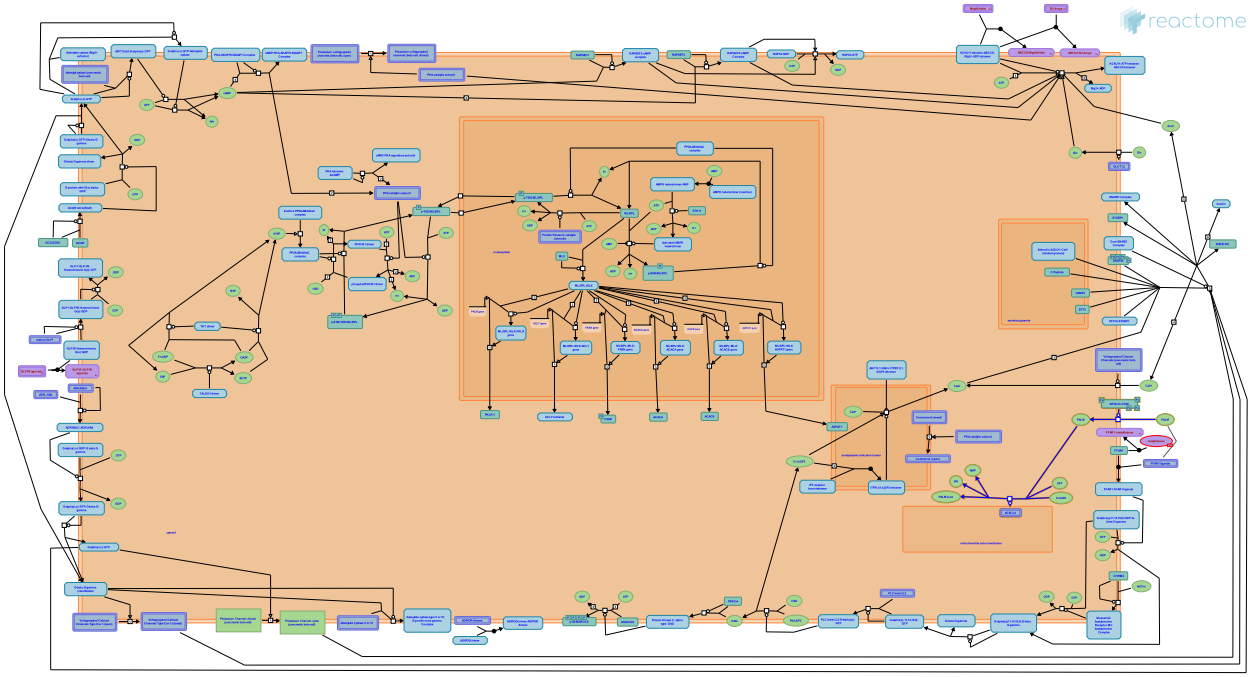
Intracellular metabolism of fatty acids regulates insulin secretion



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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. ↗

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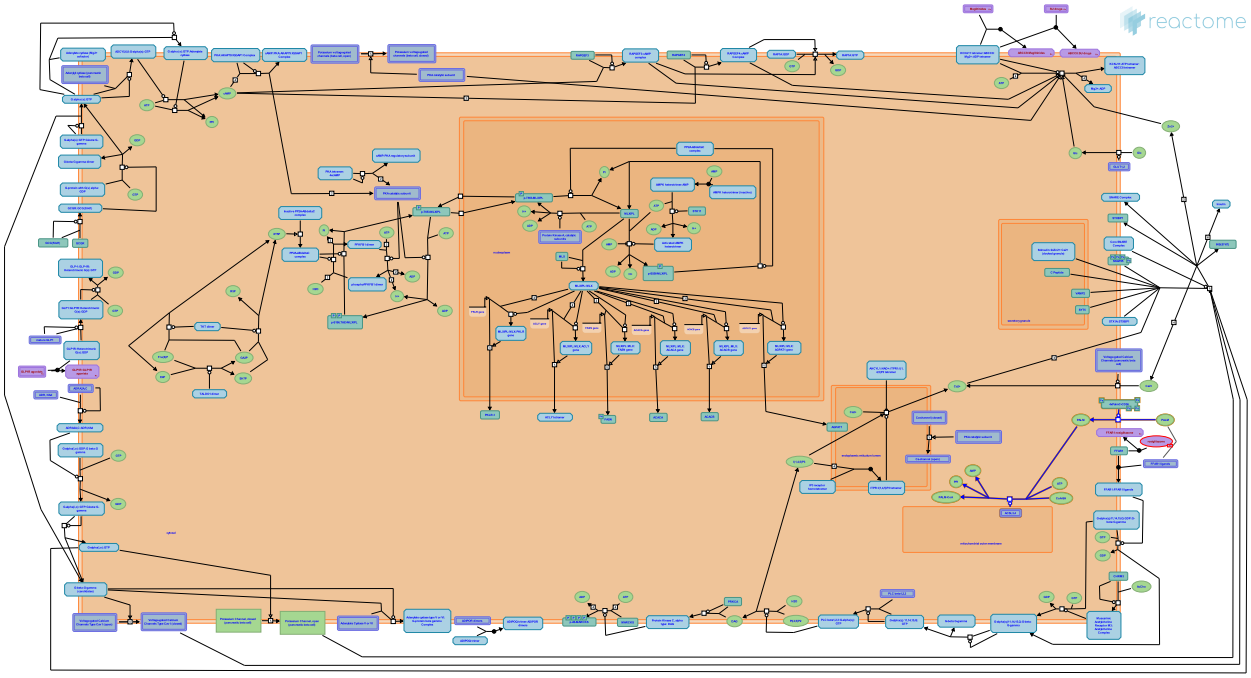
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Intracellular metabolism of fatty acids regulates insulin secretion ↗

