Cell Biology

Chapter (7): Cell Signaling Mechanisms

- Type of cell signaling
- Types of receptors
  - Internal receptors
  - Cell-surface receptors

Cell signaling and communication

- **Cell-signaling is the process by which cells communicate with their environment to mediate growth, proliferation, differentiation, survival and homeostasis.**

- **Cell signaling often refers to signal transduction because in which an event is transduced into another event.**

- **Errors in signaling interactions are responsible for diseases such as cancer, autoimmune diseases, heart diseases and diabetes mellitus.**

- **Normally, cells communicate using chemical signals which are generated by signaling molecules called ligands. These ligands are produced by a cell called sending cell, then the ligands are released into the extracellular space and finally are received by another cell called receiving cell (or target cell).**

Cell signaling and communication

- **Not all cells can be considered as a target cell (can receive a signal from a sending cell). So to be a target cell, the cell must have the right receptor for that signal.**

- **When a signaling molecule binds to its receptor, it alters the shape or activity of the receptor, triggering a change inside of the cell.**

- **There are four basic mechanisms of chemical signaling between cells: direct contact signaling, autocrine signaling, paracrine signaling, and endocrine signaling.**

- **The main difference between the different mechanisms of signaling is the distance that the signal travels through the sending cell to reach the target cell.**

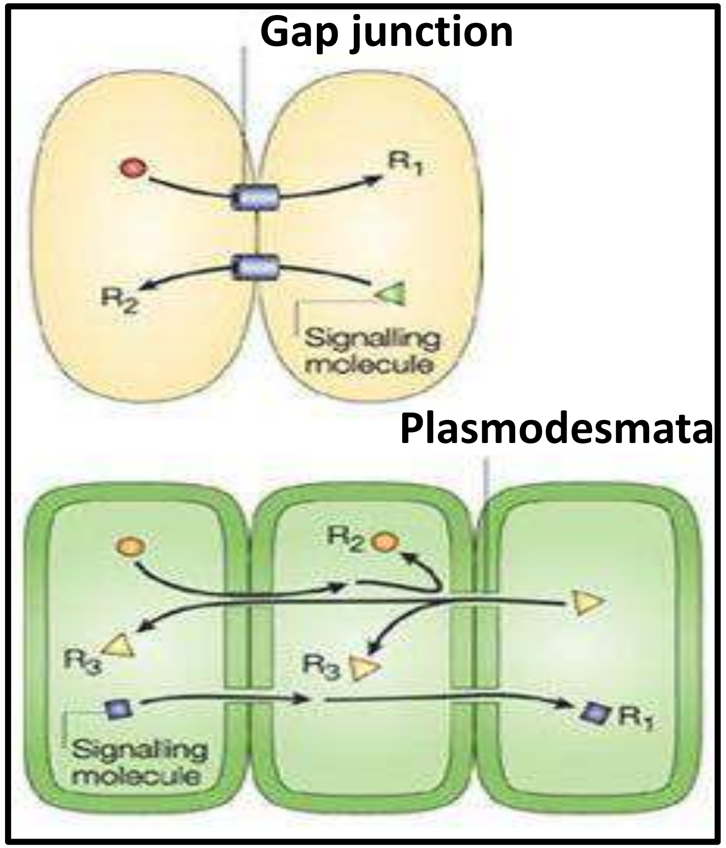
Cell signaling and communication

1. **Direct contact signaling**

- **It occurs when the cells are very close to each others where some molecules on the plasma membrane of the cells bind together in specific ways such as tight junctions, anchoring junctions, gap junctions and plasmodesmata.**

- **Neither tight junctions nor anchoring junctions are involved in cell signaling and communication.**

- **Gap junctions and plasmodesmata are connections between the plasma membranes of neighboring cells which allow small signaling molecules such as calcium ions (Ca^{2+}) to diffuse between the two neighboring cells.**



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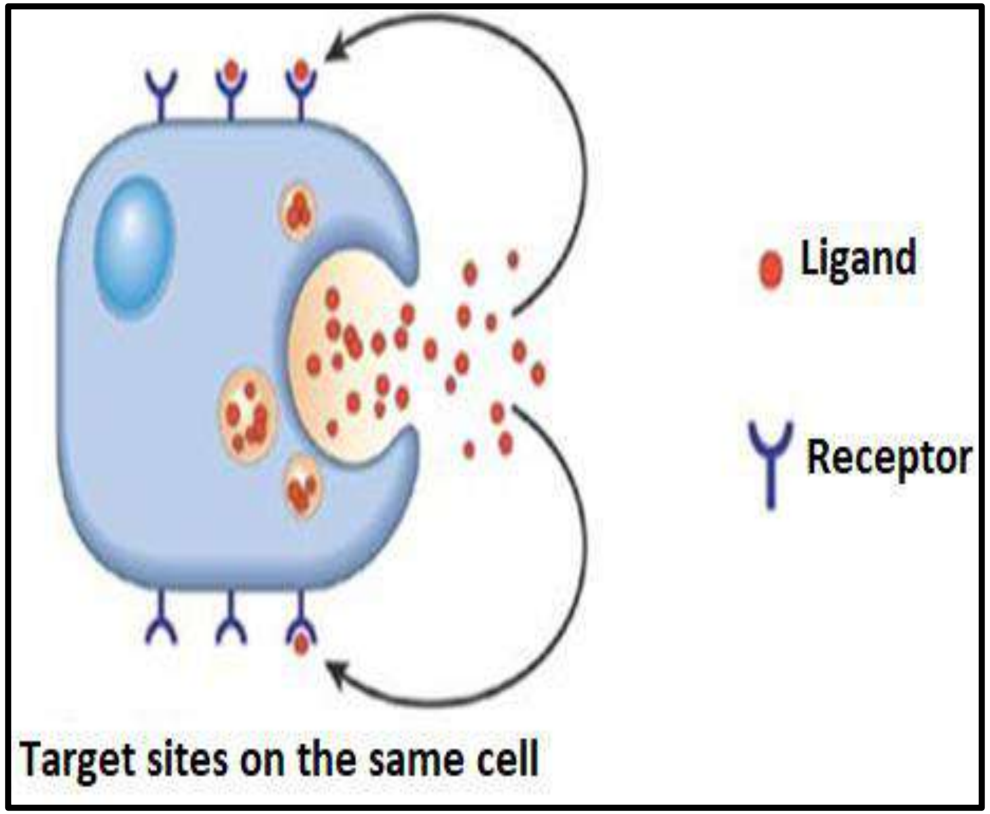
2. Autocrine signaling

