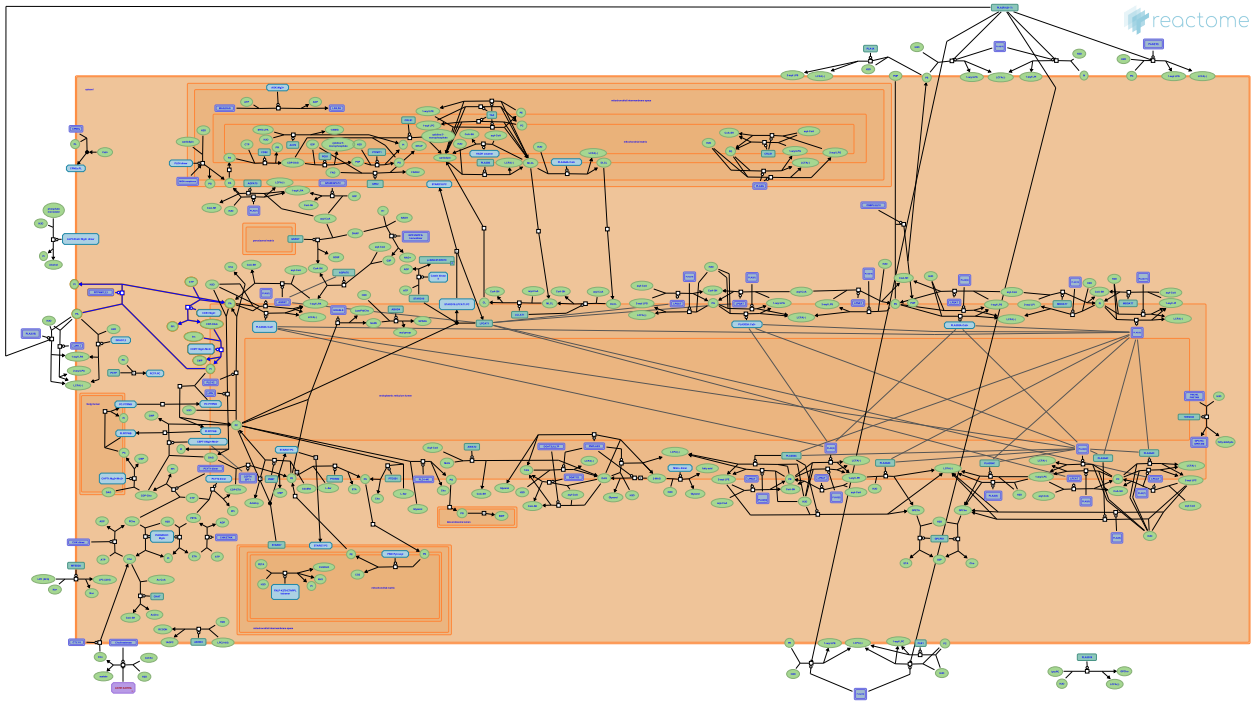
Synthesis of PI



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19/10/2020

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.

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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. ↗

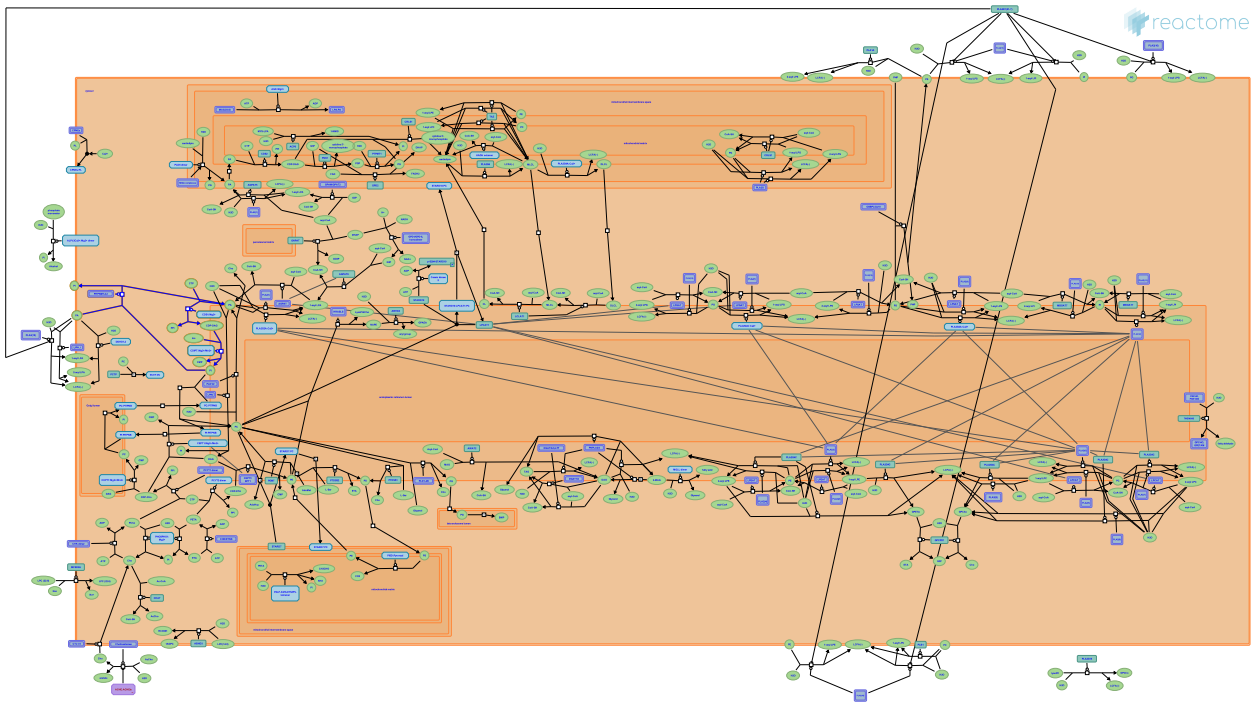
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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 PI ↗

