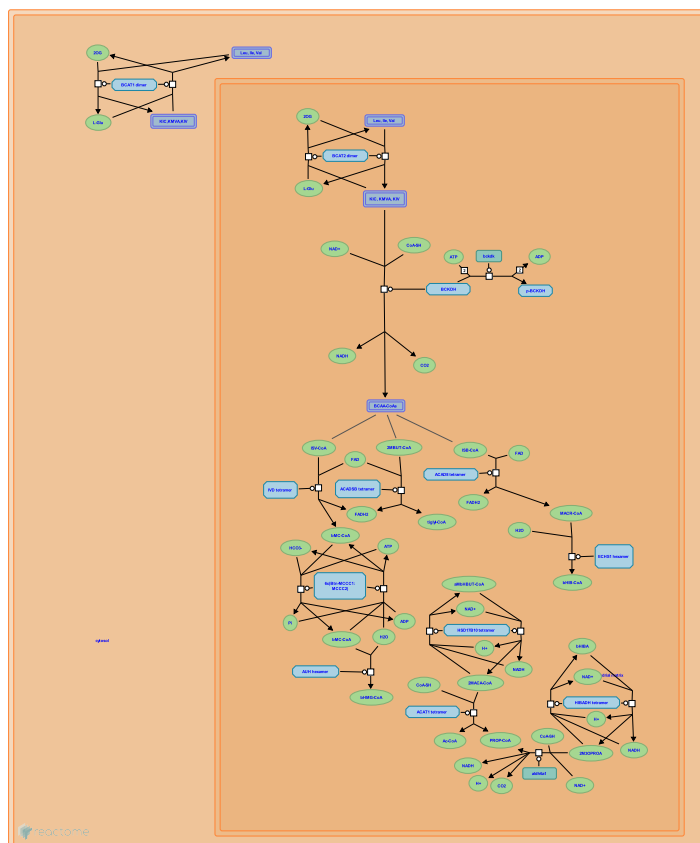# Branched-chain amino acid catabolism

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.

19/05/2024

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. ↗
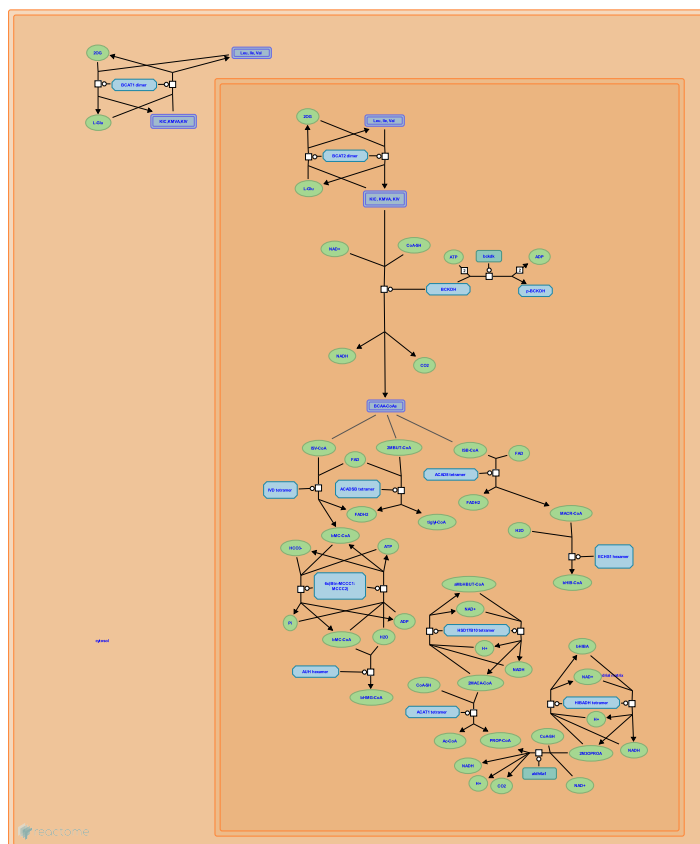
Reactome database release: 88

This document contains 1 pathway and 19 reactions (see Table of Contents)

Branched-chain amino acid catabolism ↗

Stable identifier: R-XTR-70895

Inferred from: Branched-chain amino acid catabolism (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

leu, ile, or val + alpha-ketoglutarate <=> a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate [BCAT1] ↗

