

Cell Signalling

PHYA-Sem-II-CC3

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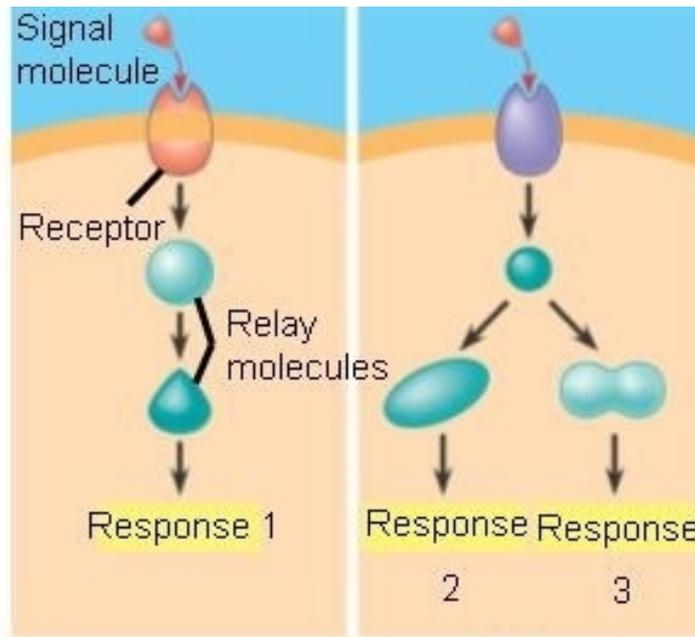
PHYA-Sem-II-Cell Signalling Syllabus (CU)

- CC3TH.

- Cell Surface receptor proteins ----
 1. Ion channel coupled
 2. G-protein coupled
 3. Enzyme coupled
- Intracellular messengers -----
 1. cAMP, cGMP
 2. IP3
 3. DAG
 4. Protein kinases
 5. Ca²⁺
 6. CO and NO
- Signal transduction pathways -----
 1. Phosphatidylinositides
 2. MAP kinase
 3. JAK-STAT
 4. SMAD

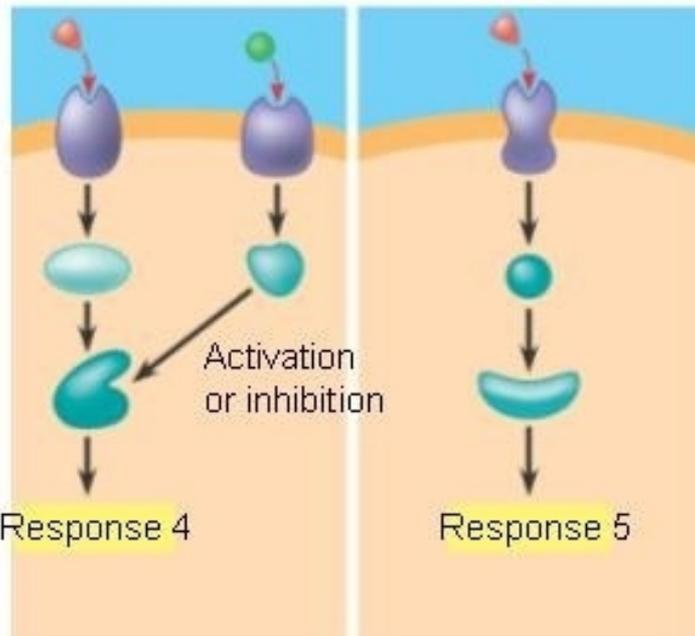
CELL SIGNALING

- How do cells receive and respond to signals from their surroundings.
- Prokaryotes and unicellular eukaryotes are largely independent and autonomous.
- In multicellular organisms there is a variety of signaling molecules that are secreted or expressed on the cell surface of one cell and bind to receptors and expressed by other cells. These molecules integrate and coordinate the functions of the cells that make up the organism.



A. Pathway leads to single response

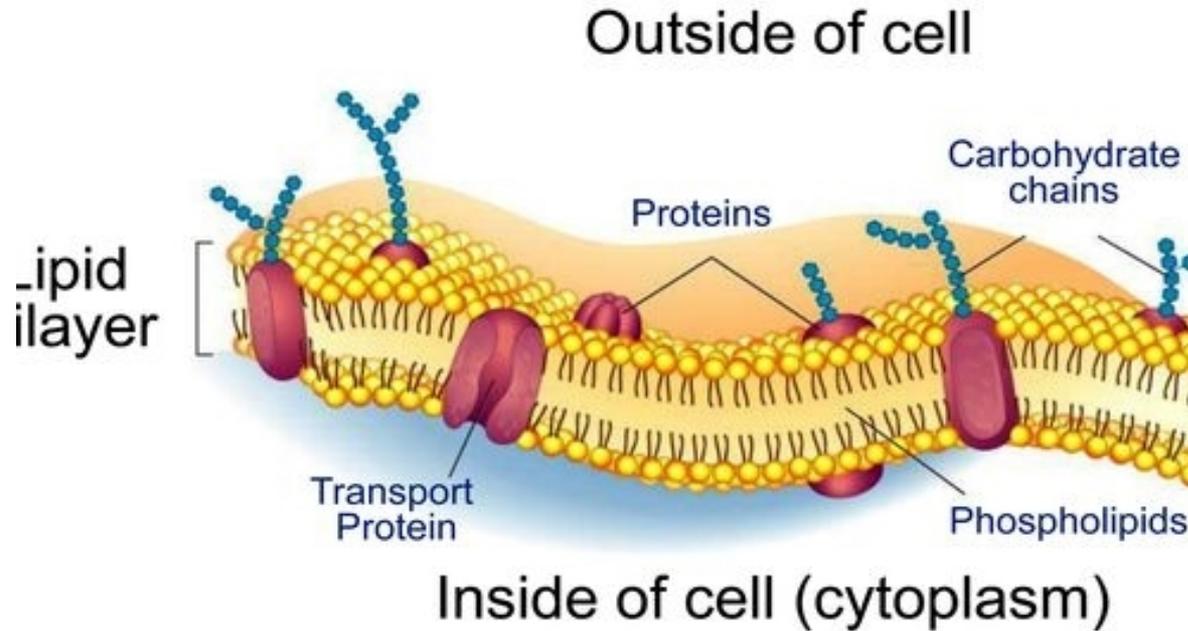
Cell B. Pathway branches leading to two responses



