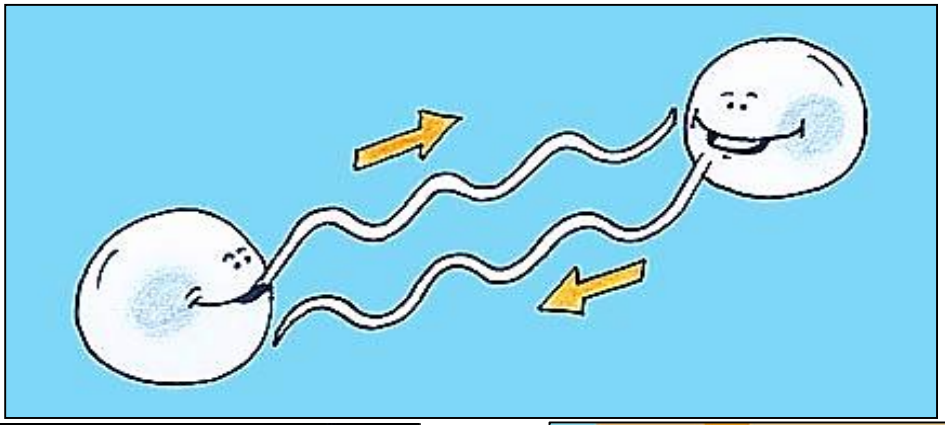
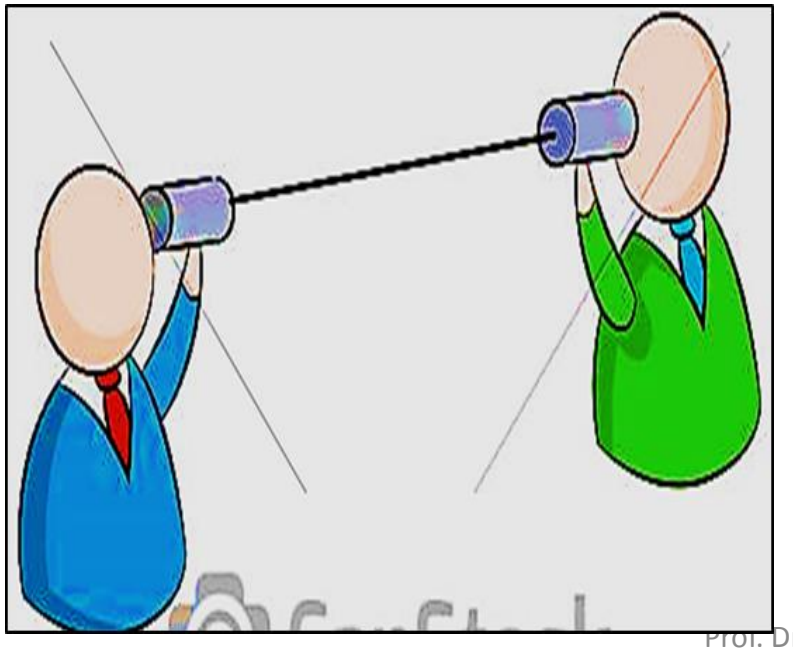
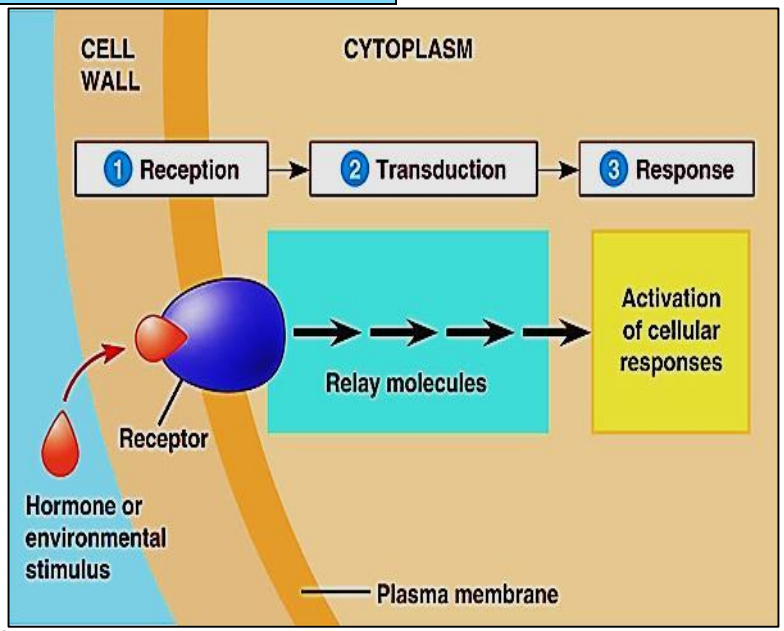
Cell Bio 8
Cell Communication







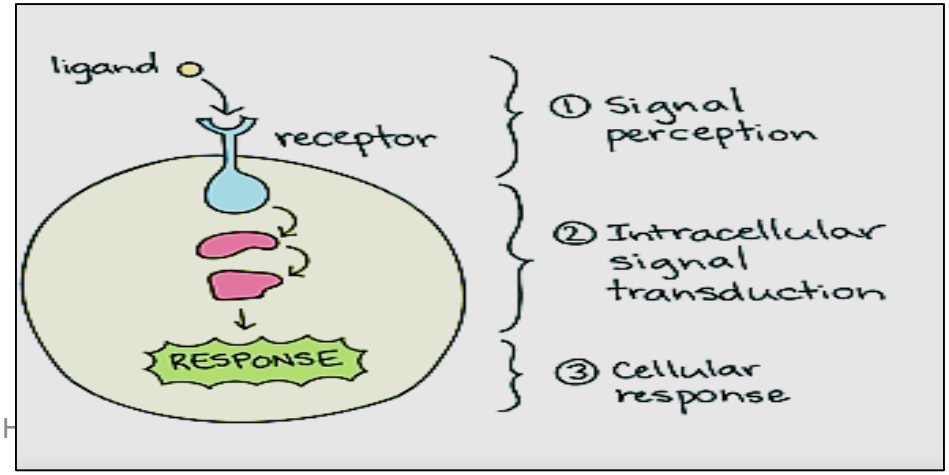
Cell signaling

- Living cells in a multicellular organism have to communicate e each others in order to maintain homeostasis & life.

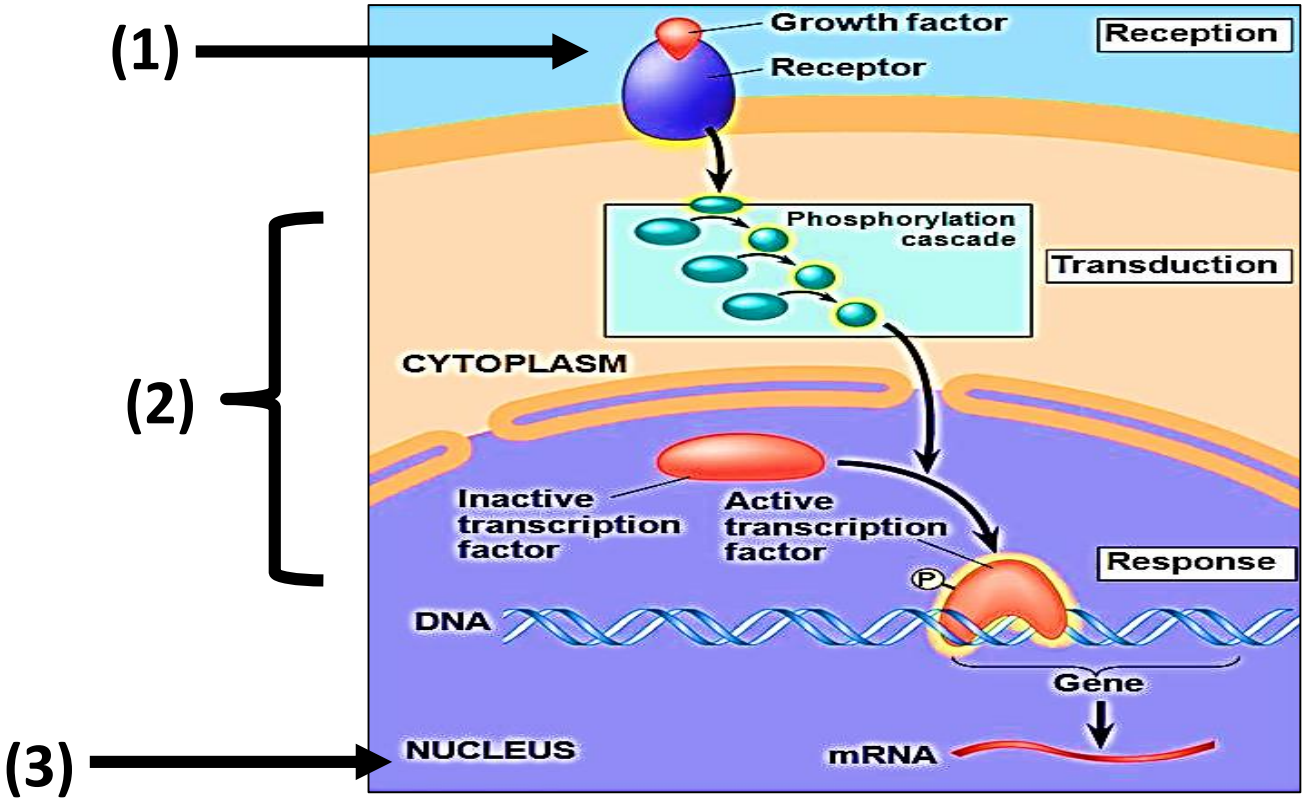
- Cells communicate e each through **signals** which result in **responses** within the cells

