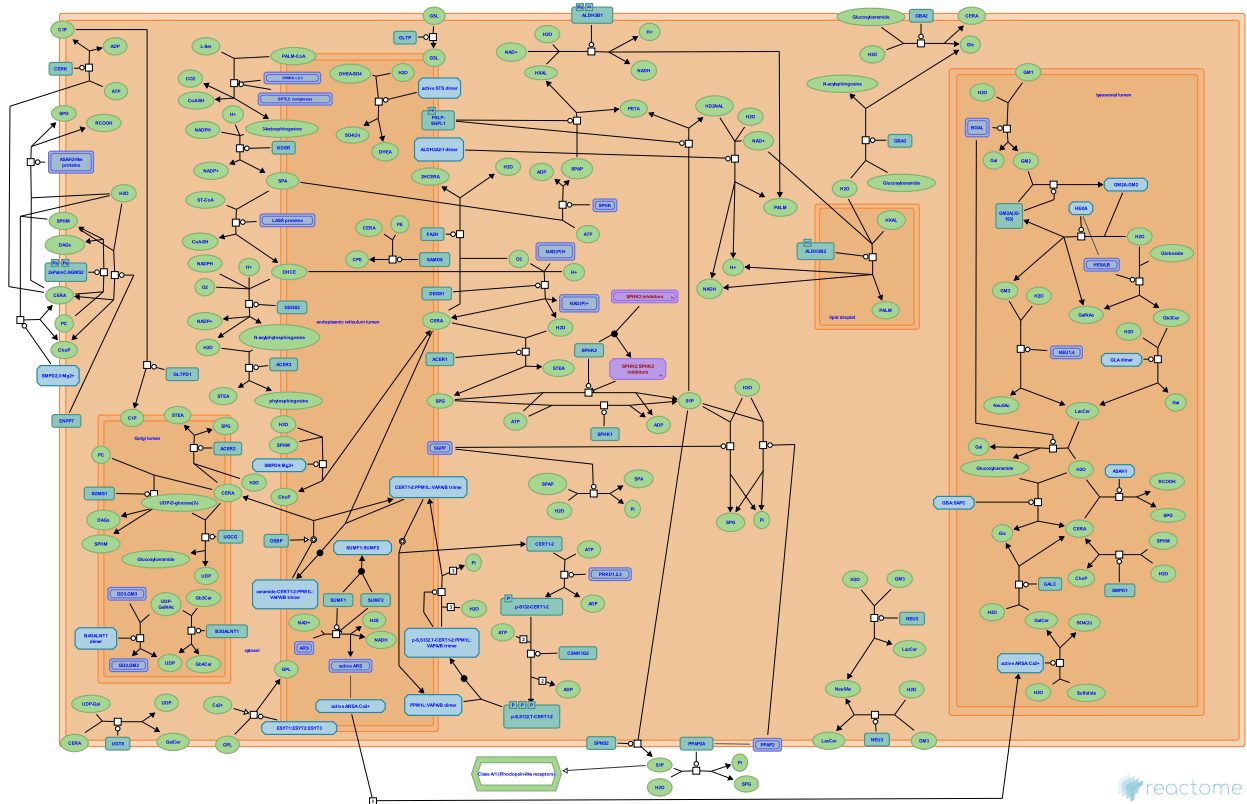


Sphingolipid metabolism



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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/).