C. Cross-talk occurs between two pathways

Cell D. Different receptors lead to different responses

Structure of the Cell Membrane



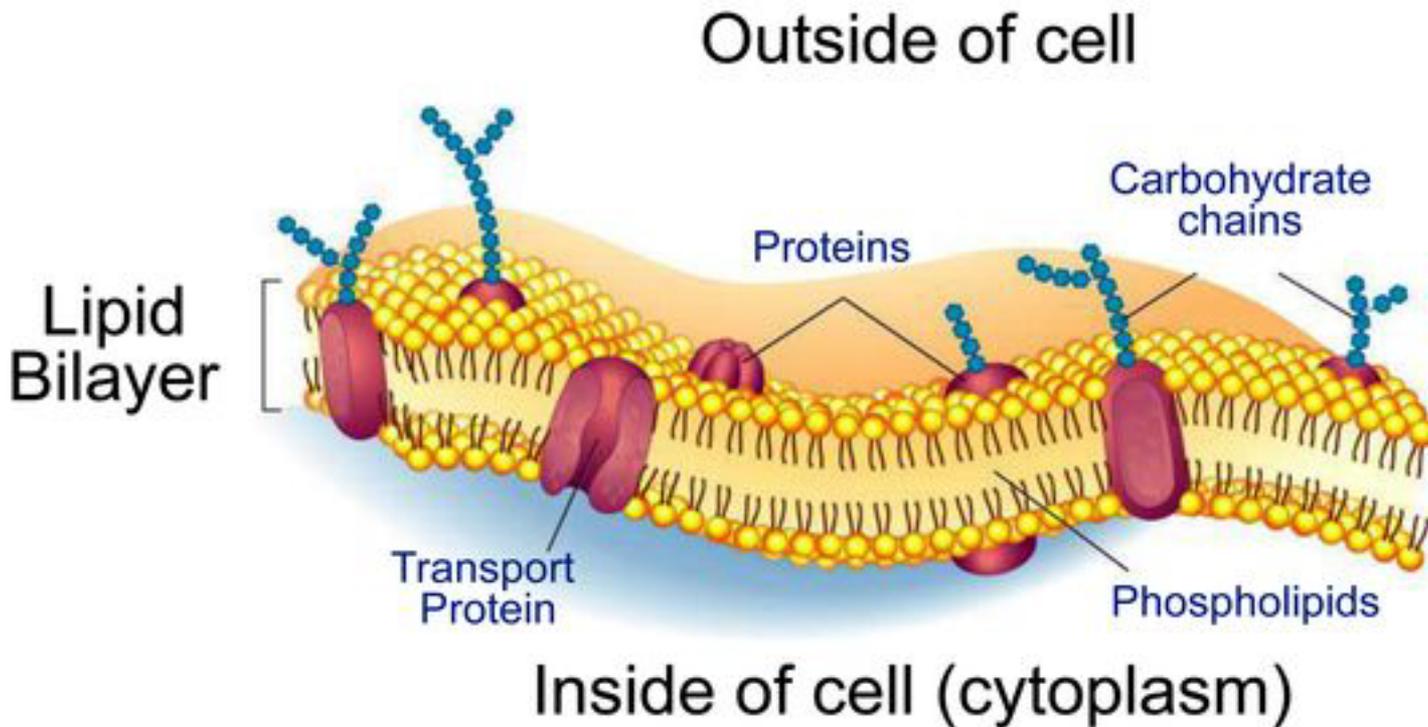
Signalling molecules: **Neurotransmitters**

They signal from neuron to neuron or from neuron to other target cell (ex. muscle cell).

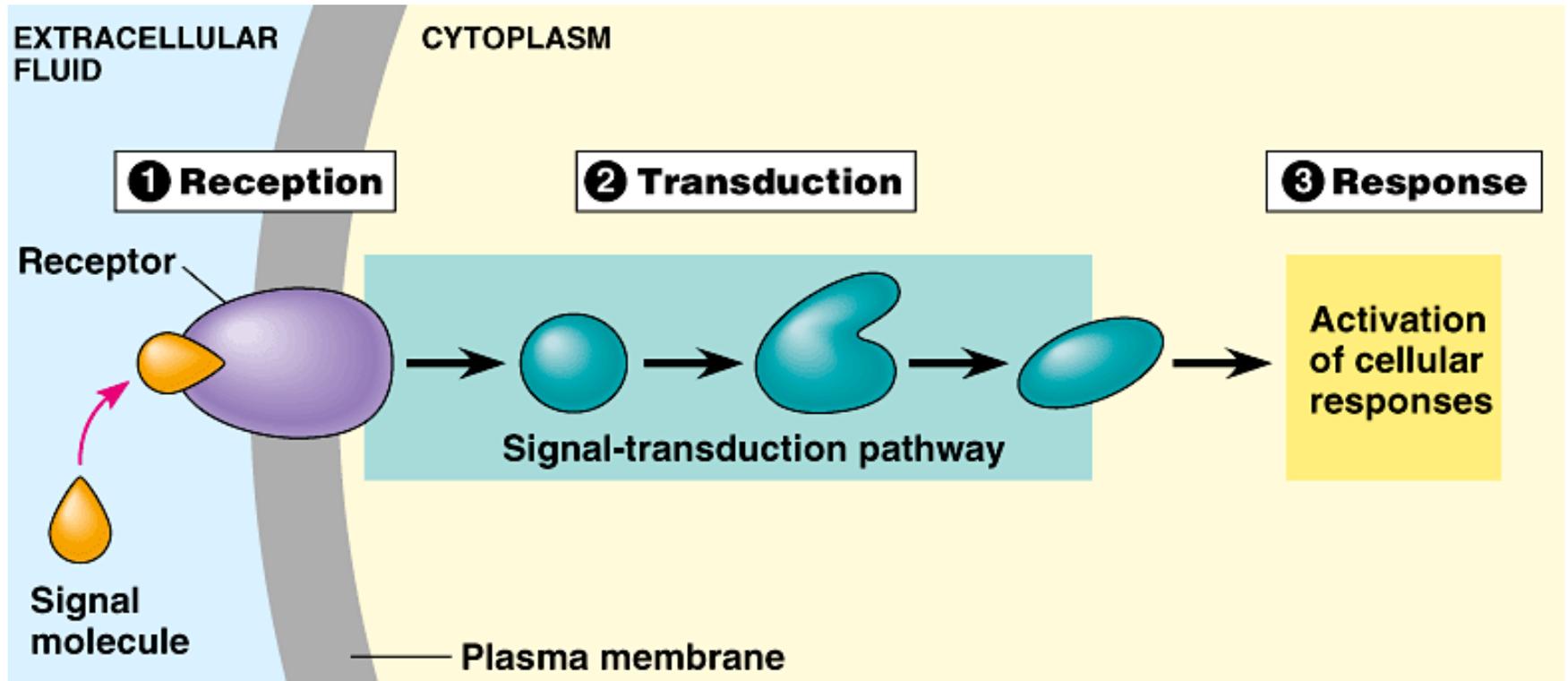
1. Acetylcholine
2. Glycine
3. Glutamate
4. Dopamine
5. Epinephrine
6. Serotonin
7. Histamine
8. GABA.

