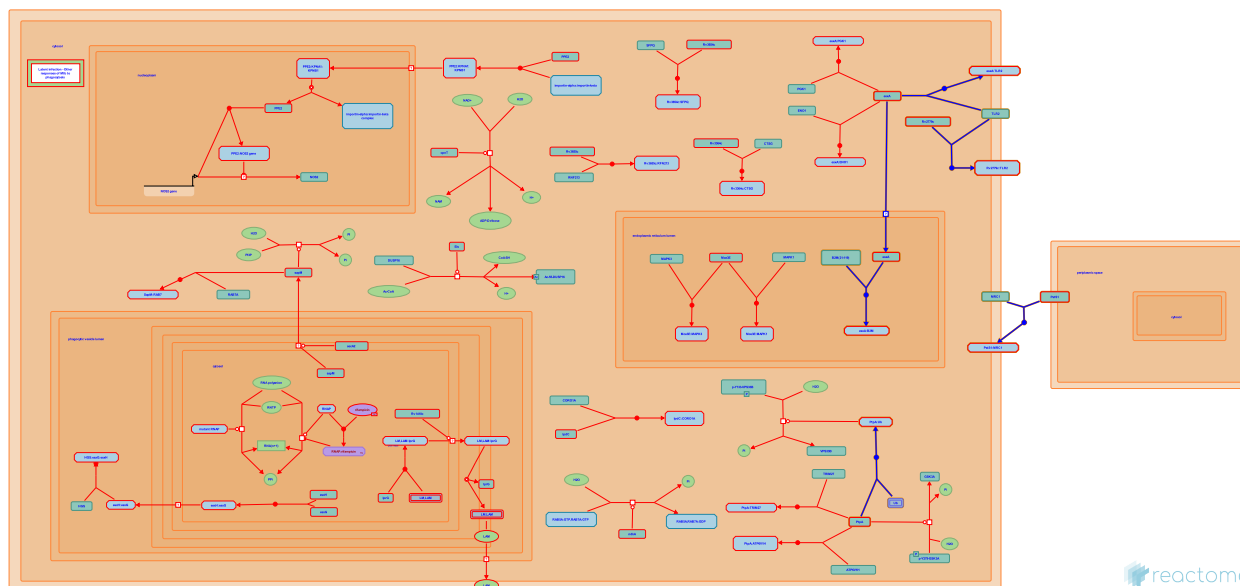


# Modulation by Mtb of host immune system



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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

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

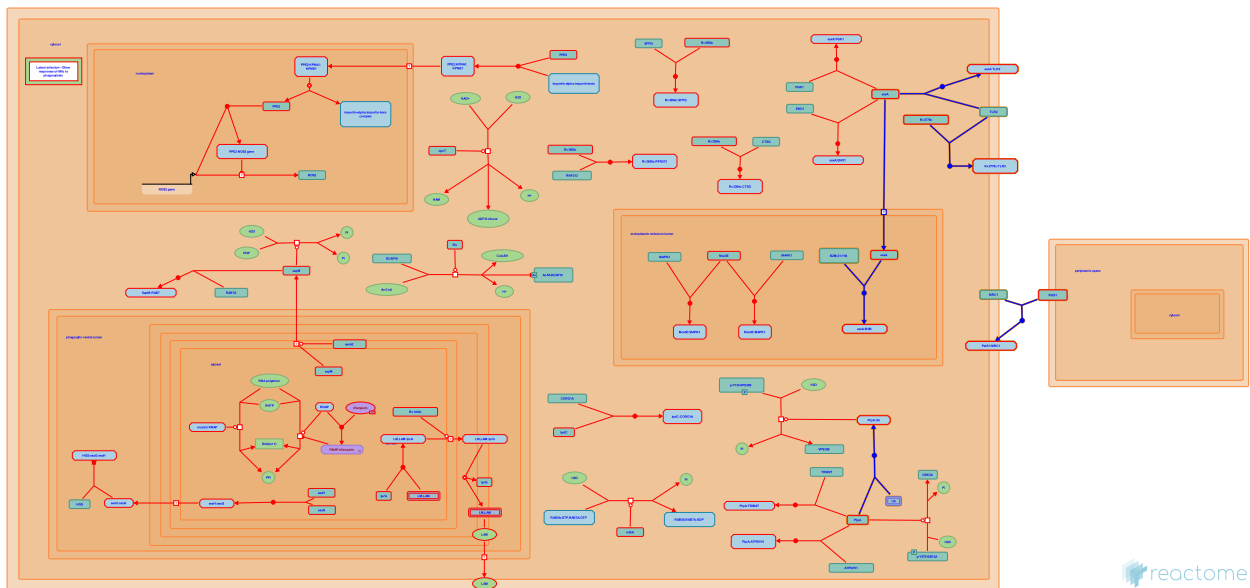
Reactome database release: 88

This document contains 1 pathway and 6 reactions ([see Table of Contents](#))