Stable identifier: R-HSA-1483226



Phosphatidylinositol (PI) is synthesized when phosphatidic acid (PA) and cytidine triphosphate (CTP) are converted into cytidine diphosphate-diacylglycerol (CDP-DAG) followed by conversion into PI and cytidine monophosphate (CMP) (Stuhne-Sekalec et al 1986, Lykidis et al. 1997).

Literature references

Lykidis, A., Jackson, PD., Rock, CO., Jackowski, S. (1997). The role of CDP-diacylglycerol synthetase and phosphatidylinositol synthase activity levels in the regulation of cellular phosphatidylinositol content. *J Biol Chem, 272* , 33402-9. ↗

Stuhne-Sekalec, L., Chudzik, J., Stanacev, NZ. (1986). Participation of the microsomal CDP-diglycerides in the mitochondrial biosynthesis of phosphatidylglycerol. *Biochem Cell Biol, 64*, 309-14. ↗

Editions

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

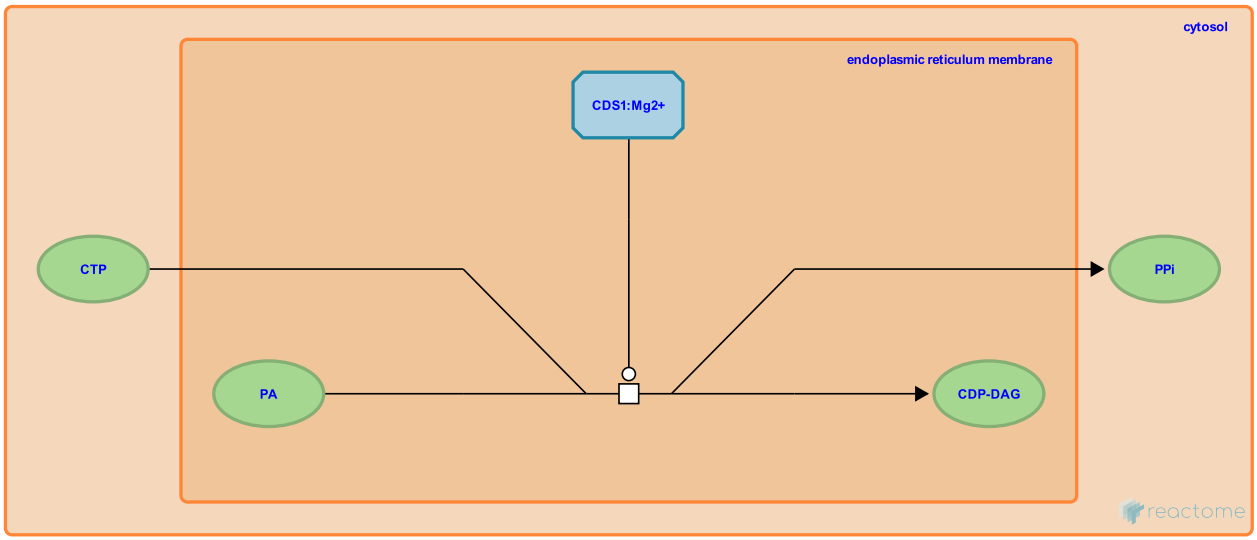
PA is converted to CDP-DAG by CDS1 ↗

Location: Synthesis of PI

Stable identifier: R-HSA-1483121

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



At the endoplasmic reticulum (ER) membrane, phosphatidate cytidylyltransferase 1 (CDS1) converts phosphatidic acid (PA) and cytidine triphosphate (CTP) into cytidine diphosphate-diacylglycerol (CDP-DAG). Both ER and mitochondrial membranes have the