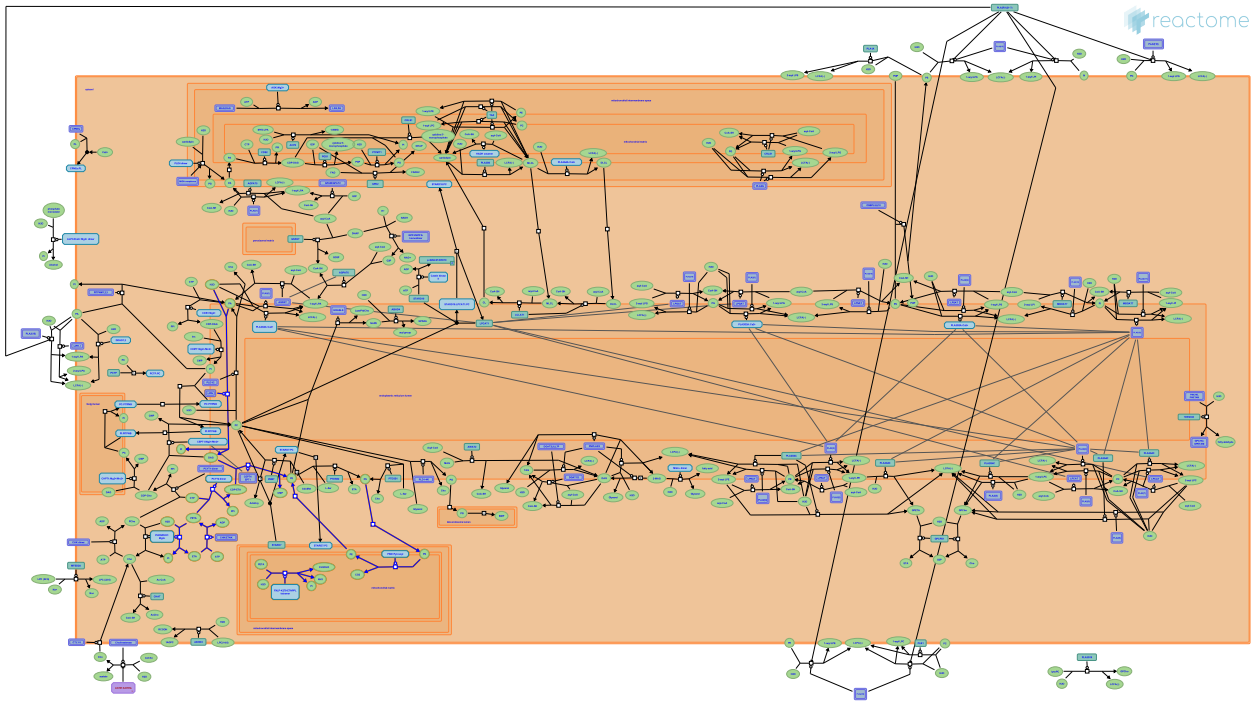
Synthesis of PE



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22/10/2020

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. ↗

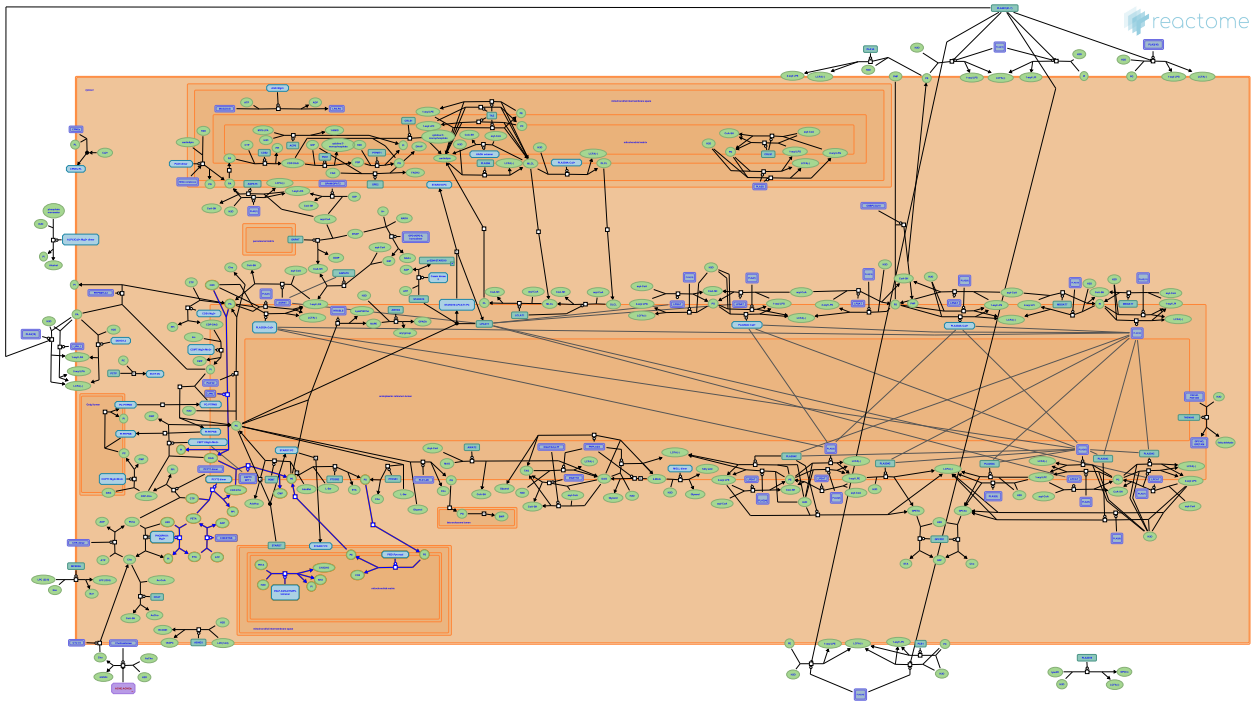
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Synthesis of PE ↗

