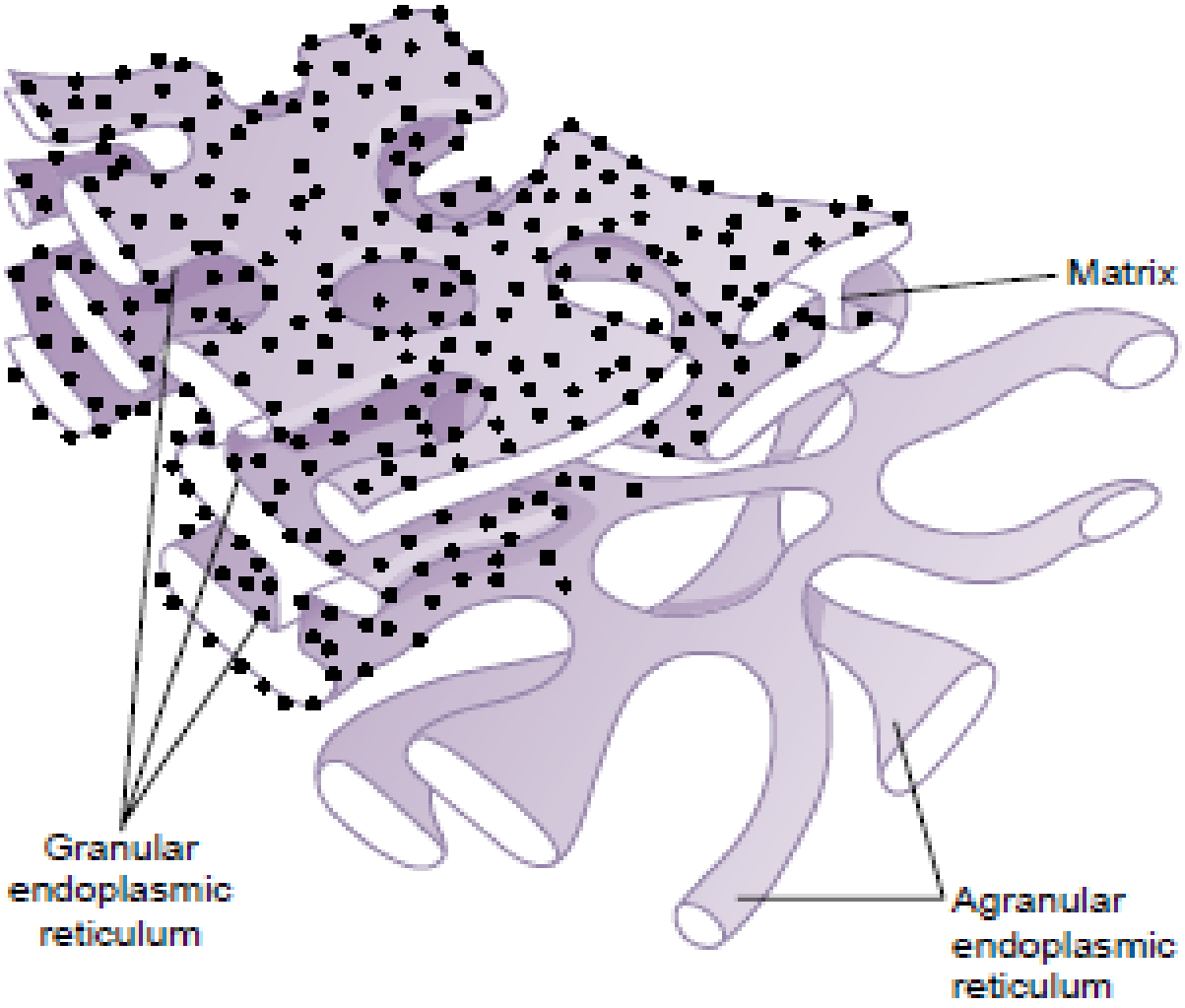
- Complex meshwork of canals & vesicles extending from the nucleus to the exterior of the cell.
- Two types of EPR

1)Smooth endoplasmic reticulum:-

- Has no ribosomes on it's surface
- For synthesis of lipid steroids
- Contain enzyme for certain metabolic functions within the cell (e.g. detoxification of foreign substance e.g. drugs)

