



# Membranes and receptors module

**Session6**

**Lecture 6.1**

## **RECEPTORS IN CELL SIGNALLING** **RECEPTOR STRUCTURE**

**Lecturer: Dr. Ayam mohammed salih.**

# Objectives

**1-Describe and compare biological communication processes involving hormones, local mediators and neurotransmitters**

**2-Give an overview of the role of membrane proteins as receptors for responding to external stimuli**

**3-Contrast in general terms the mechanisms of polypeptide hormones and the steroid and thyroid hormones**

**Objective number (1):**

- **Describe and compare biological communication processes involving hormones, local mediators and neurotransmitters**

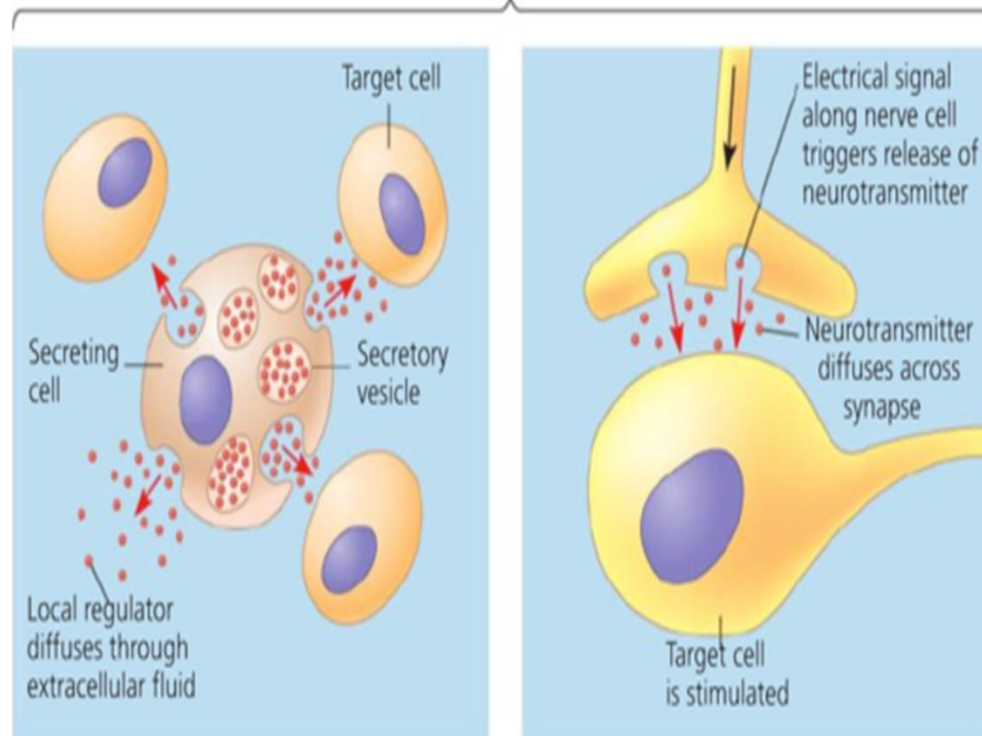
# Chemical Signaling

- **According to their functions:**
- **Hormones:**) signaling between cells in different tissues via the circulation . (Thyroxin hormone ).
- **Neurotransmitters:** (signaling at specialized cell junctions in the nervous system, synapses. (Acetylcholine)

**Local chemical mediators :**(signaling between adjacent cells in the same tissue (cytokines)

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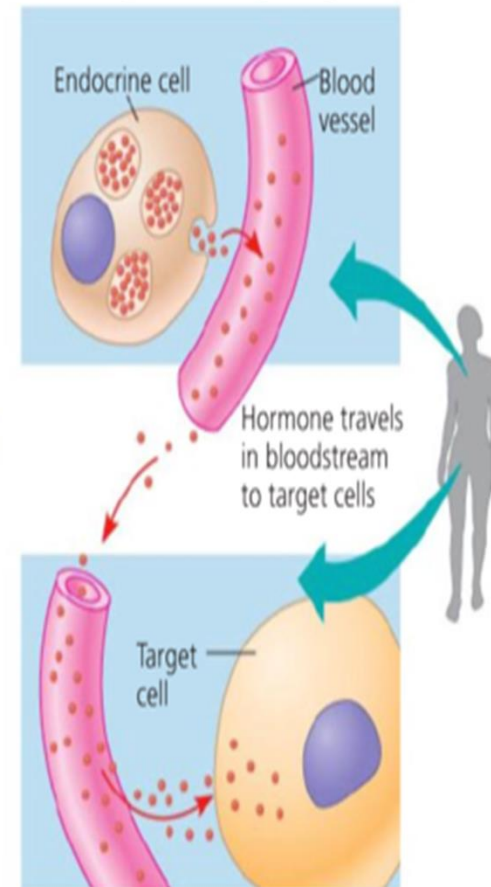
## Local signaling



**(a) Paracrine signaling.** A secreting cell acts on nearby target cells by discharging molecules of a local regulator (a growth factor, for example) into the extracellular fluid.

**(b) Synaptic signaling.** A nerve cell releases neurotransmitter molecules into a synapse, stimulating the target cell.

## Long-distance signaling



**(c) Hormonal signaling.** Specialized endocrine cells secrete hormones into body fluids, often the blood. Hormones may reach virtually all body cells.

## How Do Cells Recognize Signals?

Cells have proteins called **receptors** that bind to signaling molecules and initiate a physiological response. Different receptors are specific for different molecules, **Dopamine** receptors bind dopamine, **insulin** receptors bind insulin, nerve **growth factor** receptors bind nerve growth factor, and so on.

we have also **intracellular** receptors for hydrophobic Molecules

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# Receptor

**Receptors:** are transmembrane proteins , which bind to signaling molecules(ligand) outside the cell and then transmit the signal through a sequence of molecular switches to internal signaling pathway. and which in response to ligand binding brings about regulation of a cellular process. In the unbound state a receptor is functionally silent.

