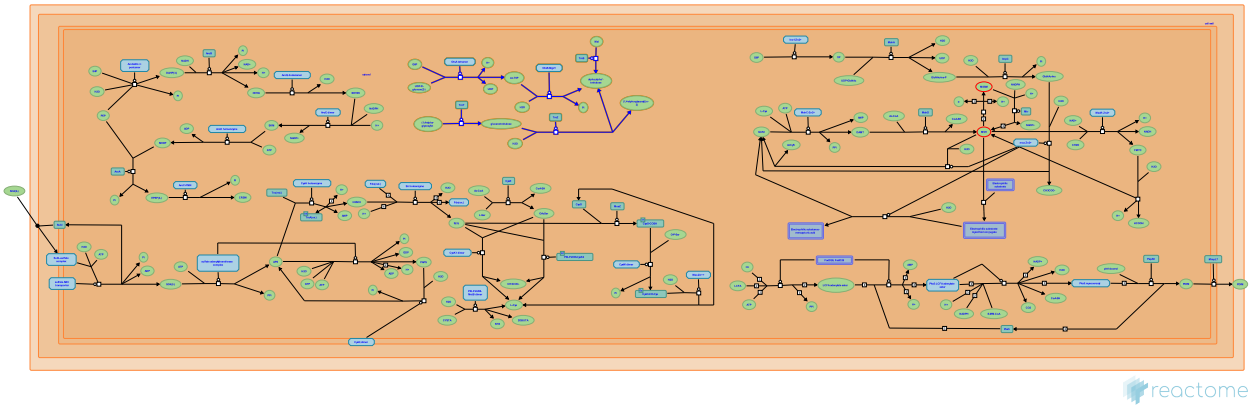
Trehalose biosynthesis



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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. ↗

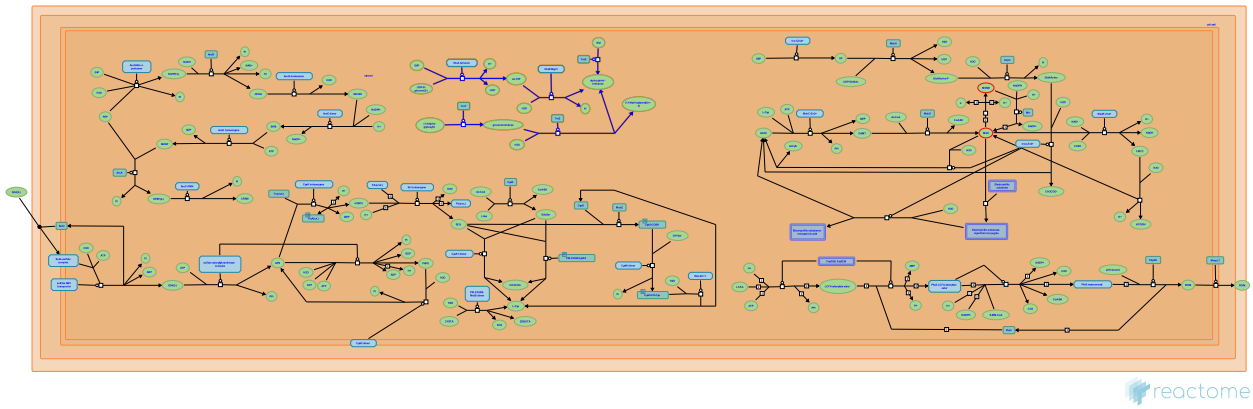
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Trehalose biosynthesis ↗

Stable identifier: R-MTU-868688

Compartments: cytosol



The non-reducing disaccharide trehalose is found in insects, plants, and microorganisms. In bacteria, it is a storage energy source and is essential for the survival of many stress conditions. In mycobacteria, trehalose is also part of the cell wall and of the 'cord factor' which is important for entry into the host (Elbein et al, 2003; Tropis et al, 2005; Jain & Roy, 2009)

M. tuberculosis has three ways to synthesize trehalose: from UDP-glucose and glucose phosphate (the OtsAB pathway), from maltose (the TreS pathway), and from glycogen (TreYZ pathway). The OtsAB pathway was shown to be essential for the organism. It is not known, however, whether or not the essentiality of trehalose for the mycobacterial growth is directly connected to the biosynthesis of cell wall mycolates (De Smet et al, 2000; Murphy et al, 2005)