- **Autocrine signals are produced by the same cell meaning that the signaling cell and the target cell are the same.**

- **In autocrine signaling, a cell signals to itself by releasing a ligand that binds to a receptor on its own surface.**

- **This type of signaling often occurs during the early development of an organism to ensure that cells develop into the correct tissues and take on the proper function.**

- **Further, if a cell is infected with a virus, the cell can signal itself to undergo programmed cell death, killing the virus in the process.**



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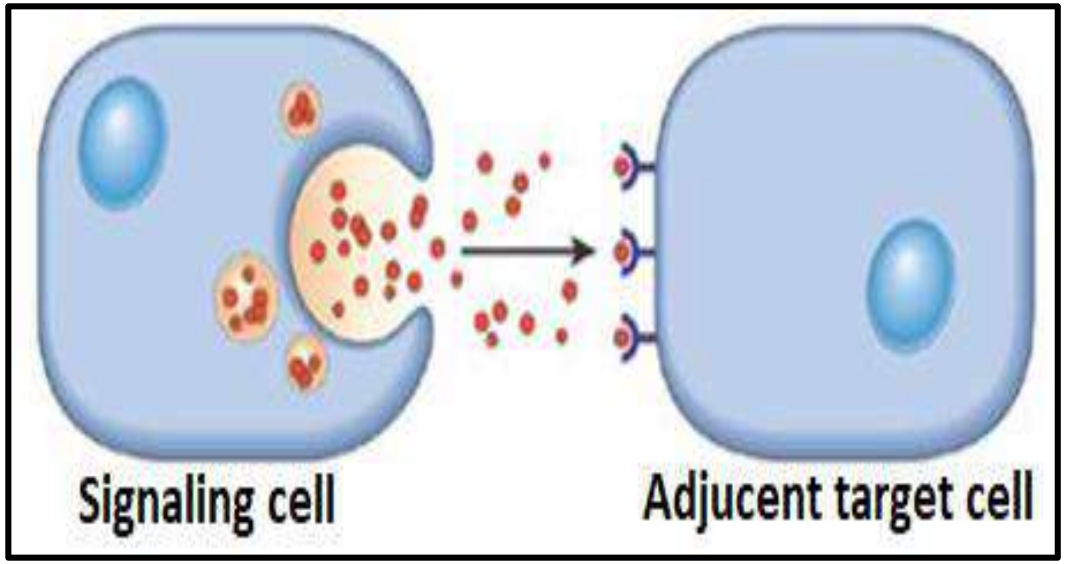
3. Paracrine signaling

- Paracrine signaling occurs between adjacent cells through the release of chemical messengers (ligands) that can diffuse through the space between the cells.

- In this type of signaling, cells communicate over relatively short distances and the signals usually produce quick responses that last for short time because the paracrine ligands are quickly degraded by enzymes.

- One example of paracrine signaling is the transfer of signals across synapses between nerve cells.

- The junction between nerve cells where signal transmission occurs is called a synapse.

