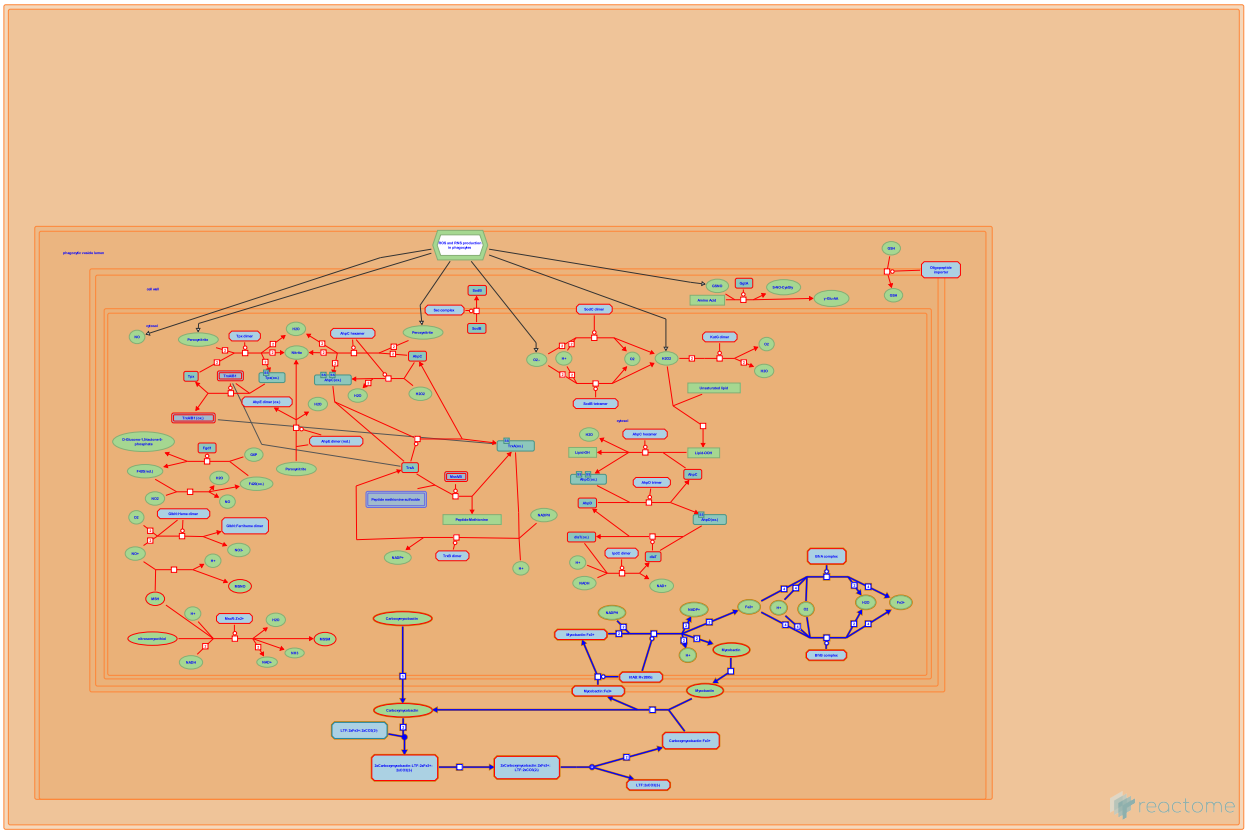
Mtb iron assimilation by chelation



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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.