**Hydrophilic receptors** :- outside the cell On the membrane

**Hydrophobic receptors**:- inside the cell On the Nucleus or cytosol

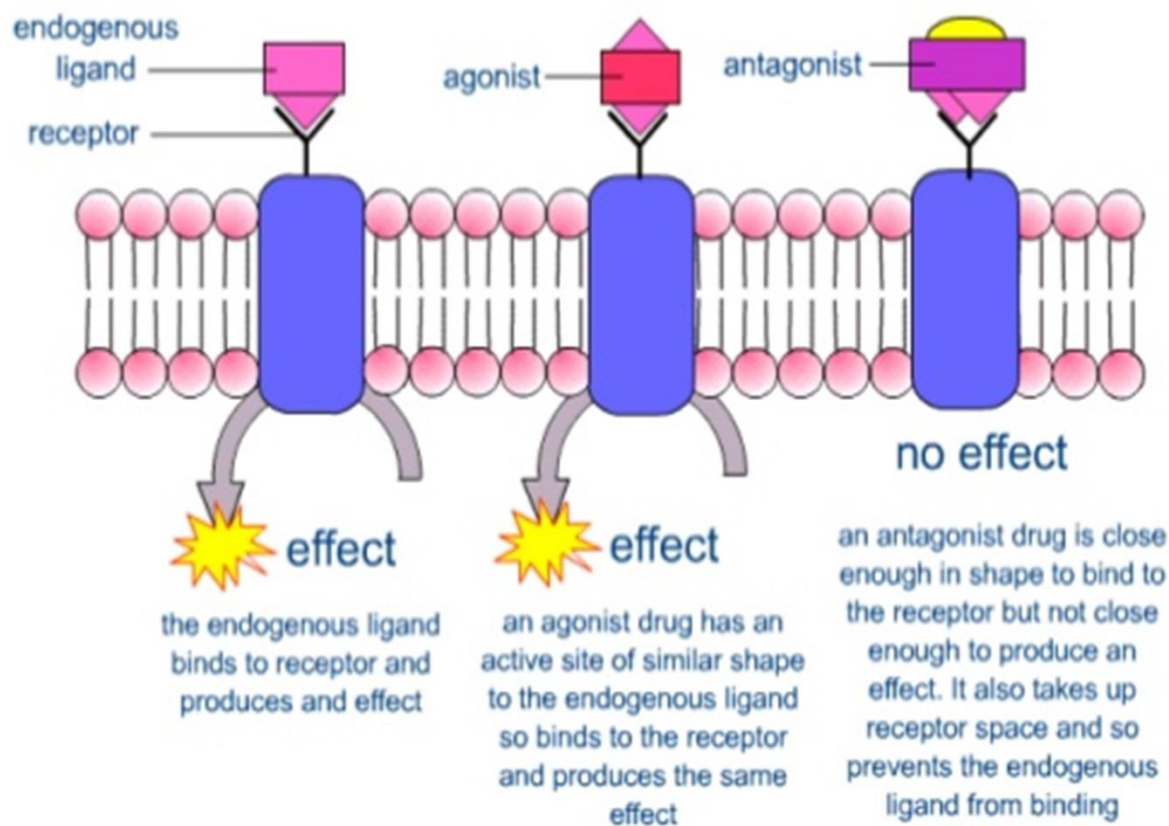
# Ligand

A ligand is any small molecule that bind specifically to a receptor site.

- Ligand binding may produce an activation of a receptor in this case the ligand is termed an **agonist**.
- Ligand may combine with a receptor site without causing activation this type of ligand is termed an **antagonist**.
- **Partial agonist**: stimulate a receptor but are unable to elicit the maximum cell response possible.



# Basics of agonist and antagonist



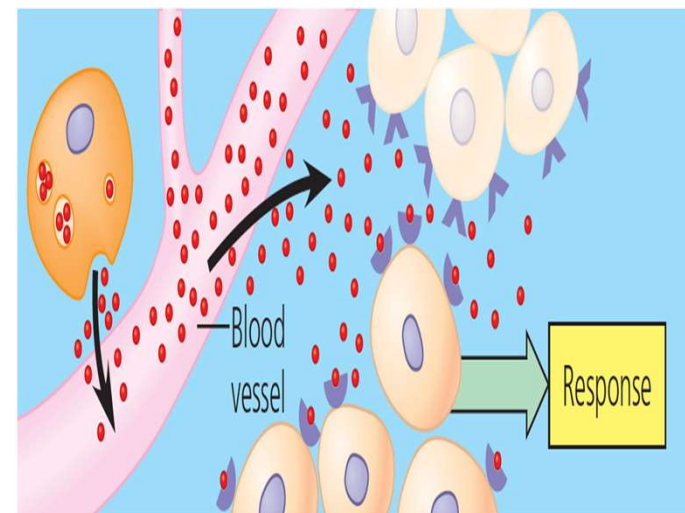
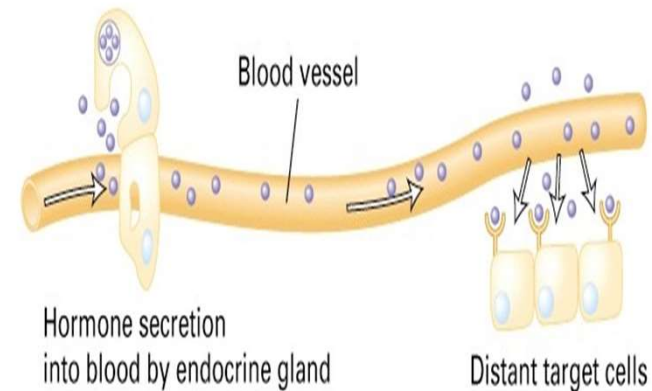
## **Q2) How many types of Signaling are there?**

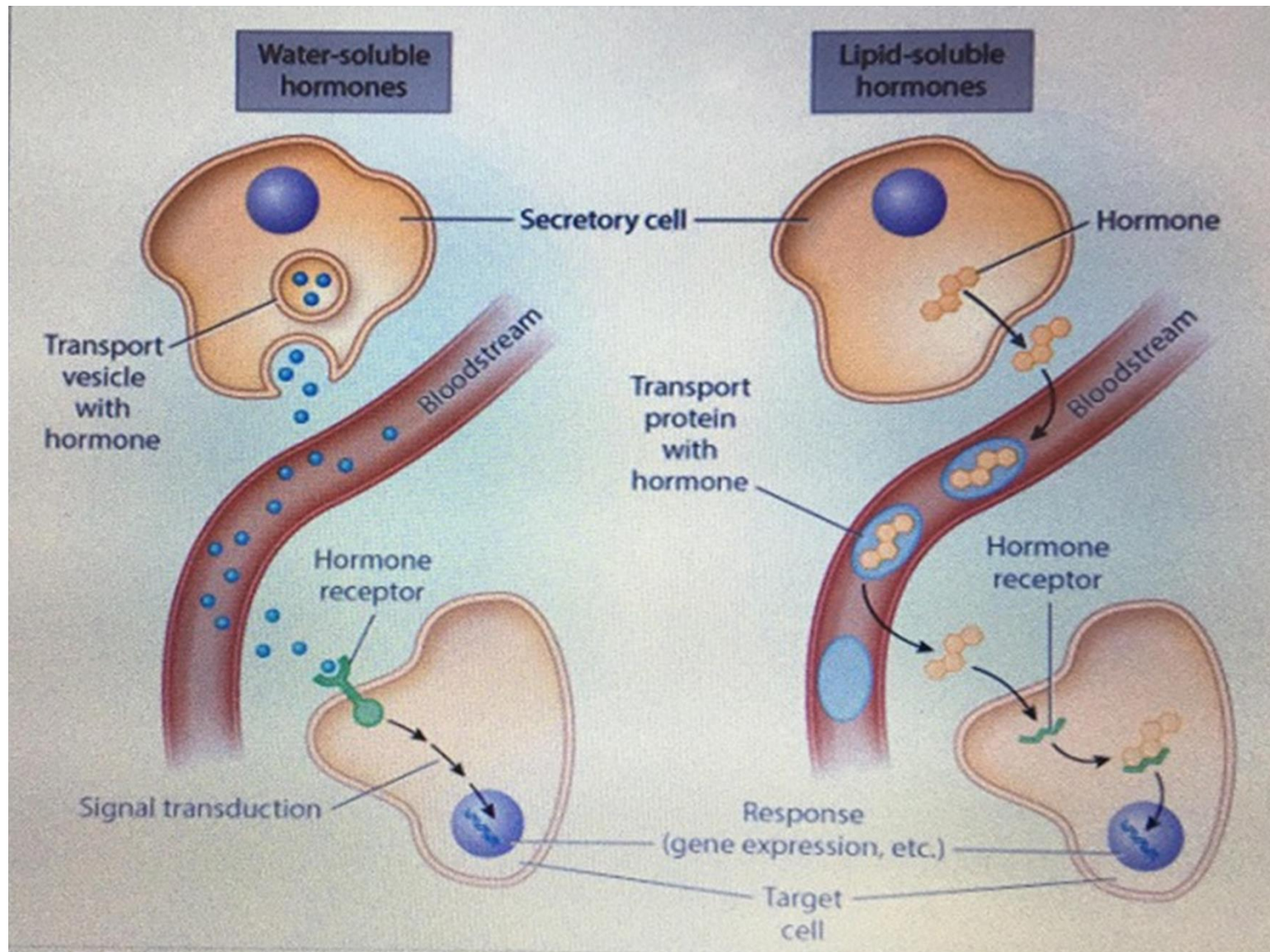
- Depending on the distance that the signaling molecule has to travel, we can talk about