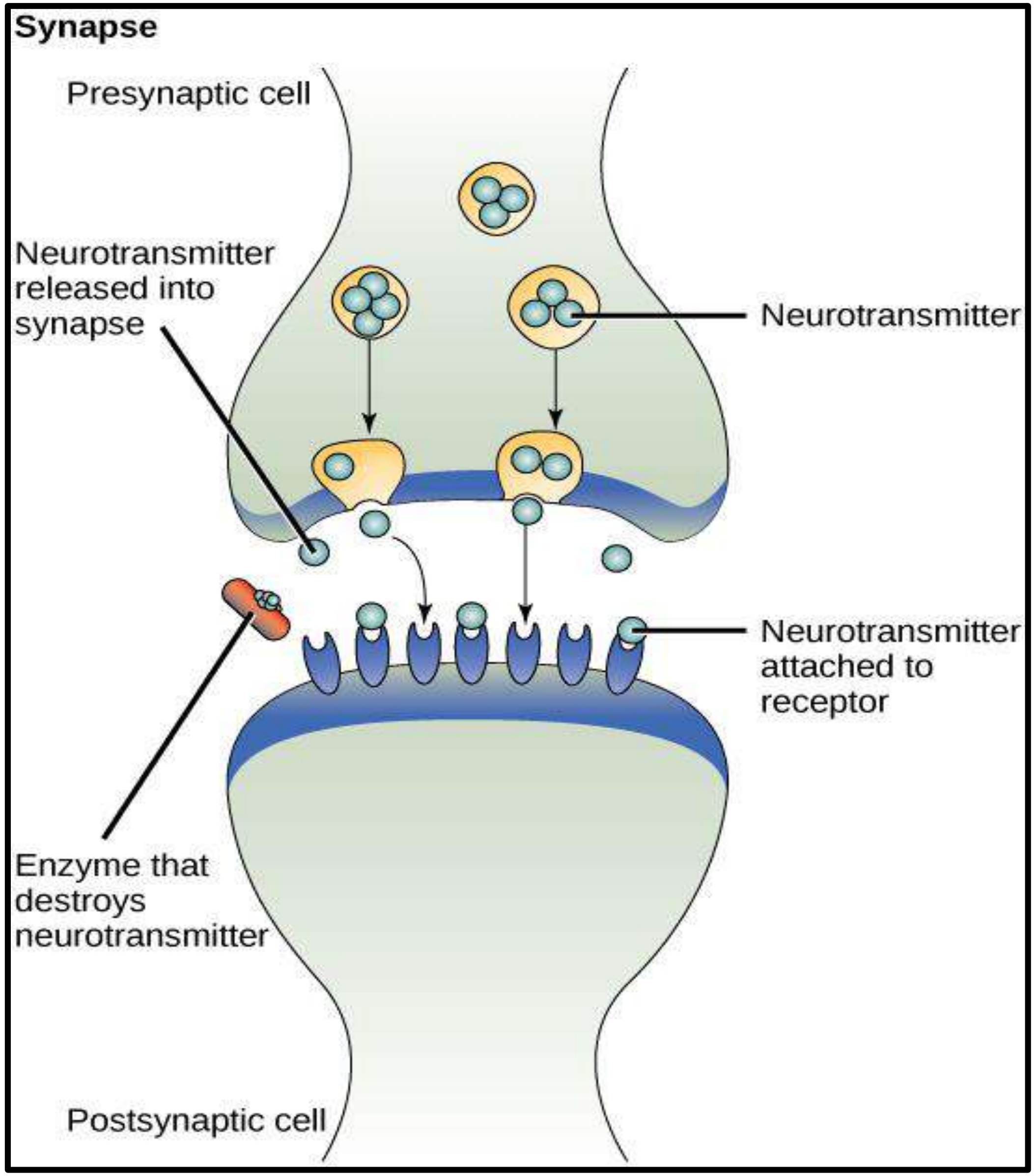


Cell signaling and communication

3. Paracrine signaling

- **Signals between nerve cells are generated by fast-moving electrical impulses called action potentials.**

- **When these impulses reach the end of one nerve cell called presynaptic cell (the cell generating the signal), the signal continues on to the next nerve cell called postsynaptic cell (the cell receiving the signal) by the release of chemical ligands called neurotransmitters from the presynaptic cell.**