02/05/2024

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. ↗

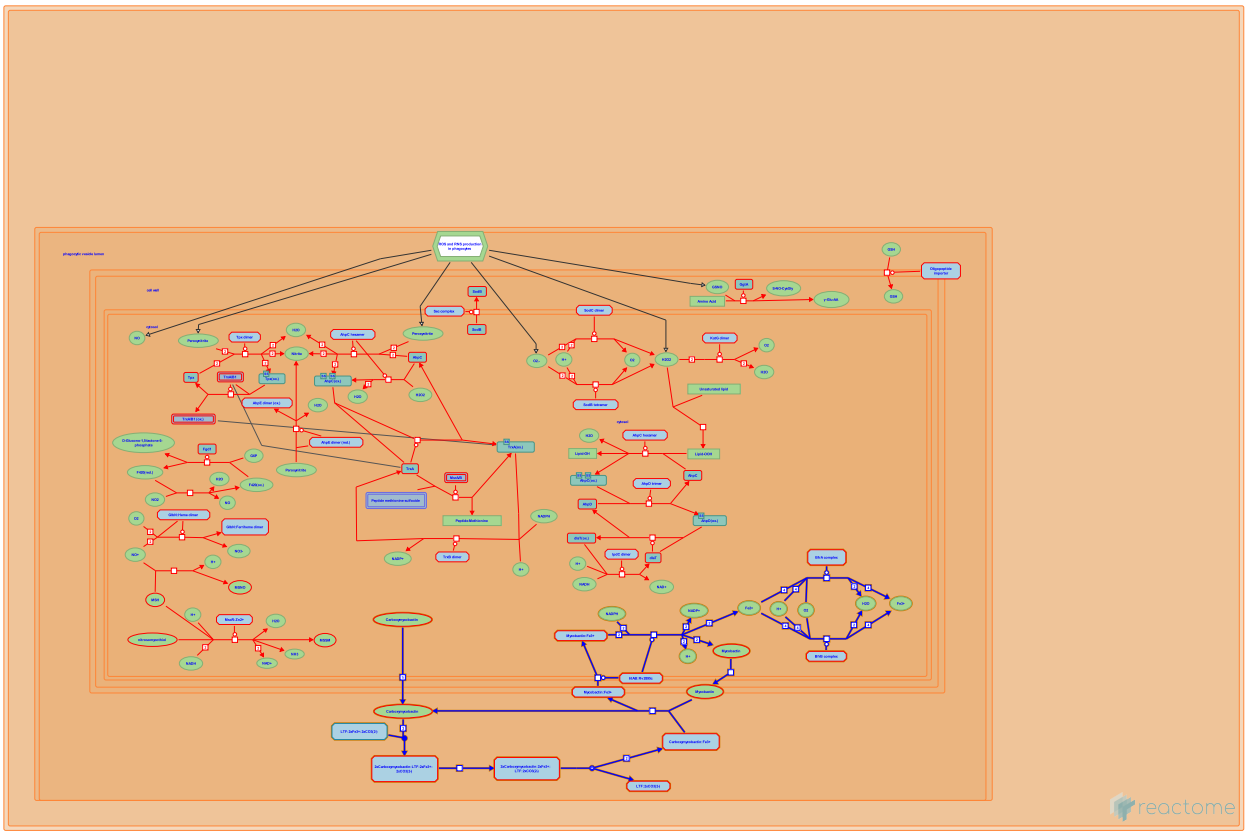
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Mtb iron assimilation by chelation ↗

Stable identifier: R-HSA-1222449

Diseases: tuberculosis



Uptake of iron in *Mtb*, especially when the bacterium is in the host, strongly depends on siderophores. Humans, through secretion of lactoferrin, maintain an iron concentration of 10^(-18) M within macrophages, and the bacterium has evolved the siderophores mycobactin T and exomycobactin T (formerly exochelin) to cope with this shortage. While nonpolar mycobactin T stays in the cell wall and only moves around in liquid droplets, polar exochelin is abundantly secreted. As it can bind iron with higher affinity than lactoferrin, it frequently scavenges iron ions from this molecule (Miethke & Marahiel 2007).

Literature references

Marahiel, MA., Miethke, M. (2007). Siderophore-based iron acquisition and pathogen control. *Microbiol Mol Biol Rev, 71*, 413-51. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

