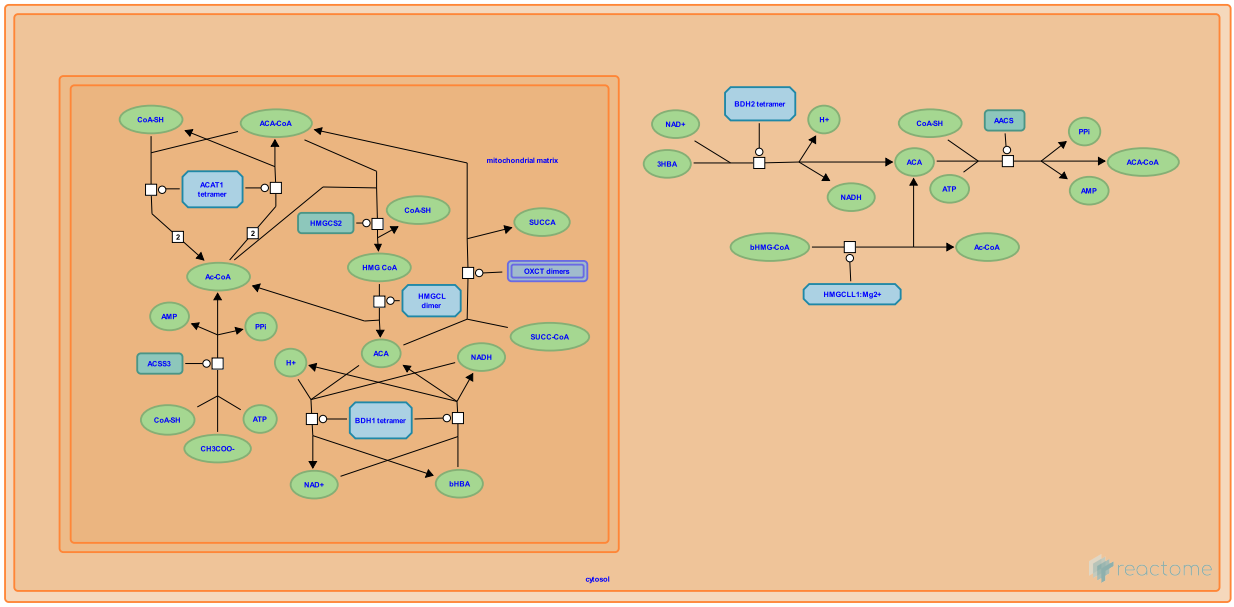
Ketone body metabolism



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.

10/04/2024

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. ↗

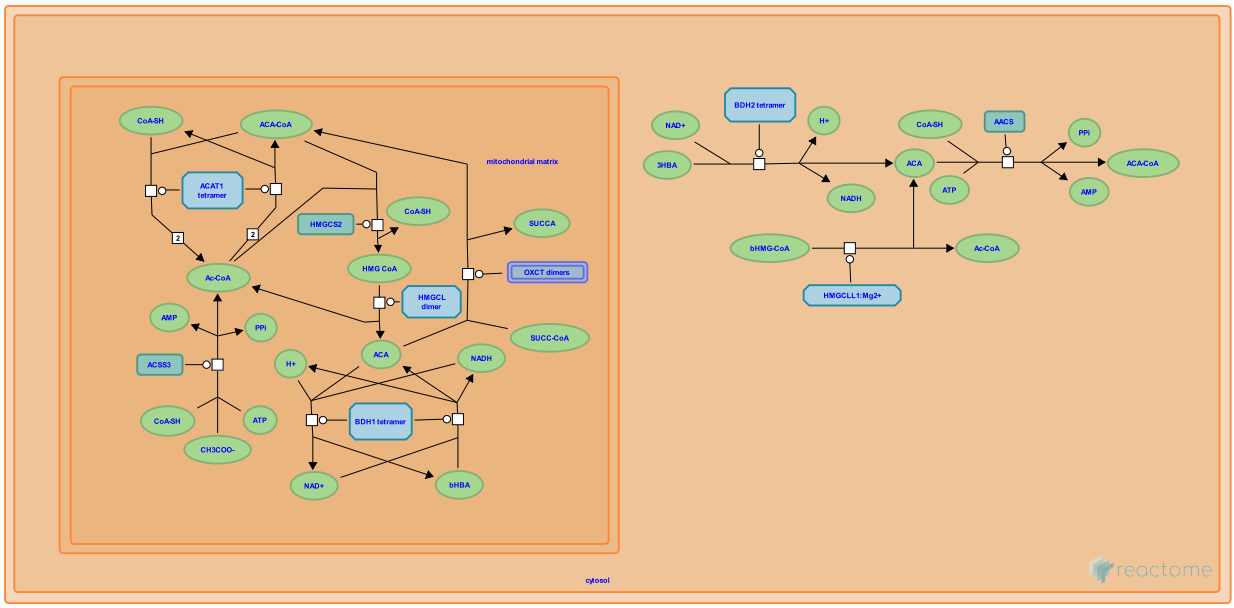
Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

