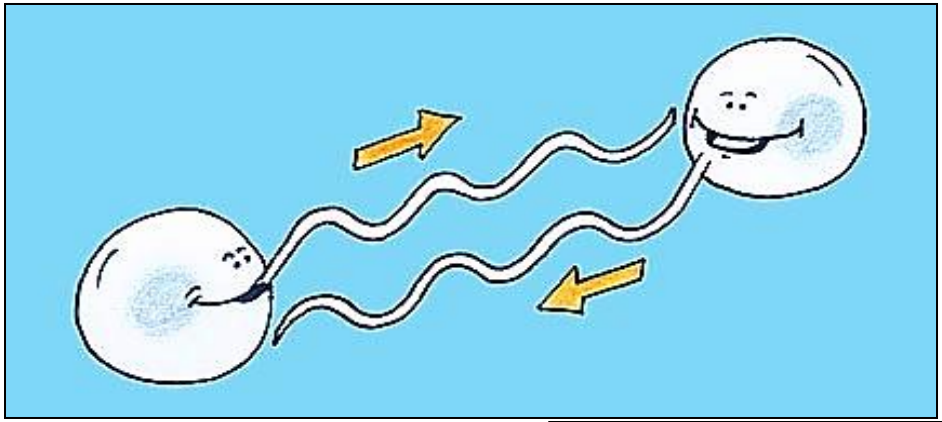
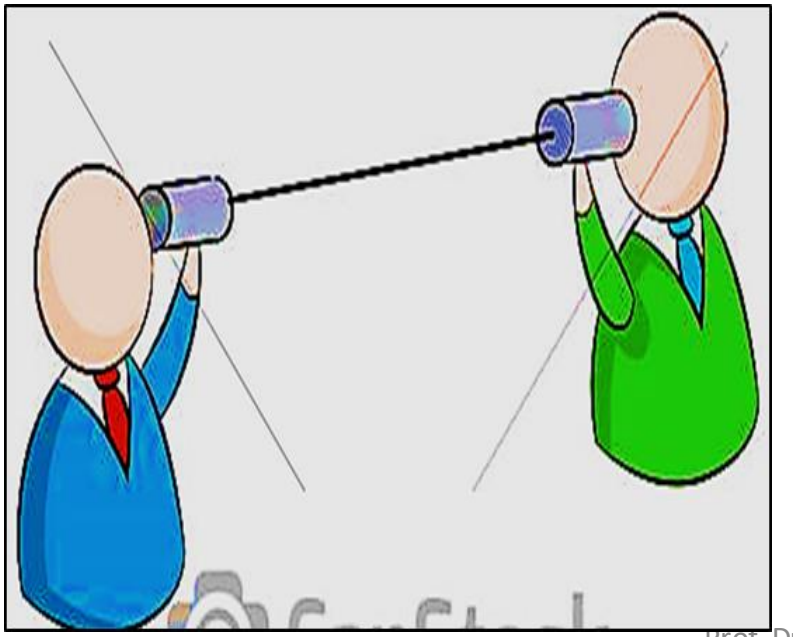
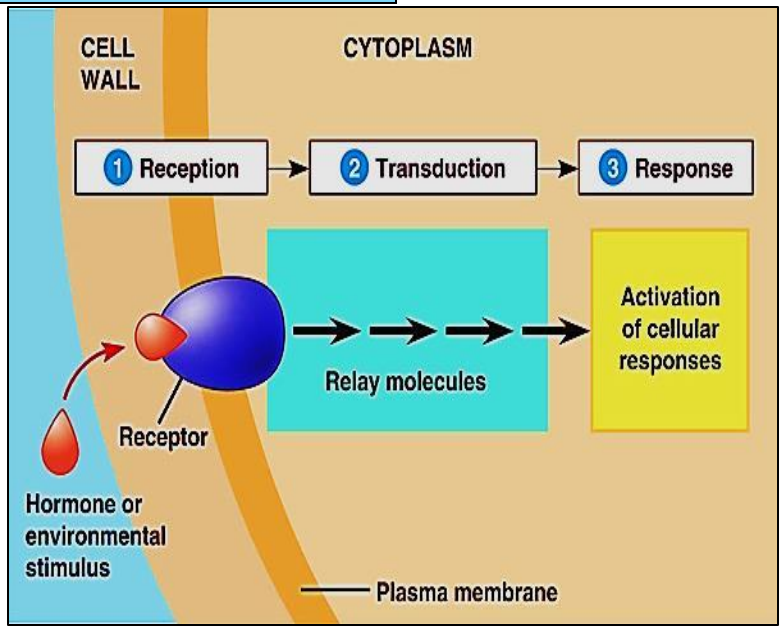
Cell Bio
Cell Communication







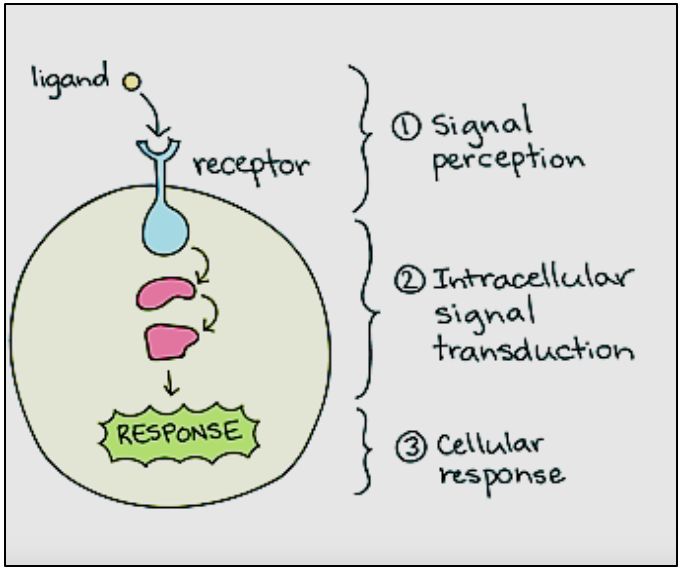
Cell signaling

- Living cells in a multicellular organism have to communicate e each others & respond to the environment in order to regulate many biological process & to maintain homeostasis & life.

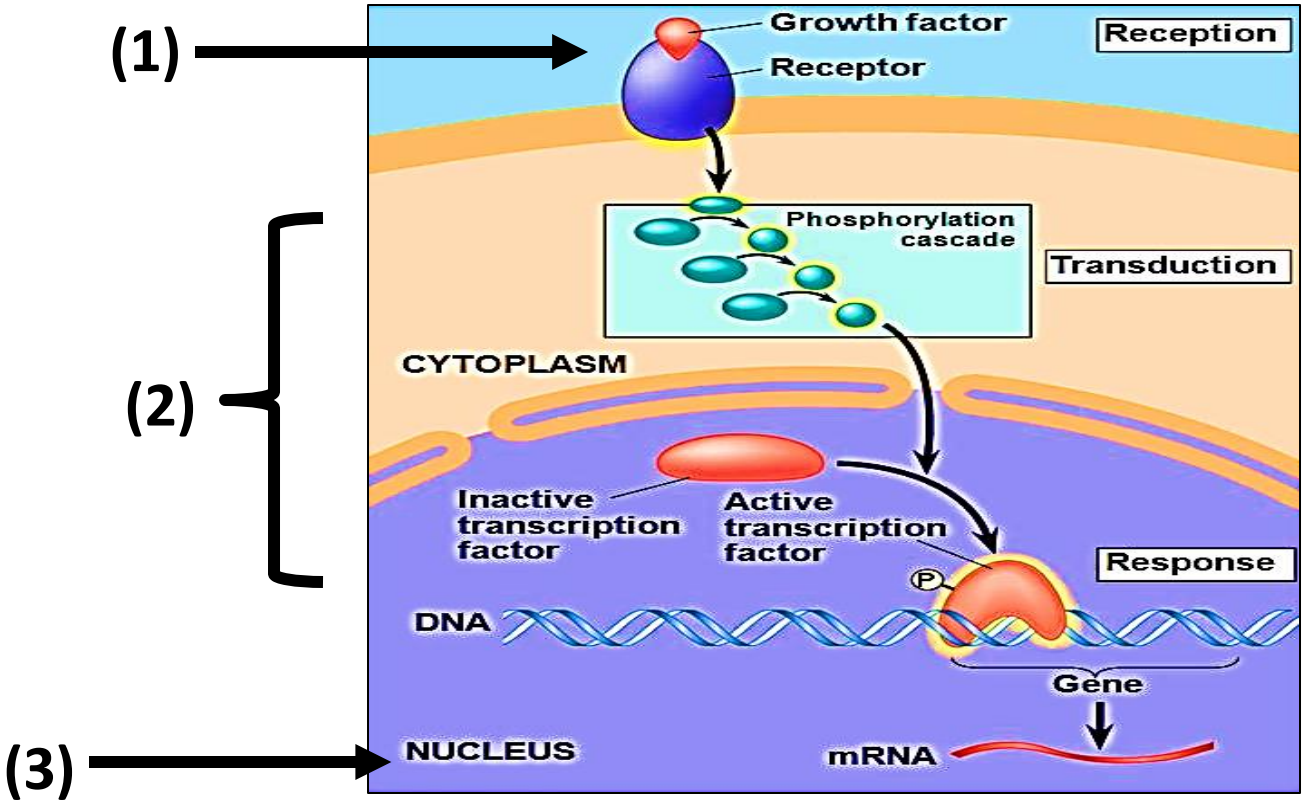
- Cells communicate e each through **signals** which result in **responses** within the cells

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:

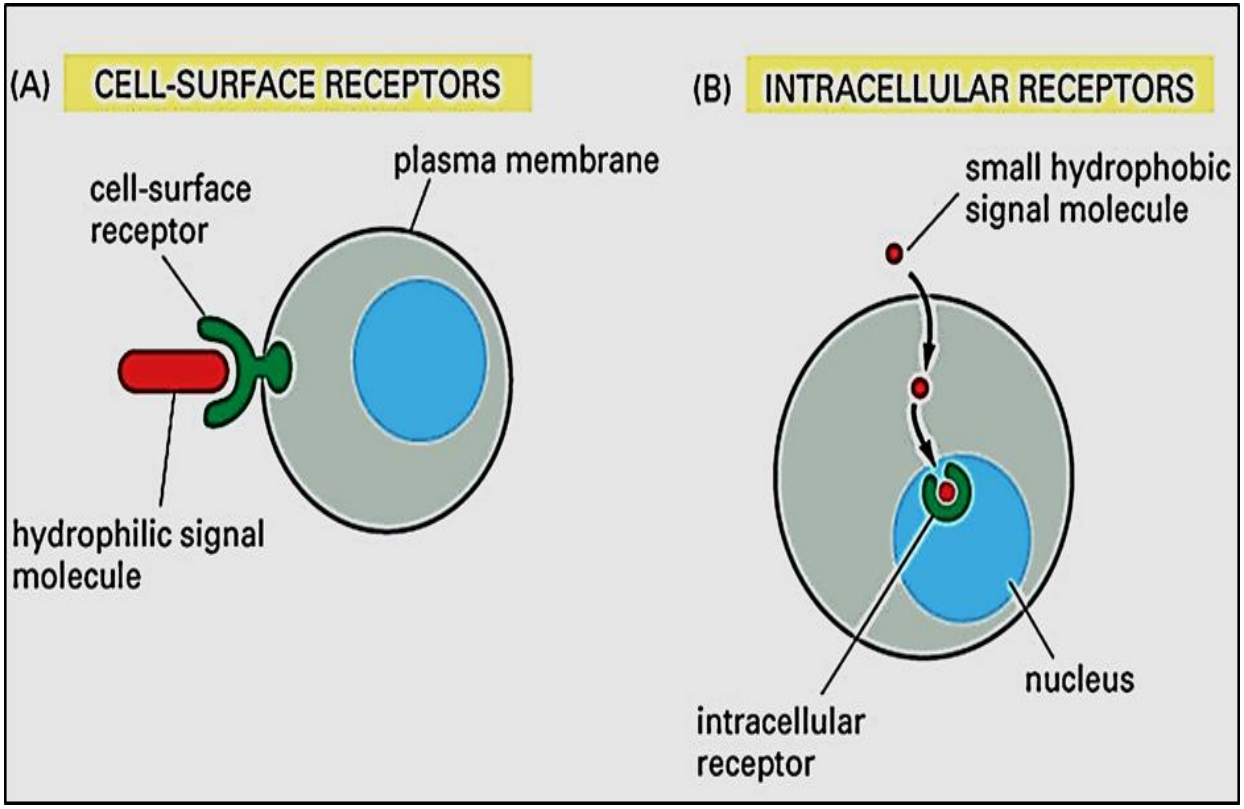
- Sound
- Light
- Temperature
- Odorants
- Substances that we taste

Within the body (hormones):

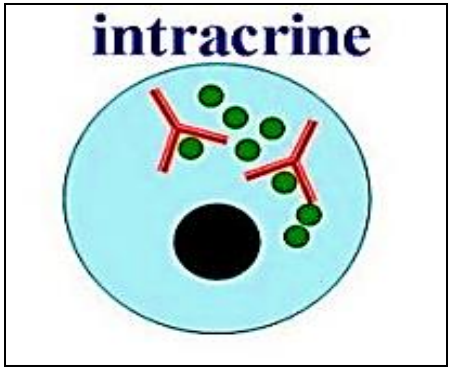
- Epinephrine (Adrenaline)
- Insulin
- Testosterone
- Estrogen

All these signals will bind to receptors & cause the cell to respond in certain way.

