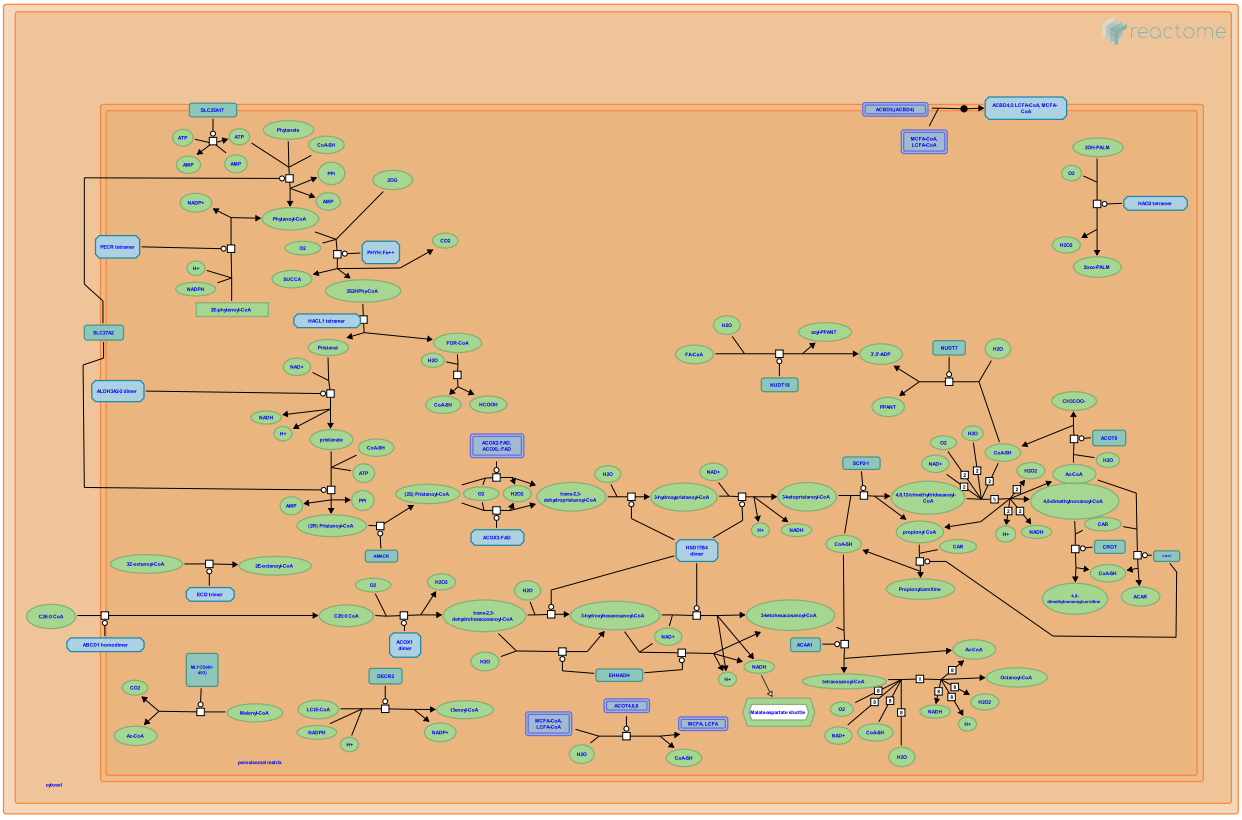
Peroxisomal lipid metabolism



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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.