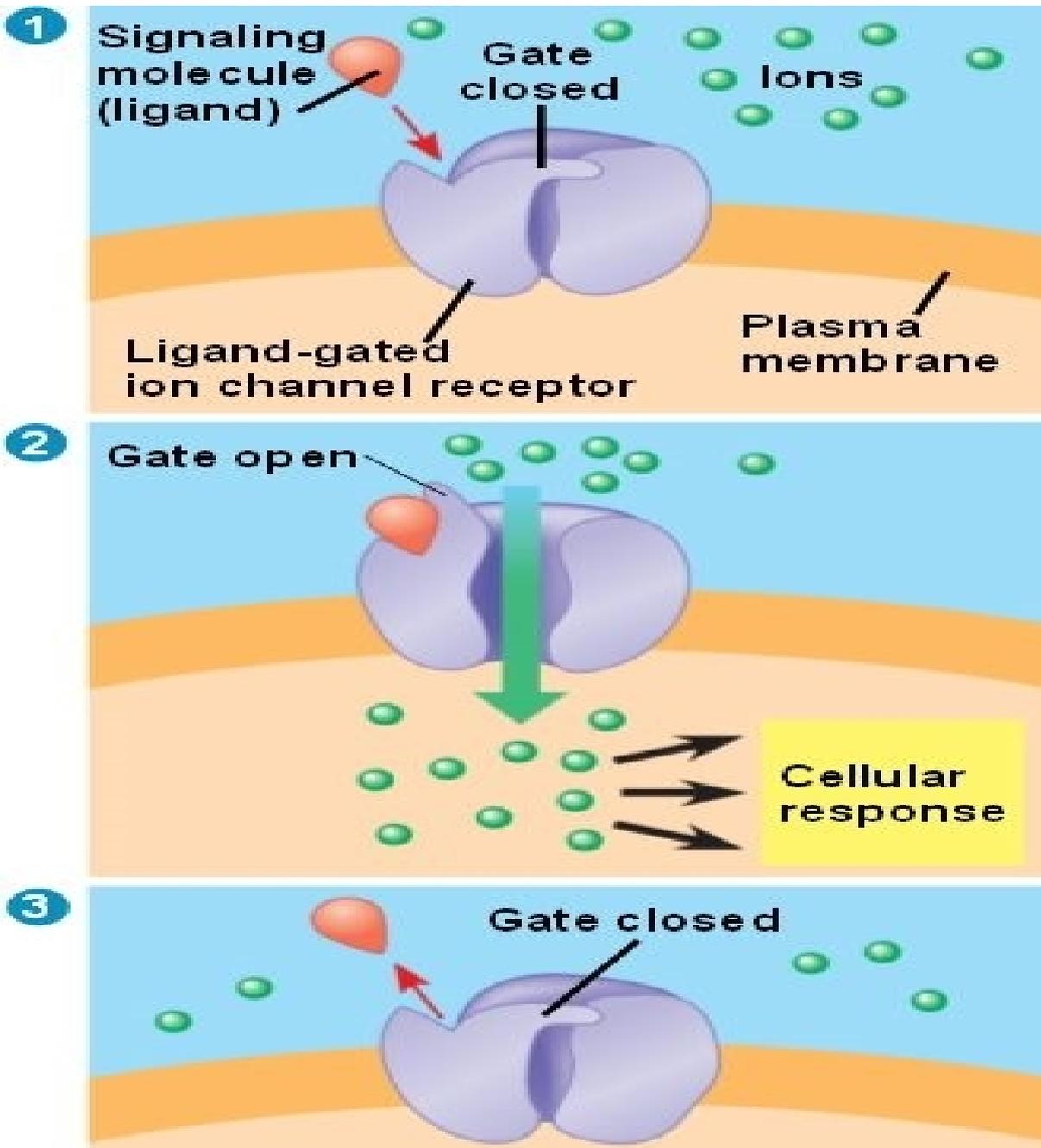
Common features: hydrophilic molecules that bind to cell surface receptors. The binding induces conformational changes that open ion channels → ion fluxes in the cell.