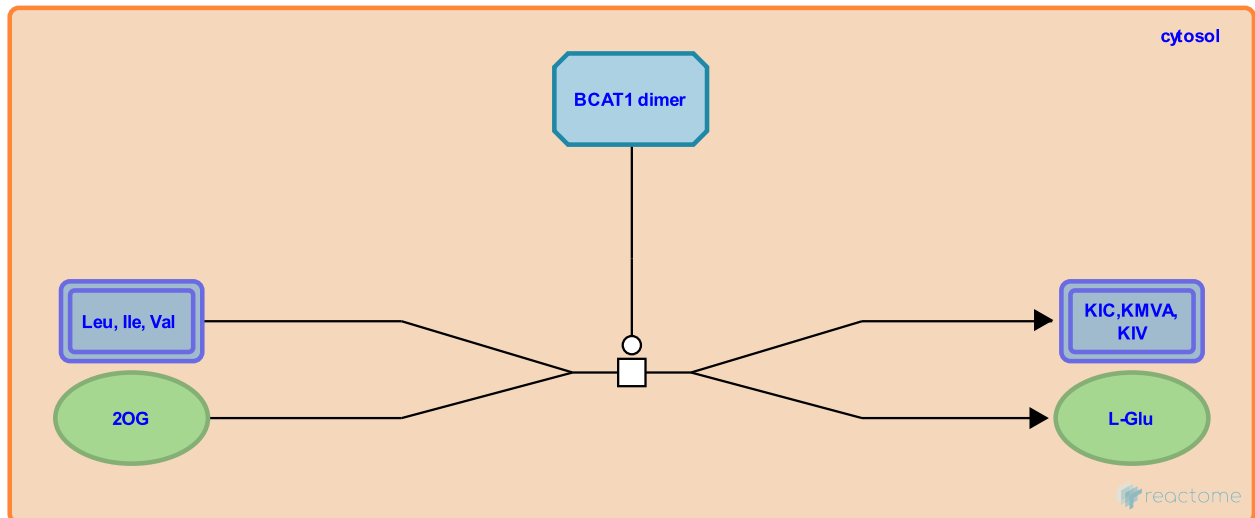**Location:** Branched-chain amino acid catabolism

Stable identifier: R-XTR-70723

Type: transition

Compartments: cytosol

Inferred from: leu, ile, or val + alpha-ketoglutarate <=> a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate [BCAT1] (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate <=> leu, ile, or val + alpha-ketoglutarate [BCAT1] ↗

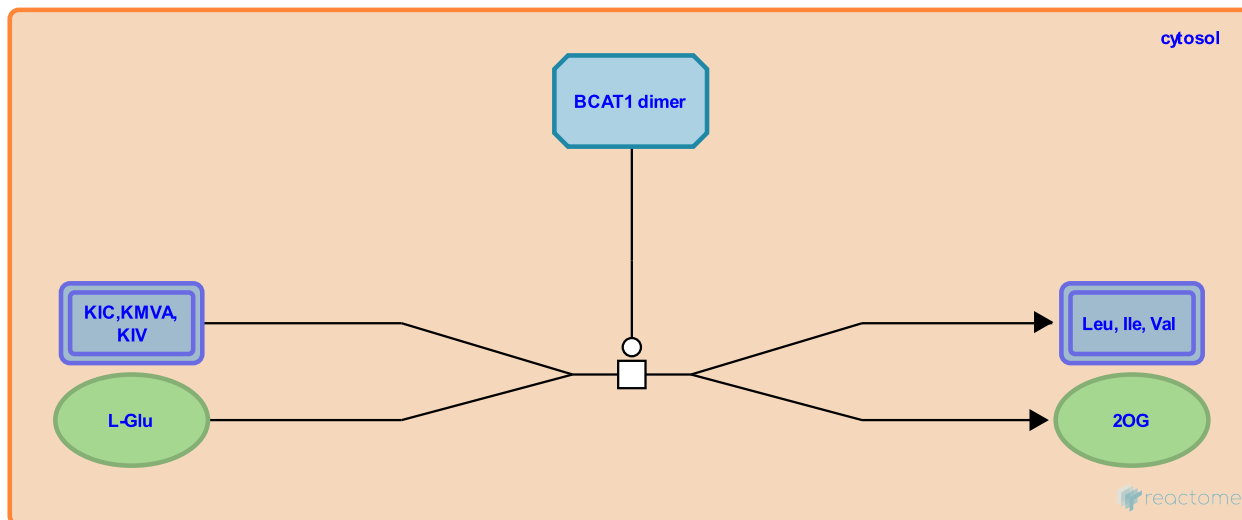**Location:** Branched-chain amino acid catabolism

Stable identifier: R-XTR-508189

Type: transition

Compartments: cytosol

Inferred from: a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate <=> leu, ile, or val + alpha-ketoglutarate [BCAT1] (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

leu, ile, or val + alpha-ketoglutarate <=> a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate [BCAT2] ↗

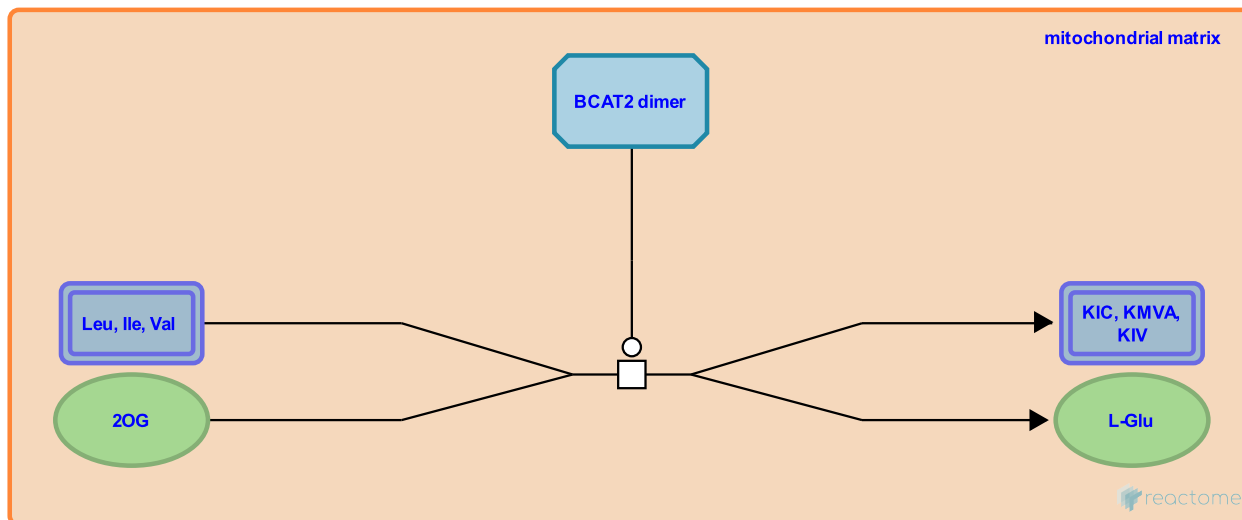**Location:** Branched-chain amino acid catabolism