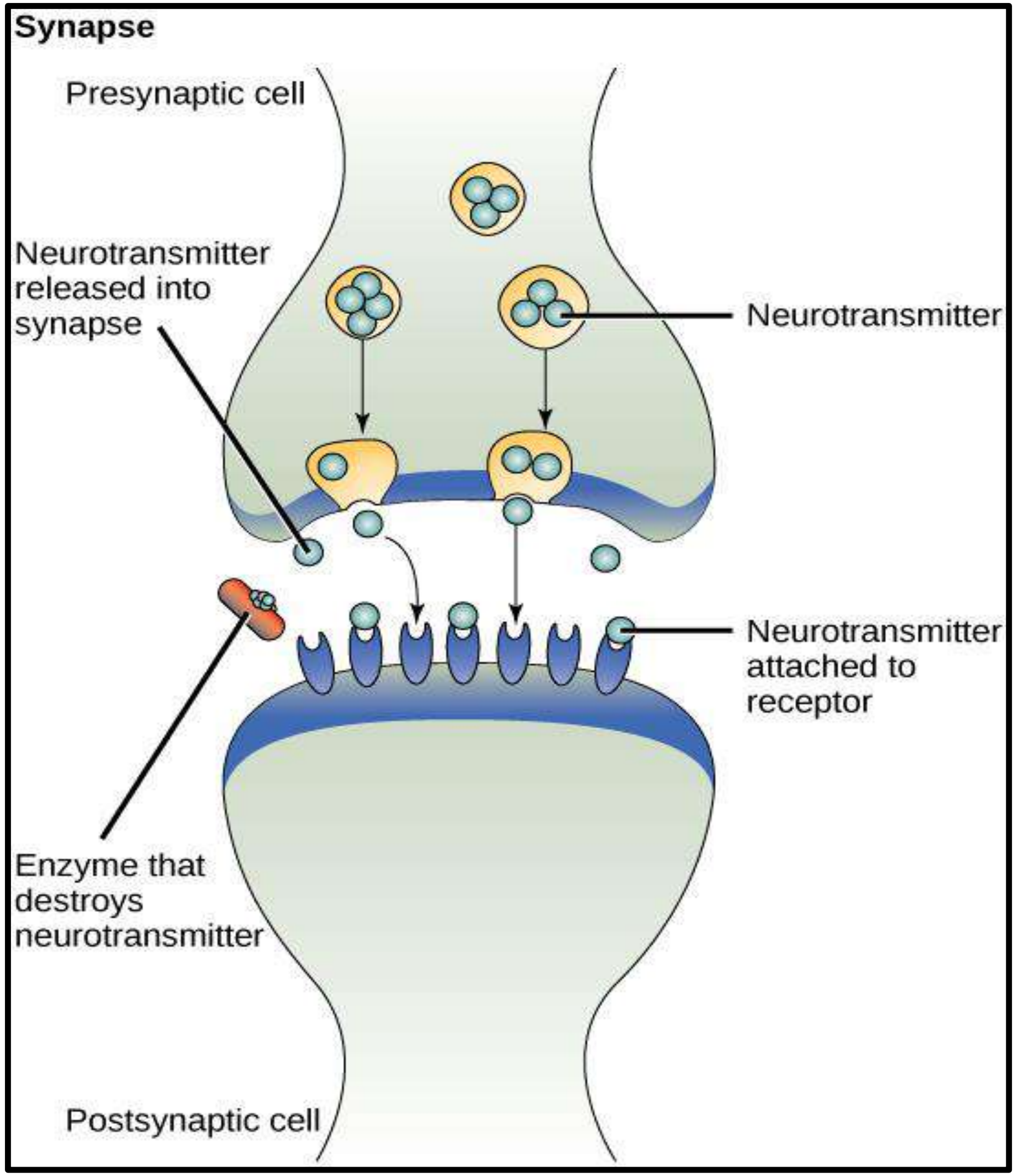


Cell signaling and communication

3. Paracrine signaling

- **The neurotransmitters are transported across the very small distances between nerve cells, which are called chemical synapses and then bind to specific receptors on the surface of the postsynaptic cell.**

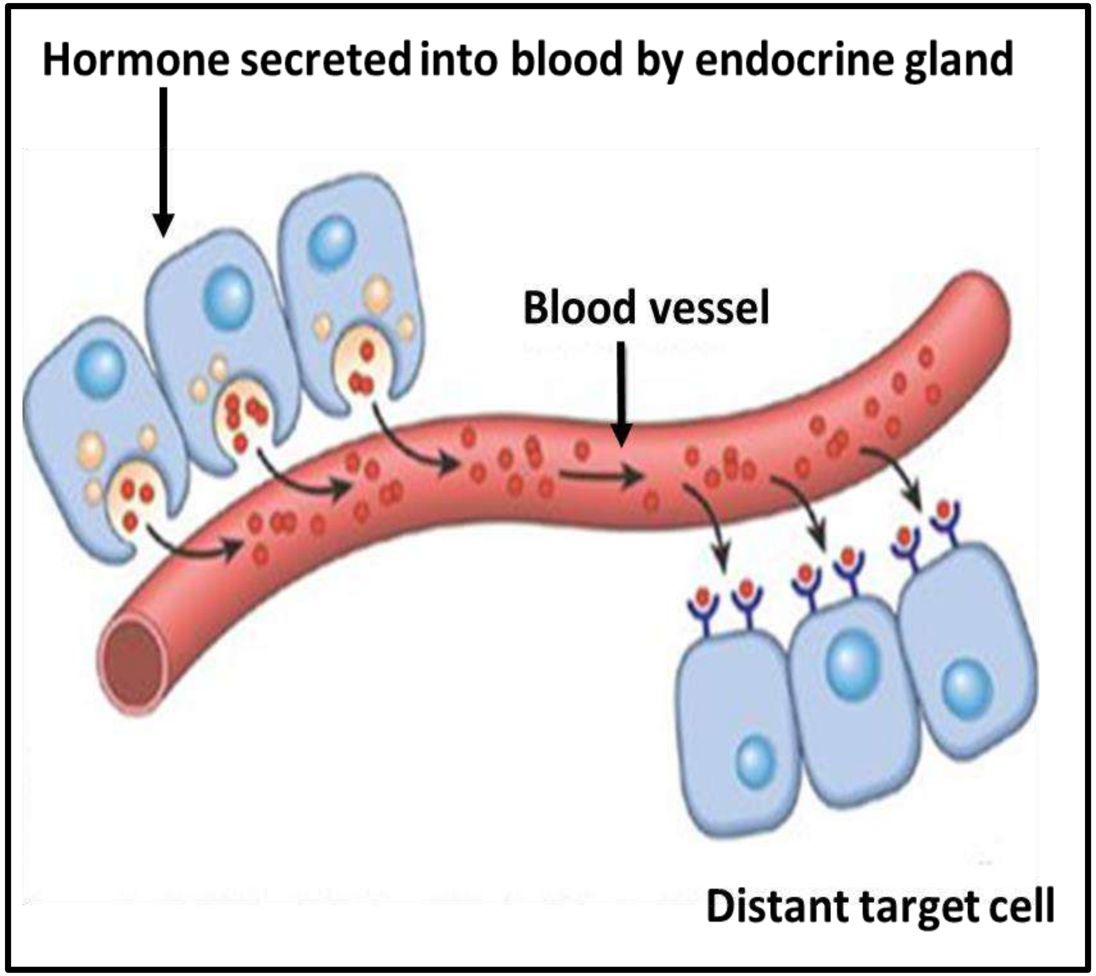
- **When the neurotransmitter binds the receptor on the surface of the postsynaptic cell, the electrochemical potential of the target cell changes, and the next electrical impulse is generated.**



Cell signaling and communication

4. Endocrine signaling

- In this type of signaling, cells transmit signals over long distances by using the circulatory system.
- These types of signals usually produce a slower response but have a longer-lasting effect.
- The signals are originated from endocrine cells which are located in endocrine glands, such as the thyroid gland, the hypothalamus, and the pituitary gland.
- The ligands released in endocrine signaling are called hormones, which are signaling molecules produced in one part of the body but affect other body regions some distance away.
- Hormones travel large distances from endocrine cells via the bloodstream to reach their target cells, and then they bind with their specific receptors.