Structure of the Cell Membrane



Three Stages of Signal Transduction

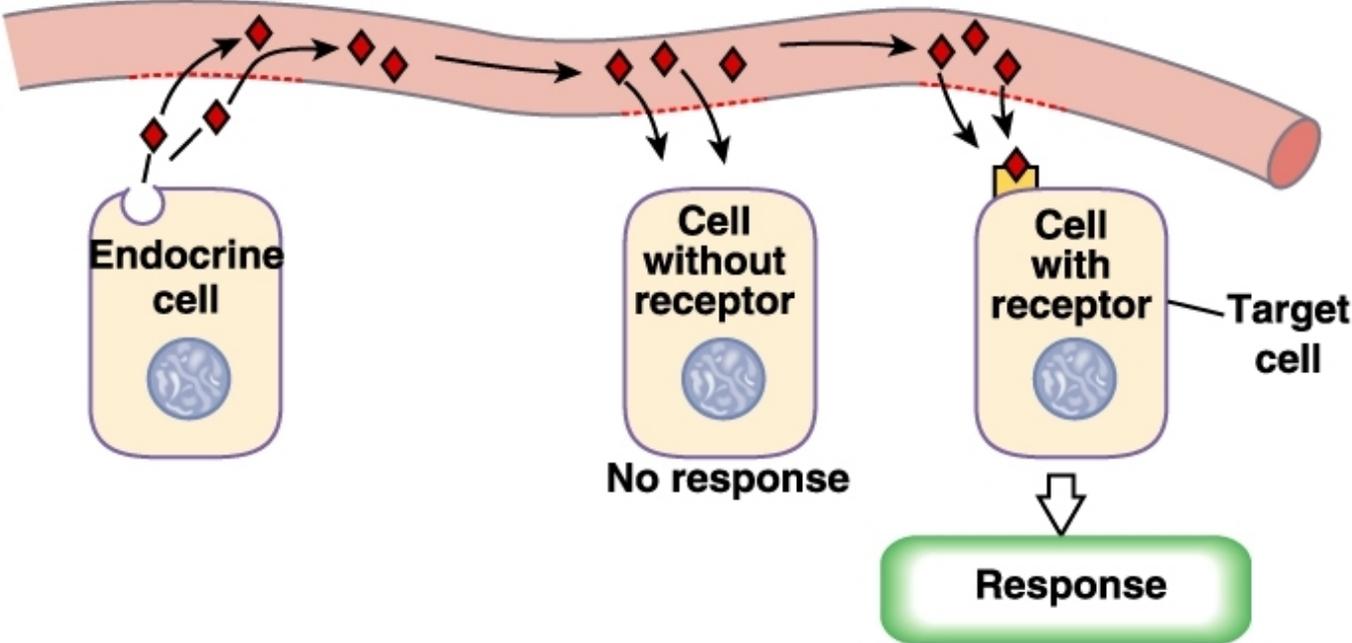




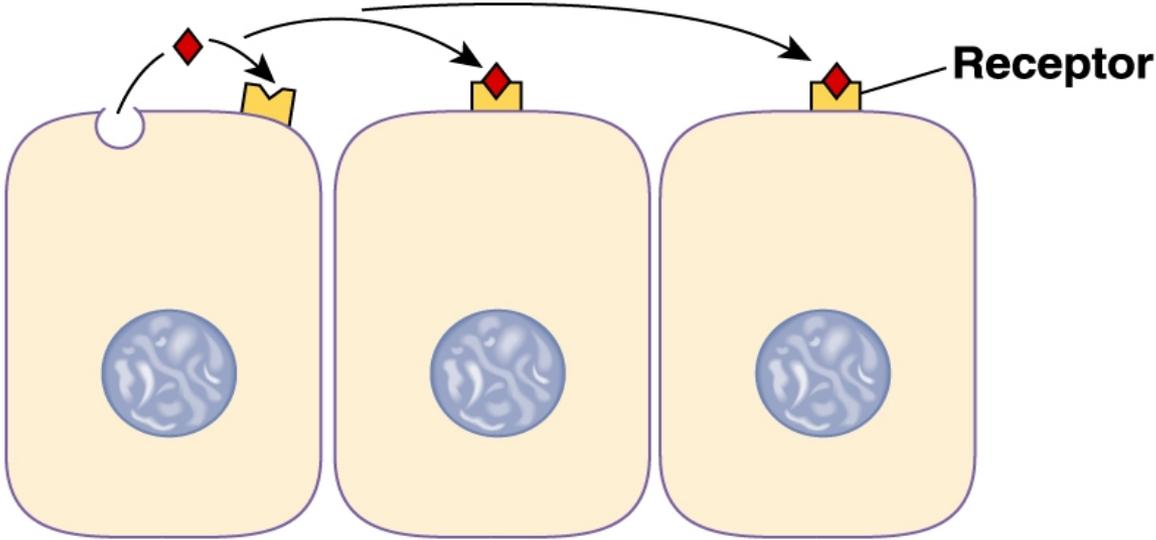
Modes of cell-cell signaling

1. Direct cell-cell or cell-matrix (integrins and cadherins)
2. Indirect: Secreted molecules.
 - A. **Endocrine** signaling. The signaling molecules are **hormones** secreted by endocrine cells and carried through the circulation system to act on target cells at distant body sites.
 - B. **Paracrine** signaling. The signaling molecules released by one cell act on neighboring target cells (**neurotransmitters**).
 - C. **Autocrine** signaling. Cells respond to signaling molecules that they themselves produce (response of the immune system to **foreign antigens, and cancer cells**).

Hormone



Autocrine and paracrine signals



Autocrine signaling

- cells respond to substances that they themselves release. Many growth factors act in this fashion, and cultured cells often secrete growth factors that stimulate their own growth and proliferation. This type of signaling is particularly common in tumor cells, many of which overproduce and release growth factors that stimulate inappropriate, unregulated proliferation of themselves as well as adjacent non-tumor cells; this process may lead to formation of tumor mass.

paracrine signaling

- In **paracrine signaling**, the signaling molecules released by a cell only affect target cells in close proximity to it. The conduction of an **electric impulse** from one nerve cell to another or from a nerve cell to a muscle cell (inducing or inhibiting muscle contraction) occurs via paracrine signaling.