Stable identifier: R-XTR-70724

Type: transition

Compartments: mitochondrial matrix

Inferred from: leu, ile, or val + alpha-ketoglutarate <=> a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate [BCAT2] (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: BCKDH synthesizes BCAA-CoA from KIC, KMVA, KIV

a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate <=> leu, ile, or val + alpha-ketoglutarate [BCAT2] ↗
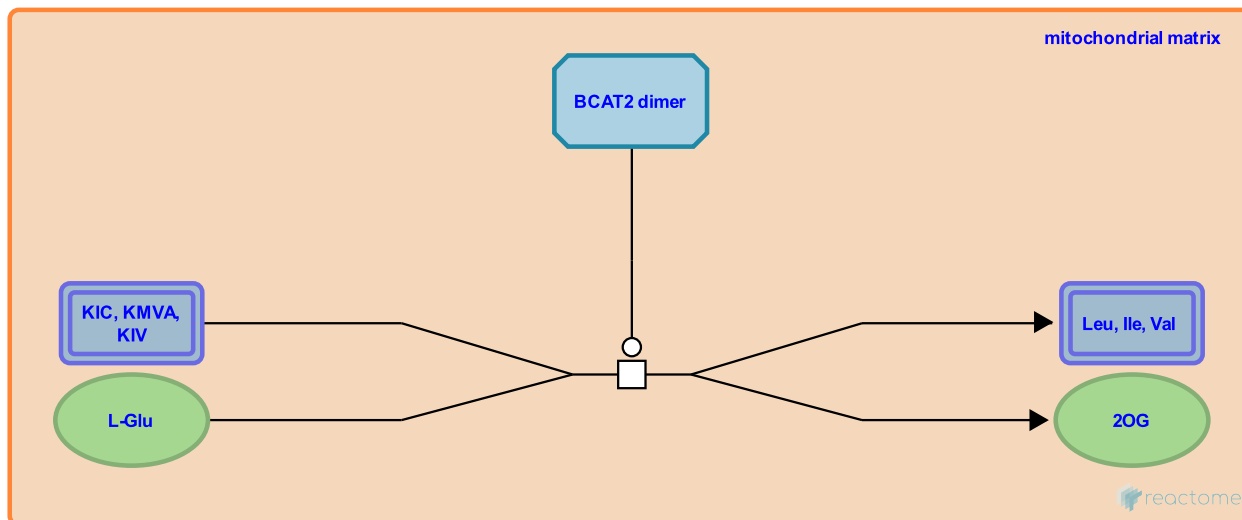
Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-508179

Type: transition

Compartments: mitochondrial matrix

Inferred from: a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate <=> leu, ile, or val + alpha-ketoglutarate [BCAT2] (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

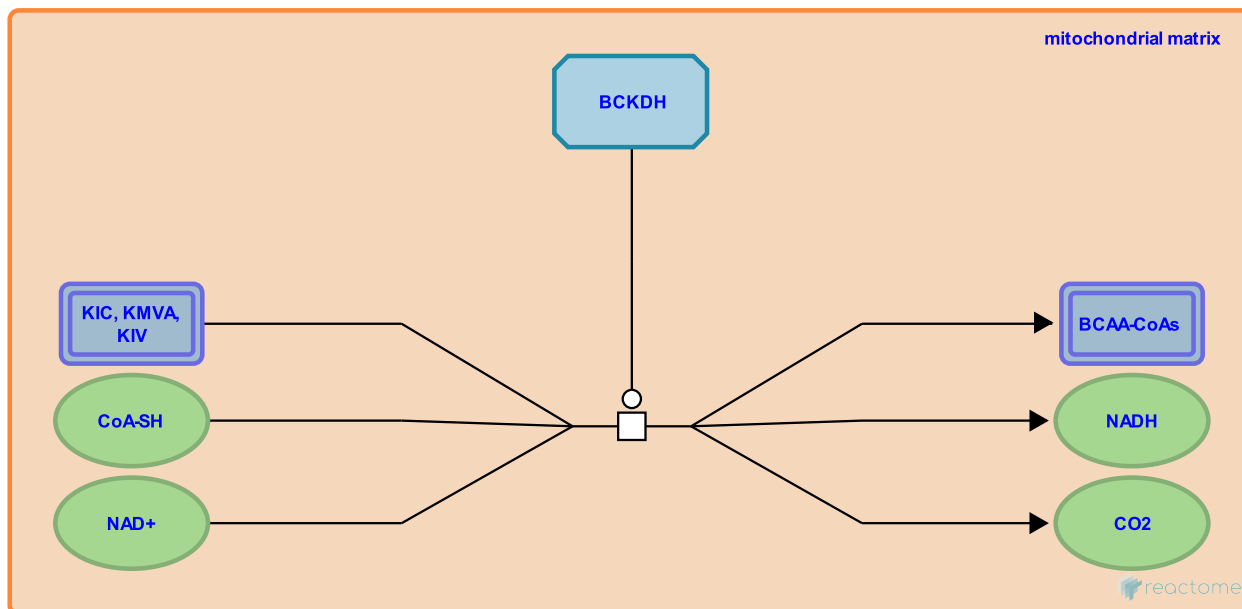# BCKDH synthesizes BCAA-CoA from KIC, KMVA, KIV ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70713