Carboxymycobactin gets secreted ↗

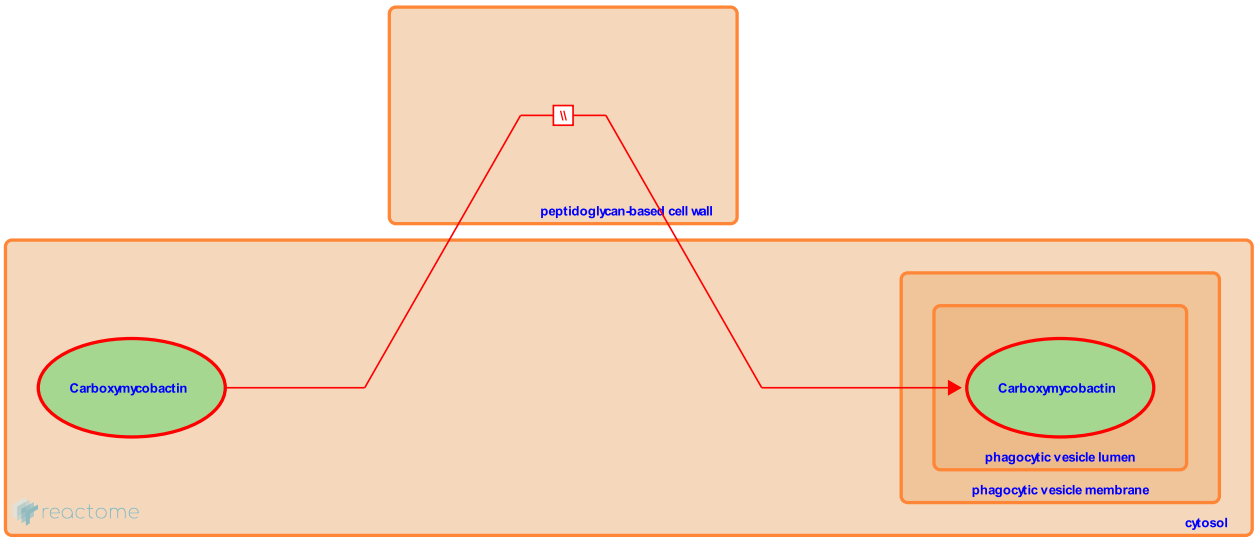
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1222738

Type: omitted

Compartments: peptidoglycan-based cell wall

Diseases: tuberculosis



Carboxymycobactin is the more polar siderophore of *Mtb* and it is localized, after its secretion, in the phagosomal lumen. The transporters for export and secretion of this molecule are still unknown (Madigan et al. 2012).

Followed by: Carboxymycobactin binds LTF:2xFe3+:2xCO3(2-)

Literature references

Layre, E., McConnell, MJ., Rodriguez, GM., Barry CE, 3rd., Debono, CA., Moody, DB. et al. (2012). Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in Mycobacterium tuberculosis. *Proc Natl Acad Sci U S A, 109*, 1257-62. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

Mycobactin is exported ↗

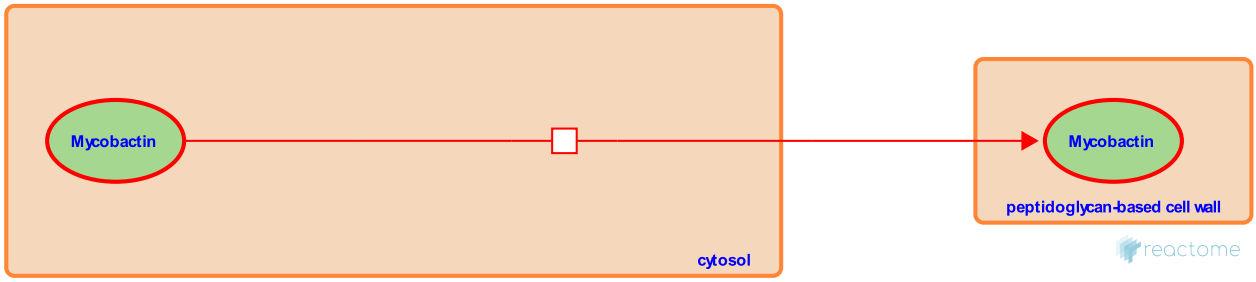
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1222722

Type: transition

Compartments: cytosol, peptidoglycan-based cell wall

Diseases: tuberculosis



Mycobactin is the lipophilic siderophore of *Mtb*. After export into the periplasmic space, it localizes to the bacterium's cell wall. The responsible transporter activity is still unknown (Madigan et al. 2012).