1)Rough endoplasmic reticulum:-

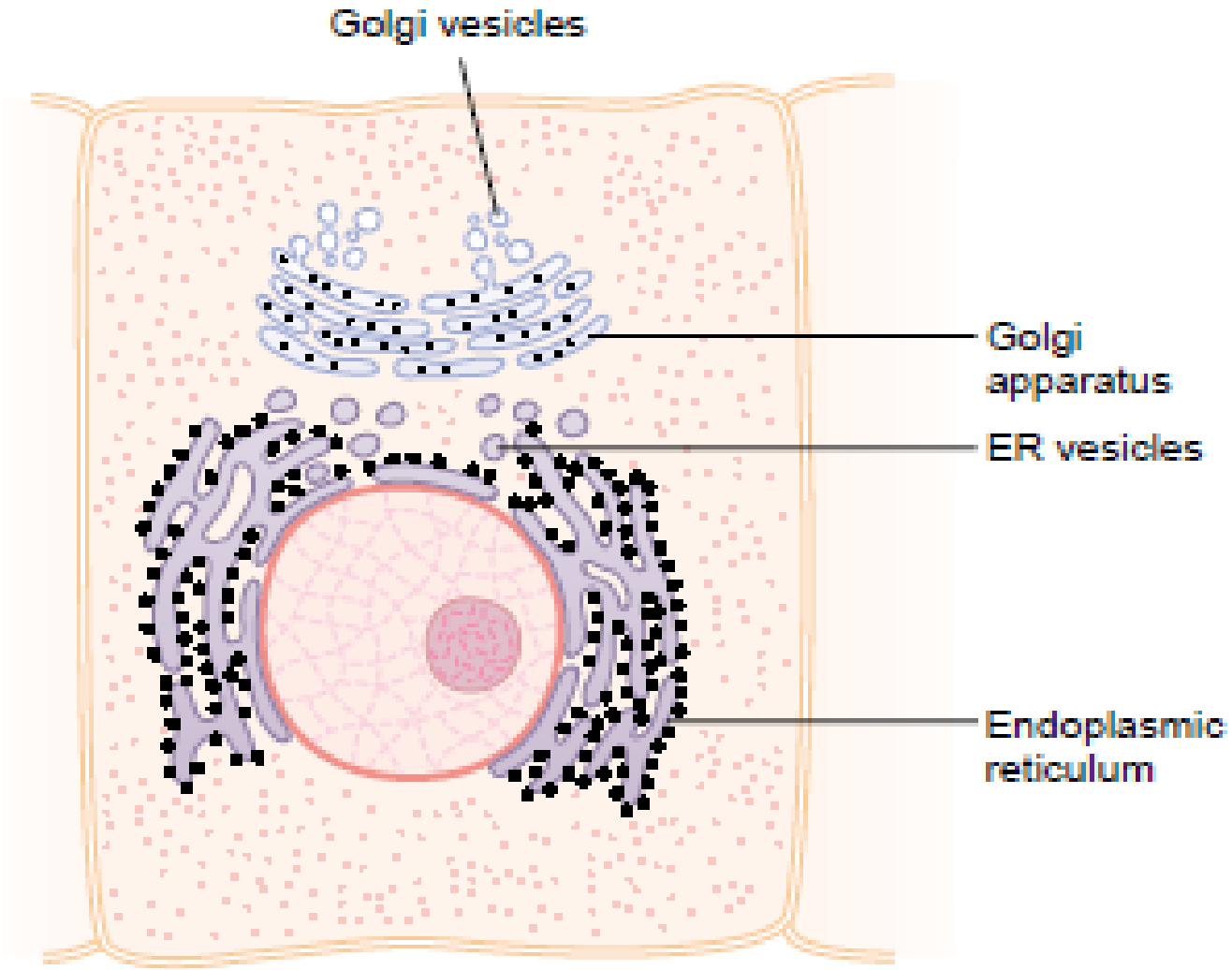
- Has ribosome on it is surface
- For protein synthesis