26/04/2024

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. ↗

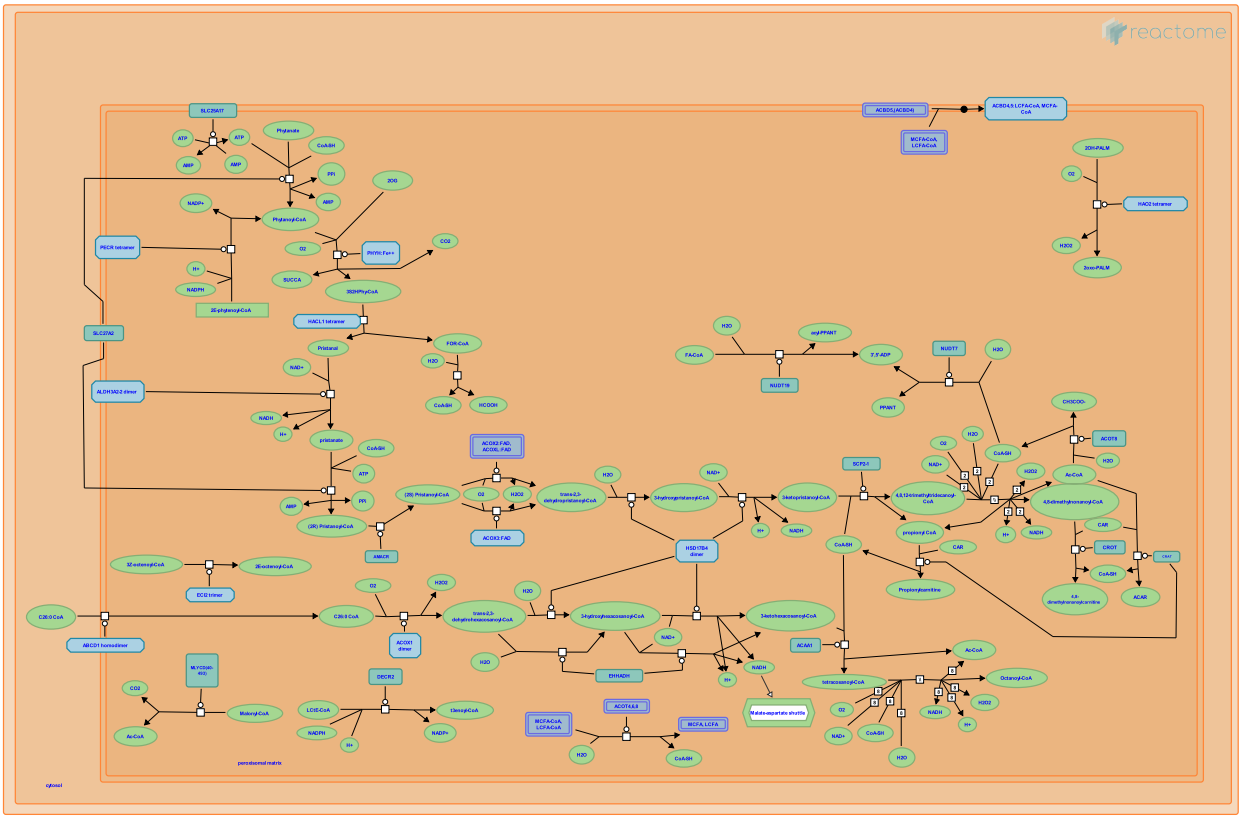
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Peroxisomal lipid metabolism ↗

Stable identifier: R-HSA-390918



In humans, the catabolism of phytanate, pristanate, and very long chain fatty acids as well as the first four steps of the biosynthesis of plasmalogens are catalyzed by peroxisomal enzymes. Defects in any of these enzymes or in the assembly of peroxisomes are associated with severe developmental disorders (Wanders and Watherham 2006).

Literature references

Wanders, RJA., Waterham, HR. (2006). Biochemistry of mammalian peroxisomes revisited. *Annu Rev Biochem, 75*, 295-332. ↗

Editions

2009-02-11	Authored, Edited	D'Eustachio, P.
2009-02-27	Reviewed	Jassal, B.

