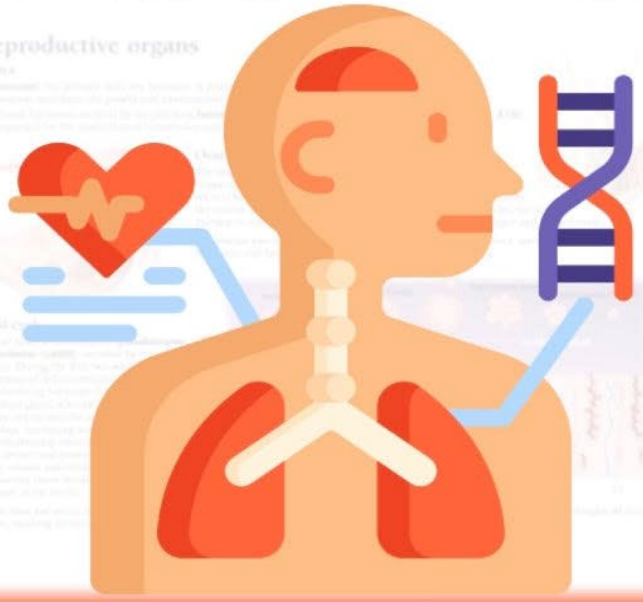
Doctor 022

Physiology

Sheet no.04



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-INTRODUCTION:

-**osmotic pressure**: is the pressure exerted to prevent the movement of free solvent molecules across a semi-permeable membrane (as you have learnt in the last lecture)

-**oncotic pressure**: is the pressure which can be generated but by the presence of protein particles.

-In our bodies we have fluids (nearly made from vesicular fluid) and also, we have plenty of proteins which are dissolved also in that fluid, and these proteins are creating oncotic pressure instead of osmotic pressure (which can be created by ions and other types of particles). but sometimes they combined to create what we call **colloid-osmotic pressure**.

-other important thing you need to know is the importance of **hydrostatic pressure** that made by pumping of heart to cause filtration of fluids across the membrane of capillaries.

TABLE 3.1 Passive Membrane Transport Processes

PROCESS	ENERGY SOURCE	DESCRIPTION	EXAMPLES
DIFFUSION			
Simple diffusion	Kinetic energy	Net movement of particles (ions, molecules, etc.) from an area of their higher concentration to an area of their lower concentration, that is, along their concentration gradient	Movement of fats, oxygen, carbon dioxide through the lipid portion of the membrane
Facilitated diffusion	Kinetic energy	Same as simple diffusion, but the diffusing substance is attached to a lipid-soluble membrane carrier protein or moves through a membrane channel	Movement of glucose and some ions into cells
Osmosis	Kinetic energy	Simple diffusion of water through a selectively permeable membrane	Movement of water into and out of cells directly through the lipid phase of the membrane or via membrane pores (aquaporins)
FILTRATION			
	Hydrostatic pressure	Movement of water and solutes through a semipermeable membrane (either through the plasma membrane or between cells) from a region of higher hydrostatic pressure to a region of lower hydrostatic pressure, that is, along a pressure gradient	Movement of water, nutrients, and gases through a capillary wall; formation of kidney filtrate

(The table above is describing some modalities of transport that we can have across membranes in general).

-ACTIVE MODALITIES OF TRANSPORT:

-In that case we need to consume macro energetic molecules, we have primary active transport and secondary active transport also we have vesicular transport.

1-Primary active transport:

-in this type we have **carriers** that must be phosphorylated (the addition of phosphorus group and here where we consume macro energetic) to move particles from the low concentration to the high concentration.

- We have a lot of types of carriers that can work as primary active transport carrier such as: **Na+/K+ pump, H+ (proton pump), H+/k+ pump and Ca++ pump.** (Whenever you hear pump, you must know that this type of transport is primary active transport).

-Mechanism of action of these pumps:

-Na+/K+ pump: they are carriers that move 3 Na (which have higher concentration outside) from inside to outside and 2 K (which have higher concentration inside) from outside to inside (from high concentration to low concentration).