**Three (3) types of signaling:**

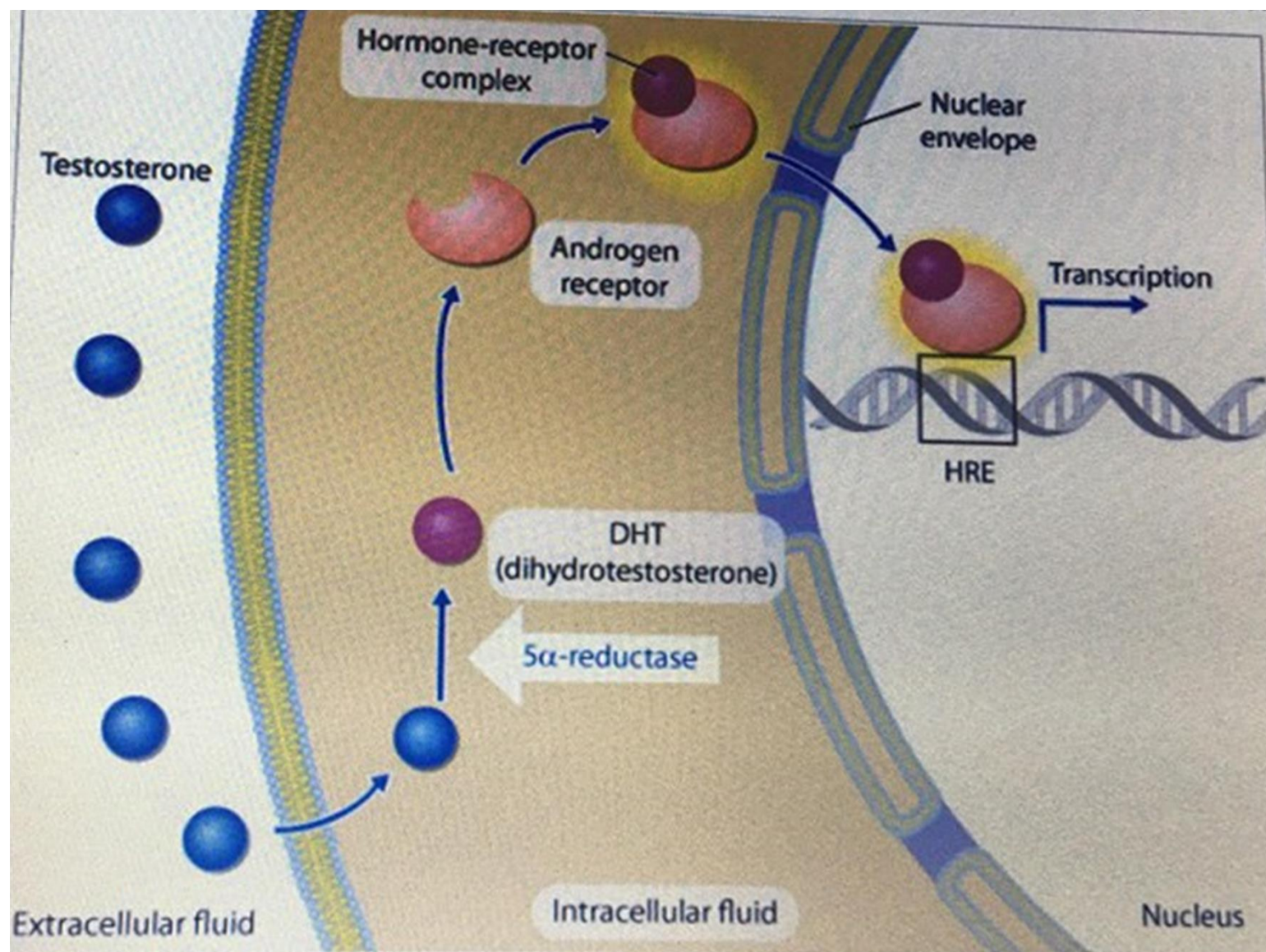
- **Endocrine signaling:** hormones are produce by an endocrine gland and sent through the blood stream to distant cells.
- **Hormones can be:**
- Small **lipophilic** molecules that **diffuse through** the cell membrane to reach cytosolic or nuclear receptors.
- **Examples** are progesterone and testosterone, They generally regulate transcription
- or water soluble molecules (**Hydrophilic**) that bind to receptors **on** the plasma membrane.
- They are either proteins **like** insulin and glucagons, or small, charged molecules like histamine and epinephrine.