Literature references

Jain, NK., Roy, I. (2009). Effect of trehalose on protein structure. *Protein Sci, 18*, 24-36. ↗

Apt, AS., Young, DB., Stewart, GR., McAlister, MS., Robertson, BD., Harris, R. et al. (2005). The OtsAB pathway is essential for trehalose biosynthesis in Mycobacterium tuberculosis. *J Biol Chem, 280*, 14524-9. ↗

Morbach, S., Wolf, A., Krämer, R., Meniche, X., Tropis, M., Gebhardt, H. et al. (2005). The crucial role of trehalose and structurally related oligosaccharides in the biosynthesis and transfer of mycolic acids in Corynebacterineae. *J Biol Chem, 280*, 26573-85. ↗

Young, DB., De Smet, KA., Robertson, BD., Brown, IN., Weston, A. (2000). Three pathways for trehalose biosynthesis in mycobacteria. *Microbiology, 146*, 199-208. ↗

Elbein, AD., Pastuszak, I., Carroll, D., Pan, YT. (2003). New insights on trehalose: a multifunctional molecule. *Glycobiology, 13*, 17R-27R. ↗

Editions

2010-05-29	Authored	Stephan, R.
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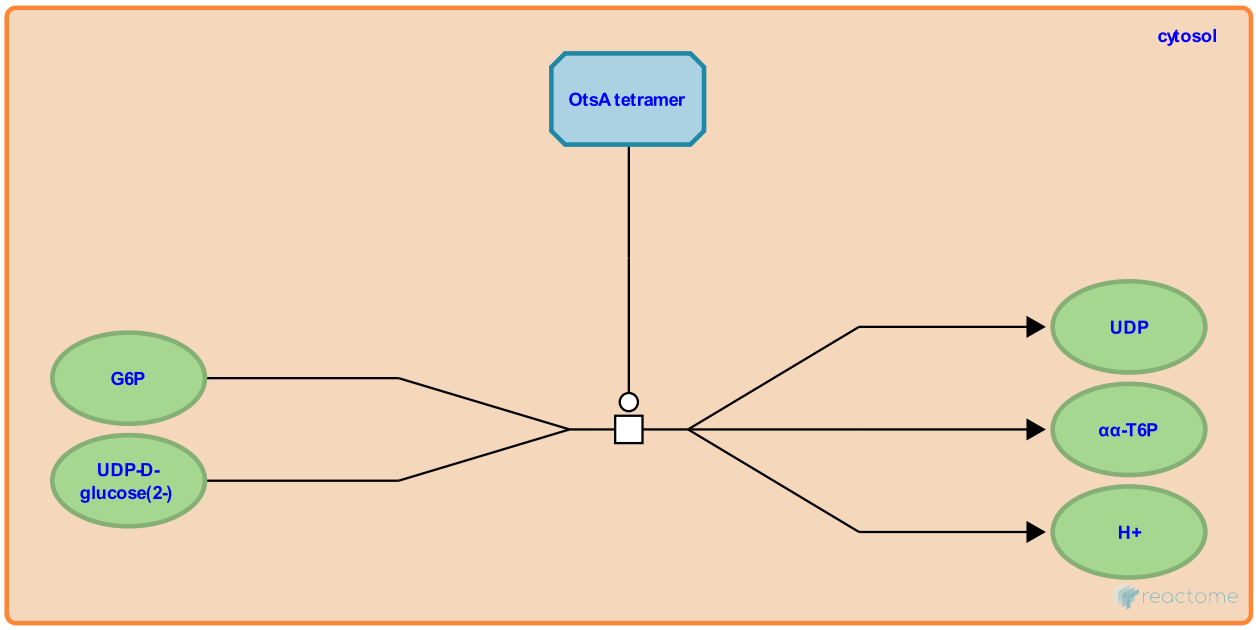
Glucose is transferred from UDP-glucose onto glucose-6-phosphate ↗

Location: Trehalose biosynthesis

Stable identifier: R-MTU-868622

Type: transition

Compartments: cytosol



Trehalose phosphate synthase, which is a tetramer in solution (OtsA tetramer), catalyzes the transfer of glucose from UDP-glucose (UDP-Glc) onto glucose-6-phosphate (G6P) to form alpha,alpha-trehalose-6-phosphate (αα-T6P). The enzyme is stimulated by manganese ions and can also accept ADP-, CDP-, GDP- and TDP-glucose as well as UDP-glucose (De Smet et al. 2000, Pan et al. 2008).