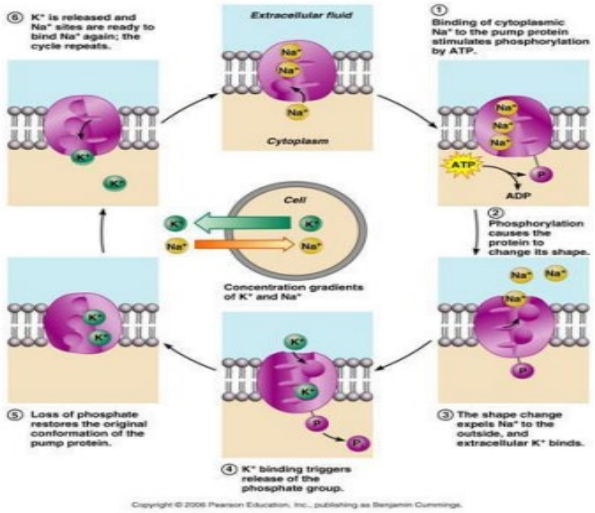
-proton pump: transport of H^+ (which have higher concentration outside) from inside to outside.

-H+/k+ pump: transport of H^+ and K^+ from low concentration to high concentration.

- Ca++ pump: transport Ca from cytosol (low concentration) to endoplasmic reticulum (high concentration).

-now let's know how Na+/K+ pump work exactly:

As you see in the picture, we have Na+/K+ pump that have 3 sites for attachment of Na. once we have Na attached to their sites the carrier will be phosphorylated to induce conformational changes that transport 3 Na from inside to outside. After the realising of Na ions, the carrier will have 2 sites for attachment of K. now once we have K attached to their site



the carrier will induce conformational change by the process of dephosphorylation to transport K from outside to inside.

-as a conclusion, these carriers are transporting 3 Na from inside to outside by the process of phosphorylation and 2 k from outside to inside by the process of dephosphorylation.

-The importance of pumps for cell functions:

a-maintaining cell volume:

Almost all of our cells have Na+/K+ pump, which is needed to keep the low concentration of Na+ inside cells and the low concentration of K+ outside cells, and why is it important?

As you can see above in Na+/K+ pump, we have transported 3 Na+ ions from inside to outside and introduced back only 2 K+ ions from outside to inside. If these pumps stop functioning, Na+ concentration inside will increase and as a result cell's osmolarity will increase so does its volume which results in cell rupturing and inhibiting cell activity.

b-Maintaining cell functionality:

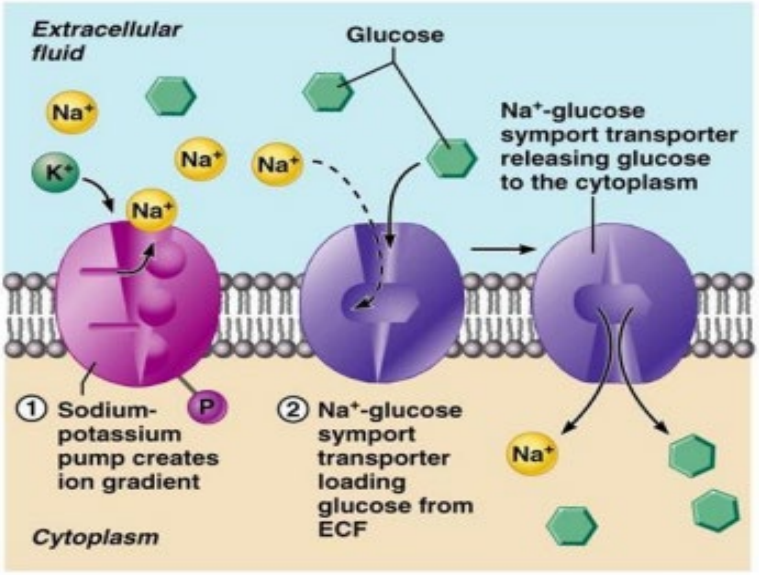
as an example, there are some structures in our bodies that need more HCL inside it like the stomach, to help in the process of digestion, we have specialized cells that transport protons from inside to outside (from low to high concentration) in these structure to maintain their functions.