Stable identifier: R-HSA-1483213



De novo (Kennedy pathway) synthesis of phosphatidylethanolamine (PE) involves phosphorylation of ethanolamine (ETA) to phosphoethanolamine (PETA) followed by condensing with cytidine triphosphate (CTP) to form CDP-ethanolamine (CDP-ETA). Diacylglycerol (DAG) and CDP-ETA together then form PE. Alternatively, PE is formed when phosphatidylserine (PS) is decarboxylated by phosphatidylserine decarboxylase proenzyme (PISD) (Henneberry et al. 2002, Vance 1991, Vance 1990).

Literature references

Vance, JE. (1990). Phospholipid synthesis in a membrane fraction associated with mitochondria. *J Biol Chem, 265*, 7248-56. ↗

Vance, JE. (1991). Newly made phosphatidylserine and phosphatidylethanolamine are preferentially translocated between rat liver mitochondria and endoplasmic reticulum. *J Biol Chem, 266*, 89-97. ↗

Henneberry, AL., Wright, MM., McMaster, CR. (2002). The major sites of cellular phospholipid synthesis and molecular determinants of Fatty Acid and lipid head group specificity. *Mol Biol Cell, 13*, 3148-61. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.
2012-05-14	Reviewed	Wakelam, M.

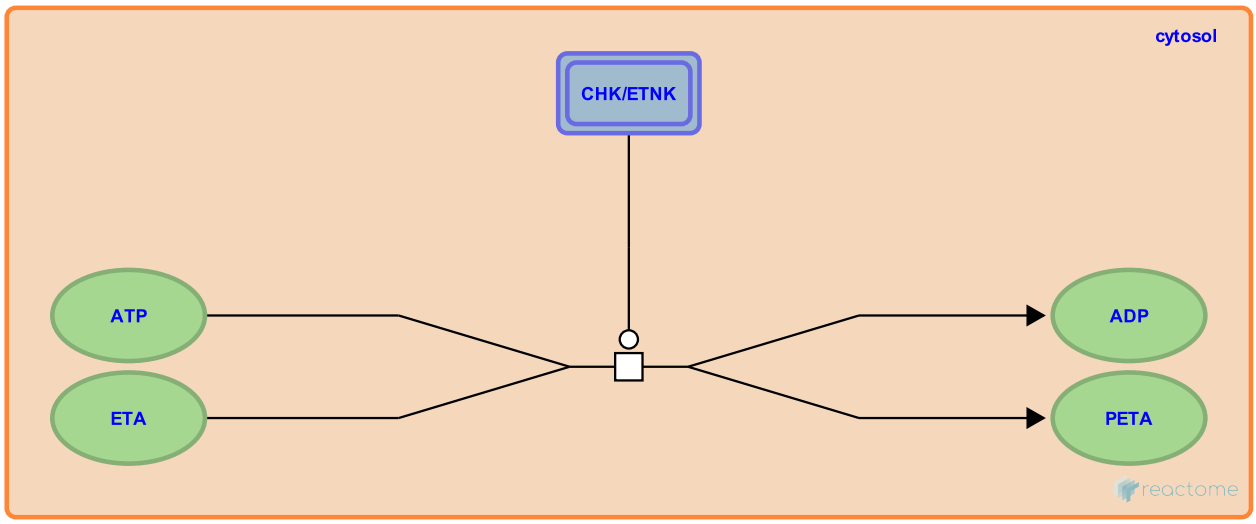
ETA is phosphorylated to PETA by CHK/ETNK ↗