Type: transition

Compartments: mitochondrial matrix

Inferred from: BCKDH synthesizes BCAA-CoA from KIC, KMVA, KIV (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: leu, ile, or val + alpha-ketoglutarate <=> a-ketoisocaproate, a-keto-b-methylvalerate, or a-ketoisovalerate + glutamate [BCAT2]

Followed by: isovaleryl-CoA + FAD => beta-methylcrotonyl-CoA + FADH2, alpha-methylbutyryl-CoA + FAD => tiglyl-CoA + FADH2, isobutyryl-CoA + FAD => methacrylyl-CoA + FADH2

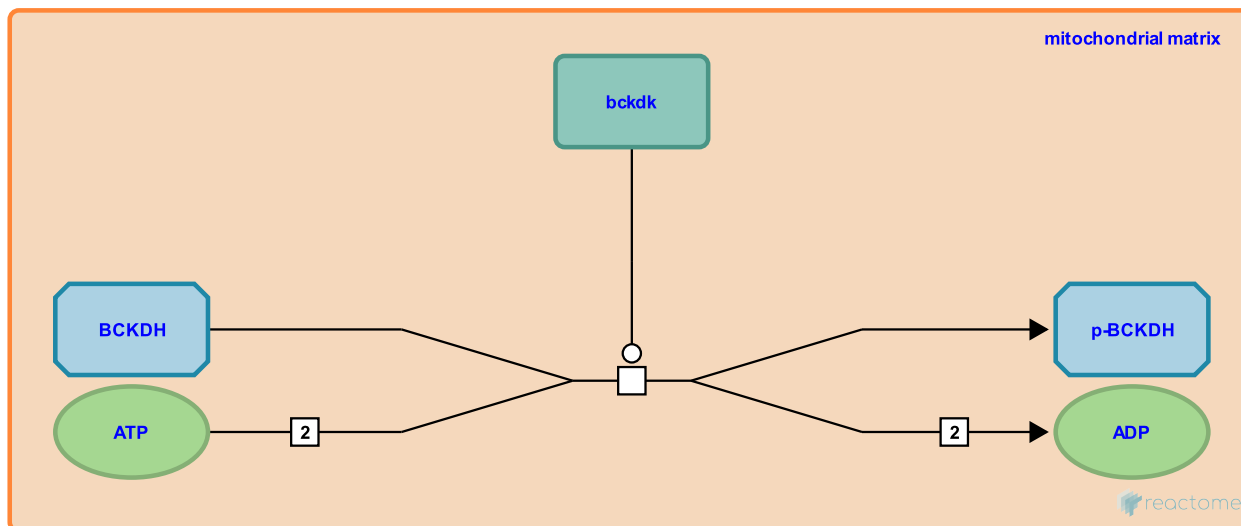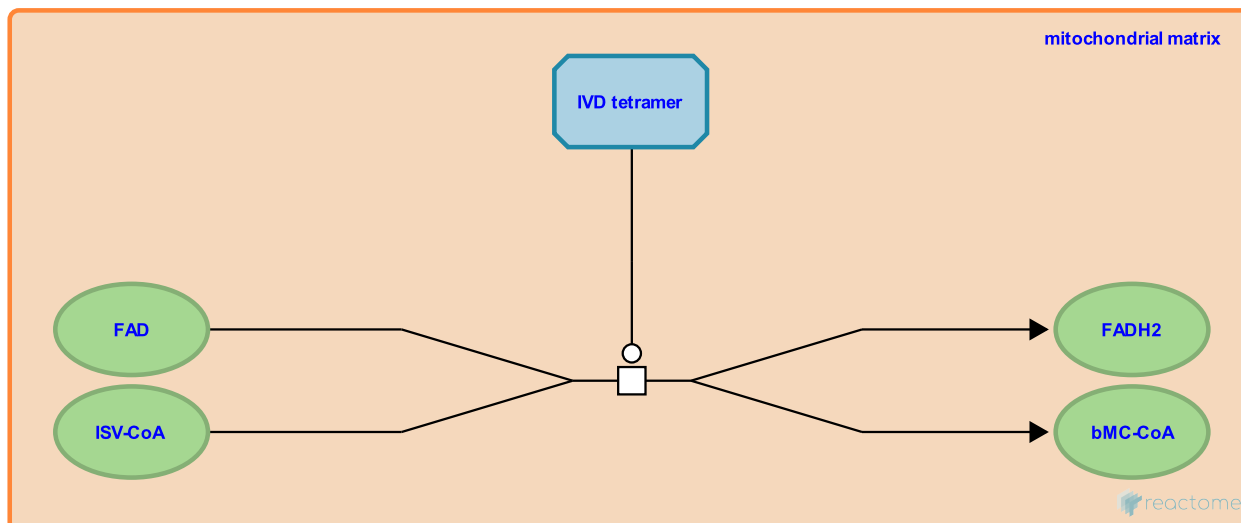# BCKDK phosphorylates BCKDH ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-5693148