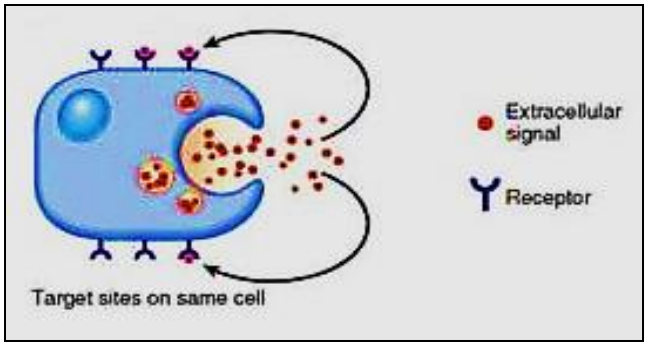
Receptors : are specialized proteins, usually located on the cell membrane or within the cell that recognize and bind to specific signals



Modes of cell signaling

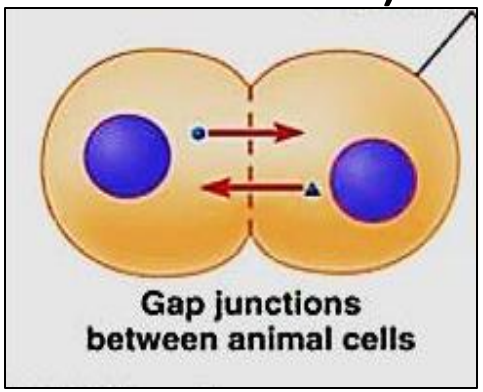


1- Intracrine: signal either hormones or growth factors act on receptors inside the cell (either: cytosolic /nuclear receptors)

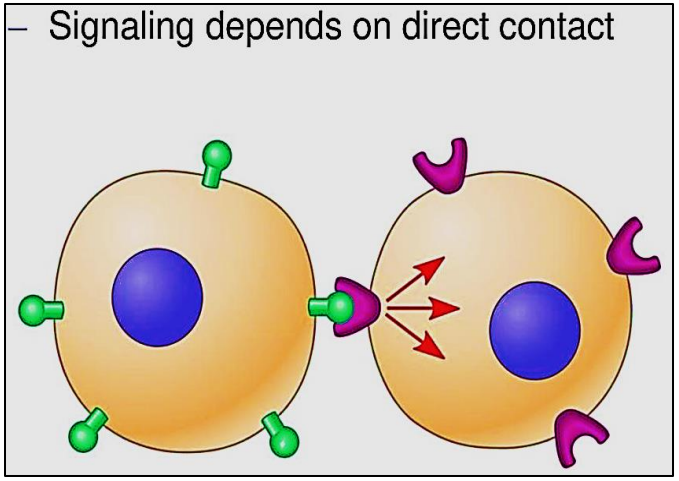


2- Autocrine : the cell secretes signals: hormone or chemical substance that binds to receptors on that surface of The cell itself, leading to changes in the cell. (Autocrine signaling plays critical roles in cancer activation)

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

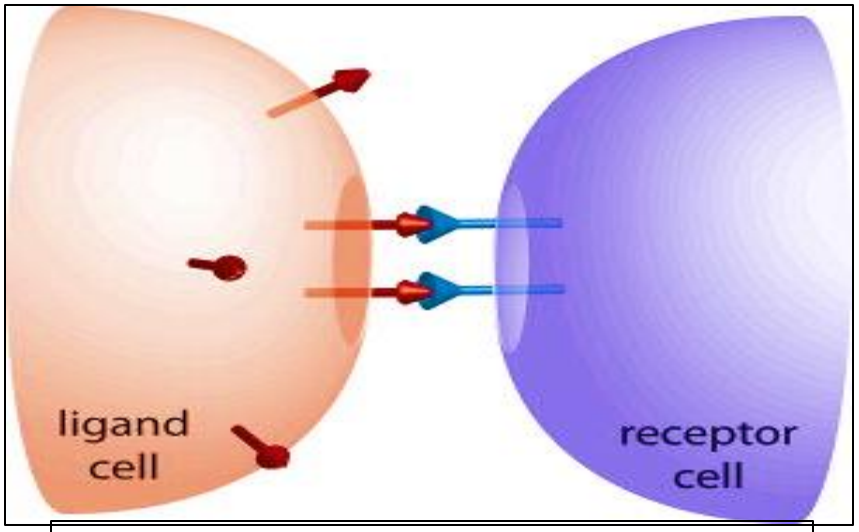


Types of juxtracrine signaling:

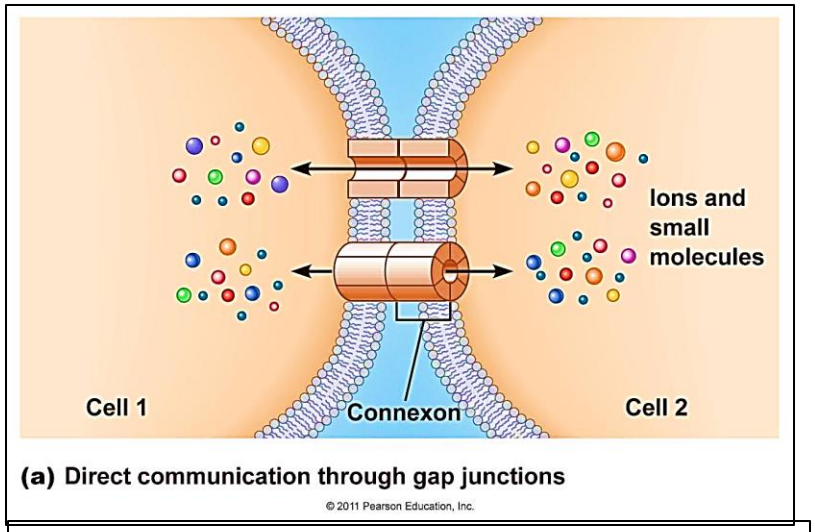
1- A membrane ligand & a membrane Receptor of two adjacent cells interact

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

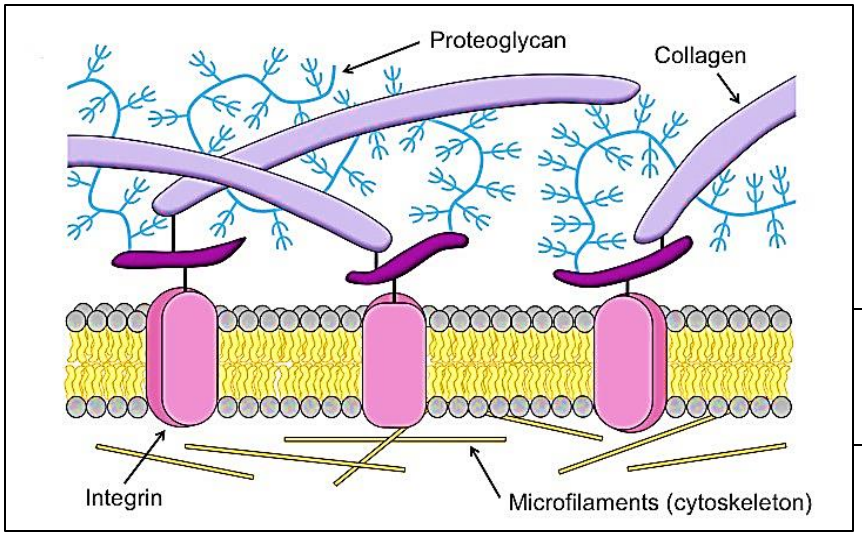
3- An extracellular matrix protein & a cell membrane protein interact with each other



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



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



An extracellular matrix protein & a cell membrane protein interact

Types of juxtracrine signaling

4- Short distance: act locally on different nearby cells

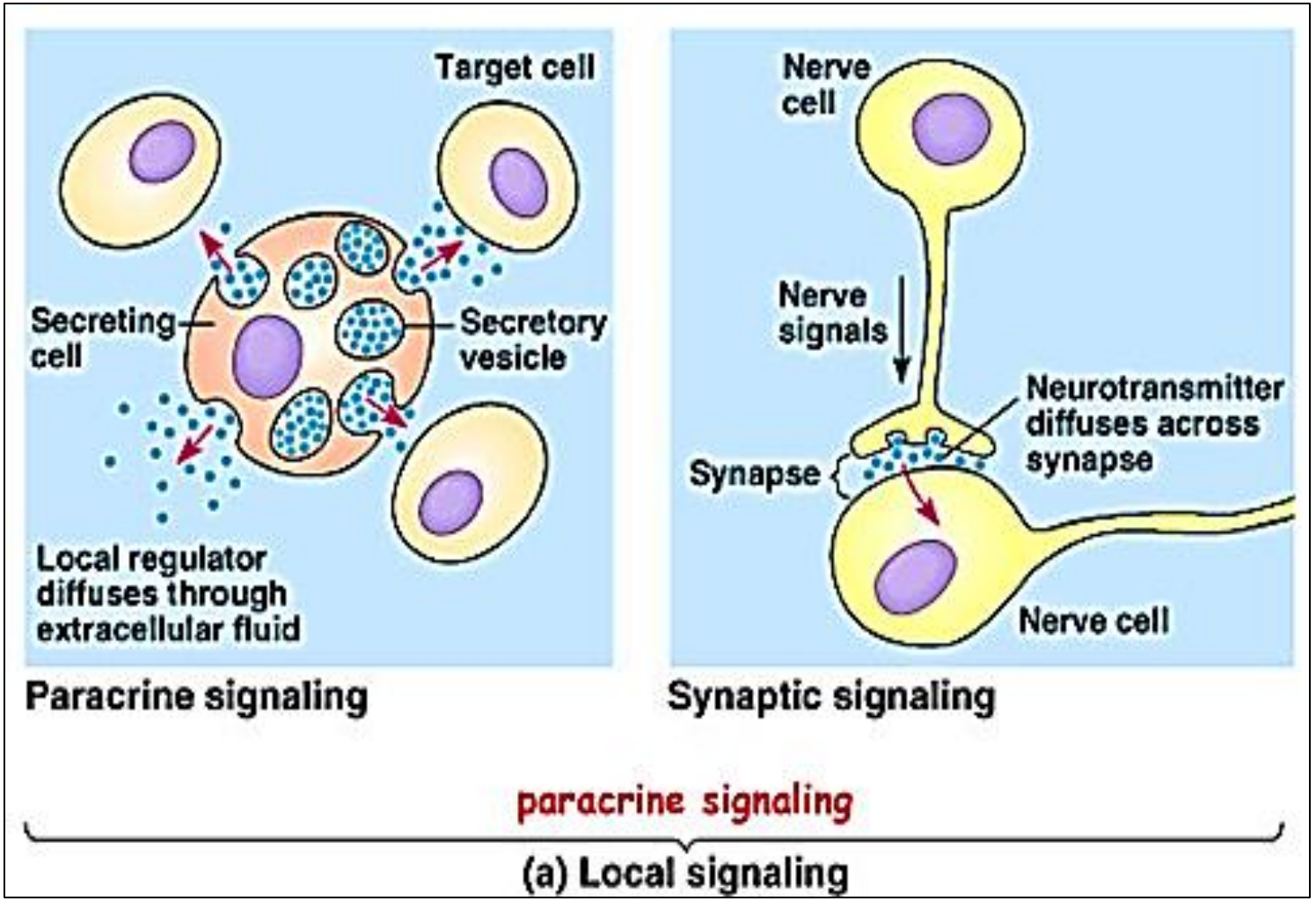
@ **Paracrine** (nearby) signaling (cytokines, histamine)