- **The cell signaling system has 3 parts**:

I. Reception
II. Transduction
III. Response



The signal transduction pathway: is a series of steps by which a signal received on a cell's surface is converted into a specific cellular metabolic activities which result in specific cell response



Steps of signaling system

The **signals** can be received from either:

External environment:

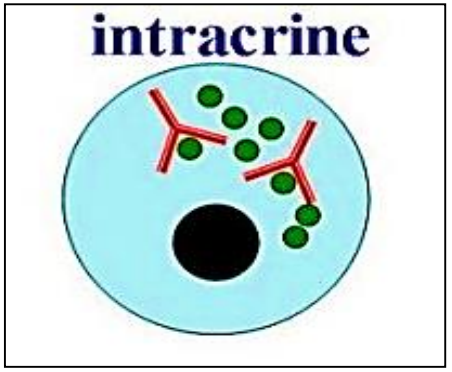
- Sound
- Light
- Temperature
- Odorants
- Substances that we taste

Within the body (hormones):

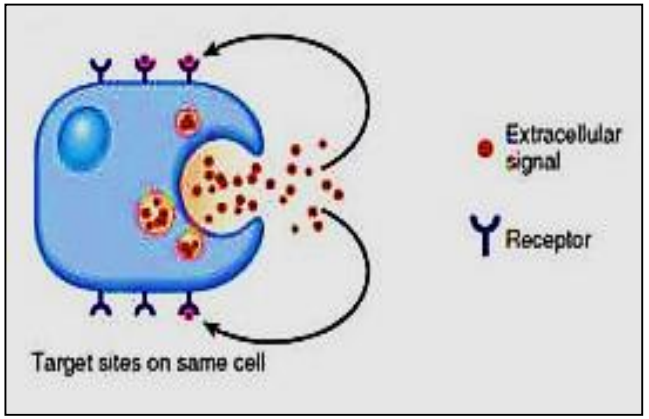
- Epinephrine (Adrenaline)
- Insulin
- Testosterone
- Estrogen

All these factors will cause the cell to respond in some way.

Modes of cell signaling

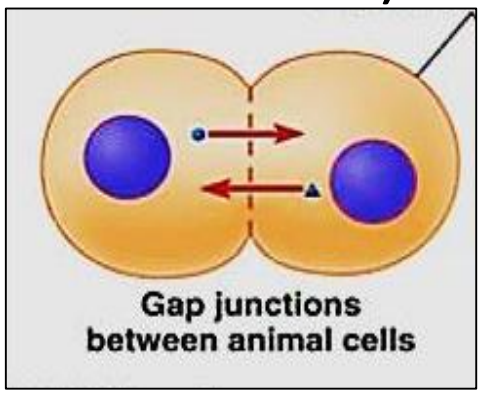


1- Intracrine: hormones or growth factors act on receptors inside the cell (cytosolic /nuclear receptors)

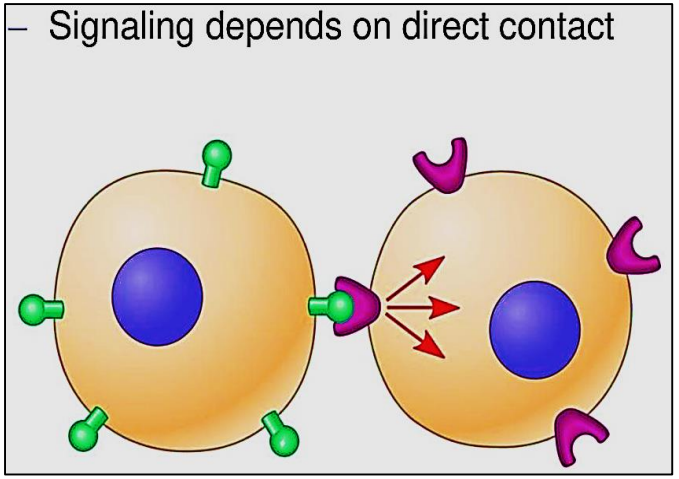


2- Autocrine : the cell secretes a hormone or chemical substance that binds to receptors on that surface of same cell, leading to changes in the cell. (Autocrine signaling plays critical roles in cancer activation)

3- Direct (Juxtacrine signaling): gap junctions (Cardiac muscles, embryonic development)



Juxtracrine or contact /dependent signaling :is a type of cell-cell or cell matrix signaling in multicellular organism



Types of juxtracrine signaling:

1- A membrane ligand & a membrane protein of two adjacent cells interact

2- Communicating junction(gap J) links the intracellular compartments of two adjacent cells allowing the exchange of small molecules

3- An extracellular matrix protein & a cell membrane protein interact

4- Short distance: act locally on different nearby cells

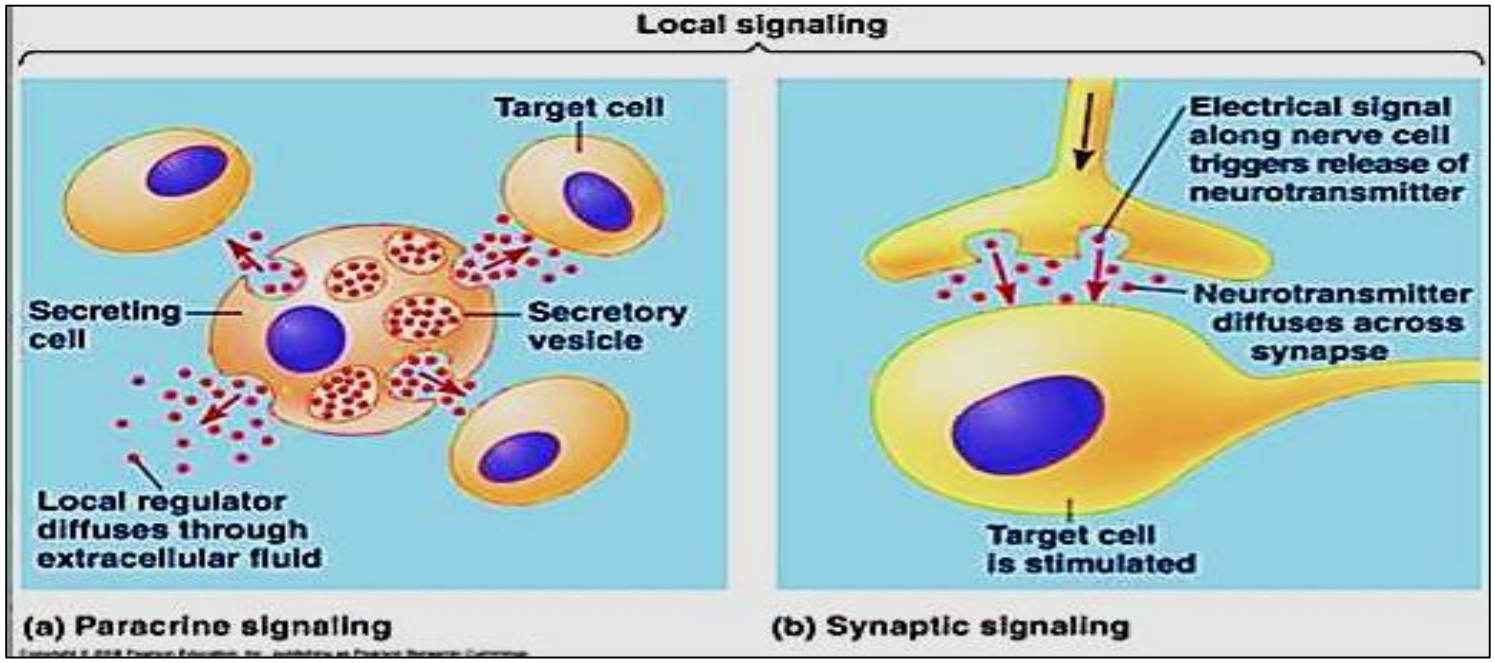
@ **Paracrine** (nearby) signaling (cytokines, histamine)

@ **Synaptic** signaling (neurotransmitters : AC)

- **Paracrine:** signals are carried by messenger molecules called "**local regulators**", that are released by one cell and move to make contact with another nearby cells

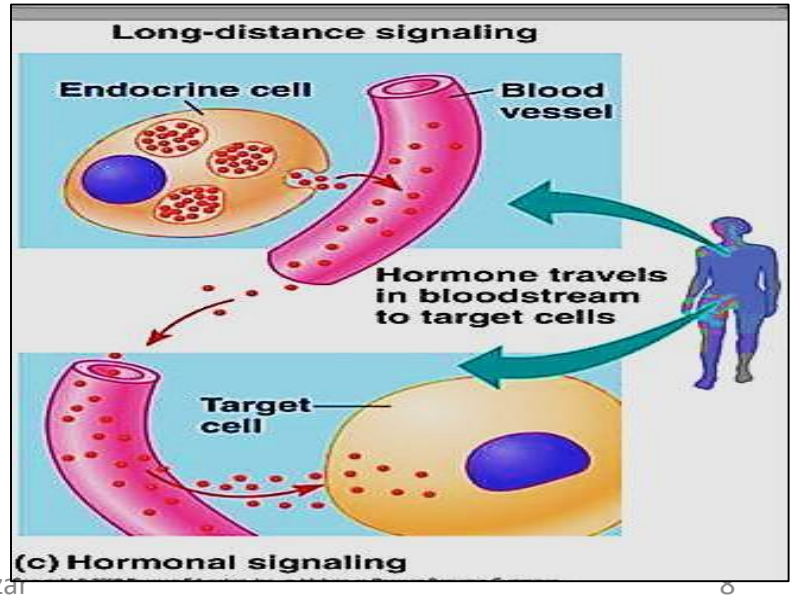
  (e.g.; blood clotting, local allergic skin reaction, wound healing)

- **Synaptic**: (**neurotransmitters**). Neurotransmitters are **endogenous chemicals** that transmit signals from a **neuron** to another nerve cells or muscle cells across the synapse.