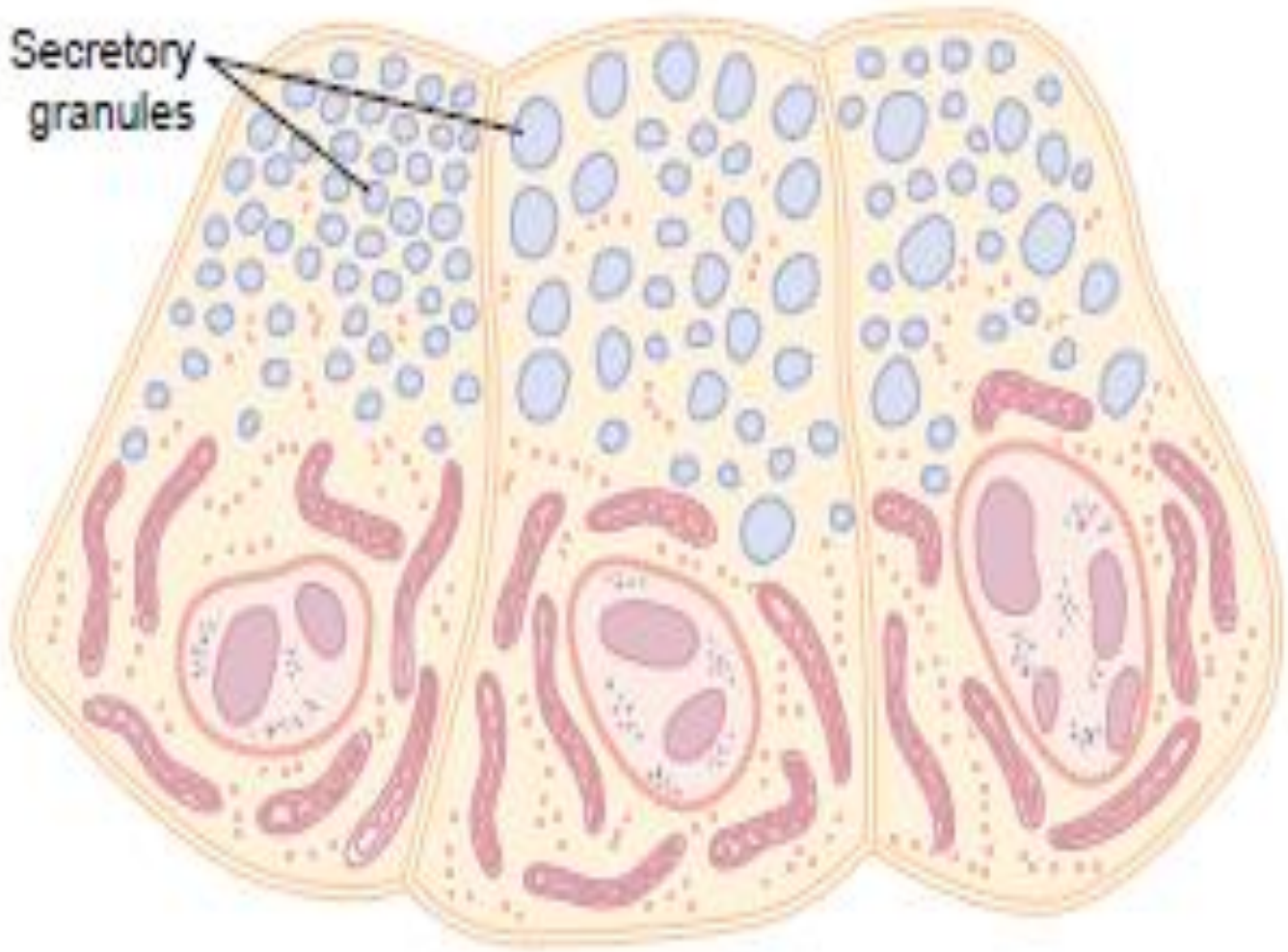
Structure of the endoplasmic reticulum

The Golgi apparatus

The Golgi apparatus is closely related to the endoplasmic reticulum. It has membranes similar to those of the smooth endoplasmic reticulum. It usually is composed of enclosed vesicles lying near one side of the nucleus. This apparatus is prominent in secretory cells, where it is located on the side of the cell from which the secretory substances are extruded. The Golgi apparatus functions in association with the endoplasmic reticulum. **Small "transport vesicles" (also called endoplasmic reticulum vesicles, or *ER vesicles*)** continually pinch off from the endoplasmic reticulum and shortly thereafter fuse with the Golgi apparatus. In this way, substances entrapped in the ER vesicles are transported from the endoplasmic reticulum to the Golgi apparatus. The transported substances are then processed in the Golgi apparatus to form lysosomes, secretory vesicles, and other cytoplasmic components.



typical Golgi apparatus and its relationship to the endoplasmic reticulum (ER) and the nucleus



