Phagocytosis

Many cells need to bring a variety of materials, like bacteria, dead host cells, and debris from other cells or the environment, across their plasma membrane and into their cytoplasm for many different reasons. Some cells can use various methods, such as ion pumps, voltage-gated channels, or osmosis, to pull smaller molecules and chemicals across the plasma membrane and into their cytoplasm. But larger objects, like viruses, bacteria, or other particles are too large to use small channels to transport through the plasma membrane. So, cells engulf the larger objects and pull them in, which are generally called *endocytosis*. There are many different types of endocytosis, one of which is called **phagocytosis.**

Phagocytosis is a process wherein a cell binds to the item it wants to engulf on the cell surface and draws the item inward while engulfing around it. The process of phagocytosis often happens when the cell is trying to destroy something, like a virus or an infected cell, and is often used by immune system cells.

Phagocytosis differs from other methods of endocytosis because it is very specific and depends on the cell being able to bind to the item it wants to engulf by way of cell surface receptors. Phagocytosis won't happen unless the cell is in physical contact with the particle it wants to engulf.

The cell surface receptors used for phagocytosis depend on the type of cell that is doing the phagocytizing. These are the most common ones:

- **Opsonin receptors**: Opsonin receptors are used to bind bacteria or other particles that have been coated with immunoglobulin G (or "IgG") antibodies by the immune system. The immune system coats potential threats in antibodies so that other cells know it needs to be destroyed. The immune system can also use something called the "complement system", which is a group of proteins used to tag the bacteria. The complement system is another way for the immune system to destroy pathogens and threats to the host.
- **Scavenger receptors**: Scavenger receptors bind to molecules that are produced by bacteria. Most bacteria and other cellular species produce a matrix of proteins surrounding themselves (called an "extracellular matrix"). This matrix is a perfect way for the immune system to identify foreign species in the body, because human cells do not produce the same protein matrix.
- **Toll-like receptors**: Toll-like receptors, named after a similar receptor in fruit flies encoded by the Toll gene, bind to specific molecules produced by bacteria. Toll-like receptors are a key part of the innate immune system because, once bound to a bacterial pathogen, they recognize the specific bacteria and activate

the immune response. There are lots of different types of Toll-like receptors produced by the body, all which bind different molecules.

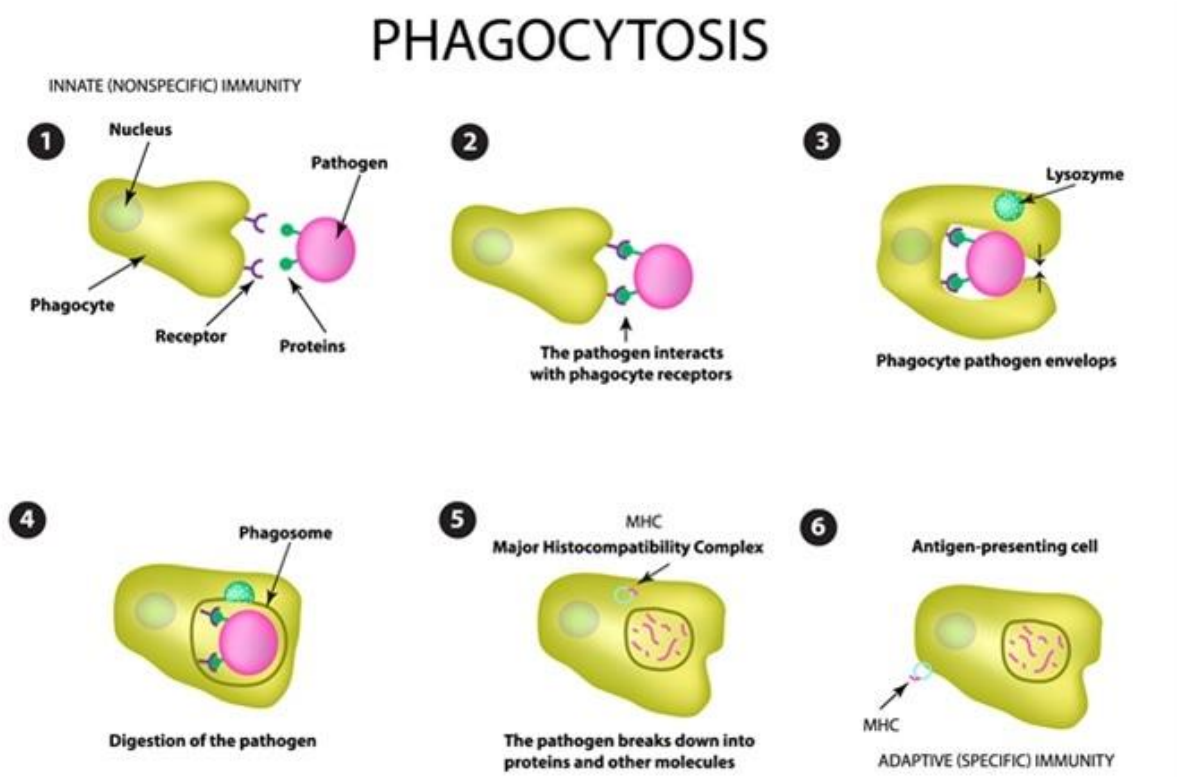
- **Antibodies**: Some immune cells make antibodies that can bind to specific antigens. This is a process similar to how toll-like receptors recognize and identify what type of bacteria is infecting the host. Antigens are molecules that act like a pathogen "calling card", because they help the immune system know what threat it has to fight.

