Introduction to cell signalling

Learn how cells communicate with one another using different kinds of short- and long-range signalling in our bodies.

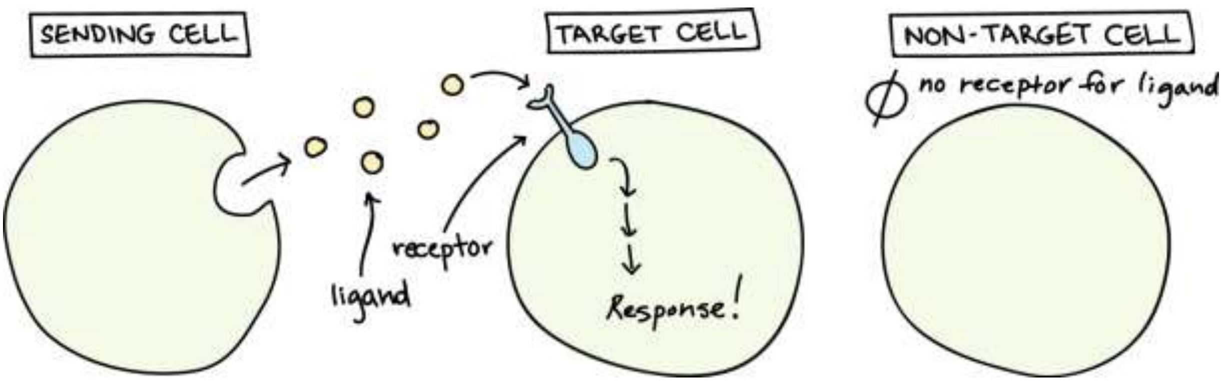
Introduction

Think your cells are just simple building blocks, unconscious and static as bricks in a wall? If so, think again! Cells can detect what's going on around them, and they can respond in real time to cues from their neighbours and environment. At this very moment, your cells are sending and receiving millions of messages in the form of chemical signalling molecules!

In this article, we'll examine the basic principles of how cells communicate with one another. We'll first look at how cell-cell signalling works, then consider different kinds of short- and long-range signalling that happen in our bodies.

Overview of cell signalling

Cells typically communicate using chemical signals. These chemical signals, which are proteins or other molecules produced by a **sending cell**, are often secreted from the cell and released into the extracellular space. There, they can float – like messages in a bottle – over to neighbouring cells.



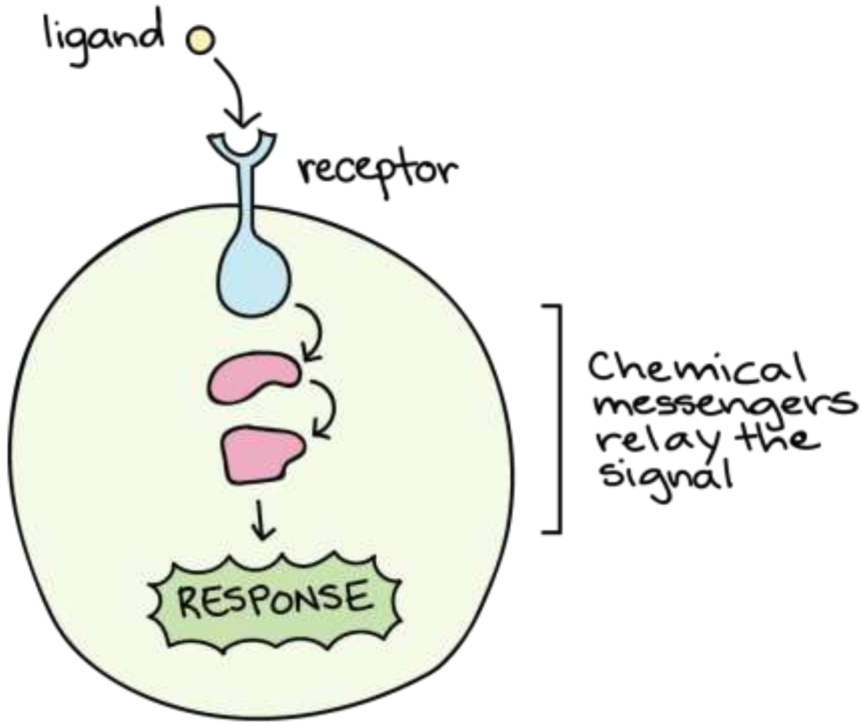
Sending cell: this cell secretes a ligand.

Target cell: this cell has a receptor that can bind the ligand. The ligand binds to the receptor and triggers a signalling cascade inside the cell, leading to a response.

