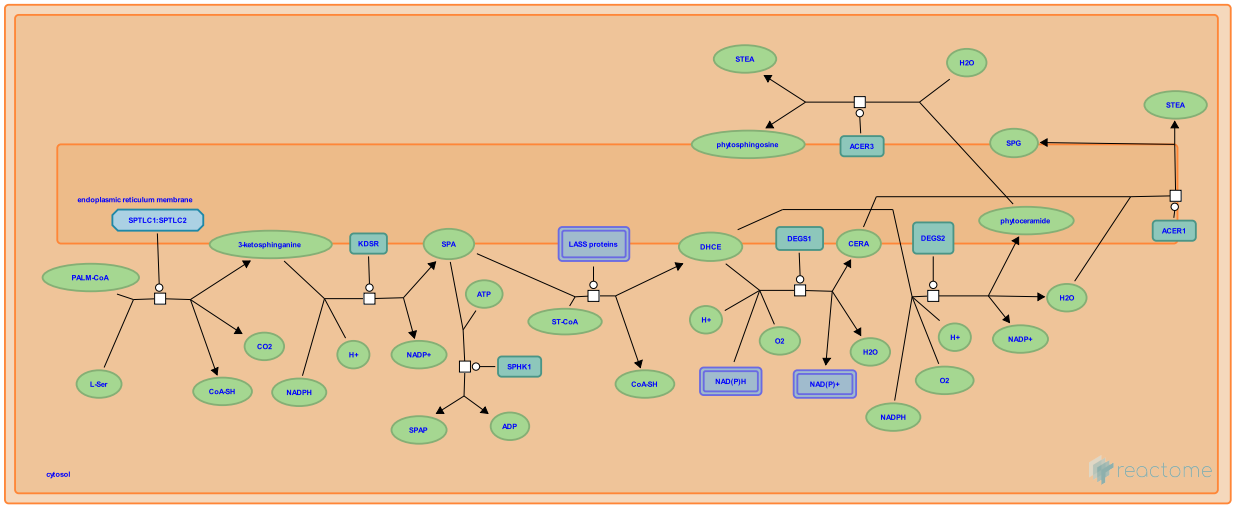
Sphingolipid metabolism



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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. ↗

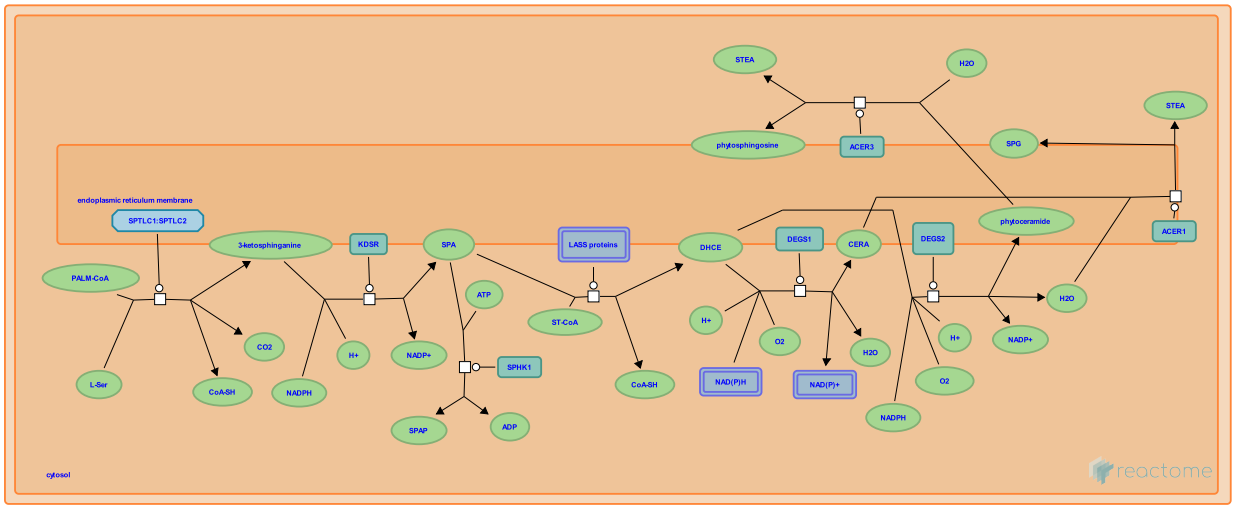
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Sphingolipid metabolism ↗

