Adv. Cell Biology **MSc Student** **Dr. Treefa Farouq Ismail**

Signaling Molecules

In multicellular organisms, cells send and receive chemical messages constantly to coordinate the actions of distant organs, tissues, and cells. The ability to send messages quickly and efficiently enables cells to coordinate and fine-tune their functions.

Signaling molecules interact with a target cell as a ligand to cell surface receptors, and/or by entering into the cell through its membrane or endocytosis for intracrine signaling. This generally results in the activation of second messengers, leading to various physiological effects.

A particular molecule is generally used in diverse modes of signaling, and therefore a classification by mode of signaling is not possible. At least three important classes of signaling molecules are widely recognized:

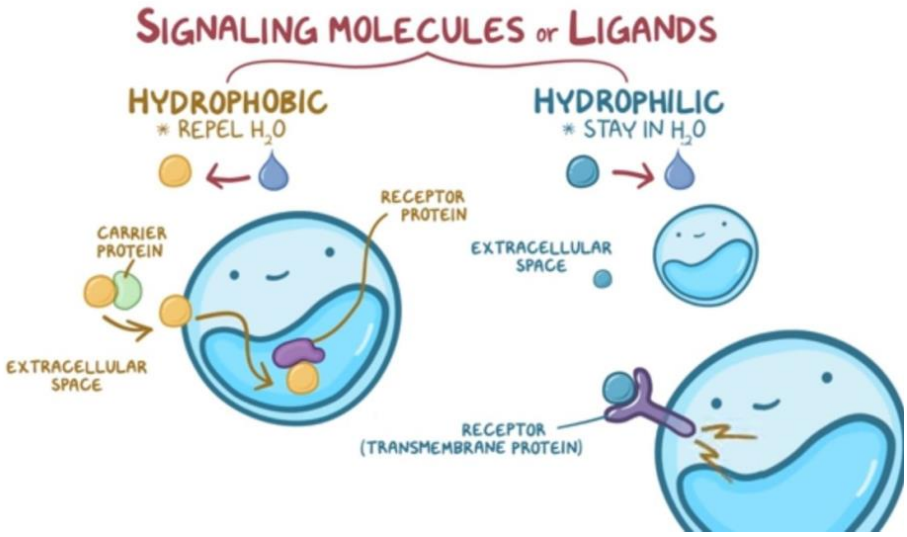
- Hormones are the major signaling molecules of the endocrine system, though they often regulate each other's secretion via local signaling (e.g. islet of Langerhans cells).
- Neurotransmitters are signaling molecules of the nervous system, also including neuropeptides and neuromodulators. Neurotransmitters like the catecholamines are also secreted by the endocrine system into the systemic circulation.
- Cytokines are signaling molecules of the immune system, with a primary paracrine or juxtacrine role, though they can during significant immune responses have a strong presence in the circulation, with systemic effect (altering iron metabolism or body temperature). Growth factors can be considered as cytokines or a different class.

Signaling molecules can belong to several chemical classes: lipids, phospholipids, amino acids, monoamines, proteins, glycoproteins, or gases.

Signaling molecules binding surface receptors are generally large and hydrophilic (e.g. TRH (Thyrotropin-releasing hormone is the master regulator of **thyroid gland growth** and function (including the **secretion** of the **thyroid** hormones thyroxine and triiodothyronine). These hormones control the body's metabolic rate, heat generation, neuromuscular function and heart rate, among other things.), Vasopressin (**Antidiuretic Hormone**), the primary function of AVP in the body is to regulate extracellular fluid

volume by regulating renal handling of water) , Acetylcholine (is an organic chemical that functions in the brain and body as a neurotransmitter—a chemical message released by nerve cells to send signals to other cells, such as neurons, muscle cells and gland cells.), while those entering the cell are generally small and hydrophobic (e.g. glucocorticoids, thyroid hormones, cholecalciferol, retinoic acid), but important exceptions to both are numerous, and a same molecule can act both via surface receptor or in an intracrine manner to different effects.

Hydrogen sulfide is produced in small amounts by some cells of the human body and has a number of biological signaling functions. Only two other such gases are currently known to act as signaling molecules in the human body: nitric oxide and carbon monoxide.