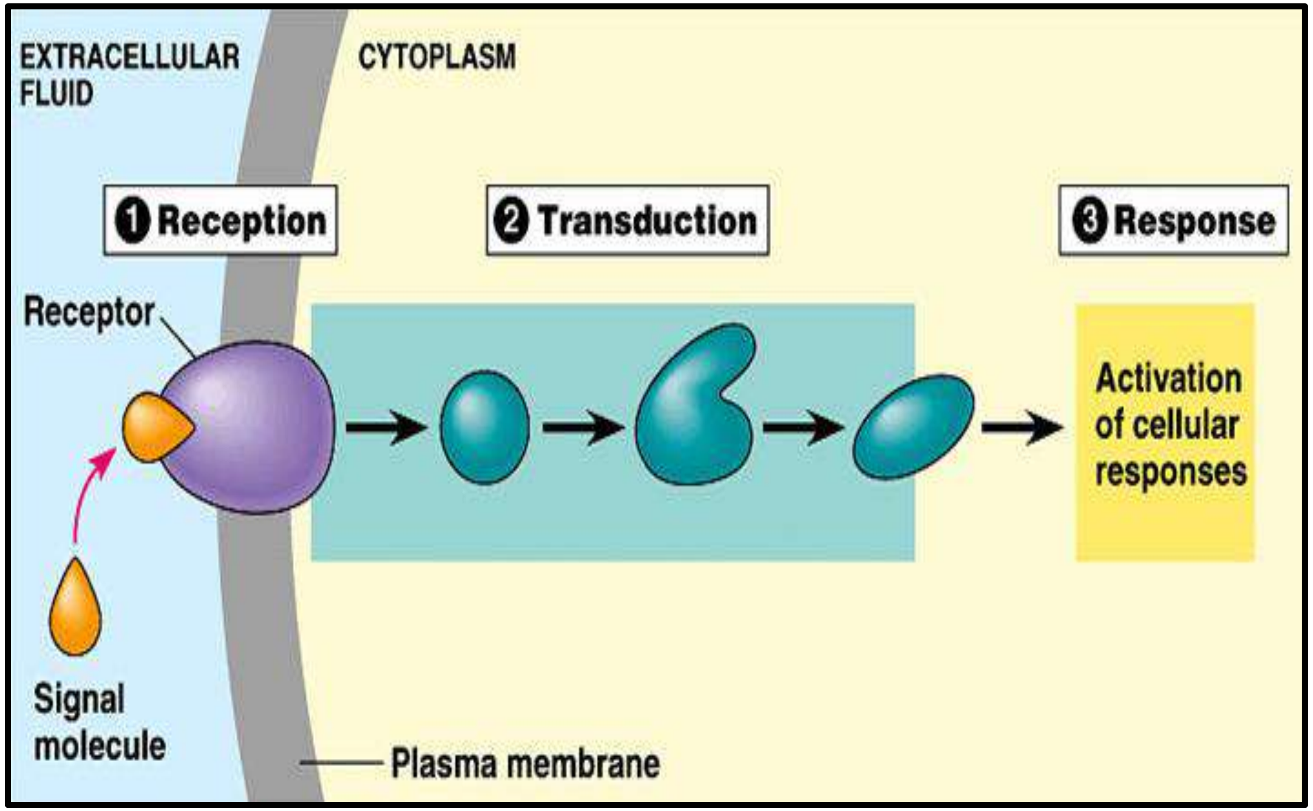


Cell signaling and communication

Stages of cell signaling

- The signaling process from signal detection to final response is called signal transduction pathway.
- There are three stages during signal transduction pathway:

1. Reception: in which the signal molecule binds to the receptor.
2. Transduction: in which the chemical signal results in a series of enzyme activation required to produce the final response.
3. Response: which is the final stage of the signaling process resulting cellular responses.



