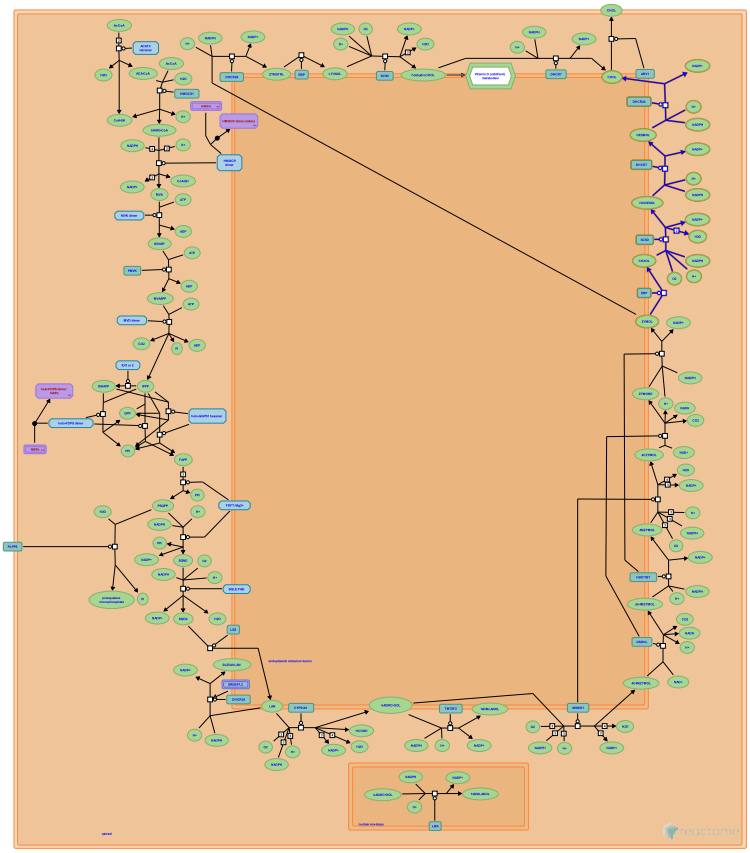
Cholesterol biosynthesis via desmosterol



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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. ↗

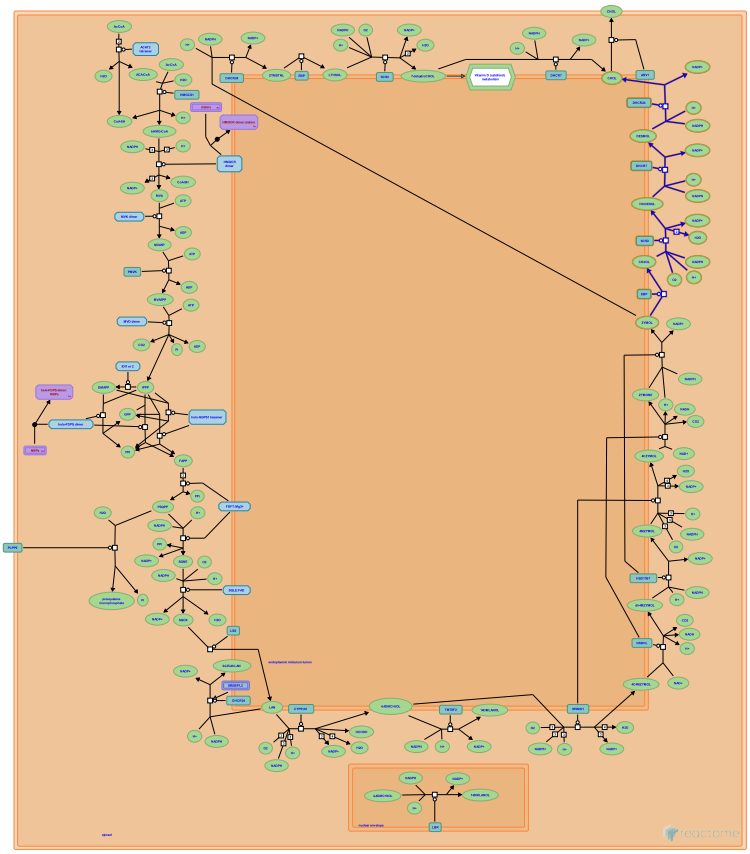
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Cholesterol biosynthesis via desmosterol ↗