Location: Synthesis of PE

Stable identifier: R-HSA-1483222

Type: transition

Compartments: cytosol



In the cytosol, ethanolamine (ETA) is phosphorylated to phosphoethanolamine (PETA) by choline kinase (CHK) dimer or by ethanolamine kinase 1/2 (ETNK1/2) (Lykidis et al. 2001, Gallego-Ortega et al. 2009). CHK dimer consists of either choline kinase alpha subunit (CHKA) or beta subunit (CHKB) homodimer, or of CHKA:CHKB heterodimer.

Preceded by: PETA is dephosphorylated to ETA by PHOSPHO1

Followed by: PXLP-K278-ETNPPL tetramer hydrolyses PETA, PETA and CTP are condensed to CDP-ETA by PCY2, PETA is dephosphorylated to ETA by PHOSPHO1

Literature references

Gallego-Ortega, D., Ramirez de Molina, A., Ramos, MA., Valdes-Mora, F., Barderas, MG., Sarmentero-Estrada, J. et al. (2009). Differential role of human choline kinase alpha and beta enzymes in lipid metabolism: implications in cancer onset and treatment. *PLoS One, 4*, e7819. ↗

Lykidis, A., Wang, J., Karim, MA., Jackowski, S. (2001). Overexpression of a mammalian ethanolamine-specific kinase accelerates the CDP-ethanolamine pathway. *J Biol Chem, 276*, 2174-9. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

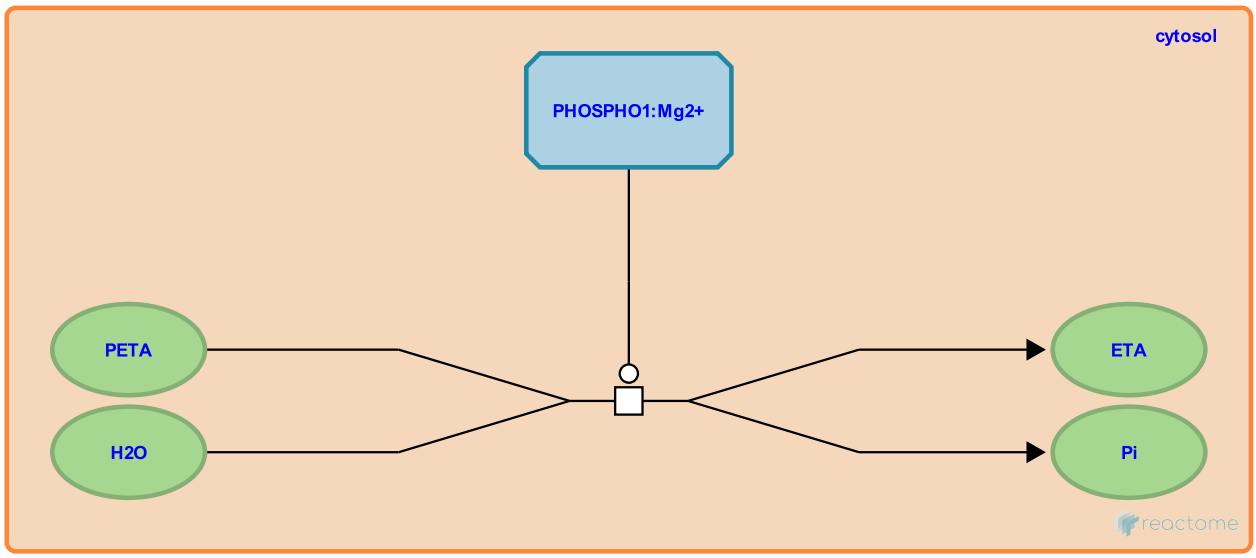
PETA is dephosphorylated to ETA by PHOSPHO1 ↗

Location: Synthesis of PE

Stable identifier: R-HSA-1483096

Type: transition

Compartments: cytosol



In the cytosol, phosphoethanolamine (PETA) is dephosphorylated to ethanolamine (ETA) by phosphoethanolamine/phosphocholine phosphatase (PHOSPHO1) (Roberts et al. 2004).