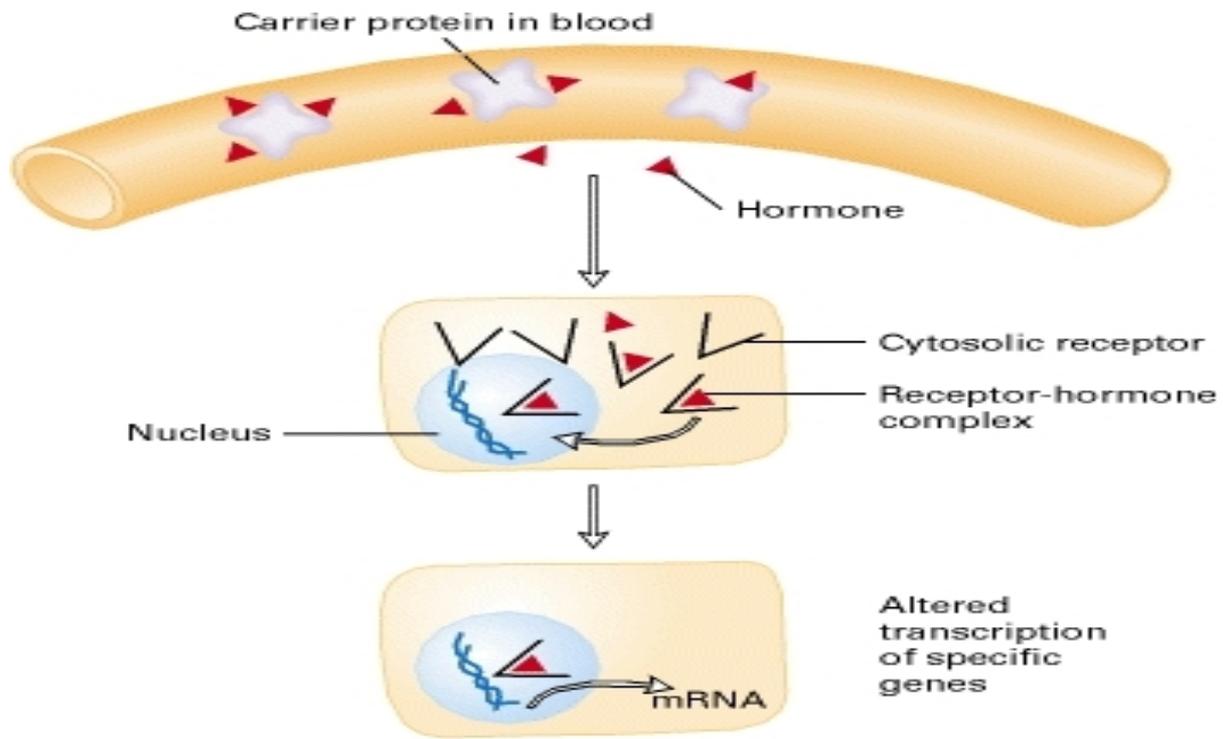
Four Stages of Signal Transduction

Signal transduction through membrane receptors usually requires four characters:

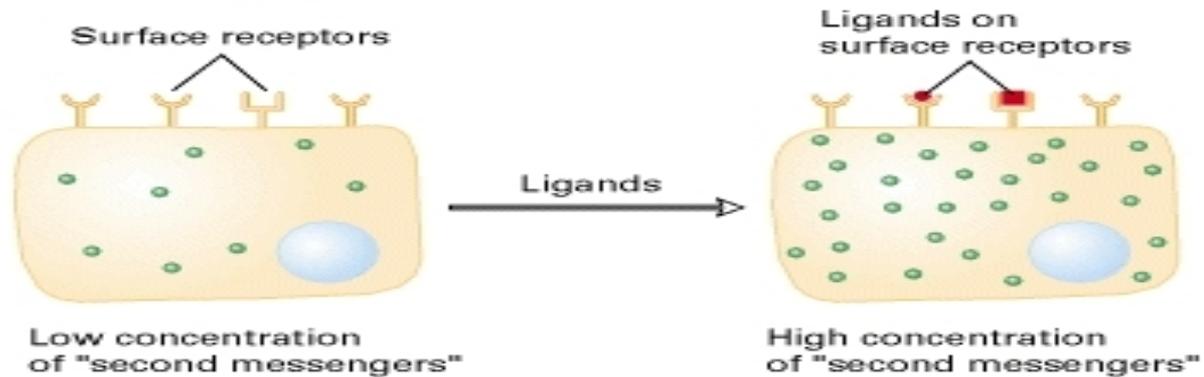
- ✓ **Extracellular signal molecule:** an extracellular signal molecule is produced by one cell and is capable of traveling to neighboring cells, or to cells that may be far away.
- ✓ **Receptor protein:** the cells in an organism must have cell surface receptor proteins that bind to the signal molecule and communicate its presence inward into the cell.

- ✓ **Intracellular signaling proteins:** these distribute the signal to the appropriate parts of the cell. The binding of the signal molecule to the receptor protein will activate intracellular signaling proteins that initiate a signaling cascade (a series of intracellular signaling molecules that act sequentially).
- ✓ **Target proteins:** the conformations or other properties of the target proteins are altered when a signaling pathway is active and changes the behavior of the cell.

