Phagocytosis: An Evolutionarily Conserved Mechanism to Remove Apoptotic Bodies and Microbial Pathogens

Phagocytosis of IgG-coated Targets by Macrophages

3 min 10 min

Mast Cells Can Phagocytose Too!

Extension of an F-actin-rich "Phagocytic Cup" Around Phagocytic Targets

Motor Proteins and Exocytosis Power Phagocytosis

From: Chavrier, Nature Cell Biol. 4:E169, 2002
Post-phagocytic Events: Phagosome-Lysosome Fusion

Phagocytosis of Bacteria is Followed by Phagosome-Lysosome Fusion

0-3 min  1-5 min  30 min-hrs

Granulomatous inflammation consists of epithelioid macrophages, giant cells, lymphocytes, plasma cells, and fibroblasts.

Epithelioid cells accumulate around the center of a granuloma. They get their name from the fact that they have pink cytoplasm similar to squamous epithelium.

Langhans-type giant cells represent fused macrophages. The nuclei are lined up around the periphery of the cell.

The Granuloma: a Delayed Response to Indigestible Pathogens and Particles in Macrophages

Oxidant-dependent Killing of Bacteria and Fungi

Post-phagocytic Events: "Phagosome-Oxidase Fusion"

Post-phagocytic Events: Generation of H₂O₂
**Post-phagocytic Events: Myeloperoxidase Activity**

**Post-phagocytic Events: Peroxynitrite Production**

**Bacterial Virulence Factors Subvert Host Defenses**

**Immunological Consequences of Phagocytosis**

**Dendritic Cells Engulf Influenza-infected Monocytes and Cross-present Antigen**

**Biology of Fcγ Receptors**

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**From**: Albert et al., *Nature* 392:86, 1998
Functional Sites on the IgG Molecule

FcγR binding site
Glycosylation site
VH
VL

Fc, Receptor Signaling: ITAM Phosphorylation

Opsonized Bacterium

FcγRIIIA
γ subunit
Src family TK

Fc, Receptor Signaling: Syk Activation

Opsonized Bacterium

PTPase

Syk

TK substrates

Activating FcγR
Inhibitory FcγR

ITAM
Syk

Phagocytosis

Clustering of the BCR by Antigen Initiates Signaling
Hypersensitivity Diseases

The "Dark Side" of Fc Receptors: Immune Complex-mediated Injury

The Arthus Reaction: A Model of Type III Hypersensitivity

Requirement of Activating FcRs in Immune Complex-mediated Glomerulonephritis

Absence of the γ subunit of Fc receptors leads to enhanced survival in the F1 generation of NZB/NZW (lupus-prone) mice, a model for autoimmune, immune complex-mediated glomerulonephritis.

Glomerulonephritis is blocked in γ chain-deficient NZB/NZW (lupus-prone) mice. Pathological features include mesangial thickening and hypercellularity evolving into end-stage sclerotic and crescentic changes.

**Summary**

1. Phagocytosis is a component of innate and acquired immunity. It is the principal means of destroying pathogenic bacteria and fungi. Phagocytosis initiates the process of antigen presentation.
2. Many phagocytic receptors recognize a diverse array of microbial pathogens. Some pathogens (e.g., S. pneumoniae) require opsonization for their clearance.
4. Phagocytosis is an essential component of development and tissue remodeling. Ingestion of apoptotic bodies is immunologically "silent" and is normally accompanied by a suppression of inflammation.
5. Failure of this mechanism may result in autoimmunity.
6. Fc receptors come in two basic types: activating (ITAM-associated) and inhibitory (ITIM-associated).
7. The relative expression of activating and inhibitory Fc receptors determines the outcome of a given engagement of Fc receptors.
8. Fc receptor-driven pathology includes formation and deposition of immune complexes, which play a major role in autoimmunity.