Preceded by: ETA is phosphorylated to PETA by CHK/ETNK

Followed by: ETA is phosphorylated to PETA by CHK/ETNK

Literature references

Roberts, SJ., Stewart, AJ., Sadler, PJ., Farquharson, C. (2004). Human PHOSPHO1 exhibits high specific phosphoethanolamine and phosphocholine phosphatase activities. *Biochem J, 382*, 59-65. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

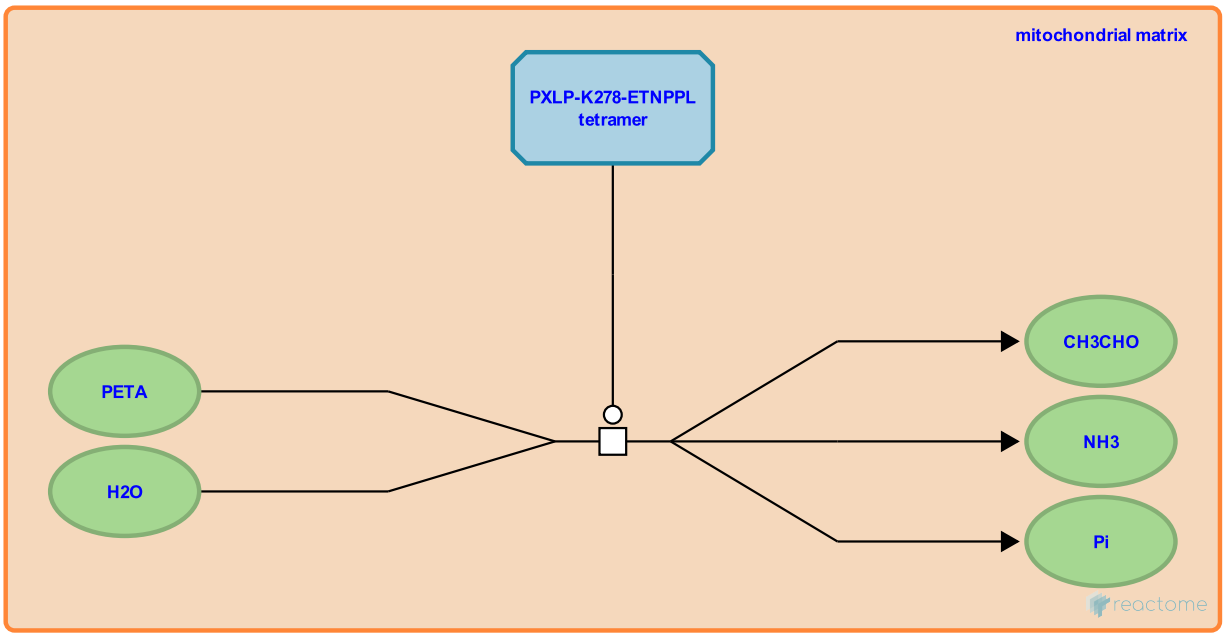
PXLP-K278-ETNPPL tetramer hydrolyses PETA ↗

Location: Synthesis of PE

Stable identifier: R-HSA-5696415

Type: transition

Compartments: mitochondrial matrix



In mitochondria, ethanolamine-phosphate phospho-lyase and 5-phosphohydroxy-L-lysine phospho-lyase (ETNPPL and PHYKPL respectively) are two closely related pyridoxal-phosphate-dependent, homotetrameric ammoniophospholyases that hydrolyse phosphoethanolamine (PETA) and 5-phosphohydroxylysine (5PHL) respectively (Veiga-da-Cunha et al. 2012). PETA is a component and a precursor of phospholipids whereas 5PHL is a breakdown product of collagen. ETNPPL utilises one pyridoxal 5'-phosphate (PXLP) as cofactor per subunit.

Preceded by: ETA is phosphorylated to PETA by CHK/ETNK

Literature references

Veiga-da-Cunha, M., Hadi, F., Balligand, T., Stroobant, V., Van Schaftingen, E. (2012). Molecular identification of hydroxylysine kinase and of ammoniophospholyases acting on 5-phosphohydroxy-L-lysine and phosphoethanolamine. *J. Biol. Chem., 287*, 7246-55. ↗

Editions

2015-05-29	Authored, Edited	Jassal, B.
2015-06-26	Reviewed	D'Eustachio, P.

