

Autophagy

In Infectious diseases

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Autophagy

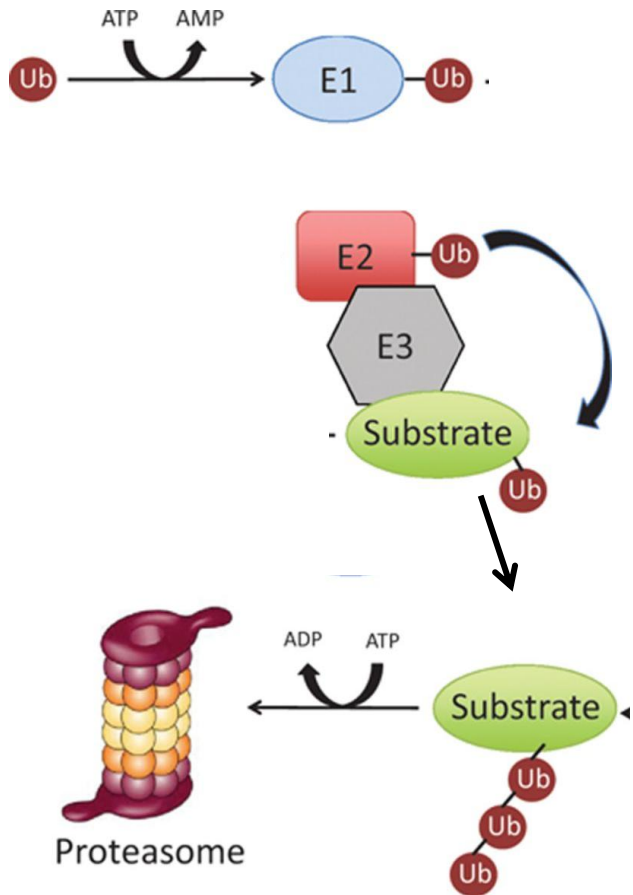
In Infectious diseases

Part I: Introduction to Autophagy

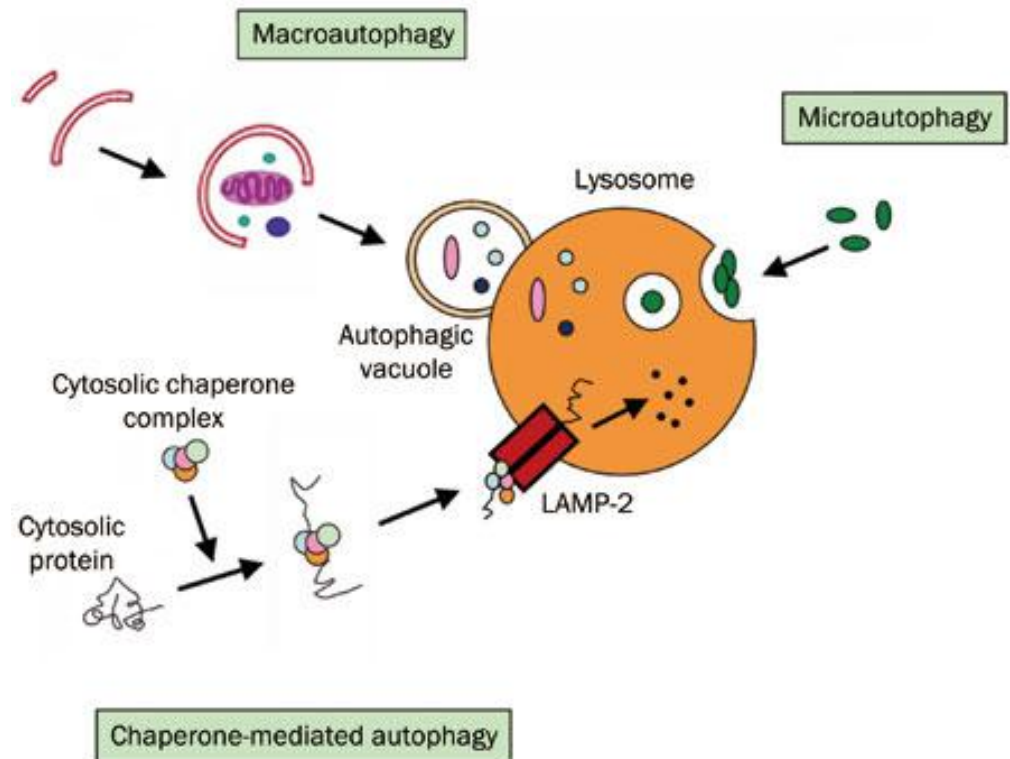
Part II: Role of Autophagy in Infectious Diseases

Intracellular mechanisms of degradation of cellular waste

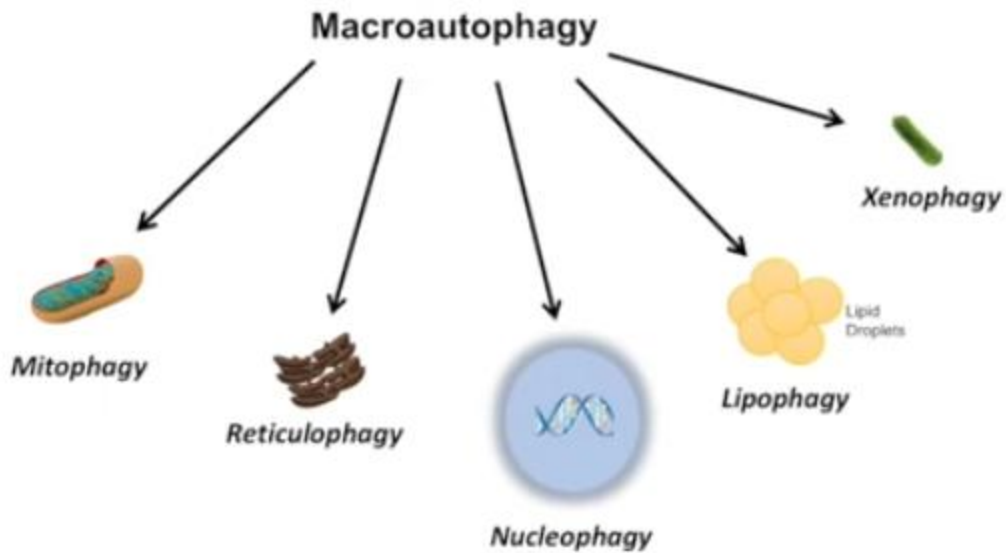
Ub-Proteasome system



Autophagy pathways



Macroautophagy



Schematic of major steps in autophagy.