capability to synthesize cytidine diphosphate-diacylglycerol (CDP-DAG) with phosphatidate cytidylyltransferase 1 and 2 (CDS1 and CDS2) (Lykidis et al. 1997). However, transport of CDP-DAG between organelles cannot be ruled out (Stuhne-Sekalec et al. 1986).

Followed by: CDP-DAG is converted to PI by CDIPT

Literature references

Lykidis, A., Jackson, PD., Rock, CO., Jackowski, S. (1997). The role of CDP-diacylglycerol synthetase and phosphatidylinositol synthase activity levels in the regulation of cellular phosphatidylinositol content. *J Biol Chem, 272* , 33402-9. ↗

Stuhne-Sekalec, L., Chudzik, J., Stanacev, NZ. (1986). Participation of the microsomal CDP-diglycerides in the mitochondrial biosynthesis of phosphatidylglycerol. *Biochem Cell Biol, 64*, 309-14. ↗

Editions

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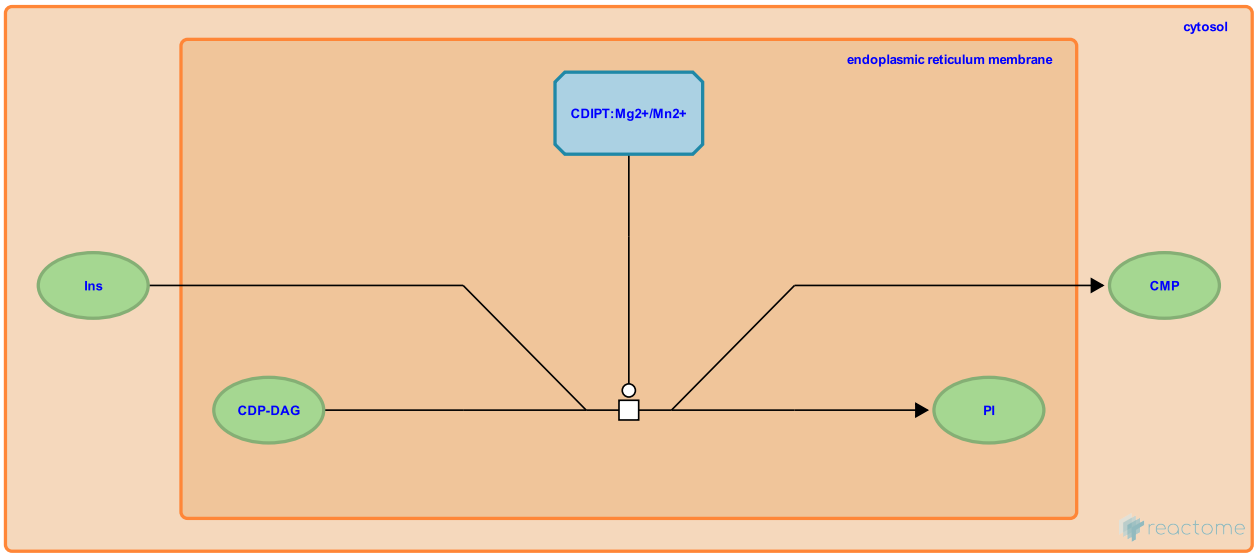
CDP-DAG is converted to PI by CDIPT ↗

Location: Synthesis of PI

Stable identifier: R-HSA-1482976

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



At the endoplasmic reticulum (ER) membrane, CDP-diacylglycerol-inositol 3-phosphatidyltransferase (CDIPT) converts cytidine diphosphate-diacylglycerol (CDP-DAG) and inositol (Ins) into phosphatidylinositol (PI) and cytidine monophosphate (CMP) (Lykidis et al. 1997).