Stable identifier: R-GGA-433584



Sphingolipids are derivatives of sphingosine (trans-1,3-dihydroxy 2-amino-4-octadecene), an 18-carbon unsaturated amino alcohol. Amide linkage of a fatty acid to sphingosine yields ceramides. Esterification of choline to ceramides yields sphingomyelin, and ceramide glycosylation yields gangliosides. These molecules appear to be essential components of cell membranes, and intermediates in the pathways of sphingolipid synthesis and breakdown modulate processes including apoptosis.

De novo synthesis proceeds in four steps: the reaction of palmitoyl-CoA and serine to form 3-dehydrosphinganine, the reduction of 3-dehydrosphinganine to sphinganine, the reaction of sphinganine and a long-chain fatty acyl CoA to form dihydroceramide, and the desaturation of dihydroceramide to form ceramide.

Other sphingolipids involved in signaling are derived from ceramide and its biosynthetic intermediates. These include sphinganine (dihydrosphingosine) 1-phosphate, phytoceramide, sphingosine, and sphingosine 1-phosphate.

Sphingomyelin is synthesized in a single step in the membrane of the Golgi apparatus from ceramides generated in the endoplasmic reticulum (ER) membrane and transferred to the Golgi by CERT (ceramide transfer protein), an isoform of COL4A3BP that is associated with the ER membrane as a complex with PPM1L (protein phosphatase 1-like) and VAPA or VAPB (VAMP-associated proteins A or B). Sphingomyelin synthesis appears to be regulated primarily at the level of this transport process through the reversible phosphorylation of CERT.

These processes have not been experimentally studied in chickens, but are inferred here from their human counterparts.

Editions

2009-08-22	Authored, Edited, Reviewed	D'Eustachio, P.

palmitoyl-CoA + serine => 3-dehydrosphinganine + CoASH + CO2 ↗

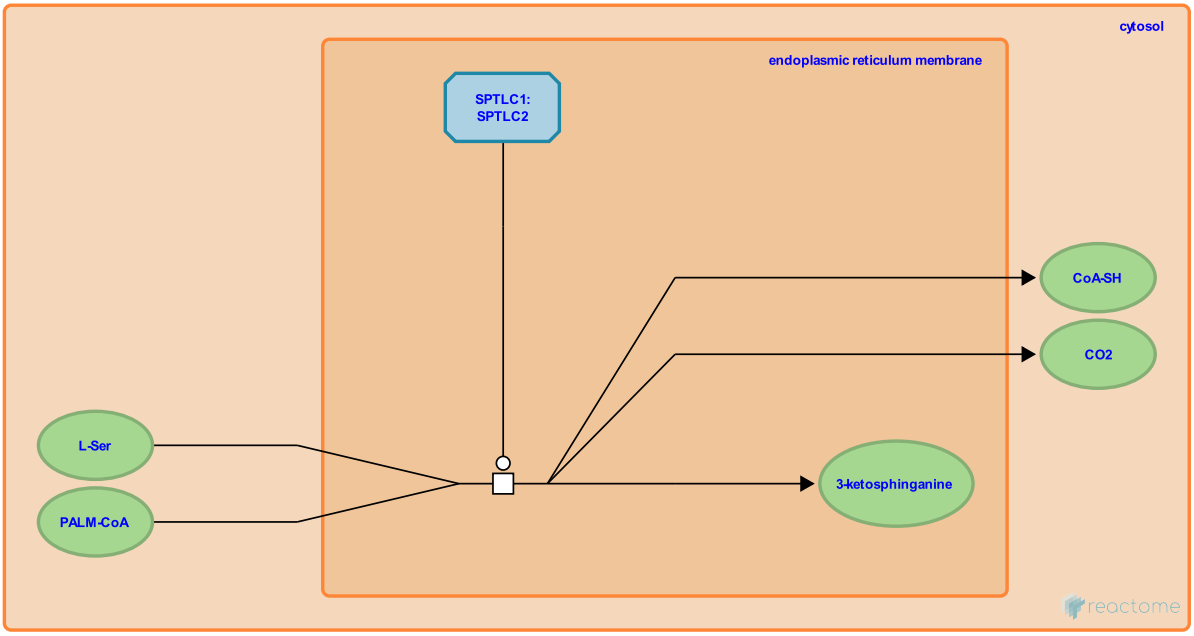
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433550