Stable identifier: R-HSA-6807047

Compartments: endoplasmic reticulum membrane, cytosol



The transformation of zymosterol into cholesterol can follow either of routes, one in which reduction of the double bond in the isooctyl side chain is the final step (cholesterol synthesis via desmosterol, also known as the Bloch pathway) and one in which this reduction is the first step (cholesterol biosynthesis via lathosterol, also known as the Kandutsch-Russell pathway). The former pathway is prominent in the liver and many other tissues while the latter is prominent in skin, where it may serve as the source of the 7-dehydrocholesterol that is the starting point for the synthesis of D vitamins (Mitsche et al. 2015).

Literature references

Hobbs, HH., Mitsche, MA., Cohen, JC., McDonald, JG. (2015). Flux analysis of cholesterol biosynthesis in vivo reveals multiple tissue and cell-type specific pathways. *Elife, 4*, e07999. ↗

Editions

2015-11-02	Authored, Edited	D'Eustachio, P.
2015-11-02	Reviewed	Jassal, B.

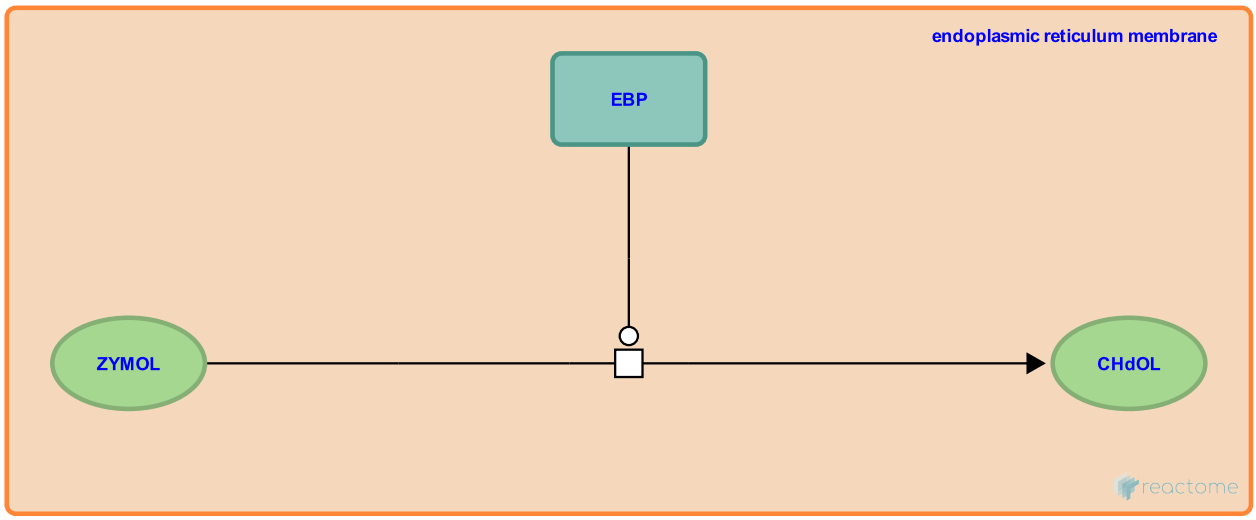
Zymosterol is isomerized to cholesta-7,24-dien-3beta-ol ↗

Location: Cholesterol biosynthesis via desmosterol

Stable identifier: R-HSA-195690

Type: transition

Compartments: endoplasmic reticulum membrane



Isomerization of zymosterol to cholesta-7,24-dien-3beta-ol is catalyzed by EBP in the endoplasmic reticulum. The biochemical details of the reaction have been established through studies of purified rat EBP; the role of the human enzyme has been established through studies of patients deficient in it (Derry et al. 1999; Braverman et al. 1999).