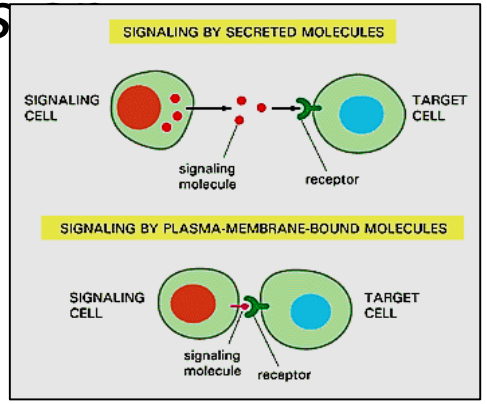
5- Endocrine signaling : act on target cells at distant body sites (long distance)

e.g. (**Hormones** produced by **endocrine cells**, travel through the **circulatory system** to affect other cells all over the body



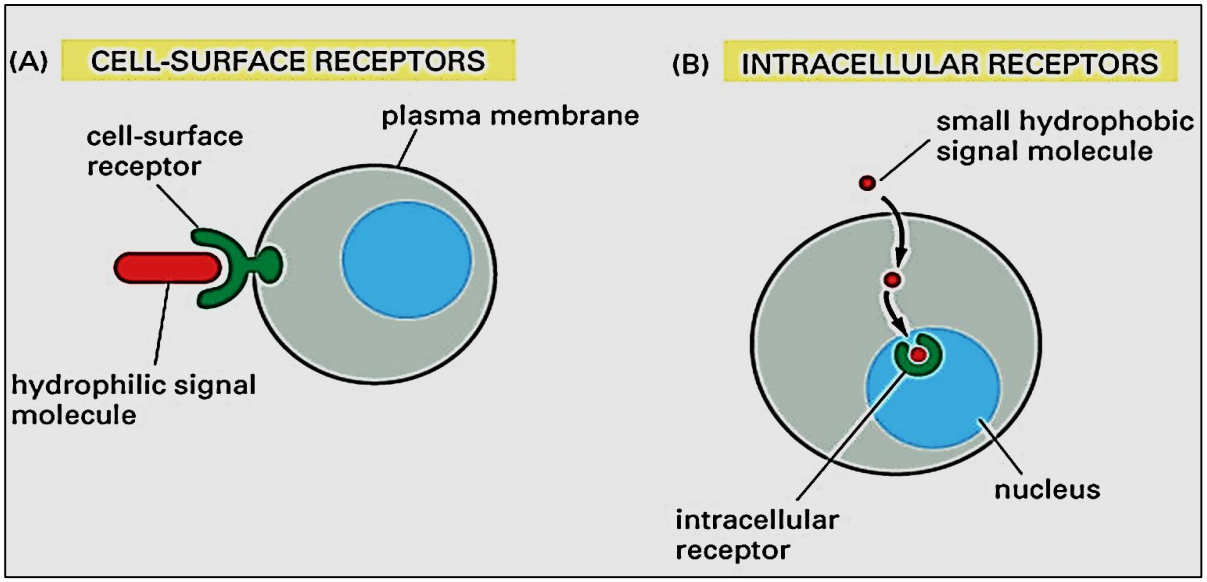
I. Reception

Signaling molecules: are either secreted by or expressed on the surface of some cells **will bind** to *receptors* *other cells* causing changes in target cells



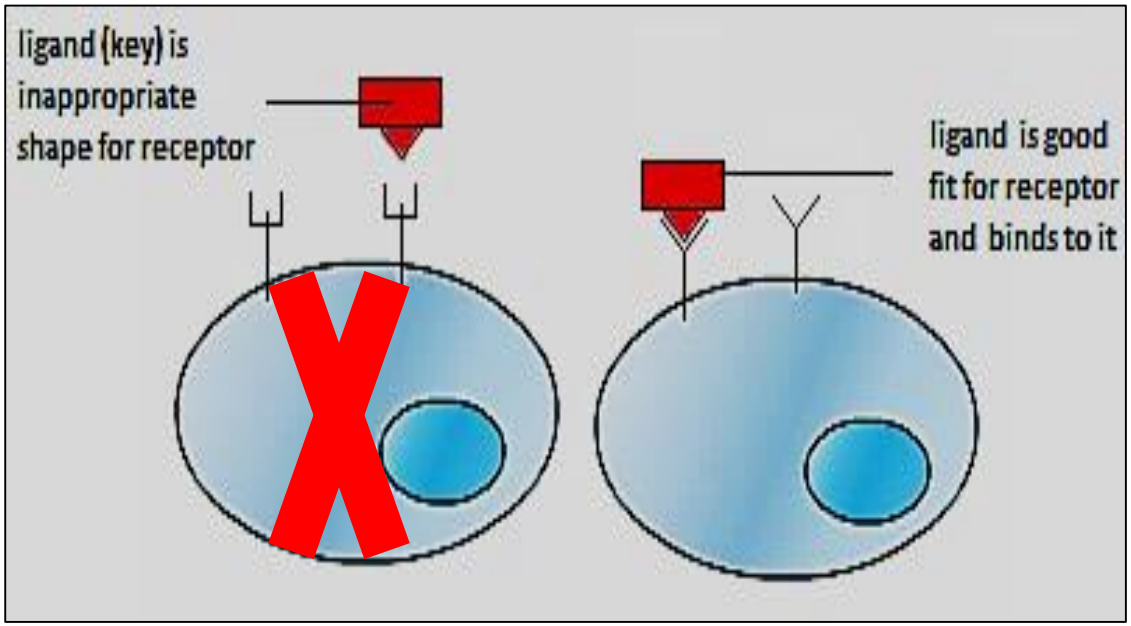
Receptors: Protein molecules found either:

- On the cell surface (*embedded within the cell membrane*)
- In the cytoplasm (intracellular)

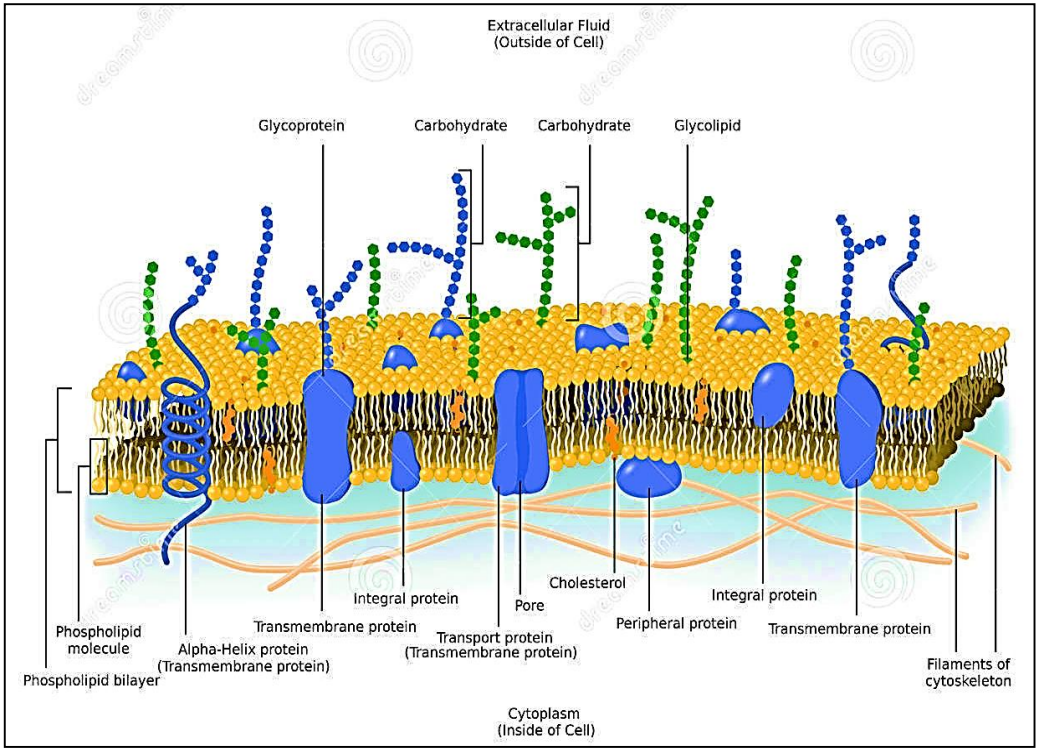


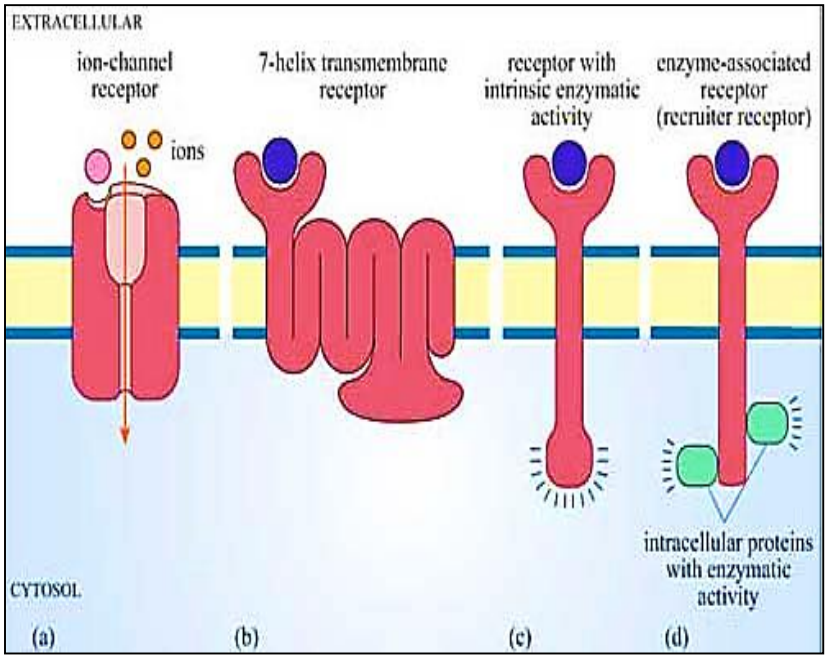
- Signaling molecules (Ligands): **could be:** proteins, small peptides, amino acids, nucleotides, steroids, retinoids (vit. A), fatty acid derivatives, nitric oxide, carbon monoxide…. (Hormones, neurotransmitters, drugs, toxins, gases)