Non target cell: this cell does not have a receptor for the ligand (though it may have other kinds of receptors). The cell does not perceive the ligand and thus does not respond to it.

Not all cells can “hear” a particular chemical message. In order to detect a signal (that is, to be a **target cell**), a neighbour cell must have the right **receptor** for that signal. When a signalling molecule binds to its receptor, it alters the shape or activity of the receptor, triggering a change inside of the cell. Signalling 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.



You can learn more about how this works in the articles on ligands and receptors, signal relay, and cellular responses.

Forms of signalling

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

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

Paracrine signalling

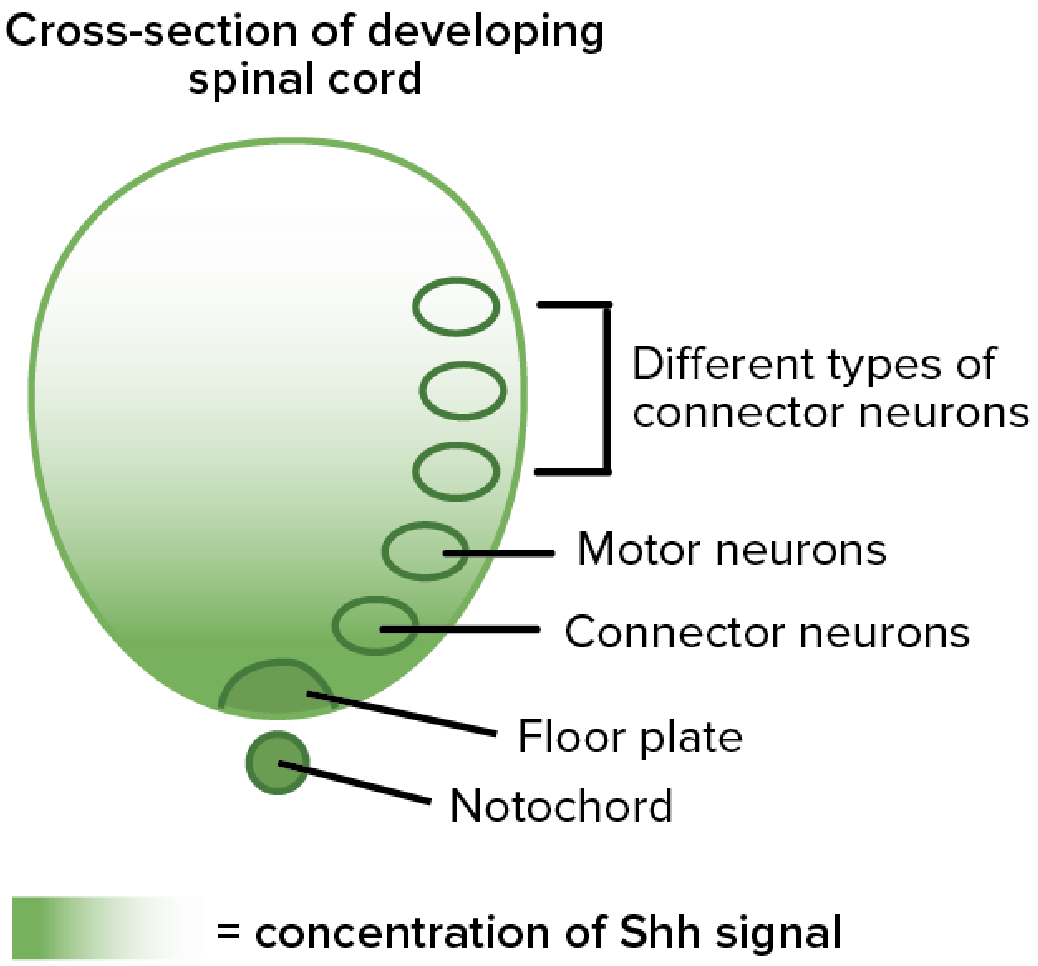
Often, cells that are near one another communicate through the release of chemical messengers (ligands that can diffuse through the space between the cells). This type of signalling, in which cells communicate over relatively short distances, is known as **paracrine signalling**.

Paracrine signalling allows cells to locally coordinate activities with their neighbours. 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 neighbouring group of cells what cellular identity to take on.

Sonic hedgehog and morphogens

The developing spinal cord of an embryo contains a hollow tube of cells that runs along the embryo's back, called the notochord, and a column of cells that runs parallel to the notochord, called the floor plate. Together, the notochord and floor plate release a signalling molecule called Sonic hedgehog (Shh).