Followed by: Carboxymycobactin and mycobactin exchange their iron load

Literature references

Layre, E., McConnell, MJ., Rodriguez, GM., Barry CE, 3rd., Debono, CA., Moody, DB. et al. (2012). Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in Mycobacterium tuberculosis. *Proc Natl Acad Sci U S A, 109*, 1257-62. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

Carboxymycobactin binds LTF:2xFe3+:2xCO3(2-) ↗

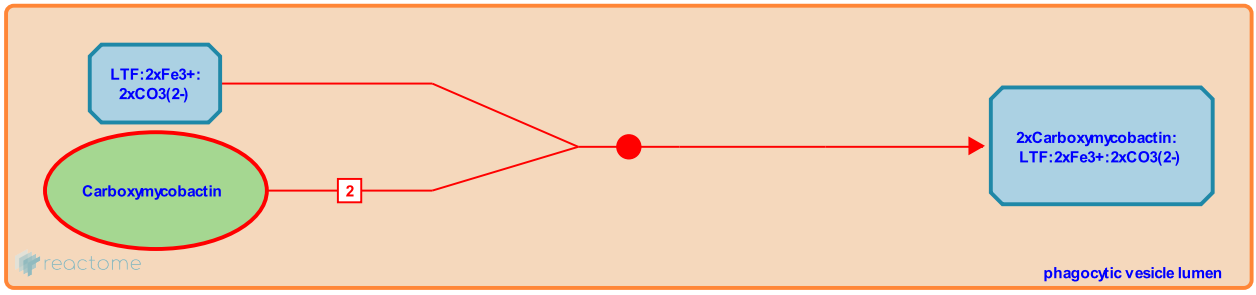
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1222641

Type: binding

Compartments: phagocytic vesicle lumen

Diseases: tuberculosis



Since bacterial siderophores bind iron with much greater affinity, they can scavenge iron ions from loaded lactoferrin (Madigan et al. 2012).

Preceded by: Carboxymycobactin gets secreted

Followed by: Carboxymycobactin and mycobactin exchange their iron load, Carbocymycobactin binds Fe3+ from LTF:2xFe3+:2xCO3(2-)

Literature references

Layre, E., McConnell, MJ., Rodriguez, GM., Barry CE, 3rd., Debono, CA., Moody, DB. et al. (2012). Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in Mycobacterium tuberculosis. *Proc Natl Acad Sci U S A, 109*, 1257-62. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

Carbocymycobactin binds Fe3+ from LTF:2xFe3+:2xCO3(2-)

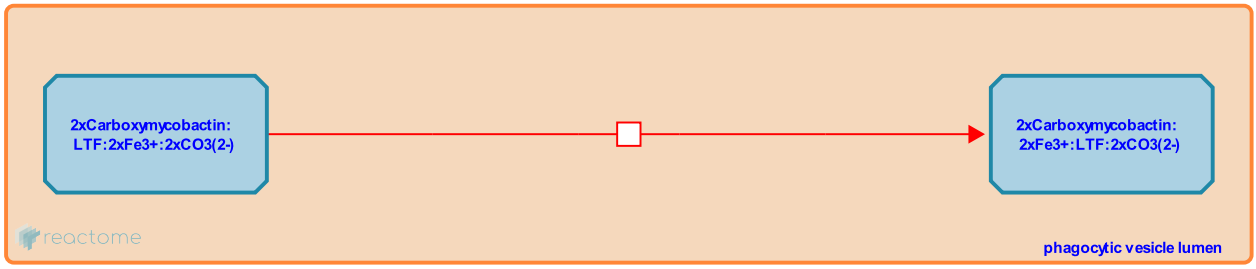
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-8951549

Type: transition

Compartments: phagocytic vesicle lumen

Diseases: tuberculosis



Since bacterial siderophores bind iron with much greater affinity, they can scavenge iron ions from loaded lactoferrin (Madigan et al. 2012).

Preceded by: Carboxymycobactin binds LTF:2xFe3+:2xCO3(2-)

Followed by: LTF:2xCO3(2-) dissociates from Carbocymycobactin:Fe3+

Literature references

Layre, E., McConnell, MJ., Rodriguez, GM., Barry CE, 3rd., Debono, CA., Moody, DB. et al. (2012). Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in Mycobacterium tuberculosis. *Proc Natl Acad Sci U S A, 109*, 1257-62.

Editions

2011-01-10	Authored	Stephan, R.
2012-04-30	Reviewed	Warner, D.
2016-12-08	Edited	Jassal, B.