- Ligand: signal molecule with a "key" that fit with the receptor "Lock" → Ligand – Receptor complex → biological changes in the cell



Receptors on the cell membrane

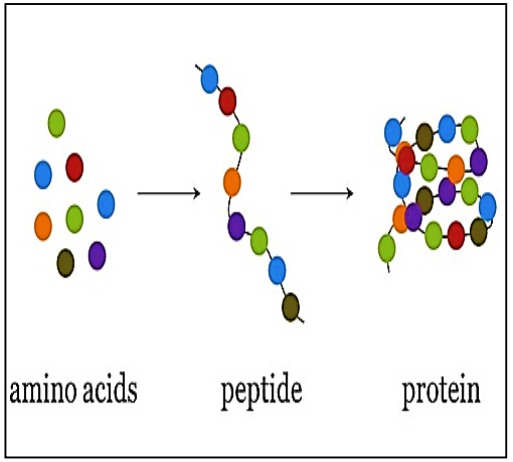




Receptors are integral proteins embedded in The lipid bilayer of the cell membrane

Types /Mechanism of action of hormones

- **Amino acid derivatives**: Melatonin



- **Peptide/ protien (non-steroid) hormones:**

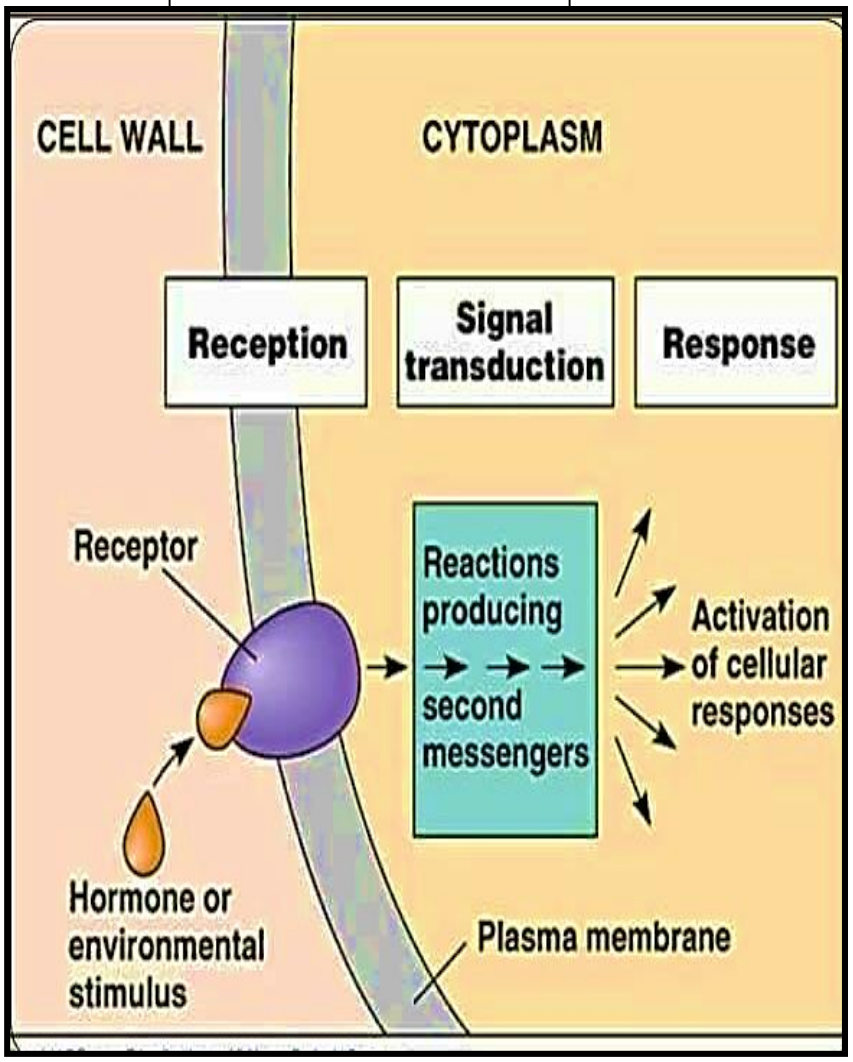
E.g. : Insulin, glucagon, epinephrine, LH,
FSH, Histamine, Ach, ... etc.

- **Steroid hormones:**

E.g. Estrogen, Testosterone , Aldosterone, Calcitrol, vit D,
cortisol…. etc.

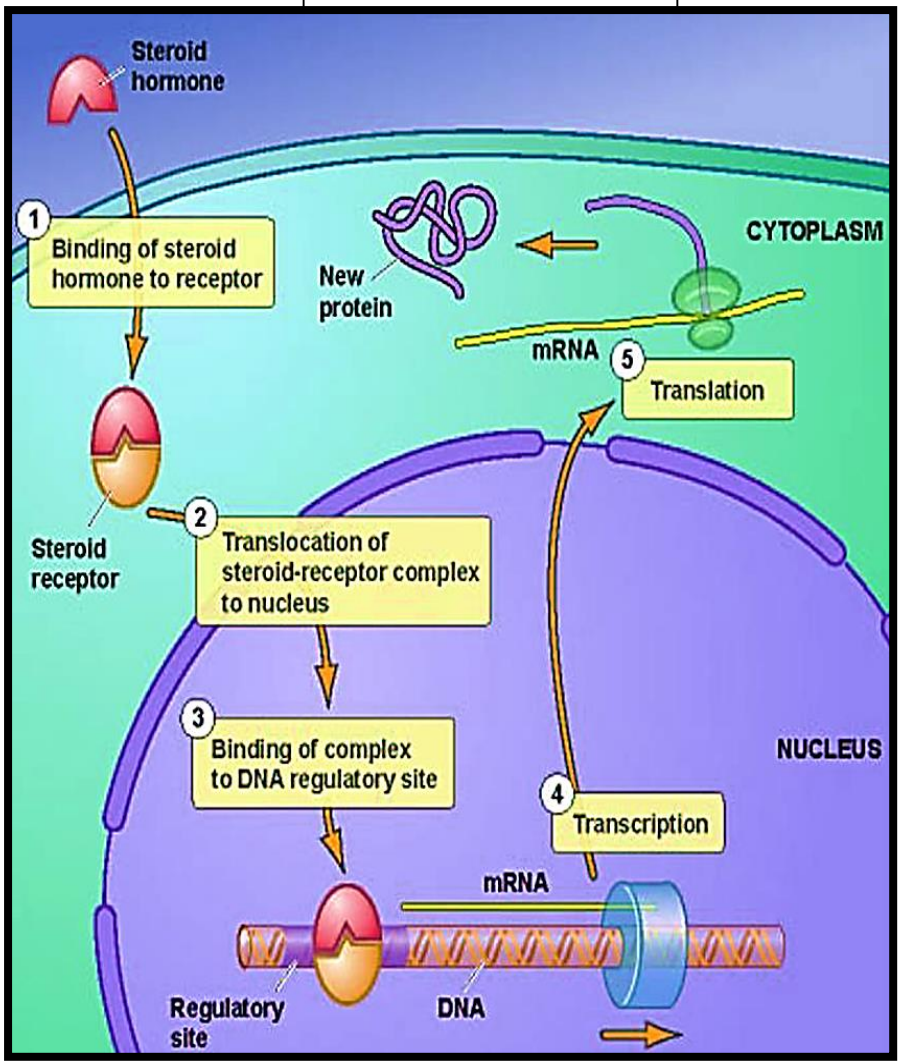
Up to the nature of the signaling molecule the action will be either alteration in protein function or alteration in protein synthesis

