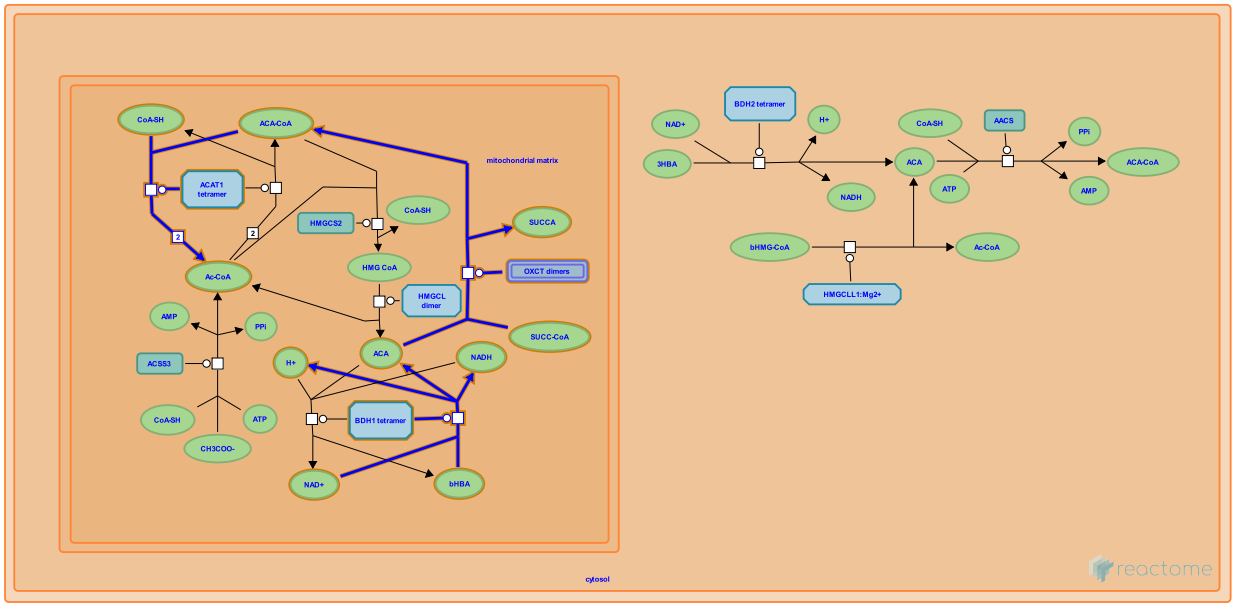
Utilization of Ketone Bodies



Gopinathrao, G., Jassal, B., Joshi-Tope, G.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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.

01/05/2024

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. ↗

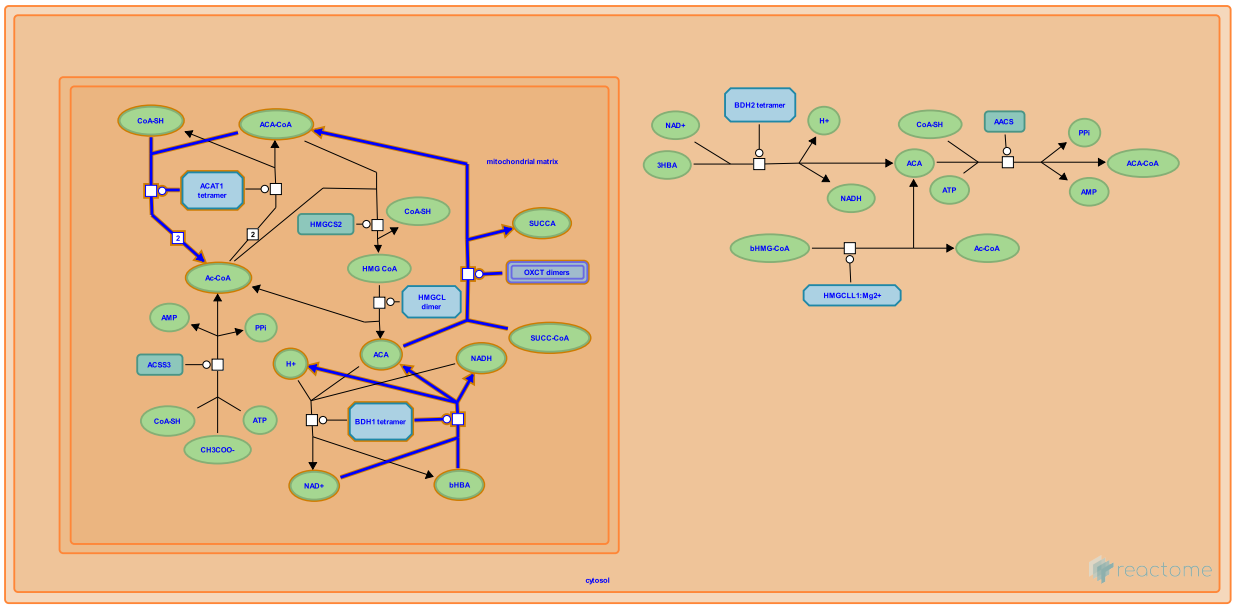
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Utilization of Ketone Bodies ↗