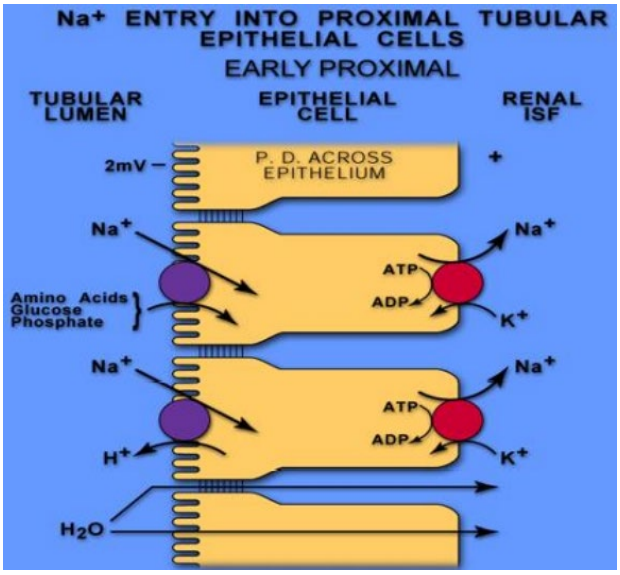
Another example is Ca pump which important for moving Ca from cytosol to endoplasmic reticulum in muscles to stop contraction.

2-Secondary active transport:

-We have high concentration of Na+ outside and low concentration inside, that's why soluble has very high tendency to move from outside to inside, but there are protein structures working like carriers (Not channels!) that help Na+ to move from outside to inside with a condition to move with it another substance.

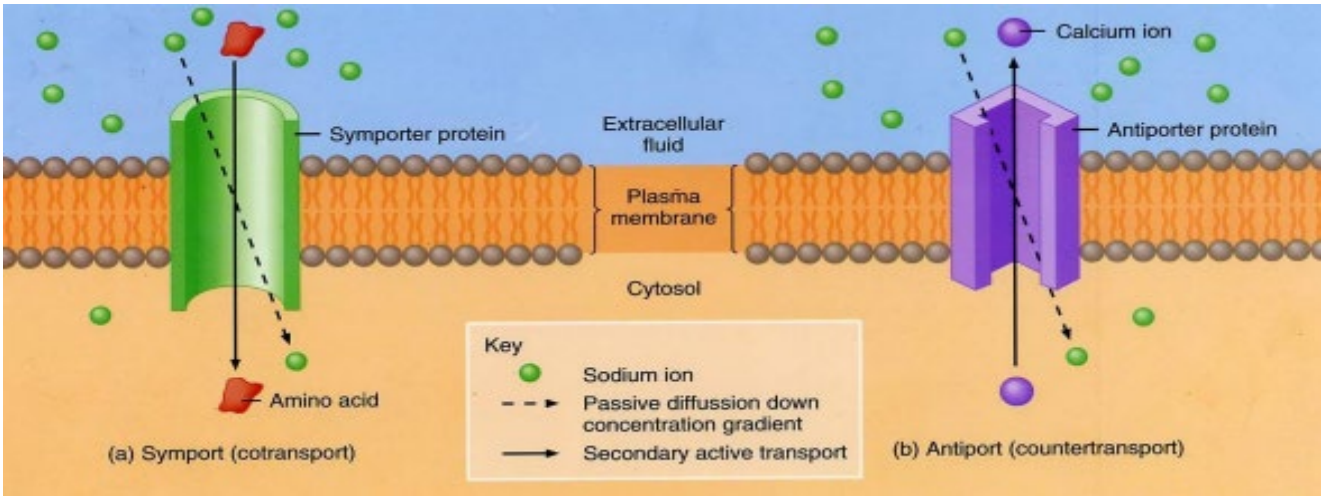
In the following picture these carriers have two sites, one for Na+ and the other one is for glucose (it might be galactose or other molecules) once the two binding sites are filled a change in conformation occurs in order to transport Na+ from high concentration to low concentration, but the other substance moves from the low concentration to the high concentration. We haven't consumed directly macro energetic molecules but it is still considered active transport and we call it secondary active transport; because we already have the energy created to get concentration gradient for Na+ to perform this type of transport, the low concentration of Na+ inside is used to transport other particles (like amino acids, glucose and galactose) from the low concentration (for example: in the lumen of the small intestine -to absorb nutrients-) to the high concentration (in the cytosol), this is secondary active transport mechanism. If the two transported particles where in the same direction we call it co-transport (symport), but if the two transported particles where in the opposite direction then it is called counter transport (Antiport).