Secretory granules (secretory vesicles) in acinar cells of the pancreas

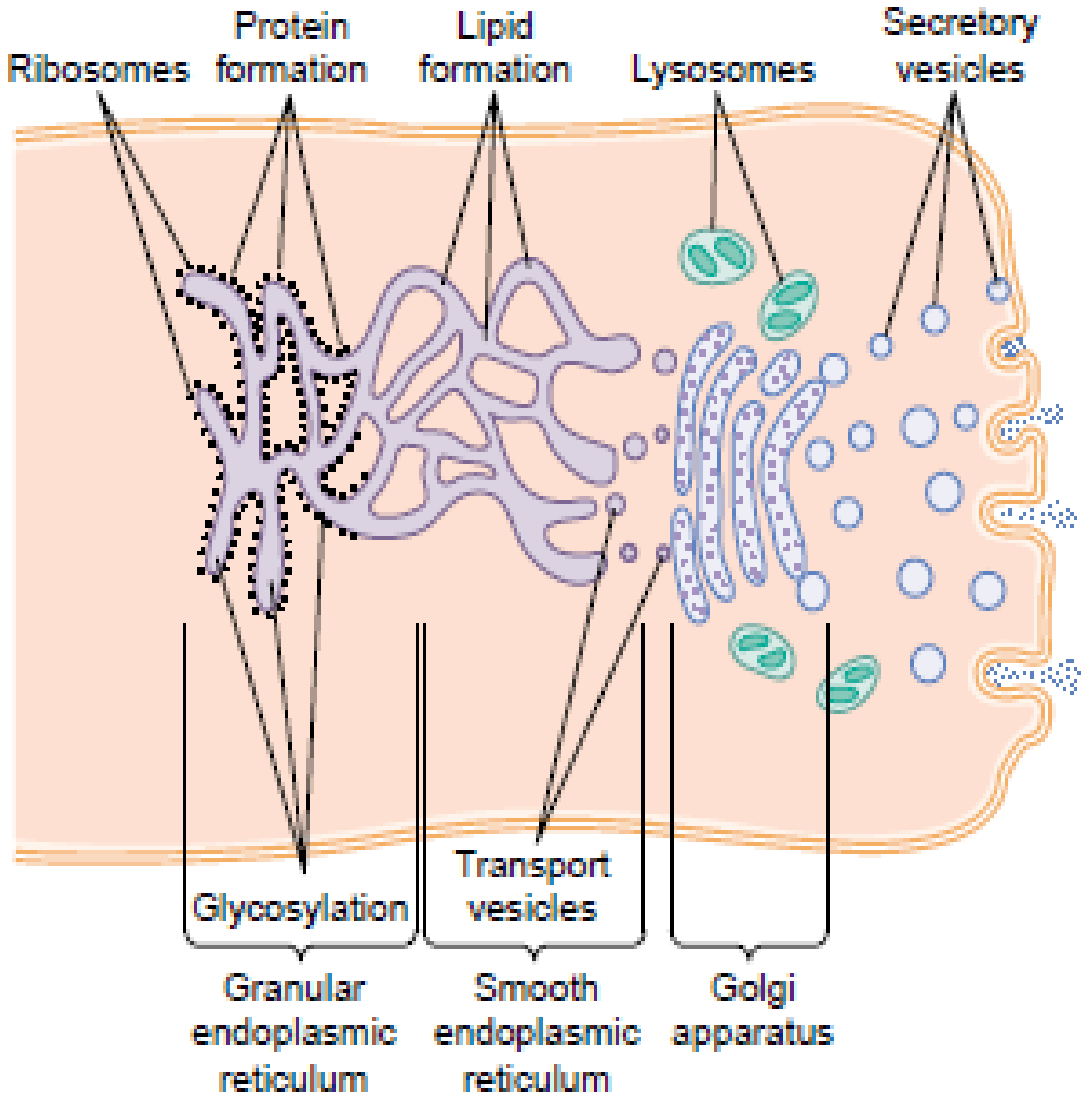


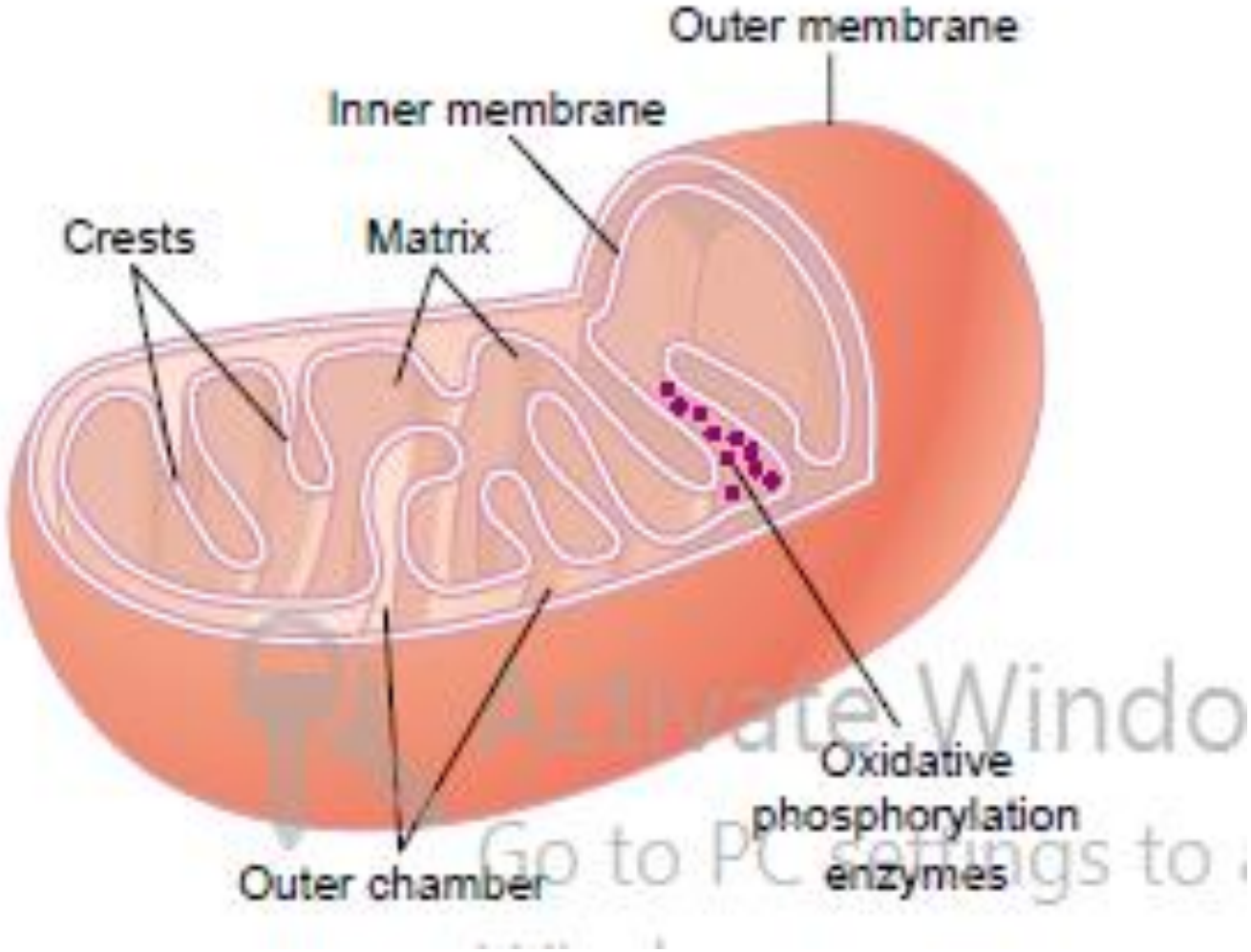
Figure 6

Formation of proteins, lipids, and cellular vesicles by the endoplasmic reticulum and Golgi apparatus

The mitochondria

- The power houses of the cells (provide the energy used by the cell to perform its functions). They are abundant in certain cells like endocrine cells, parietal cells& renal cells (because these cells need energy for synthesis of hormones or active transport of ion “like parietal cells in the body of stomach”).
- Each mitochondria is surrounded by two phospholipid bilayer membrane. the cristae & the inner cavity of mitochondria (the matrix) contain the respiratory enzymes needed for oxidative phosphorylation of glucose to release large amount of energy in the form of ATP (Adenosine Triphosphate).

- Each mitochondria contain DNA that plays a role in the formation of few mitochondrial proteins (using mitochondrial ribosomes) & in its own replication
- Abnormalities of mitochondrial DNA may result in certain diseases usually affect the high energy tissues (muscles, heart&brain). These diseases always inherited from mothers (Mitochondrial DNA (mtDNA) is not transmitted through nuclear DNA (nDNA). In humans, as in most multicellular organisms, mitochondrial DNA is inherited only from the mother's ovum. There are theories, however, that paternal mtDNA transmission in humans can occur under certain circumstances.



Structure of a mitochondrion

Mitochondrial inheritance

In most multicellular organisms, **mtDNA** is inherited from the mother (maternally inherited). Mechanisms for this include:-

1. An egg contains on average 200,000 mtDNA molecules, whereas a healthy human sperm was reported to contain on average 5 molecules

2. Degradation of sperm mtDNA in the female genital tract, in the fertilized egg, and some times failure of sperm mtDNA to enter the egg.