LTF:2xCO3(2-) dissociates from Carbocymycobactin:Fe3+ ↗

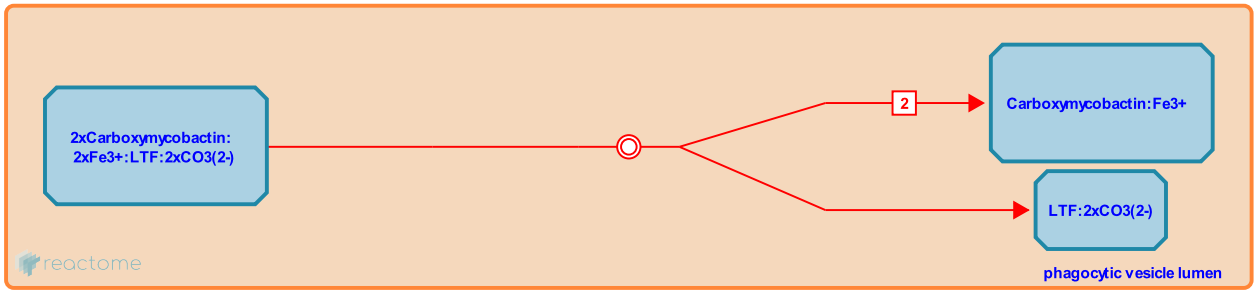
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-8951552

Type: dissociation

Compartments: phagocytic vesicle lumen

Diseases: tuberculosis



Since bacterial siderophores bind iron with much greater affinity, they can scavenge iron ions from loaded lactoferrin (Madigan et al. 2012).

Preceded by: Carbocymycobactin binds Fe3+ from LTF:2xFe3+:2xCO3(2-)

Literature references

Layre, E., McConnell, MJ., Rodriguez, GM., Barry CE, 3rd., Debono, CA., Moody, DB. et al. (2012). Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in Mycobacterium tuberculosis. *Proc Natl Acad Sci U S A, 109*, 1257-62. ↗

Editions

2011-01-10	Authored	Stephan, R.
2012-04-30	Reviewed	Warner, D.
2016-12-08	Edited	Jassal, B.

Carboxymycobactin and mycobactin exchange their iron load ↗

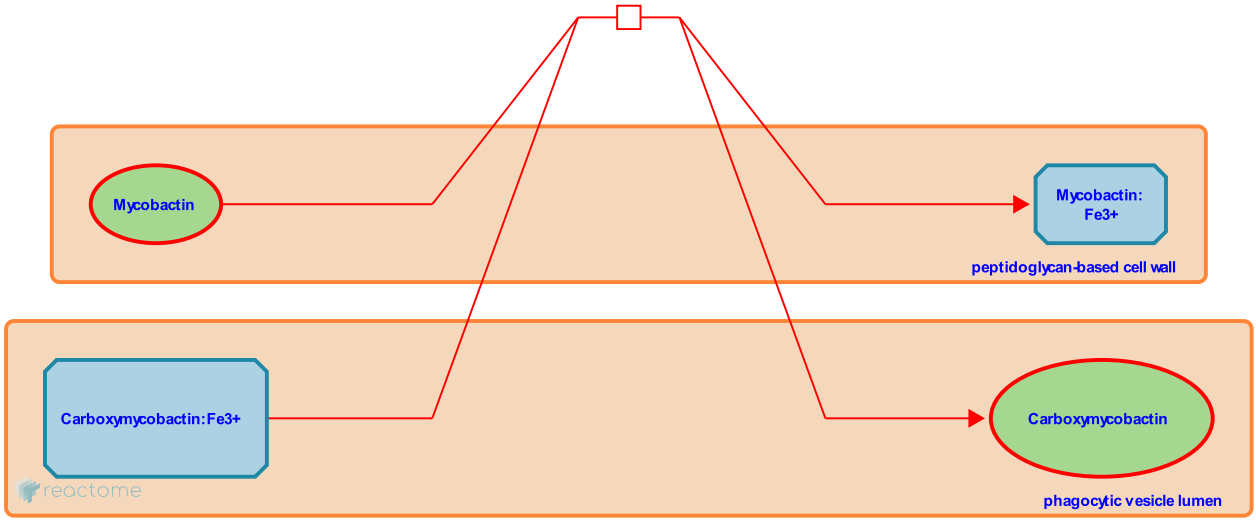
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1222325

Type: transition

Compartments: extracellular region, peptidoglycan-based cell wall

Diseases: tuberculosis



Carboxymycobactin and mycobactin exchange their iron loads. This interplay between polar and nonpolar siderophore is unique to *Mtb*. However, mycobactin can gather iron from nonpolar regions of the host cell by itself too (Madigan et al. 2012).