## Modulation by Mtb of host immune system ↗

**Stable identifier:** R-HSA-9637628

**Diseases:** tuberculosis



Mtb enhances its chances for being taken up by a phagocyte by blocking adaptive immune responses, as well as other innate immune system responses. Components of the bacterial cell wall also specifically promote phagocytosis via both the opsonic pathway and the presentation of adhesins (Esparza et al. 2015).

### Literature references

Zenteno, E., García, T., Esparza, M., Mancilla, R., Espinosa, P., Palomares, B. (2015). PstS-1, the 38-kDa Mycobacterium tuberculosis glycoprotein, is an adhesin, which binds the macrophage mannose receptor and promotes phagocytosis. *Scand. J. Immunol.*, 81, 46-55. ↗

### Editions

2019-02-19	Edited	Pardo, AM.
2019-02-19	Authored	Stephan, R.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## PstS1 binds MRC1 ↗

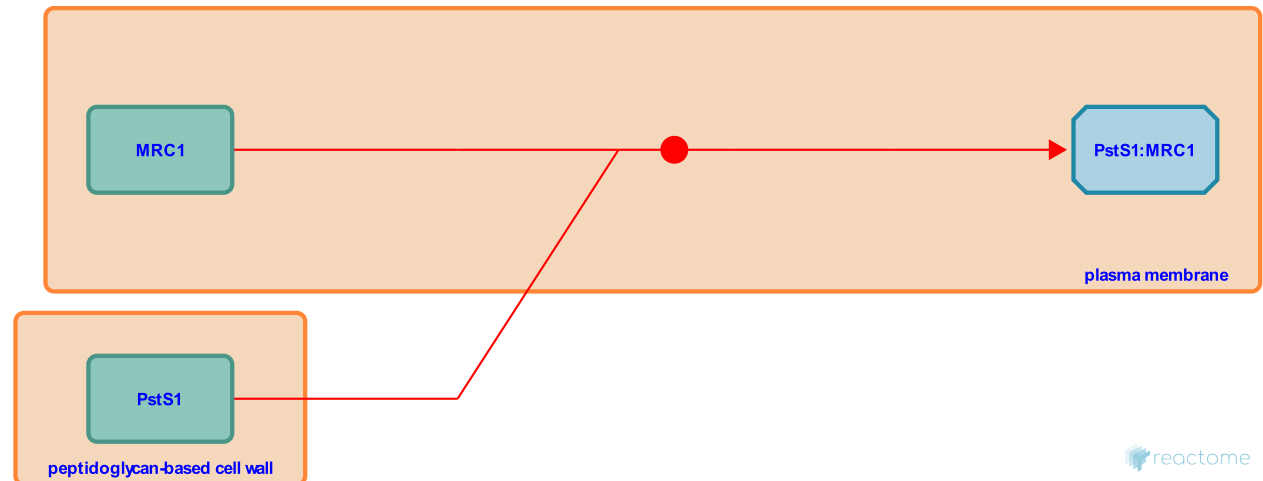
**Location:** [Modulation by Mtb of host immune system](#)

**Stable identifier:** R-HSA-9637605

**Type:** binding

**Compartments:** plasma membrane, peptidoglycan-based cell wall

**Diseases:** tuberculosis



Human macrophage mannose receptor (MRC1) recognizes Mtb by binding to phosphate-binding protein PstS1 (PstS1), which contains two molecules of mannose (Esparza et al. 2015).

