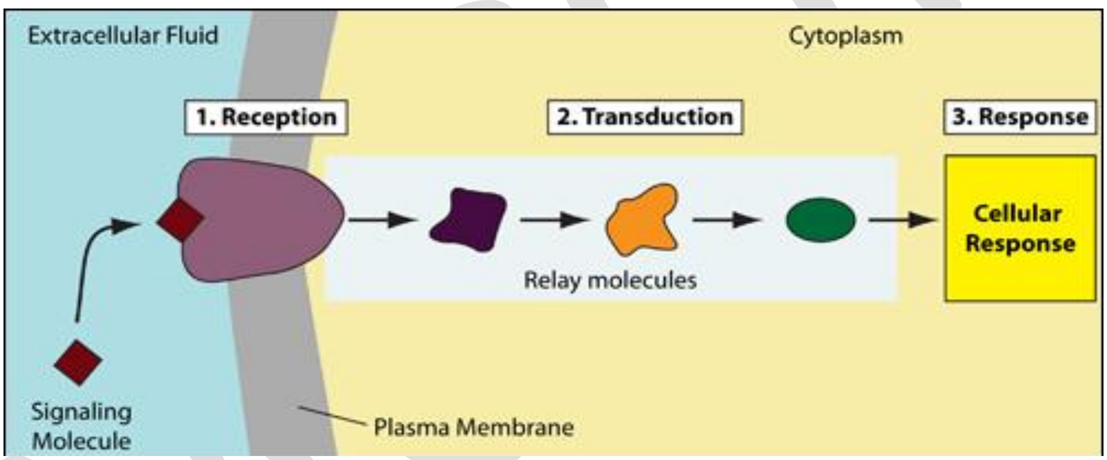
Signal Reception & Transduction

Cells in a multicellular organism communicate with one another to regulate tissue and organ development, to control their growth and division, and to coordinate their functions.

- **Cell signaling** (also known as **Signal transduction**) is the transmission of molecular signals (These chemical signals, which are proteins or other molecules) from a cell's exterior to its interior. Signals received by cells must be transmitted effectively into the cell to ensure an appropriate response. This step is initiated by cell receptors.

- **Phases of Signal Transduction:** There are three stages in the process of cell signaling:

1. **Reception**: It's the cell's detection of a signaling molecule (**ligand**) coming from outside of the cell. The signal is detected when the molecule binds to the receptor located at the cell's surface or inside the cell.
2. **Transduction**: The receptor protein is changed when the signaling molecule binds to it which initiates the process of transduction. In transduction the signal is converted to a form that can bring specific cellular response.
3. **Response**: It's the stage of cell signaling where the signal finally triggers a specific cellular response.



- **Signaling Molecules (ligands):** Signaling molecules are necessary for the coordination of cellular responses by serving as ligands and binding to cell receptors.

Types of the Signaling Molecules

The types of molecules that serve as **ligands** are incredibly varied and range from small proteins to small ions like calcium.

1. Small Hydrophobic Ligands

Small hydrophobic ligands can directly diffuse through the plasma membrane and interact with internal receptors. Important members of this class of ligands are the steroid hormones, such as female sex hormone, estradiol; the male sex hormone, testosterone; and cholesterol. Other hydrophobic hormones include thyroid hormones and vitamin D. In order to be soluble in blood, hydrophobic ligands must bind to carrier proteins while they are being transported through the bloodstream.

2. Water-Soluble Ligands

Water-soluble ligands are polar and, therefore, cannot pass through the plasma membrane unaided; sometimes, they are too large to pass through the membrane at all. Instead, most water-soluble ligands bind to the extracellular domain of cell-surface receptors.

These water soluble ligands are quite diverse and include small molecules, peptides, and proteins.

3. Other Ligands

Nitric oxide (NO) is **a gas** that also acts as a ligand. It is able to diffuse directly across the plasma membrane; one of its roles is to interact with receptors in smooth muscle and induce relaxation of the tissue.

NO has a very short half-life; therefore, it only functions over short distances. Nitroglycerin, a treatment for heart disease, acts by triggering the release of NO, which causes blood vessels to dilate (expand), thus restoring blood flow to the heart.

❖ Types of Cell Receptors

Receptors are protein molecules in the target cell or on its surface that bind ligands. There are two types of receptors: internal receptors and cell-surface receptors.