Type: transition

Compartments: mitochondrial matrix

Inferred from: BCKDK phosphorylates BCKDH (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

isovaleryl-CoA + FAD => beta-methylcrotonyl-CoA + FADH2 ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70745

Type: transition

Compartments: mitochondrial matrix

Inferred from: isovaleryl-CoA + FAD => beta-methylcrotonyl-CoA + FADH2 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: BCKDH synthesizes BCAA-CoA from KIC, KMVA, KIV

Followed by: beta-methylcrotonyl-CoA + ATP + CO2 <=> beta-methylglutaconyl-CoA + ADP + orthophosphate + H2O [MCCA]

beta-methylcrotonyl-CoA + ATP + CO2 <=> beta-methylglutaconyl-CoA + ADP + ortho-phosphate + H2O [MCCA] ↗
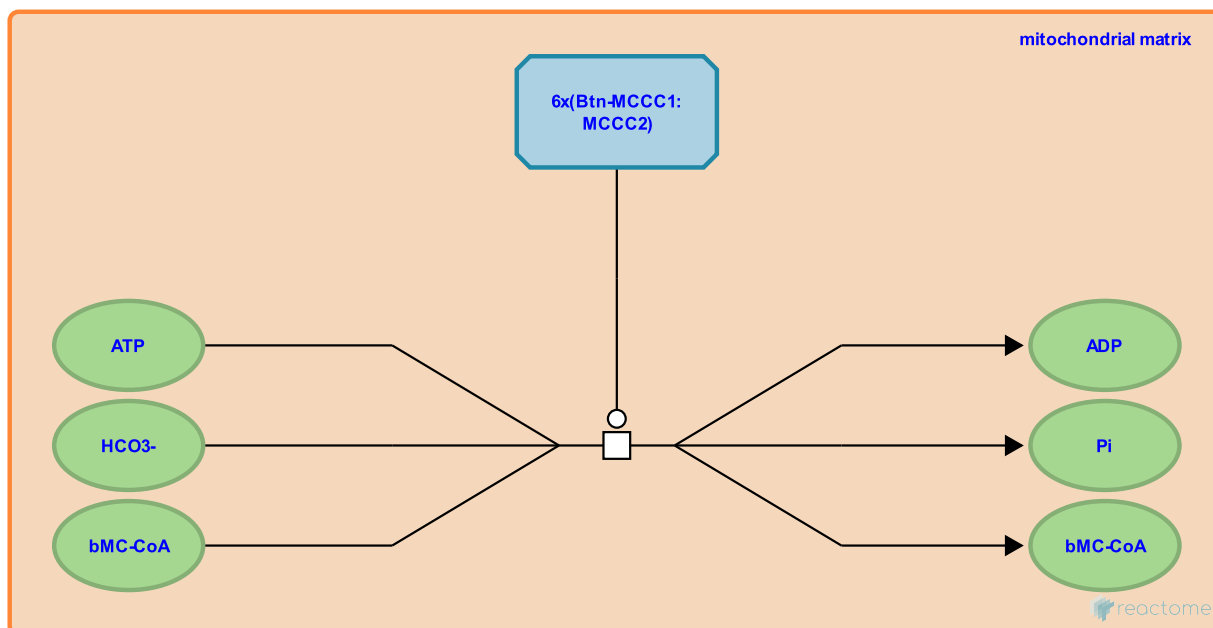
Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70773

Type: transition

Compartments: mitochondrial matrix

Inferred from: beta-methylcrotonyl-CoA + ATP + CO2 <=> beta-methylglutaconyl-CoA + ADP + ortho-phosphate + H2O [MCCA] (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: isovaleryl-CoA + FAD => beta-methylcrotonyl-CoA + FADH2

Followed by: beta-methylglutaconyl-CoA + H2O <=> beta-hydroxy-beta-methylglutaryl-CoA