Stable identifier: R-HSA-77108

Compartments: mitochondrial matrix



The levels of acetone in ketone bodies are much lower than those of acetoacetic acid and beta-hydroxybutyric acid. Acetone cannot be converted back to acetyl-CoA, and is excreted in urine, or breathed out through the lungs. Extrahepatic tissues utilize ketone bodies by converting the beta-hydroxybutyrate successively to acetoacetate, acetoacetatyl-CoA, finally to acetyl-CoA (Sass 2011).

Literature references

Sass, JO. (2011). Inborn errors of ketogenesis and ketone body utilization. *J Inherit Metab Dis.* ↗

Editions

2003-10-19	Authored	Joshi-Tope, G.
2016-06-30	Edited	Jassal, B.

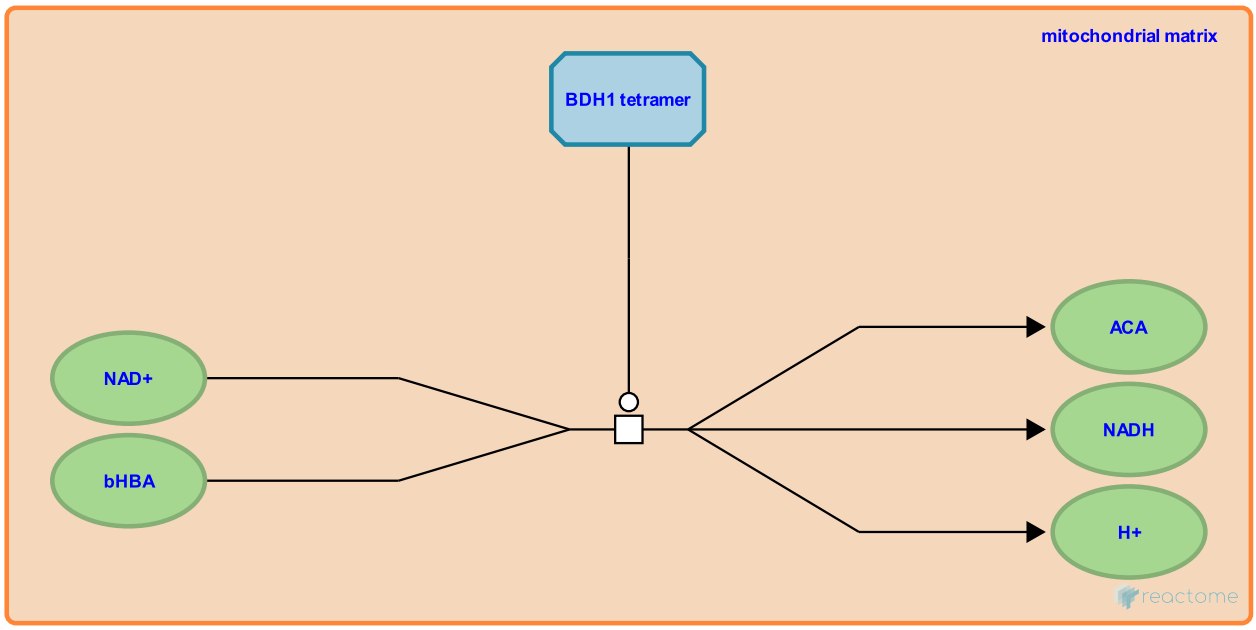
D-beta hydroxybutyrate+NAD+ <=> acetoacetate+NADH+H+ ↗

Location: Utilization of Ketone Bodies

Stable identifier: R-HSA-73920

Type: transition

Compartments: mitochondrial matrix



D-beta-hydroxybutyrate dehydrogenase tetramer (BDH1) in the mitochondrial matrix catalyzes the reversible reaction of D-beta hydroxybutyrate and NAD+ to form acetoacetate and NADH + H+ (Marks et al. 1992).