Hydrophilic ligand



Peptide based hormones are water soluble

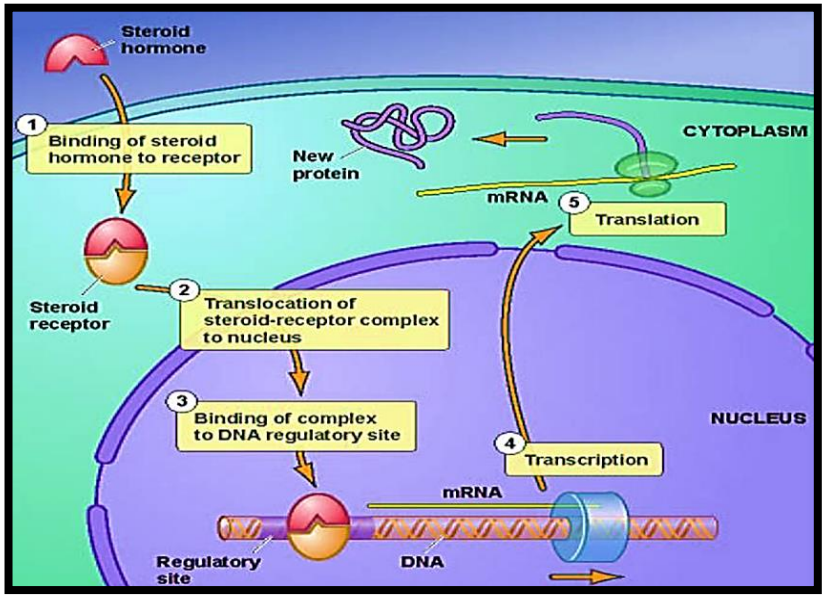
Lipophilic ligand



Steroid based hormones are lipid soluble

Intracellular receptors

- They are Proteins found in the cytoplasm or nucleus of target cells

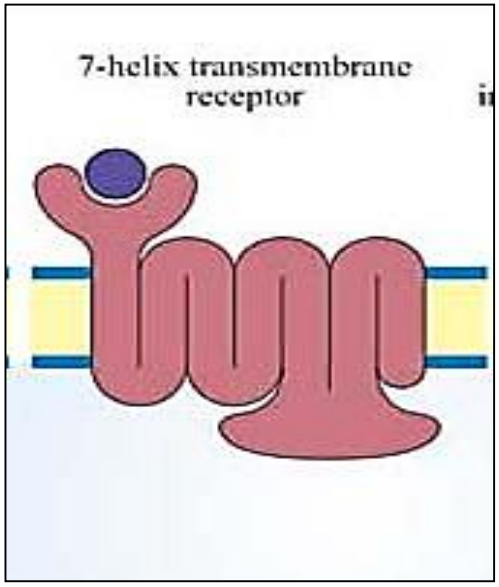


- The small, hydrophobic Ligands can easily cross the lipid bilayer membrane and activate these receptors ,e.g. steroid and thyroid hormones

- The ligand –receptor complex moves to the nucleus → binds to specific regulatory regions of the chromosomal DNA → promote the initiation of transcription of m-RNA (mediate gene expression) i.e. transforming the information on cell's DNA into a sequence of amino acids that ultimately forms a protein

Extracellular receptors: There are 3 types of membrane receptors

1. G protein–coupled receptors (7–transmembrane protein)
2. Tyrosine kinases (enzyme – linked) receptors
3. Ion channel receptor



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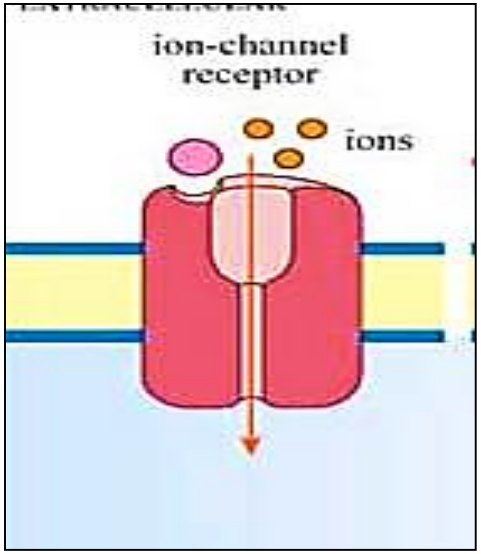

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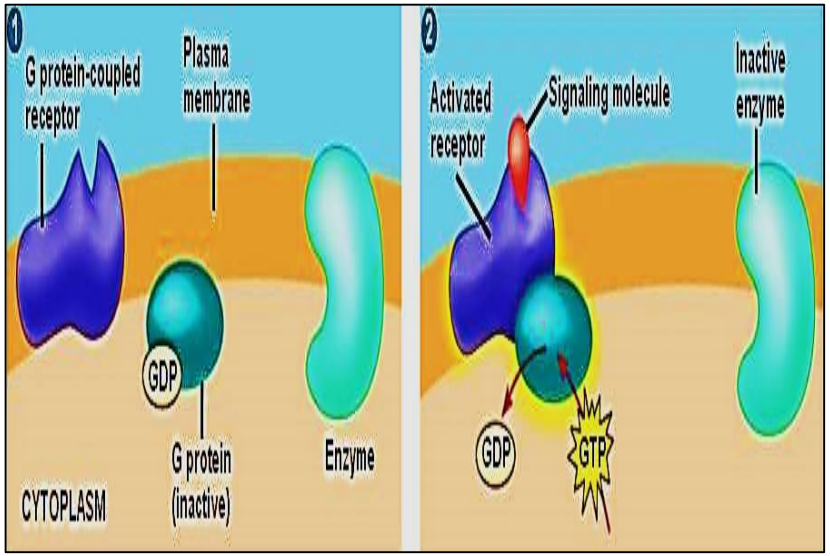
1- G- protein coupled receptors

Step 1:

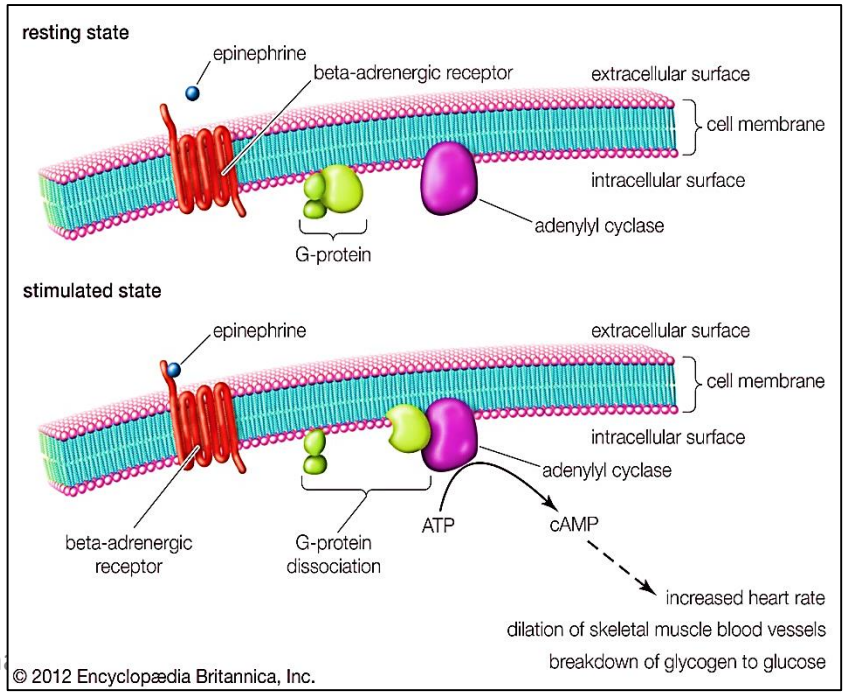
G protein – linked receptors + ligand → activate a membrane protein called G- protein



Step 2:

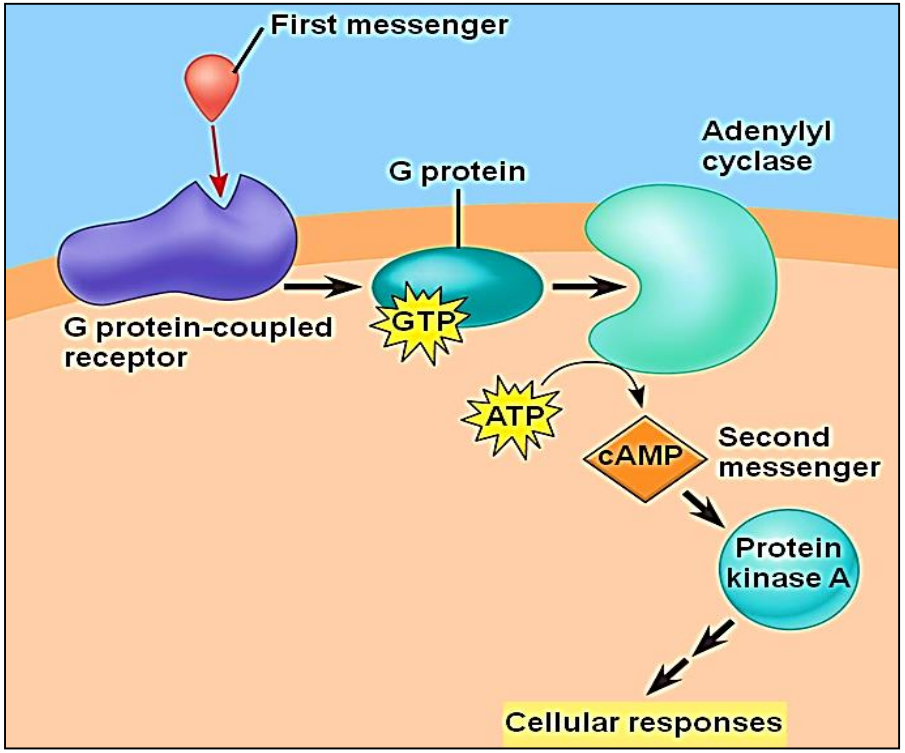
Binding of the ligand to the receptor changes the shape of the receptor→ release GTP that attach to the G protein → **ON switch** → activates G protein