Stable identifier: R-HSA-434313



Fatty acids augment the glucose triggered secretion of insulin through two mechanisms: activation of FFAR1 (GPR40) and intracellular metabolism of fatty acids. Fatty acids are transported into the cell by CD36 (FAT) (Noushmehr et al. 2005) and metabolized by ligation to coenzyme A (Ansari et al. 2017), transport into mitochondria, and beta oxidation which generates ATP. The ATP increases the intracellular ratio of ATP:ADP and thereby closes potassium channels (K(ATP) channels) at the plasma membrane (reviewed in Acosta-Montano and Garcia-Gonzalez 2018). The enzymes that metabolize fatty acids in beta cells also metabolize fatty acids in other tissues however their combinations and subcellular locations may differ.

Literature references

Doria, A., Noushmehr, H., Wawrowsky, KA., Farilla, L., Mlynarski, W., D'Amico, E. et al. (2005). Fatty acid translocase (FAT/CD36) is localized on insulin-containing granules in human pancreatic beta-cells and mediates fatty acid effects on insulin secretion. *Diabetes, 54*, 472-81. ↗

García-González, V., Acosta-Montaño, P. (2018). Effects of Dietary Fatty Acids in Pancreatic Beta Cell Metabolism, Implications in Homeostasis. *Nutrients, 10*. ↗

Stoker, SW., Ansari, IH., MacDonald, MJ., Fernandez, LA., Kendrick, MA., Ntambi, JM. et al. (2017). Characterization of Acyl-CoA synthetase isoforms in pancreatic beta cells: Gene silencing shows participation of ACSL3 and ACSL4 in insulin secretion. *Arch. Biochem. Biophys., 618*, 32-43. ↗

Editions

2009-08-28	Authored, Edited	May, B.
2018-12-22	Reviewed	D'Eustachio, P.

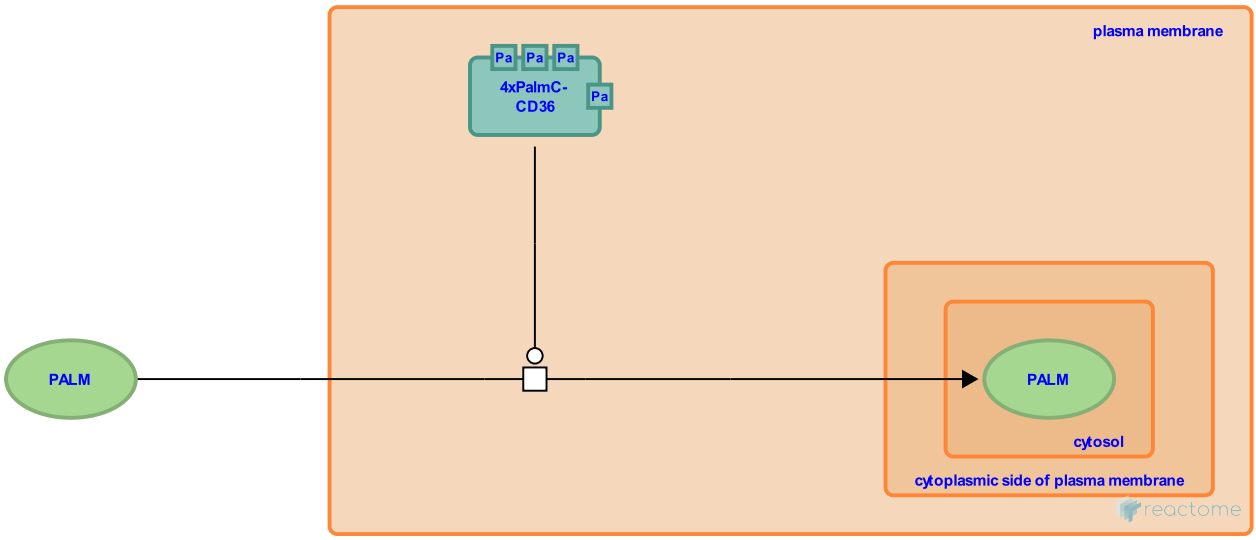
CD36 (FAT) translocates palmitate from the extracellular region to the cytosol ↗

Location: Intracellular metabolism of fatty acids regulates insulin secretion

Stable identifier: R-HSA-434381

Type: transition

Compartments: plasma membrane



CD36 (FAT) located in the plasma membrane of pancreatic beta cells transports fatty acids such as palmitate into the cell (Noushmehr et al. 2005).