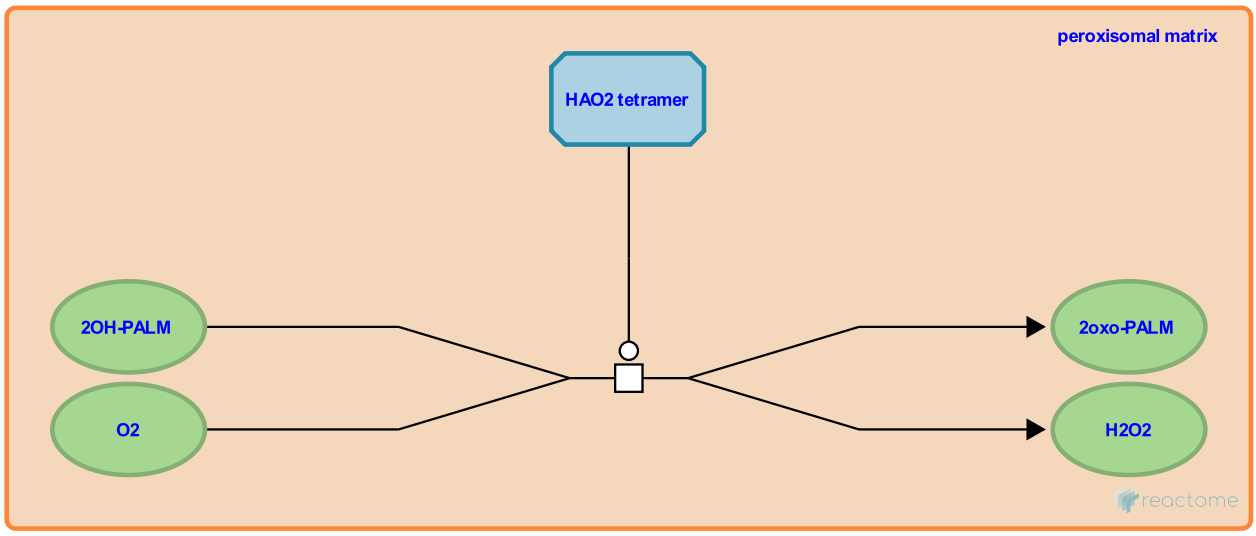
HAO2 tetramer oxidises 2OH-PALM ↗

Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-6787811

Type: transition

Compartments: peroxisomal matrix



Fatty acids can be metabolised by two distinct pathways; alpha- and beta-oxidation. Peroxisomal hydroxyacid oxidase 2 (HAO2) is thought to take part in alpha-oxidation of long chain fatty acids such as 2-hydroxypalmitate (2OH-PALM). HAO2 functions as a homotetramer and is highly expressed in liver and kidney (Jones et al. 2000).

Literature references

Gould, SJ., Morrell, JC., Jones, JM. (2000). Identification and characterization of HAOX1, HAOX2, and HAOX3, three human peroxisomal 2-hydroxy acid oxidases. *J Biol Chem, 275*, 12590-7. ↗

Editions

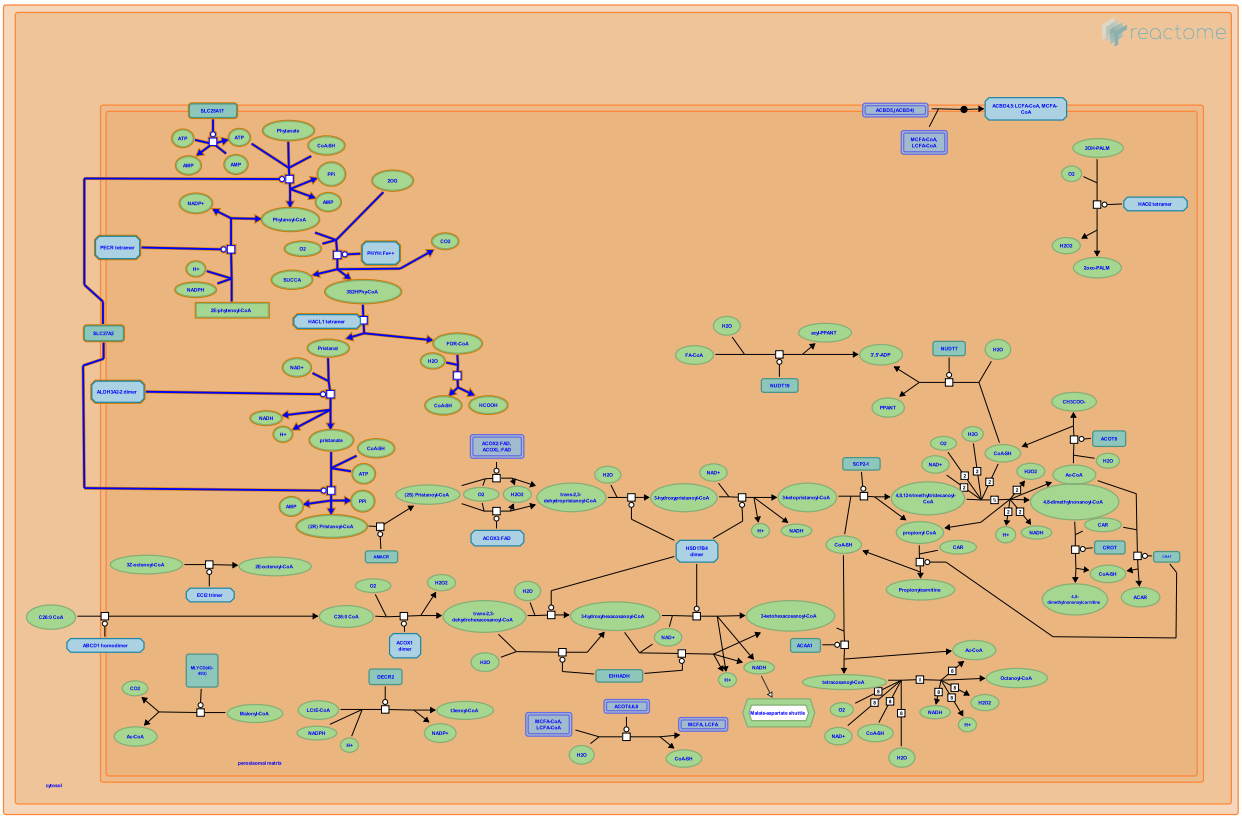
2015-07-17	Authored, Edited	Jassal, B.
2015-09-14	Reviewed	D'Eustachio, P.