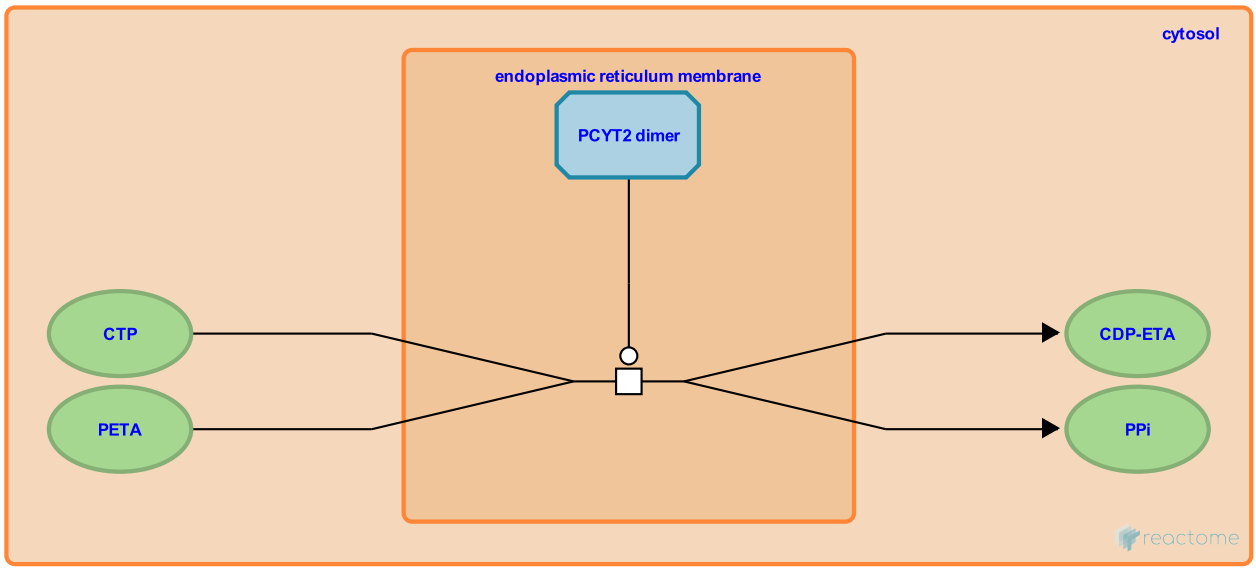
PETA and CTP are condensed to CDP-ETA by PCY2 ↗

Location: Synthesis of PE

Stable identifier: R-HSA-1483190

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



At the endoplasmic reticulum (ER) membrane, active membrane-bound ethanolamine-phosphate cytidylyltransferase (PCY2) dimer condenses phosphoethanolamine (PETA) and cytidine triphosphate (CTP) to produce CDP-ethanolamine (CDP-ETA) (Zhu et al. 2008, Nakashima et al. 1997).

Preceded by: ETA is phosphorylated to PETA by CHK/ETNK

Followed by: CDP-ETA and DAG are converted to PE by CEPT1/EPT1

Literature references

Nakashima, A., Hosaka, K., Nikawa, J. (1997). Cloning of a human cDNA for CTP-phosphoethanolamine cytidylyl-transferase by complementation in vivo of a yeast mutant. *J Biol Chem, 272*, 9567-72. ↗

Zhu, L., Johnson, C., Bakovic, M. (2008). Stimulation of the human CTP:phosphoethanolamine cytidylyltransferase gene by early growth response protein 1. *J Lipid Res, 49*, 2197-211. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