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: SPTLC complexes transfer acyl-CoA onto serine (Homo sapiens)



SPTLC (serine palmitoyltransferase) enzyme complexes associated with the endoplasmic reticulum membrane catalyze the reaction of palmitoyl-CoA and serine to form 3-dehydrosphinganine. SPTLC2 and SPTLC3 polypeptides exhibit enzyme activity when either is complexed with SPTLC1. These chicken proteins are known only as the inferred products of genes predicted from the chicken genome sequence; their functional properties are inferred from those of their better-studied mammalian orthologues.

Followed by: 3-dehydrosphinganine + NADPH + H+ => sphinganine + NADP+

3-dehydrosphinganine + NADPH + H+ => sphinganine + NADP+ ↗

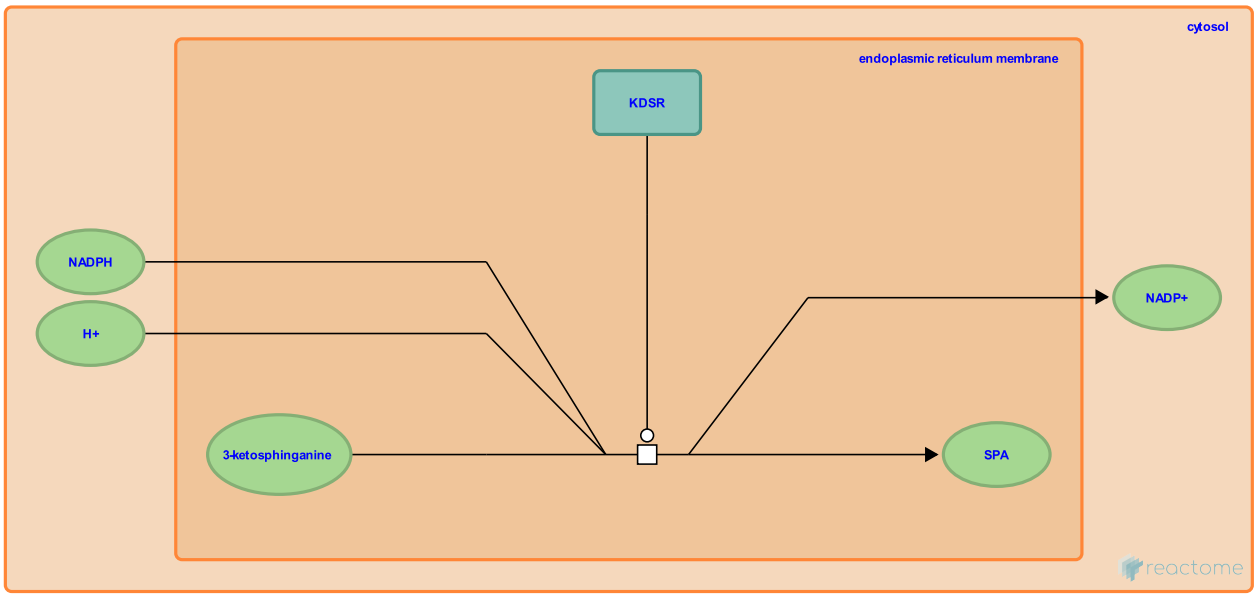
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433576