Followed by: Cholesta-7,24-dien-3beta-ol is desaturated to form cholesta-5,7,24-trien-3beta-ol

Literature references

Wilcox, WR., Obie, C., Lin, P., Valle, D., Moser, A., Moebius, FF. et al. (1999). Mutations in the gene encoding 3 beta-hydroxysteroid-delta 8, delta 7-isomerase cause X-linked dominant Conradi-Hunermann syndrome. *Nat Genet, 22* , 291-4. ↗

Boyd, Y., Herman, GE., Gormally, E., Zhao, W., Means, GD., Derry, JM. et al. (1999). Mutations in a delta 8-delta 7 sterol isomerase in the tattered mouse and X-linked dominant chondrodysplasia punctata. jderry@immunex.com. *Nat Genet, 22*, 286-90. ↗

Editions

2007-04-21	Authored, Edited	D'Eustachio, P.
2007-04-21	Reviewed	Jassal, B.

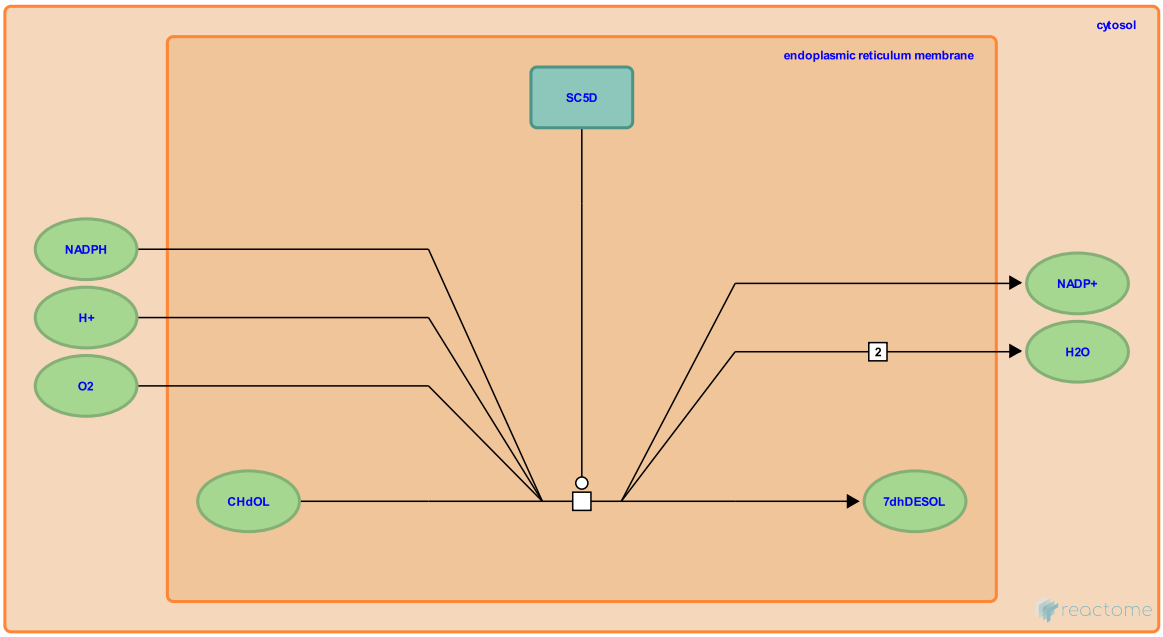
Cholesta-7,24-dien-3beta-ol is desaturated to form cholesta-5,7,24-trien-3beta-ol ↗

Location: Cholesterol biosynthesis via desmosterol

Stable identifier: R-HSA-195664

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



Cholesta-7,24-dien-3beta-ol, NADPH + H+, and O2 react to form cholesta-5,7,24-trien-3beta-ol, NADP+, and 2 H2O, catalyzed by SC5D. This reaction takes place in the endoplasmic reticulum. Its biochemical details are inferred from those of the reaction catalyzed by the purified rat protein (Kawata et al. 1985). The role of human SC5D in catalyzing this reaction in vivo is established from studies of patients in whom the enzyme is defective (Brunetti-Pierri et al. 2002; Krakowiak et al. 2003).