Followed by: Trehalose-6-phosphate is hydrolyzed to trehalose

Literature references

Elbein, AD., Carroll, JD., Pan, YT. (2002). Trehalose-phosphate synthase of Mycobacterium tuberculosis. Cloning, expression and properties of the recombinant enzyme. *Eur J Biochem, 269*, 6091-100. ↗

Young, DB., De Smet, KA., Robertson, BD., Brown, IN., Weston, A. (2000). Three pathways for trehalose biosynthesis in mycobacteria. *Microbiology, 146*, 199-208. ↗

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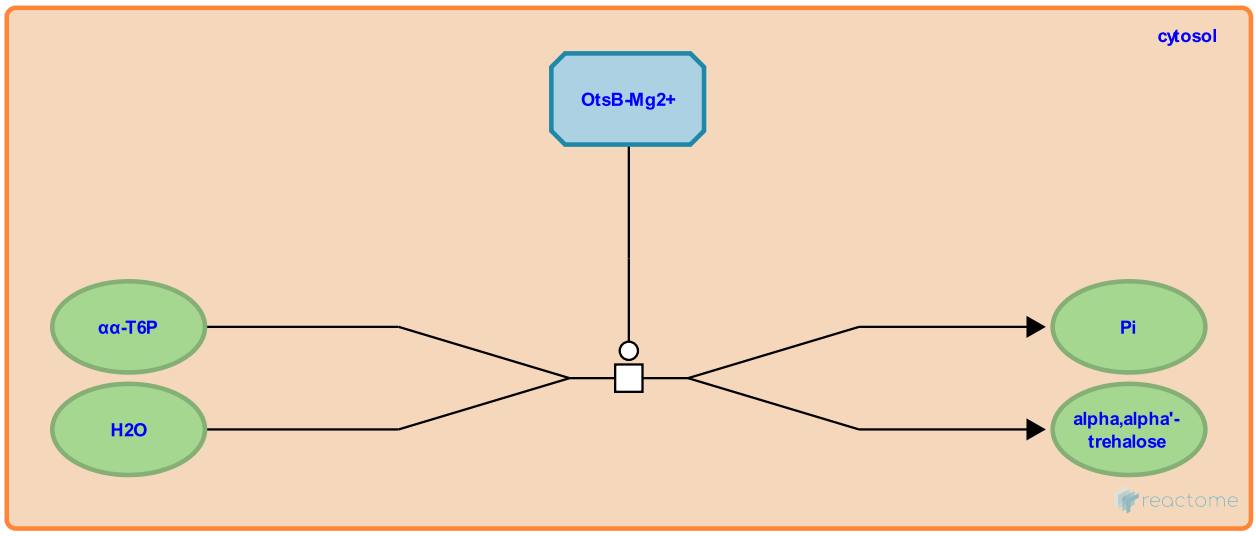
Trehalose-6-phosphate is hydrolyzed to trehalose ↗

Location: Trehalose biosynthesis

Stable identifier: R-MTU-868608

Type: transition

Compartments: cytosol



Hydrolysis of trehalose phosphate, catalyzed by OtsB2, gives trehalose. The enzyme needs magnesium for its activity. A second homologue, OtsB1 is non-functional (De Smet et al, 2000; Edavana et al, 2004).