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

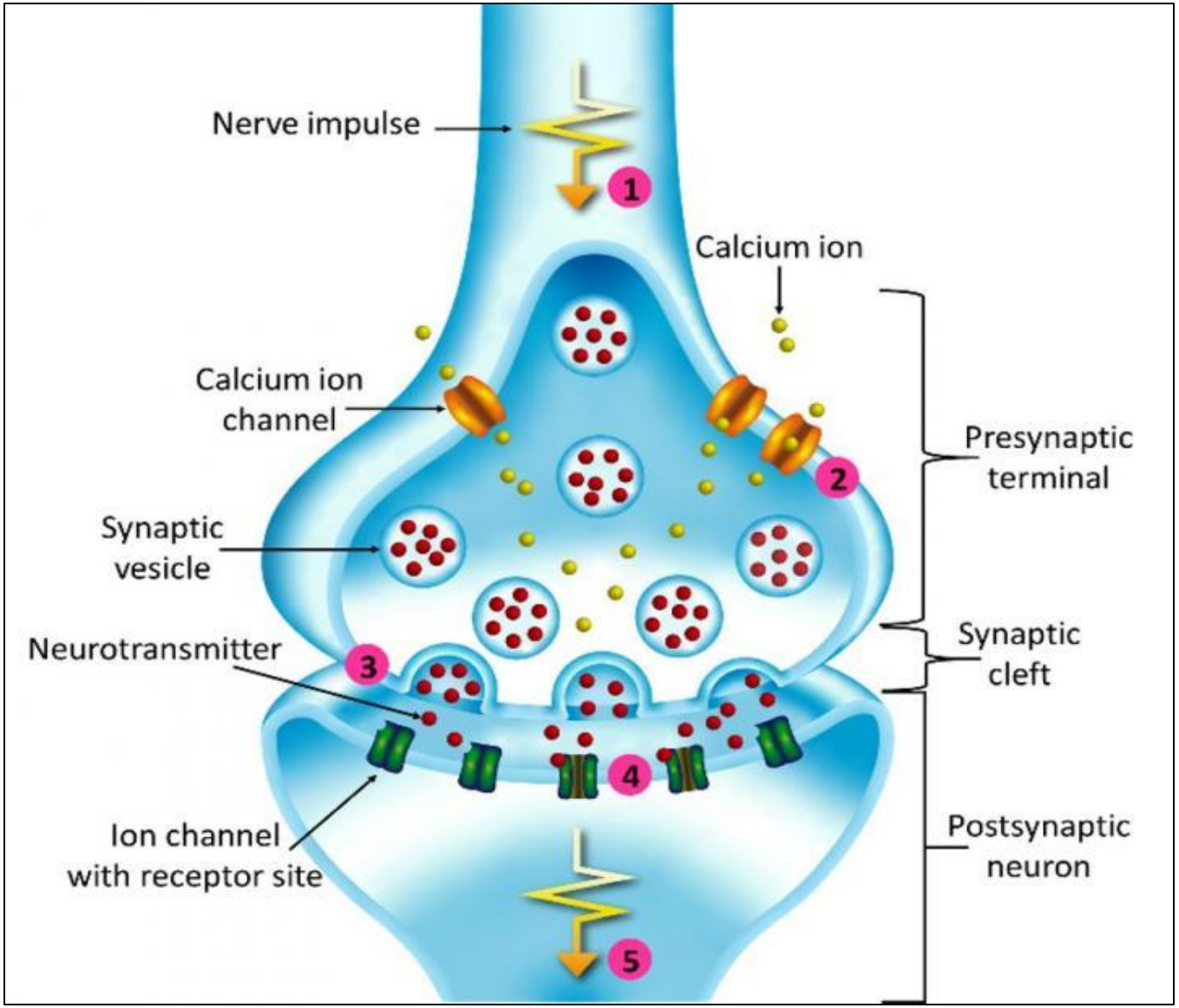
- **Paracrine:** signals are carried by messenger molecules called "**local regulators**", that are released by one cell and diffuse to make contact with another nearby cells

  (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.



