

*Commentary*

# Macrophage-mediated phagocytosis: Mechanisms and clinical implications

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## DESCRIPTION

Macrophages, as an important component of the immune system, play an important role in maintaining homeostasis and defending the body against pathogens. One of their primary functions is phagocytosis, a process by which they engulf and digest cellular debris, foreign substances, microbes, and apoptotic cells. This study discusses about the mechanisms of macrophage-mediated phagocytosis and its clinical implications, highlighting its significance in health and disease.

### Mechanisms of macrophage-mediated phagocytosis

Phagocytosis involves a series of steps that enable macrophages to identify, engulf, and degrade targets. These steps can be broadly categorized into recognition and attachment, engulfment, and digestion.

**Recognition and attachment:** Macrophages recognize and attach to targets through a variety of receptors on their surface. These receptors can be broadly classified into two categories they are opsonic and non-opsonic receptors. Opsonic receptors recognize opsonins, which are molecules that coat the surface of pathogens and apoptotic cells. Common opsonins include antibodies and complement proteins. For example, Fc Receptors (FcRs) on macrophages bind to the Fc region of antibodies, while Complement Receptors (CRs) bind to complement-coated targets. Non-opsonic receptors directly recognize Pathogen-Associated Molecular Patterns (PAMPs) on the surface of microbes and Damage-Associated Molecular Patterns (DAMPs) on apoptotic cells. Examples include Toll-Like Receptors (TLRs) and scavenger receptors.

**Engulfment:** Once the target is recognized and attached, macrophages extend their plasma membrane around the target, forming a phagocytic cup. This process is driven by the actin cytoskeleton, which undergoes rapid remodeling. The phagocytic cup eventually closes around the target, engulfing it in a membrane-bound vesicle known as a phagosome.

**Digestion:** The phagosome containing the engulfed target undergoes a series of maturation steps, during which it fuses with lysosomes to form a phagolysosome. Lysosomes contain a variety

of hydrolytic enzymes, such as proteases, lipases, and nucleases, as well as antimicrobial peptides. The acidic environment within the phagolysosome facilitates the degradation of the engulfed material. Additionally, macrophages produce Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) within the phagolysosome, further aiding in the destruction of pathogens.

### Clinical implications

Macrophage-mediated phagocytosis has significant clinical implications in various contexts, macrophages play an important role in the defense against infectious agents. Through phagocytosis, they can eliminate bacteria, viruses, fungi, and parasites. However, some pathogens have evolved mechanisms to evade or exploit macrophage phagocytosis. Macrophages can have dual roles in cancer, acting as both tumor suppressors and promoters, depending on their polarization state (M1 vs. M2 macrophages). M1 macrophages exhibit anti-tumor properties through their ability to phagocytose tumor cells and produce pro-inflammatory cytokines. Enhancing the phagocytic activity of M1 macrophages can be a therapeutic approach in cancer treatment. Tumor promotion by promoting angiogenesis, suppressing anti-tumor immune responses, and aiding in tissue remodeling. Targeting the factors that drive M2 polarization or reprogramming M2 macrophages to an M1 phenotype could help in inhibiting tumor progression. In autoimmune diseases, the dysregulation of macrophage-mediated phagocytosis can contribute to pathogenesis. For example, in Systemic Lupus Erythematosus (SLE), impaired clearance of apoptotic cells by macrophages can lead to the accumulation of cellular debris and the production of autoantibodies. Therapies aimed at restoring normal phagocytic function could potentially ameliorate autoimmune symptoms. Macrophages are essential for tissue repair and regeneration following injury. They remove dead cells and debris, secrete cytokines and growth factors, and orchestrate the transition from inflammation to tissue repair. In the context of wound healing, efficient phagocytosis by macrophages is important for clearing necrotic tissue and preventing chronic inflammation. Strategies to enhance macrophage function could improve healing outcomes, especially in chronic wounds and diabetic ulcers. Macrophages also play a role in regenerative medicine. For instance, they are

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involved in the clearance of senescent cells and the promotion of stem cell activity. Modulating macrophage activity could enhance tissue engineering and regenerative therapies.

### **Therapeutic strategies targeting macrophage-mediated phagocytosis**

Given the central role of macrophage-mediated phagocytosis in various diseases, several therapeutic strategies are being investigated to modulate this process. Enhancing phagocytosis cytokine therapy administering cytokines such as Interferon-Gamma (IFN- $\gamma$ ) can enhance macrophage activation and phagocytic activity. Opsonization using therapeutic antibodies or complement proteins to opsonize pathogens or tumor cells can enhance their recognition and phagocytosis by macrophages. Inhibiting pathogen evasion developing drugs that inhibit the mechanisms used by pathogens to evade macrophage phagocytosis, such as blocking phagosome-lysosome fusion,

can improve pathogen clearance. Modulating macrophage polarization in cancer therapy, reprogramming Tumor-Associated Macrophages (TAMs) from a pro-tumor M2 phenotype to an anti-tumor M1 phenotype can enhance anti-tumor immunity. Promoting tissue repair administering growth factors that promote macrophage-mediated tissue repair can enhance wound healing and tissue regeneration. Macrophage-mediated phagocytosis is a fundamental process in immune defense, tissue homeostasis, and disease. Understanding the mechanisms underlying this process and its clinical implications can lead to novel therapeutic strategies for a wide range of diseases, including infections, cancer, autoimmune disorders, and tissue repair. By harnessing the power of macrophages and modulating their activity, people can improve disease outcomes and enhance the body's ability to heal and regenerate. The continued analysis of macrophage biology potential to yield significant advancements in medical science and therapeutic interventions.