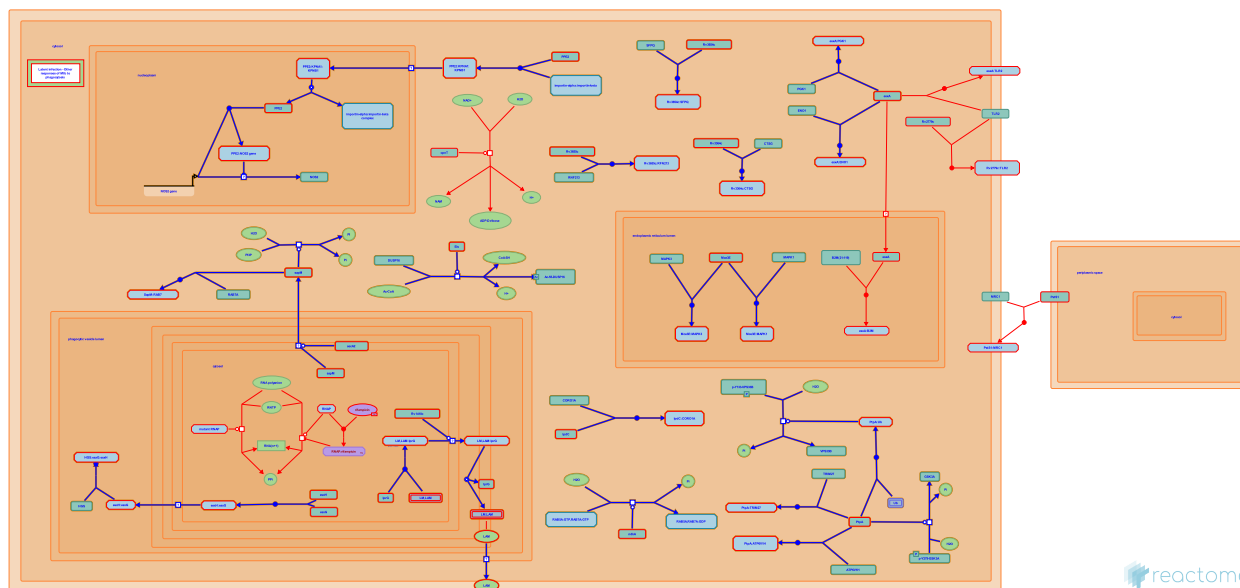


# Response of Mtb to phagocytosis



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/textbook/).

30/04/2024

## Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

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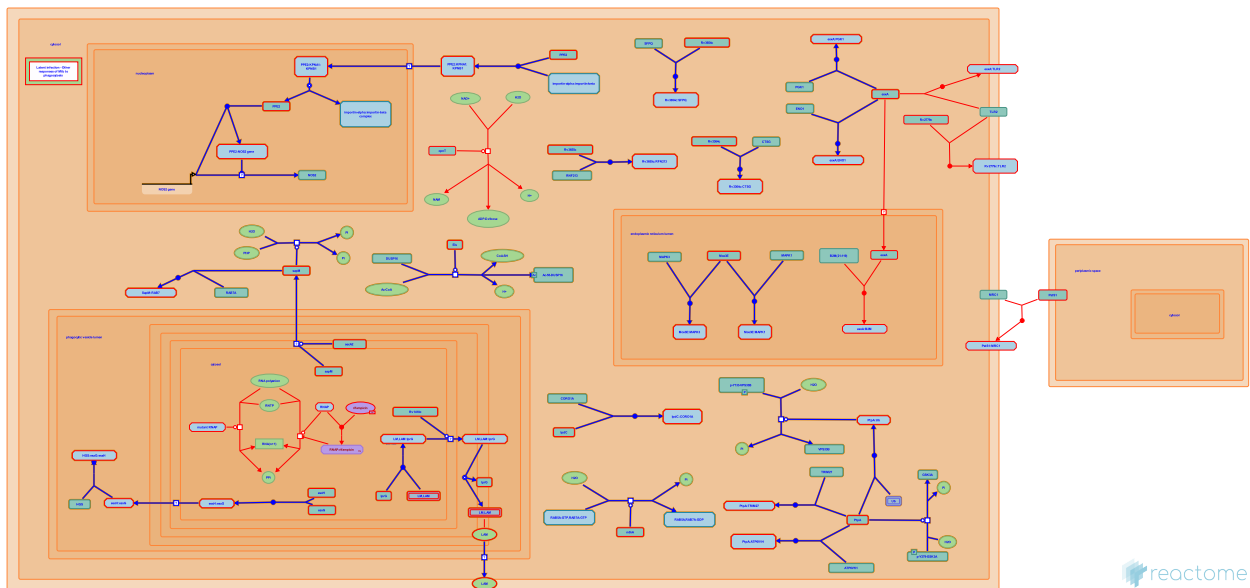
Reactome database release: 88