Preceded by: Carboxymycobactin binds LTF:2xFe3+:2xCO3(2-), Mycobactin is exported

Followed by: Loaded mycobactin gets imported

Literature references

Layre, E., McConnell, MJ., Rodriguez, GM., Barry CE, 3rd., Debono, CA., Moody, DB. et al. (2012). Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in Mycobacterium tuberculosis. *Proc Natl Acad Sci U S A, 109*, 1257-62. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

Loaded mycobactin gets imported ↗

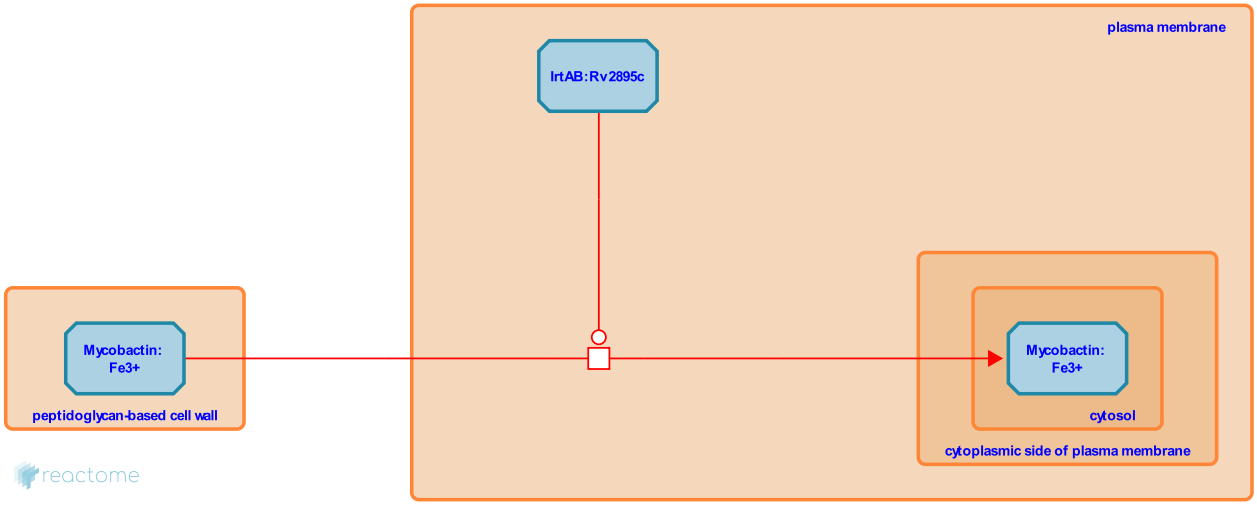
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1222597

Type: transition

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

Diseases: tuberculosis



The ABC-type transporter IrtA, probably complexed with IrtB and ViuB (Rv2895c), specifically transports iron-loaded mycobactin into the cytosol (Ryndak et al. 2009).

Preceded by: Carboxymycobactin and mycobactin exchange their iron load

Followed by: Iron is reduced and separates from mycobactin

Literature references

Smith, I., Ryndak, MB., Rodriguez, GM., Wang, S. (2010). The Mycobacterium tuberculosis high-affinity iron importer, IrtA, contains an FAD-binding domain. *J Bacteriol, 192*, 861-9. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