Signaling molecules are often called **ligands**, a general term for molecules that bind specifically to other molecules (such as receptors).

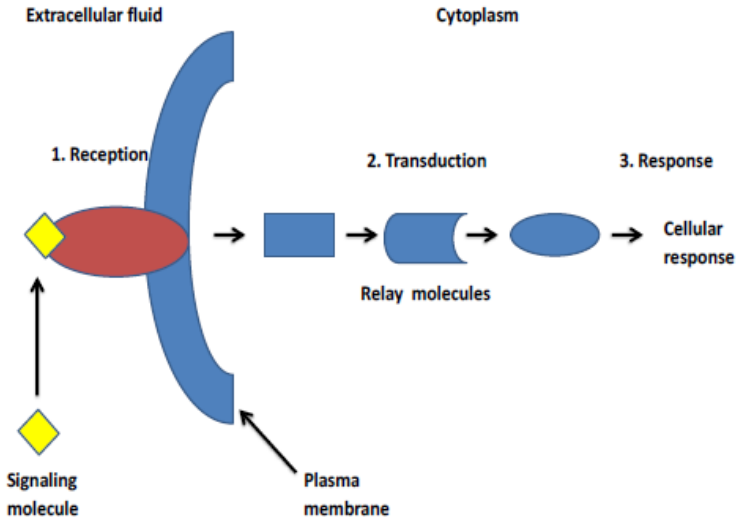
The message carried by a ligand is often relayed through a chain of chemical messengers inside the cell. Ultimately, it leads to a change in the cell, such as alteration in the activity of a gene or even the induction of a whole process, such as cell division. Thus, the original **intercellular** (between-cells) signal is converted into an **intracellular** (within-cell) signal that triggers a response.

Cell signaling can be divided into 3 stages:

1. Reception: A cell detects a signaling molecule from the outside of the cell. A signal is detected when the ligand binds to a receptor protein on the surface of the cell or inside the cell.

2. Transduction: When the signaling molecule binds to the receptor, it changes the receptor protein. This change initiates the process of transduction. Each relay molecule in the signal transduction pathway changes the next molecule in the pathway.

3. Response: Finally, the signal triggers a specific cellular response



Forms of Signaling

Cell-cell signaling involves the transmission of a signal from a sending cell to a receiving cell. However, not all sending and receiving cells are next-door neighbors, nor do all cell pairs exchange signals in the same way.

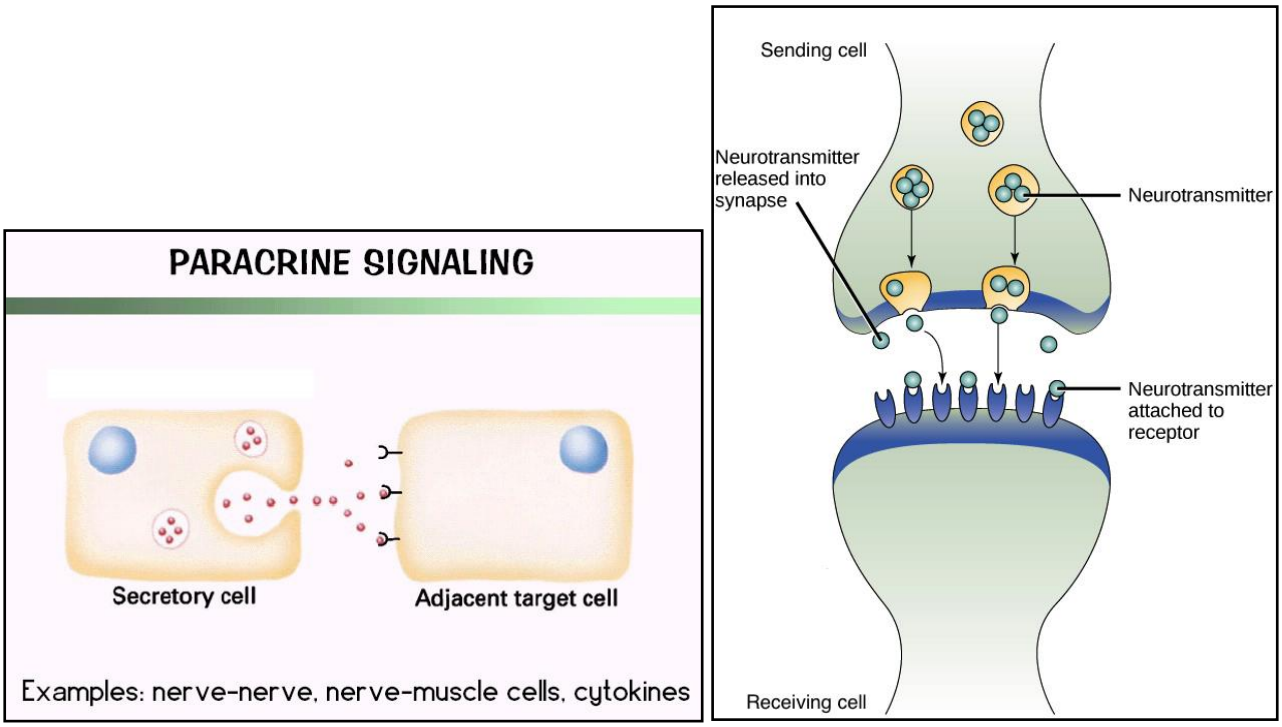
There are four basic categories of chemical signaling found in multicellular organisms: paracrine signaling, autocrine signaling, endocrine signaling, and signaling by direct contact. The main difference between the different categories of signaling is the distance that the signal travels through the organism to reach the target cell.