Followed by: OXCT dimers transfer CoA from SUCC-CoA to ACA, forming ACA-CoA

Literature references

Duncan, TM., McIntyre, JO., Fleischer, S., Tempst, P., Erdjument-Bromage, H., Marks, AR. (1992). Molecular cloning and characterization of (R)-3-hydroxybutyrate dehydrogenase from human heart. *J Biol Chem, 267*, 15459-63. ↗

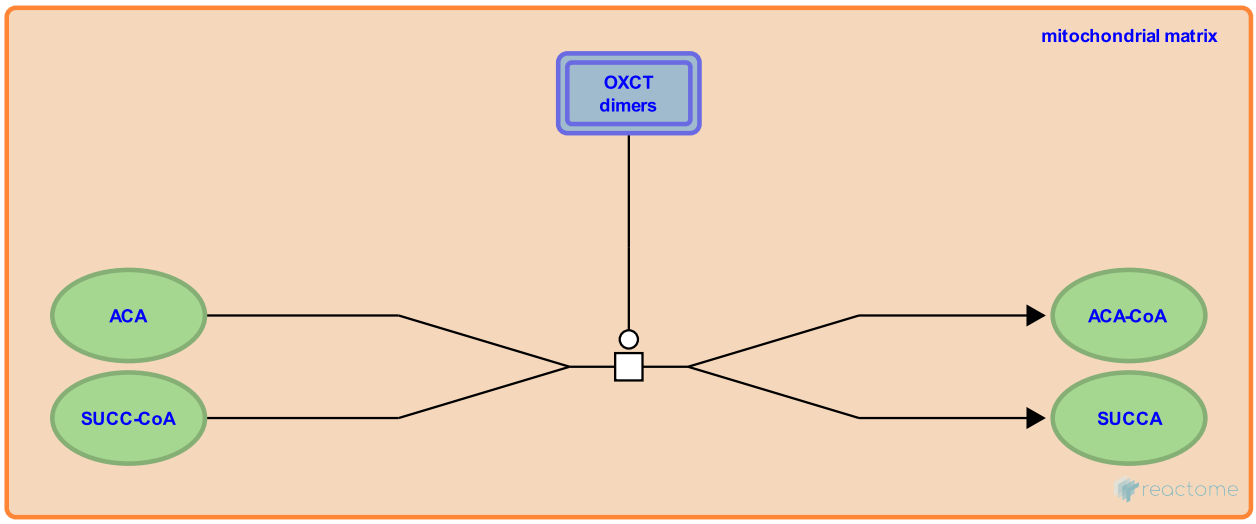
OXCT dimers transfer CoA from SUCC-CoA to ACA, forming ACA-CoA ↗

Location: Utilization of Ketone Bodies

Stable identifier: R-HSA-74177

Type: transition

Compartments: mitochondrial matrix



Mitochondrial succinyl-CoA:3-ketoacid coenzyme A transferases 1 and 2 (OXCT1 and OXCT2) are key enzymes for the metabolism of ketone bodies, catalysing the first rate-limiting step of ketone body utilisation in peripheral tissues. In dimeric form, they mediate the transfer of a CoA moiety from succinyl-CoA (SUCC-CoA) to acetoacetate (ACA) to form acetoacetyl-CoA (ACA-CoA) and succinate (SUCCA) (Kassovska-Bratinova et al. 1996, Tanaka et al. 2002). ACA-CoA can be converted to acetyl-CoA which can be utilised by the tricarboxylic acid cycle for energy production.