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: KDSR reduces 3-ketosphingoid (Homo sapiens)



KDSR (3-ketodihydrosphingosine reductase) enzyme associated with the cytosolic face of the endoplasmic reticulum membrane catalyzes the reduction of 3-dehydrosphinganine by NADPH to form sphinganine (dihydrosphingosine). Chicken KDSR is known only as the predicted product of a cDNA identified in a high-throughput experiment. This reaction is inferred from its well-studied human counterpart.

Preceded by: palmitoyl-CoA + serine => 3-dehydrosphinganine + CoASH + CO2

Followed by: sphinganine + stearyl-CoA => dihydroceramide + CoASH, sphinganine (dihydrosphingosine) +ATP => sphinganine 1-phosphate + ADP

sphinganine + stearyl-CoA => dihydroceramide + CoASH ↗

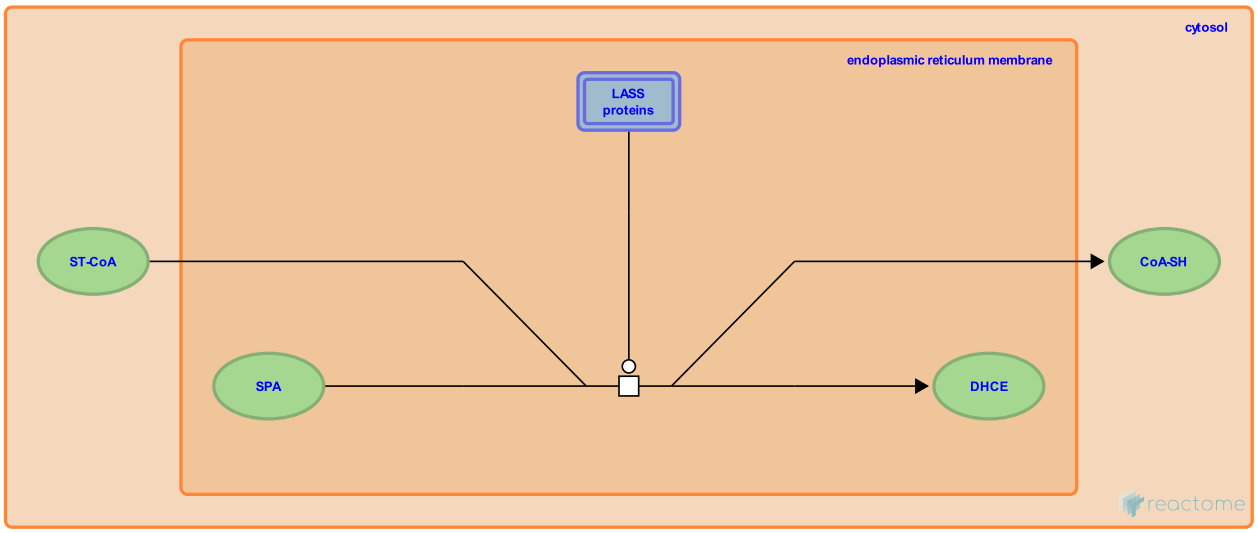
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433592

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: Ceramide synthases transfer acyl-CoA onto sphingoid (Homo sapiens)



LASS (ceramide synthase / "longevity assurance homolog") enzymes associated with the endoplasmic reticulum membrane catalyze the reaction of sphinganine (dihydrosphingosine) and a long-chain fatty acyl CoA such as stearyl-CoA to form a dihydroceramide and CoASH. Chicken LASS proteins are known only as the predicted products of open reading frames predicted from analysis of the chicken genome sequence. This reaction is inferred from its well-studied human counterpart.