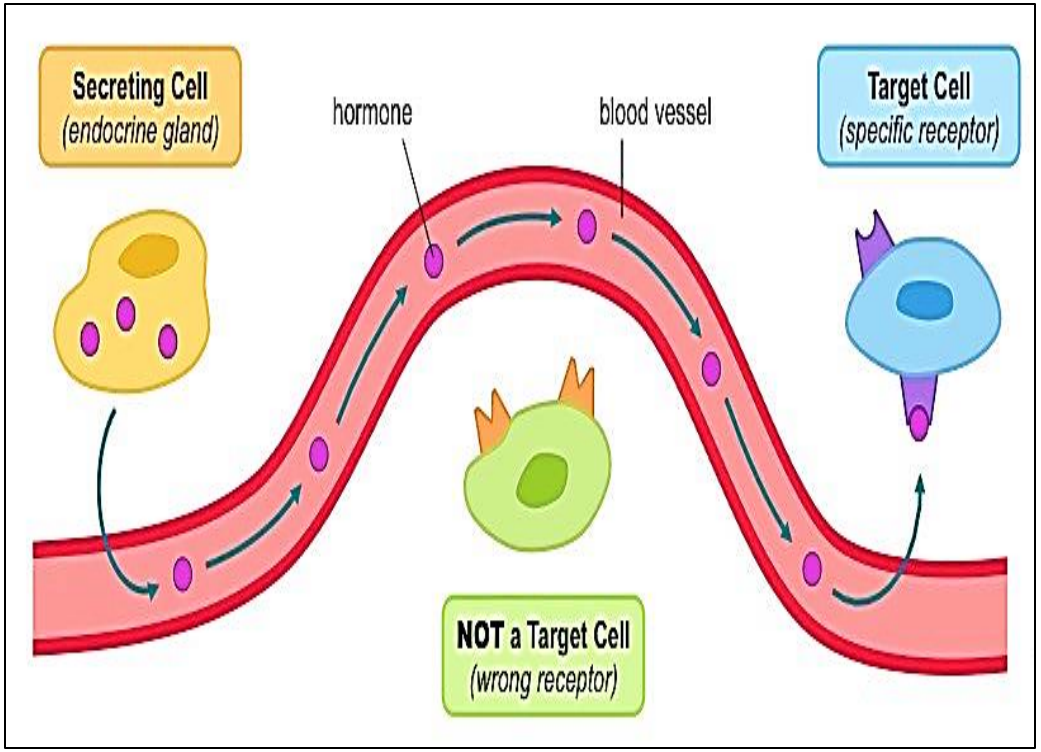
LOCAL OR SHORT DISTANT SIGNALING

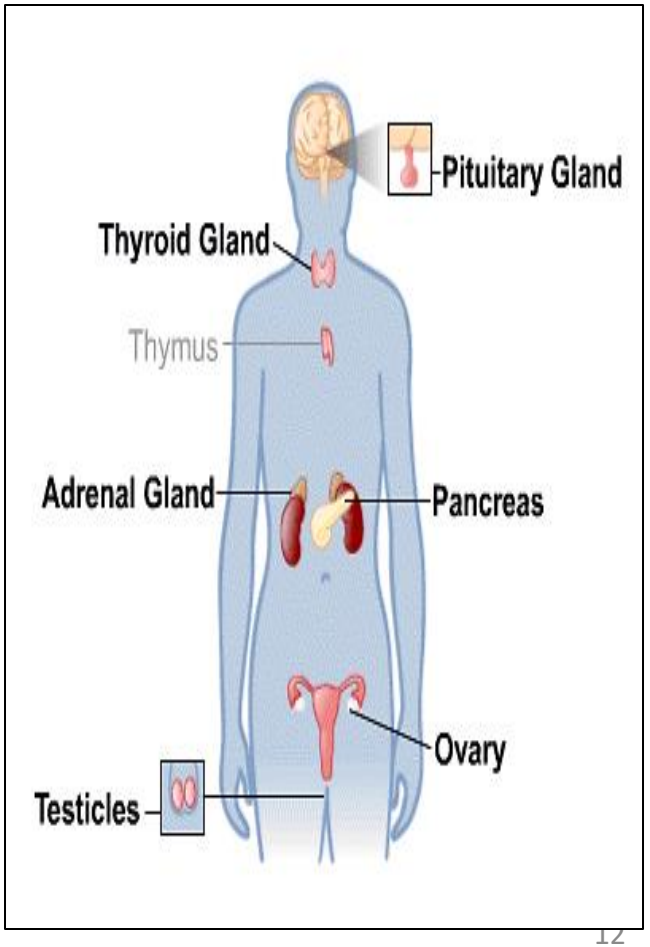


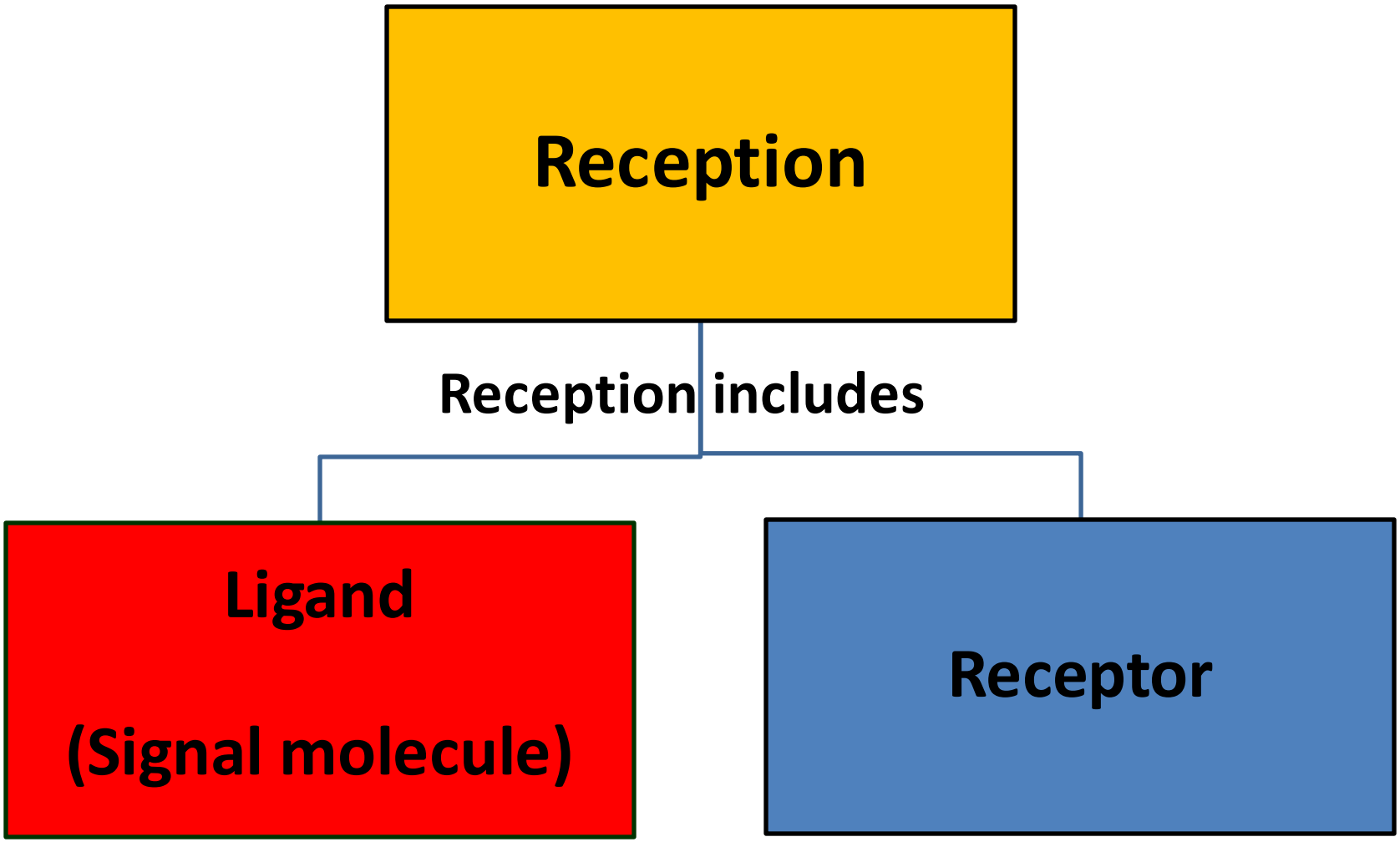
Synaptic signaling

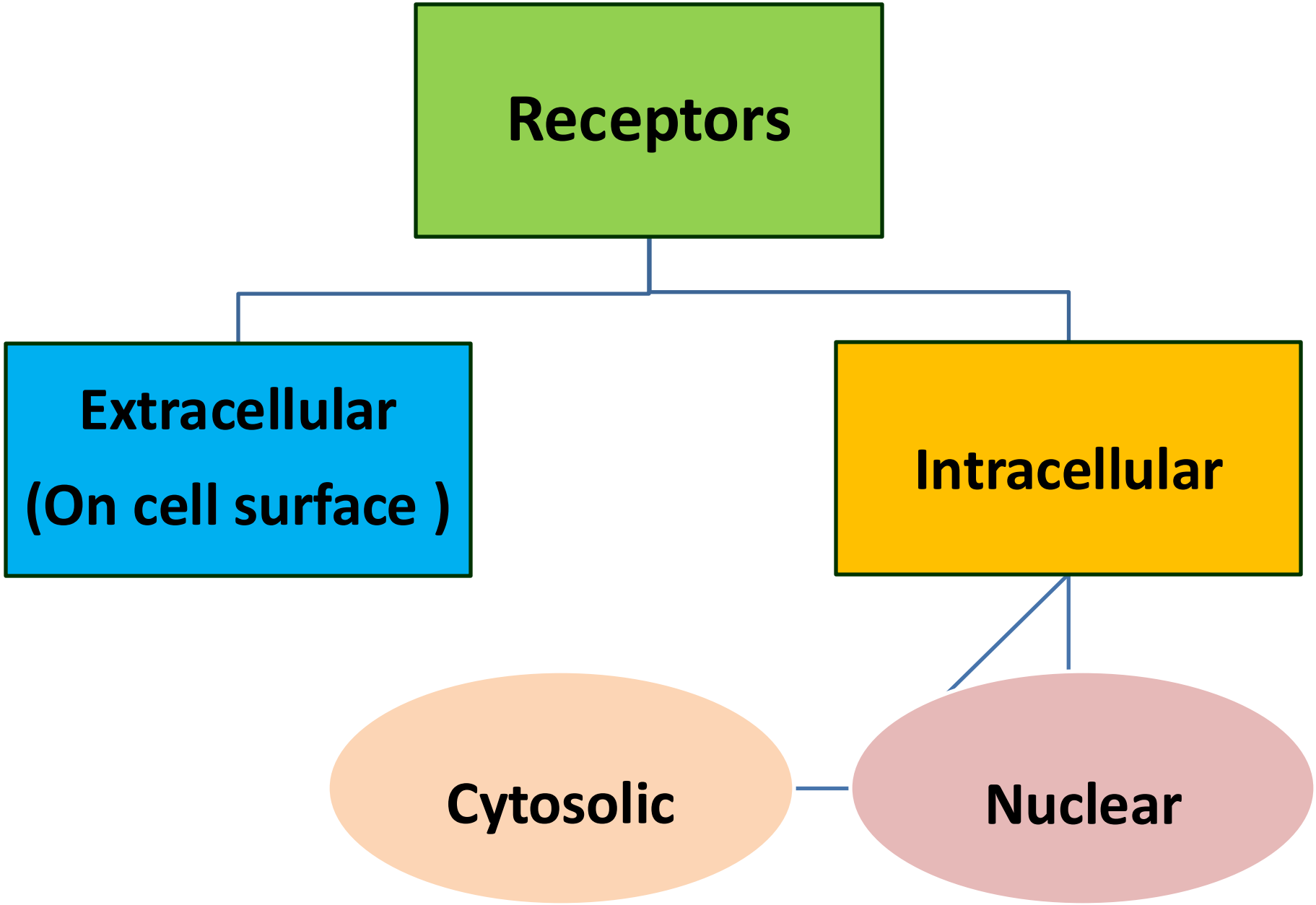
5- Endocrine signaling : act on distant target cells located at distant body sites (long distance cell communication)

e.g. (**Hormones** secreted by **endocrine cells** and released into the **bloodstream** to affect other cells all over the body






Reception
Reception includes
Ligand
(Signal molecule)
Receptor


Receptors
Extracellular
(On cell surface)
Intracellular
Cytosolic
Nuclear

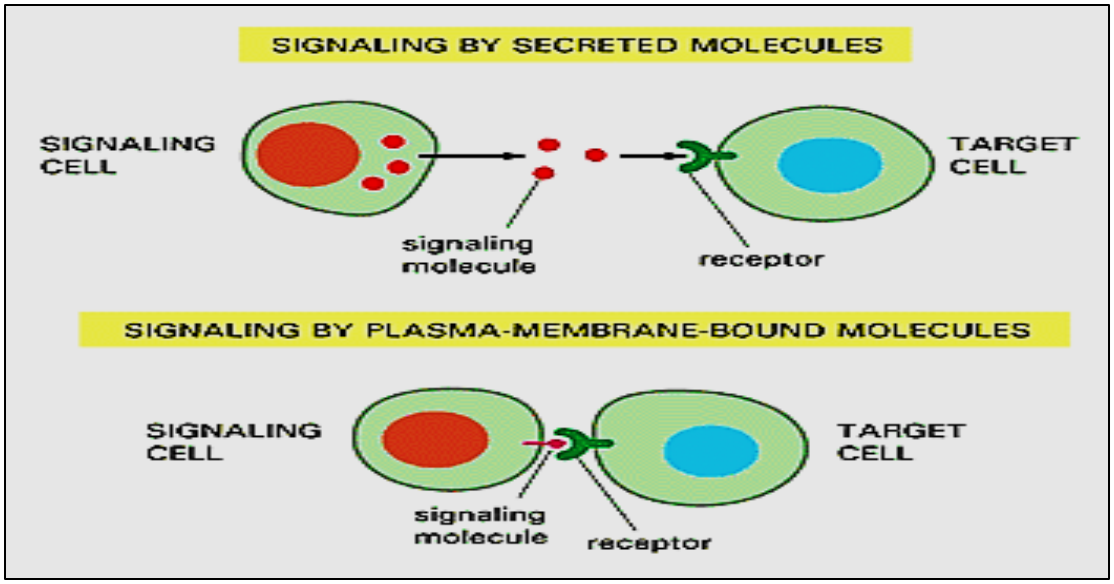
I. Reception

1- Signaling molecule (Ligand)

Are either

Molecules secreted

Protein expressed on cell surface

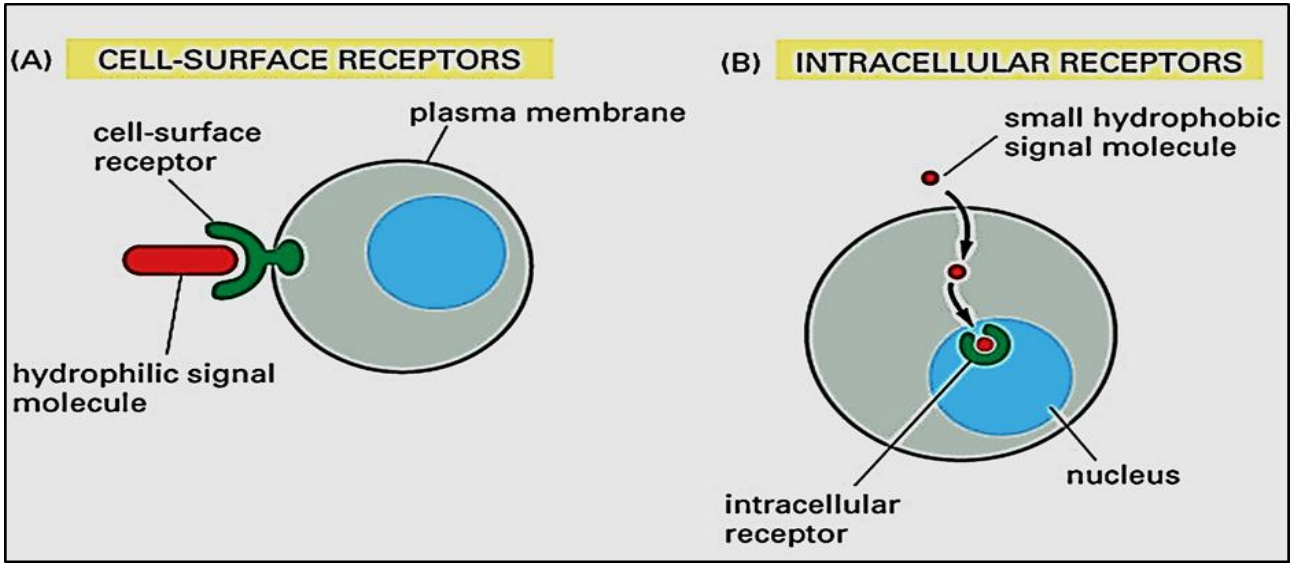


2- Receptors

Are either

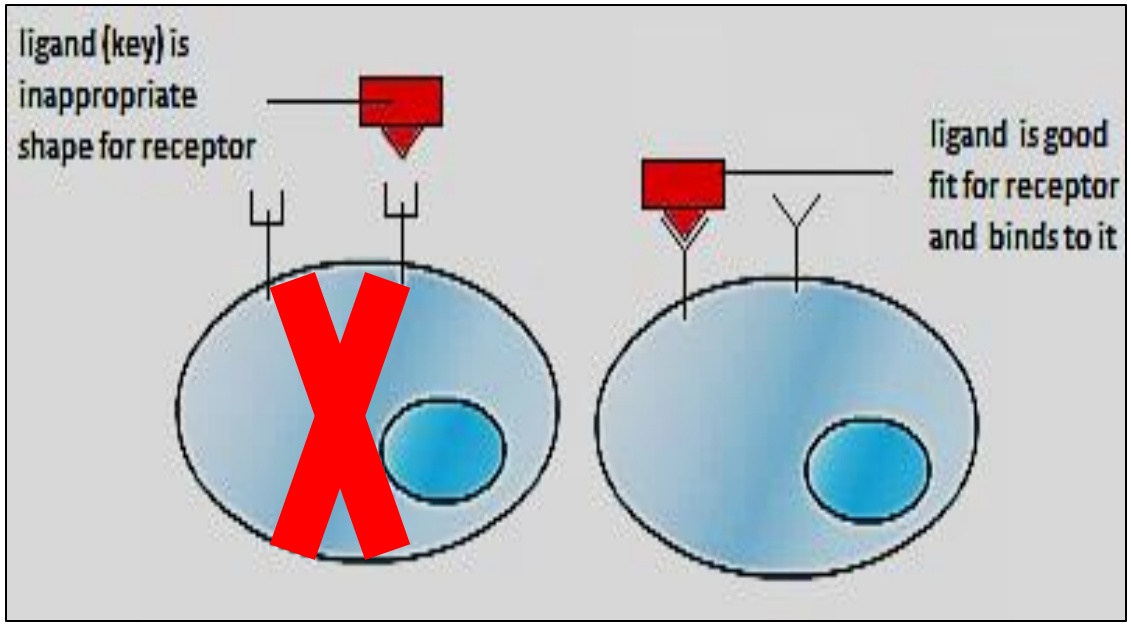
On the Cell Surface

Inside the Cytoplasm or Nucleus



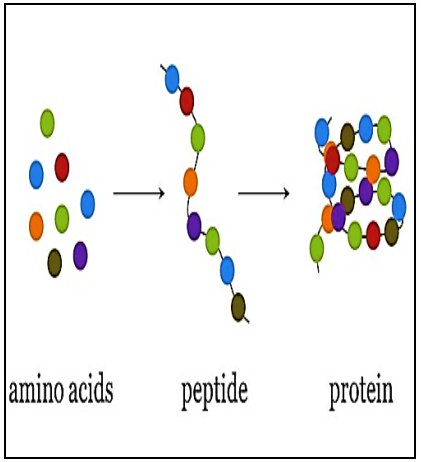
- Signaling molecules (Ligands): **could be:** proteins, small peptides, amino acids, nucleotides, steroids, retinoids (vit. A), fatty acid derivatives, nitric oxide, carbon monoxide…. (Hormones, neurotransmitters, drugs, toxins, gases)

- Ligand (signal molecule) has a "key" that fit in the receptor "Lock" → Ligand – Receptor complex → that will cause biological changes in the cell



Types of hormones ligands

- **Amino acid derivatives**: Melatonin



- **Protein (peptide) hormones (non-steroid) :**

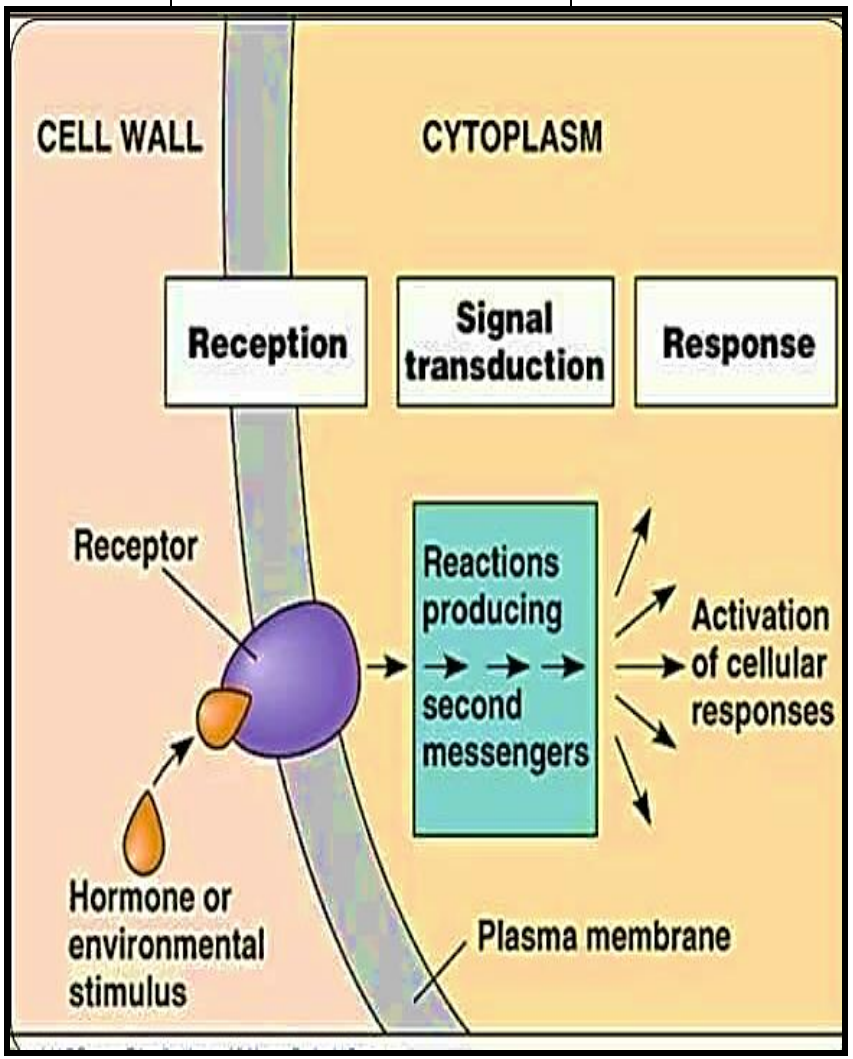
E.g. :Insulin, glucagon, epinephrine (adrenaline),
LH, FSH, Histamine, Ach