As Shh diffuses away from the notochord and floor plate, it forms a gradient, with high levels near the source and low levels further away. The different concentrations of Shh at different points along the gradient help tell nearby cells what types of neurons they should become.



Cross-section of the developing spinal cord, showing the distribution of Shh and the specification of different types of neurons. As Shh diffuses away from the notochord and floor plate, it forms a gradient, with high levels near the source and low levels further away. The different concentrations of Shh at different points along the gradient help tell nearby cells what types of neurons they should become.

- Cells that are close to the notochord and floor plate receive a high dose of signal and become a specific type of connector neuron (interneuron).
- Cells that are a little further away get a lower dose of signal and become motor neurons (neurons that connect up to muscles).

- Cell that are even more distant from the notochord and floor plate receive progressively lower doses of signal and become other types of interneurons.

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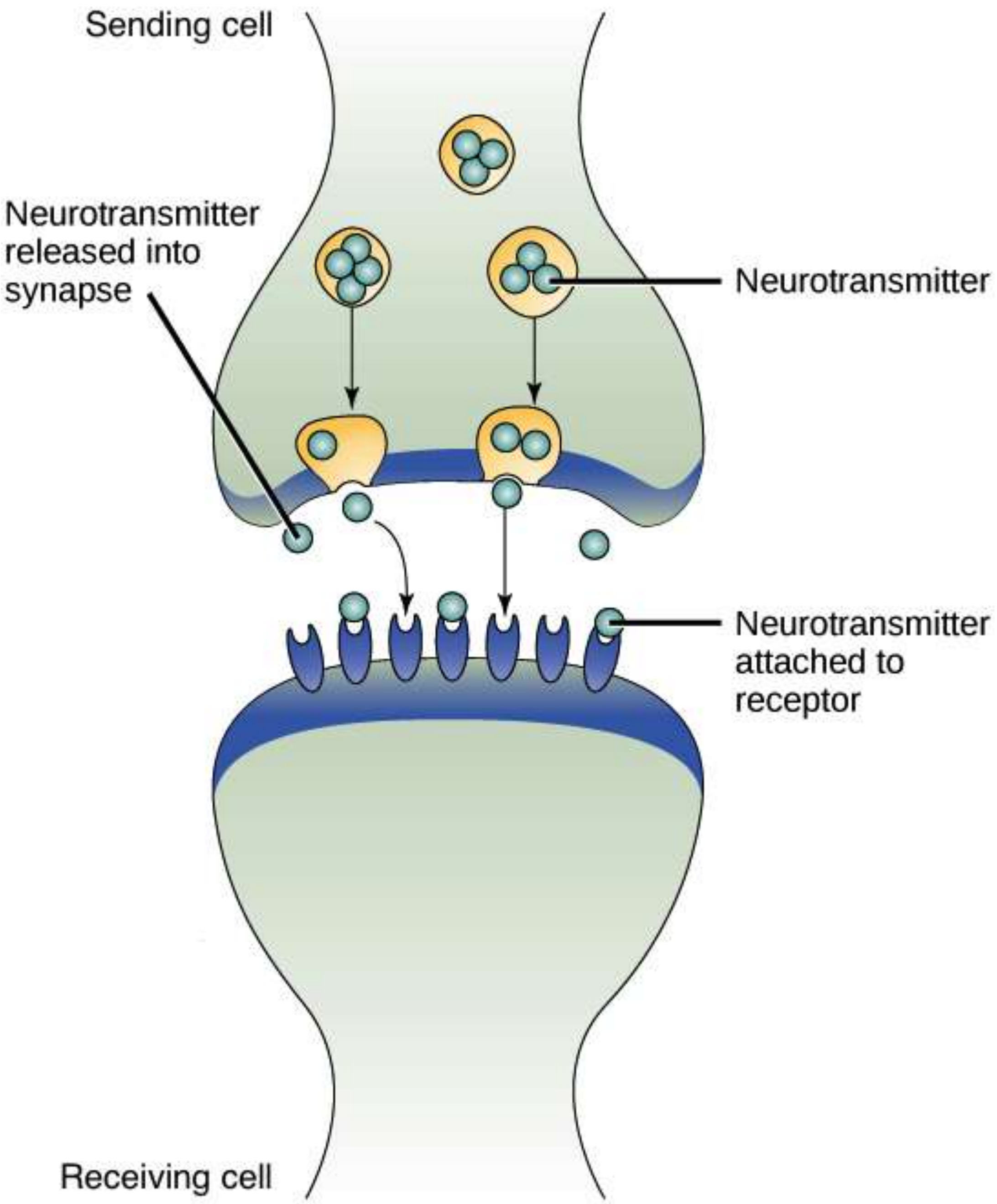
Different levels of Shh signal trigger different responses in cells, causing them to take on distinct identities and characteristics. Signals like Shh, which form gradients and produce different developmental effects depending on the dose of signal, are known as **morphogens**.
The specification of different types of neurons in the spinal cord also depends on other, non-Shh signalling pathways and on the timing of signals. We've simplified the discussion here to highlight the role of Shh as a morphogen.