Preceded by: 3-dehydrosphinganine + NADPH + H+ => sphinganine + NADP+

Followed by: dihydroceramide + NADPH + H+ + O2 => phytoceramide + NADP+ + H2O, dihydroceramide + NAD(P)H + H+ + O2 => ceramide + NAD(P)+ + H2O

dihydroceramide + NAD(P)H + H+ + O2 => ceramide + NAD(P)+ + H2O ↗

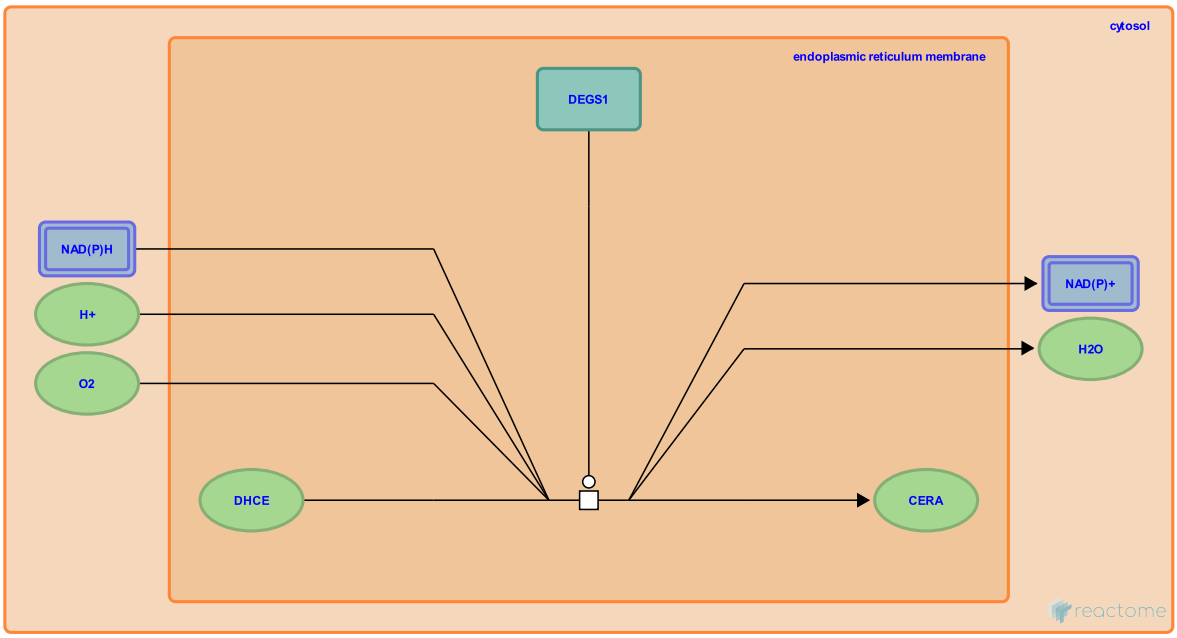
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433599

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: DEGS1 dehydrogenates dihydroceramide (Homo sapiens)



DEGS1 (sphingolipid delta(4)-desaturase 1 / "degenerative spermatocyte homolog 1") enzyme associated with the cytosolic face of the endoplasmic reticulum catalyzes the desaturation of dihydroceramide to form ceramide. Chicken DEGS1 protein is known only as the inferred product of a cDNA identified in a high-throughput survey. This reaction is inferred from its well-studied mammalian counterpart.

Preceded by: sphinganine + stearyl-CoA => dihydroceramide + CoASH

Followed by: ceramide + H2O => stearate + sphingosine [endoplasmic reticulum]