(a) Endocrine signaling





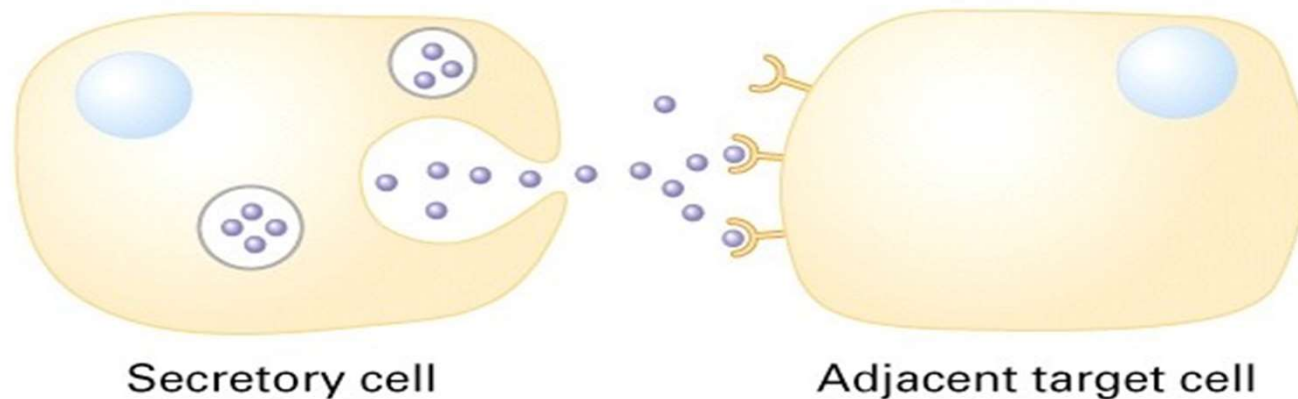




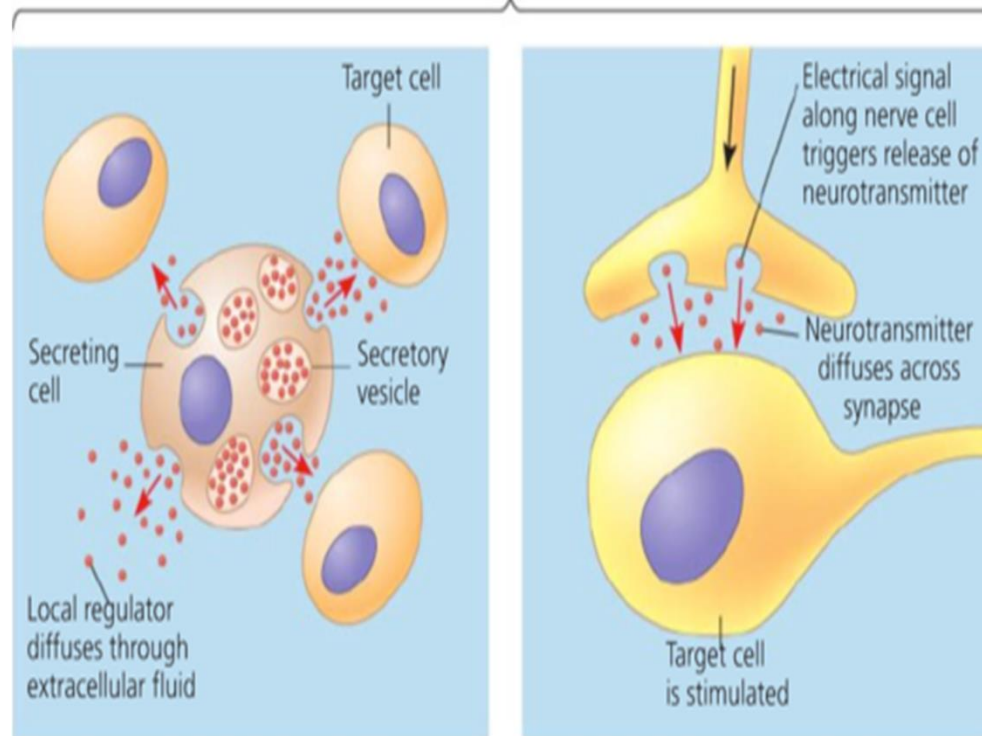
## paracrine signaling

- signaling molecule affects only target cells in the proximity of the signaling cell.
- An **example** is the conduction of an electric signal from one nerve cell to another or to a muscle cell.
- In this case the signaling molecule is a **neurotransmitter**.

(b) Paracrine signaling



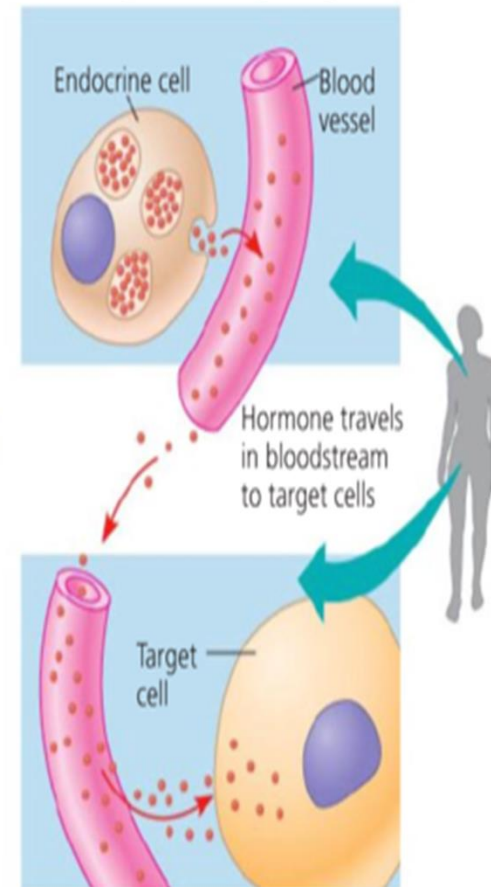
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## Long-distance signaling

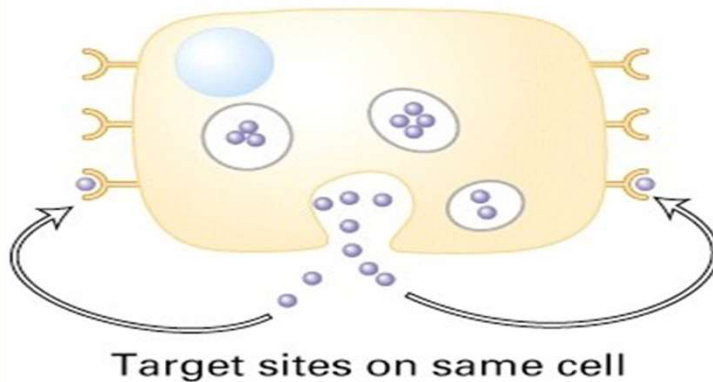


**(c) Hormonal signaling.** Specialized endocrine cells secrete hormones into body fluids, often the blood. Hormones may reach virtually all body cells.

## Autocrine signaling

Are produced by signaling cell that can also bind to the ligand that is released . This type of signaling often occurs during the early development of an organism to ensure that cells develop into correct tissue and take on the proper function. Further if a cell infected with a virus the cell can signal itself to undergo programmed cell death, killing the virus in the process.

(c) Autocrine signaling



Key:

- Extracellular signal
- Y Receptor
- Membrane-attached signal



**Objective number (2):**

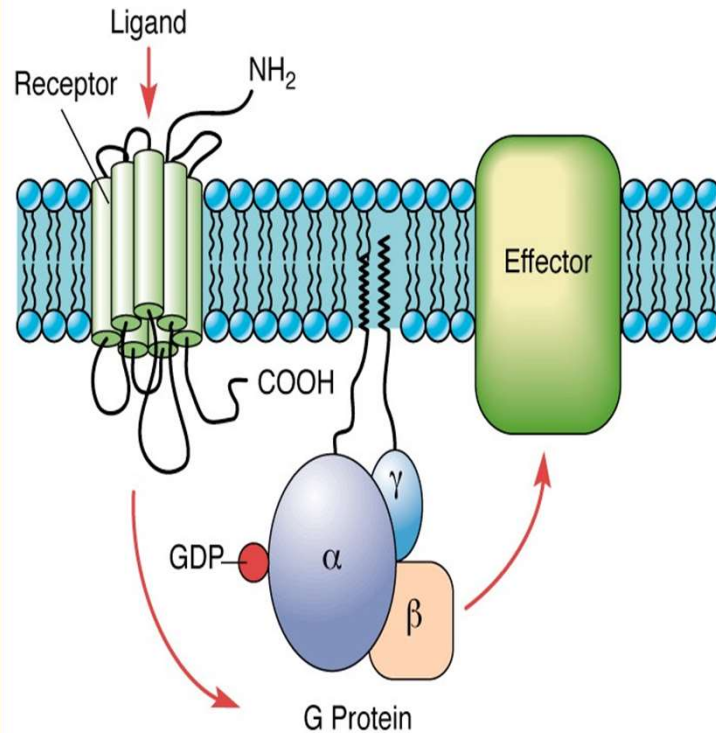
**Give an overview of the role of membrane proteins as receptors for responding to external stimuli, and for the uptake of external molecules via endocytosis**

## Types of Receptors

- Membrane receptors fall into **three major classes:**
- **G-protein-coupled receptors**,
- **ion channel receptors** ,
- **Tyrosine –kinase receptors.**

