Phagocytosis

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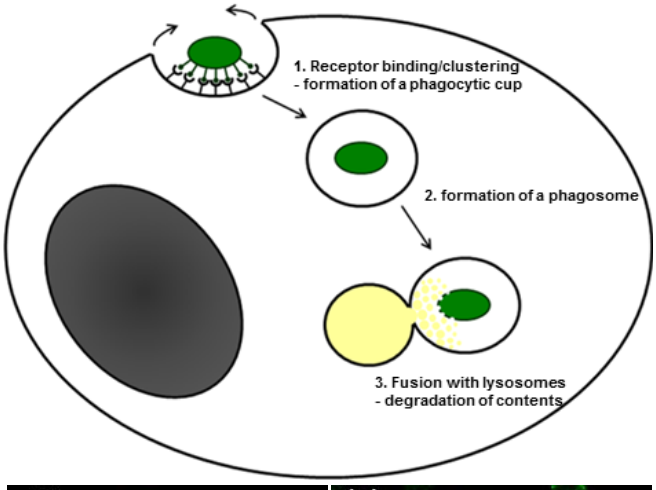
Phagocytosis is a specific form of **endocytosis** by which cells internalise solid matter, including microbial pathogens. While most cells are capable of phagocytosis, it is the professional phagocytes of the immune system, including **macrophages**, **neutrophils** and immature **dendritic cells**, that truly excel in this process. In these cells, phagocytosis is a mechanism by which microorganisms can be contained, killed and processed for antigen presentation and represents a vital facet of the innate immune response to pathogens, and plays an essential role in initiating the **adaptive immune response**.

The process of phagocytosis begins with the binding of **opsonins** (i.e. **complement** or **antibody**) and/or specific molecules on the pathogen surface (called pathogen-associated molecular pathogens [**PAMPs**]) to cell surface receptors on the phagocyte. This causes receptor clustering and triggers phagocytosis. The cell membrane then extends around the target, eventually enveloping it and pinching-off to form a discreet **phagosome**. This vesicle can mature and acidify through fusion with late endosomes and lysosomes to form a **phagolysosome**, in which degradation of the contents can occur via the action of lysosomal hydrolases.

Numerous receptors are involved in phagocytosis. **Complement receptors** and **Fc receptors** are particularly important for the recognition and phagocytosis of opsonised microbes and other solid matter. Other receptors, including the Toll-like receptors (**TLRs**), scavenger receptors (SR) and **lectins** (such as DC-SIGN, dectin-1 and the **mannose receptor**) are also important in the uptake of many pathogenic microorganisms. Phagocytosis is typically a dynamic process that requires reorganisation of the actin cytoskeleton and the involvement of actin-binding proteins and signalling molecules.

Moreover, phagocytosis can be influenced by numerous pathogen-associated and endogenous molecules, including **lipopolysaccharide** (**LPS**) and **cytokines**. In particular **TNFα** and **IFNγ** drive the formation and maturation of phagosomes. This process triggers the phagocyte to produce cytokines, which act as chemoattractants to enhance migration and activation of other immune cells to the site of infection.

Some **intracellular pathogens**, including *Mycobacterium tuberculosis*, have evolved strategies to inhibit phagosomal maturation and can survive and replicate within the immature phagosome. Other pathogens, such as *Escherichia coli* and *Neisseria meningitides,* have developed mechanisms to fix, shed and/or degrade opsonins to prevent activation of the immune response and thus evade immune surveillance and phagocytosis.



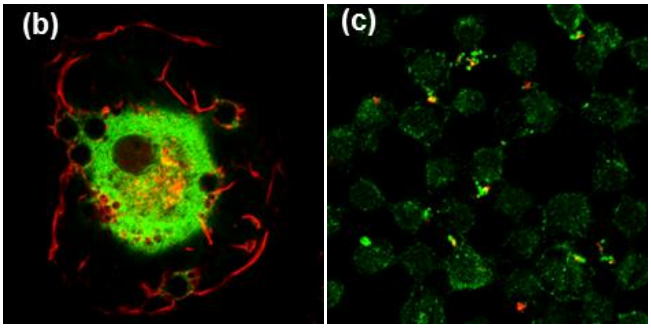


Figure 1. (a) Three stages of phagocytosis; receptor binding and formation of a phagocytic cup, pinching-off and formation of a discreet phagosome and fusion with lysosomes. **(b)** Human macrophage phagocytosing *Candida albicans*. Arrows: phagosomes stained for actin (red) and calreticulin, an endoplasmic reticulum marker (green). **(c)** IFN-g-treated mouse macrophages infected with *Mycobacterium bovis* BCG (red) and stained for the lysosomal marker CD69 (LAMP3, green).