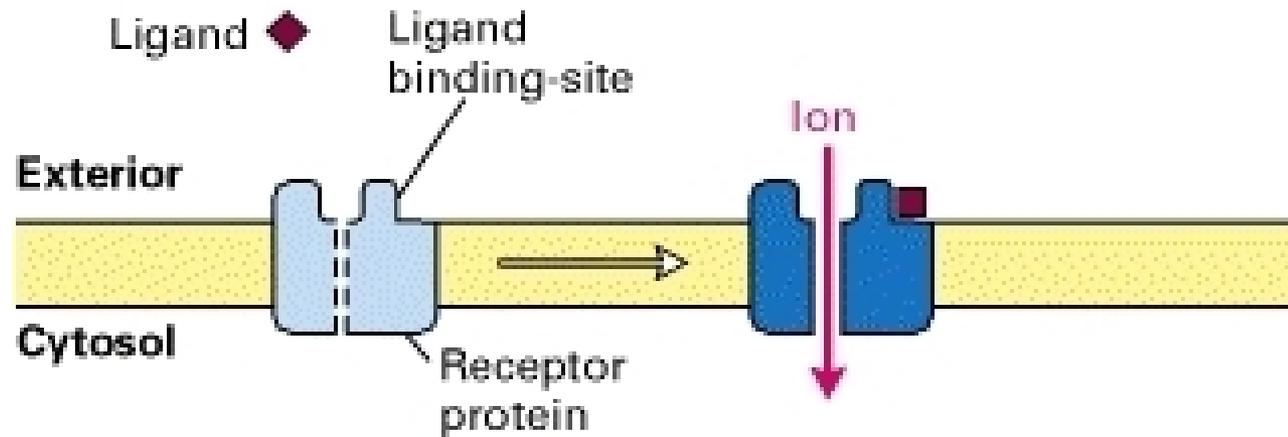
(a) Intracellular receptors



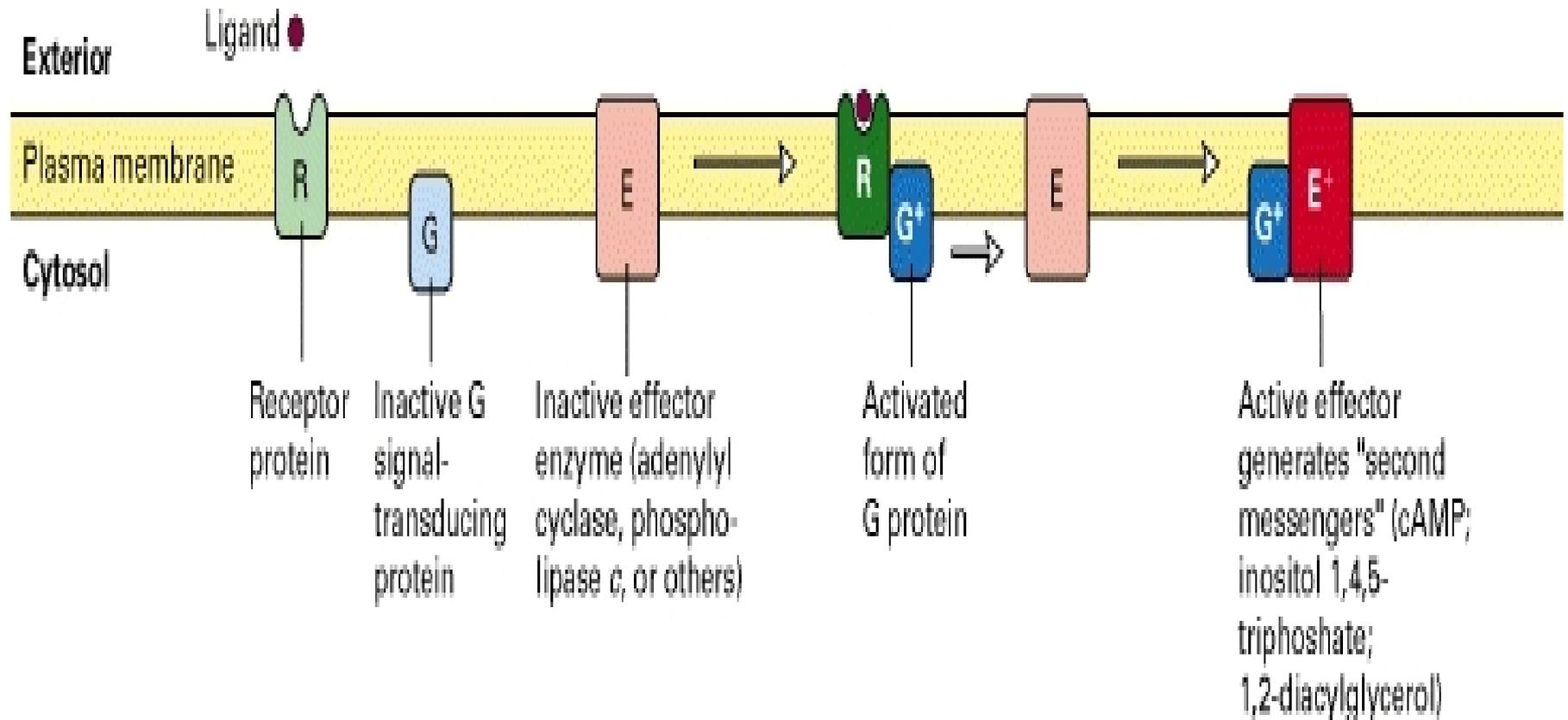
(b) Cell surface receptors



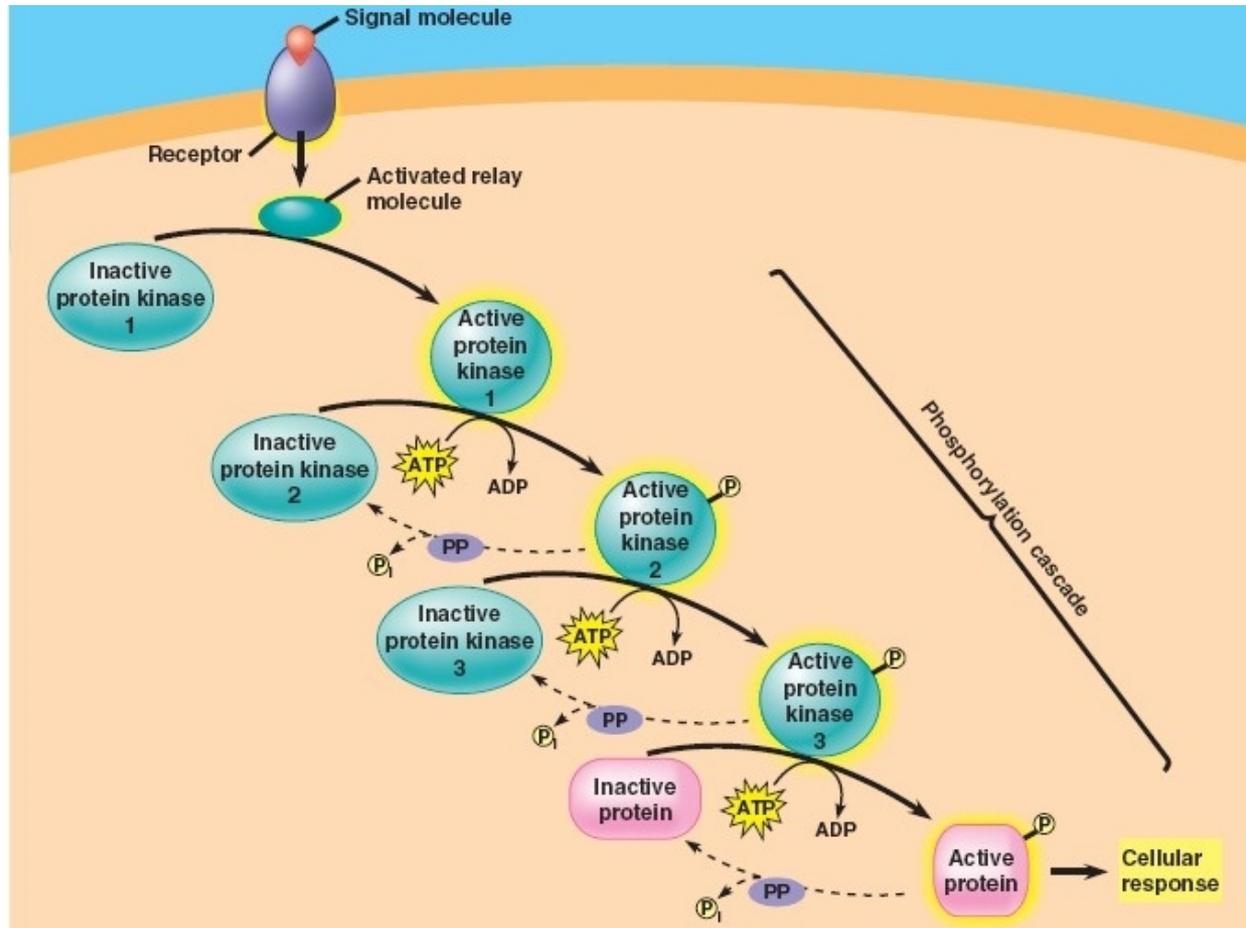