Whatever the mechanism, this single parent (uniparental inheritance) pattern of mtDNA inheritance is found in most animals, most plants and in fungi as well.

- Mitochondrial inheritance is therefore non-Mendelian , as Mendelian inheritance presumes that half the genetic material of a fertilized egg (zygote) derives from each parent.

Lysosomes

Are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm. The lysosomes provide an intracellular digestive system that allows the cell to digest :-

(1)Damaged cellular structures,

(2) Food particles that have been ingested by the cell, and

(3)Unwanted matter such as bacteria.

Lysosomes contain hydrolytic enzymes (protease, lipase, carbohydras& nucleases) that are used in hydrolysis or digestion of engulfed material (e.g. digestion of bacteria with in vacuoles of WBCs.

- Ordinarily, the membrane surrounding the lysosome prevents the enclosed hydrolytic enzymes from coming in contact with other substances in the cell and, therefore, prevents their digestive actions. However, some conditions of the cell break the membranes of some of the lysosomes, allowing release of the digestive enzymes. These enzymes then split the organic substances with which they come in contact into small, highly diffusible substances such as amino acids and glucose.

Transport mechanism across the cell membrane

- There are constant movement of O_2,CO_2, nutrients, electrolytes& waste products across the cell membrane. A variety of transport mechanisms are involved, these are generally classified into passive& active transport mechanisms.

Passive transport mechanisms:-

- Don’t consume energy in transport
- Transport substances from area of higher concentration to area of low concentration (i.e. down the concentration or electrical gradient)
- Either don’t use carriers (as simple diffusion) or use carrier (as facilitated diffusion)

Active transport mechanisms:-

- Consume energy in transport
- Transport substances from area of lower concentration to area of higher concentration (i.e. against concentration or electrical gradient)
- Always need carriers for transport.

Remembers:-

1. Transport of a substance against its chemical or electrical gradient with consumption of energy& usage of carrier is known as primary active transport.
2. Transport of a substance with another substance that's transported activity is known as secondary active transport. The substance uses the same carrier that used by other substance.
3. Secondary active transport (also known as co-transport) may occur in the same direction of the primary substance (=symport), or in the opposite direction (= antiport).

Substances transported by simple diffusion

- Diffusion is the process by which a substance expands, because of random movement of its particles to fill the available volume.
- Nonpolar substances transported by simple diffusion include:

- Fatty acids.
- Steroid hormones synthesized from cholesterol.
- Gasses (O_2 &CO_2)

- Simple diffusion of polar substances (water soluble substances) like ion is low. However, it can occur through certain ion channels (integral proteins in the cell membrane)
- Passive diffusion of water through cell membrane is known as osmosis. It occurs through certain water channels known as aquaporin. Water moves from the side of low concentration of solute to the side of higher concentration of solute.

Substances transported by facilitated diffusion:-

- Don’t consume energy.
- Have maximum rate of transport that depends on the density of carriers on the cell membrane. The maximum rate is reached when all carriers are saturated.
- Example includes transport of glucose from basolateral membrane of renal & intestinal cells& its absorption from ECF by most cells of body.

substance transported actively:

- The well-known example of primary active transport is the pump that transport sodium& potassium against their concentration (= the Na^+/ K^+ pump). It transports 3 atoms of sodium from ICF to ECF in exchange to 2 atoms of potassium from ECF to ICF.
- The well-known example of secondary active transport is transport of glucose (coupled to sodium) through the luminal membrane of the bowel& renal cells.
- Secretion of hydrogen by renal cells is another example of secondary active transport. However hydrogen ion moves in opposite direction to sodium (antiport).

Other transport mechanisms

- ***Endocytosis (active vesicular transport)***

- Endocytosis is the uptake of molecules into cells. Here a molecule fuses with the cell membrane. Inviginates it& then the invagination is separated from the cell membrane to form a vesicles.
- Special protein may facilitated the process of endocytosis (Clathrin& dynamin)
- When engulfed substance is dissolved in fluid, the process is known as **pinocytosis** **(cell drinking)**; & when particulate matter or bacteria, the process known as **phagocytosis** **(cell eating).**

Exocytosis (active vesicular transport)

- Exocytosis is the release of substance from cells, (i.e. opposite endocytosis). Proteins synthesized with in the cell are usually packed into secretory vesicles& secreted by exocytosis.
- Notice that exocytosis requires calcium, energy,& certain proteins.