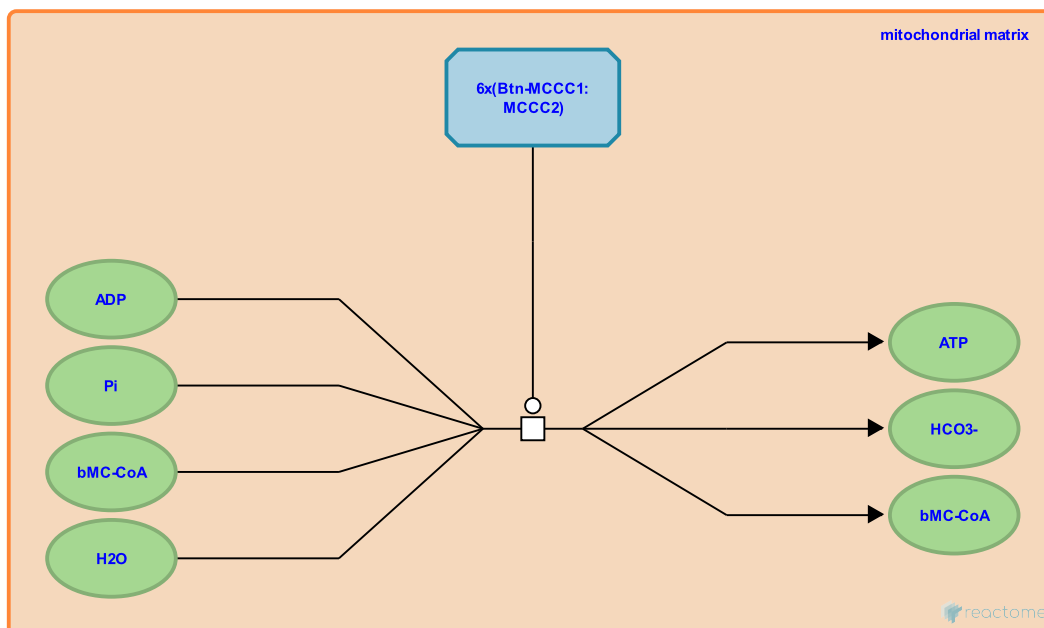# beta-methylglutaconyl-CoA + ADP + orthophosphate + H2O <=> beta-methylcrotonyl-CoA + ATP + CO2 [MCCA] ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-508308

Type: transition

Compartments: mitochondrial matrix

Inferred from: beta-methylglutaconyl-CoA + ADP + orthophosphate + H2O <=> beta-methylcrotonyl-CoA + ATP + CO2 [MCCA] (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

beta-methylglutaconyl-CoA + H2O <=> beta-hydroxy-beta-methylglutaryl-CoA ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70785

Type: transition

Compartments: mitochondrial matrix

Inferred from: beta-methylglutaconyl-CoA + H2O <=> beta-hydroxy-beta-methylglutaryl-CoA (Homo sapiens)
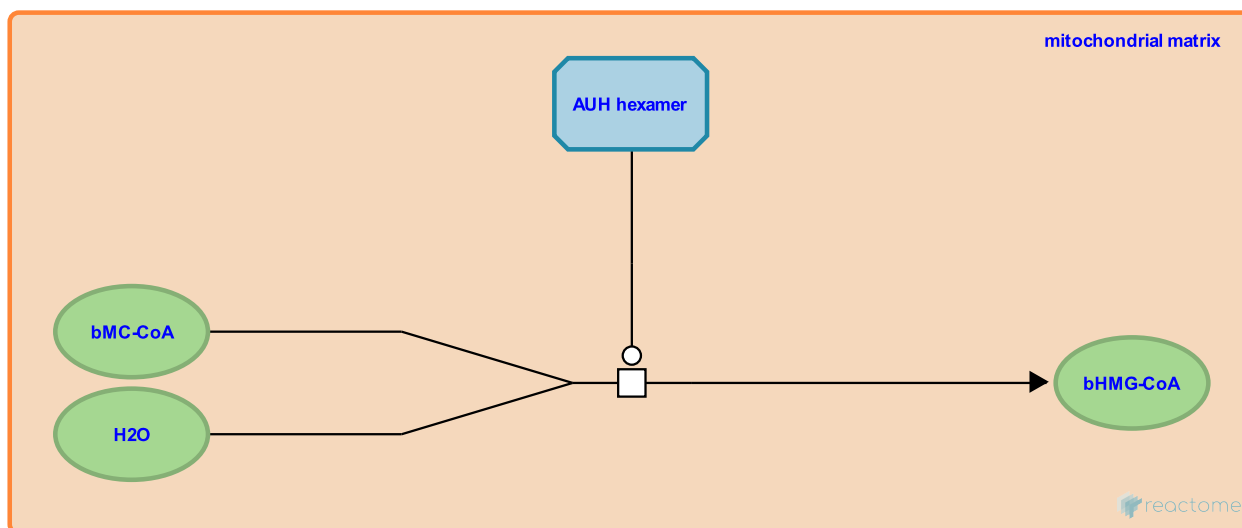
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: beta-methylcrotonyl-CoA + ATP + CO2 <=> beta-methylglutaconyl-CoA + ADP + orthophosphate + H2O [MCCA]
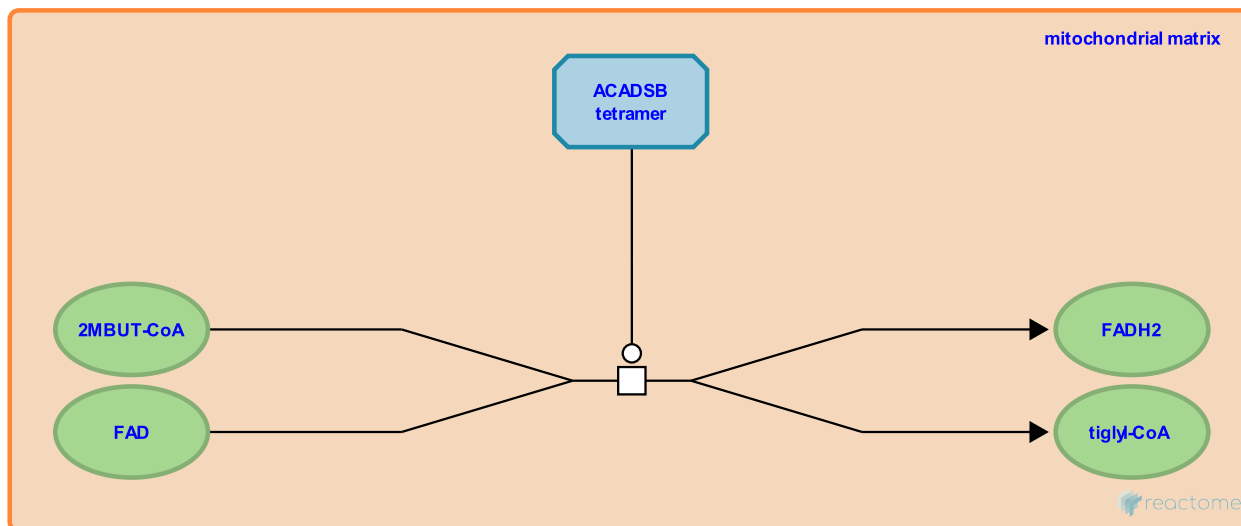
alpha-methylbutyryl-CoA + FAD => tiglyl-CoA + FADH2 ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70800