This document contains 6 pathways ([see Table of Contents](#))

## Response of Mtb to phagocytosis ↗

**Stable identifier:** R-HSA-9637690

**Diseases:** tuberculosis



*Mycobacterium tuberculosis* (Mtb) encounters a vastly changed environment shortly after being internalized by macrophages. The compartment it resides in, the phagosome, is acidified and devoid of important metal ions and is flooded with reactive oxygen and nitrogen species. Steps will be soon taken by the macrophage to "mature" the phagosome with all kinds of lysosomal digestive enzymes. However, unlike most other bacteria species, Mtb has evolved solutions to each of these threats. As a last resort to a strong immune response, some bacteria will enter a dormant state (de Chastellier 2009, Flannagan et al. 2009). To what extent this is true is still unclear (McDaniel et al. 2016). Upon weakening of the immune defense, Mtb reawakens from its dormant state and starts to multiply inside the phagocyte (Repasy et al. 2013).

### Literature references

- Kotton, DN., Repasy, T., Martinez, N., Hendricks, G., Kornfeld, H., Kirschner, DE. et al. (2013). Intracellular bacillary burden reflects a burst size for *Mycobacterium tuberculosis* in vivo. *PLoS Pathog.*, 9, e1003190. ↗
- Eda, S., Ganusov, VV., Krishna, N., McDaniel, MM., Handagama, WG. (2016). Quantifying Limits on Replication, Death, and Quiescence of *Mycobacterium tuberculosis* in Mice. *Front Microbiol*, 7, 862. ↗
- Cosio, G., Grinstein, S., Flannagan, RS. (2009). Antimicrobial mechanisms of phagocytes and bacterial evasion strategies. *Nat Rev Microbiol*, 7, 355-66. ↗
- de Chastellier, C. (2009). The many niches and strategies used by pathogenic mycobacteria for survival within host macrophages. *Immunobiology*, 214, 526-42. ↗

### Editions

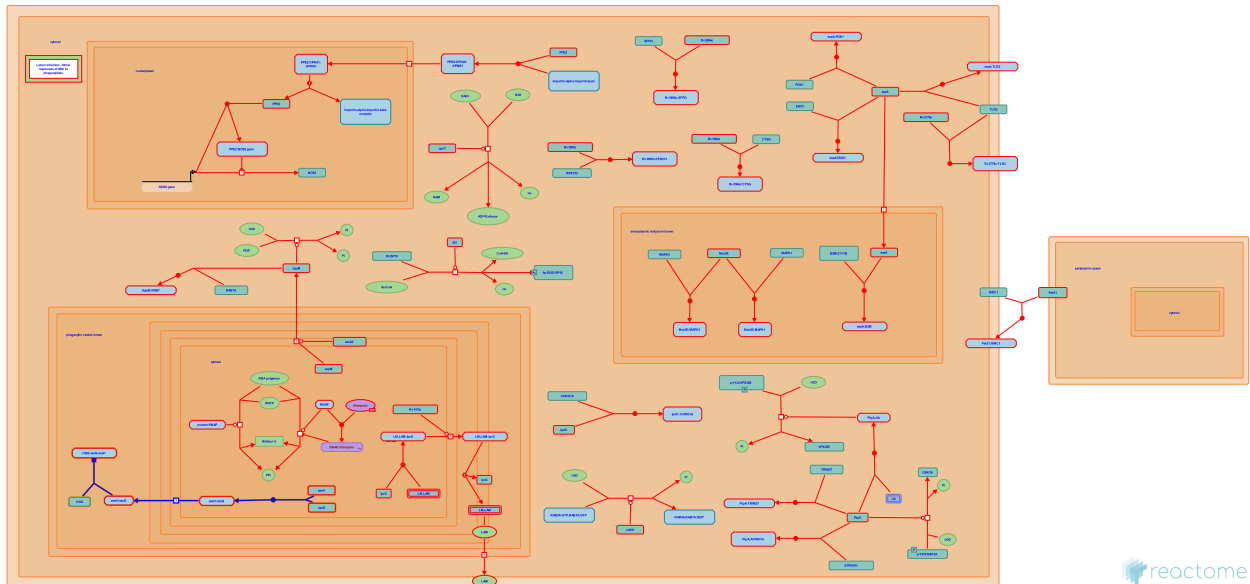
2019-02-06	Authored	Stephan, R.
2019-02-19	Edited	Jassal, B.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## Inhibition of membrane repair ↗

**Location:** [Response of Mtb to phagocytosis](#)

**Stable identifier:** R-HSA-9635644

**Diseases:** tuberculosis



When the phagosomal membrane is injured, this is sensed and acted upon both by the host phagocyte and Mtb. While the host repair system is activated, the bacterium is secreting proteins that block host repair components, effectively inhibiting repair (Mittal et al. 2018).