As you may have guessed, the signalling molecule is named after the Sega video game character of the same name. The first gene similar to *Sonic hedgehog* was discovered in fruit flies, and flies lacking activity of this gene had a spiky-looking appearance, causing the gene to be named *hedgehog*. When a similar gene was discovered in vertebrates, it was given the related name of *Sonic hedgehog*. The researcher who named the gene had never actually played the video game, but rather, borrowed Sonic's name from a pre-release comic book belonging to his daughter.

Synaptic signalling

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

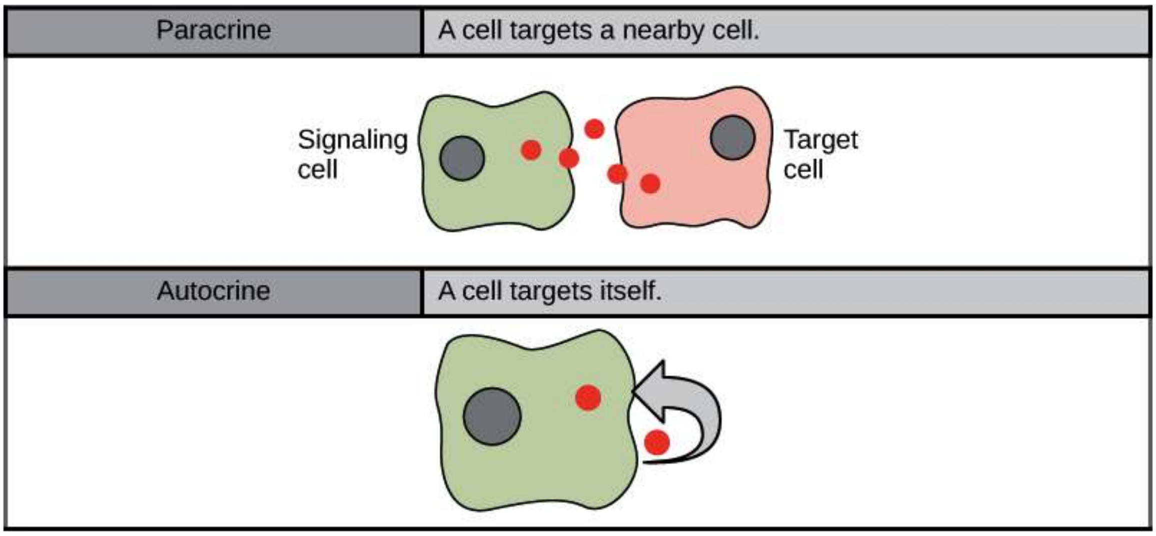
When the sending neuron fires, an electrical impulse moves rapidly through the cell, traveling down a long, fibre-like extension called an axon. When the impulse reaches the synapse, it triggers the release of ligands called **neurotransmitters**, which quickly cross the small gap between the nerve cells. When the neurotransmitters arrive at the receiving cell, they bind to receptors and cause a chemical change inside of the cell (often, opening ion channels and changing the electrical potential across the membrane).



Synaptic signalling. 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.

Image modified from "Signalling molecules and cellular receptors: Figure 2," by OpenStax College, Biology (CC BY 3.0).

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.



Paracrine signalling: a cell targets a nearby cell (one not attached by gap junctions). The image shows a signalling molecule produced by one cell diffusing a short distance to a neighbouring cell.

Autocrine signalling: a cell targets itself, releasing a signal that can bind to receptors on its own surface.

Image modified from "Signalling molecules and cellular receptors: Figure 1," by OpenStax College, Biology (CC BY 3.0).

Autocrine signalling

In **autocrine signalling**, 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 signalling plays an important role in many processes.