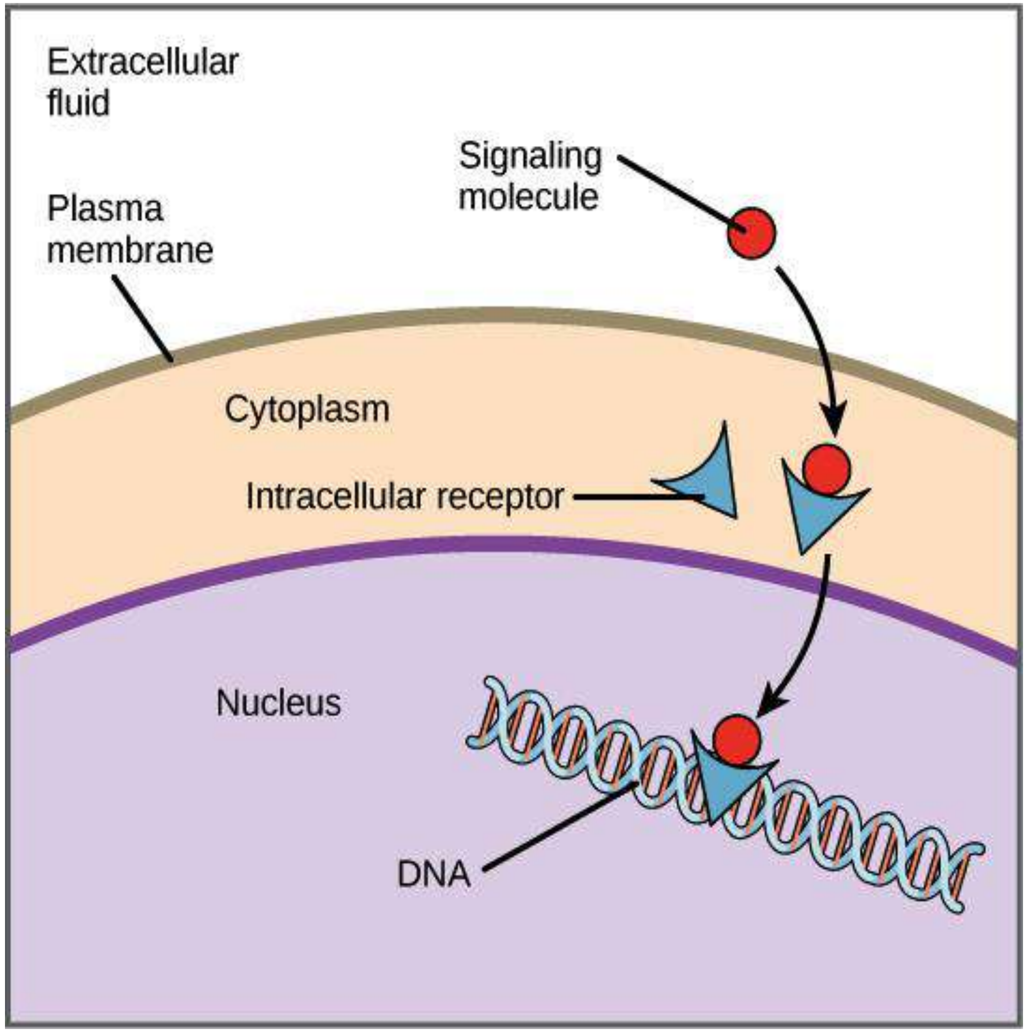
Cell signaling and communication

Types of receptors

- Receptor is a protein molecule in the target cell or on its surface that binds a specific ligand.
- There are two types of receptors, internal receptors and cell-surface receptors.

1. Internal receptors

- They are receptor proteins found inside the cell, typically in the cytoplasm (cytoplasmic receptors) or nucleus (nuclear receptors) and respond to hydrophobic ligands that are able to travel across the plasma membrane.
- Many of these ligands bind to proteins regulating mRNA synthesis to mediate protein synthesis.



- When the ligand binds to the internal receptor, a conformational change is triggered that exposes a DNA-binding site on the receptor. The ligand-receptor complex moves into the nucleus, then binds to the specific region of the DNA and promotes the initiation of transcription.

Cell signaling and communication

Types of receptors

2. Cell-surface receptors

- **Cell-surface receptors, also known as transmembrane receptors, are membrane- proteins that bind to ligands on the outside surface of the cell.**
- **These receptors span the plasma membrane and performs signal transduction, in which an extracellular signal is converted into an intercellular signal.**
- **In this type of signaling, the ligand does not need to cross the plasma membrane. So, many different kinds of molecules (including large molecules, and hydrophilic molecules) can act as ligands.**
- **Each cell-surface receptor has three main components:**
  - **External ligand-binding domain (extracellular domain)**
  - **Hydrophobic membrane-spanning region**
  - **Intracellular domain inside the cell which often transmits a signal**
- **The size and extent of each of these domains vary widely, depending on the type of receptor.**

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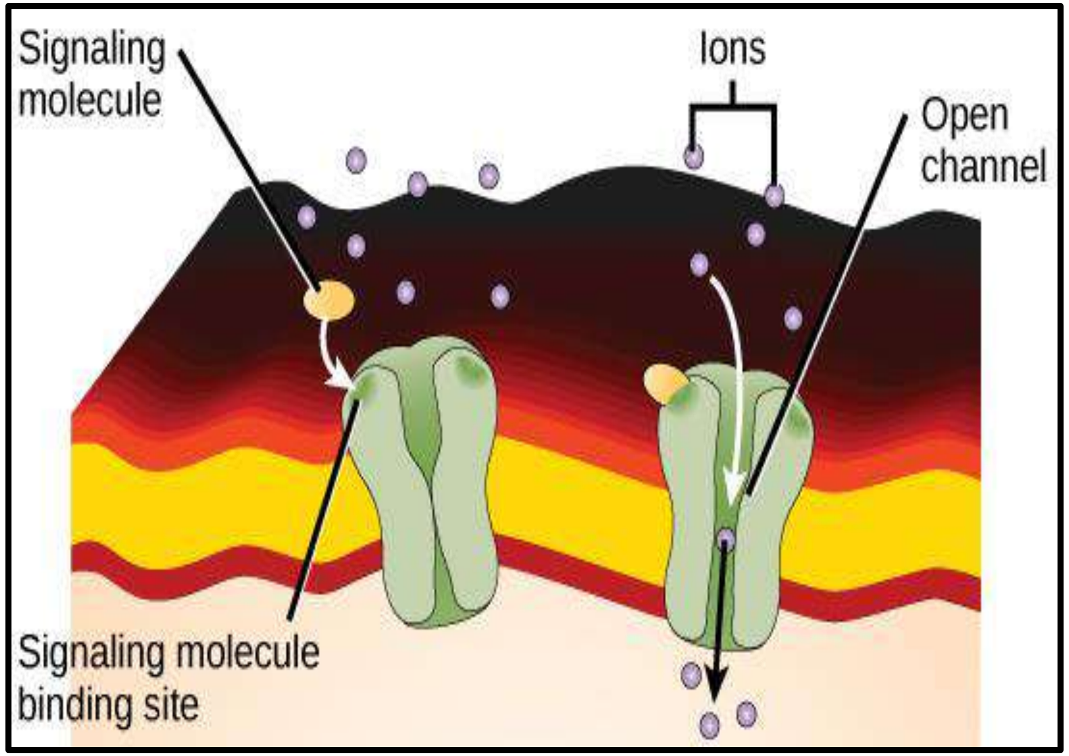
Types of receptors