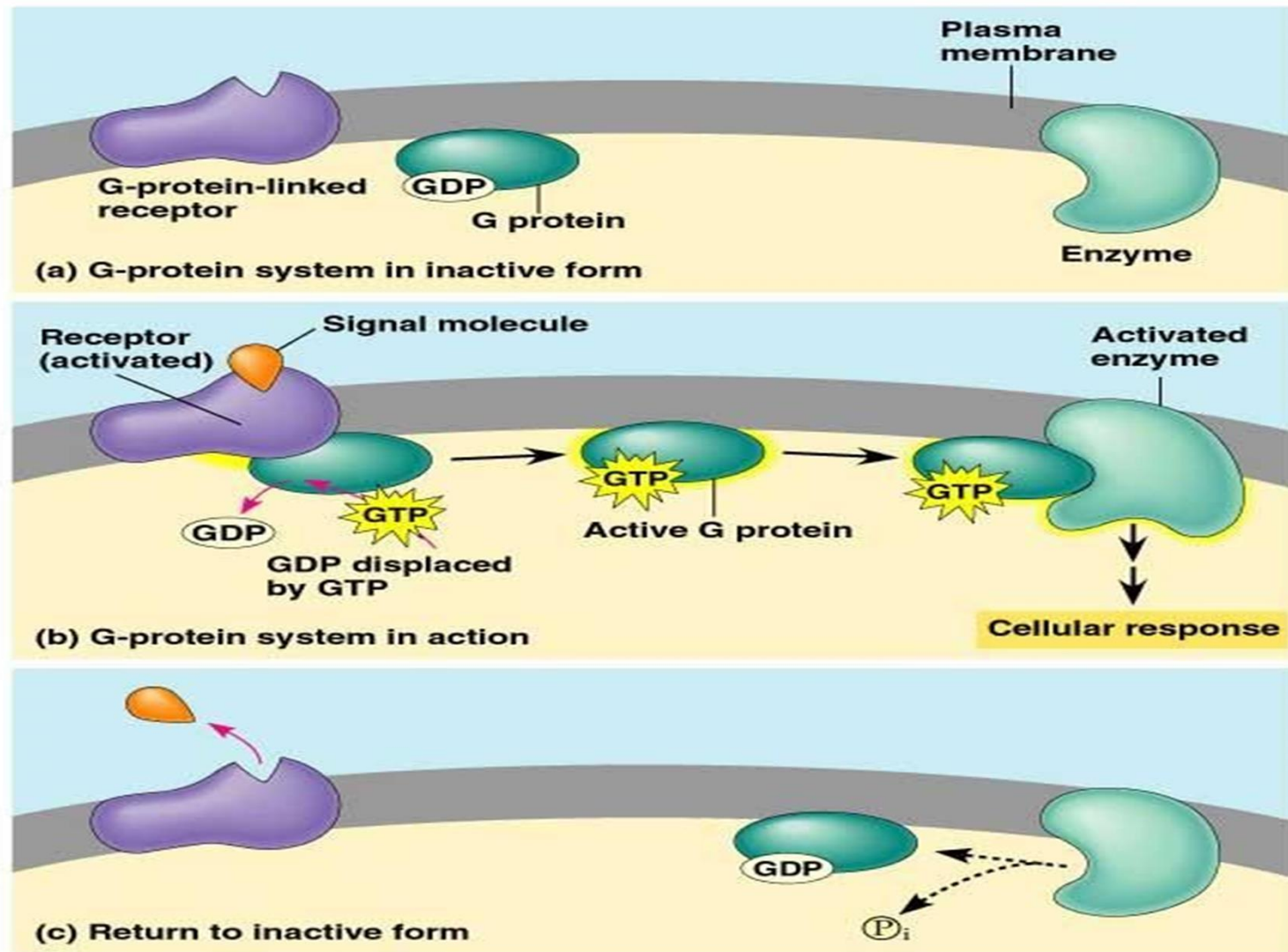
G-protein –linked receptor is a plasma membrane receptor that work with the help of a protein called a G protein .

Each G-protein-linked receptor has seven  $\alpha$ -helices spanning the membrane and functions as a switch that is on or off depending on which of two guanine nucleotides is attached , GDP or GTP. When GDP is bound , the G protein is inactive , when GTP is bound it is active .



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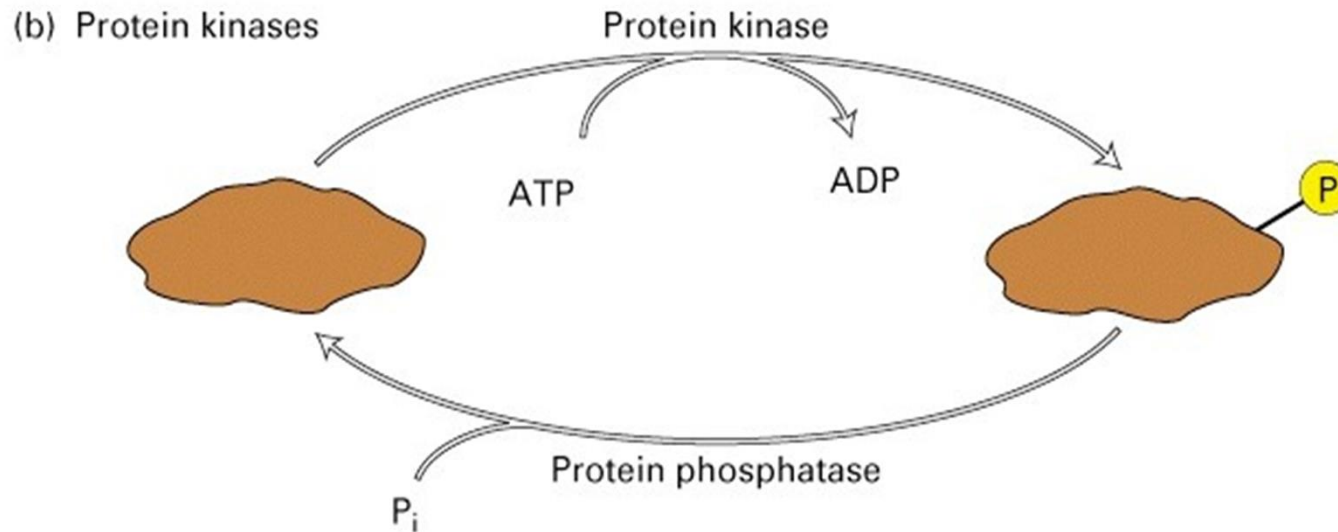
- The ligand bonds to the extracellular side of the G-protein –linked receptor which is then activated and changes its conformation so that it can activate a G-protein .
- The G-protein then bind to another protein (usually an enzyme) and alter it to become active.
- The absence of a signal they are bound to GDP. Signal results in the release of GDP and the binding of GTP. After a short period of time they hydrolyze GTP and back to their off state





G-Protein Signaling - YouTube.MP4

- )b) **Protein Kinases** - Upon activation they add phosphate groups to themselves and/or other proteins at either serine/threonine, or at tyrosine residues.
- Their activity can be regulated by **second messengers**, interaction with other proteins, or by phosphorylation itself. They are opposed by phosphatases that remove phosphate groups from specific phosphorylated proteins.