Followed by: ACSL3,4 ligates coenzyme A (CoA-SH) to palmitate yielding palmitoyl-coenzyme A in the pancreatic beta cell

Literature references

Doria, A., Noushmehr, H., Wawrowsky, KA., Farilla, L., Mlynarski, W., D'Amico, E. et al. (2005). Fatty acid translocase (FAT/CD36) is localized on insulin-containing granules in human pancreatic beta-cells and mediates fatty acid effects on insulin secretion. *Diabetes, 54*, 472-81. ↗

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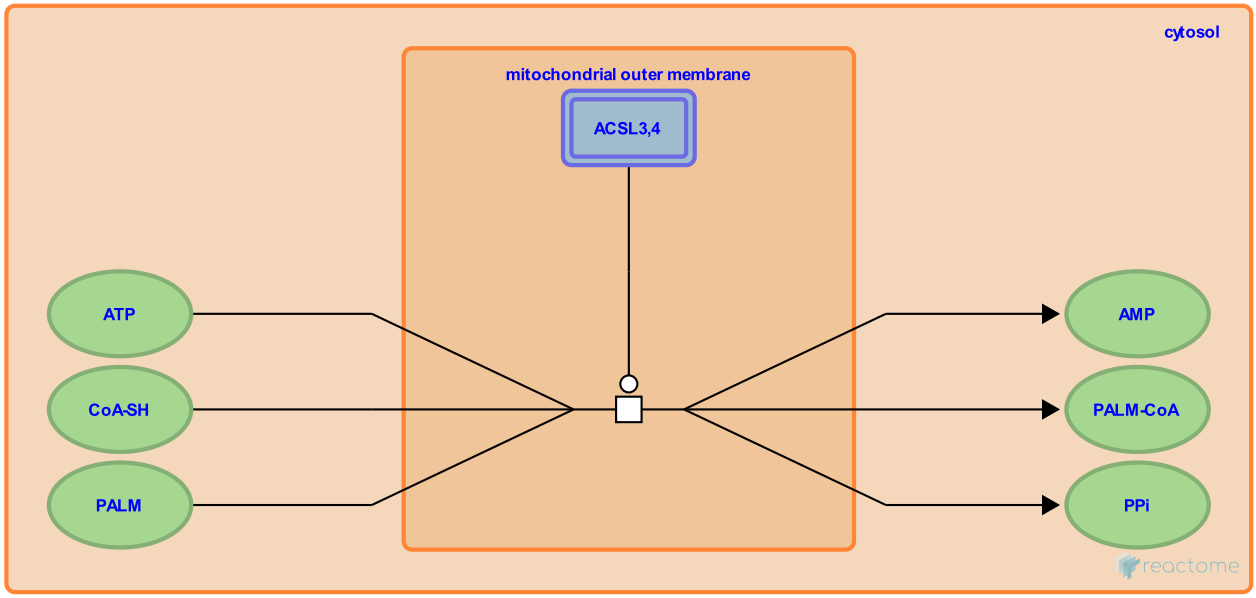
ACSL3,4 ligates coenzyme A (CoA-SH) to palmitate yielding palmitoyl-coenzyme A in the pancreatic beta cell ↗

Location: Intracellular metabolism of fatty acids regulates insulin secretion

Stable identifier: R-HSA-434382

Type: transition

Compartments: mitochondrial outer membrane



ACSL3 and ACSL4 found on the mitochondria of pancreatic beta cells ligate coenzyme A (Co-A) to fatty acids such as palmitate (Ansari et al. 2017) prior to transport into mitochondria by the carnitine system and beta oxidation in the mitochondrial matrix yielding ATP.

Preceded by: CD36 (FAT) translocates palmitate from the extracellular region to the cytosol

Literature references

Stoker, SW., Ansari, IH., MacDonald, MJ., Fernandez, LA., Kendrick, MA., Ntambi, JM. et al. (2017). Characterization of Acyl-CoA synthetase isoforms in pancreatic beta cells: Gene silencing shows participation of ACSL3 and ACSL4 in insulin secretion. *Arch. Biochem. Biophys., 618*, 32-43. ↗

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