Iron is reduced and separates from mycobactin ↗

Location: Mtb iron assimilation by chelation

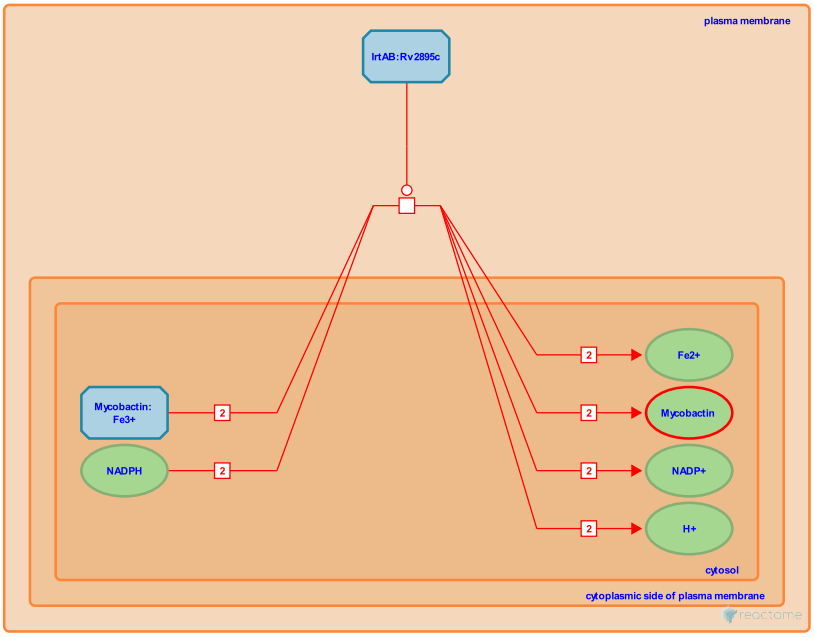
Stable identifier: R-HSA-1222399

Type: transition

Compartments: plasma membrane, cytosol

Diseases: tuberculosis

Inferred from: Iron is reduced and separates from enterobactin (Escherichia coli)



The IrtA transporter has a flavin reductase domain very much like Fre from E.coli that can probably act as ferrisiderophore reductase to relieve incoming loaded mycobactin from its Fe3+ by reducing it to Fe2+. Furthermore Rv2895c, which co-precipitates with IrtB and therefore is probably part of the transporter complex, has such a domain as well (Farhana et al. 2008).

Preceded by: Loaded mycobactin gets imported

Literature references

Tyagi, AK., Ehtesham, NZ., Farhana, A., Hasnain, SE., Rathore, SS., Kumar, S. et al. (2008). Mechanistic insights into a novel exporter-importer system of Mycobacterium tuberculosis unravel its role in trafficking of iron. *PLoS One, 3*, e2087. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

BfrA stores iron ↗

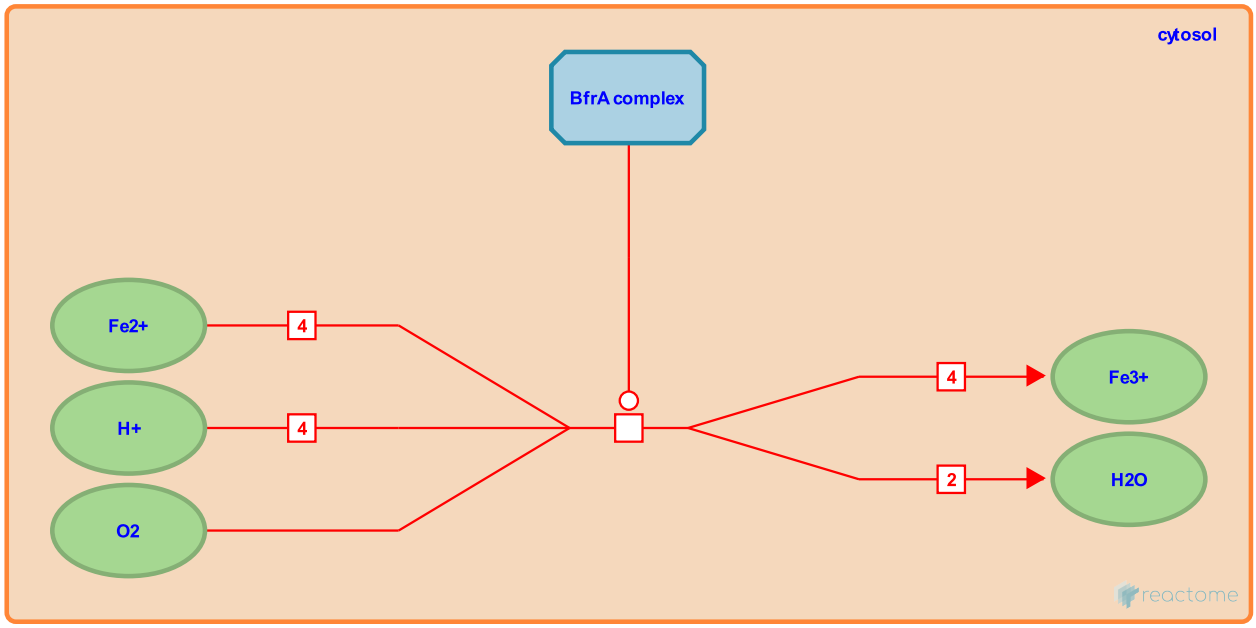
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1562604

Type: transition

Compartments: cytosol

Diseases: tuberculosis



Mtb bacterioferritin BfrA oxidises Fe2+ to Fe3+, migrates them to its centre, and collects thousands of them as FeO(OH) in the central mineral core from which they can be later remobilised (Reddy et al. 2012).