G protein is active



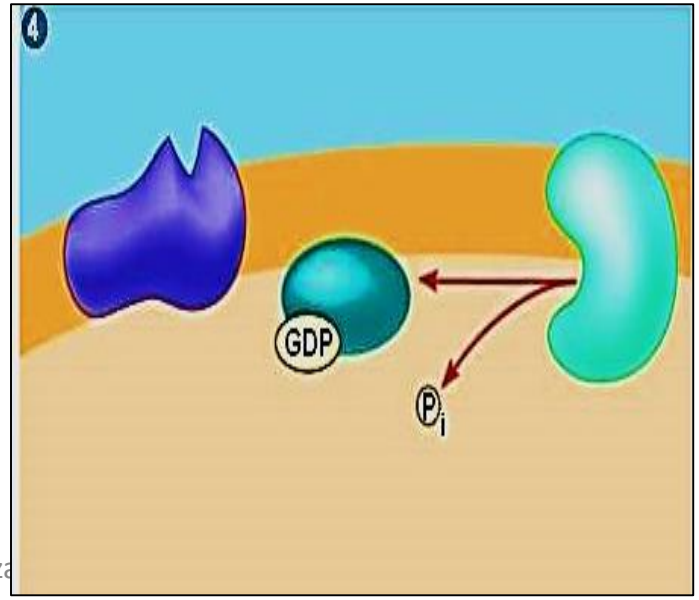
Step 3:

The activated G protein moves to catalyze the Adenylyl cyclase enzyme. The activated enzyme will change ATP→ cAMP → is a 2nd messenger→ phosphorylation cascade → cellular response



Step 4:

G protein returns to the inactive form by moving away from the enzyme & rejoined with GDP. The whole system is ready to receive new signal.



Importance of G protein-coupled receptor system

1. Most widespread class of receptors in mammals

1. Regulates the process of transcription, , motility, secretion, embryonic development, homeostasis, memory

2. Play significant role in controlling vision, smell & taste, hearing sensations

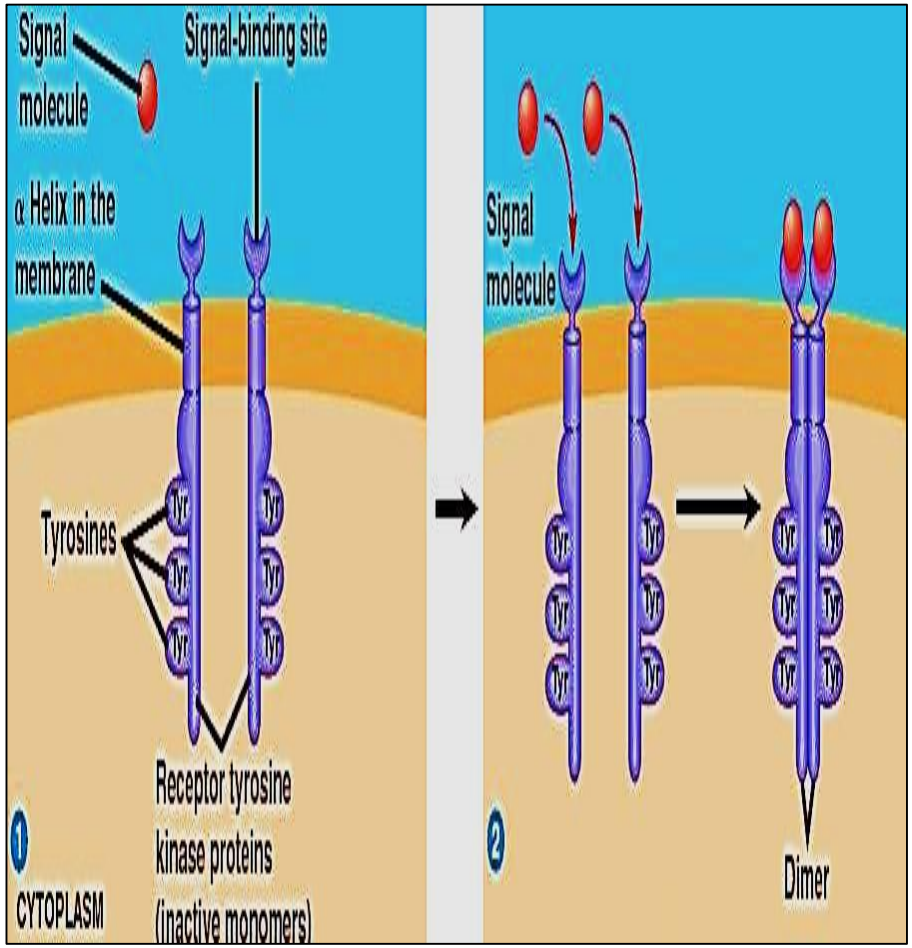
3. 45% of all Pharmaceutical & therapeutics targets & interact e G protein system.

4. Ligand binding produces signaling to a **2nd messenger**

2- Tyrosine kinase receptors

Step 1:

- **TK are receptor proteins located in the cell membrane.**
- **Its intracellular domains are associated with an enzyme**
- **start out as inactive monomers.**
- **Each has a ligand binding site**
- **The signal molecules are often growth factors**

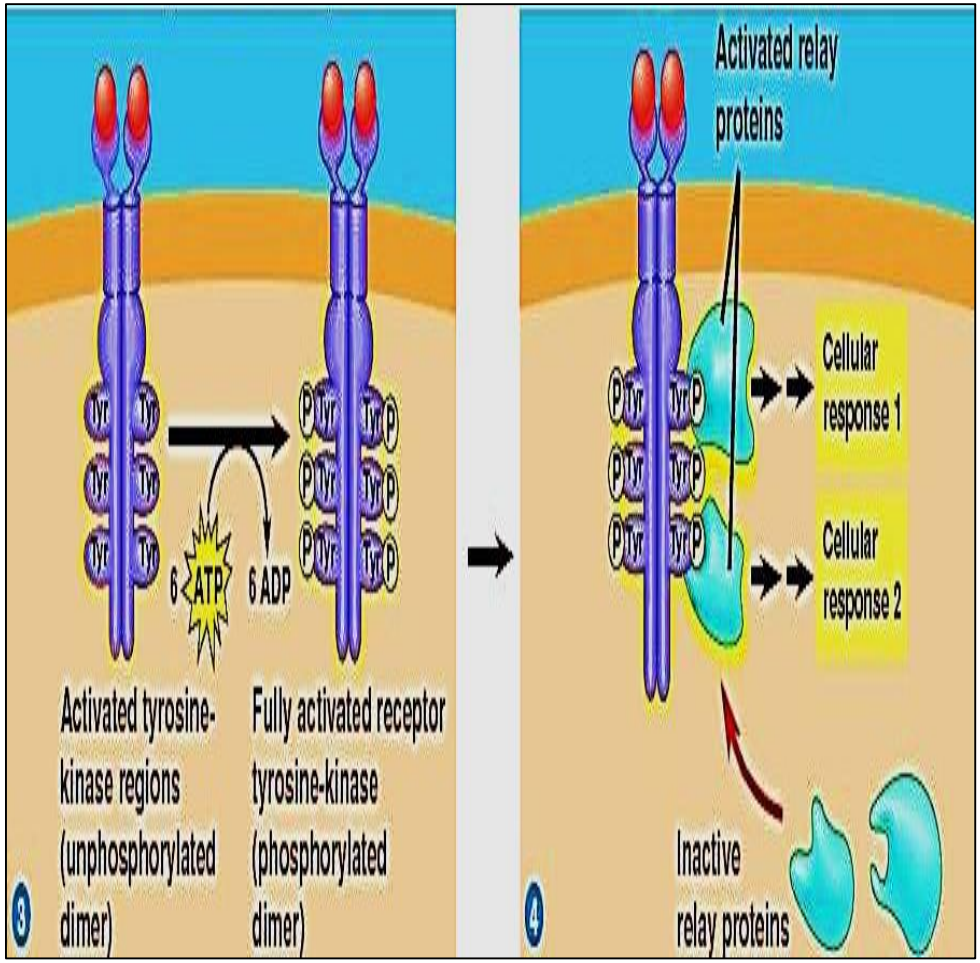


Step 2:

- **When signal molecules bind with receptor sites, monomers combine to form dimers → shape in change of TK → start activation, yet not phosphorylated**

Step 3:

- **Dimerization** activates → phosphorylation process(it takes multiple ATPs {6})
- **Fully phosphorylation** → fully active receptors



Step 4:

- Fully phosphorylated & active receptor → initiate signal transduction → multiple cellular respons
- Each TK system can trigger many separate cellular responses