Ketone body metabolism ↗

Stable identifier: R-HSA-74182

Compartments: mitochondrial matrix



Acetoacetate, beta-hydroxybutyrate, and acetone collectively are called ketone bodies. The first two are synthesized from acetyl-CoA, in the mitochondria of liver cells; acetone is formed by spontaneous decarboxylation of acetoacetate. Ketone body synthesis in liver is effectively irreversible because the enzyme that catalyzes the conversion of acetoacetate to acetoacetyl-CoA is not present in liver cells.

Ketone bodies, unlike fatty acids and triglycerides, are water-soluble. They are exported from the liver, and are taken up by other tissues, notably brain and skeletal and cardiac muscle. There, they are broken down to acetyl-CoA which is oxidized via the TCA cycle to yield energy. In a normal person, this pathway of ketone body synthesis and utilization is most active during extended periods of fasting. Under these conditions, mobilization and breakdown of stored fatty acids generates abundant acetyl-CoA acetyl-CoA in liver cells for synthesis of ketone bodies, and their utilization in other tissues minimizes the demand of these tissues for glucose (Sass 2011).

Literature references

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

Editions

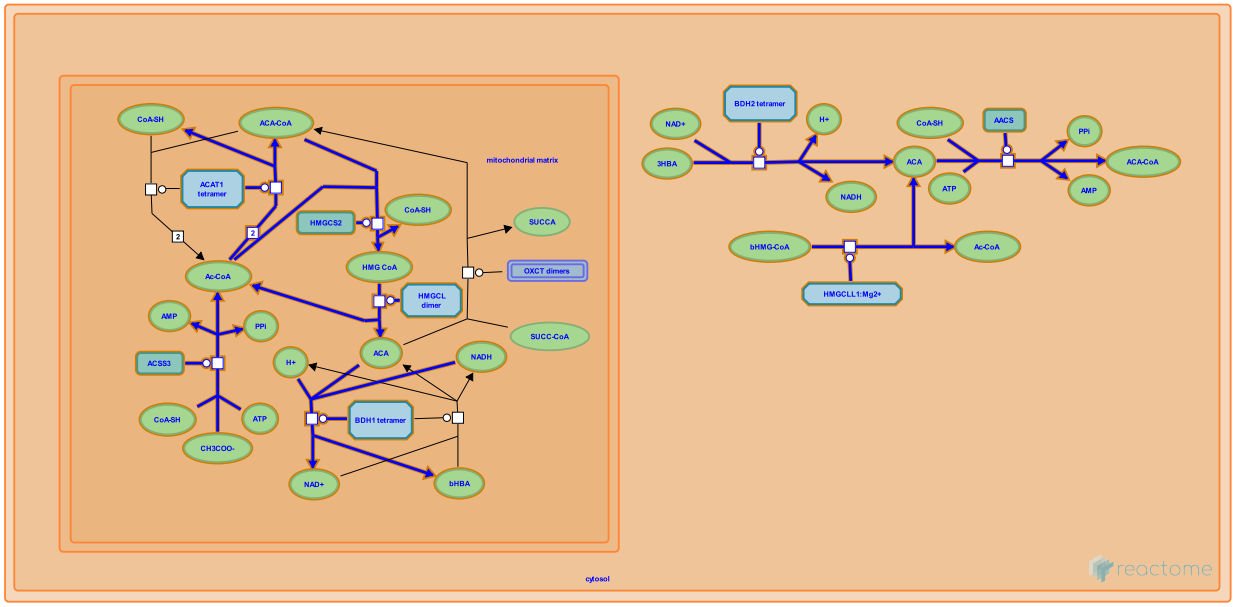
2003-07-16	Edited	Gopinathrao, G.
2003-07-23	Authored	Gopinathrao, G.
2016-06-30	Revised	Jassal, B.