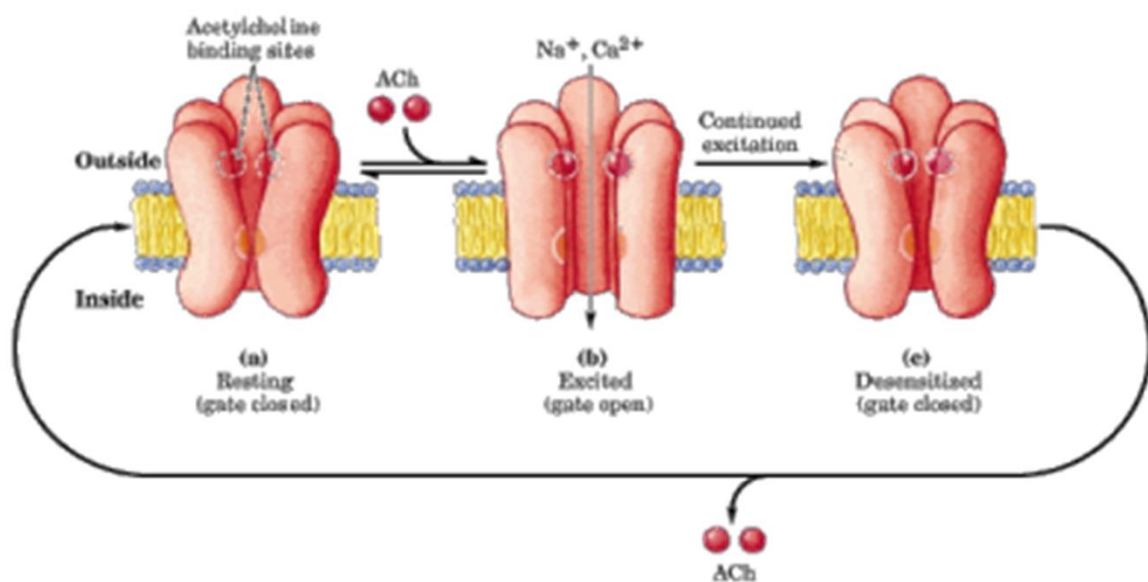


## Ligand-gated ion channels

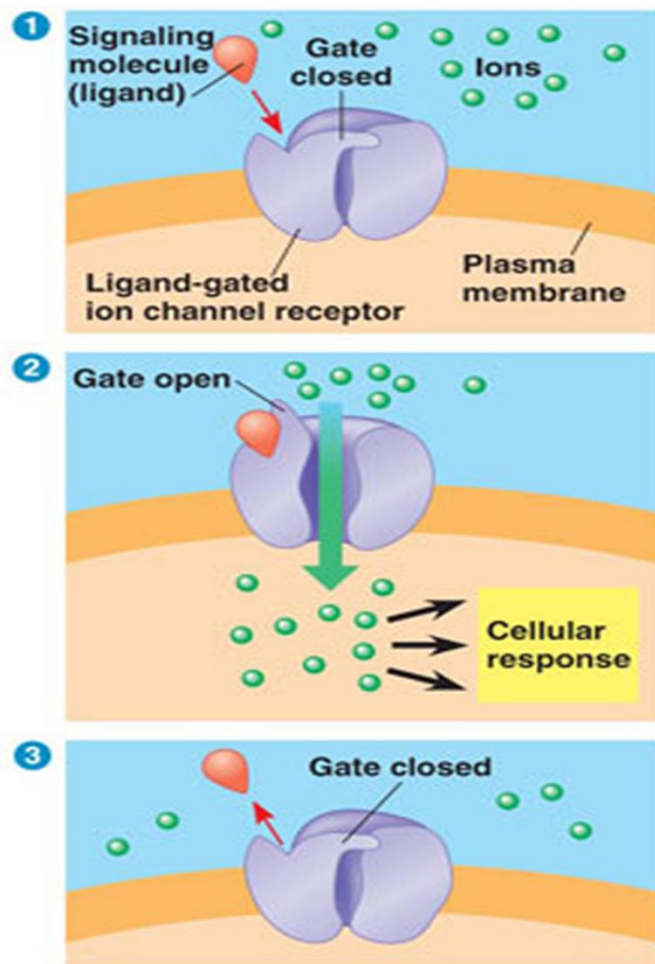
- Have a heteropentameric structure.
- Each subunit consist of the extracellular ligand-binding domain and a transmembrane domain where the transmembrane domain in turn includes four transmembrane alpha helixes. The ligand binding cavities are located at the interface between the subunits.



# Ligand-gated Ion channel



Acetylcholine binding --> Either  $\text{Na}^+$  or  $\text{Ca}^{2+}$  pass --> initiate membrane depolarization --> Normally acetylcholine is lowered by acetylcholinesterase --> if abnormally remain high --> conformation change --> desensitization.

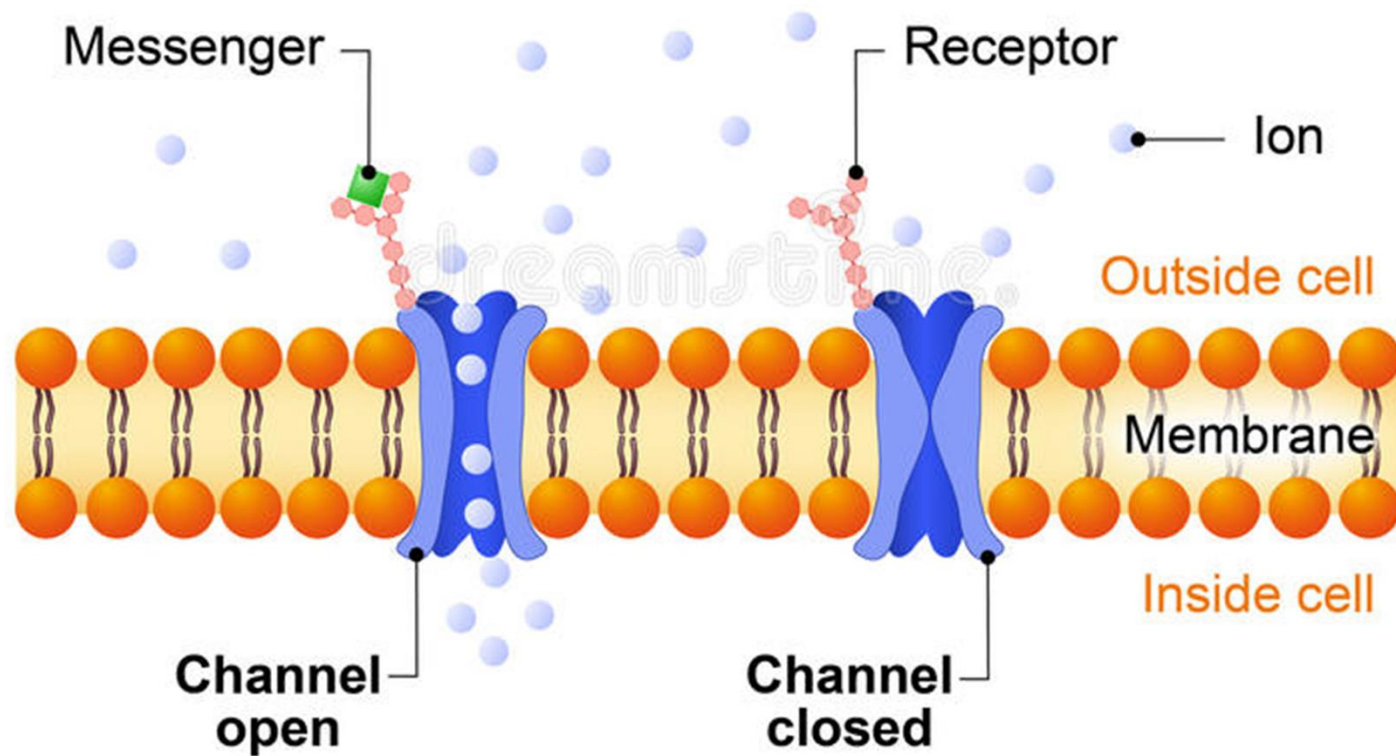


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AP1 - NEURON - LIGAND GATED CHANNELS - YouTube.MP4