1. Internal receptors

Internal receptors, also known as intracellular receptors (cytoplasmic or nuclear) are found inside the cell (the cytoplasm or the nucleus) and respond to hydrophobic ligand molecules that are able to travel across the plasma membrane. Once inside the cell, many of these molecules bind to proteins that act as regulators of mRNA synthesis to mediate gene expression. Internal receptors can directly influence gene expression without having to pass the signal on to other receptors or messengers.

2. Cell-Surface Receptors

Cell-surface receptors, also known as transmembrane receptors, are cell surface, membrane-anchored (peripheral), or integral proteins that bind to external ligand molecules. This type of receptor spans the plasma membrane and performs signal transduction, converting an extracellular signal into an intracellular signal. Ligands that interact with cell-surface receptors do not have to enter the cell that they affect. Cell-surface receptors are also called cell-specific proteins or markers because they are specific to individual cell types.

Types of Cell Surface Receptors: There are three general categories of cell-surface receptors:

1. Ion Channel-Linked Receptors

Ion channel-linked receptors bind a ligand and open a channel through the membrane that allows specific ions to pass through. When a ligand binds to the extracellular region of the channel, there is a conformational change in the protein’s structure that allows ions such as chloride ions and hydrogen ions to pass through.

2. Enzyme-Linked Receptors

Enzyme-linked receptors are cell-surface receptors with intracellular domains that are associated with an enzyme. When a ligand binds to the extracellular domain, a signal is transferred through the membrane and activates the enzyme, which sets off a chain of events within the cell that eventually leads to a response. An example of this type of enzyme-linked receptor is **the tyrosine kinase receptor**.

3. G-Protein Linked Receptors

G-protein-linked receptors bind a ligand and activate a membrane protein called a G-protein. The activated G-protein then interacts with either an ion channel or an enzyme in the membrane.