### Literature references

Zenteno, E., García, T., Esparza, M., Mancilla, R., Espinosa, P., Palomares, B. (2015). PstS-1, the 38-kDa Mycobacterium tuberculosis glycoprotein, is an adhesin, which binds the macrophage mannose receptor and promotes phagocytosis. *Scand. J. Immunol.*, 81, 46-55. ↗

### Editions

2019-02-19	Edited	Pardo, AM.
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## esxA translocates from Mtb cytosol to the host's ER [↗](#)

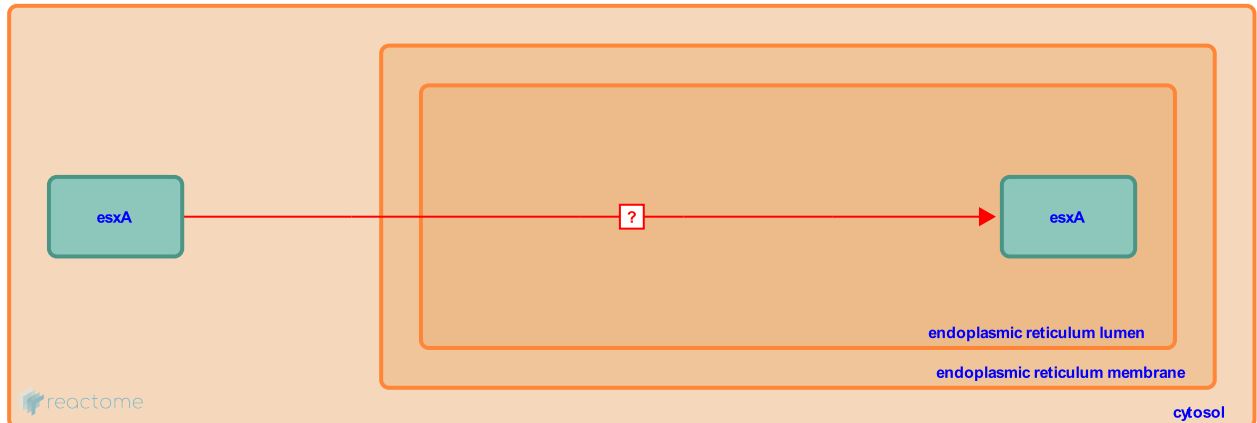
**Location:** [Modulation by Mtb of host immune system](#)

**Stable identifier:** R-HSA-9637651

**Type:** uncertain

**Compartments:** endoplasmic reticulum lumen, cytosol

**Diseases:** tuberculosis



Mtb secreted 6 kDa early secretory antigenic target (esxA) succeeds in entering the endoplasmic reticulum of host macrophages by an unknown mechanism (Sreejit et al. 2014).

**Followed by:** [esxA binds B2M](#)

## Literature references

Sreejit, G., Parveen, N., Ghosh, S., Mukhopadhyay, S., Jha, V., Valluri, VL. et al. (2014). The ESAT-6 protein of Mycobacterium tuberculosis interacts with beta-2-microglobulin ( $\beta$ 2M) affecting antigen presentation function of macrophage. *PLoS Pathog.*, 10, e1004446. [↗](#)

## Editions

2019-02-19	Edited	Pardo, AM.
2019-02-19	Authored	Stephan, R.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## esxA binds TLR2 ↗

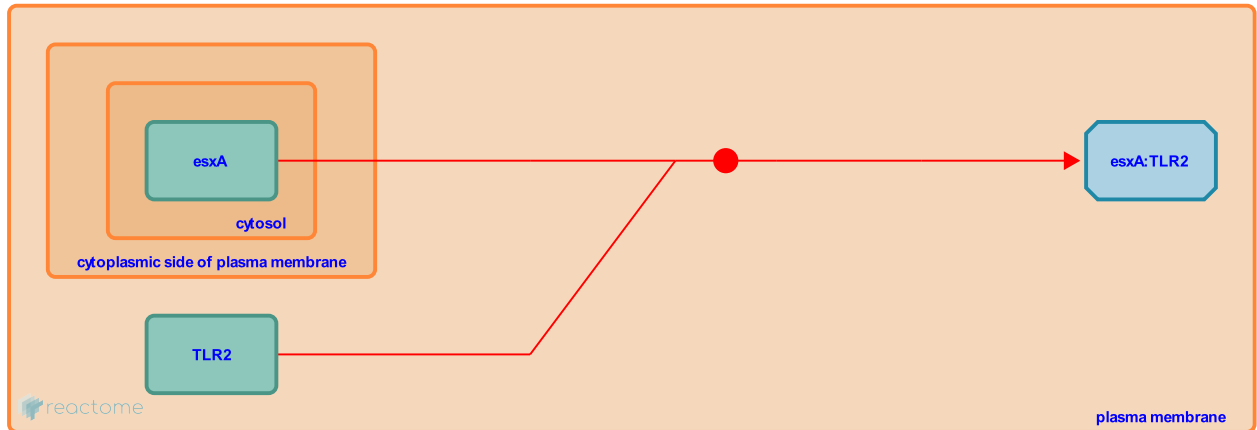
**Location:** [Modulation by Mtb of host immune system](#)