  Cells have to complete some steps in order to successfully phagocytise something. In order to illustrate this a little easier, let's say we are following a macrophage (a type of immune cell) phagocytizing a virus. Keep in mind, a lot of different types of cells perform phagocytosis, though.

1. **The virus and the cell need to come into contact with each other.** Sometimes the immune cell accidentally bumps into a virus in the blood stream. Other times, cells move by way of a process called "chemotaxis". Chemotaxis means the movement of an organism or cell in response to a chemical stimulus. Many immune system cells move in response to cytokines, small proteins used specifically for cell signalling. Cytokines signal cells to move to certain area in the body where the particle (in our case, a virus) is found. This is common with infections that are specific to a certain area (like a skin wound infected with bacteria).

2. **The virus binds to the cell surface receptors on the macrophage.** Remember that different cell types express different receptors. Some receptors are general, meaning that they can identify a self-produced molecule versus a potential threat (and that's about it), and others are very specific, like toll-like receptors or antibodies. The macrophage will not initiate phagocytosis without successful binding of the cell surface receptors.

   Viruses can also have surface receptors which can be specific to those on the macrophage. Viruses need to access the host cell's cytoplasm or nucleus in order to replicate and cause an infection, so they use their surface receptors to interact with immune system cells and exploit the immune response for entry into the cell. Sometimes, when a virus and a host cell interact, the host cell is able to successfully destroy the virus and stop the spread of infection. Other times, the host cell engulfs the virus, and the virus tricks the cell, gaining access to what it needs to replicate. Once this happens, the infected cell is identified and destroyed by other cells of the immune system in order to stop viral replication and infection



3. **The macrophage starts to surround the virus and engulf it into the cell.** Instead of moving the large item across the plasma membrane, which might damage the membrane permanently, phagocytosis uses extensions of the cytoplasm (pseudopods) to surround the particle and enclose it in a membrane. For our virus example, the macrophage and virus are bound at the cell surface. The pseudopods protrude outward on either side of the virus until both sides meets and the virus is enclosed. Remember, cells are reasonably flexible and fluid.

For our virus example, the macrophage and virus are bound at the cell surface. The cell pulls the virus inward, creating a pocket-like indentation without damaging the plasma membrane. Remember, cells are reasonably flexible and fluid.

4. **The surrounded virus becomes completely enclosed in a bubble-like structure, called a "phagosome", within the cytoplasm.**
The lips of the pocket, formed as a result of the extensions of the pseudopods extend towards each other in order to close the gap. This action creates a phagosome, where the plasma membrane has moved around the particle, encasing it safely inside the cell.

5. **The phagosome fuses with a lysosome, becoming a "phagolysosome".**
Lysosomes are also bubble-like structures, similar to phagosomes, which process wastes inside the cell. "Lysis" means "to break down", is making it easy to

remember the function of a lysosome. Without fusing with a lysosome, the phagosome wouldn't be able to do anything with the contents inside.

6. **Phagolysosome lowers the pH to break down its contents.**
   A lysosome or phagolysosome is able to break down the stuff inside of itself by drastically lowering the pH of its internal environment. Lowering the pH makes the environment inside the phagolysosome makes it very acidic. This is an effective way of killing or neutralizing whatever is inside the phagolysosome so it cannot infect them cell.

   Some viruses actually exploit the lowered pH to escape the phagolysosome and start replicating inside the cell. For example, influenza (the flu virus) uses the drop in pH to activate a conformational change, allowing it to escape into the cytoplasm.

7. **Once the contents have been neutralized, the phagolysosome forms a residual body that contains the waste products from the phagolysosome.** The residual body is eventually discharged from the cell.