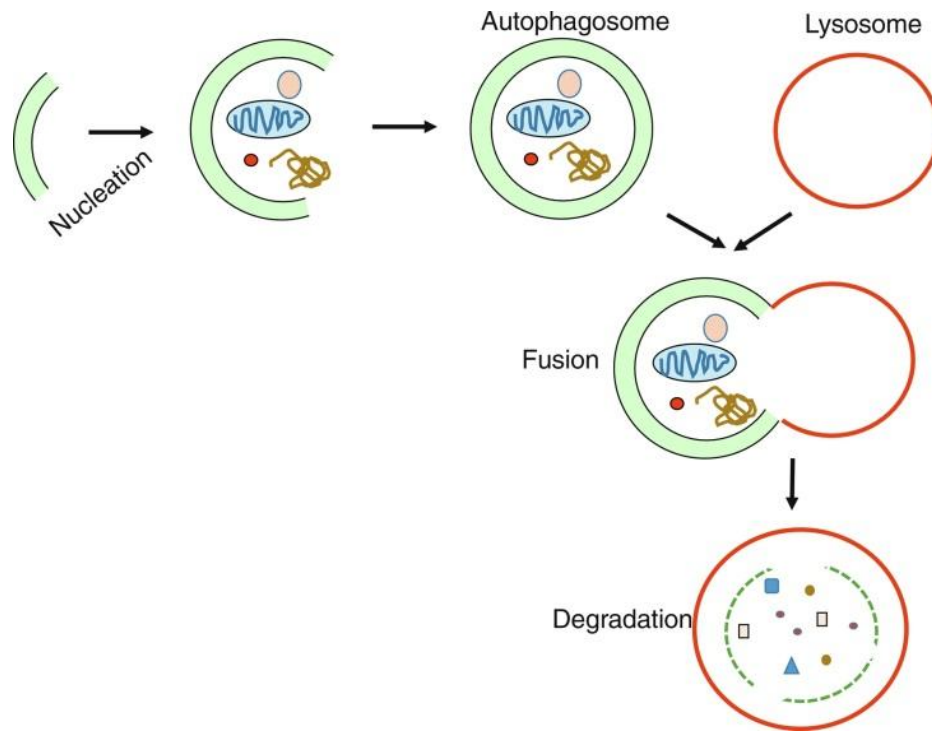
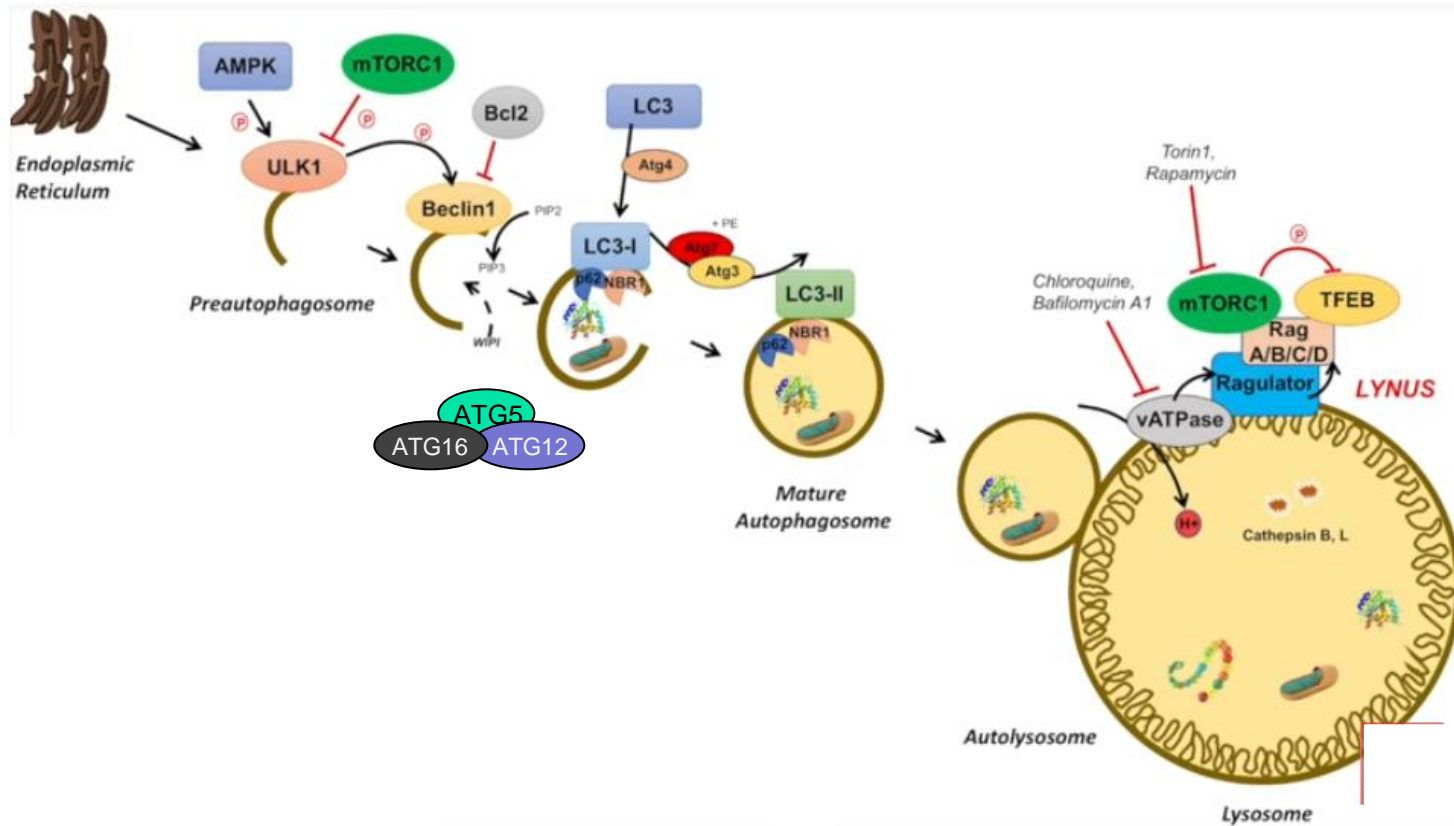
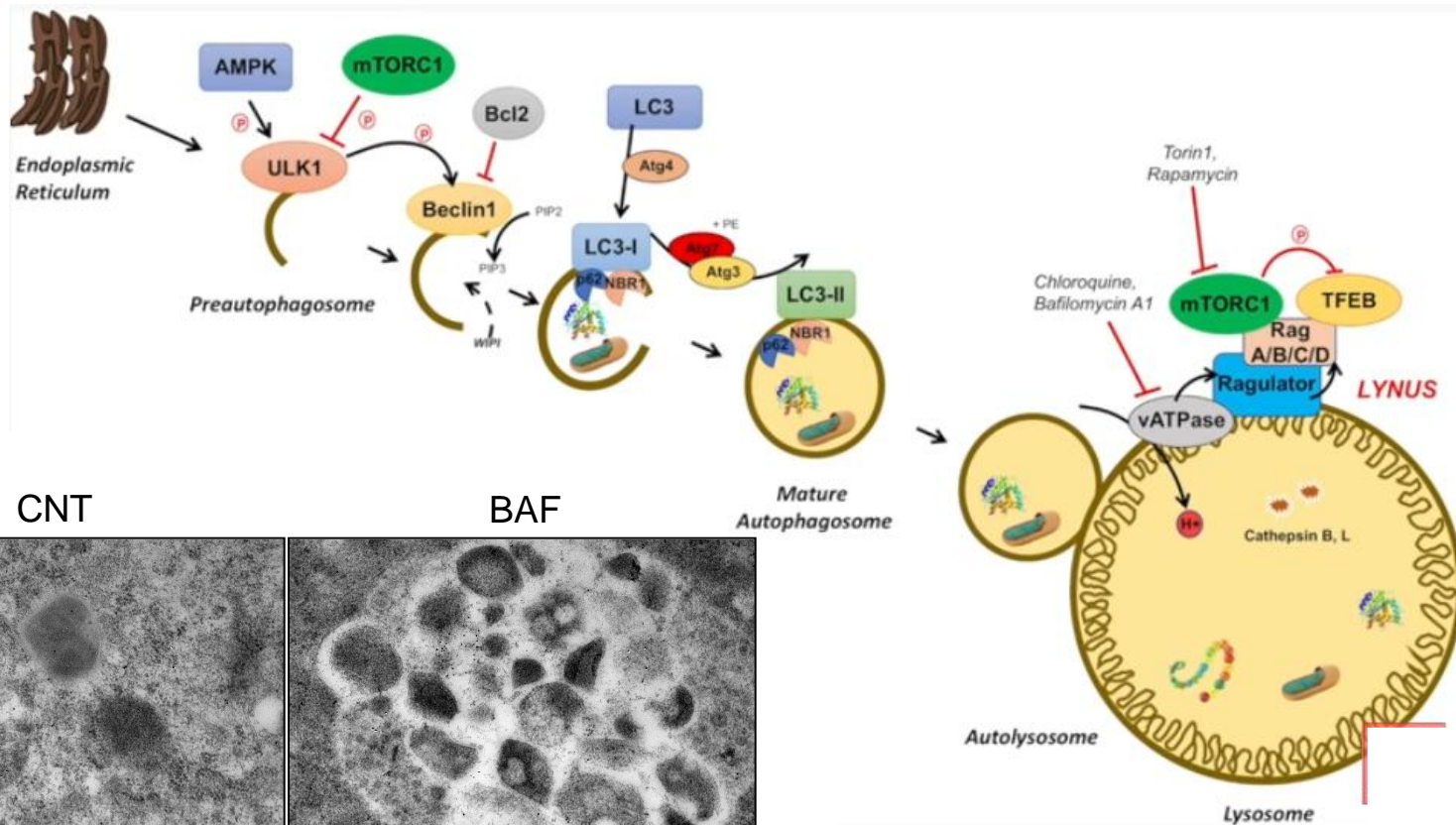


Figure 11–12. Expansion of a membrane derived from the ER membrane, or possibly other sources, leads to the formation of a cuplike structure that engulfs cytoplasmic material, including organelles such as mitochondria. This extends further to form a double-membrane vesicle called the autophagosome, which fuses with the lysosome. The cargo of the autophagosome is digested by lysosomal enzymes.