Alpha-oxidation of phytanate ↗

Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-389599

Compartments: peroxisomal matrix



Phytanic acid arises through ruminant metabolism of chlorophyll and enters the human diet as a constituent of dairy products (Baxter 1968). It can act as an agonist for PPAR and other nuclear hormone receptors, but its normal role in human physiology, if any, is unclear. It is catabolized via a five-step alpha-oxidation reaction sequence that yields pristanoyl-CoA, which is turn is a substrate for beta-oxidation. These reactions take place in the peroxisomal matrix and their failure is associated with Refsum disease (Wanders et al. 2003).

Literature references

Baxter, JH. (1968). Absorption of chlorophyll phytol in normal man and in patients with Refsum's disease. *J Lipid Res, 9*, 636-41. ↗

Jansen, GA., Wanders, RJA., Lloyd, MD. (2003). Phytanic acid alpha-oxidation, new insights into an old problem: a review. *Biochim Biophys Acta, 1631*, 119-35. ↗

Editions

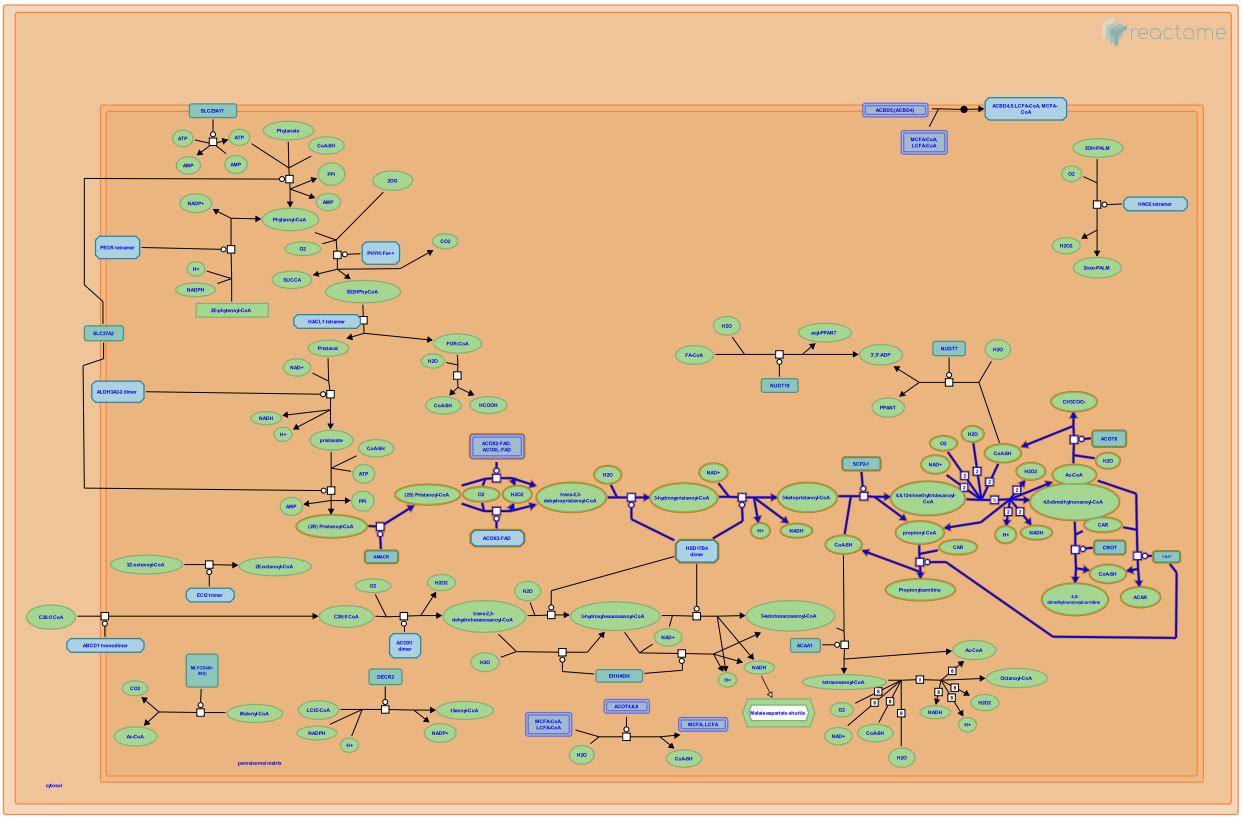
2009-01-11	Authored, Edited	D'Eustachio, P.
2009-02-27	Reviewed	Jassal, B.