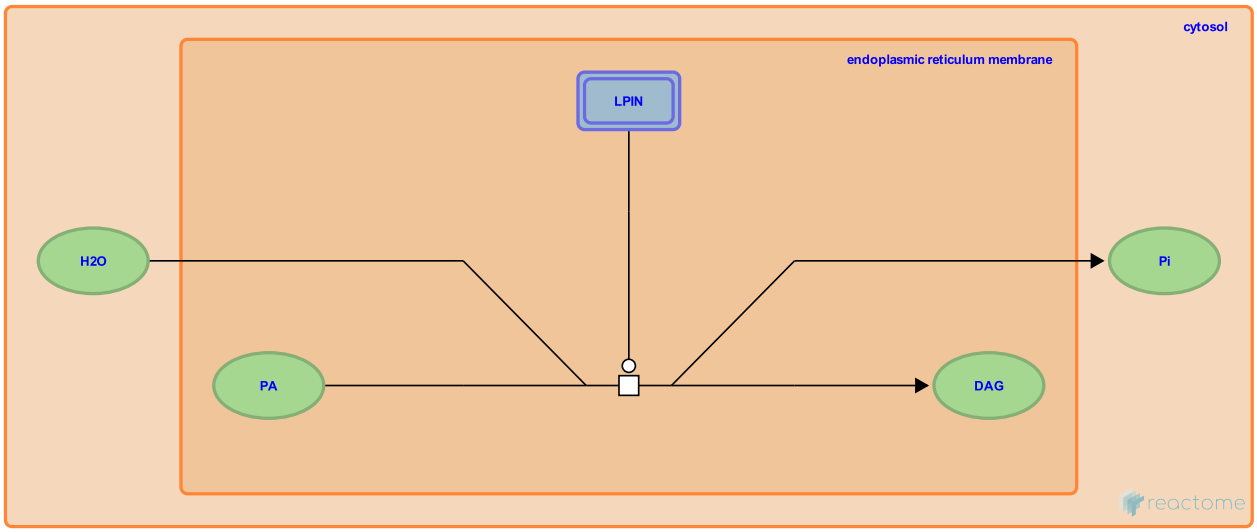
PA is dephosphorylated to DAG by LPIN ↗

Location: Synthesis of PE

Stable identifier: R-HSA-1483203

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



At the endoplasmic reticulum (ER) membrane, phosphatidate phosphatase 1-3 (LPIN) dephosphorylates phosphatidic acid (PA) to form diacylglycerol (DAG) (Grimsey et al. 2008, Donkor et al. 2007).

Followed by: CDP-ETA and DAG are converted to PE by CEPT1/EPT1

Literature references

Donkor, J., Sariahmetoglu, M., Dewald, J., Brindley, DN., Reue, K. (2007). Three mammalian lipins act as phosphatidate phosphatases with distinct tissue expression patterns. *J Biol Chem, 282,* 3450-7. ↗

Grimsey, N., Han, GS., O'Hara, L., Rochford, JJ., Carman, GM., Siniossoglou, S. (2008). Temporal and spatial regulation of the phosphatidate phosphatases lipin 1 and 2. *J Biol Chem, 283*, 29166-74. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

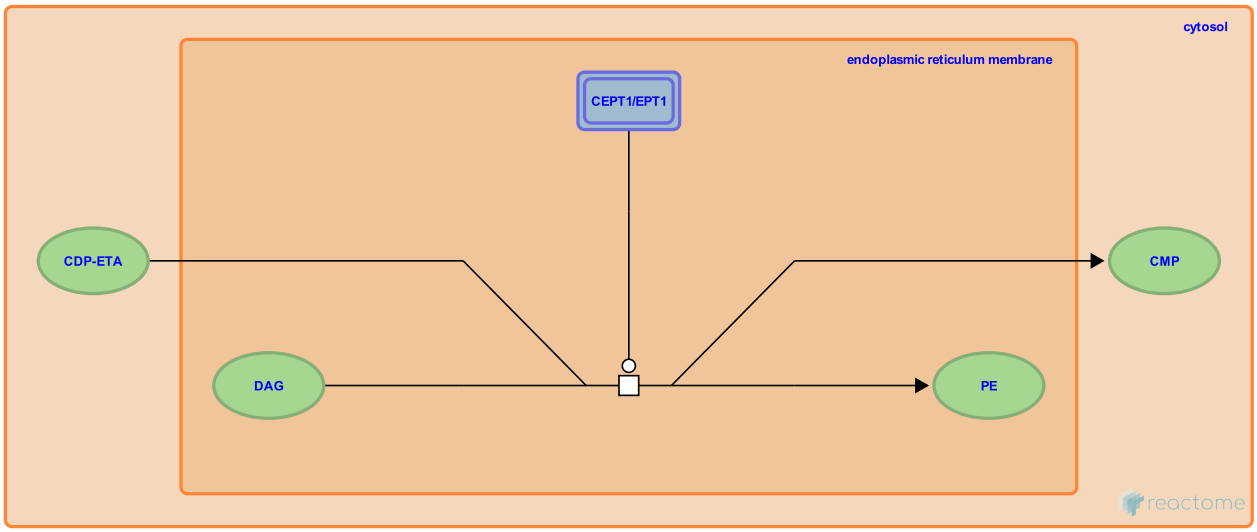
CDP-ETA and DAG are converted to PE by CEPT1/EPT1 ↗

Location: Synthesis of PE

Stable identifier: R-HSA-1482962

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



At the endoplasmic reticulum (ER) membrane, choline/ethanolaminephosphotransferase 1 (CEPT1) or ethanolaminephosphotransferase 1 (EPT1) converts CDP- ethanolamine (CDP-ETA) and diacylglycerol (DAG) to phosphatidylethanolamine (PE) and cytidine monophosphate (CMP) (Horibata et al. 2007, Wright et al. 2002, Henneberry et al. 1999, Henneberry et al. 2002, Henneberry et al. 2000).