To sum up, we have used the energy which is created **by the activity of the Na+/K+ pump** to achieve the second type of transport, **WE HAVEN'T CONSUMED MACRO ENERGETIC MOLECULES** by these protein structures, we already have consumed macro energetic molecules to reduce Na+ concentration inside.

Example of secondary transport: The exchange of Na+ with Ca++ which occurs in the heart, Na+ has high tendency to get inside the cell but with that we transport a Ca++ ion from inside to outside (from low to high concentration), this is called Sodium-Calcium exchange, and these carriers (again NOT channels) are called sodium dependent carriers (in secondary active transport). If we say sodium independent carriers it means FACILITATED DIFFUSION.



3-Vesicular transport:

-as you know, plenty of proteins are synthesized in the endoplasmic reticulum and then they are transported by vesicles toward the plasma membrane to do their function or to be secreted.

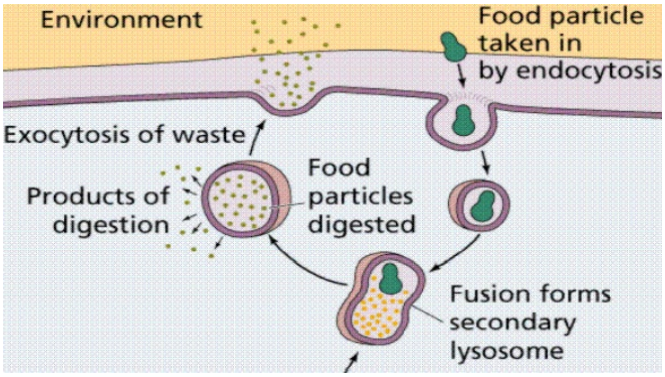
-in our cells we have a system of microtubules to transport vesicles inside the cells in which the vesicles will bind to microtubules by a protein and then move along the microtubules by a process of phosphorylation and dephosphorylation (consuming ATP).

-before the transport of protein toward the membrane, vesicles containing proteins will move to Golgi complex to be packed and sent to their exact destination in process that called sorting.

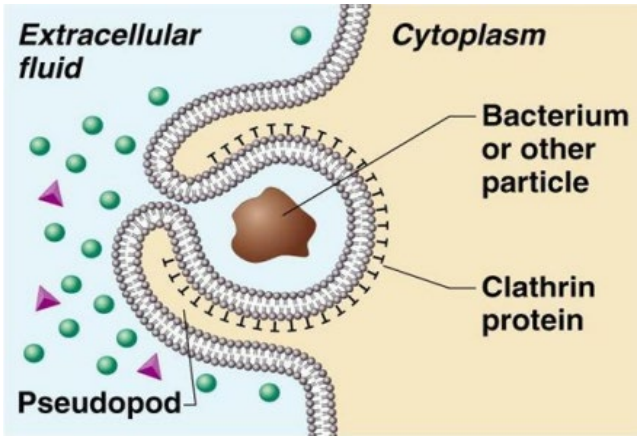
-the proteins inside the vesicles have a sequence called **address** (sequence of amino acids), Golgi complex will read this address and according to this address the Golgi complex will know where these proteins must go and send them to their destination by vesicular transport. If the protein is for secretion, then it is found inside a vesicle, but if it is a functional protein (must be inserted over the plasma membrane) it remains inserted over the membrane of the vesicle which fuse with the plasma membrane.