Mechanism

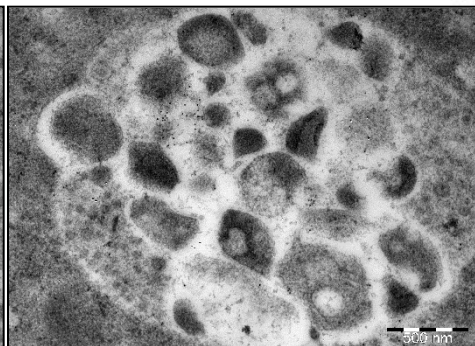
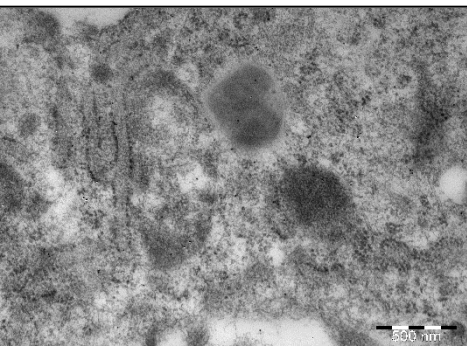


Mechanism

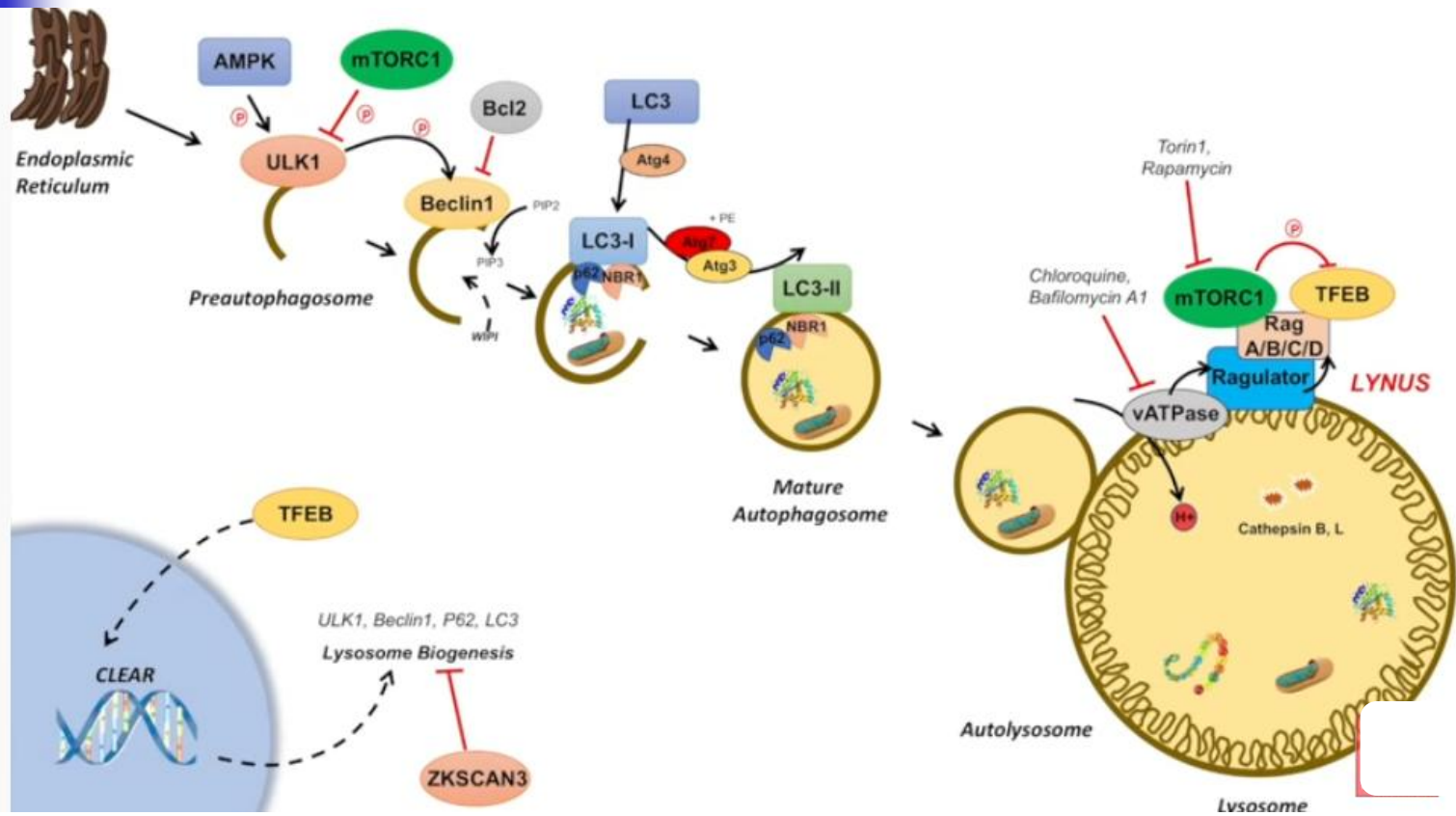


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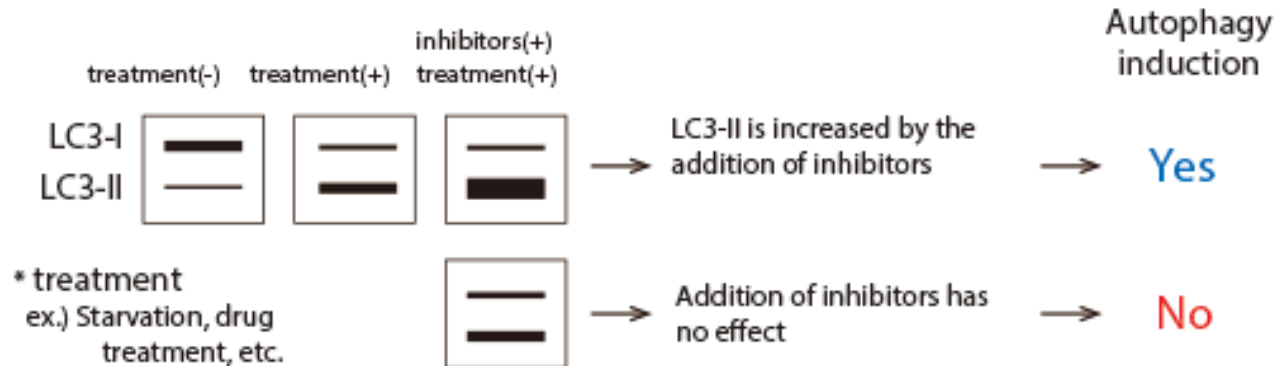
BAF



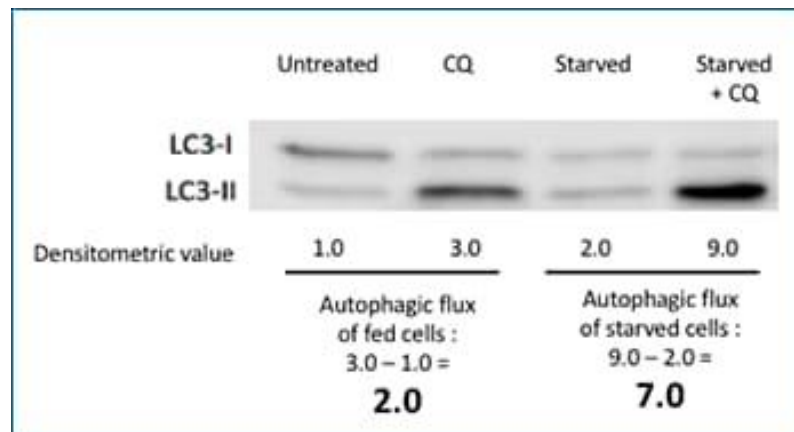
Mechanism



Autophagic flux



(Source) Mizushima, N. and Yoshimori, T. How to Interpret LC3 Immunoblotting. *Autophagy* 3, 542-545 (2007) (PMID:17611390)

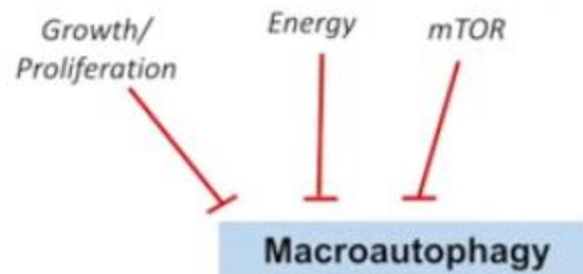




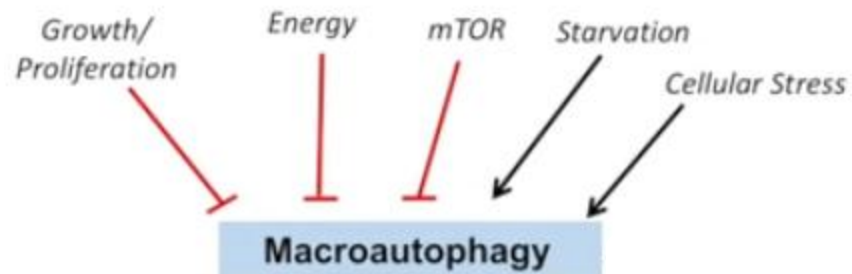
Autophagy: Summary

- Autophagosome: A double membrane bound compartment that engulfs cytosol and degrades the cytoplasmic contents.
- Large: 400-1500 nm (larger than lysosome)
- May originate from ER or from fusion of lipid-containing vesicles that form 'sequestration crescent'.