12/05/2023

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

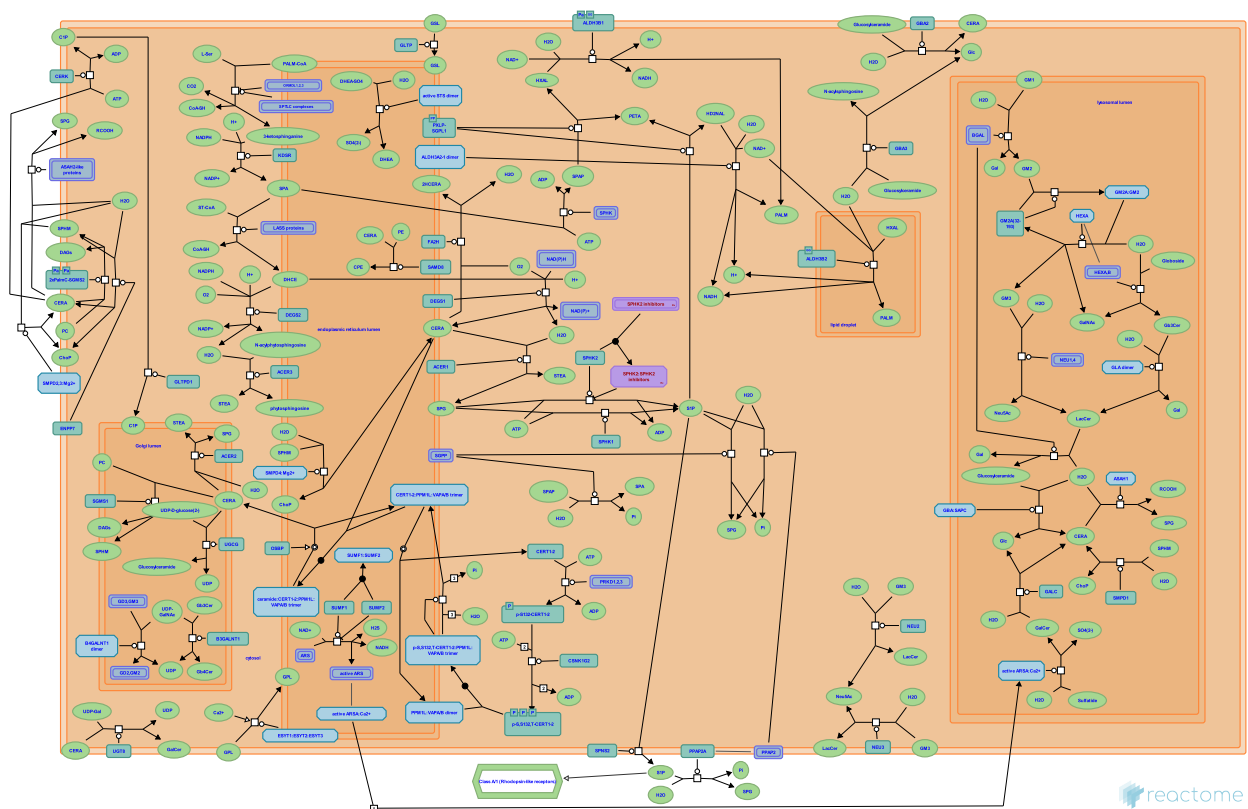
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Reactome database release: 84

This document contains 3 pathways ([see Table of Contents](#))

Sphingolipid metabolism ↗

Stable identifier: R-HSA-428157



Sphingolipids are derivatives of long chain sphingoid bases such as sphingosine (trans-1,3-dihydroxy-2-amino-4-octadecene), an 18-carbon unsaturated amino alcohol which is the most abundant sphingoid base in mammals. Amide linkage of a fatty acid to sphingosine yields ceramides. Esterification of phosphocholine to ceramides yields sphingomyelin, and ceramide glycosylation yields glycosylceramides. Introduction of sialic acid residues 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 and T cell trafficking.

While sphingolipids are abundant in a wide variety of foodstuffs, these dietary molecules are mostly degraded by the intestinal flora and intestinal enzymes. The body primarily depends on de novo synthesis for its sphingolipid supply (Hannun and Obeid 2008; Merrill 2002). De novo synthesis proceeds in four steps: the condensation of palmitoyl-CoA and serine to form 3-ketosphinganine, the reduction of 3-ketosphinganine to sphinganine, the acylation of sphinganine with 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 (Saito et al. 2008).