(b) **Ion-channel receptors (acetylcholine)**



(a) G protein-coupled receptors (epinephrine, glucagon, serotonin)

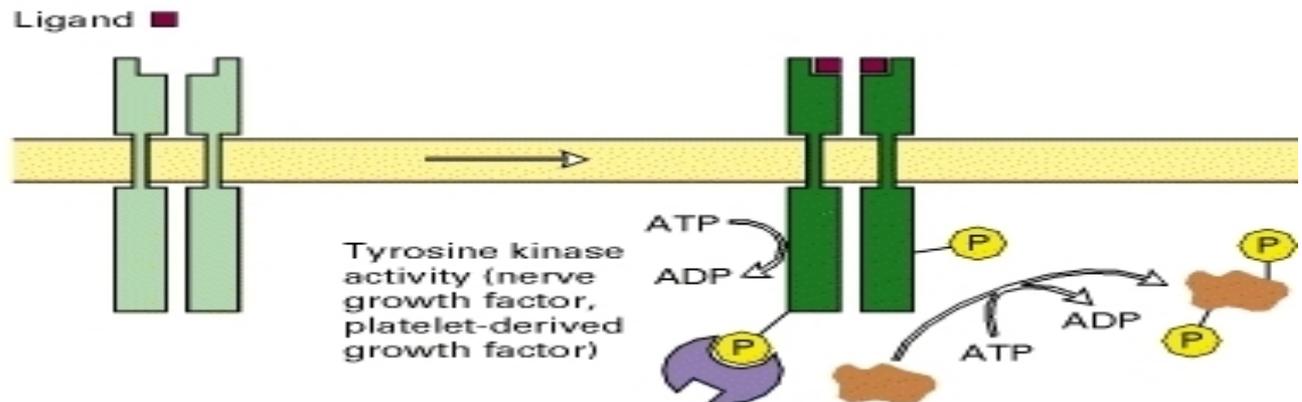
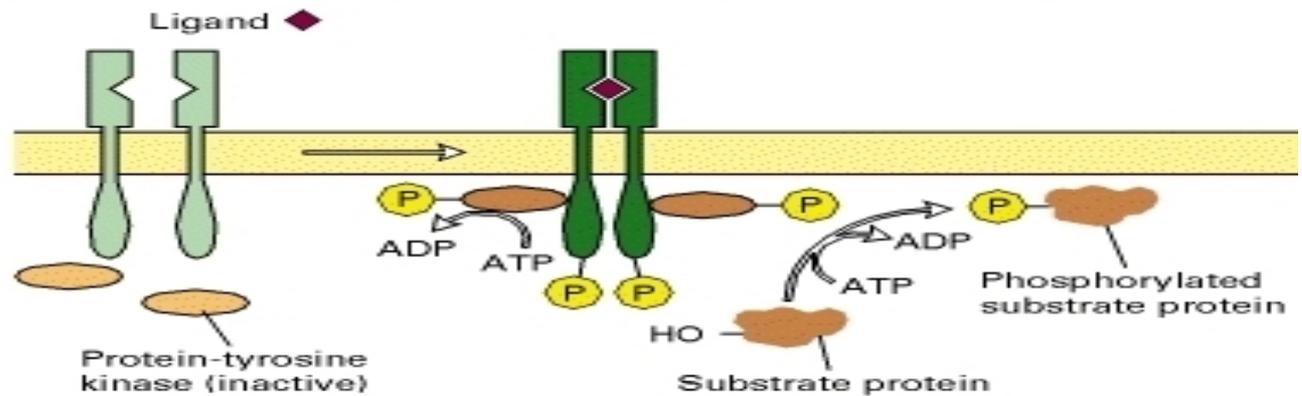