Preceded by: D-beta hydroxybutyrate+NAD+ <=> acetoacetate+NADH+H+

Followed by: acetoacetyl-CoA + CoA <=> 2 acetyl-CoA

Literature references

Kondo, N., Pérez-Cerda, C., Kassovska-Bratinova, S., Vobecky, S., Fukao, T., Ugarte, M. et al. (1996). Succinyl CoA: 3-oxoacid CoA transferase (SCOT): human cDNA cloning, human chromosomal mapping to 5p13, and mutation detection in a SCOT-deficient patient. *Am J Hum Genet, 59*, 519-28. ↗

Kohroki, J., Tanaka, H., Nishimune, Y., Onishi, M., Iguchi, N. (2002). Cloning and characterization of a human orthologue of testis-specific succinyl CoA: 3-oxo acid CoA transferase (Scot-t) cDNA. *Mol. Hum. Reprod., 8*, 16-23. ↗

Editions

2003-07-16	Authored	Gopinathrao, G.
2017-01-12	Edited, Revised	Jassal, B.

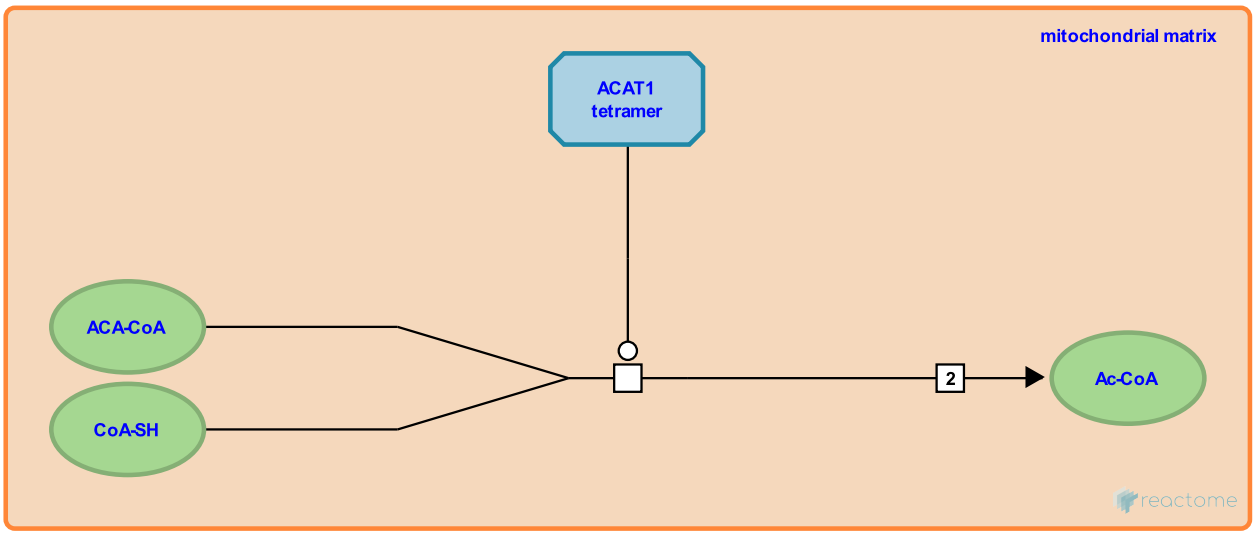
acetoacetyl-CoA + CoA <=> 2 acetyl-CoA ↗

Location: Utilization of Ketone Bodies

Stable identifier: R-HSA-74181

Type: transition

Compartments: mitochondrial matrix



Acetyl-CoA acetyltransferase tetramer (ACAT1) in the mitochondrial matrix catalyzes the reversible reaction of acetoacetyl-CoA and CoA to form two molecules of acetyl-CoA (Middleton et al. 1986).

Preceded by: OXCT dimers transfer CoA from SUCC-CoA to ACA, forming ACA-CoA

Literature references

Romanos, A., Middleton, B., Cannon, RA., Conde, C., Nyhan, WL., Lipson, M. et al. (1986). 3-Ketothiolase deficiency. *Eur J Pediatr, 144*, 586-9. ↗

Table of Contents

Introduction 1

Utilization of Ketone Bodies 2

- D-beta hydroxybutyrate+NAD+ <=> acetoacetate+NADH+H+ 3
- OXCT dimers transfer CoA from SUCC-CoA to ACA, forming ACA-CoA 4
- acetoacetyl-CoA + CoA <=> 2 acetyl-CoA 5

Table of Contents 6