Type: transition

Compartments: mitochondrial matrix

Inferred from: alpha-methylbutyryl-CoA + FAD => tiglyl-CoA + FADH2 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: BCKDH synthesizes BCAA-CoA from KIC, KMVA, KIV

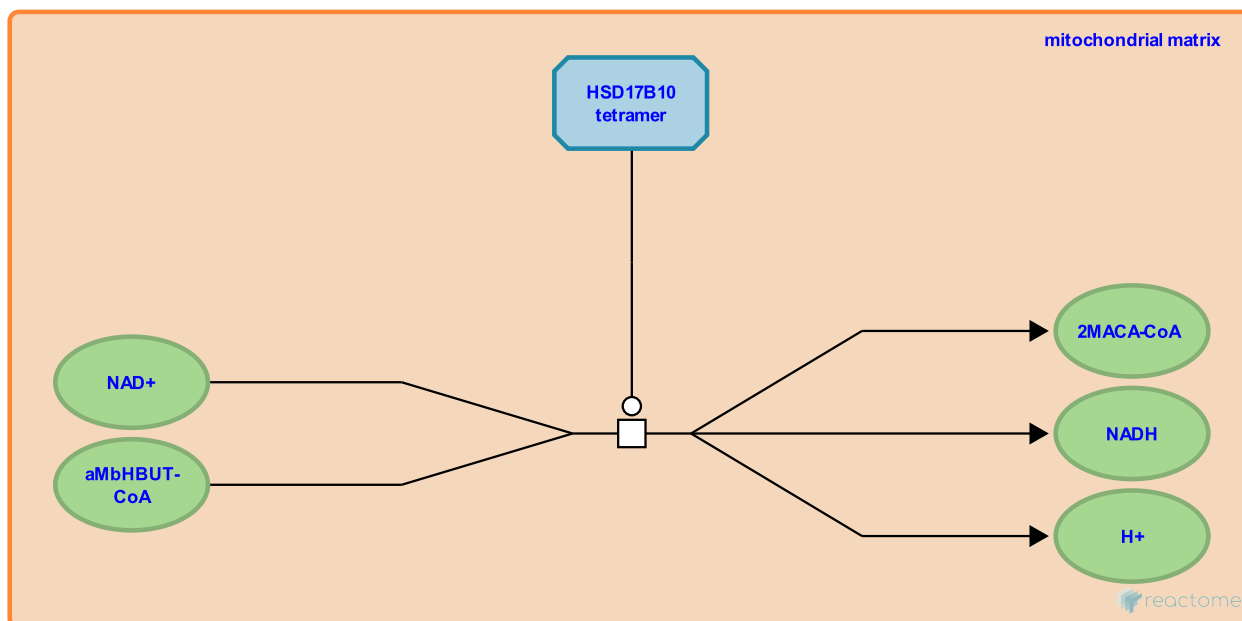## alpha-methyl-beta-hydroxybutyryl-CoA + NAD+ <=> alpha-methylacetoacetyl-CoA + NADH + H+ ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70837

Type: transition

Compartments: mitochondrial matrix

Inferred from: alpha-methyl-beta-hydroxybutyryl-CoA + NAD+ <=> alpha-methylacetoacetyl-CoA + NADH + H+ (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: alpha-methyl-acetoacetyl-CoA + CoA => propionyl-CoA + acetyl-CoA