Preceded by: Zymosterol is isomerized to cholesta-7,24-dien-3beta-ol

Followed by: Cholesta-5,7,24-trien-3beta-ol is reduced to desmosterol

Literature references

Balli, F., Andria, G., Rivasi, F., Dello Russo, A., Brunetti-Pierri, N., Ferrari, P. et al. (2002). Lathosterolosis, a novel multiple-malformation/mental retardation syndrome due to deficiency of 3beta-hydroxysteroid-delta5-desaturase. *Am J Hum Genet, 71*, 952-8. ↗

Wassif, CA., Kovarova, M., Harris, G., Tsokos, M., Porter, FD., Grinberg, A. et al. (2003). Lathosterolosis: an inborn error of human and murine cholesterol synthesis due to lathosterol 5-desaturase deficiency. *Hum Mol Genet, 12*, 1631-41. ↗

Editions

2007-04-21	Authored, Edited	D'Eustachio, P.
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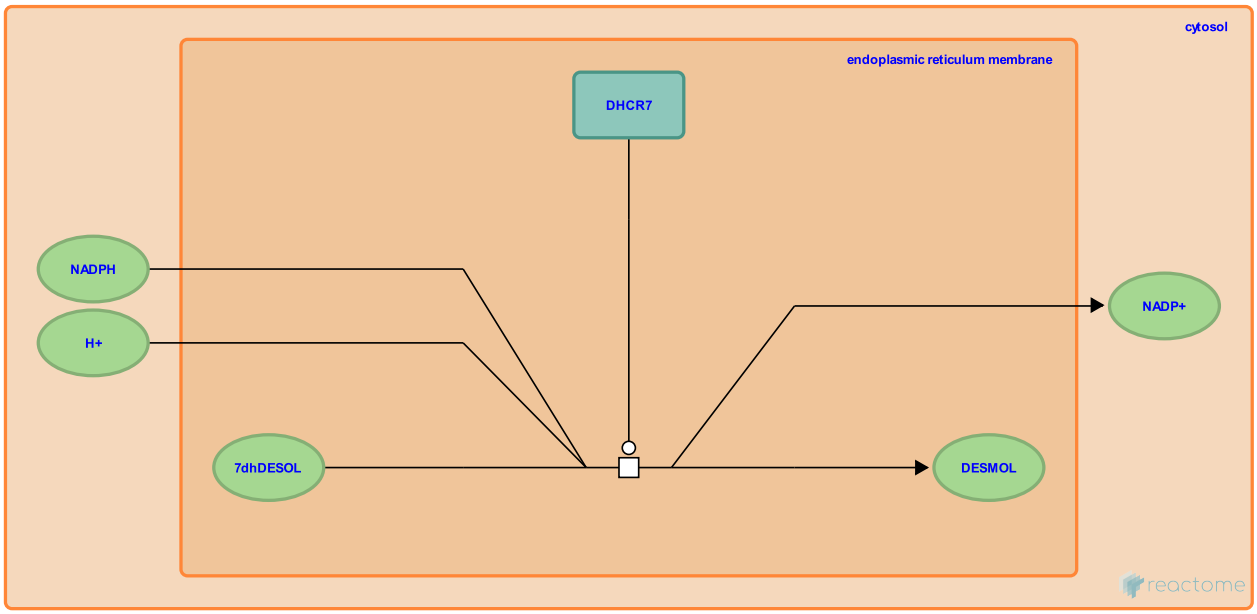
Cholesta-5,7,24-trien-3beta-ol is reduced to desmosterol ↗

Location: Cholesterol biosynthesis via desmosterol

Stable identifier: R-HSA-196402

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



Cholesta-5,7,24-trien-3beta-ol and NADPH + H+ react to form desmosterol and NADP+. This reaction is catalyzed by DHCR7, associated with the endoplasmic reticulum membrane. The biochemical details of the reaction are inferred from those of the reaction catalyzed by the well-studied rat enzyme (Bae et al. 1999).