2. Cell-surface receptors

- There are different kinds of cell-surface receptors: ligand-gated ion channels, G protein-coupled receptors, and enzyme-linked receptors .

a. ligand-gated ion channels

- They are also called ion channel-linked receptors that bind an external ligand at their extracellular region.
- When a ligand binds to the extracellular region of the channel, a conformational change in the protein structure occurs that allows ions such as sodium, calcium, magnesium, and hydrogen to pass through.
- Nerve cells have ligand-gated channels that are bound by neurotransmitters as acetylcholine.



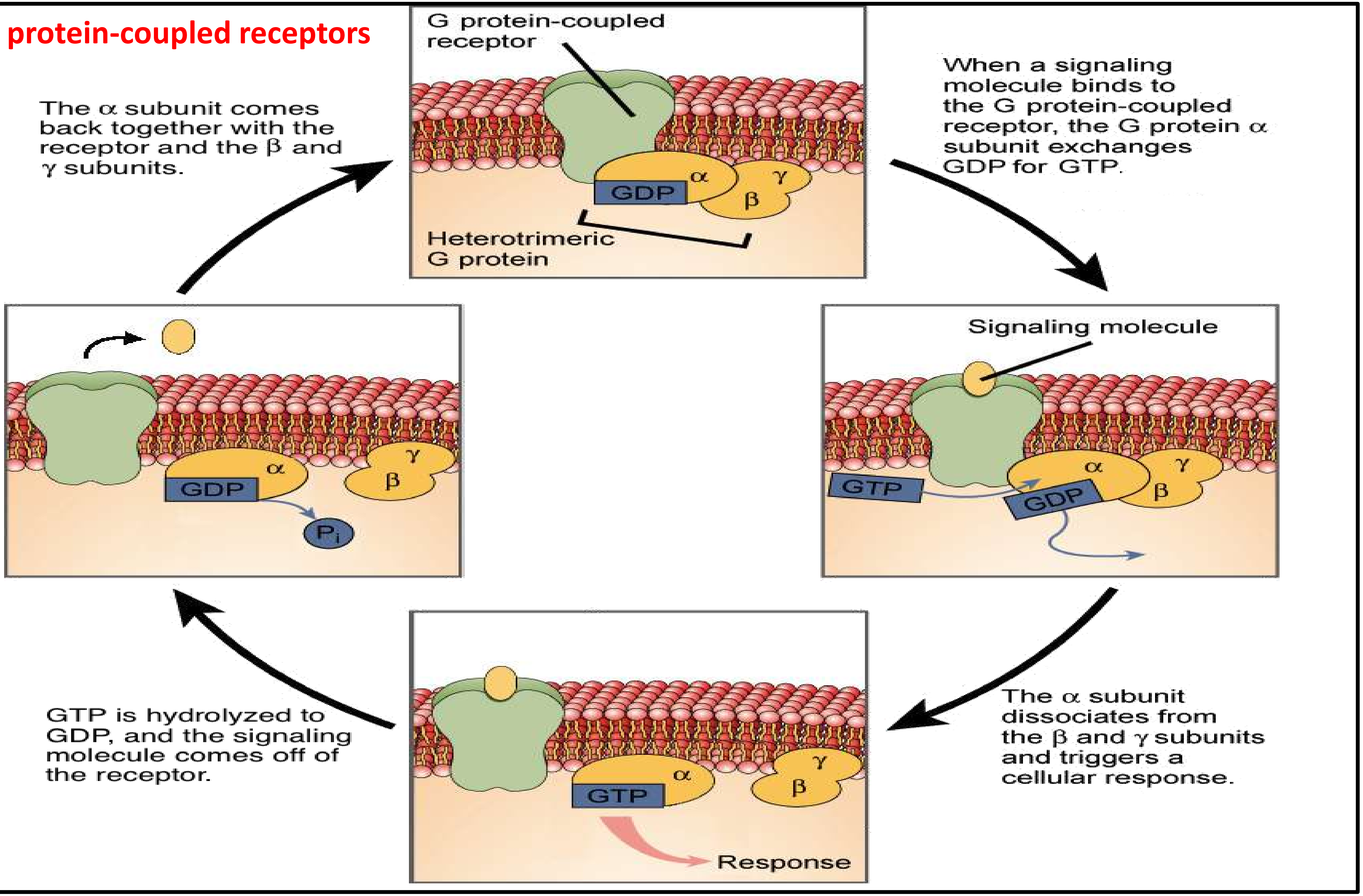
Cell signaling and communication

Types of receptors

b. G protein-coupled receptors

- **They are the largest family of cell surface receptors that share a common structure and signaling method.**
- **They transmit signals inside the cell through a type of protein called a G protein.**
- **When its ligand is not present, a G protein-coupled receptor is found in an inactive state, where α, β and γ subunits are associated together and guanosine diphosphate (GDP) is bound to α subunit.**
- **Once the ligand binds to the receptor, the G-protein is activated where GDP is released and guanosine triphosphate (GTP) is bound to α subunit.**
- **Then the subunits of the G-protein are separated into α subunit with GTP and βγ subunit. One or both of these G-protein fragments are be able to activate other enzymes and second messenger activators to generate the cell response.**
- **After awhile, the GTP on the active α subunit of the G-protein is hydrolyzed to GDP, and α, β and γ subunits are re-associated to form the inactive G-protein and the cycle begins again.**