Paracrine signaling

Often, cells that are near one another communicate through the release of chemical messengers (ligands that can diffuse through the space between the cells). This type of signaling, in which cells communicate over relatively short distances, is known as **paracrine signaling**.

Paracrine signaling allows cells to locally coordinate activities with their neighbors. Although they're used in many different tissues and contexts, paracrine signals are especially important during development, when they allow one group of cells to tell a neighboring group of cells what cellular identity to take on.

One unique example of paracrine signaling is **synaptic signaling**, in which nerve cells transmit signals. This process is named for the **synapse**, the junction between two nerve cells where signal transmission occurs.



Synaptic signaling. Neurotransmitter is released from vesicles at the end of the axon of the sending cell. It diffuses across the small gap between sending and target neurons and binds to receptors on the target neuron.

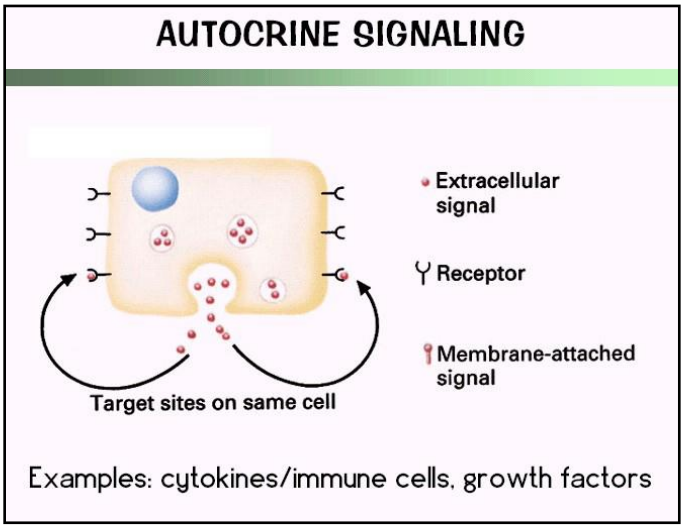
The neurotransmitters that are released into the chemical synapse are quickly degraded or taken back up by the sending cell. This "resets" the system so they synapse is prepared to respond quickly to the next signal.

Autocrine signaling

In **autocrine signaling**, a cell signals to itself, releasing a ligand that binds to receptors on its own surface (or, depending on the type of signal, to receptors inside of the cell).

This may seem like an odd thing for a cell to do, but autocrine signaling plays an important role in many processes.

For instance, autocrine signaling is important during development, helping cells take on and reinforce their correct identities. From a medical standpoint, autocrine signaling is important in cancer and is thought to play a key role in metastasis (the spread of cancer from its original site to other parts of the body). In many cases, a signal may have both autocrine and paracrine effects, binding to the sending cell as well as other similar cells in the area.