Preceded by: PA is converted to CDP-DAG by CDS1

Literature references

Lykidis, A., Jackson, PD., Rock, CO., Jackowski, S. (1997). The role of CDP-diacylglycerol synthetase and phosphatidylinositol synthase activity levels in the regulation of cellular phosphatidylinositol content. *J Biol Chem, 272* , 33402-9. ↗

Editions

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

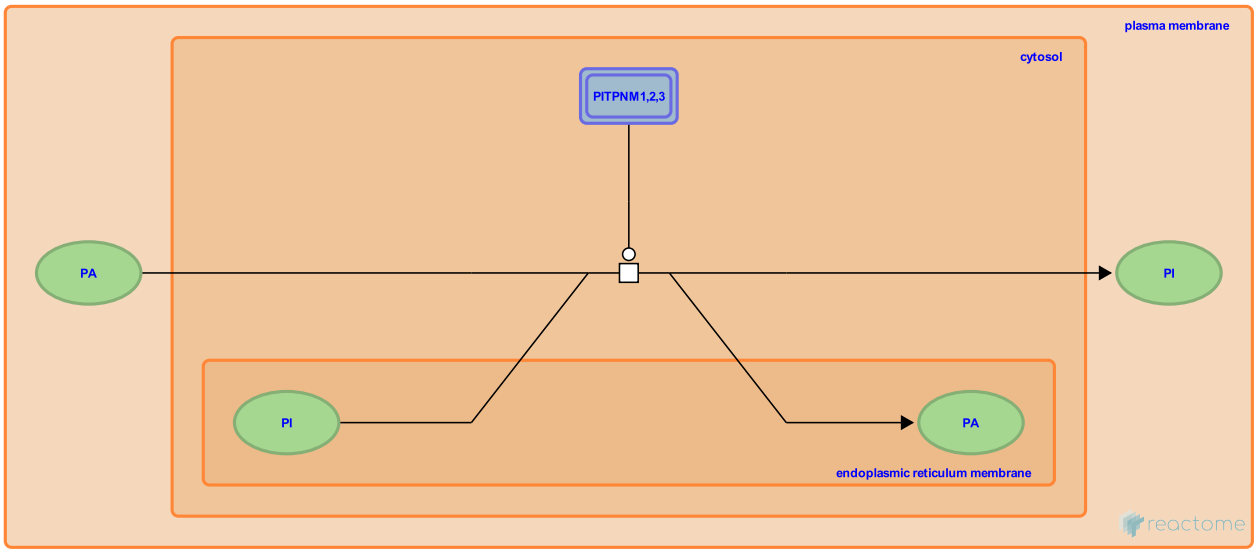
PITPNM1,2,3 exchange PI for PA ↗

Location: Synthesis of PI

Stable identifier: R-HSA-8869241

Type: transition

Compartments: cytosol, endoplasmic reticulum membrane, plasma membrane



Phosphatidylinositol 4,5-bisphosphate (PIP2) at the plasma membrane (PM) constitutively controls many cellular functions, and its hydrolysis via receptor stimulation can mediate cell signalling. A steady delivery of phosphatidylinositol (PI) from its site of synthesis in the endoplasmic reticulum (ER) to the PM is essential to maintain PIP2 levels. In addition, phosphatidic acid (PA), generated from diacylglycerol in the PM, has to reach the ER for PI resynthesis. The ubiquitously-expressed membrane-associated phosphatidylinositol transfer proteins 1, 2 and 3 (PITPNM1,2,3) (Lev et al. 1999) detect PIP2 hydrolysis and translocate to ER-PM junctions where they mediate the exchange of PI for PA (Kim et al. 2015, Chang & Liou 2015). Defects in PITPNM3 can cause cone-rod dystrophy 5 (CORD5; MIM:600977), a retinal dystrophy manifested as progressive loss of central vision, defective color vision, and photophobia. The missense mutation Q626H lacks the N-terminal PIT domain needed for transport of phospholipids and renewal of photoreceptors membranes is impaired (Kohn et al. 2007).

Literature references

Kim, YJ., Guzman-Hernandez, ML., Wisniewski, E., Balla, T. (2015). Phosphatidylinositol-Phosphatidic Acid Exchange by Nir2 at ER-PM Contact Sites Maintains Phosphoinositide Signaling Competence. *Dev. Cell, 33*, 549-61. ↗

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Köhn, L., Kadzhaev, K., Burstedt, MS., Haraldsson, S., Hallberg, B., Sandgren, O. et al. (2007). Mutation in the PYK2-binding domain of PITPNM3 causes autosomal dominant cone dystrophy (CORD5) in two Swedish families. *Eur. J. Hum. Genet., 15*, 664-71. ↗

Editions

2016-04-26	Authored, Edited	Jassal, B.
2016-07-15	Reviewed	D'Eustachio, P.

Table of Contents