### Literature references

Uwase, G., Philips, JA., Köster, S., Hanson, PI., Tinaztepe, E., Mittal, E. et al. (2018). Mycobacterium tuberculosis Type VII Secretion System Effectors Differentially Impact the ESCRT Endomembrane Damage Response. *MBio*, 9 . ↗

### Editions

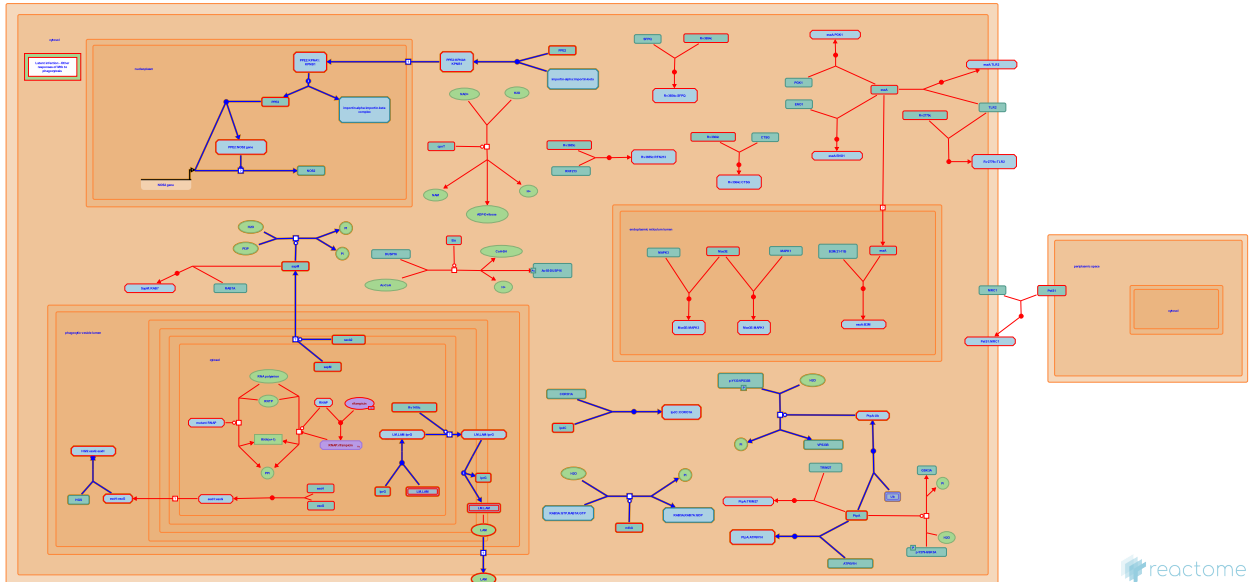
2019-02-06	Edited	Pardo, AM., Koile, I.
2019-02-06	Authored	Stephan, R.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## Suppression of phagosomal maturation ↗

**Location:** [Response of Mtb to phagocytosis](#)

**Stable identifier:** R-HSA-9637687

**Diseases:** tuberculosis



The fate of phagosomes is usually directed by factors in the host phagocyte and involves flooding itself with superoxide, nitric oxide, and protons. Acidification is the prerequisite for later fusion with a lysosome. *Mycobacterium tuberculosis* (Mtb) releases substances that inhibit all of these processes, effectively arresting the phagosome in the present state and creating a protected niche for Mtb multiplication (Russell 2011, Stutz et al. 2018).