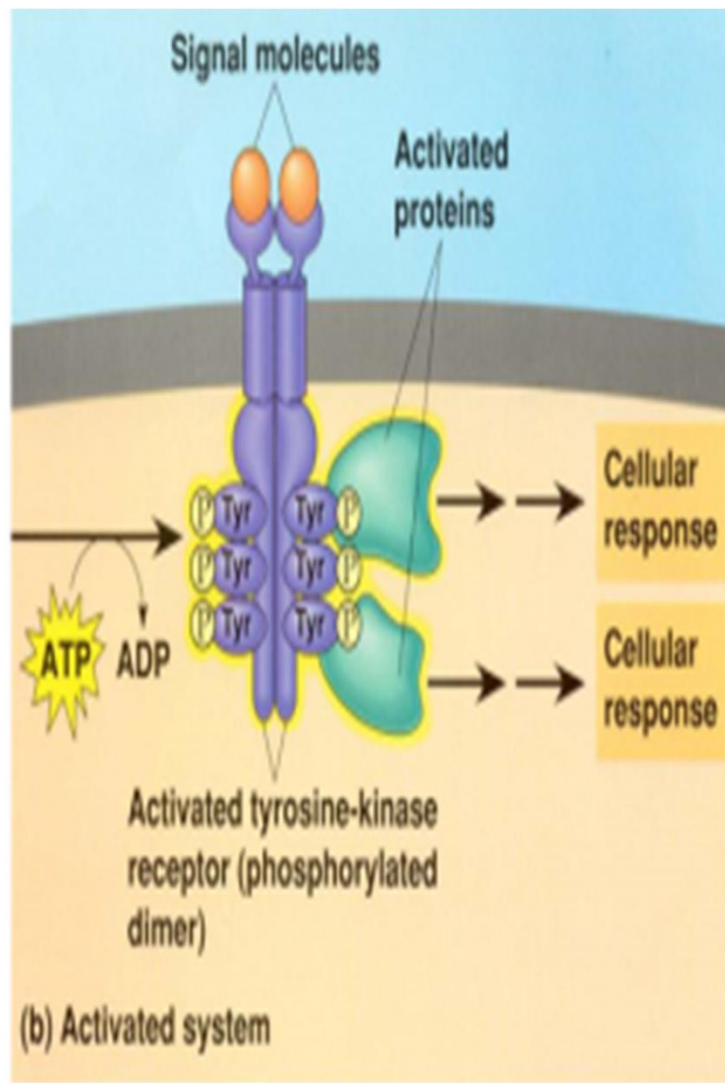
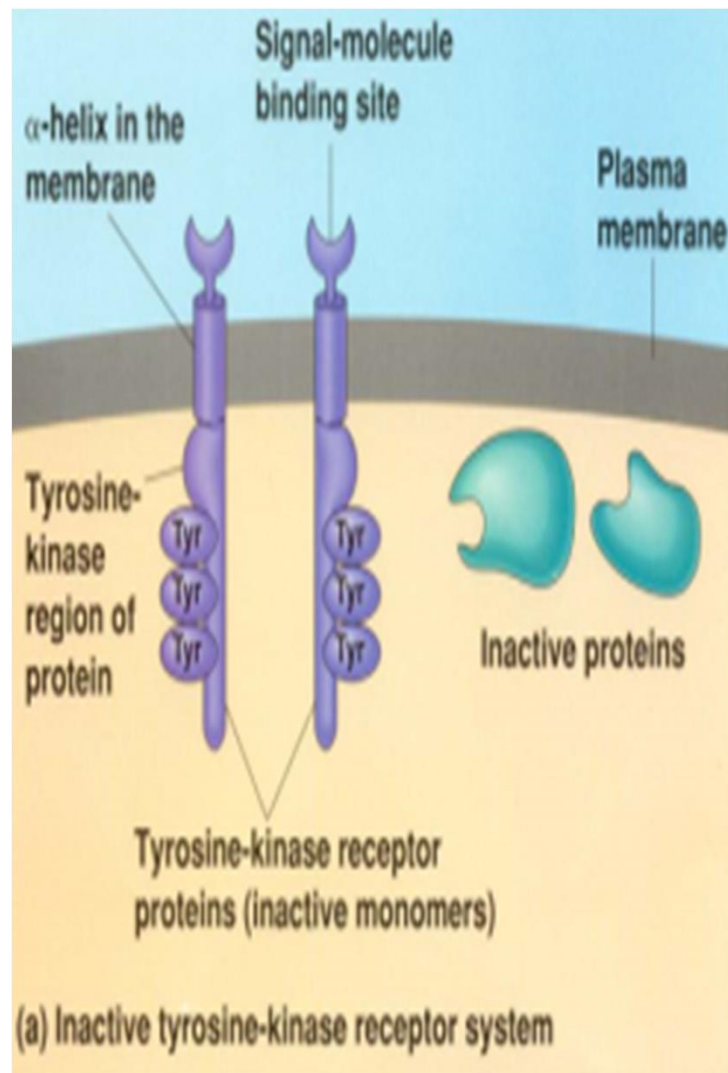
# Ligand-gated ion channel



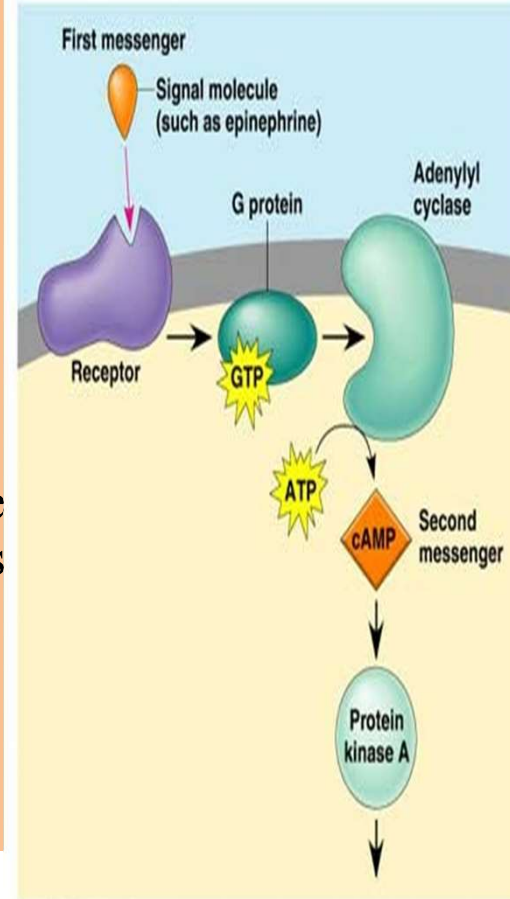
## Tyrosine-kinase receptor

- catalyzes the transfer of phosphate groups from ATP to the amino acid tyrosine on a substrate protein; they are membrane receptors that attach phosphates to protein tyrosine
- The effect of the signal molecule on a tyrosine-kinase receptor is polypeptide aggregation and phosphorylation (the addition of a phosphate  $\text{PO}_4$  group to a protein or other organic molecule) of the receptor. To go into more depth, activation occurs in 3 steps:

- 1-The ligand binding causes 2 receptor polypeptides to aggregate, forming a dimer (a protein consisting of 2 polypeptides).
- 2- This aggregation activates the tyrosine-kinase parts of both polypeptides, each of which then
- 3- phosphorylates the tyrosines on the tail of the polypeptide. Proteins inside the cell recognize the tyrosine-kinase receptor once its activated and bind to its specific phosphorylated tyrosine, changing the conformation and activating it where one tyrosine-kinase receptor dimer then activates 10 or more different intracellular proteins