- **Steroid (lipid) hormones:**

E.g. Estrogen, Testosterone , Aldosterone, Calcitrol, cortisone

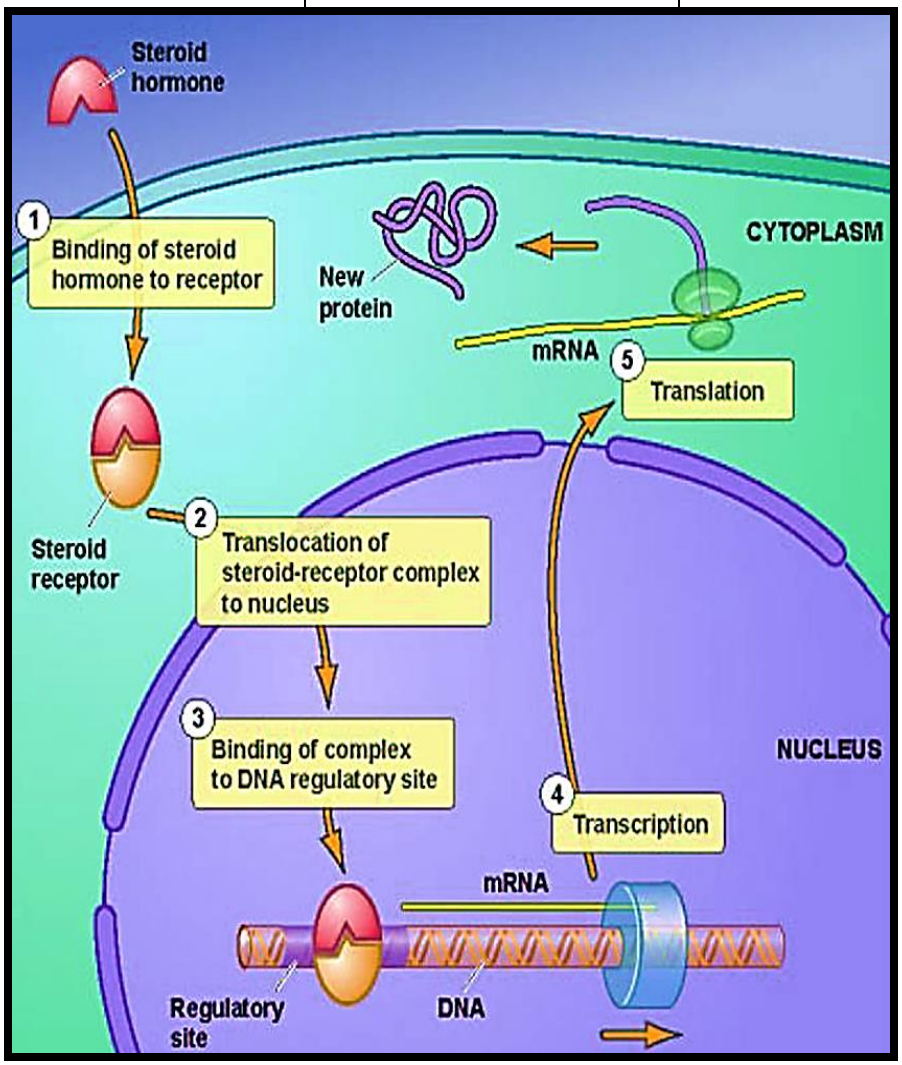
the message carried by the signaling molecule will translated either as alteration in protein function
or alteration in protein synthesis } of the cell

Hydrophilic ligand



protein based hormones are water soluble

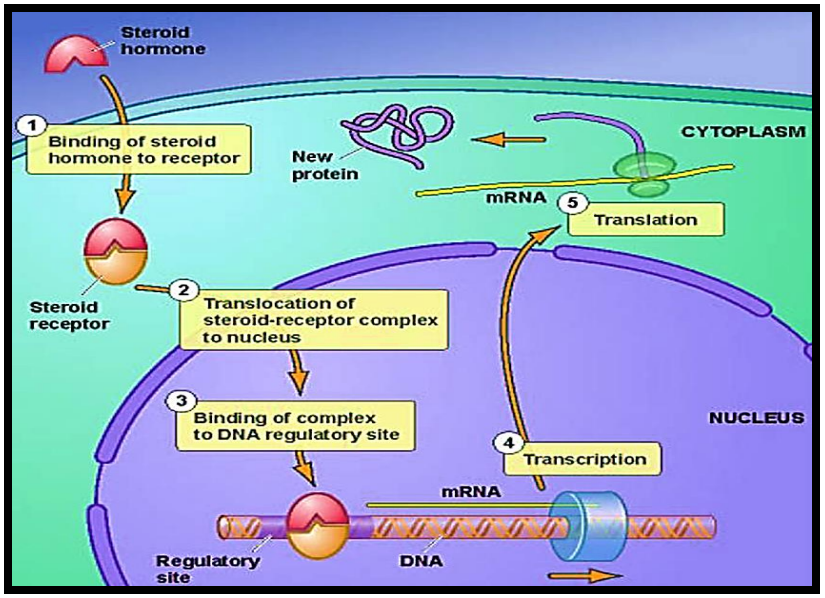
Lipophilic ligand



lipid based hormones are lipid soluble

Intracellular Receptors

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

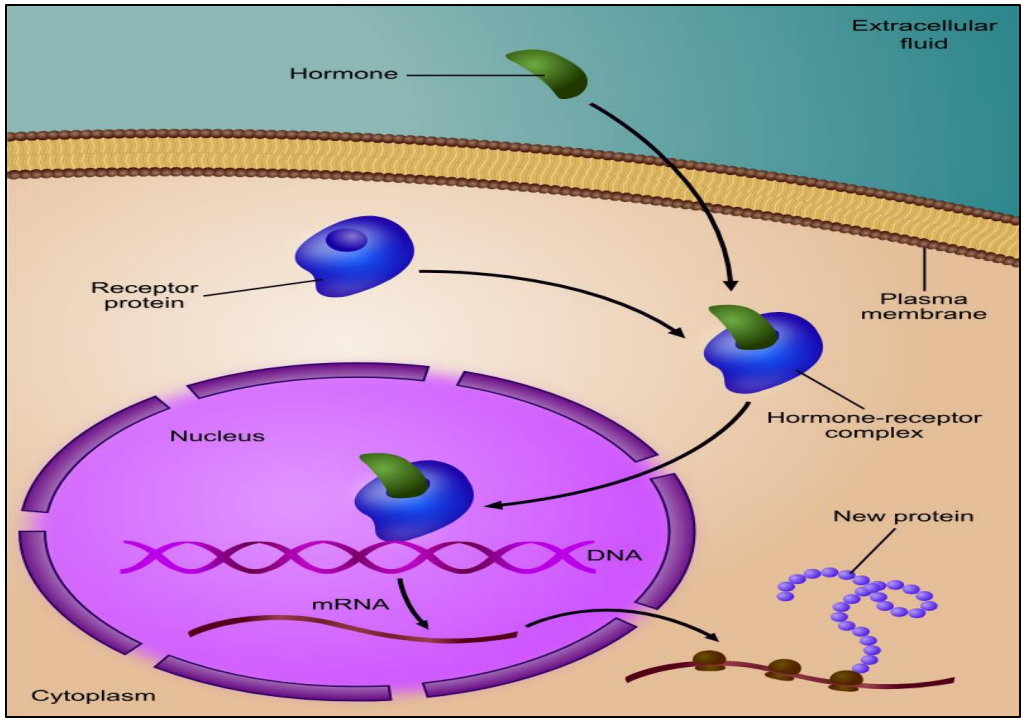


- The Ligands (small, hydrophobic) can easily cross the lipid bilayer membrane and activate these receptors ,e.g. steroid and thyroid hormones are hydrophobic ligands

- The ligand –receptor complex moves to the nucleus → binds to specific regulatory regions of the chromosomal DNA → promote the transcription of m-RNA (mediate gene expression)

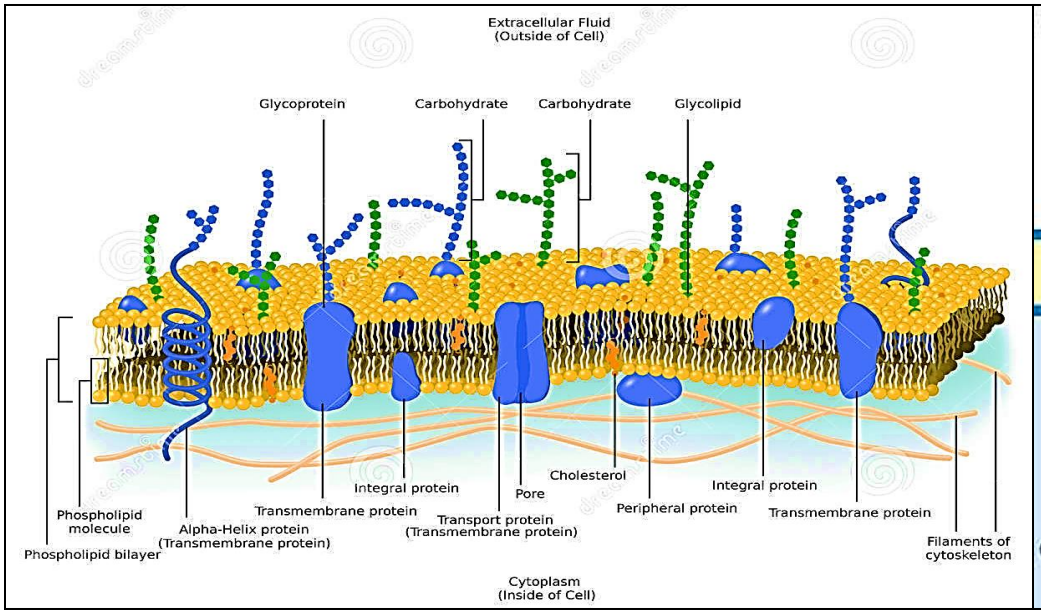
- Gene expression

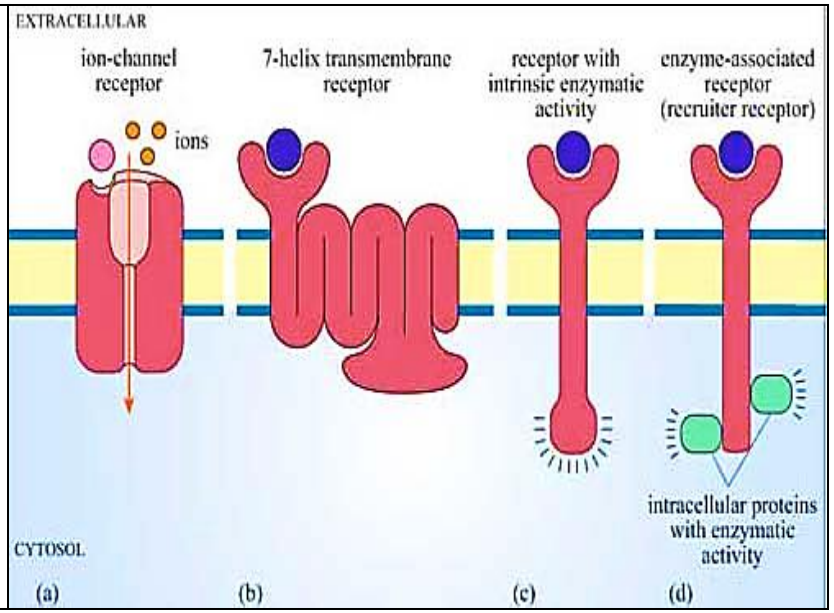
Transforming the information on cell's DNA (encoded in a gene) into a sequence of amino acids that ultimately forms a protein or RNA allowing the cell to respond & perform specialized roles