Literature references

Tamura, S., Saito, S., Kobayashi, T., Echigo, S., Kawano, M., Matsui, H. et al. (2008). Protein phosphatase 2Cepsilon is an endoplasmic reticulum integral membrane protein that dephosphorylates the ceramide transport protein CERT to enhance its association with organelle membranes. *J Biol Chem*, 283, 6584-93. [↗](#)

Merrill AH, Jr. (2002). De novo sphingolipid biosynthesis: a necessary, but dangerous, pathway. *J Biol Chem*, 277, 25843-6. [↗](#)

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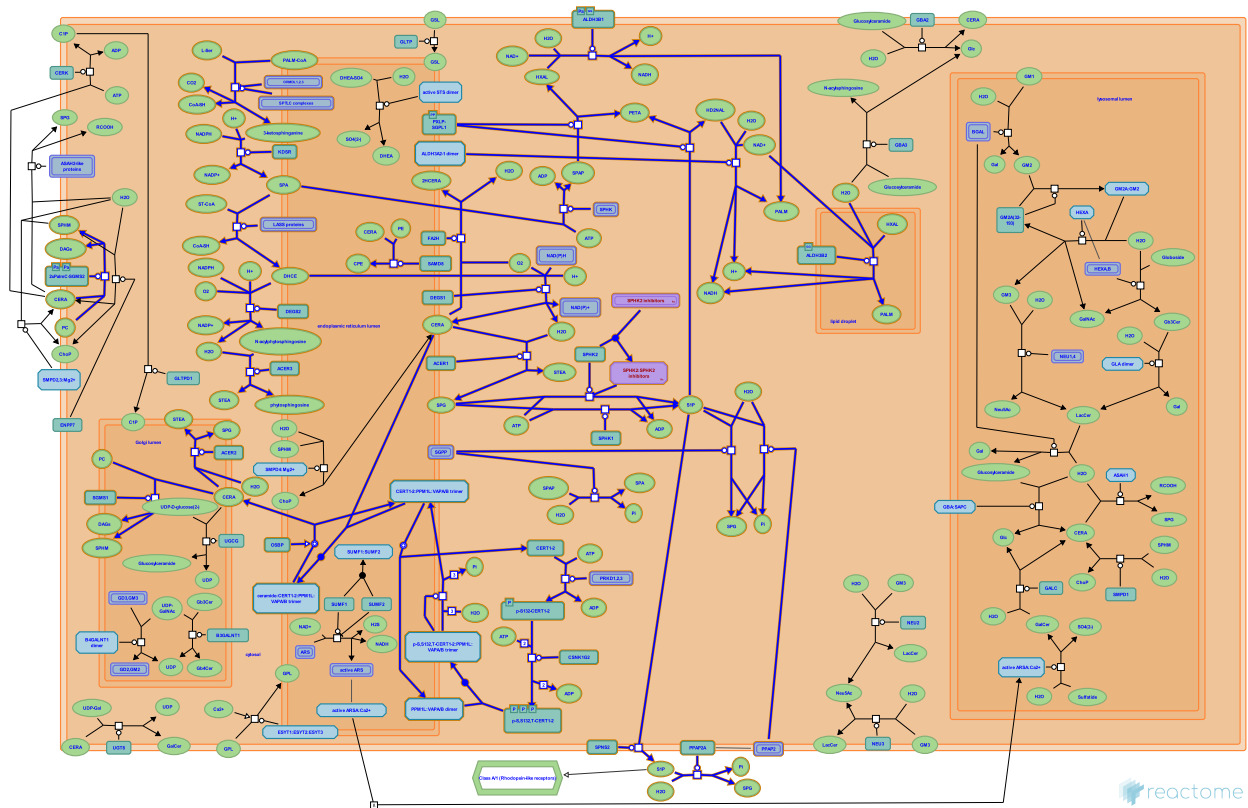
Editions

2009-08-21	Authored, Edited	D'Eustachio, P.
2009-08-21	Reviewed	Jassal, B.
2009-11-19	Reviewed	Hannun, YA., Luberto, C.

Spingolipid de novo biosynthesis ↗

Location: Spingolipid metabolism

Stable identifier: R-HSA-1660661



The main steps involved in de novo sphingolipid synthesis are annotated here (Merrill 2002, Gault et al. 2010).