**Stable identifier:** R-HSA-9637638

**Type:** binding

**Compartments:** plasma membrane, cytosol

**Diseases:** tuberculosis



Mtb secreted Mtb 6 kDa early secretory antigenic target (esxA) binds to toll-like-receptor 2 (TLR2), inhibiting the human immune response (Pathak et al. 2007).

## Literature references

Bhattacharyya, A., Basu, J., Banerjee, A., Basu, KK., Kundu, M., Pathak, SK. et al. (2007). Direct extracellular interaction between the early secreted antigen ESAT-6 of Mycobacterium tuberculosis and TLR2 inhibits TLR signaling in macrophages. *Nat. Immunol.*, 8, 610-8. ↗

## Editions

2019-02-19	Edited	Pardo, AM.
2019-02-19	Authored	Stephan, R.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.

## Rv2779c binds TLR2 [↗](#)

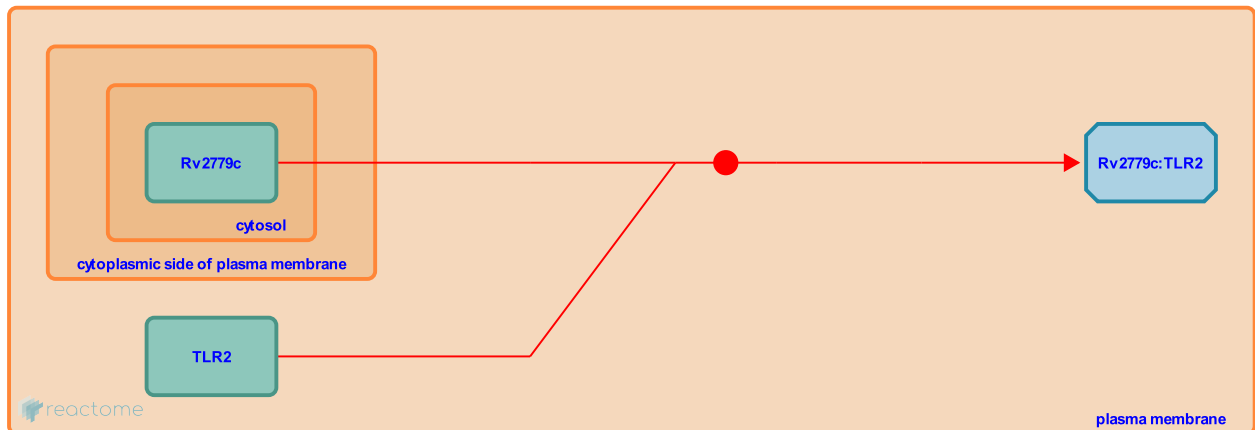
**Location:** [Modulation by Mtb of host immune system](#)

**Stable identifier:** R-HSA-9637641

**Type:** binding

**Compartments:** plasma membrane, cytosol

**Diseases:** tuberculosis



Mtb Rv2779c protein binds to toll-like-receptor 2 (TLR2), inhibiting the human immune response (Liu et al. 2015).

### Literature references

Cai, H., Liu, Y., Huang, HR., Chen, ST., Li, JY. (2016). The rLrp of Mycobacterium tuberculosis inhibits proinflammatory cytokine production and downregulates APC function in mouse macrophages via a TLR2-mediated PI3K/Akt pathway activation-dependent mechanism. *Cell. Mol. Immunol.*, 13, 729-746. [↗](#)

### Editions

2019-02-19	Edited	Pardo, AM.
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## esxA binds B2M ↗