Beta-oxidation of pristanoyl-CoA ↗

Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-389887

Compartments: peroxisomal matrix



Pristanoyl-CoA, generated in the peroxisome by alpha-oxidation of dietary phytanic acid, is further catabolized by three cycles of peroxisomal beta-oxidation to yield 4,8-dimethylnonanoyl-CoA, acetyl-CoA and two molecules of propionyl-CoA. These molecules in turn are converted to carnitine conjugates, which can be transported to mitochondria (Wanders and Waterham 2006, Verhoeven et al. 1998, Ferdinandusse et al. 1999).

Literature references

Wanders, RJA., Waterham, HR. (2006). Biochemistry of mammalian peroxisomes revisited. *Annu Rev Biochem, 75*, 295-332. ↗

Verhoeven, NM., Roe, CR., Kok, RM., Roe, DS., Wanders, RJA., Jakobs, C. (1998). Phytanic acid and pristanic acid are oxidized by sequential peroxisomal and mitochondrial reactions in cultured fibroblasts. *J Lipid Res, 39*, 66-74. ↗

IJlst, L., Denis, S., Wanders, RJA., Dacremont, G., Mulders, J., Waterham, HR. et al. (1999). Molecular cloning and expression of human carnitine octanoyltransferase: evidence for its role in the peroxisomal beta-oxidation of branched-chain fatty acids. *Biochem Biophys Res Commun, 263*, 213-8. ↗