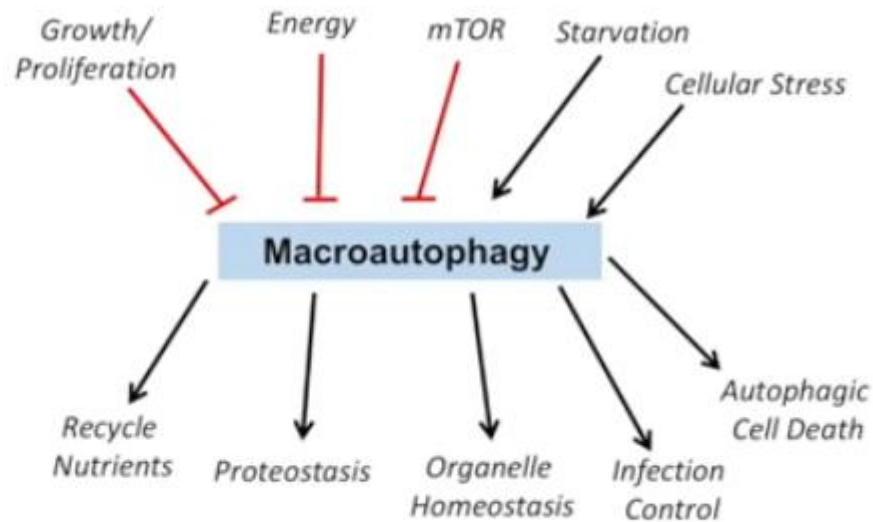
Autophagy: Summary



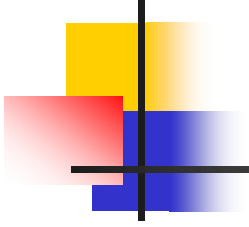
Autophagy: Summary



Autophagy: Summary



Part II



Part II



Role of autophagy in infection

- Does autophagy benefit the host as a defense mechanism?
- Does autophagy benefit the microbe by facilitating survival and replication?
- Or both?



Role of autophagy in bacterial infection

- Autophagy functions as an **antibacterial mechanism**. The induction and recognition mechanisms for several bacterial species have been elucidated.
- Bacteria can **escape killing by autophagy** and some can even **use autophagy** to promote infection of host cells, through the interaction between bacterial effector proteins and autophagy components.

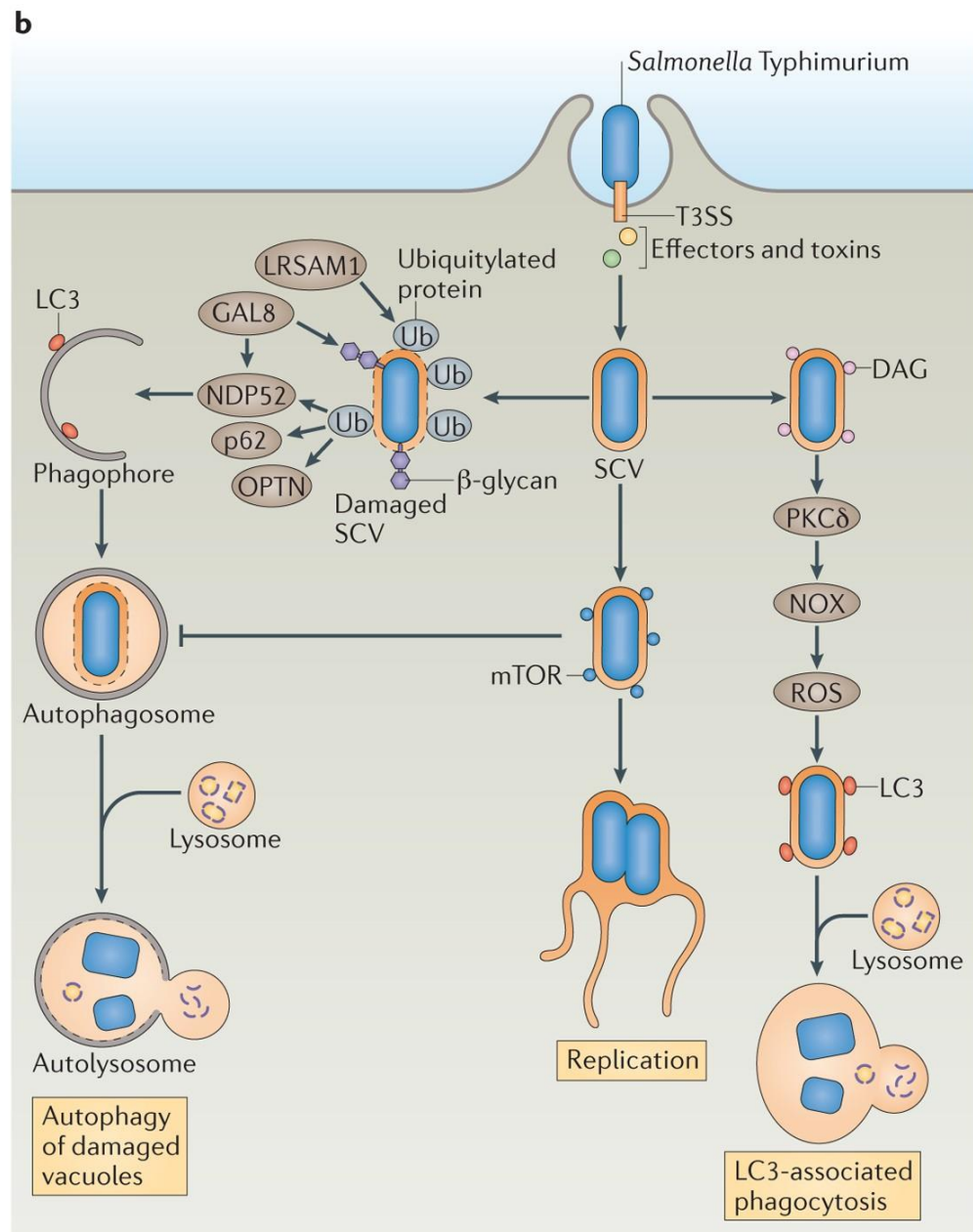
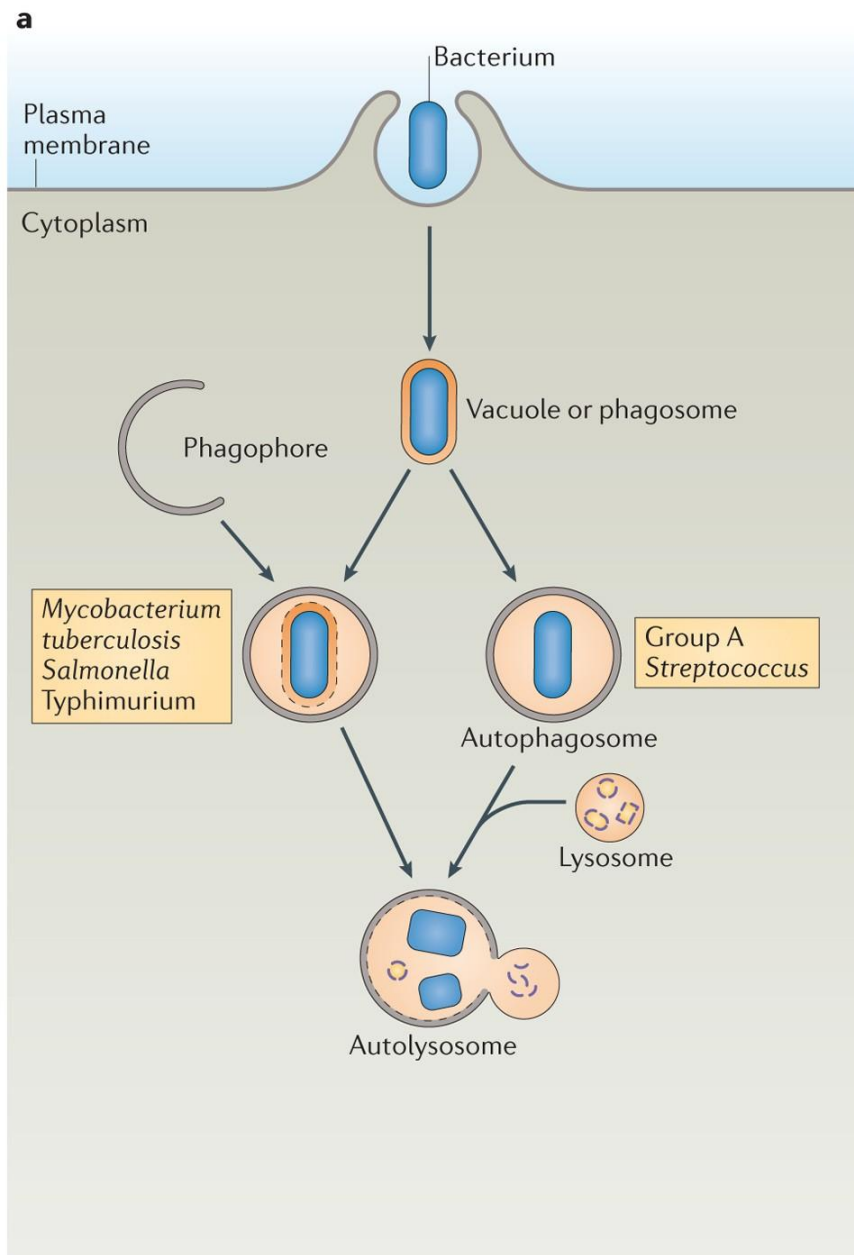