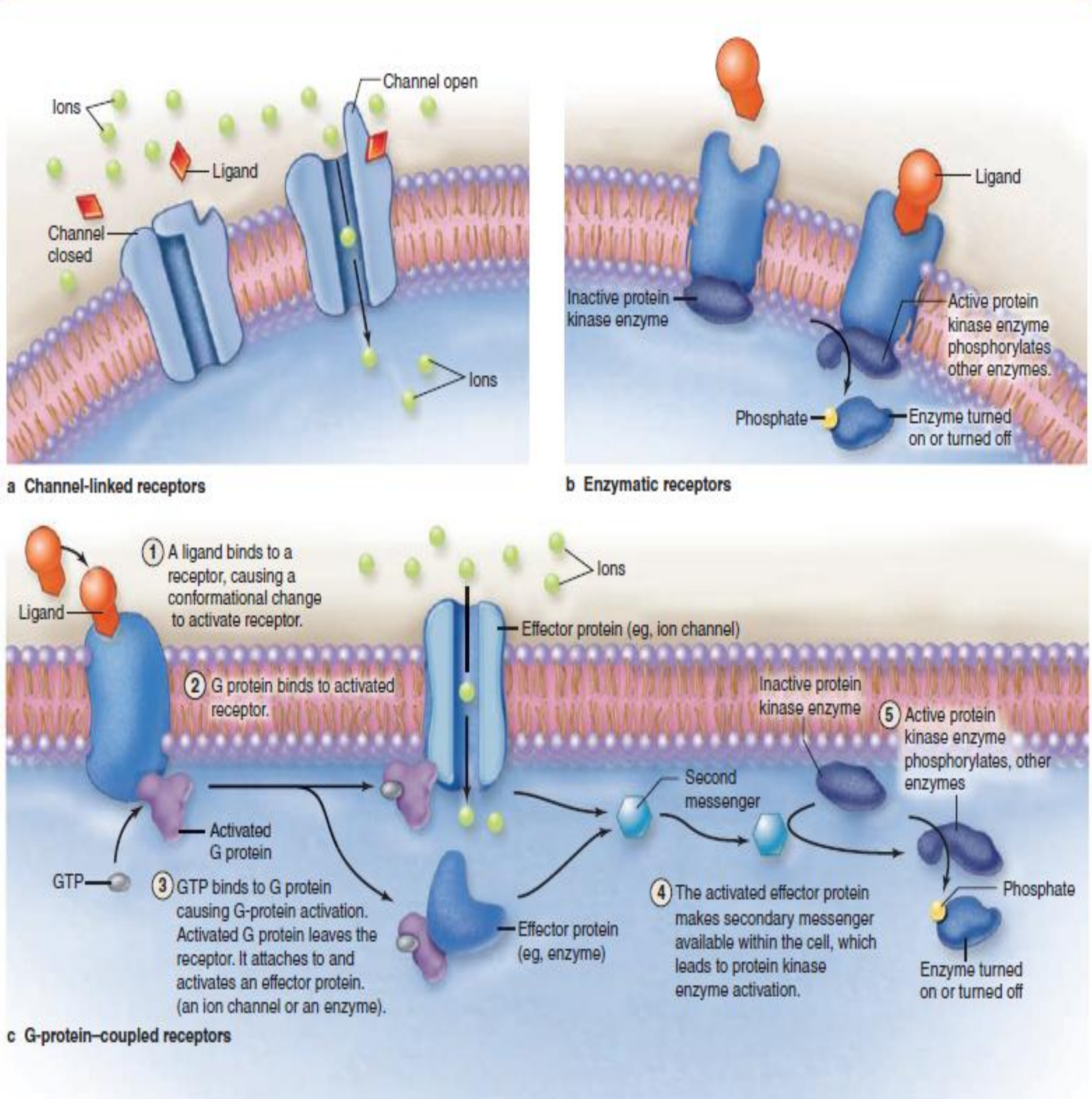


Figure of major types of membrane receptors

❖ MEDICAL APPLICATION

Many diseases are caused by defective receptors. For example, pseudohypoparathyroidism and one type of dwarfism are caused by nonfunctioning parathyroid and growth hormone receptors, respectively. In these two conditions the glands produce the respective hormones, but the target cells cannot respond because they lack normal receptors.

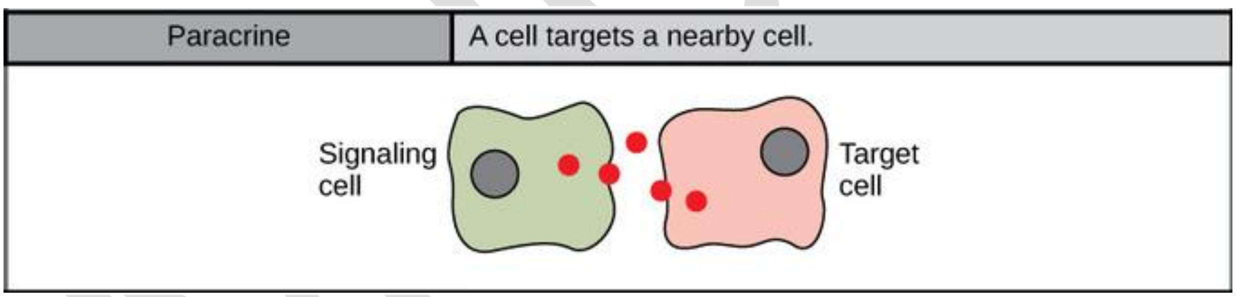
❖ Types of Signaling

The major types of signaling mechanisms that occur in multicellular organisms are**: Paracrine, Endocrine, Autocrine, and Direct Signaling (Juxtacrine).** The main difference between the different categories of signaling is the distance that the signal travels through the organism to reach the target cell.

1. Paracrine Signaling

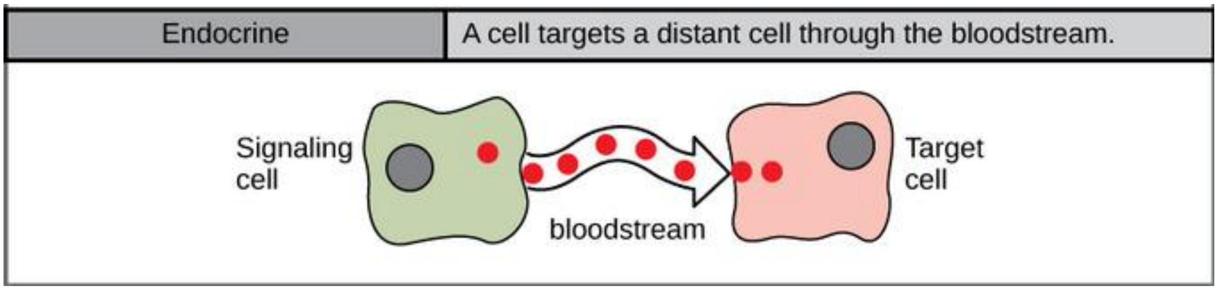
Signals that act locally between cells those are close together. Paracrine signals move by diffusion through the extracellular matrix. These types of signals usually elicit quick responses that last only a short period of time.