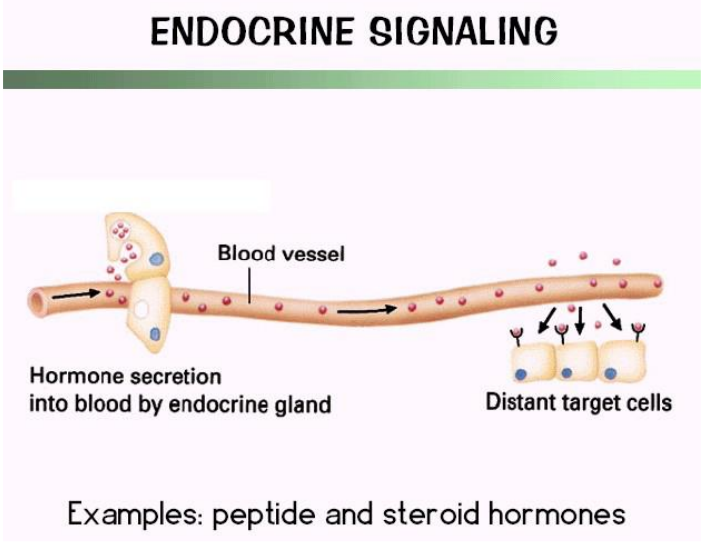
Endocrine signaling

When cells need to transmit signals over long distances, they often use the circulatory system as a distribution network for the messages they send. In long-distance **endocrine signaling**, signals are produced by specialized cells and released into the bloodstream, which carries them to target cells in distant parts of the body. Signals that are produced in one part of the body and travel through the circulation to reach far-away targets are known as **hormones**.

In humans, endocrine glands that release hormones include the thyroid, the hypothalamus, and the pituitary, as well as the gonads (testes and ovaries) and the pancreas. Each endocrine gland releases one or more types of hormones, many of which are master regulators of development and physiology.

For example, the pituitary releases **growth hormone** (**GH**), which promotes growth, particularly of the skeleton and cartilage. Like most hormones, GH affects many different types of cells throughout the body. However, cartilage cells provide one example of how

GH functions: it binds to receptors on the surface of these cells and encourages them to divide.

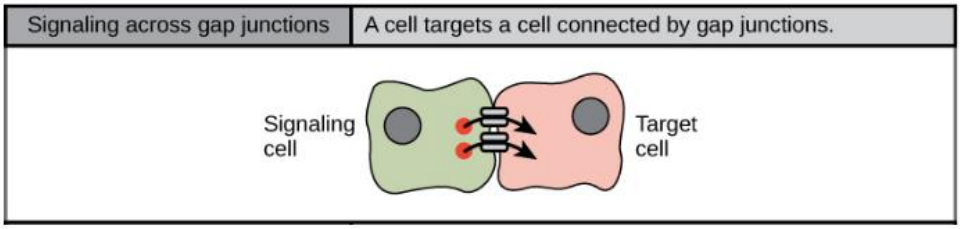


Endocrine signaling: a cell targets a distant cell through the bloodstream. A signaling molecule is released by one cell, then travels through the bloodstream to bind to receptors on a distant target cell elsewhere in the body.

Signaling through cell-cell contact

Gap junctions in animals and plasmodesmata in plants are tiny channels that directly connect neighboring cells. These water-filled channels allow small signaling molecules, called **intracellular mediators**, to diffuse between the two cells. Small molecules and ions are able to move between cells, but large molecules like proteins and DNA cannot fit through the channels without special assistance.

The transfer of signaling molecules transmits the current state of one cell to its neighbor. This allows a group of cells to coordinate their response to a signal that only one of them may have received. In plants, there are plasmodesmata between almost all cells, making the entire plant into one giant network.



Signaling across gap junctions. A cell targets a neighboring cell connected via gap junctions. Signals travel from one cell to the other by passing through the gap junctions.

In another form of direct signaling, two cells may bind to one another because they carry complementary proteins on their surfaces. When the proteins bind to one another, this interaction changes the shape of one or both proteins, transmitting a signal. This kind of signaling is especially important in the immune system, where immune cells use cell-surface markers to recognize “self” cells (the body's own cells) and cells infected by pathogens.