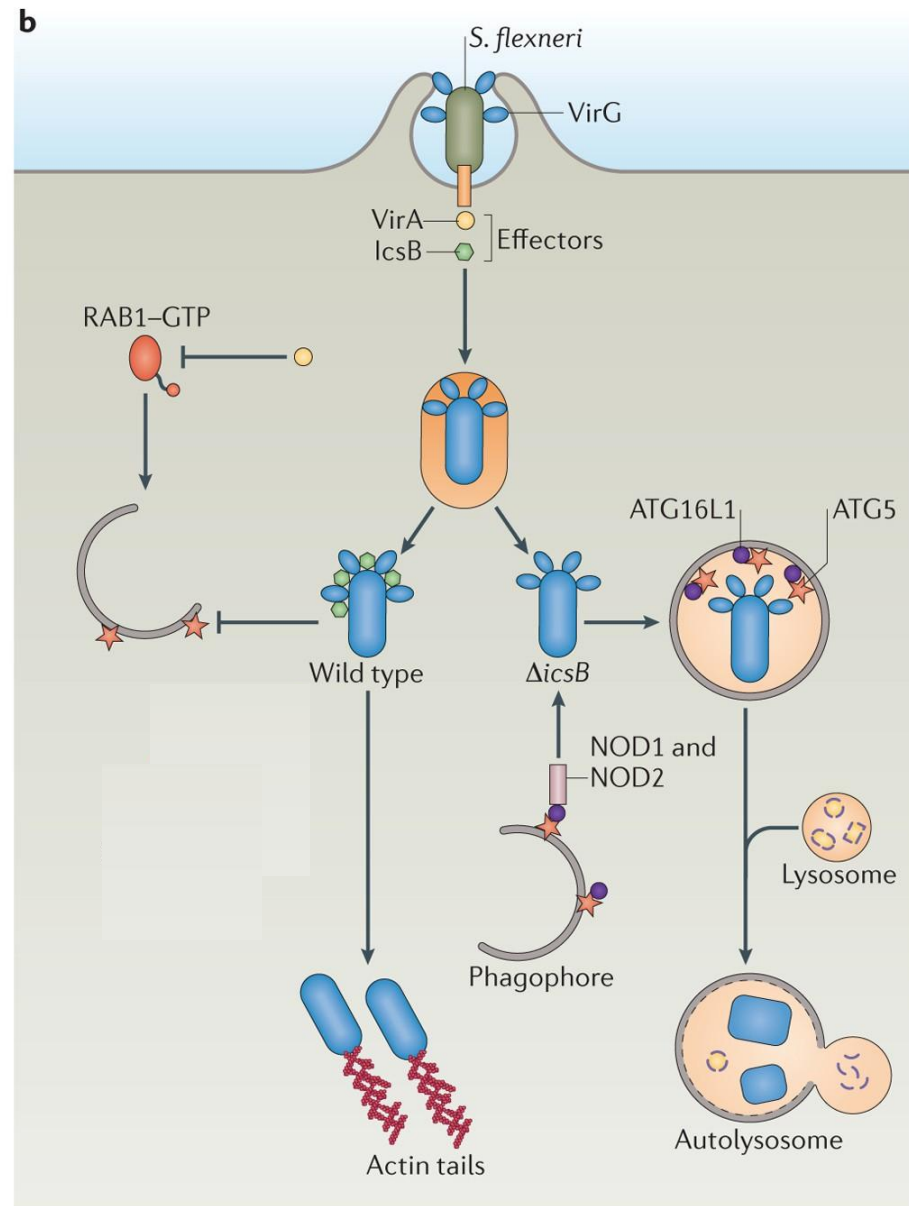
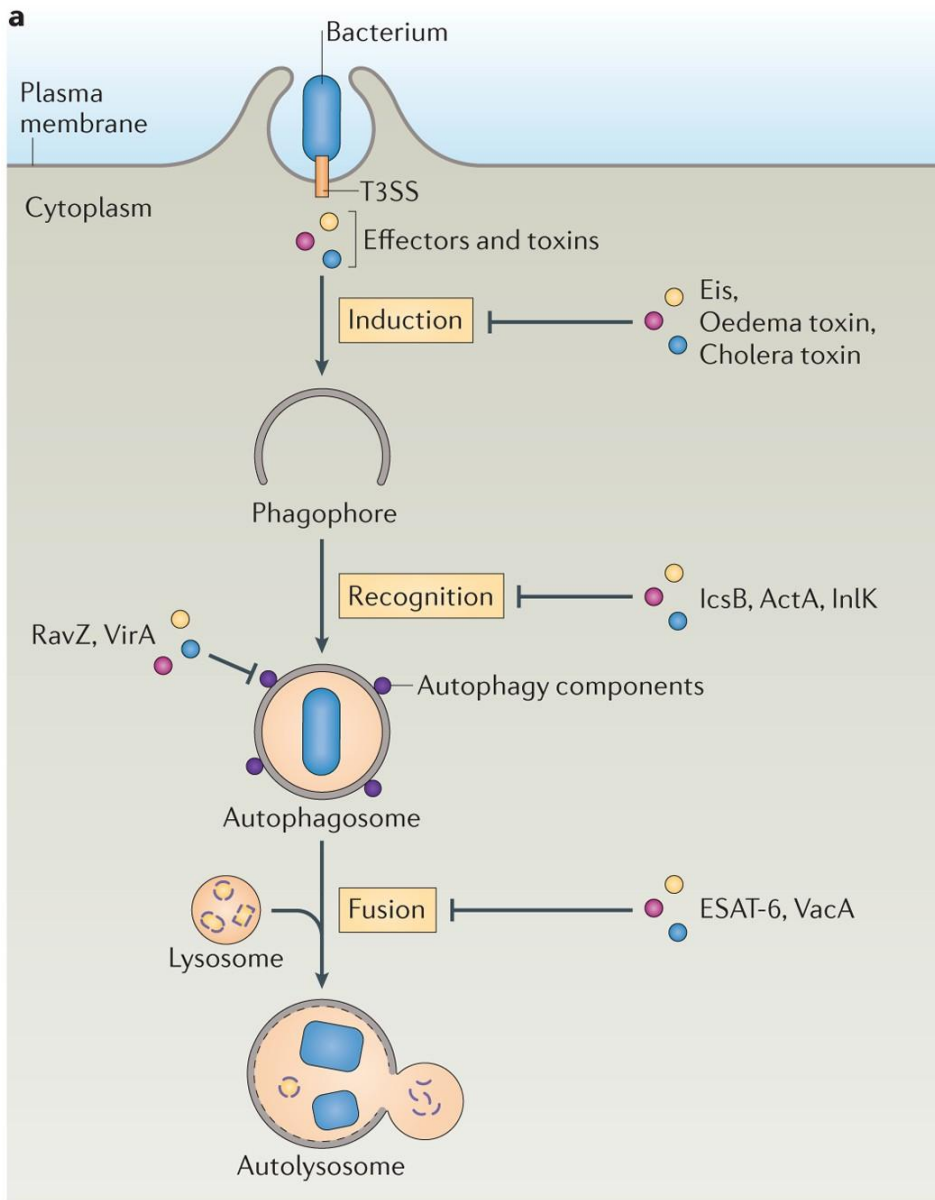
Autophagy vs Phagocytosis