Editions

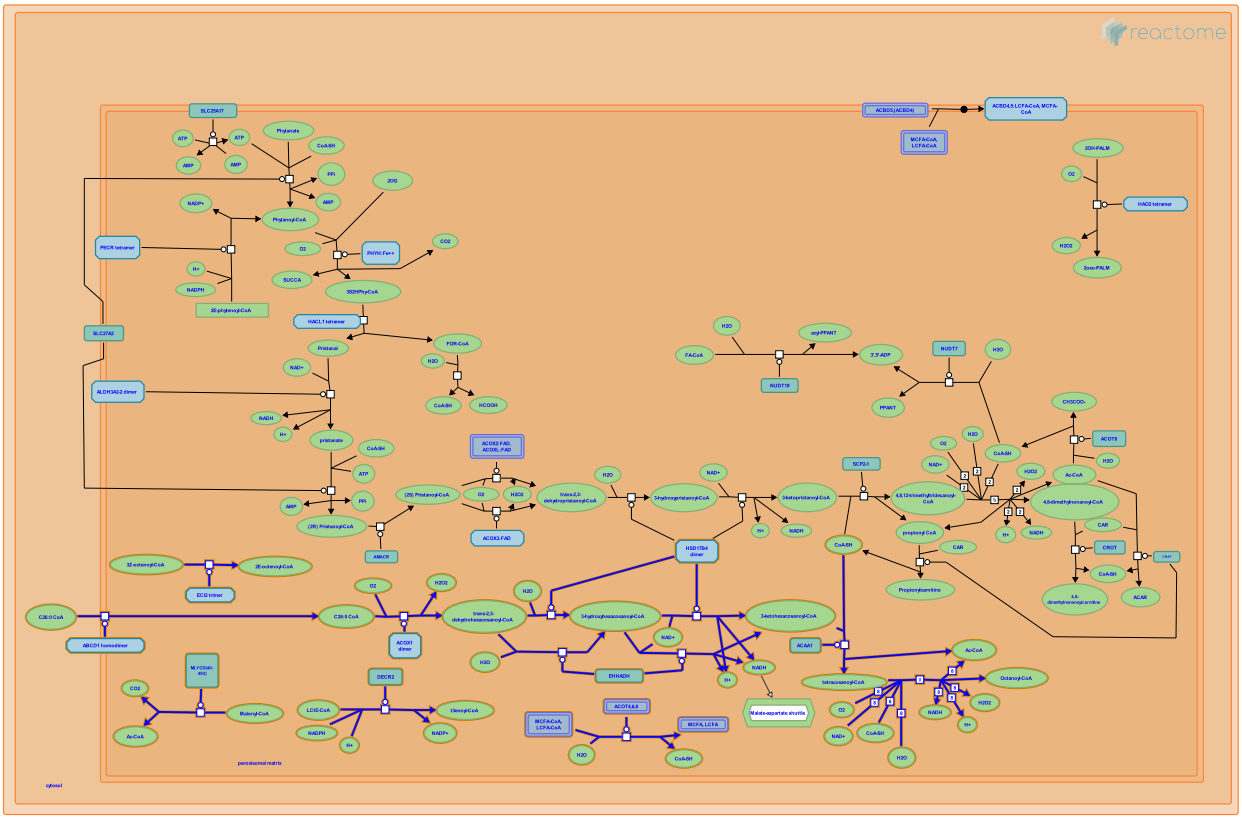
2009-02-27	Reviewed	Jassal, B.
2009-03-16	Authored	D'Eustachio, P.
2009-03-18	Edited	D'Eustachio, P.

Beta-oxidation of very long chain fatty acids ↗

Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-390247

Compartments: peroxisomal matrix



Linear fatty acids containing more than 18 carbons are broken down by beta-oxidation in peroxisomes to yield acetyl-CoA and medium chain-length fatty acyl CoA's such as octanoyl-CoA (Wanders and Waterham 2006).

Literature references

Wanders, RJA., Waterham, HR. (2006). Biochemistry of mammalian peroxisomes revisited. *Annu Rev Biochem, 75*, 295-332. ↗

Editions

2009-02-27	Reviewed	Jassal, B.
2009-03-16	Authored	D'Eustachio, P.
2009-03-18	Edited	D'Eustachio, P.