G protein-coupled receptors

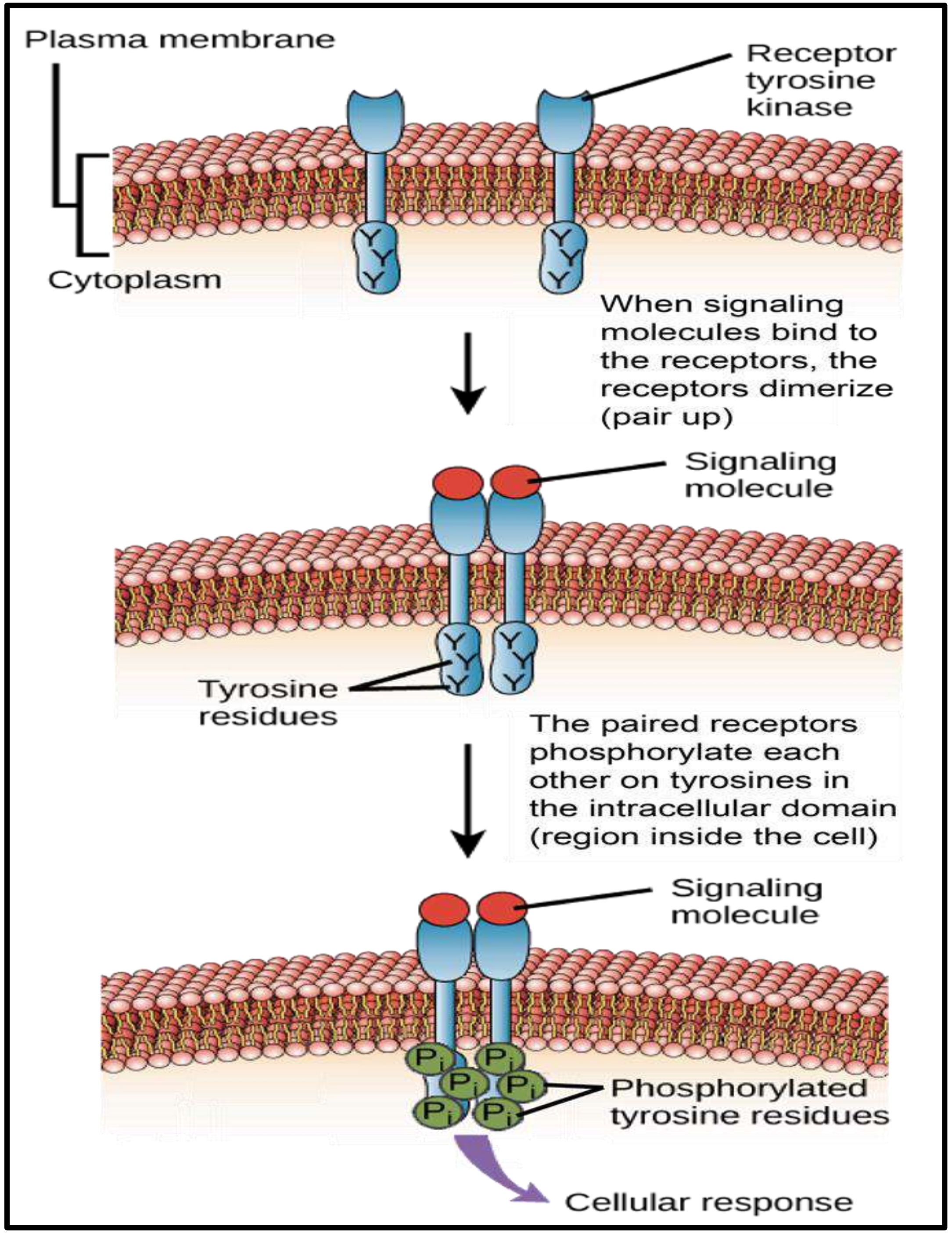


Cell signaling and communication

Types of receptors

c. Enzyme-linked receptors

- **Enzyme-linked receptors are cell-surface receptors with intracellular domains that are associated with an enzyme.**
- **In some cases, the intracellular domain of the receptor actually is an enzyme that can catalyze a reaction. Other enzyme-linked receptors have an intracellular domain that interacts with an enzyme.**
- **The best example of the enzyme-linked receptors are receptor tyrosine kinases** (**RTKs**).
- **A kinase is just a name for an enzyme that transfers phosphate groups to a protein or other target in a process known as phosphorylation.**



Cell signaling and communication

Types of receptors

c. Enzyme-linked receptors

- So, in receptor tyrosine kinases the phosphate groups are transferred to the amino acid tyrosine.
- To initiate signals through receptor tyrosine kinases, signaling molecules firstly bind to the extracellular domain of two adjacent tyrosine kinase receptors.
- The two neighboring receptors then bind together, or dimerize. Phosphates are then added to tyrosine residues on the intracellular domain of the receptors (phosphorylation).
- The phosphorylated residues can then initiate a downstream signaling cascade that leads to a cellular response.