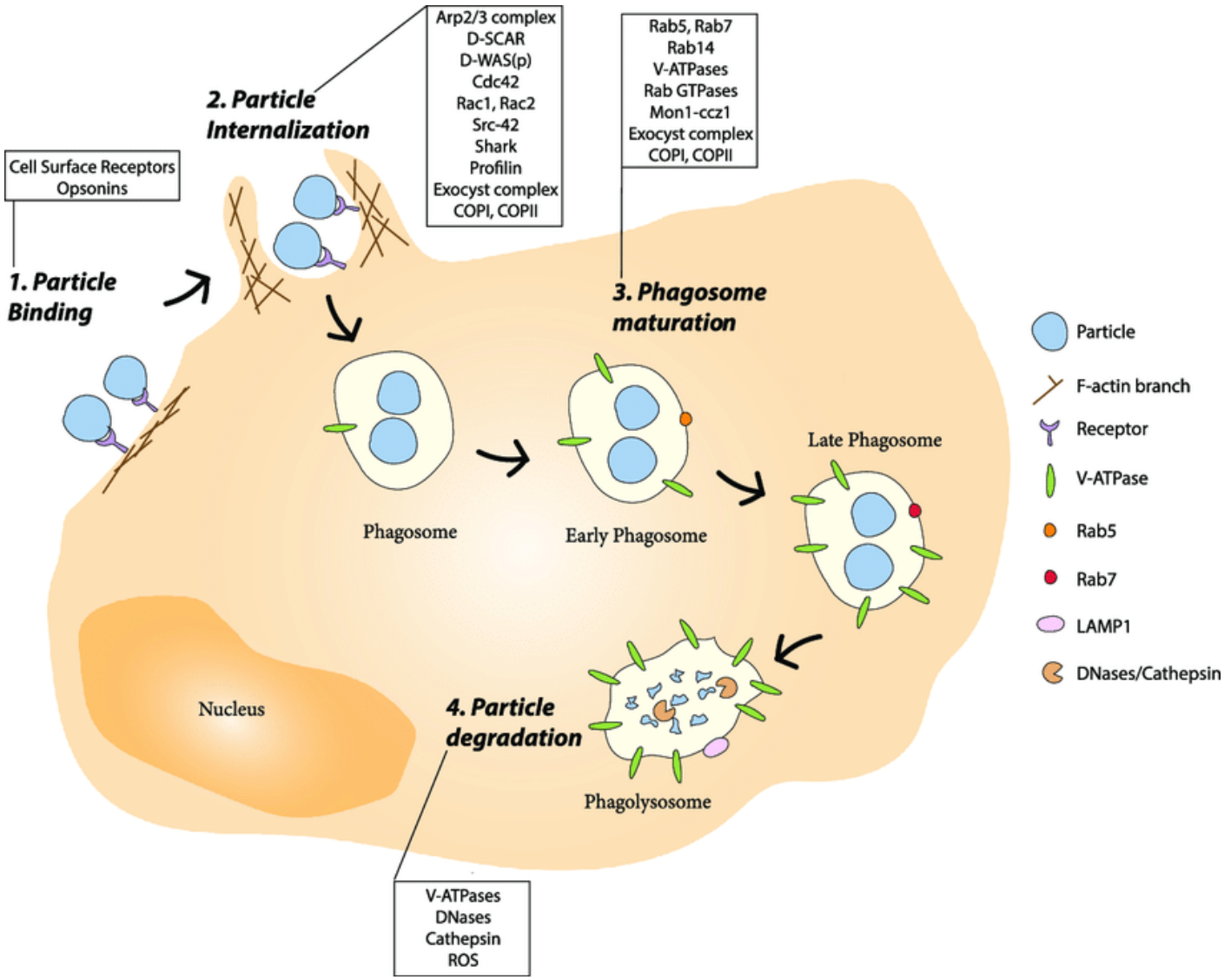
Phagocytosis and the immune system

Phagocytosis is a critical part of the immune system. Several types of cells of the immune system perform phagocytosis, such as neutrophils, macrophages, dendritic cells, and B lymphocytes. The act of phagocytizing pathogenic or foreign particles allows cells of the immune system to know what they are fighting against. By knowing the enemy, the cells of the immune system can specifically target similar particles circulating in the body.

Another function of phagocytosis in the immune system is to ingest and destroy pathogens (like viruses and bacteria) and infected cells. By destroying the infected cells, the immune system limits how quickly the infection can spread and multiply. We mentioned before that the phagolysosome creates an acidic environment to destroy or neutralize its contents. The immune system cells that perform phagocytosis can also use other mechanisms to destroy pathogens inside the phagolysosome, such as:

- **Oxygen Radicals**: Oxygen radicals are highly reactive molecules that react with proteins, lipids and other biological molecules. During physiological stress, the amount of oxygen radicals in a cell can increase dramatically, causing oxidative stress, which can destroy cell structures.
- **Nitric Oxide**: Nitric oxide is a reactive substance, similar to oxygen radicals, that reacts with superoxide to create further molecules that damage various biological molecules.

- **Antimicrobial Proteins**: Antimicrobial proteins are proteins that specifically damage or kill bacteria. Examples of antimicrobial proteins include proteases, which kill various bacteria by destroying essential proteins, and lysozyme, which attacks the cell walls of gram positive bacteria.
- **Antimicrobial Peptides**: Antimicrobial peptides are similar to antimicrobial proteins in that they attack and kill bacteria. Some antimicrobial peptides, like defensins, attack bacterial cell membranes.
- **Binding Proteins**: Binding proteins are often important players in the innate immune system because they competitively bind to proteins or ions that would have otherwise been beneficial to bacteria or viral replication. Lactoferrin, a binding protein found in mucosal membranes, binds iron ions, which are necessary for growth of bacteria.
- **********



****