Enzyme Coupled:

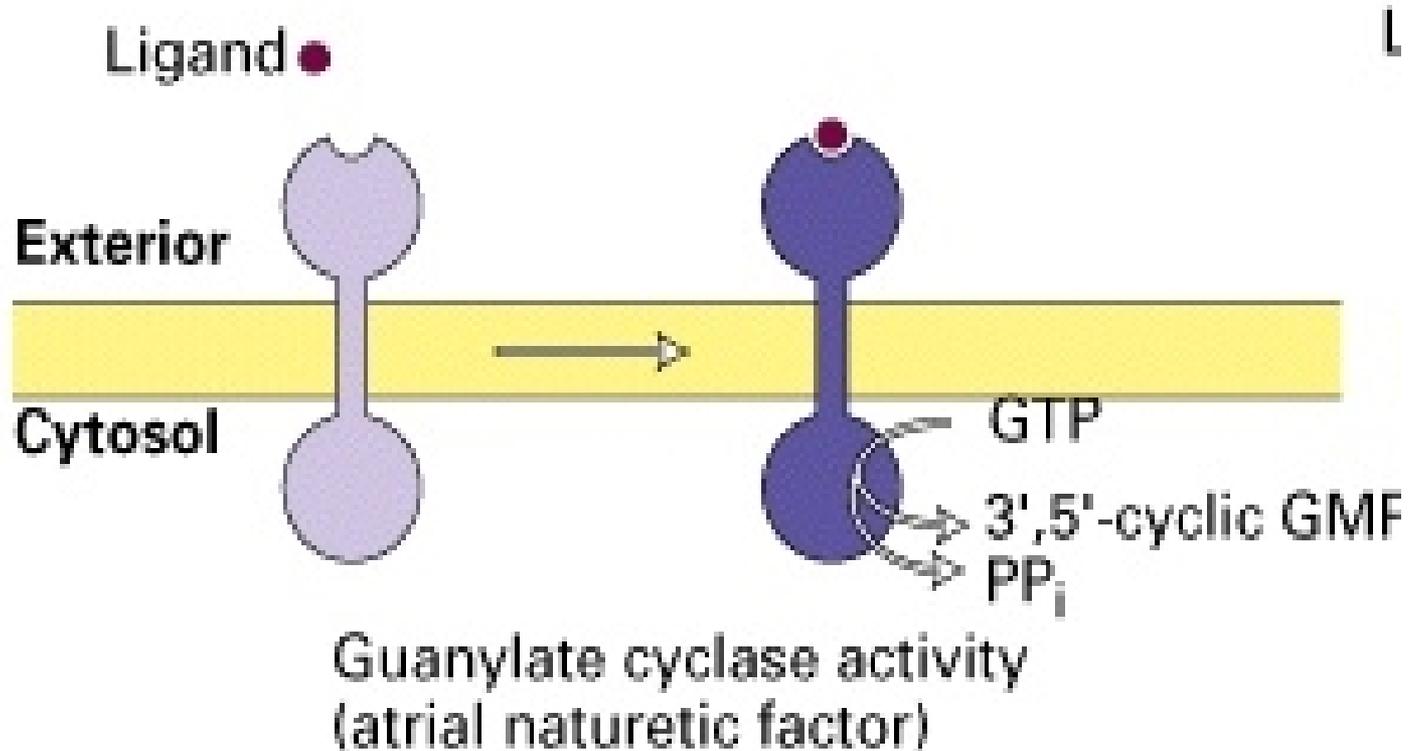


Receptor Lacking Intrinsic Enzyme activity:

(c) **Tyrosine kinase-linked receptors** (erythropoietin, interferons)



(d) Receptors with intrinsic enzymatic activity



- **Transduction:** It is the stage in cell signaling that greatly amplifies the signal. It occurs when the binding of a specific signaling molecule to a
- receptor in the plasma membrane triggers the signal transduction pathway.
- Once one signal-activated receptor activates a protein, that protein activates another, and so on. It can be thought of as a domino effect.
- This protein activity is regulated by **protein kinases**.
- One single cell can contain hundreds of different protein kinases; each responsible for a different substrate protein.
- To turn off the signal transduction pathway, **protein phosphatases** come in. These enzymes deactivate the protein kinases by rapidly removing phosphate groups from proteins, a method called **desphosphorylation**.

- Protein kinase- An enzyme that transfers phosphate groups from ATP to a protein
 - Ex: **Protein kinases** result in the phosphorylation of proteins.
- cAMP as a second messenger in a G-protein-signaling pathway.
- Protein phosphatases- Enzymes that can rapidly remove phosphate groups from proteins
 - Ex: By inactivating protein kinases, **protein phosphatases** turn off the signal transduction pathway when there is no signal present.

- Second messengers-

Small, nonprotein, water-soluble molecules or ions that relay a signal to the interior of a cell

- Ex: **Second messengers** spread throughout the cell by diffusion because they are small and water-soluble.

- cyclic AMP/cAMP- A common second messenger in eukaryotic cells made from ATP

- Ex: A **cAMP** is a regulator of some bacterial operons.

- Adenylyl cyclase- Enzyme that converts ATP to cAMP in response to an extracellular signal

- Ex: **Adenylyl cyclases** are embedded in the plasma membrane and can catalyze the synthesis of cAMP.

- Inositol trisphosphate(IP₃)- A second messenger that functions as an intermediate between certain nonsteroid hormones and a third messenger

- Ex: The pathways leading to calcium release involves **inositol trisphosphate**.

- Diacylglycerol (DAG)- A second messenger produced by the cleavage of a certain kind of phospholipid in the plasma membrane

- Ex: **DAG** is responsible for the release of calcium from the cell's ER too.

- Continued....G-Protein in next presentation....