Preceded by: Glucose is transferred from UDP-glucose onto glucose-6-phosphate

Literature references

Young, DB., De Smet, KA., Robertson, BD., Brown, IN., Weston, A. (2000). Three pathways for trehalose biosynthesis in mycobacteria. *Microbiology, 146*, 199-208. ↗

Elbein, AD., Edavana, VK., Carroll, JD., Abraham, EC., Pastuszak, I., Thampi, P. (2004). Cloning and expression of the trehalose-phosphate phosphatase of Mycobacterium tuberculosis: comparison to the enzyme from Mycobacterium smegmatis. *Arch Biochem Biophys, 426*, 250-7. ↗

Editions

2010-05-29	Authored	Stephan, R.
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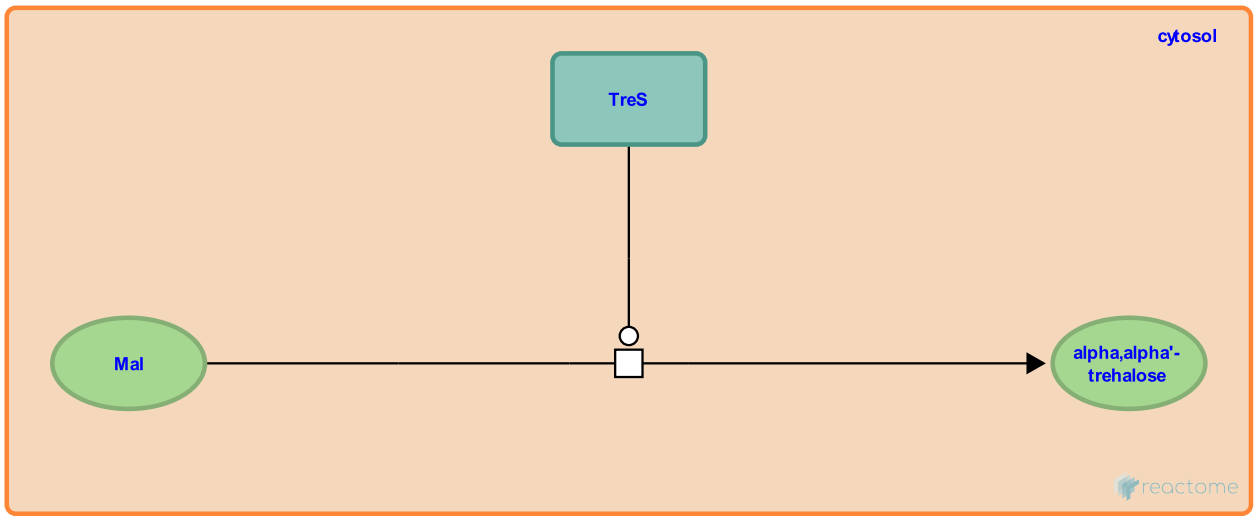
Maltose is converted to trehalose ↗

Location: Trehalose biosynthesis

Stable identifier: R-MTU-868709

Type: transition

Compartments: cytosol



Maltose is converted to trehalose. The enzymatic activity of TreS for this reaction is 2-5 fold stronger than for the reverse reaction (De Smet et al, 2000).

Literature references

Young, DB., De Smet, KA., Robertson, BD., Brown, IN., Weston, A. (2000). Three pathways for trehalose biosynthesis in mycobacteria. *Microbiology, 146*, 199-208. ↗

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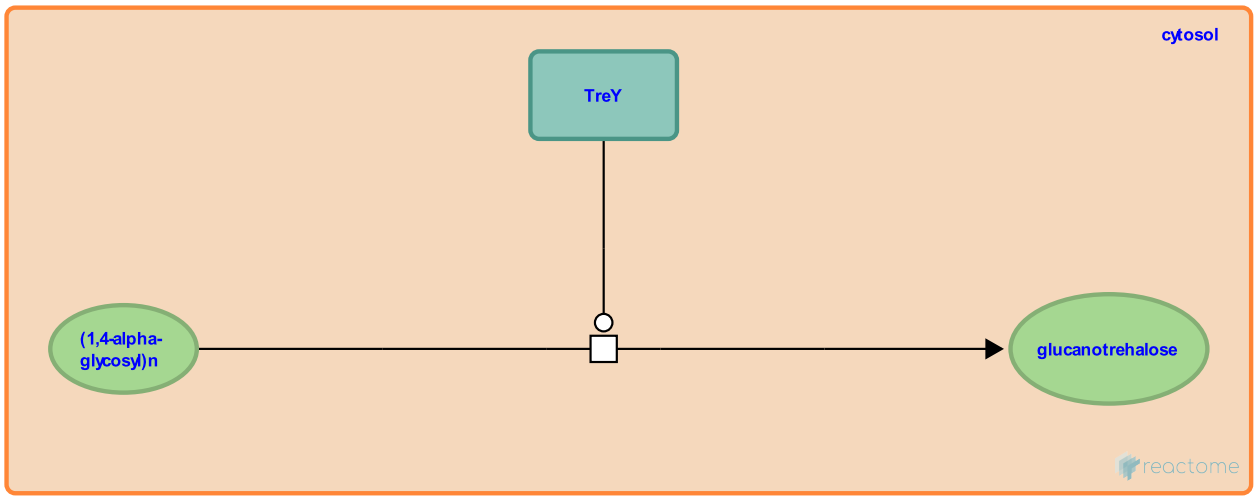
1,4-alpha-glucan is converted to glucanotrehalose ↗