Preceded by: Cholesta-7,24-dien-3beta-ol is desaturated to form cholesta-5,7,24-trien-3beta-ol

Followed by: Reduction of desmosterol to cholesterol

Literature references

Lee, JN., Fitzky, BU., Paik, YK., Moebius, FF., Glossmann, H. (1998). Molecular cloning and expression of the human delta7-sterol reductase. *Proc Natl Acad Sci U S A, 95*, 1899-902. ↗

Editions

2007-04-21	Authored, Edited	D'Eustachio, P.
2007-04-21	Reviewed	Jassal, B.

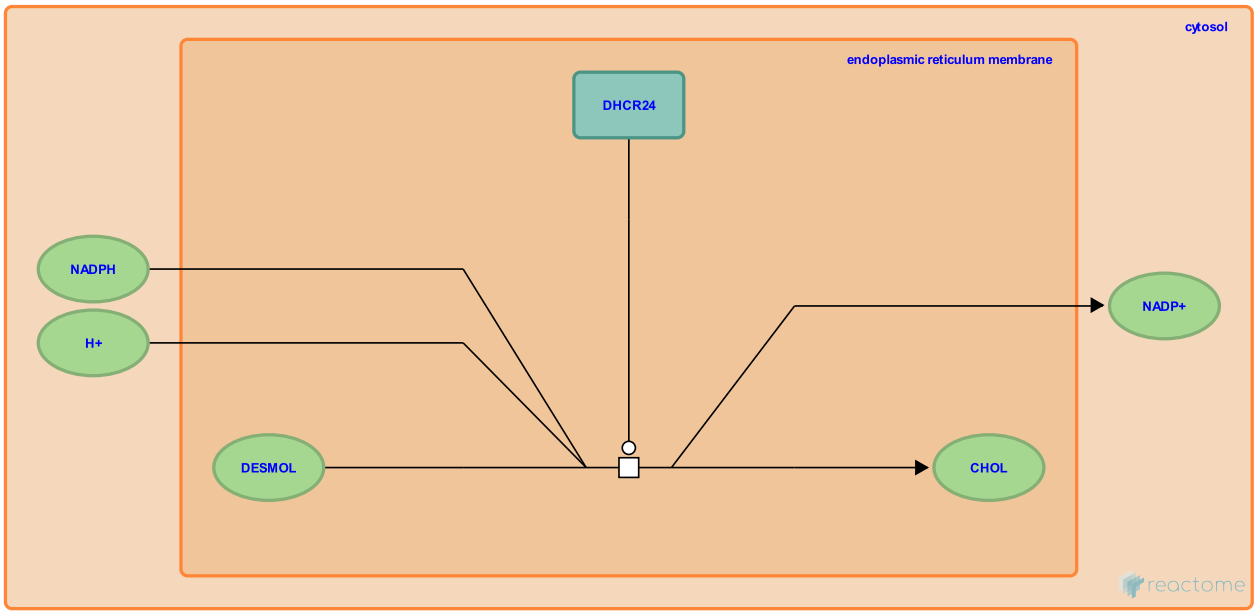
Reduction of desmosterol to cholesterol ↗

Location: Cholesterol biosynthesis via desmosterol

Stable identifier: R-HSA-196417

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



Desmosterol is reduced by NADPH + H+ to form cholesterol and NADP+, catalyzed by DHCR24 associated with the endoplasmic reticulum membrane.

Preceded by: Cholesta-5,7,24-trien-3beta-ol is reduced to desmosterol

Literature references

Vreken, P., Romeijn, GJ., FitzPatrick, DR., Hennekam, RC., Koster, J., Andersson, HC. et al. (2001). Mutations in the 3beta-hydroxysterol Delta24-reductase gene cause desmosterolosis, an autosomal recessive disorder of cholesterol biosynthesis. *Am J Hum Genet, 69*, 685-94. ↗

Editions

2007-04-21	Authored, Edited	D'Eustachio, P.
2007-04-21	Reviewed	Jassal, B.

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