Solvent drag (passive transport)

- During diffusion of solvent, it tends to drag some solute with it. This occurs in capillaries.

Transport proteins "carrier ,pumps& ion channels "

- These are highly specialized trans-membrane proteins that allow passage of water, ion, glucose, urea& other substances through the cell membrane.
- The carrier changes their shape (configuration) when they bind their substances to move them from one side of the cell membrane to other side. Usually down chemical or electrical gradients (= facilitated) diffusion.
- The pumps act as ATPase enzyme to catalyze hydrolysis of ATP. The released energy used in active transport of substances, against their chemical or electrical gradients.

- Example include Na^+ /K^+ ATPase pump, the proton pump in the parietal cells& calcium ATPase pump.
- Remember that the active transport either primary active or secondary active.

- **The ion channels allow simple diffusion (down chemical or electrical gradient) they include:**

A.Leak channels

- Always open
- Example: potassium leak channels which are responsible for the resting membrane potential.
- Resting membrane potential present in almost all cells in the body.

B. Voltage gated channels

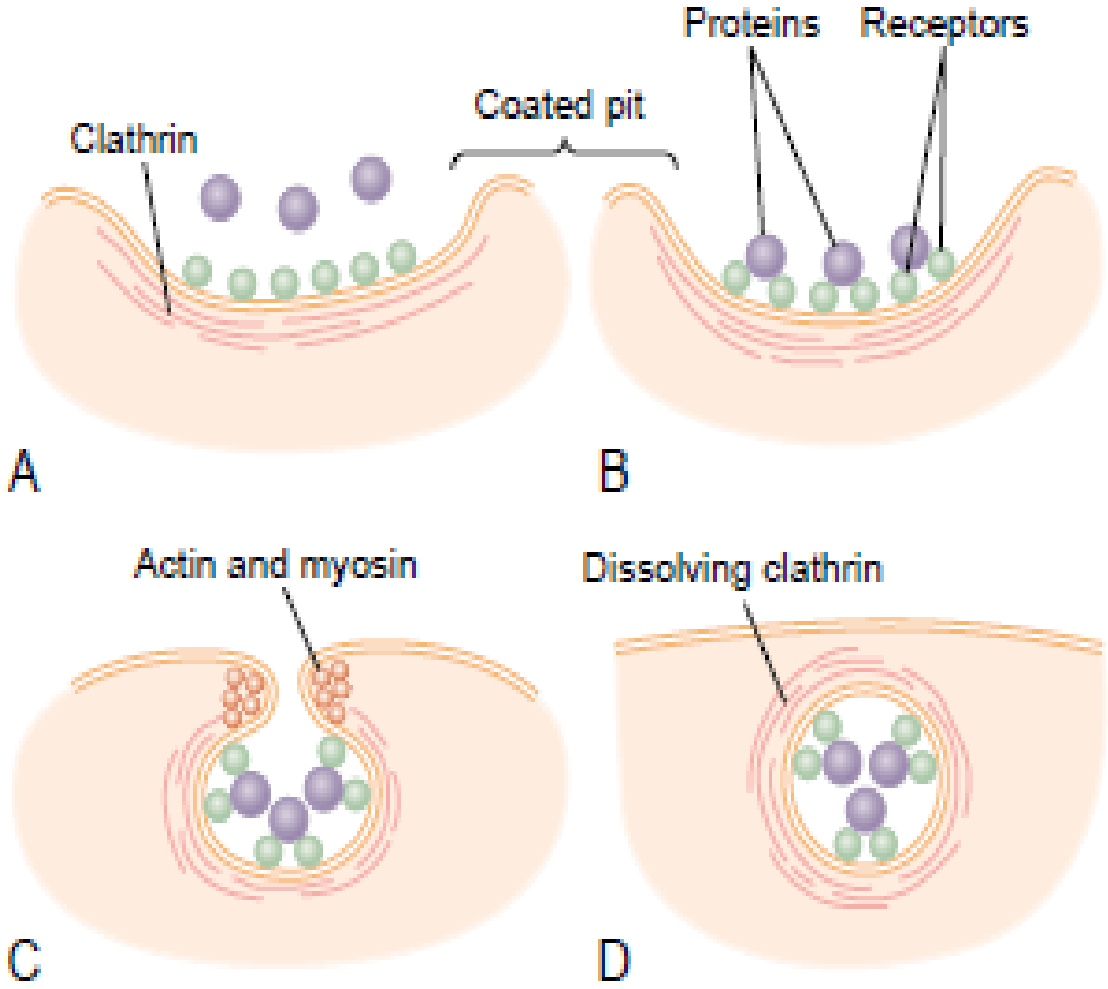
- Have gates that open or close in response to change in voltage or (potentials) in the cell membrane.
- Example: voltage gated sodium channels& voltage gated potassium channels which are responsible for depolarization& repolarization phases of action potentiate respectively.
- Action potentials are only found in excitable tissues (neuron& muscle).