Preceded by: PETA and CTP are condensed to CDP-ETA by PCY2, PA is dephosphorylated to DAG by LPIN

Literature references

Henneberry, AL., McMaster, CR. (1999). Cloning and expression of a human choline/ethanolaminephosphotransferase: synthesis of phosphatidylcholine and phosphatidylethanolamine. *Biochem J, 339*, 291-8. ↗

Henneberry, AL., Wistow, G., McMaster, CR. (2000). Cloning, genomic organization, and characterization of a human cholinephosphotransferase. *J Biol Chem, 275*, 29808-15. ↗

Wright, MM., McMaster, CR. (2002). PC and PE synthesis: mixed micellar analysis of the cholinephosphotransferase and ethanolaminephosphotransferase activities of human choline/ethanolamine phosphotransferase 1 (CEPT1). *Lipids, 37*, 663-72. ↗

Henneberry, AL., Wright, MM., McMaster, CR. (2002). The major sites of cellular phospholipid synthesis and molecular determinants of Fatty Acid and lipid head group specificity. *Mol Biol Cell, 13*, 3148-61. ↗

Horibata, Y., Hirabayashi, Y. (2007). Identification and characterization of human ethanolaminephosphotransferase1. *J Lipid Res, 48*, 503-8. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

PS transports from the ER membrane to the IM membrane ↗

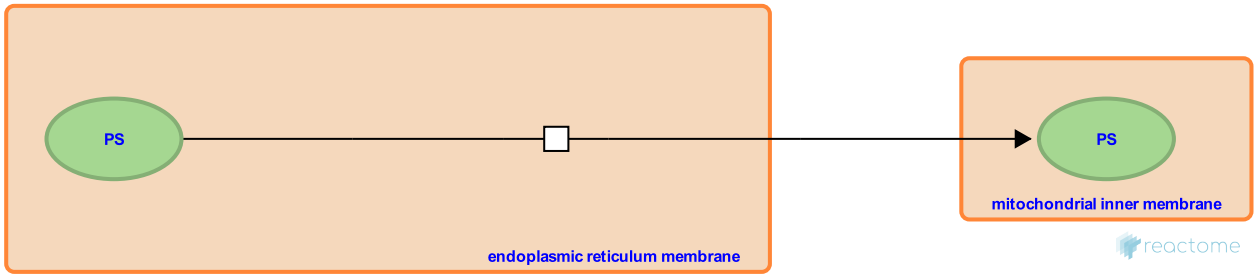
Location: Synthesis of PE

Stable identifier: R-HSA-1483170

Type: transition

Compartments: endoplasmic reticulum membrane, mitochondrial inner membrane

Inferred from: PS transports from the ER membrane to the IM membrane (Rattus norvegicus)



Transport of phosphatidylserine (PS) occurs via membrane contact sites between the endoplasmic reticulum (ER) membrane and the inner mitochondrial (IM) membrane. This event has been inferred from rats (Vance 1990, Vance 1991).

Followed by: PS is decarboxylated to PE by PISD

Literature references

Vance, JE. (1990). Phospholipid synthesis in a membrane fraction associated with mitochondria. *J Biol Chem, 265*, 7248-56. ↗

Vance, JE. (1991). Newly made phosphatidylserine and phosphatidylethanolamine are preferentially translocated between rat liver mitochondria and endoplasmic reticulum. *J Biol Chem, 266*, 89-97. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