Literature references

Puri, RV., Tyagi, AK., Reddy, PV., Khera, A. (2012). Iron storage proteins are essential for the survival and pathogenesis of Mycobacterium tuberculosis in THP-1 macrophages and the guinea pig model of infection. *J Bacteriol, 194*, 567-75. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-09-05	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

BfrB stores iron ↗

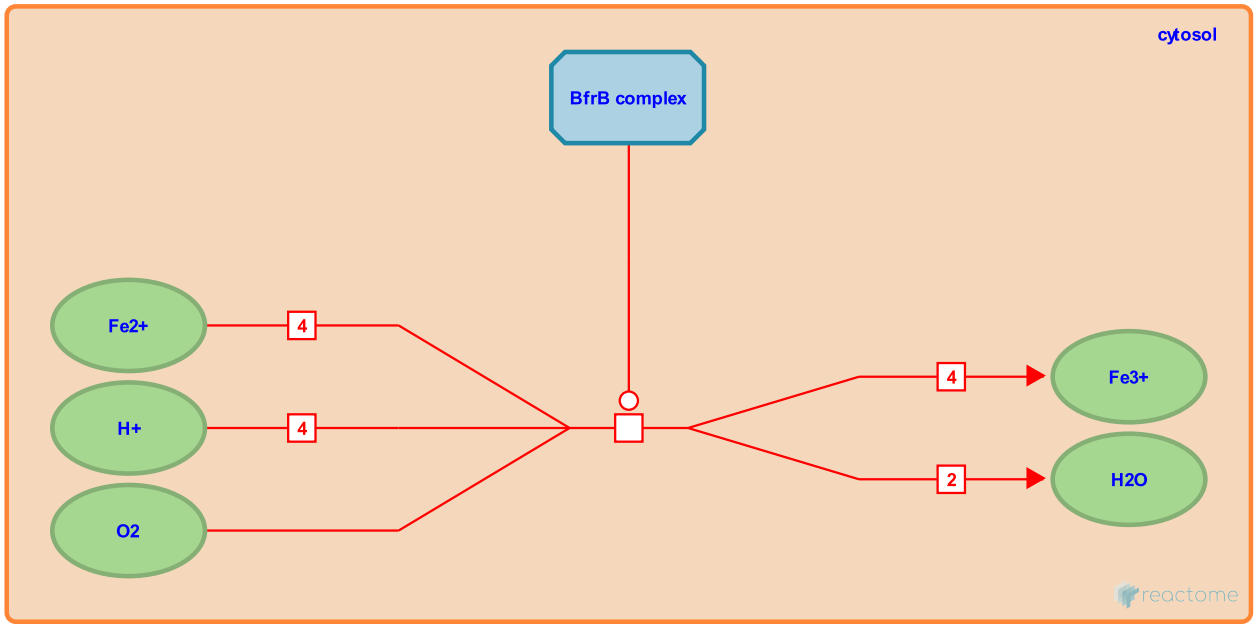
Location: Mtb iron assimilation by chelation

Stable identifier: R-HSA-1562603

Type: transition

Compartments: cytosol

Diseases: tuberculosis



Mtb bacterioferritin BfrB oxidises Fe2+ to Fe3+, migrates them to its centre, and collects thousands of them as FeO(OH) in the central mineral core from which they can be later remobilised (Harrison & Arrosio 1996, Khare et al. 2011).

Literature references

Harrison, PM., Arosio, P. (1996). The ferritins: molecular properties, iron storage function and cellular regulation. *Biochim Biophys Acta, 1275*, 161-203. ↗

Gupta, V., Sauter, NK., Tyagi, AK., Nangpal, P., Khare, G., Gupta, RK. (2011). Ferritin structure from Mycobacterium tuberculosis: comparative study with homologues identifies extended C-terminus involved in ferroxidase activity . *PLoS One, 6*, e18570. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-09-05	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.

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