Importance of Tyrosine kinase receptor system

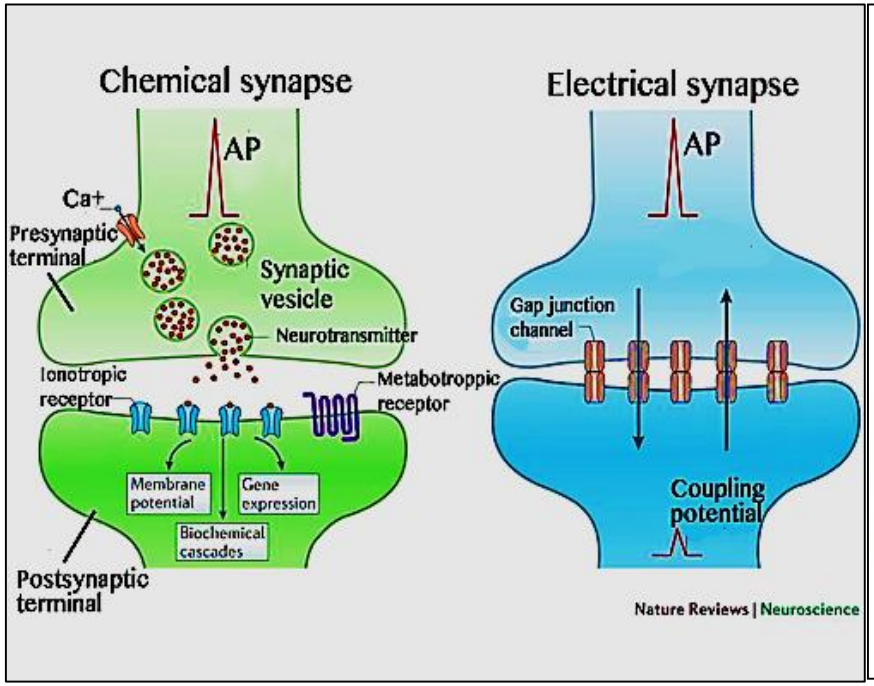
- One receptor tyrosine kinase (DIMER) can activate more different responses, providing a way for cells to regulate growth activities

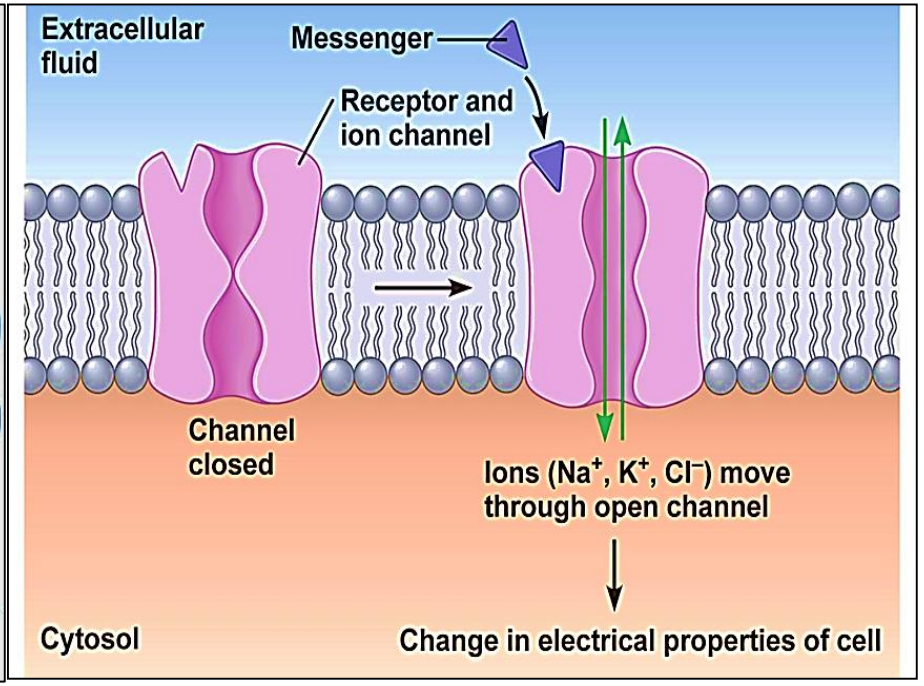
- Kinase: is the enzyme that catalyze the transfer of phosphate group → phosphorylation of the Dimer cause ON or OFF

- Many cancers are caused by mutated tyrosine receptors which get activated **without a signal molecule (cells growing out of control)**

3- Ion channel receptors

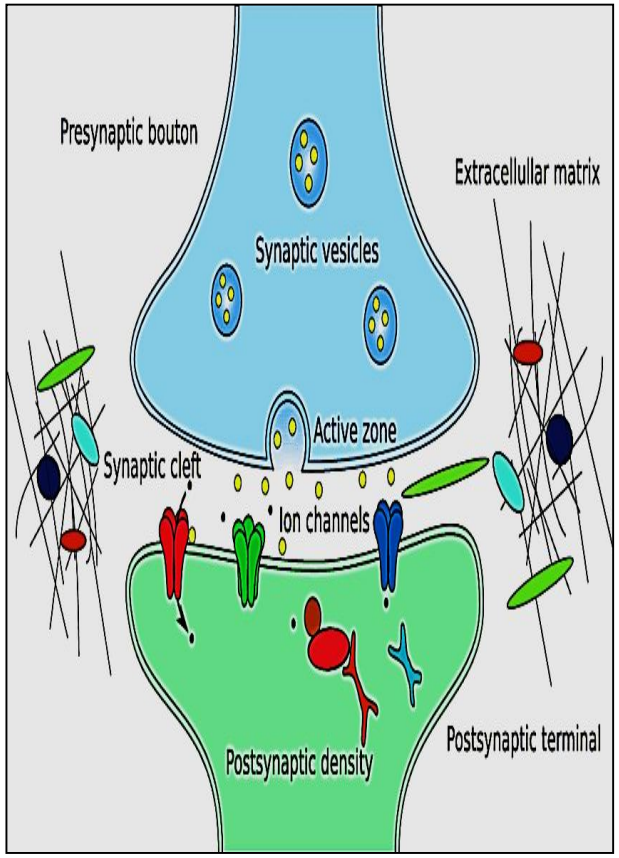
- Are the simplest form of receptors
- Also known as **ligand-gated ion channels** located on post synaptic membrane in nervous system
- Is away to regulate facilitated diffusion





Importance of ion channel receptors

- Important in the nervous system
- Neurotransmitters function as ligands which bind to receptors on target cell
- These receptors are ion channel receptors
- Once open, ions flow into the target cell
- Change in ion concentration triggers a nerve impulse



II. Signal transduction

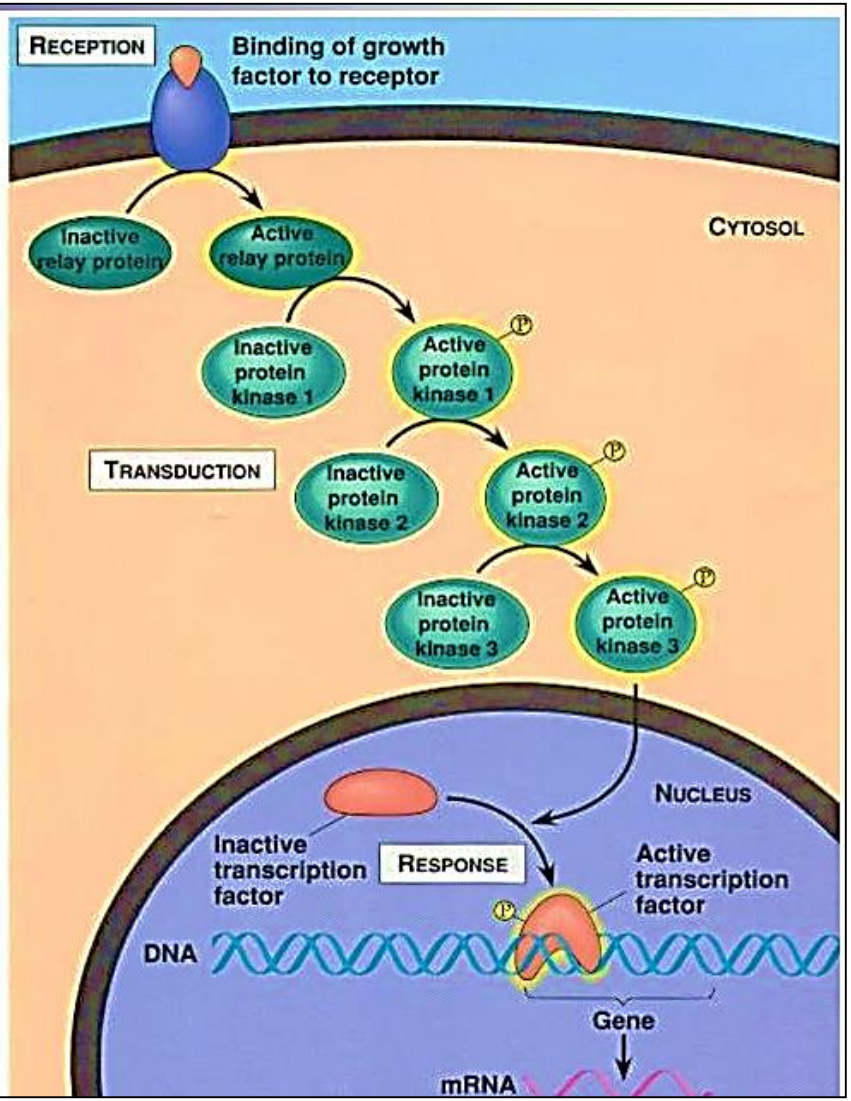
- Is the step between receiving of a signal & response of the cell to that signal
- is a biochemical chain of events occur inside the cell