In order to keep the response localized, paracrine ligand molecules are normally quickly degraded by enzymes or removed by neighboring cells. Removing the signals will reestablish the concentration gradient for the signal, allowing them to quickly diffuse through the intracellular space if released again. One example of paracrine signaling is the transfer of signals across synapses between nerve cells.Synaptic signaling is unique example of paracrine signaling; in which nerve cells transmit signals. This process is named for the **synapse**, the junction between two nerve cells where signal transmission occurs.



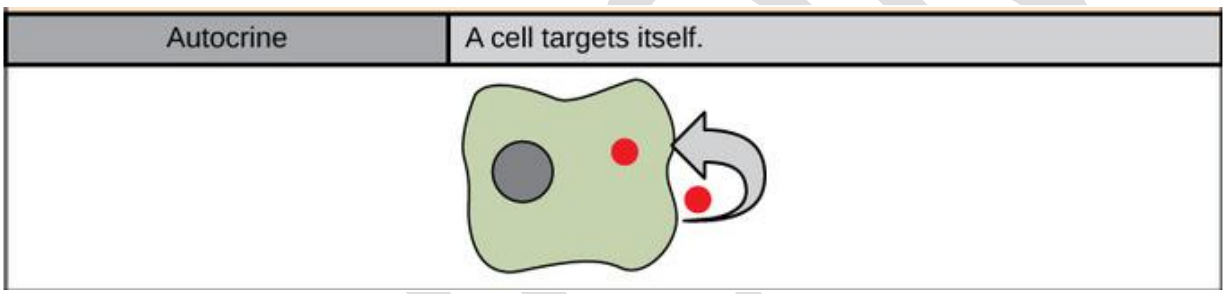
2. Endocrine Signaling

Signals from distant cells are called endocrine signals; they originate from endocrine cells, such as cells of the thyroid gland, the hypothalamus, the pituitary gland as well as the gonads (testes and ovaries) and the pancreas. These types of signals usually produce a slower response, but have a longer-lasting effect. The ligands released in endocrine signaling are called **hormones**, which are signaling molecules that are produced in one part of the body, but affect other body regions some distance away.Hormones travel the large distances between endocrine cells and their target cells via the bloodstream, which is a relatively slow way to move throughout the body.



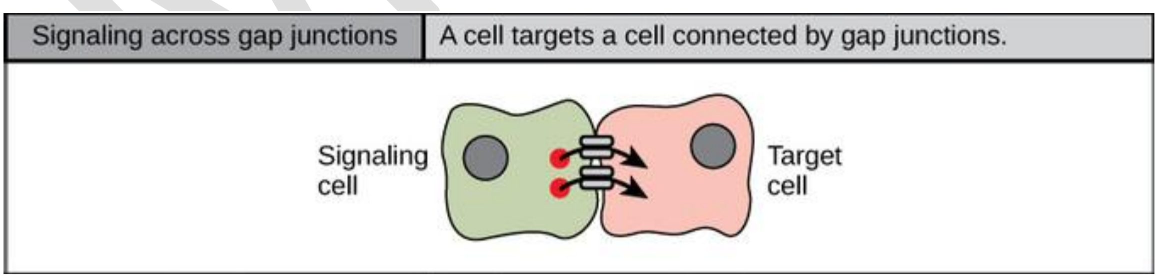
3. Autocrine Signaling

Autocrine signals are produced by signaling cells that can also bind to the ligand that is released. This means the signaling cell and the target cell can be the same or a similar cell. 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. Autocrine signaling also regulates pain sensation and inflammatory responses. 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.



4. Direct Signaling Across Gap Junctions

Gap junctions are connections between the plasma membranes of neighboring cells. These water-filled channels allow small signaling molecules, called **intracellular mediators**, to diffuse between the two cells. Small molecules, such as calcium ions, are able to move between cells, but large molecules, like proteins and DNA, cannot fit through the channels. The transfer of signaling molecules communicates the current state of the cell that is directly next to the target cell; this allows a group of cells to coordinate their response to a signal that only one of them may have received.



Medical applications of cell signaling involve targeting signaling pathways to treat diseases like cancer and inflammatory conditions. For example, some cancer therapies block signals that cause uncontrolled cell growth, while others, like those for rheumatoid arthritis, use drugs to stop inflammatory signals between immune cells. Cell signaling is also crucial for the nervous system's function and is involved in regulating the body's internal balance (homeostasis).