Both mechanisms are digestive processes and involve merging with a lysosome, where enzymes degrade the target.

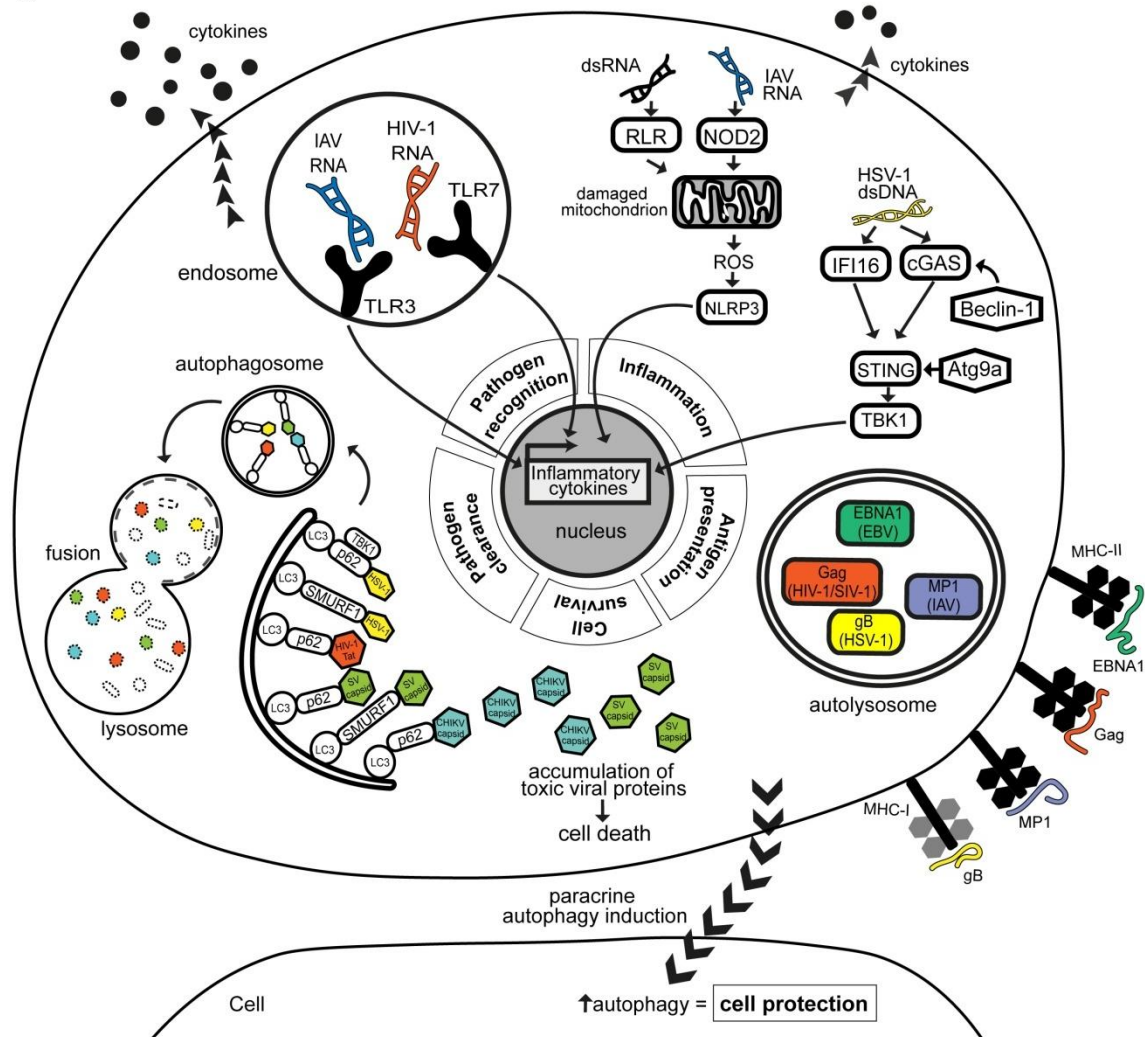
Phagocytosis is a form of endocytosis and is involved in degrading “foreign materials”, including pathogens that need to be destroyed. It mostly applies to phagocytes such as macrophages and neutrophils.

Autophagy degrades intracellular components and requires fusion of autophagosome with lysosome. Utilized by all cell types.