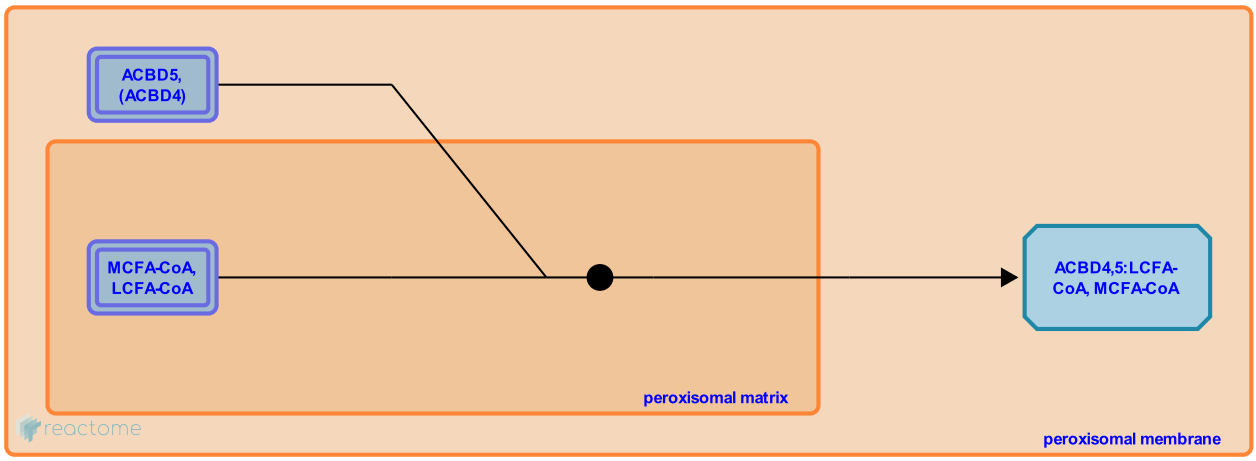
ACBD4,5 bind MCFA-CoA and LCFA-CoA ↗

Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-8848247

Type: binding

Compartments: peroxisomal matrix, peroxisomal membrane



The selective autophagy of peroxisomes (pexophagy) is controlled by autophagy receptors through the assembly of a receptor protein complex (RPC). These receptors can recruit specific proteins required for pexophagy to occur. The human orthologue of the fungal acyl-CoA-binding protein Atg37, ACBD5, is a positive regulator of the pexophagic RPC process. Palmitoyl-CoA competes with autophagy receptors thus may affect the pexophagic RPC process. Acyl-CoA-binding domain-containing proteins 4 and 5 (ACBD4,5) are peroxisomal membrane-bound proteins and thought to bind medium- and long-chain acyl-CoA esters (MCFA-CoA, LCFA-CoA) (Nazarko et al. 2014, Nazarko 2014). The function of ACBD4 has not yet been determined.

Literature references

Nazarko, TY. (2014). Atg37 regulates the assembly of the pexophagic receptor protein complex. *Autophagy, 10*, 1348-9 . ↗

Subramani, S., Nazarko, TY., Lotfi, P., Ozeki, K., Yan, M., Ramakrishnan, G. et al. (2014). Peroxisomal Atg37 binds Atg30 or palmitoyl-CoA to regulate phagophore formation during pexophagy. *J. Cell Biol., 204*, 541-57. ↗

Editions

2015-12-07	Authored, Edited	Jassal, B.
2016-04-05	Reviewed	D'Eustachio, P.

NUDT7 hydrolyses CoA-SH to 3',5'-ADP and PPANT ↗

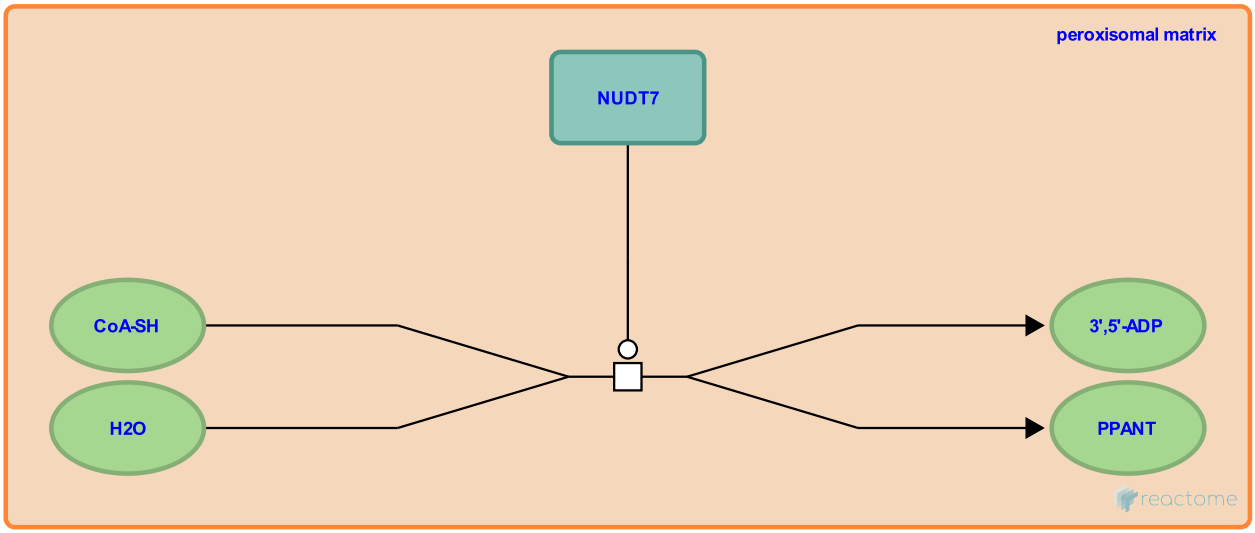
Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-6809354

Type: transition

Compartments: peroxisomal matrix

Inferred from: Nudt7 hydrolyses CoA-SH to 3',5'-ADP and PPANT (Mus musculus)



Coenzyme A (CoASH) is a necessary cofactor for the oxidation of lipids in peroxisomes. Peroxisomal coenzyme A diphosphatase (NUDT7) mediates the cleavage of CoA (and CoA esters and oxidised CoA) to produce 3',5'-ADP and 4'-phosphopantetheine (PPANT) and is suggested to be involved in the regulation of peroxisomal CoASH levels. Human NUDT7 activity is inferred from mouse Nudt7 activity (Gasmi et al. 2001, Reilly et al. 2008).