-The process in which membranes are fusing and the content is released is called **Exocytosis**, and this is how the ER form vesicles.

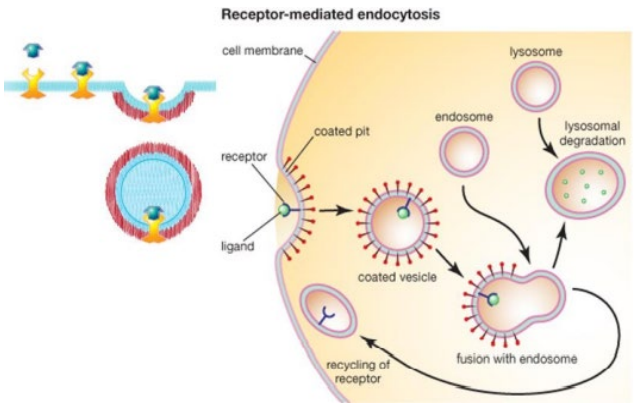
-The process in which membranes are ingulfing the content and brought it inside is called **Endocytosis**.



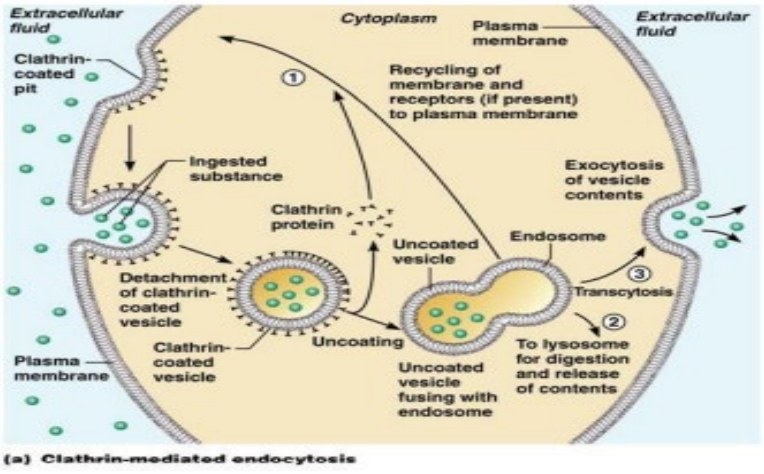
-**Phagocytosis**: it's also endocytosis but the type of particle the have been ingulfed is either a pathogen, bacteria, viruses, antigens, etc. the cells that capable of doing this type of endocytosis is called phagocytic cells.



-there are some particles that have receptor on the outer surface of plasma membrane, when these particles bind with there receptor, they activate endocytosis and that what we call **Receptor Mediated Endocytosis**. and that's what actually happens in phagocytosis. a receptor on the surface of phagocytic cells recognizes part of the antibody-antigen complex and mediate the endocytosis of it. When the vesicle get inside the cell, everything inside it will be destroyed by lysosomes including the receptor which will be recycled again.



-**Transcytosis**: the process of endocytosis the particle of one side of the cell and moving of vesicle along the cell until it reach the other side in which it will go under exocytosis.



-**Pinocytosis**: the process of ingulfing water and introducing it to cytosol in some types of bacteria.