dihydroceramide + NADPH + H+ + O2 => phytoceramide + NADP+ + H2O ↗

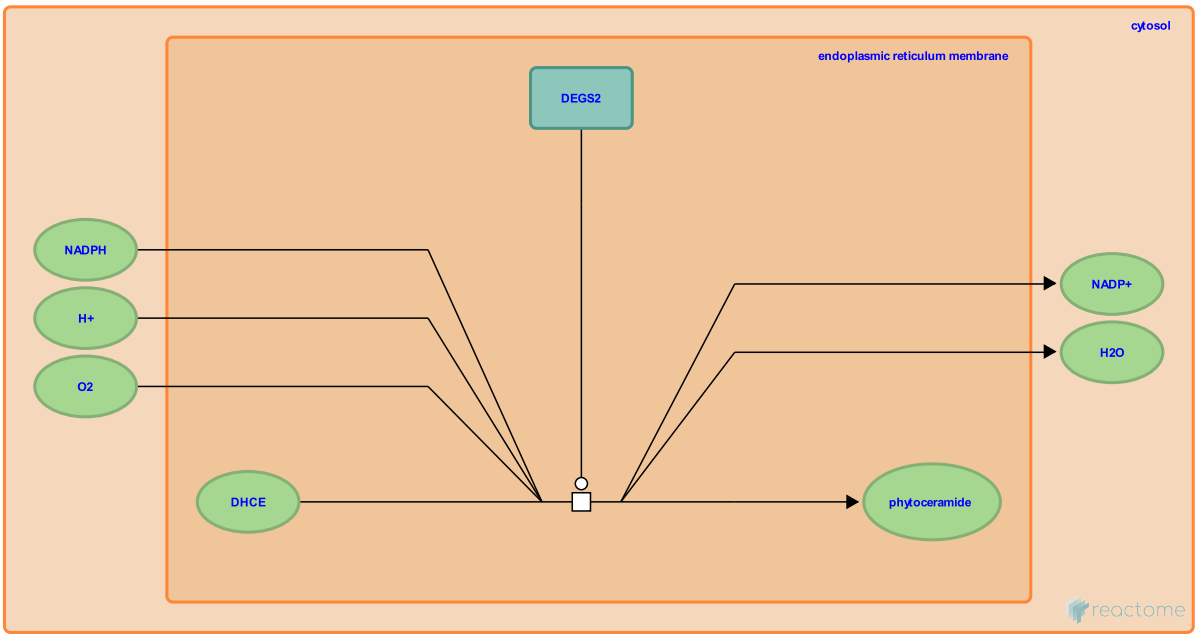
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433593

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: DEGS2 oxygenates dihydroceramide (Homo sapiens)



DEGS2 (sphingolipid C4-hydroxylase 2 / degenerative spermatocyte homolog 2) enzyme associated with the cytosolic face of the endoplasmic reticulum catalyzes the hydroxylation of dihydroceramide to form phytoceramide. Chicken DEGS2 is known only as the inferred protein product of an open reading frame identified by analysis of the chicken genome. This reaction is inferred from its well-studied mammalian counterpart.