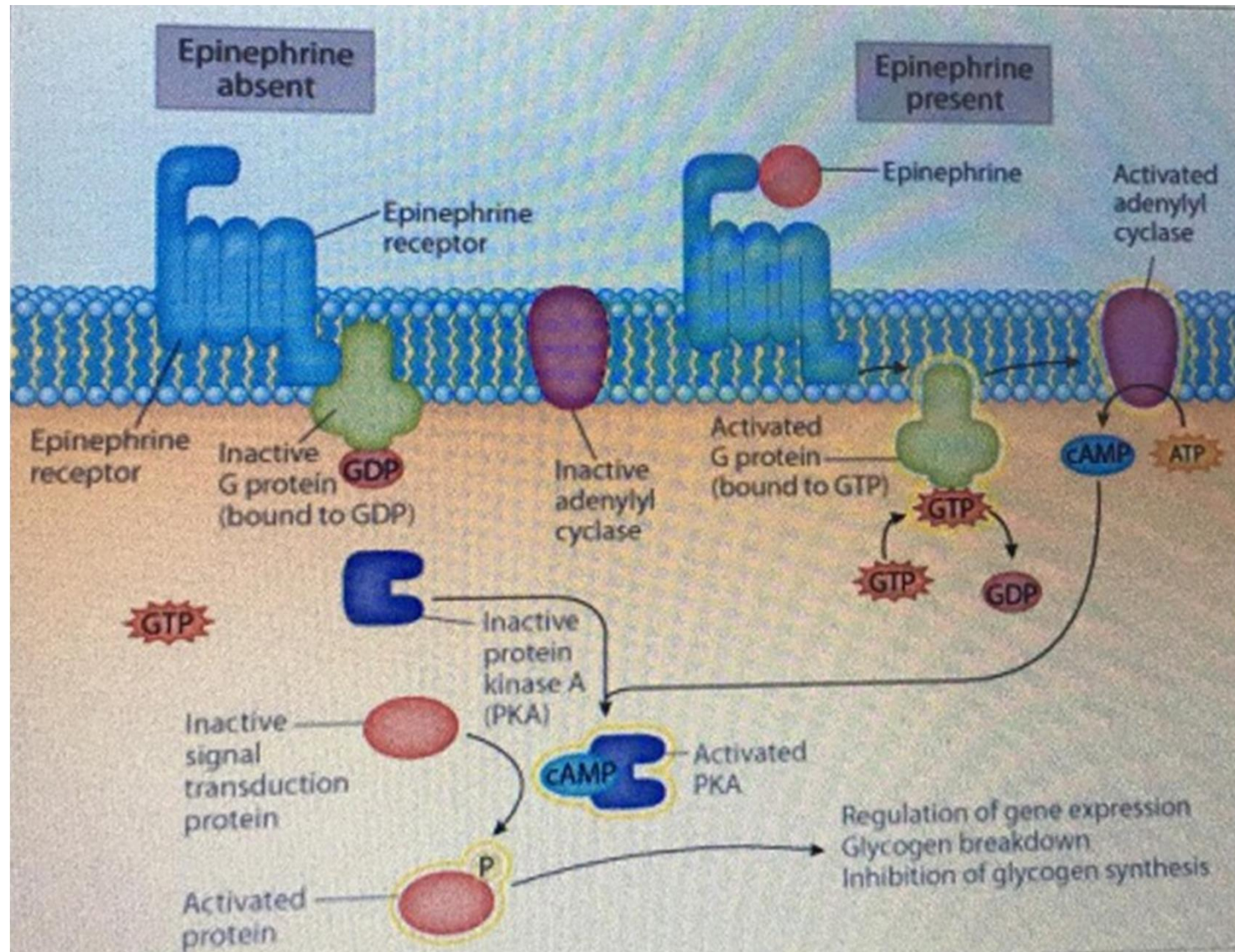
- Activation of receptors can trigger the synthesis of small molecules called **second messengers**, which initiate and coordinate intracellular signaling pathways.
- For example, **cyclic AMP** (cAMP) is a common second messenger involved in signal transduction cascades.
- cAMP is synthesized from ATP by the enzyme **adenylyl cyclase**, which resides in the cell membrane. The activation of adenylyl cyclase can result in the manufacture of hundreds or even thousands of cAMP molecules



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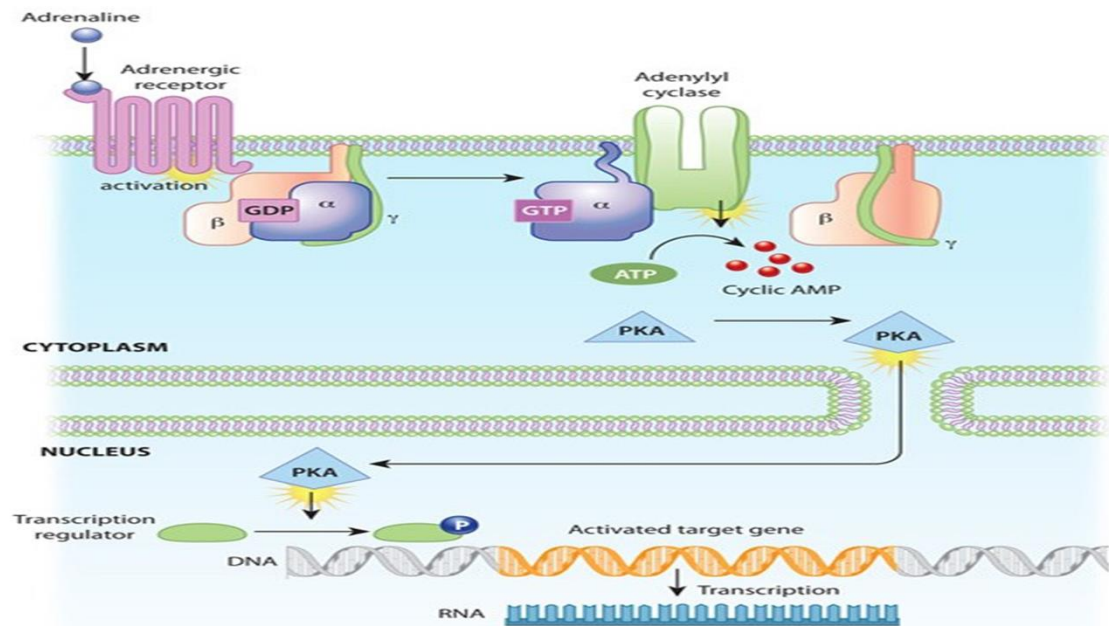


- These cAMP molecules activate the enzyme **protein kinase A** (PKA), which then **phosphorylates** multiple protein substrates by attaching phosphate groups to them. Each step in the cascade further **amplifies** the initial signal, and the phosphorylation reactions mediate both short- and long-term responses in the cell (Figure).
- How does cAMP **stop** signaling? It is degraded by the enzyme
- **phosphodiesterase**





cAMP Signaling - YouTube.MP4





action of epinephrine - YouTube.MP4

Objective number (3):

**Contrast in general terms the mechanisms of polypeptide hormones and the steroid and thyroid hormones**

- Protein and peptide hormones, catecholamines like epinephrine find their receptors decorating the plasma membrane of target cells.
- Binding of hormone to receptor initiates a series of events which leads to generation of so-called second messengers within the cell (the hormone is the first messenger).
- Receptors for steroid and thyroid hormones are located inside target cells, in the cytoplasm or nucleus, and function as ligand-dependent transcription factors.