Table 3.1 Transport of Materials Into and Out of Cells

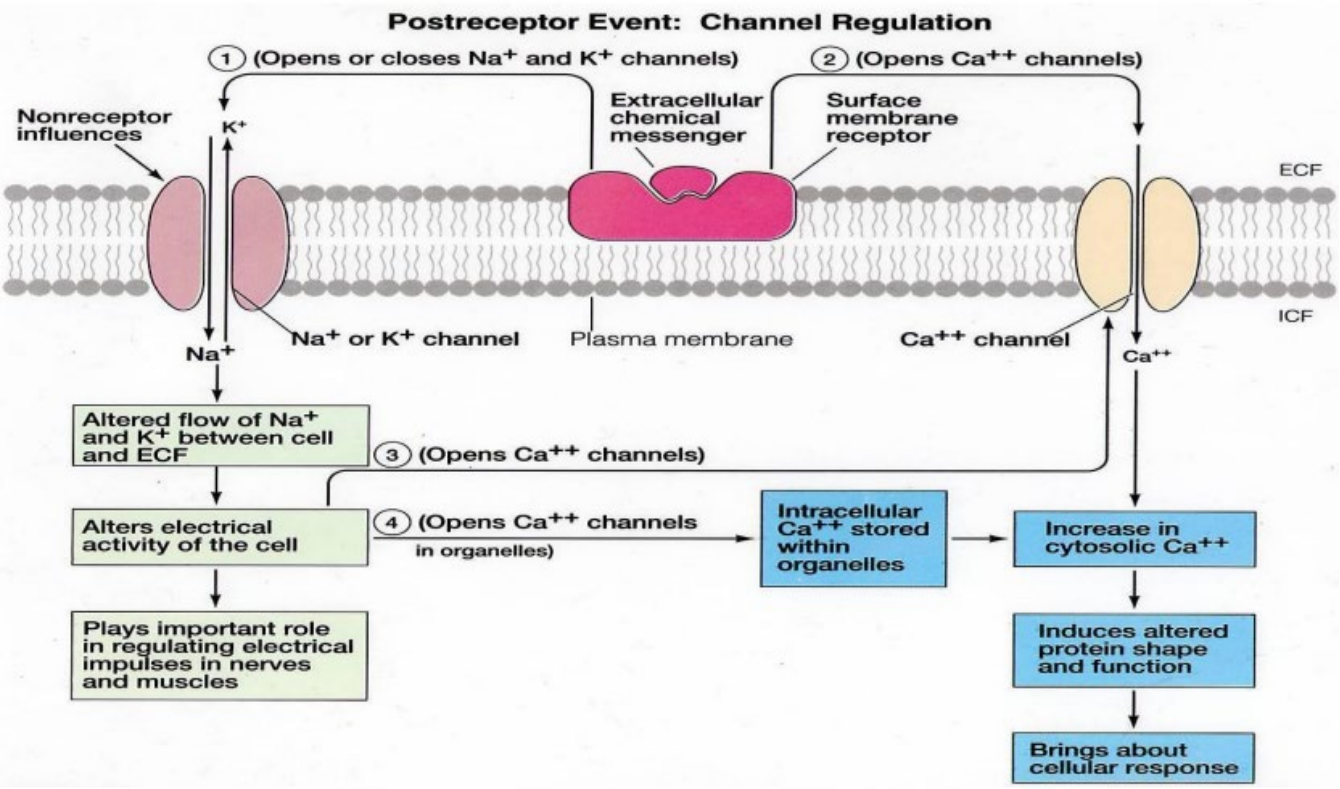
Transport Process	Description	Substances Transported
Osmosis	Movement of water molecules across a selectively permeable membrane from an area of higher water concentration to an area of lower water concentration.	Solvent: water in living systems.
Diffusion	Random mixing of molecules or ions due to their kinetic energy. A substance diffuses down a concentration gradient until it reaches equilibrium.	
Diffusion through the lipid bilayer	Passive diffusion of a substance through the lipid bilayer of the plasma membrane.	Nonpolar, hydrophobic solutes: oxygen, carbon dioxide, and nitrogen; fatty acids, steroids, and fat-soluble vitamins; glycerol, small alcohols; ammonia. Polar molecules: water and urea.
Diffusion through membrane channels	Passive diffusion of a substance down its electrochemical gradient through channels that span a lipid bilayer; some channels are gated.	Small inorganic solutes, mainly ions: K^+, Cl^-, Na^+, and Ca^{2+}. Water.
Facilitated Diffusion	Passive movement of a substance down its concentration gradient via transmembrane proteins that act as transporters; maximum diffusion rate is limited by number of available transporters.	Polar or charged solutes: glucose, fructose, galactose, and some vitamins.
Active Transport	Transport in which cell expends energy to move a substance across the membrane against its concentration gradient through transmembrane proteins that act as transporters; maximum transport rate is limited by number of available transporters.	Polar or charged solutes.
Primary active transport	Transport of a substance across the membrane against its concentration gradient by pumps; transmembrane proteins that use energy supplied by hydrolysis of ATP.	Na^+, K^+, Ca^{2+}, H^+, I^-, Cl^-, and other ions.
Secondary active transport	Coupled transport of two substances across the membrane using energy supplied by a Na^+ or H^+ concentration gradient maintained by primary active transport pumps. Antiporters move Na^+ (or H^+) and another substance in opposite directions across the membrane; symporters move Na^+ (or H^+) and another substance in the same direction across the membrane.	Antiport: Ca^{2+}, H^+ out of cells. Symport: glucose, amino acids into cells.
Transport in Vesicles	Movement of substances into or out of a cell in vesicles that bud from the plasma membrane; requires energy supplied by ATP.	
Endocytosis	Movement of substances into a cell in vesicles.	
Receptor-mediated endocytosis	Ligand-receptor complexes trigger infolding of a clathrin-coated pit that forms a vesicle containing ligands.	Ligands: transferrin, low-density lipoproteins (LDLs), some vitamins, certain hormones, and antibodies.
Phagocytosis	"Cell eating"; movement of a solid particle into a cell after pseudopods engulf it to form a phagosome.	Bacteria, viruses, and aged or dead cells.
Pinocytosis	"Cell drinking"; movement of extracellular fluid into a cell by infolding of plasma membrane to form a pinocytic vesicle.	Solutes in extracellular fluid.
Exocytosis	Movement of substances out of a cell in secretory vesicles that fuse with the plasma membrane and release their contents into the extracellular fluid.	Neurotransmitters, hormones, and digestive enzymes.