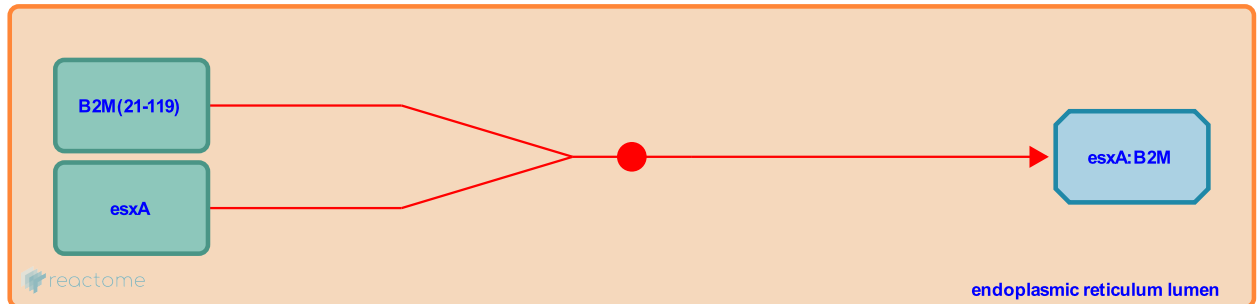
**Location:** [Modulation by Mtb of host immune system](#)

**Stable identifier:** R-HSA-9637635

**Type:** binding

**Compartments:** endoplasmic reticulum lumen

**Diseases:** tuberculosis



Mtb 6 kDa early secretory antigenic target (esxA) binds to freely available human beta-2-microglobulin (B2M) in the endoplasmic reticulum lumen, inhibiting the loading of antigen-derived peptides to B2M, a component of the class I major histocompatibility complex (MHC-I complex) (Sreejit et al. 2014).

**Preceded by:** [esxA translocates from Mtb cytosol to the host's ER](#)

## Literature references

Sreejit, G., Parveen, N., Ghosh, S., Mukhopadhyay, S., Jha, V., Valluri, VL. et al. (2014). The ESAT-6 protein of Mycobacterium tuberculosis interacts with beta-2-microglobulin ( $\beta$ 2M) affecting antigen presentation function of macrophage. *PLoS Pathog.*, 10, e1004446. ↗

## Editions

2019-02-19	Edited	Pardo, AM.
2019-02-19	Authored	Stephan, R.
2019-10-23	Reviewed	Wilkinson, RJ., Deffur, A.



## PtpA binds Ubiquitin [↗](#)

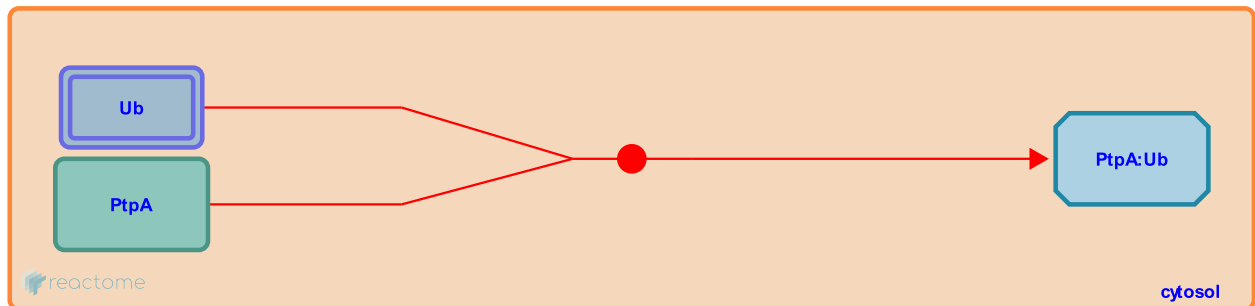
**Location:** [Modulation by Mtb of host immune system](#)

**Stable identifier:** R-HSA-9636461

**Type:** binding

**Compartments:** cytosol

**Diseases:** tuberculosis



Protein-tyrosine phosphatase (ptpA) binds human ubiquitin (Ub), which is necessary for its phosphatase activity (Wang et al. 2015).

### Literature references

Ge, PP., Gao, GF., Qiu, XB., Wang, J., Li, BX., Li, J. et al. (2015). Mycobacterium tuberculosis suppresses innate immunity by coopting the host ubiquitin system. *Nat. Immunol.*, 16, 237-45. [↗](#)

### Editions

2019-02-06	Authored	Stephan, R.
2019-02-13	Edited	Koile, I.
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