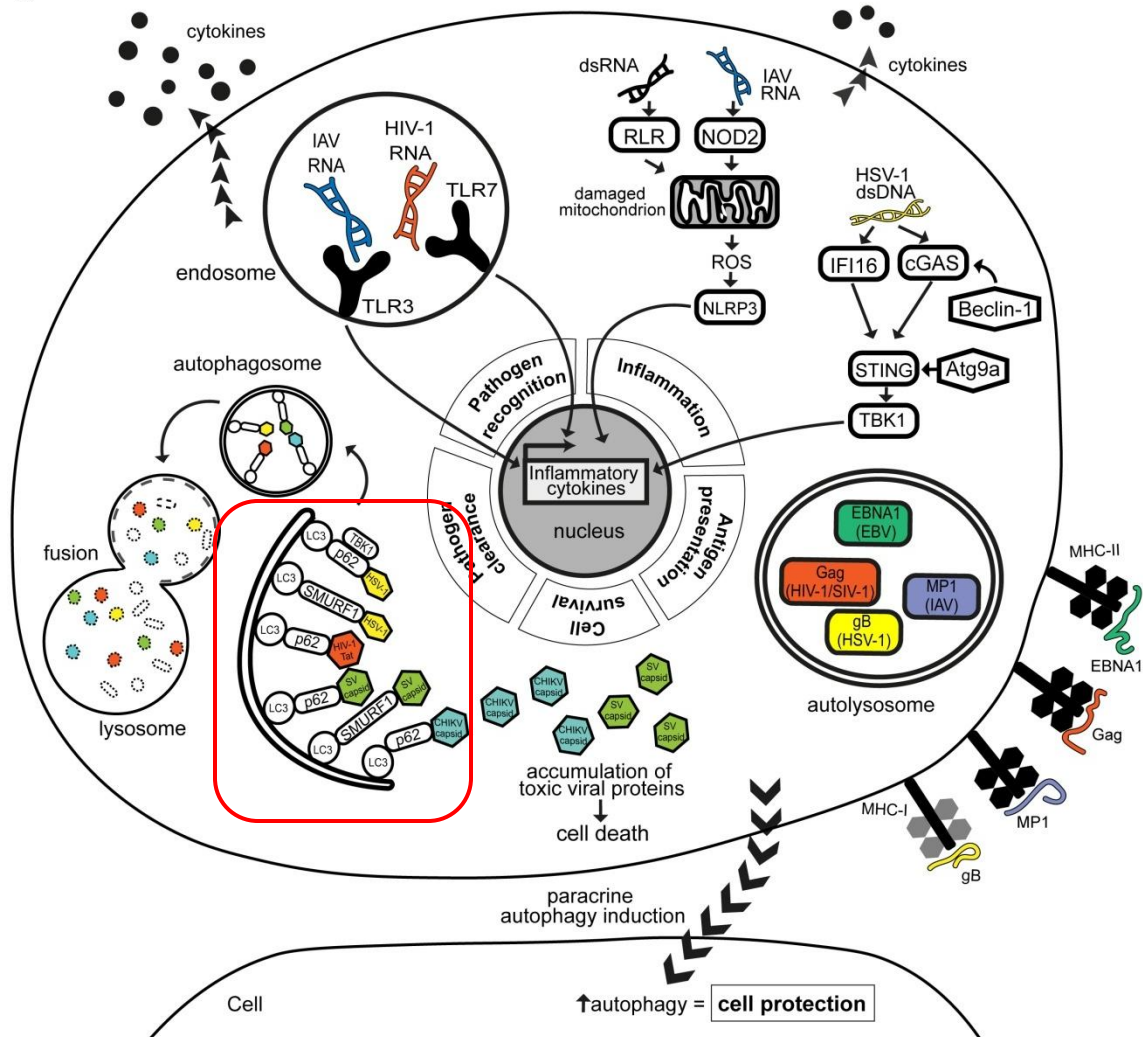




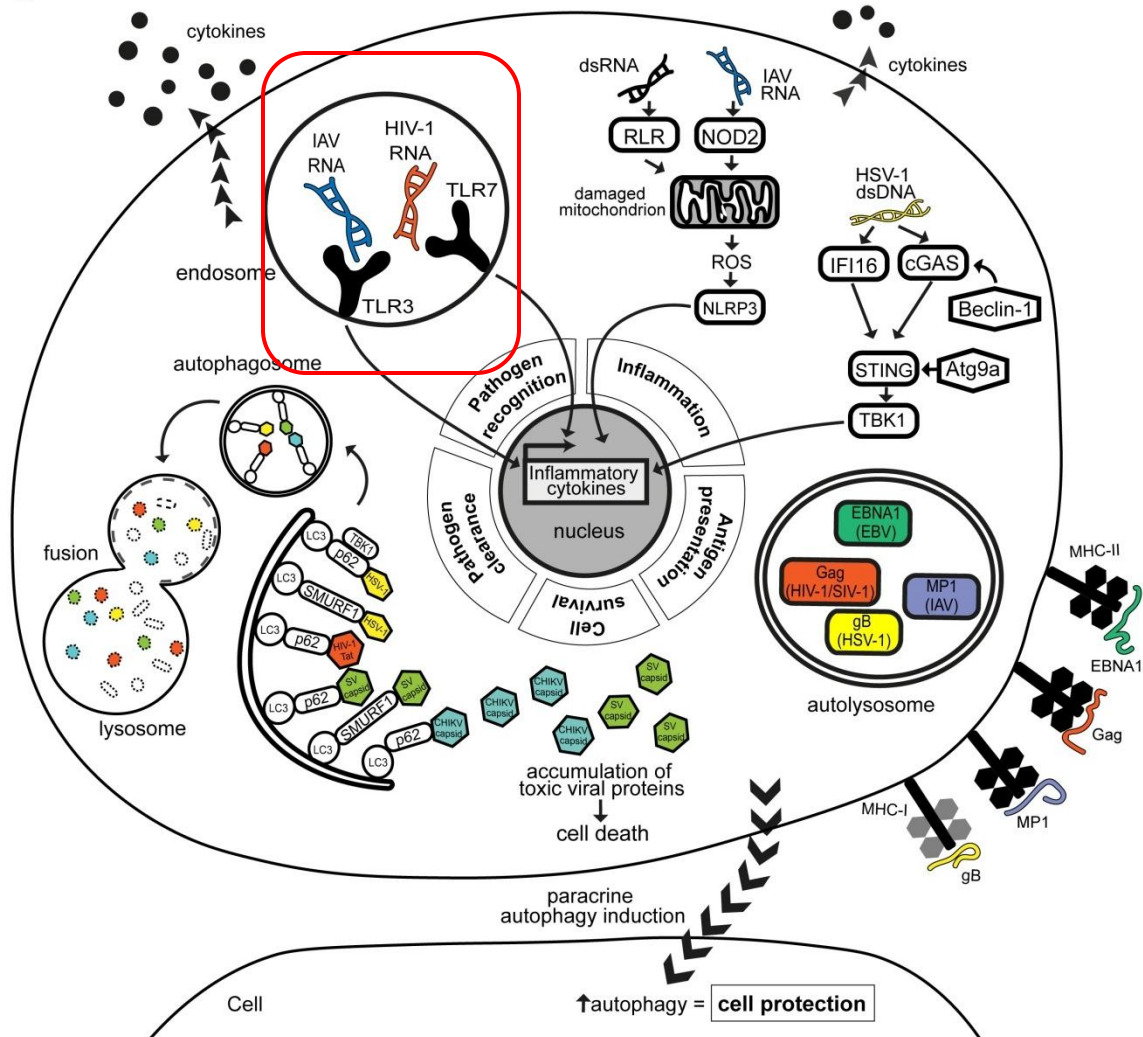
Role of autophagy in viral infection



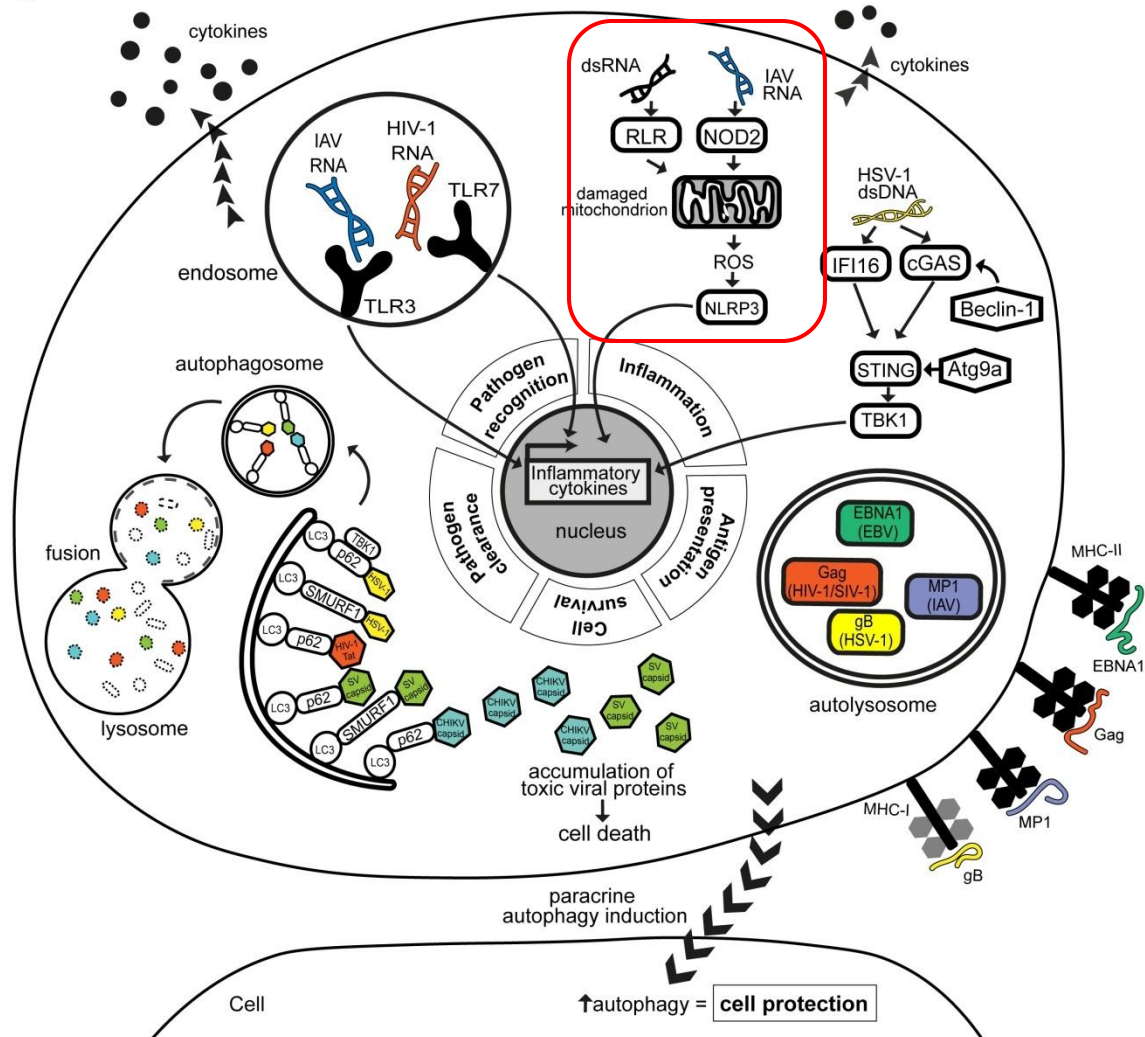
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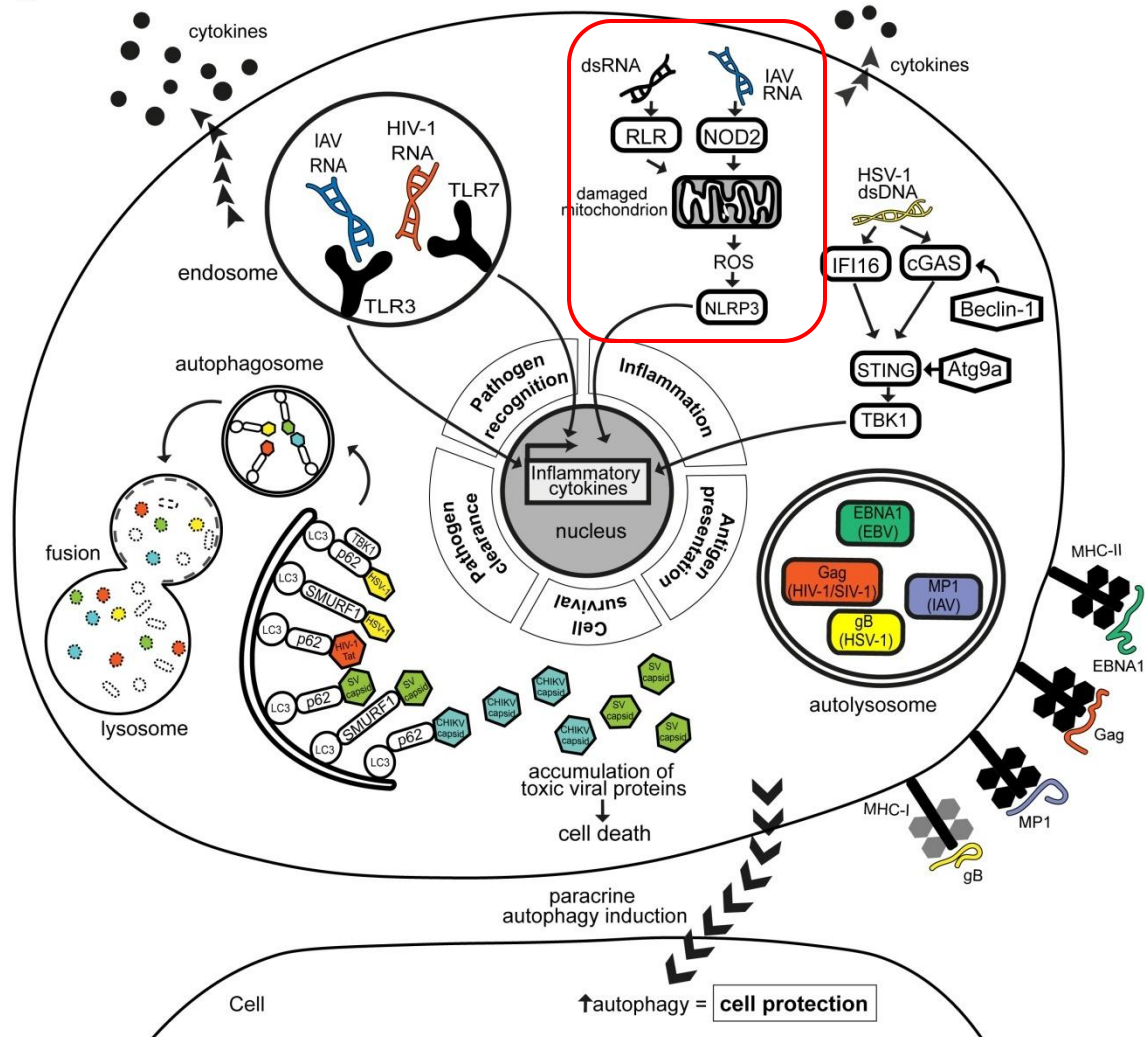
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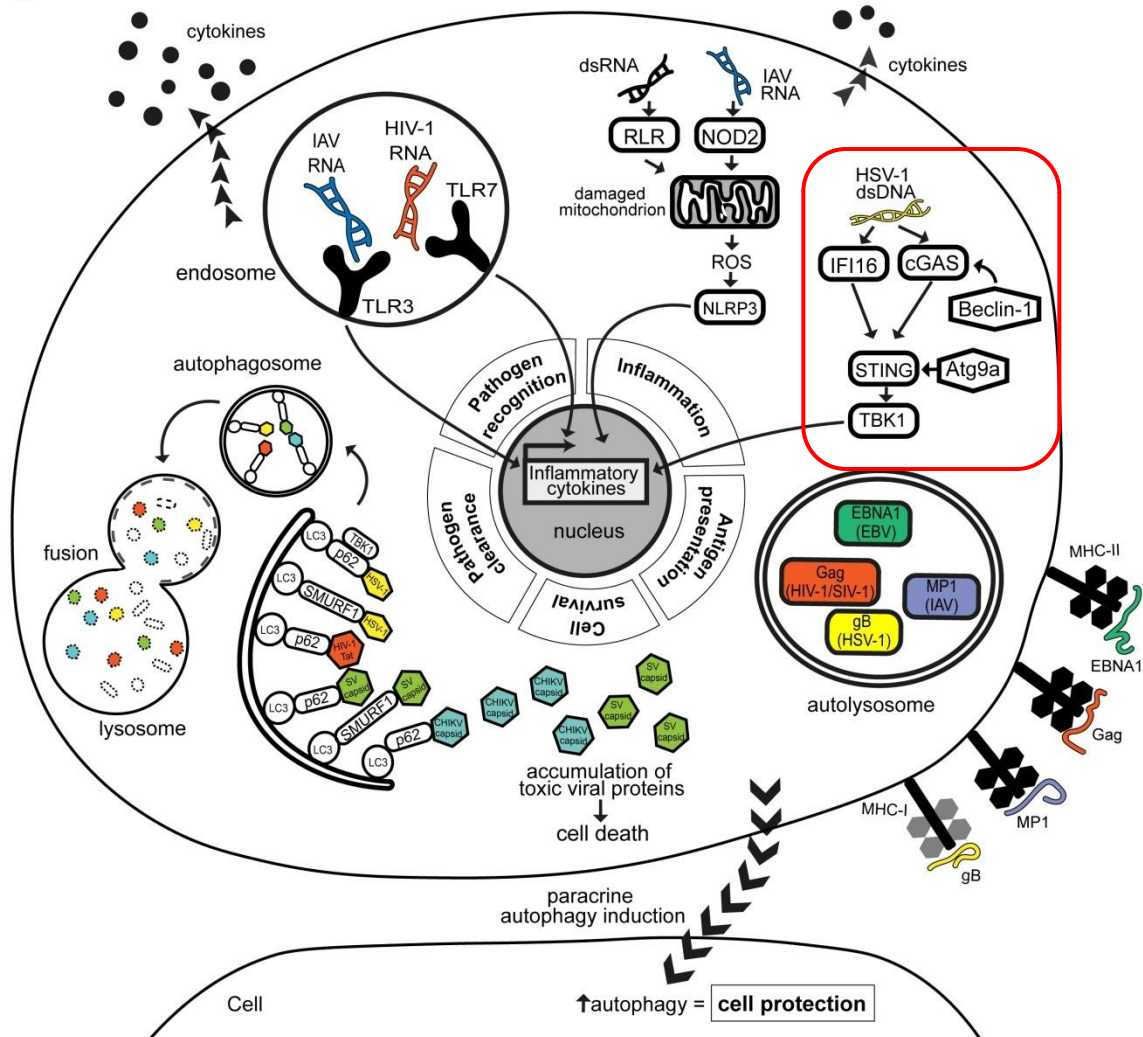
Role of autophagy in viral infection



Role of autophagy in viral infection



Role of autophagy in viral infection





Synopsis

- Autophagy is a major mechanism of self-defense against the accumulation of unwanted products.
- Complex machinery, ends up in lysosomes.
- Autophagy functions as an **antibacterial and antiviral mechanism**
- **However**, pathogens can **escape killing by autophagy** and some can even **use autophagy** to promote infection of host cells



TIP OF THE ICEBERG?