PS is decarboxylated to PE by PISD ↗

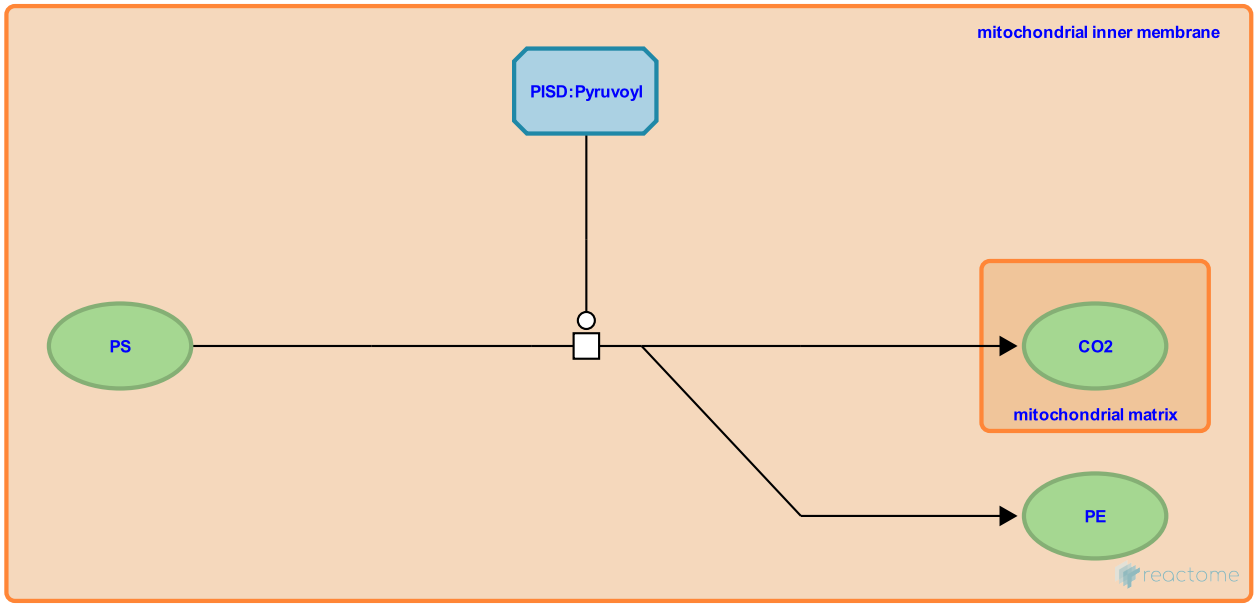
Location: Synthesis of PE

Stable identifier: R-HSA-1483212

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: PS is decarboxylated to PE by Pisd (Rattus norvegicus)



At the inner mitochondrial (IM) membrane, phosphatidylserine decarboxylase proenzyme (heterodimer of two chains from the same protein) (PISD) decarboxylates phosphatidylserine (PS) to phosphatidylethanolamine (PE). This event has been inferred from rats and limited data for a human PISD (Forbes et al. 2007).

Preceded by: PS transports from the ER membrane to the IM membrane

Followed by: PE transports from the mitochondrial membrane to the ER

Literature references

Forbes, CD., Toth, JG., Ozbal, CC., Lamarr, WA., Pendleton, JA., Rocks, S. et al. (2007). High-throughput mass spectrometry screening for inhibitors of phosphatidylserine decarboxylase. *J Biomol Screen, 12*, 628-34. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

PE transports from the mitochondrial membrane to the ER ↗

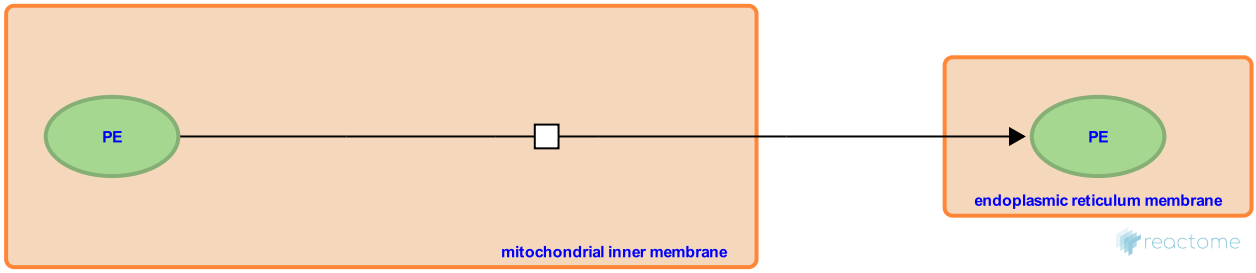
Location: Synthesis of PE

Stable identifier: R-HSA-1483077

Type: transition

Compartments: mitochondrial inner membrane, endoplasmic reticulum membrane

Inferred from: PE transports from the mitochondrial membrane to the ER (Rattus norvegicus)



Transport of phosphatidylethanolamine (PE) occurs via membrane contact sites between the mitochondrial membrane and the endoplasmic reticulum (ER) membrane. The event is inferred from rats (Vance 1990, Vance 1991).

Preceded by: PS is decarboxylated to PE by PISD

Literature references

Vance, JE. (1990). Phospholipid synthesis in a membrane fraction associated with mitochondria. *J Biol Chem, 265*, 7248-56. ↗

Vance, JE. (1991). Newly made phosphatidylserine and phosphatidylethanolamine are preferentially translocated between rat liver mitochondria and endoplasmic reticulum. *J Biol Chem, 266*, 89-97. ↗

Editions

2011-08-12	Edited	Williams, MG.
2011-09-14	Authored	Williams, MG.

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