Literature references

Gault, CR., Hannun, YA., Obeid, LM. (2010). An overview of sphingolipid metabolism: from synthesis to breakdown. *Adv Exp Med Biol*, 688, 1-23. ↗

Merrill AH, Jr. (2002). De novo sphingolipid biosynthesis: a necessary, but dangerous, pathway. *J Biol Chem*, 277, 25843-6. ↗

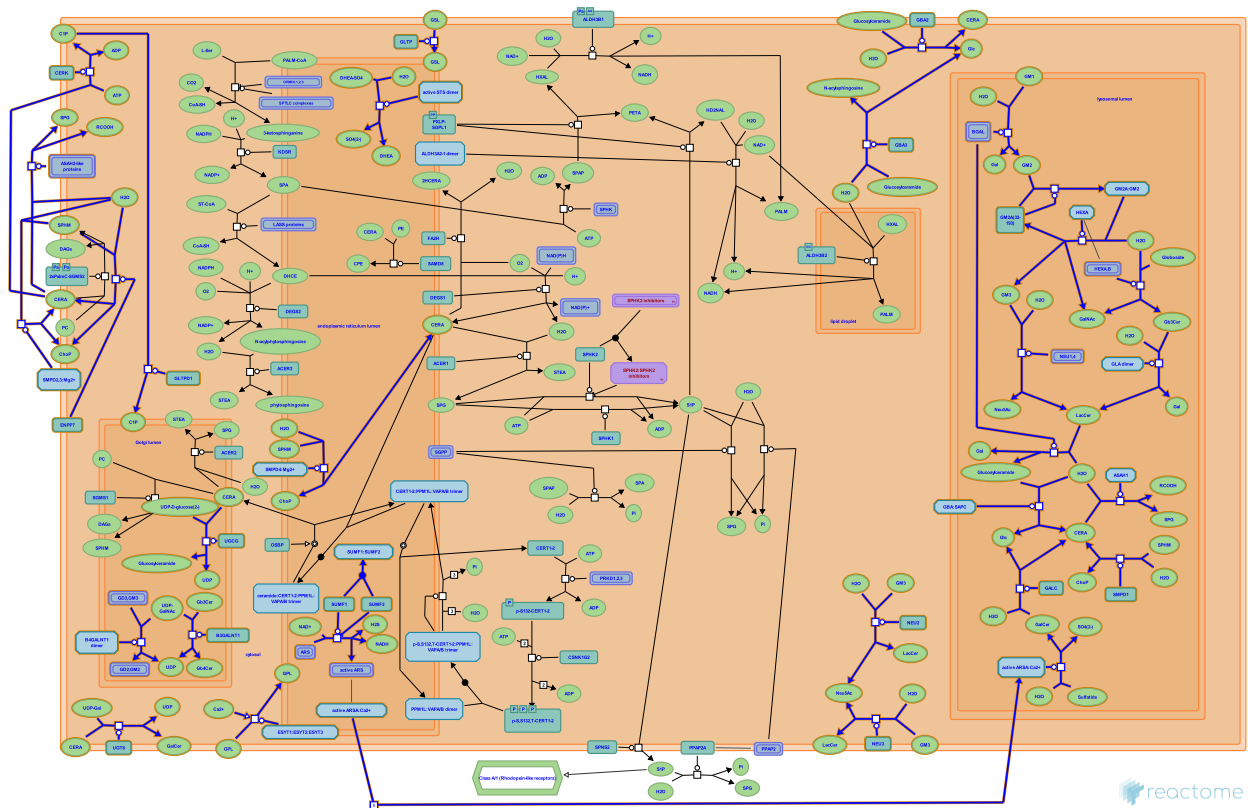
Editions

2009-08-21	Authored	D'Eustachio, P.
2011-10-14	Edited	Jassal, B.

Glycosphingolipid metabolism ↗

Location: [Sphingolipid metabolism](#)

Stable identifier: R-HSA-1660662



The steps involved in the synthesis of glycosphingolipids (sphingolipids with one or more sugars attached) are annotated here (Gault et al. 2010).

Literature references

Gault, CR., Hannun, YA., Obeid, LM. (2010). An overview of sphingolipid metabolism: from synthesis to breakdown. *Adv Exp Med Biol*, 688, 1-23. ↗

Editions

2011-10-14	Authored, Edited	Jassal, B.
2011-10-31	Reviewed	Stephan, R.
2012-05-15	Revised	Jassal, B.

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