-And now, the important question:

Is the process of transport across plasma membrane a controlled process?

The answer is: **yes, it is highly controlled**, these are some aspects of controlling:

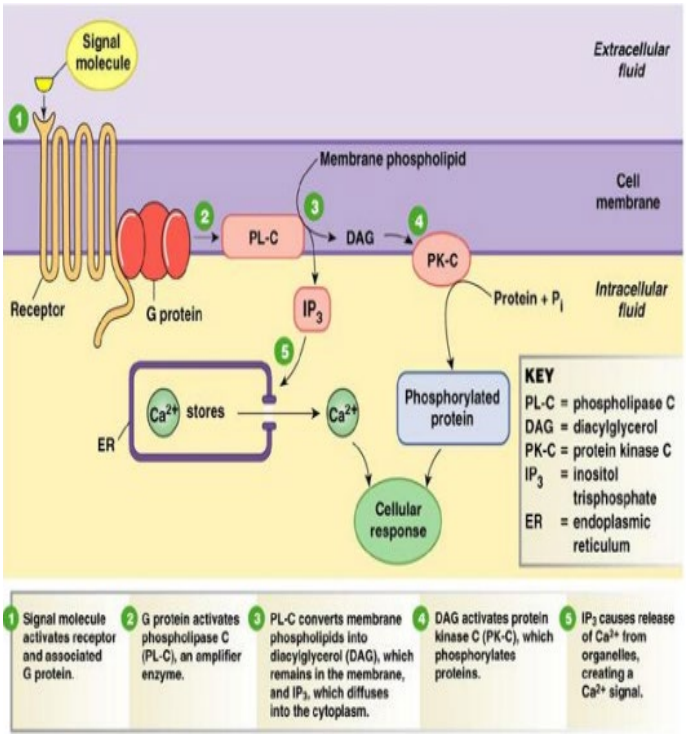
-**Receptors & G protein and Channels**: we have over the plasma membrane receptors, and these receptors are specific. Some of these receptors are connected with channels through what we call G protein (G because we use the macro energetic molecule GTP), when the ligand binds to these receptors the G protein will dissociate resulting in intracellular massages which will lead to open a sodium, potassium, calcium channel as an example (Remember: Na+ channels move sodium from outside to inside. K+ channels move potassium from inside to outside. Ca++ channels move calcium from outside to inside).