### Literature references

Russell, DG. (2011). *Mycobacterium tuberculosis* and the intimate discourse of a chronic infection. *Immunol Rev*, 240, 252-68. ↗

Stutz, MD., Doerflinger, M., Pellegrini, M., Clark, MP. (2018). *Mycobacterium tuberculosis*: Rewiring host cell signaling to promote infection. *J. Leukoc. Biol.*, 103, 259-268. ↗

### Editions

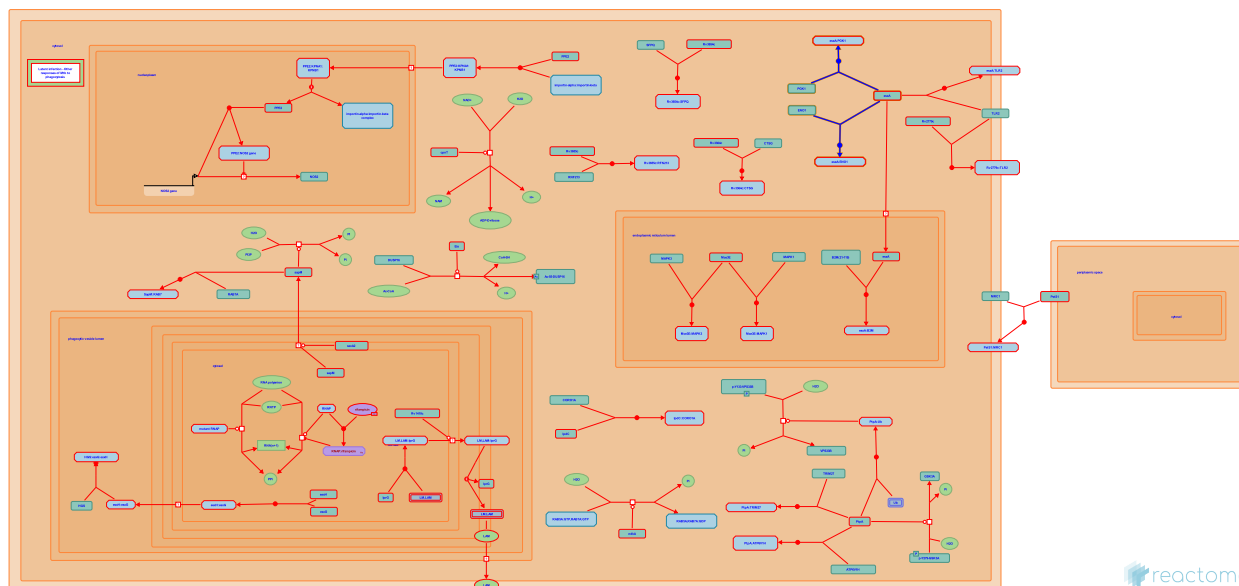
2019-02-06	Authored	Stephan, R.
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2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## Manipulation of host energy metabolism ↗

**Location:** [Response of Mtb to phagocytosis](#)

**Stable identifier:** R-HSA-963667

**Diseases:** tuberculosis



Mtb secretes proteins that enhance enzymatic activity of glucose metabolism in the phagocyte. The same proteins also appear to increase glucose uptake and to cause accumulation of DHAP, ultimately increasing the host cell's lipid production (Singh et al. 2015).

### Literature references

Rao, KV., Kaur, C., Chatterjee, S., Chaudhary, VK., Singh, V. (2015). M. tuberculosis Secretory Protein ESAT-6 Induces Metabolic Flux Perturbations to Drive Foamy Macrophage Differentiation. *Sci Rep*, 5, 12906. ↗

### Editions

2019-02-06	Authored	Stephan, R.
2019-02-13	Edited	Pardo, AM.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