Literature references

Reilly, SJ., Alexson, SE., Tillander, V., Hunt, MC., Ofman, R. (2008). The nudix hydrolase 7 is an Acyl-CoA diphosphatase involved in regulating peroxisomal coenzyme A homeostasis. *J. Biochem., 144*, 655-63. ↗

Gasmi, L., McLennan, AG. (2001). The mouse Nudt7 gene encodes a peroxisomal nudix hydrolase specific for coenzyme A and its derivatives. *Biochem. J., 357*, 33-8. ↗

Editions

2015-11-11	Authored, Edited	Jassal, B.
2016-01-11	Reviewed	D'Eustachio, P.

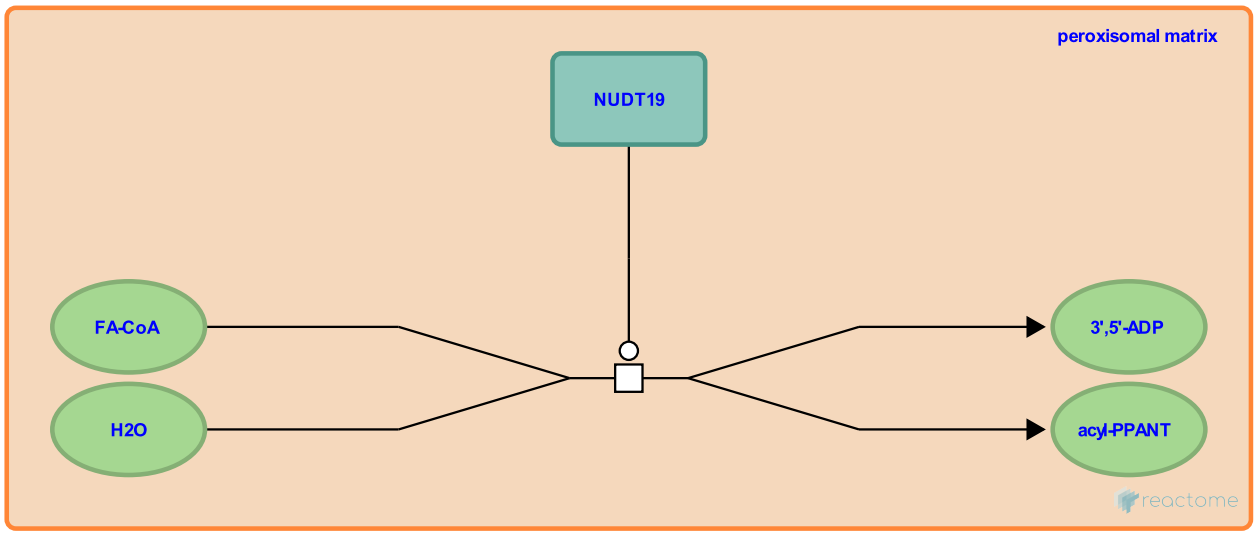
NUDT19 hydrolyses acyl-CoA to 3',5'-ADP and acyl-PPANT ↗

Location: Peroxisomal lipid metabolism

Stable identifier: R-HSA-6810474

Type: transition

Compartments: peroxisomal matrix



Coenzyme A (CoA-SH) and acyl-coenzyme A (acyl-CoA) can be degraded in peroxisomes by two members of the Nudix (nucleoside diphosphates linked to some moiety X) hydrolase superfamily; NUDT7 and NUDT19. NUDT19 hydrolyses free fatty acyl-CoA to form acyl-phosphopantetheine (acyl-PPANT) and 3′,5′-ADP. Human NUDT19 activity is inferred from mouse Nudt19 activity (Ofman et al. 2006).

Literature references

Speijer, D., Leen, R., Wanders, RJA., Ofman, R. (2006). Proteomic analysis of mouse kidney peroxisomes: identification of RP2p as a peroxisomal nudix hydrolase with acyl-CoA diphosphatase activity. *Biochem. J., 393*, 537-43. ↗

Editions

2015-11-17	Authored, Edited	Jassal, B.
2016-01-11	Reviewed	D'Eustachio, P.

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