-**Receptors & Enzymes**:

-we have some receptors that are linked to enzymes like **adenylyl cyclase**. The activation of such enzymes by the attachment of the ligand to the receptor will increase the concentration of cAMP that will lead to open some channels.

-another example: some receptor are linked to enzyme called **Phospholipase C** by G protein, when the ligand bind to its receptor it will split a phospholipid called phosphoinositol biphosphate (the phospholipid is composed of glycerol, and 2 fatty acids at carbon position number 1 and 2 on glycerol, and on carbon number 3 we have phosphate group but in this type of phospholipid we have an inositol connected to the phosphate group and a two phosphate molecules connected to inositol on carbon number 3(look down to understand what I mean)) on carbon number 3 resulting in IP3 (inositol triphosphate) which can change the activity Ca++ channels on endoplasmic reticulum resulting in transporting the Ca++ from endoplasmic reticulum to cytosol.



Fatty acid----------C1

Fatty acid----------C2

C3------Phosphate---inositol---phosphate----phosphate

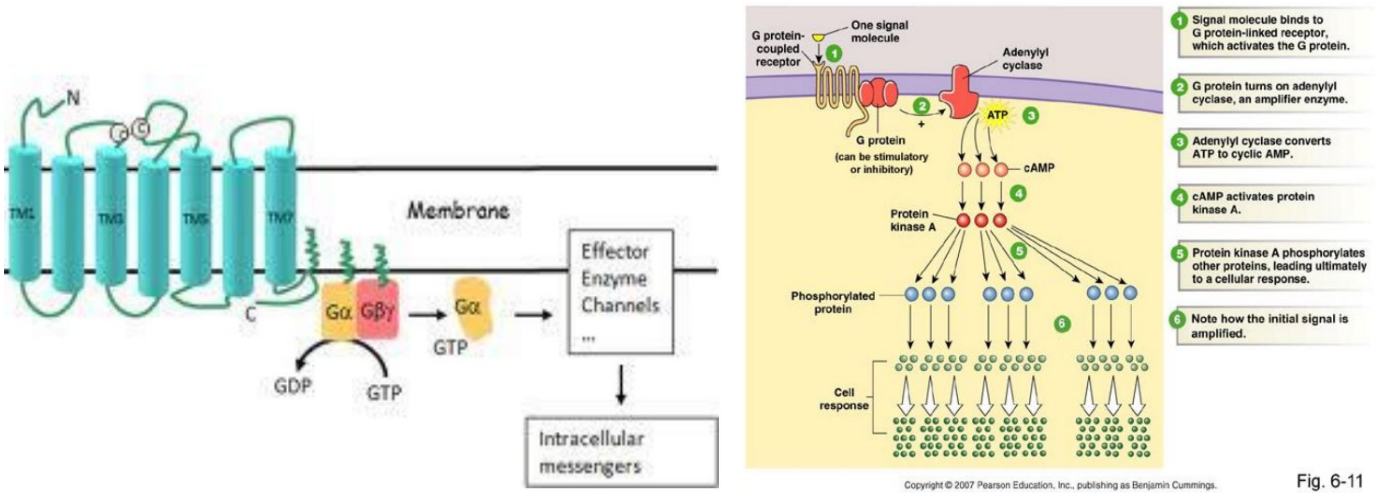


Fig. 6-11

-all of these called signal transductions mechanisms you will take it with Dr.ebae in details so don't be worry if you didn't understand.