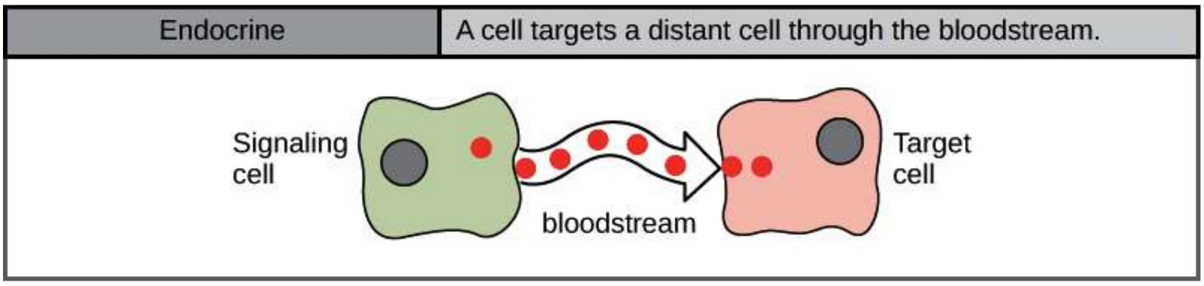
For instance, autocrine signalling is important during development, helping cells take on and reinforce their correct identities. From a medical standpoint, autocrine signalling is important in cancer and is thought to play a key role in metastasis (the spread of cancer from its original site to other 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 signalling

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

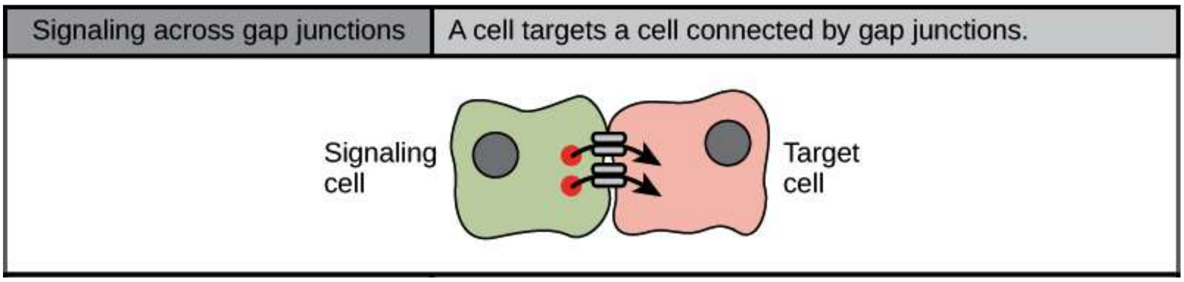
Image modified from "Signalling," by OpenStax College, Biology (CC BY 3.0).

Plants don't have endocrine cells or glands, but they do have signalling molecules that regulate growth and travel throughout the plant's body to affect distant cells. These signals are often called **plant hormones**.

Signalling through cell-cell contact

Gap junctions in animals and plasmodesmata in plants are tiny channels that directly connect neighbouring cells. These water-filled channels allow small signalling molecules, called **intracellular mediators**, to diffuse between the two cells. Small molecules, such as calcium ions (Ca_2+), are able to move between cells, but large molecules like proteins and DNA cannot fit through the channels without special assistance.

The transfer of signalling molecules transmits the current state of one cell to its neighbour. 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.



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

Image modified from "Signalling molecules and cellular receptors: Figure 1," by OpenStax College, Biology (CC BY 3.0).

In another form of direct signalling, 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 signalling 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.

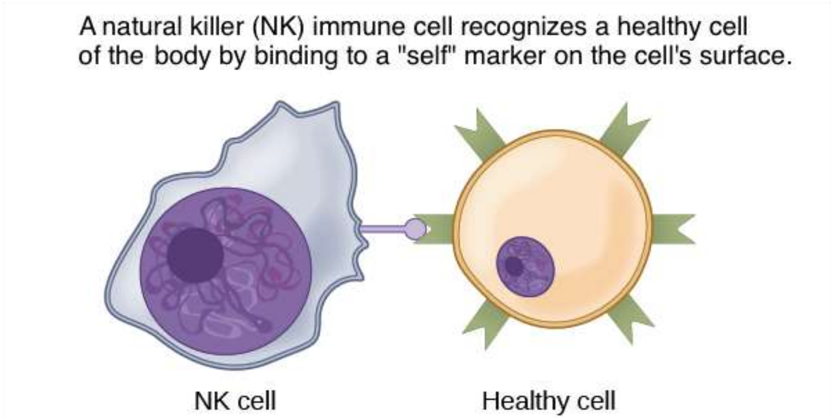


Image modified from "Adaptive immune response: Figure 7," by OpenStax College, Biology (CC BY 3.0).