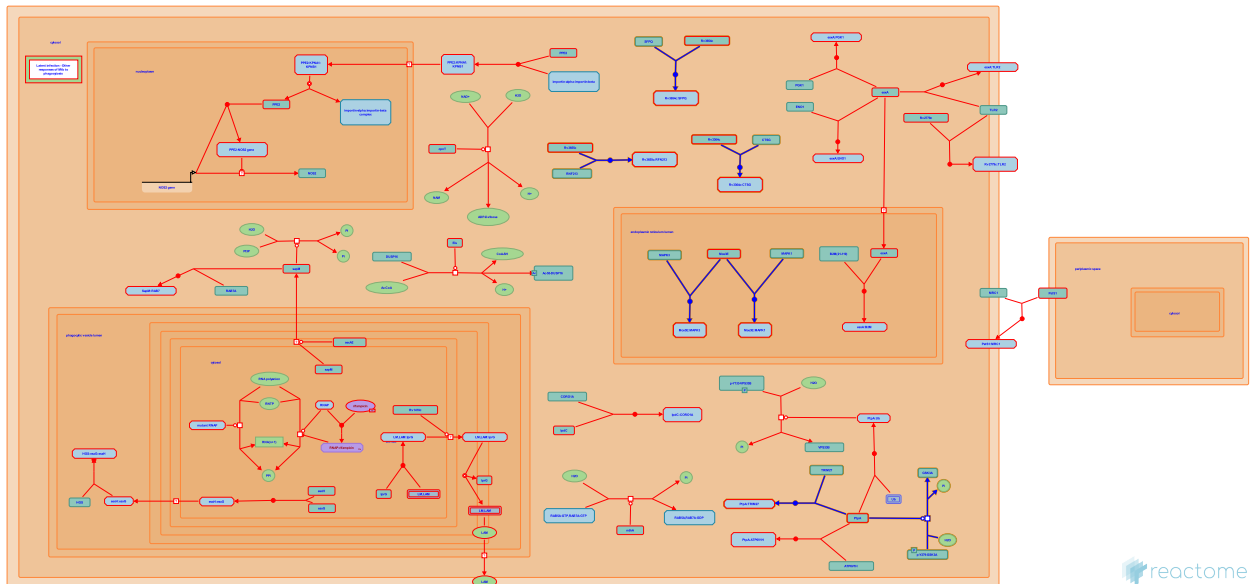
## Suppression of apoptosis ↗

**Location:** [Response of Mtb to phagocytosis](#)

**Stable identifier:** R-HSA-9635465

**Compartments:** cytosol

**Diseases:** tuberculosis



In order to survive and grow within the phagocyte, Mtb has to inhibit programmed cell death. Several proteins are secreted by Mtb that block different pathways leading to complete arrest of apoptosis (Moraco & Kornfeld 2014).

### Literature references

Kornfeld, H., Moraco, AH. (2014). Cell death and autophagy in tuberculosis. *Semin. Immunol.*, 26, 497-511. ↗

### Editions

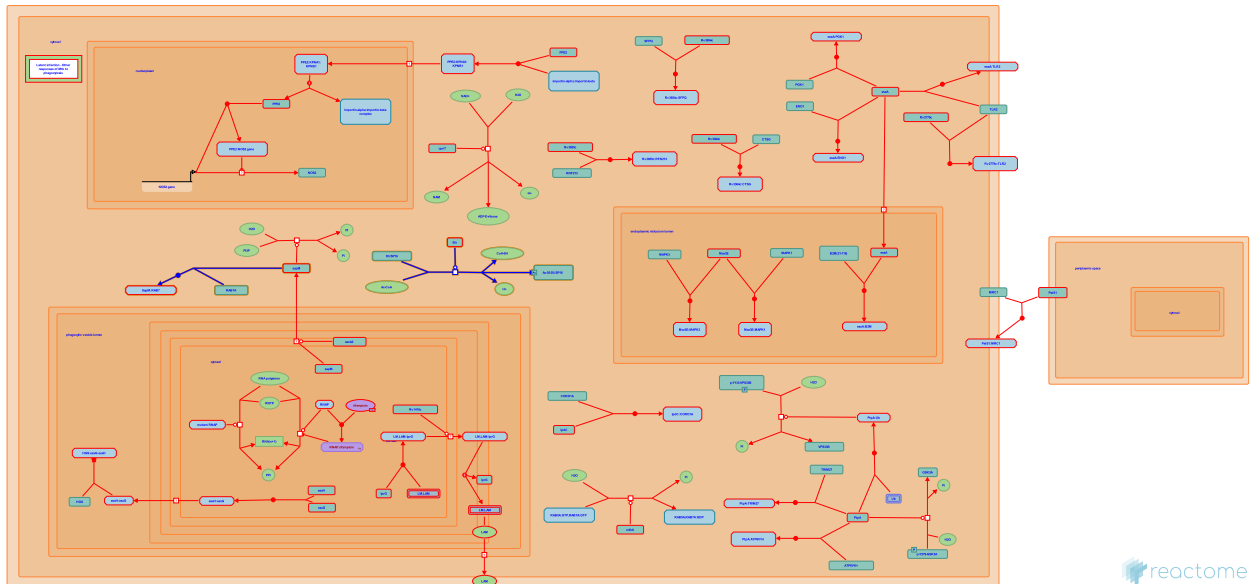
2019-02-12	Edited	Pardo, AM.
2019-02-12	Authored	Stephan, R.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## Suppression of autophagy ↗

**Location:** [Response of Mtb to phagocytosis](#)

**Stable identifier:** R-HSA-9636569

**Diseases:** tuberculosis



Autophagy, a distinct pathway of programmed cell death, is used by the phagocyte primarily to eradicate damaged cell organelles or unused proteins. As Mtb damages the phagosomal membrane it has to block autophagy processes to ensure maximum replication before exit from the cell (Jo 2013).

### Literature references

Jo, EK. (2013). Autophagy as an innate defense against mycobacteria. *Pathog Dis*, 67, 108-18. ↗

### Editions

2019-02-06	Authored	Stephan, R.
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