Location: Trehalose biosynthesis

Stable identifier: R-MTU-868658

Type: transition

Compartments: cytosol



Linear alpha-1,4-glucans are modified at one end to a glucanotrehalose by the enzyme TreY (De Smet et al, 2000).

Followed by: Glucanotrehalose is hydrolyzed to 1,4-alpha-glucan and trehalose

Literature references

Young, DB., De Smet, KA., Robertson, BD., Brown, IN., Weston, A. (2000). Three pathways for trehalose biosynthesis in mycobacteria. *Microbiology, 146*, 199-208. ↗

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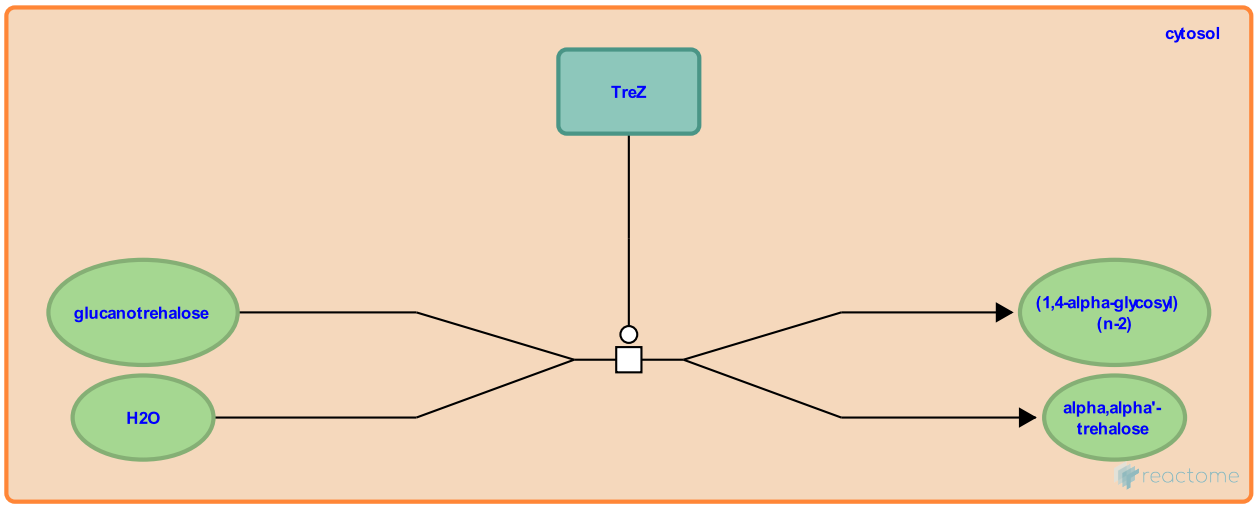
Glucanotrehalose is hydrolyzed to 1,4-alpha-glucan and trehalose ↗

Location: Trehalose biosynthesis

Stable identifier: R-MTU-868657

Type: transition

Compartments: cytosol



From the glucanotrehalose, the enzyme TreZ cleaves one molecule of trehalose, leaving a linear glucan that is two sugars shorter than before. This is the rate-limiting step in the TreYZ pathway of trehalose biosynthesis (De Smet et al, 2000).

Preceded by: 1,4-alpha-glucan is converted to glucanotrehalose

Literature references

Young, DB., De Smet, KA., Robertson, BD., Brown, IN., Weston, A. (2000). Three pathways for trehalose biosynthesis in mycobacteria. *Microbiology, 146,* 199-208. ↗

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Table of Contents