Transduction

Signal reception

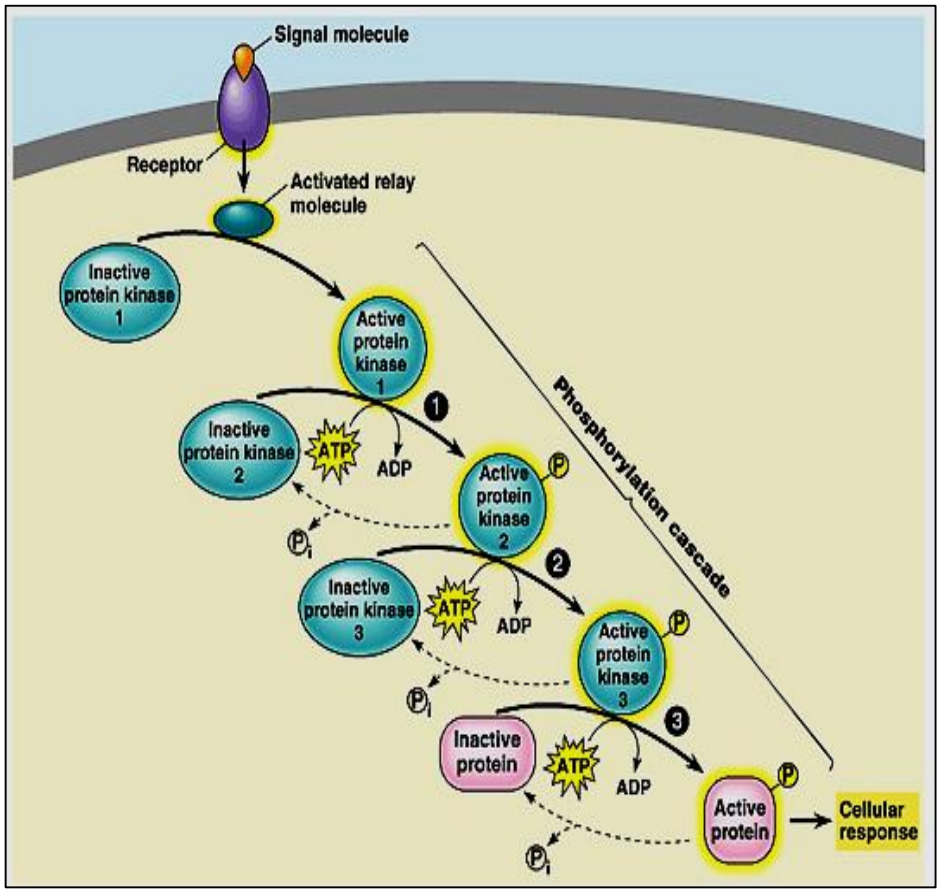
Cell response

Signal Transduction Pathways Relay Information from the Cell Surface to the Nucleus



Role of **protein kinase**

- They are protein molecules found in the cytoplasm
- Act as catalysts
- they are inactive until they are **phosphorylated**
- Each activated PK activates the next one in the chain → Phosphorylation cascade



- Finally a protein is activated which generates a cellular response

Second messengers

- 1st messenger is the extra- cellular signal molecule (ligand)

- 2nd messengers are **non protein molecules** that involve in the transduce of signals inside cells (used to relay messages), used to amplify the signal

- Examples of 2nd messengers are:

1. cAMP
2. cGMP
3. Calcium ions
4. Inositol triphosphate (IP3)

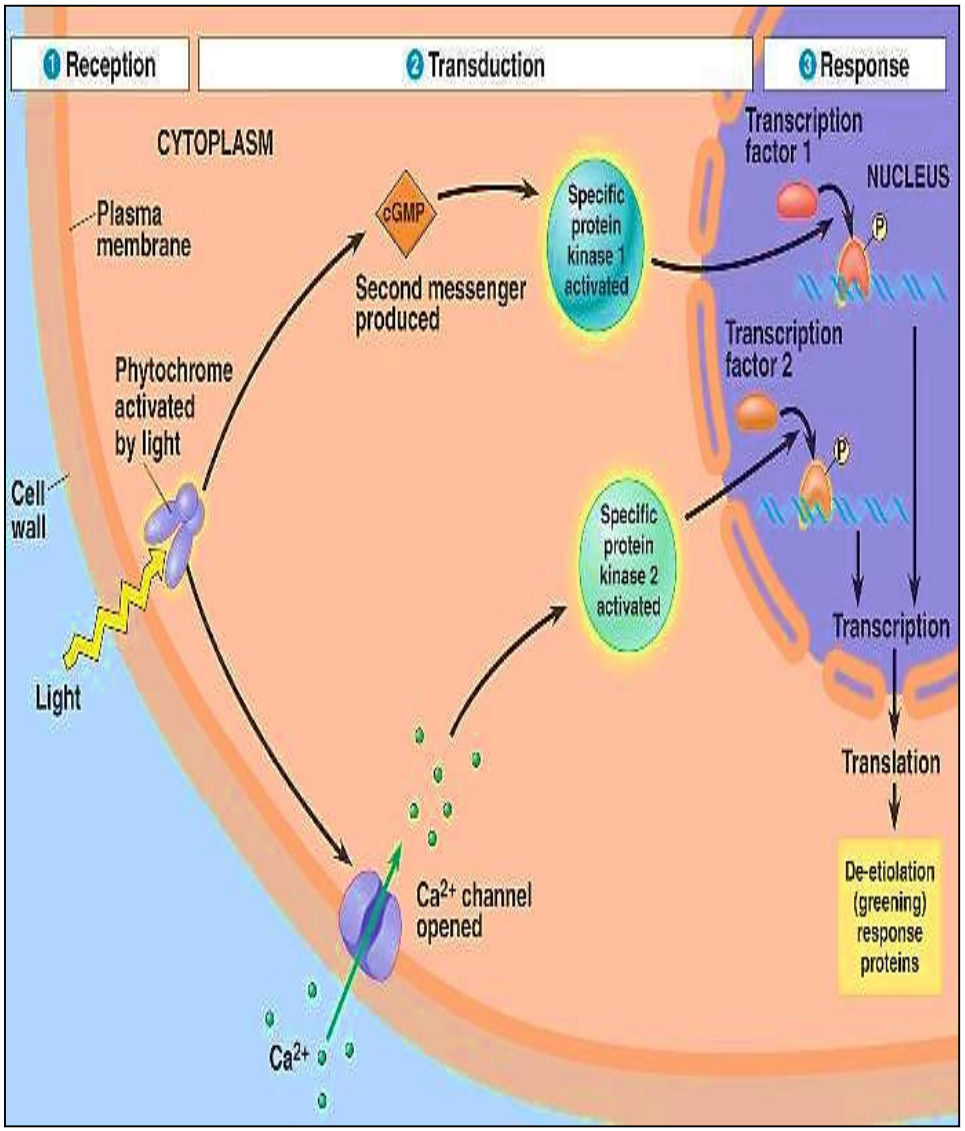
III. Responses

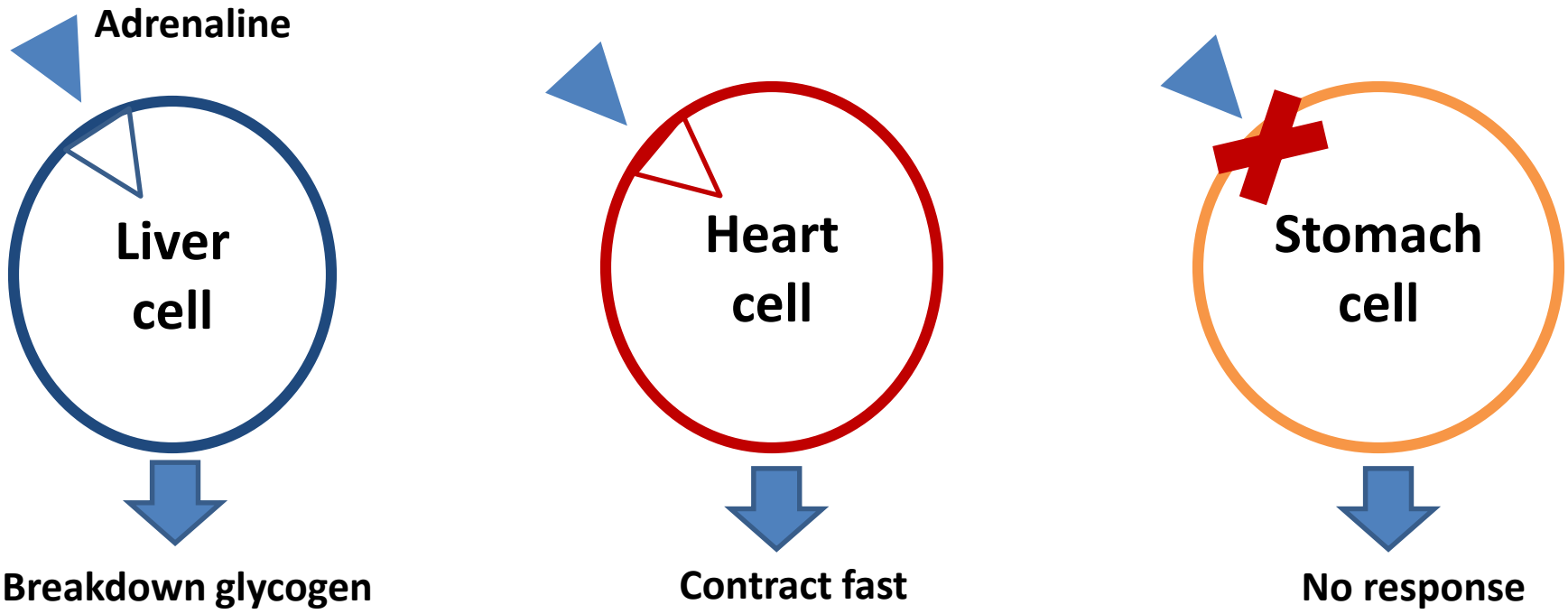
Cells respond to signaling pathways by many ways:

1- Metabolic enzyme→ alter metabolism

2- Regulatory protein→ alter gene expression

3- Cytoskeletal protein → alter cell shape or movement





(Signals can be specific only to different types cells)

Thank you