Receptors on the cell membrane

Extracellular receptors

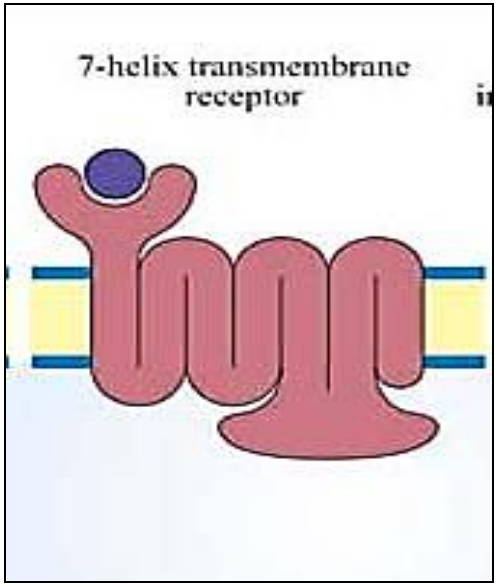




They are integral proteins embedded in The lipid bilayer of the cell membrane they detect signals from the external environment & transmit them into the cell to elicit a response

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



1

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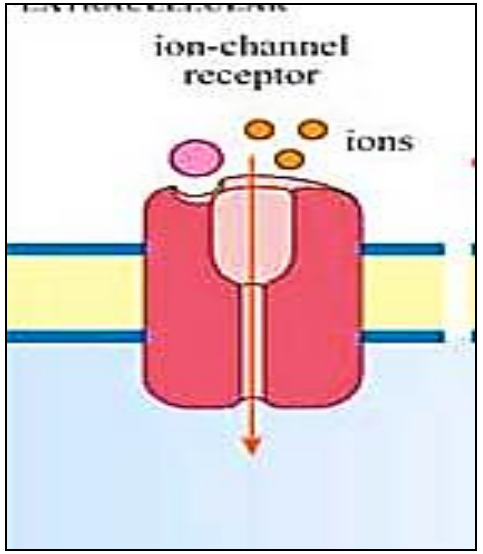

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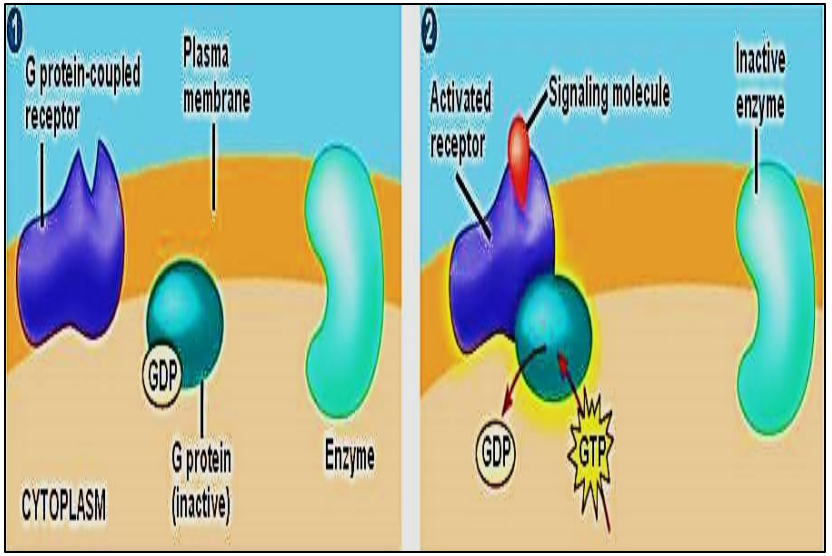
1- G- protein coupled receptors(GPCR)

Step 1:

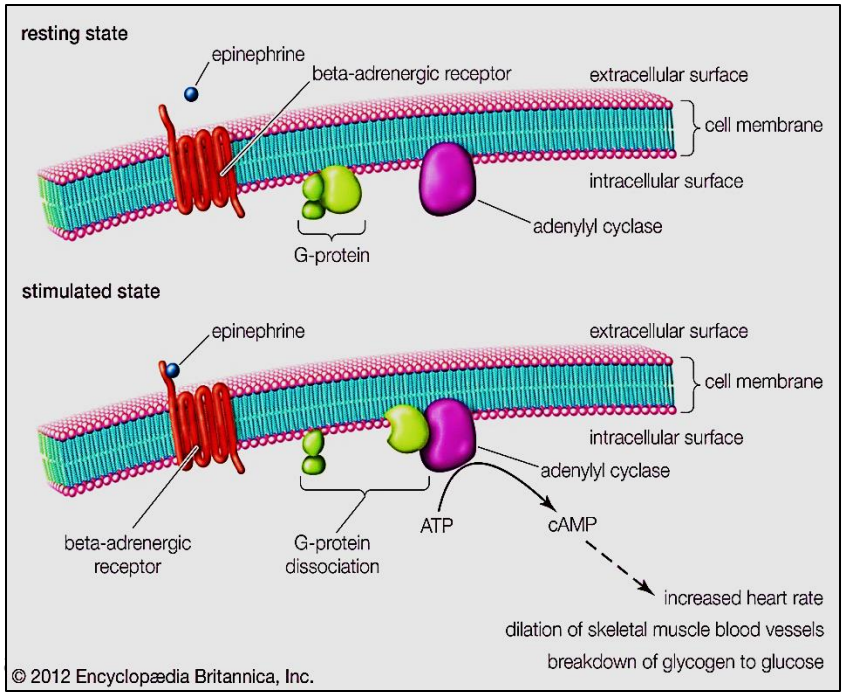
Receptors + ligand → changes the shape of the receptor → activate a membrane protein called G- protein

(G-protein is formed of 3 subunits)



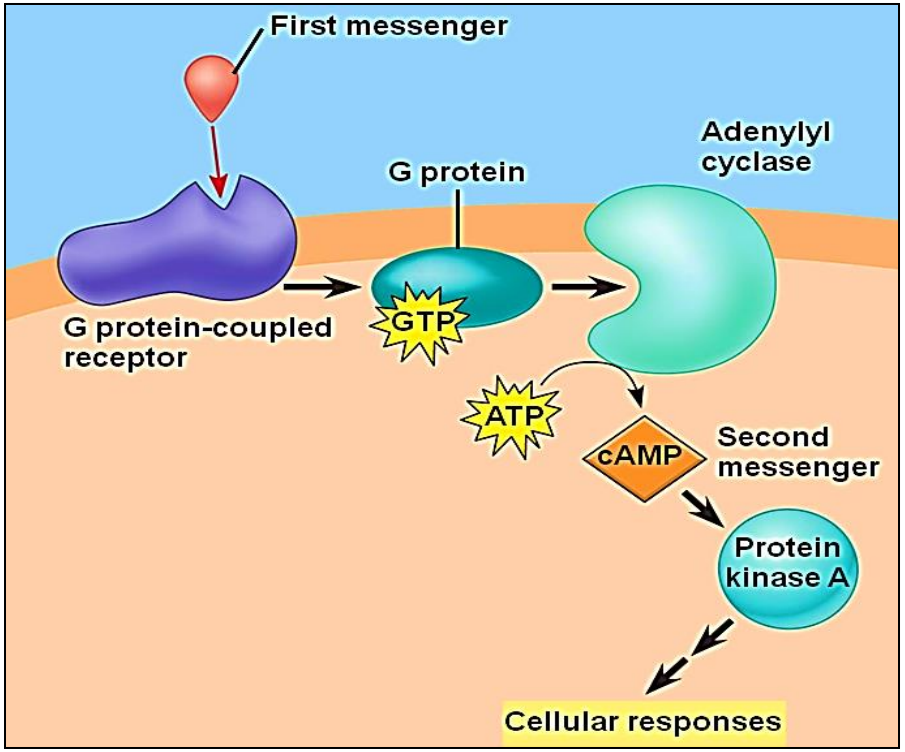
Step 2:

Activation of the G- protein → release GDP that attach to the G protein → **switch ON** → **G protein is active**



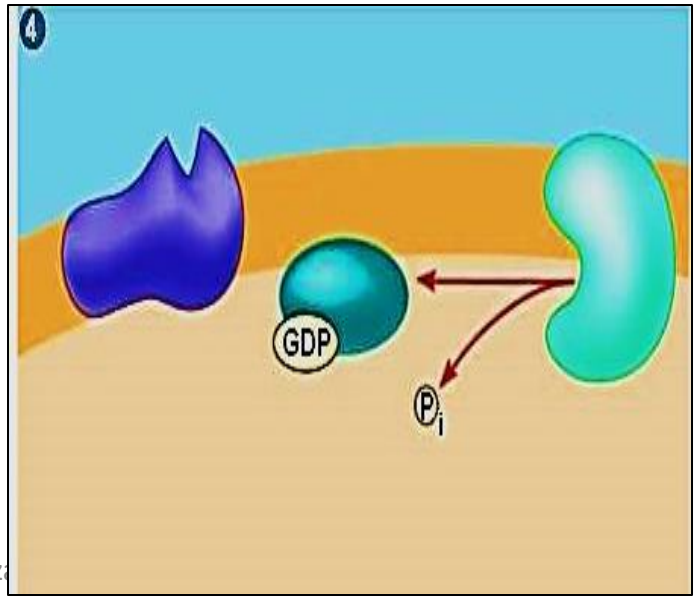
Step 3:

The activated G protein moves to catalyze the Adenylyl cyclase enzyme. The activated enzyme will change ATP→ cAMP → which 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

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

3. Play significant role in controlling vision, smell & taste, hearing sensations (sensory receptors)

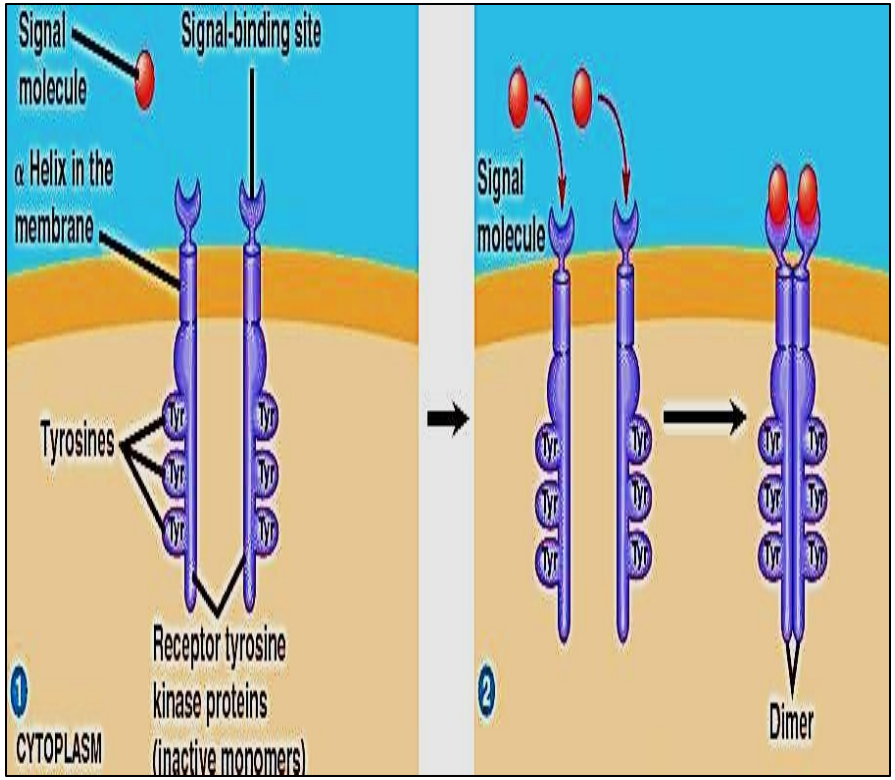
4. 45% of all Pharmaceutical & therapeutics targets & interact e G protein system.(asthma, hypertension, depression)

5. 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 (tyrosine kinase) while the extracellular domain binds to specific ligand**
- **start out as inactive monomers.**
- **The signal molecules are often growth factors**



Step 2: Dimerization (pairing of 2 receptor molecules

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

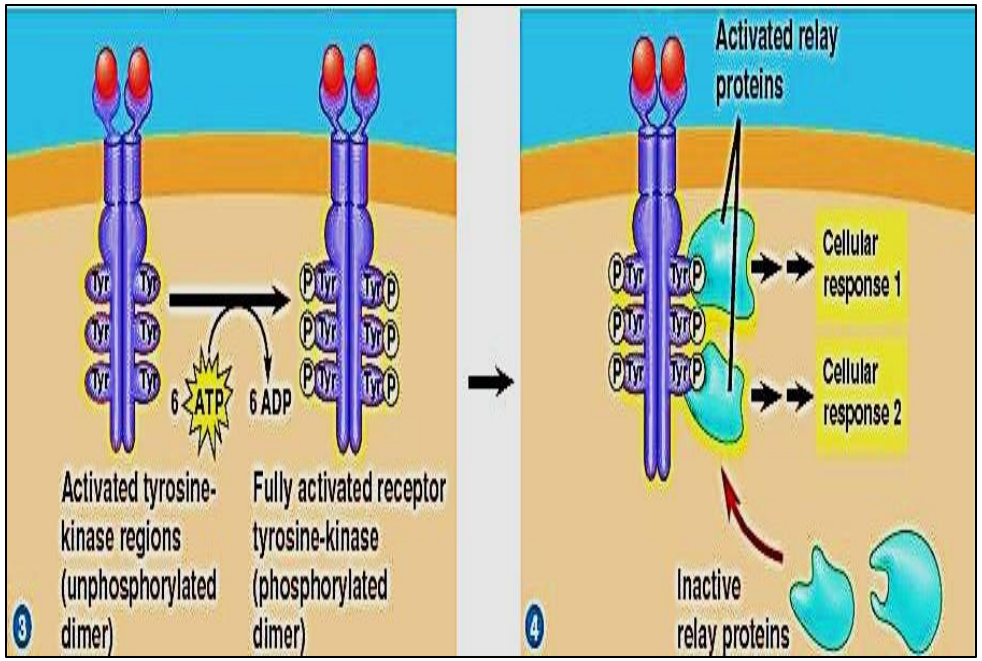
Step 3:

- **Dimerization** activates →

  Auto phosphorylation process

(it takes multiple ATPs {6})

- **Fully phosphorylation** → fully active receptors



Step 4:

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

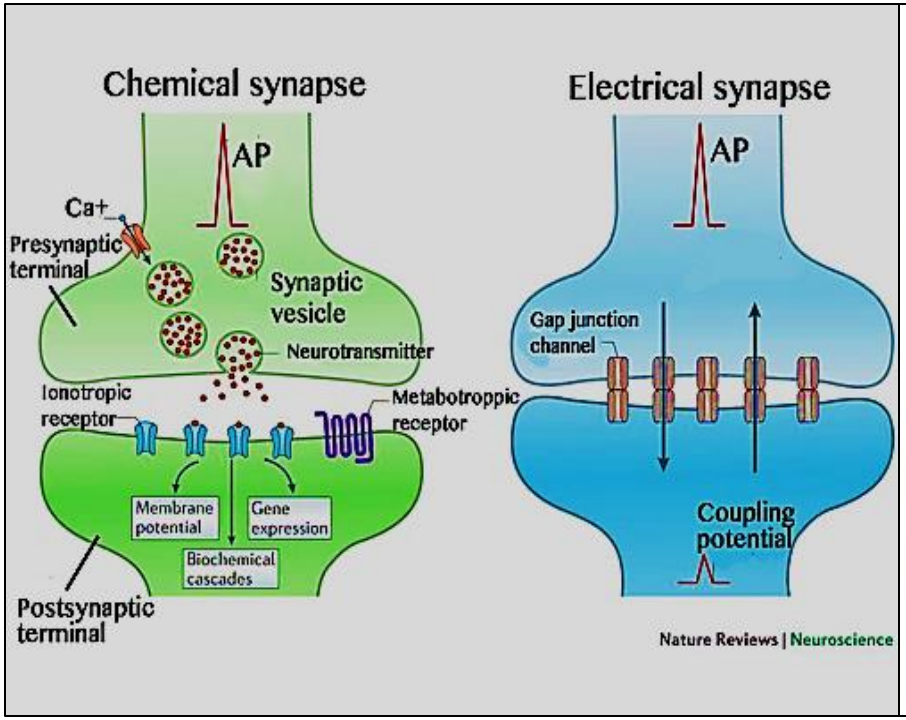
Importance of Tyrosine kinase receptor system

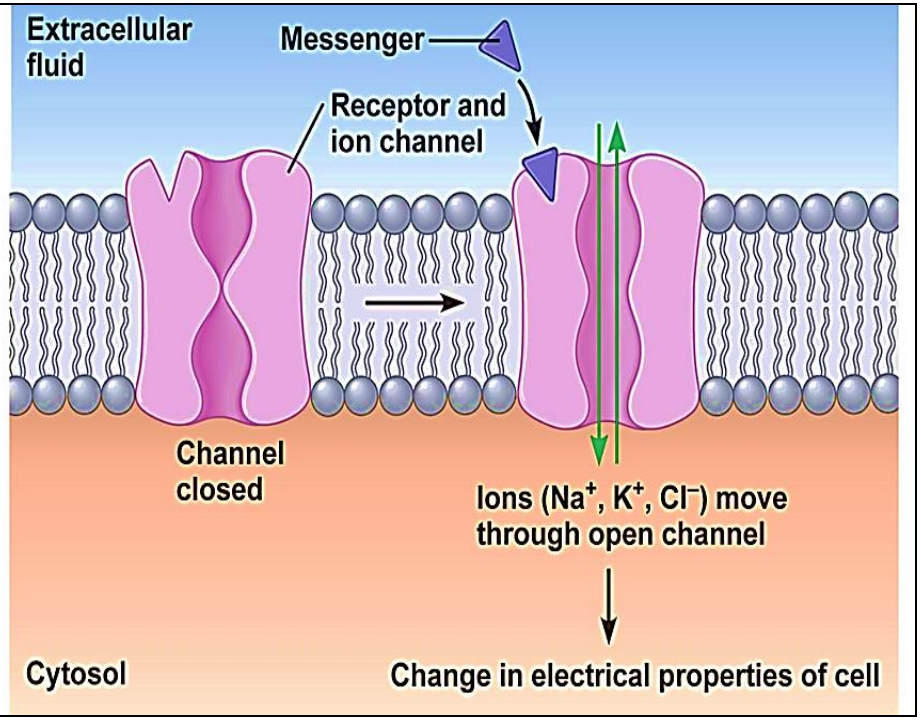
- One receptor tyrosine kinase (DIMER) can activate more different responses, providing a way for cells to regulate wide range of activities e.g. growth & proliferation

- Kinase: is the enzyme that catalyze the transfer of phosphate group → phosphorylation of the Dimer cause ON or OFF
- Insulin receptors regulate insulin uptake & metabolism (dysfunction → Diabetes)
- Many cancers are caused by mutated (dysregulated) tyrosine receptors which can get activated **without a signal molecule (cells growing out of control)**

3- Ion channel receptors

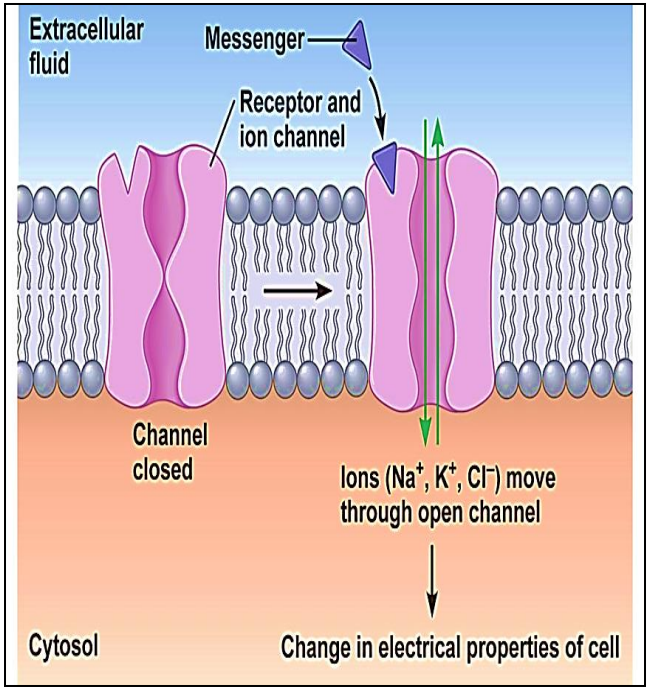
- Are the simplest form of receptors
- Also known as ligand-gated ion channels
- Receptors facilitae flow/ diffusion of ions across the cell membrane in response to specific ligands
- Essential in rapid signal transduction especially in nervous system
- located on post synaptic membrane in nervous system





Importance of ion channel receptors

- Important in the nervous system & muscle contraction
- Neurotransmitters function as ligands which bind to receptors on target cell
- The binding cause changes that lead to open or close of these ion channel



- Once open→ ions move into the target cells passively following their electrochemical gradient
- Change in ion concentration → changes in membrane potential and initiate cellular response

II. Signal transduction

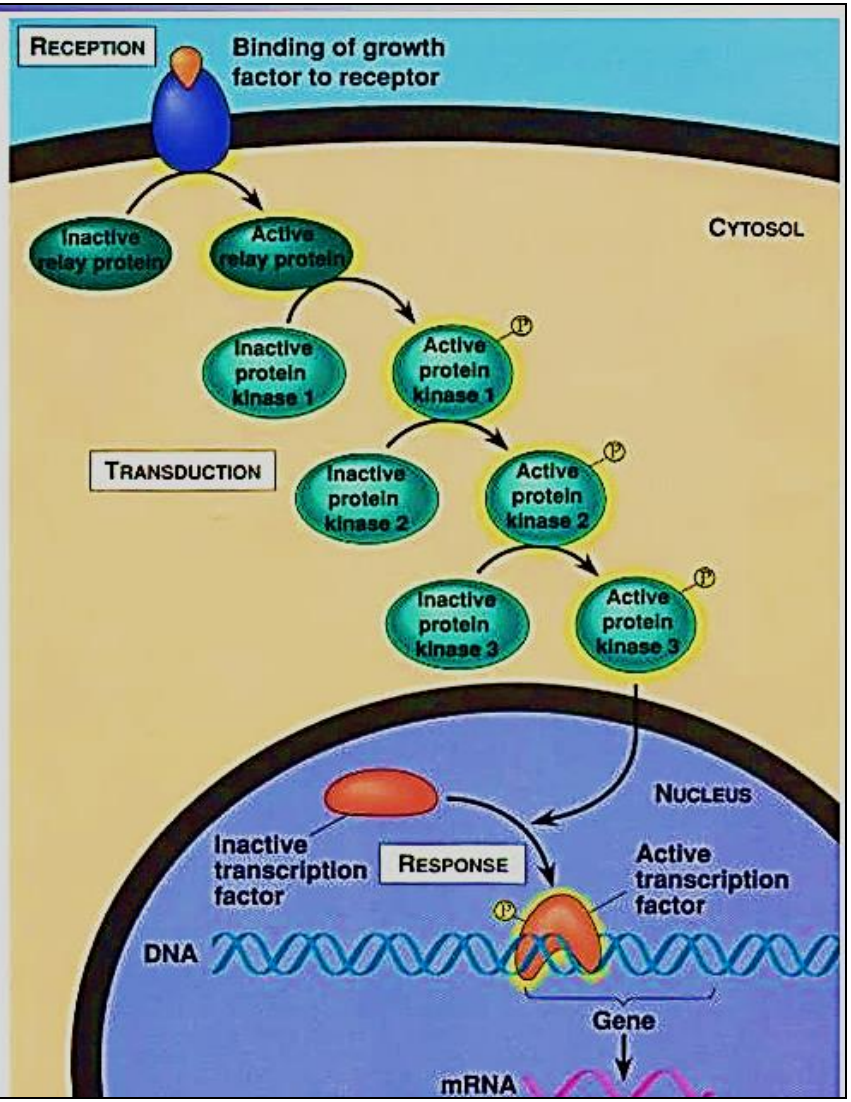
- Is the step between receiving of a signal & response of the cell to that signal
- is a biochemical chain of events occur inside the cell

Transduction

Signal reception

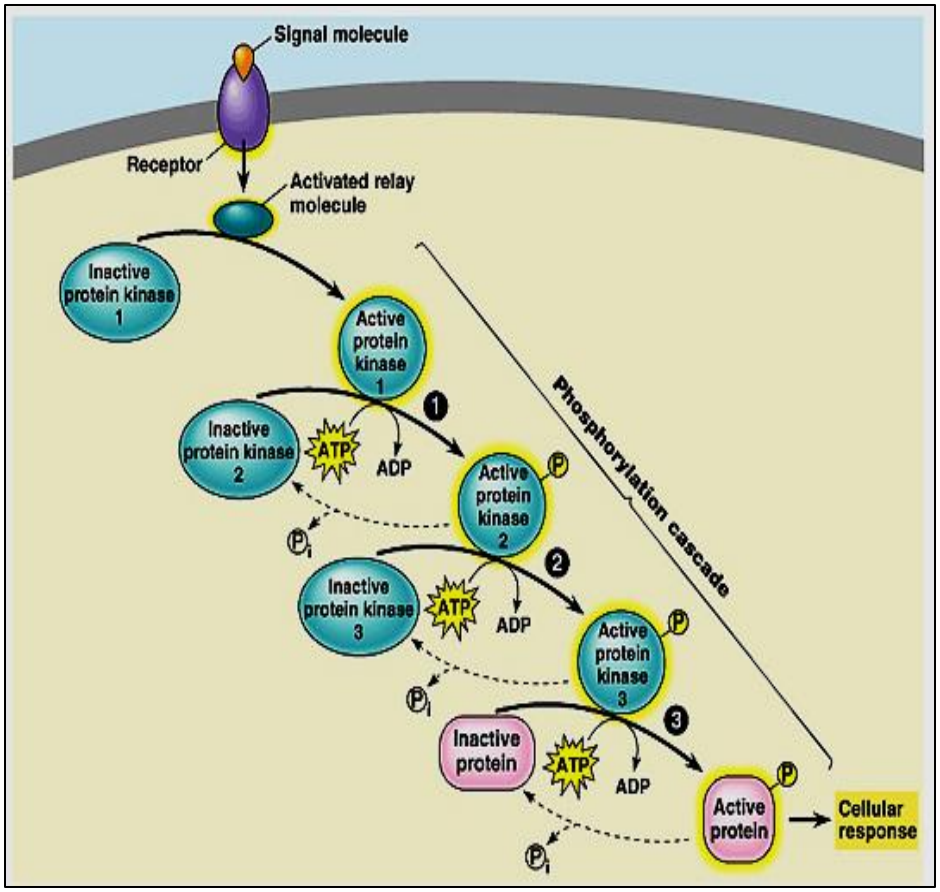
Cell response

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



Role of **protein kinases**

- They are protein molecules found in the cytoplasm
- Act as catalysts (enzymes)
- 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 intracellular 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)
5. Nitric oxide (NO)

Does intracellular receptors need 2nd messenger ?