Preceded by: sphinganine + stearyl-CoA => dihydroceramide + CoASH

Followed by: phytoceramide + H2O => stearate + phytosphingosine

ceramide + H2O => stearate + sphingosine [endoplasmic reticulum] ↗

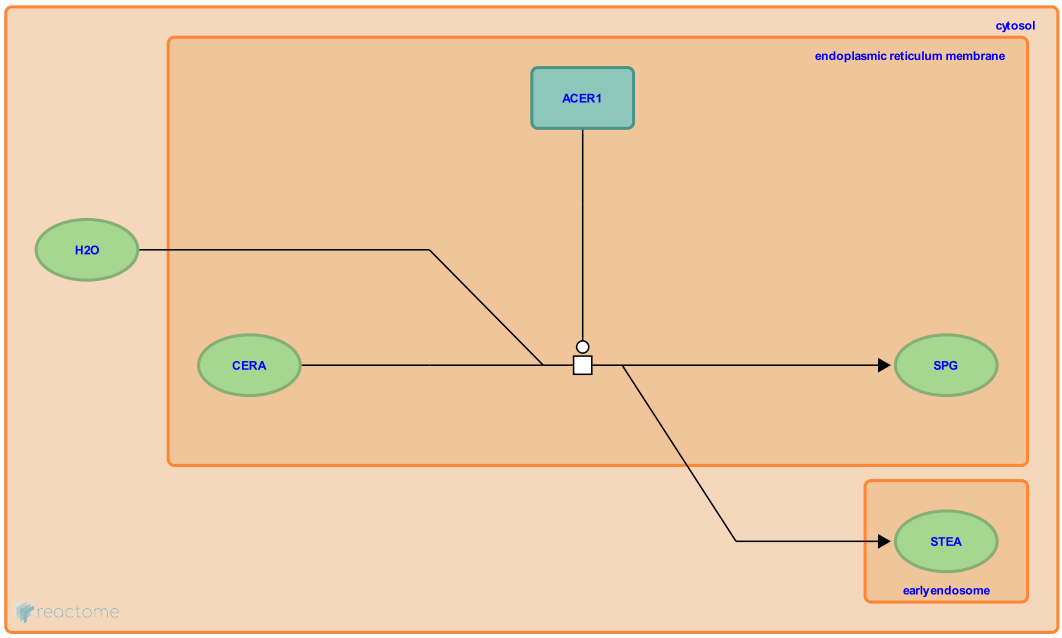
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433608

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: ACER1 hydrolyzes ceramide (endoplasmic reticulum) (Homo sapiens)



ACER1 (alkaline ceramidase 1), associated with the endoplasmic reticulum membrane, catalyzes the hydrolysis of ceramide to yield a free fatty acid (annotated here as stearate) and sphingosine. Chicken ACER1 is known only as the inferred protein product of an open reading frame found through ananlysis of the chicken genome. This reaction is inferred from its well-studied mammalian counterpart.

Preceded by: dihydroceramide + NAD(P)H + H+ + O2 => ceramide + NAD(P)+ + H2O

phytoceramide + H2O => stearate + phytosphingosine ↗

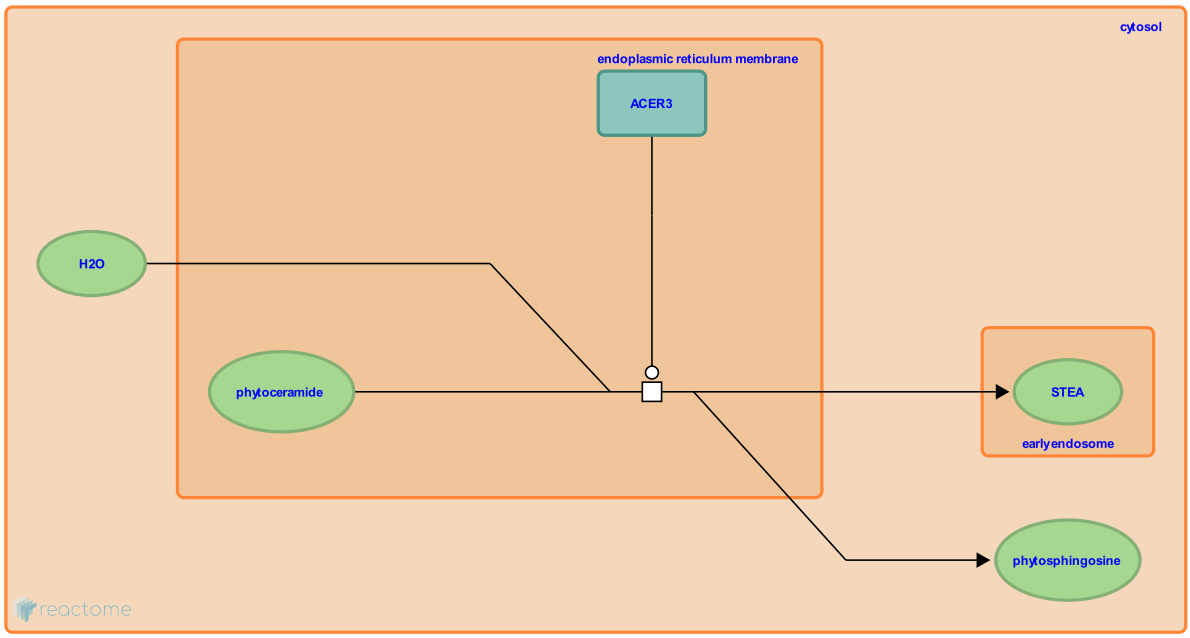
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433578