Synthesis of Ketone Bodies ↗

Location: Ketone body metabolism

Stable identifier: R-HSA-77111

Compartments: mitochondrial matrix



In a healthy, well-nourished individual, the production of ketone bodies occurs at a relatively low rate. During periods of normal physiological responses to carbohydrate shortages, the liver increases the production of ketone bodies from acetyl-CoA generated from fatty acid oxidation. This allows heart and skeletal muscle to use ketone bodies as the primary source of energy, thereby preserving the limited glucose supply for use in brain tissue.

In untreated *diabetes mellitus*, a huge buildup of ketone bodies occurs due to an increase in fatty acid oxidation. The production of ketone bodies exceeds the ability of peripheral tissues to oxidize them, and results in lowering the pH of blood. Blood acidification is dangerous, chiefly as it impairs the ability of hemoglobin to bind oxygen.

Ketone body synthesis proceeds via the synthesis of ccetoacetic acid in three steps from acetyl CoA, followed by the reduction of acetoacetic acid to beta-hydroxybutyrate. In the body, these reactions occur in the mitochondria of liver cells (Sass 2011).

Literature references

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

Editions

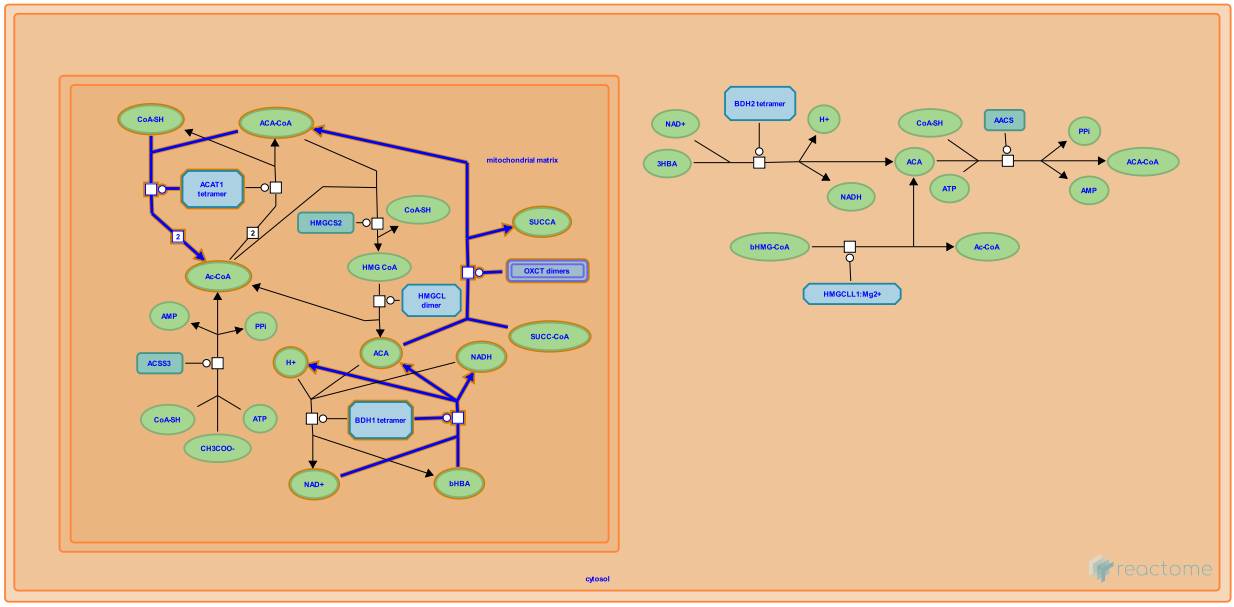
2003-10-19	Authored, Edited	Joshi-Tope, G.

Utilization of Ketone Bodies ↗

Location: Ketone body metabolism

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.

Table of Contents