Generally **they don't need 2nd mes**sengers cuz:

1- Direct action: these receptors bind directly to the lipophilic ligands

2- Gene regulation: the intracellular receptors / ligand complex usually act as transcription factors. They regulate gene expression by binding to specific DNA sequence leading to production of proteins without 2nd messenger

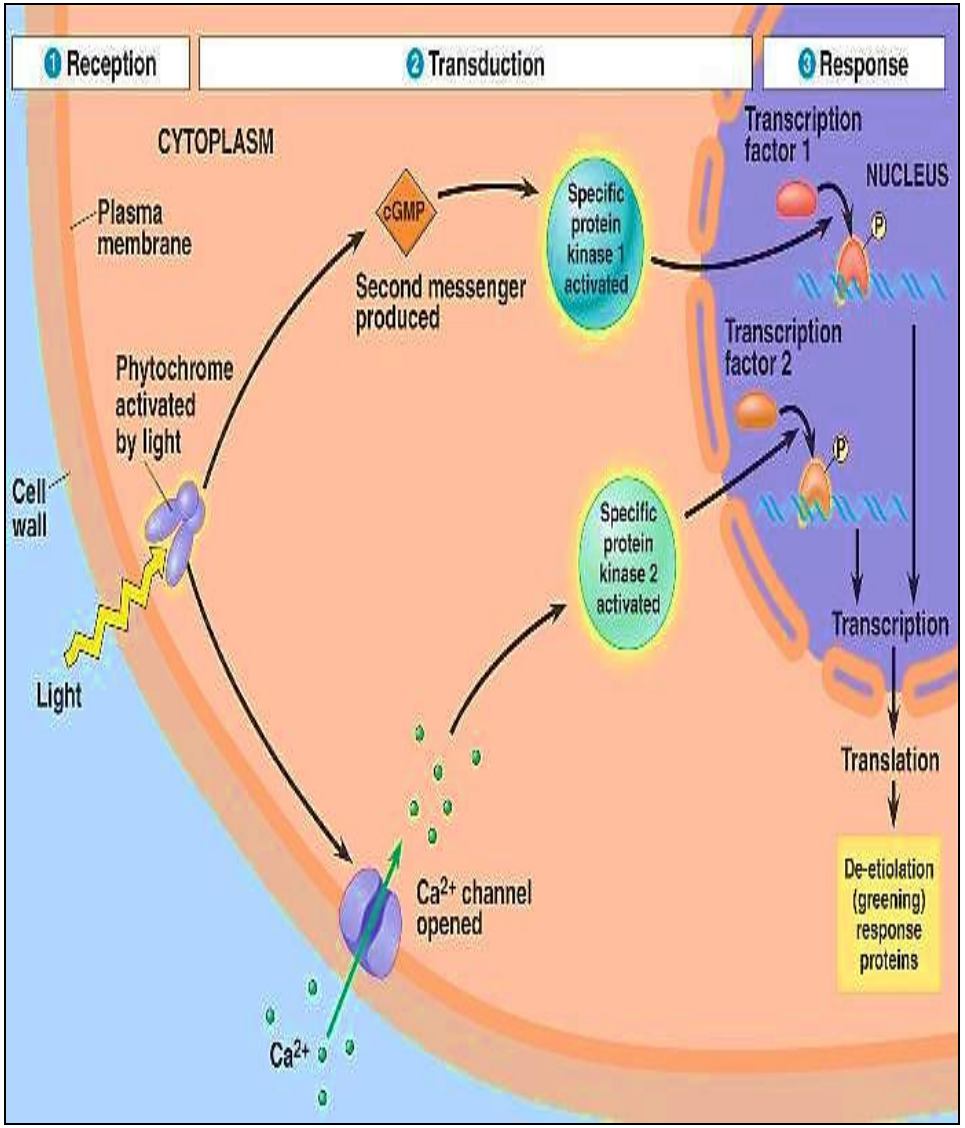
III. Responses

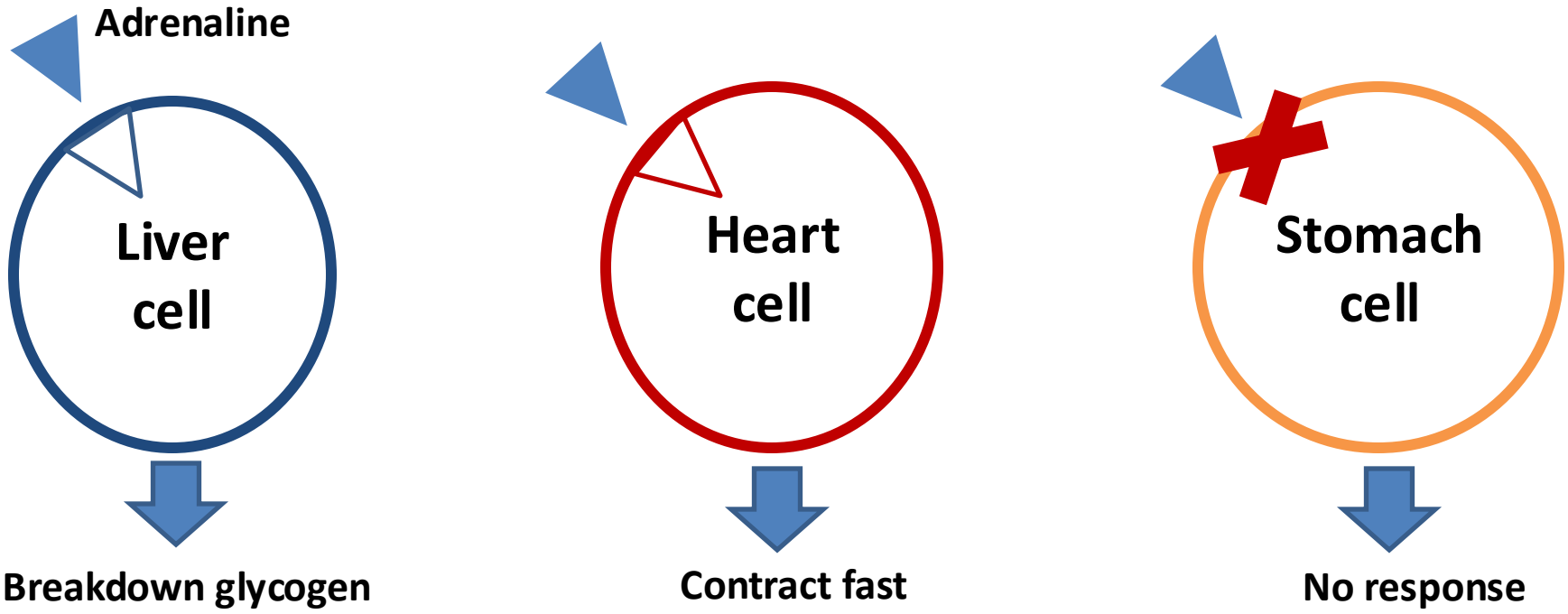
Cells respond to signaling pathways by many ways:

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)

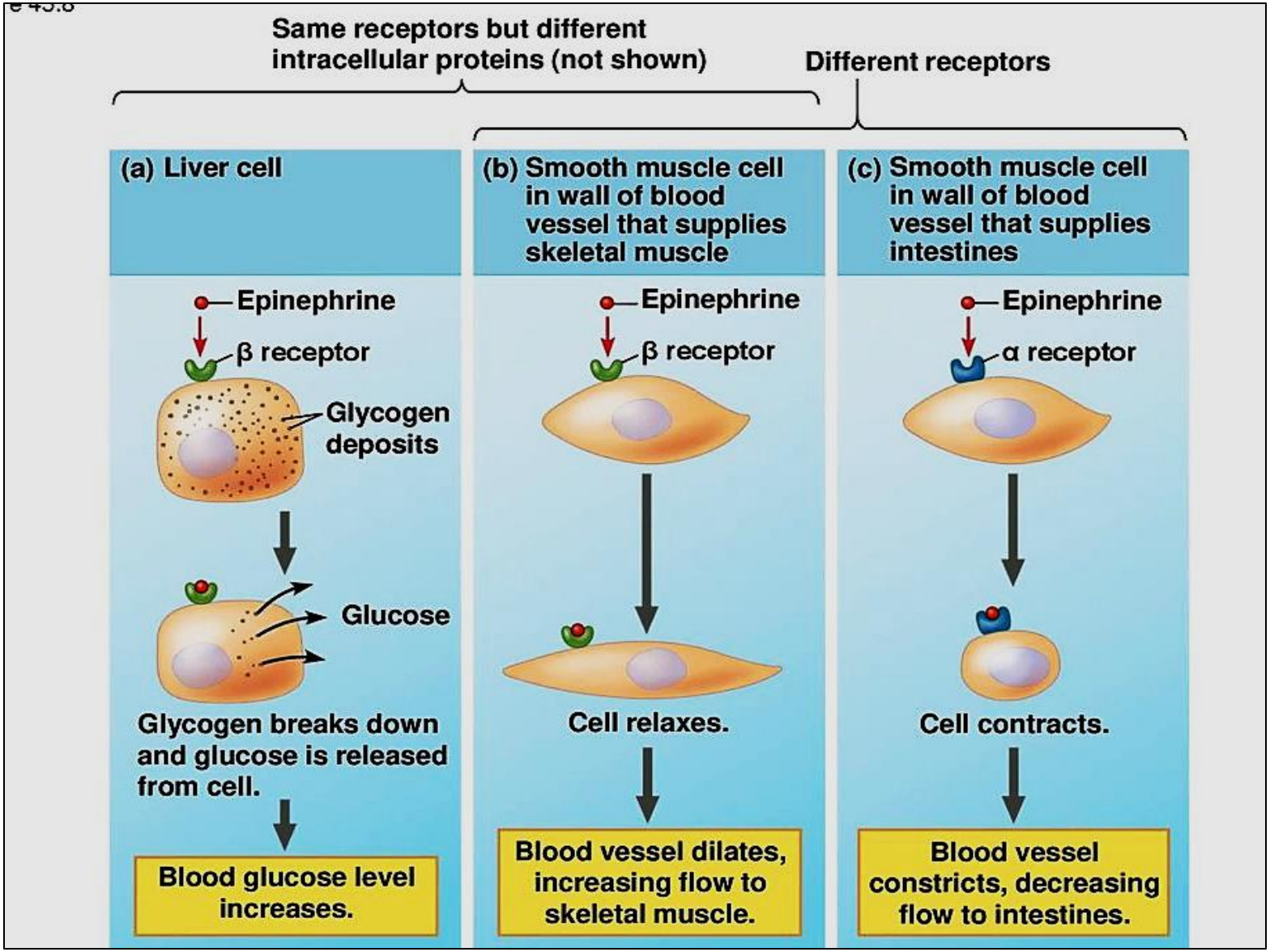
Certain signals ,receptors, or cellular responses are specific to particular type of cells this may be due to receptor specificity, signal transduction pathway specificity , or gene expression specificity

The action of adrenaline according to the type of cells

Adrenaline binds to adrenergic receptors which belong to the G-protein –coupled receptors (GPCR) family

1- There are multiple sub-types of adrenergic receptors e.g. $\alpha_{1,\ 2}$ & $\beta_{1,\ 2,\ 3}$ each receptor subtype activates specific signaling pathway

2- Receptor distribution in tissue e.g., heart cells express mainly β_1 , liver cells express β_2


Same receptors but different intracellular proteins (not shown)
Different receptors
(a) Liver cell
(b) Smooth muscle cell in wall of blood vessel that supplies skeletal muscle
(c) Smooth muscle cell in wall of blood vessel that supplies intestines
Epinephrine
β receptor
Glycogen deposits
Glucose
Glycogen breaks down and glucose is released from cell.
Blood glucose level increases.
Epinephrine
β receptor
Cell relaxes.
Blood vessel dilates, increasing flow to skeletal muscle.
Epinephrine
α receptor
Cell contracts.
Blood vessel constricts, decreasing flow to intestines.

Thank you