C. Ligand gated channels

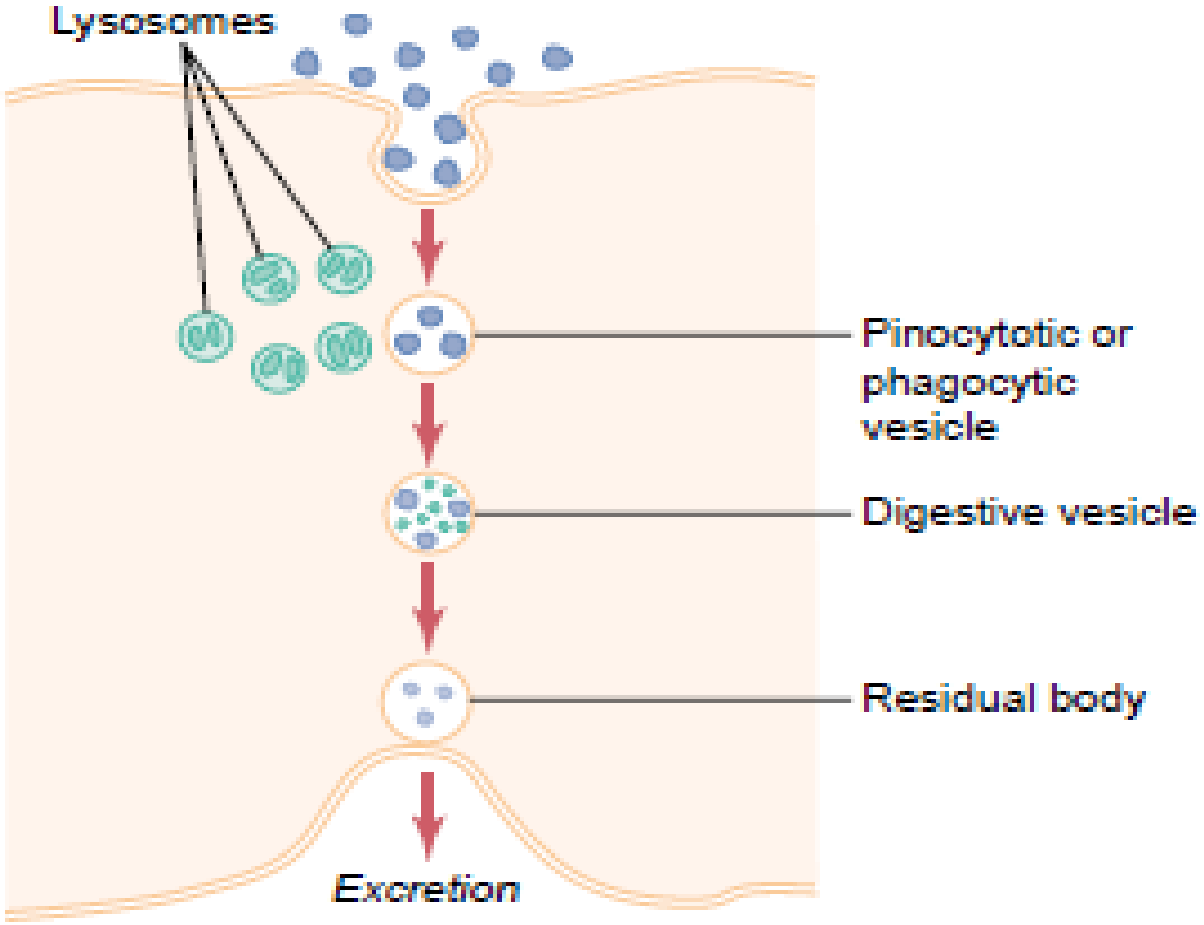
- Have gate that open when certain membrane receptor bind to specific neurotransmitters or hormones& closed when these chemical are released from the receptors.

D. Mechano-sensitive channels

- Have gates that open in response to direct mechanical stimulation of the cell membrane
- They are involved in movement of some cells.



Mechanism of pinocytosis



Digestion of substances in pinocytotic or phagocytic vesicles by enzymes derived from lysosomes

And what?

Nothing

That's all....