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: ACER3 hydrolyzes phytoceramide (Homo sapiens)



ACER3 (alkaline ceramidase 3) catalyzes the hydrolysis of phytoceramide to yield a free fatty acid (annotated here as stearate) and phytosphingosine. Chicken ACER3 protein is known only as the predicted product of an open reading frame found through analysis of the chhicken genome. This reaction is inferred from its well-studied mammalian counterpart.

Preceded by: dihydroceramide + NADPH + H+ + O2 => phytoceramide + NADP+ + H2O

sphinganine (dihydrosphingosine) +ATP => sphinganine 1-phosphate + ADP ↗

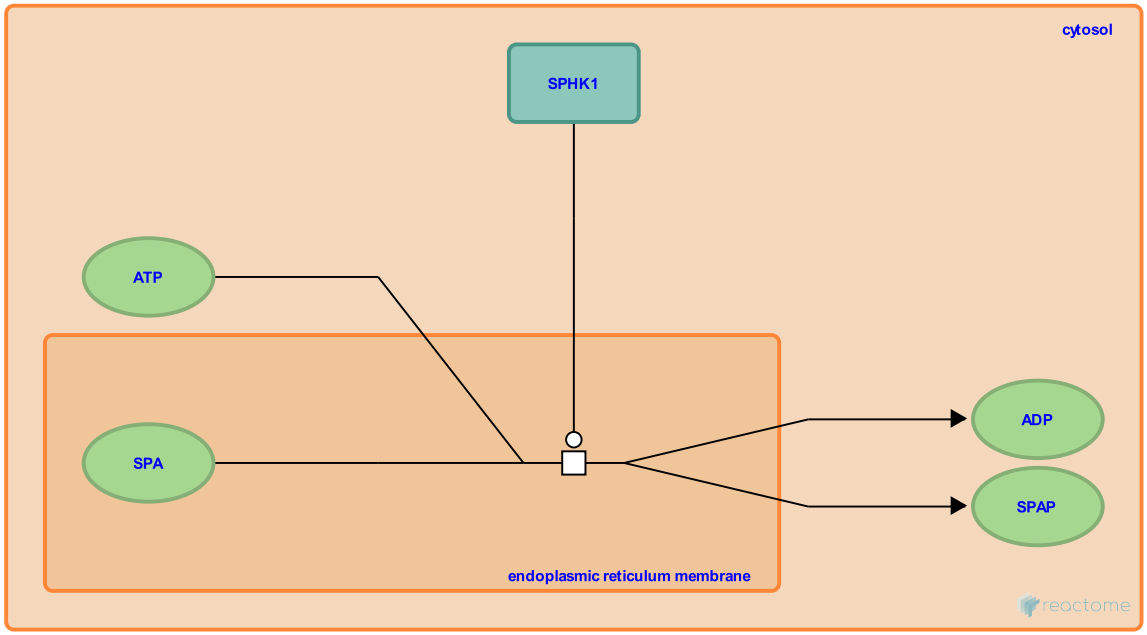
Location: Sphingolipid metabolism

Stable identifier: R-GGA-433606

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Inferred from: SPHK1 phosphorylates sphingoid (Homo sapiens)



SPHK1 (sphingosine kinase 1) catalyzes the reaction of sphinganine (dihydrosphingosine) and ATP to form dihydrosphingosine 1-phosphate and ADP. Chicken SPHK1 protein is known only as the inferred product of an open reading frame found through analysis of the chicken genome. This reaction is inferred from its well-studied mammalian counterpart.

Preceded by: 3-dehydrosphinganine + NADPH + H+ => sphinganine + NADP+

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