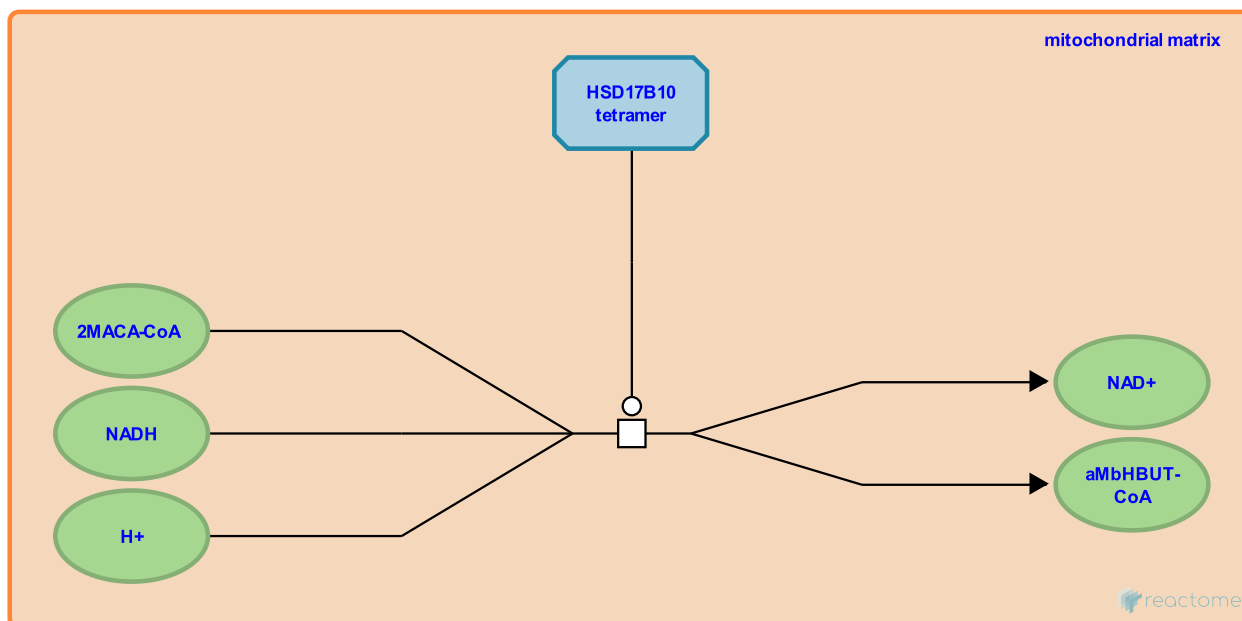## alpha-methylacetoacetyl-CoA + NADH + H+ <=> alpha-methyl-beta-hydroxybutyryl-CoA + NAD+ ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-508369

Type: transition

Compartments: mitochondrial matrix

Inferred from: alpha-methylacetoacetyl-CoA + NADH + H+ <=> alpha-methyl-beta-hydroxybutyryl-CoA + NAD+ (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

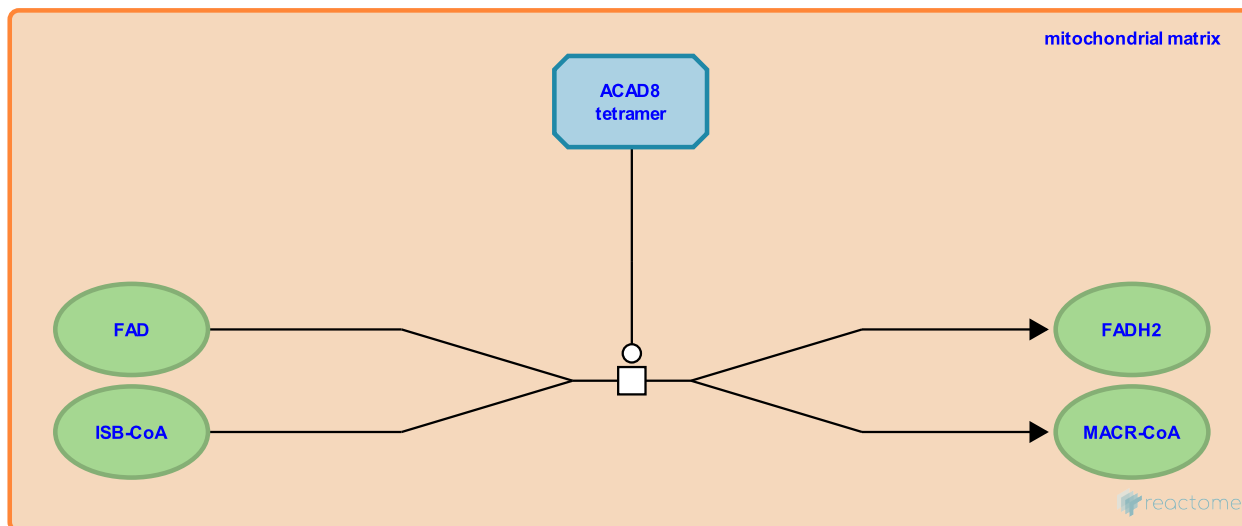# alpha-methyl-acetoacetyl-CoA + CoA => propionyl-CoA + acetyl-CoA ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70844

Type: transition

Compartments: mitochondrial matrix

Inferred from: alpha-methyl-acetoacetyl-CoA + CoA => propionyl-CoA + acetyl-CoA (Homo sapiens)
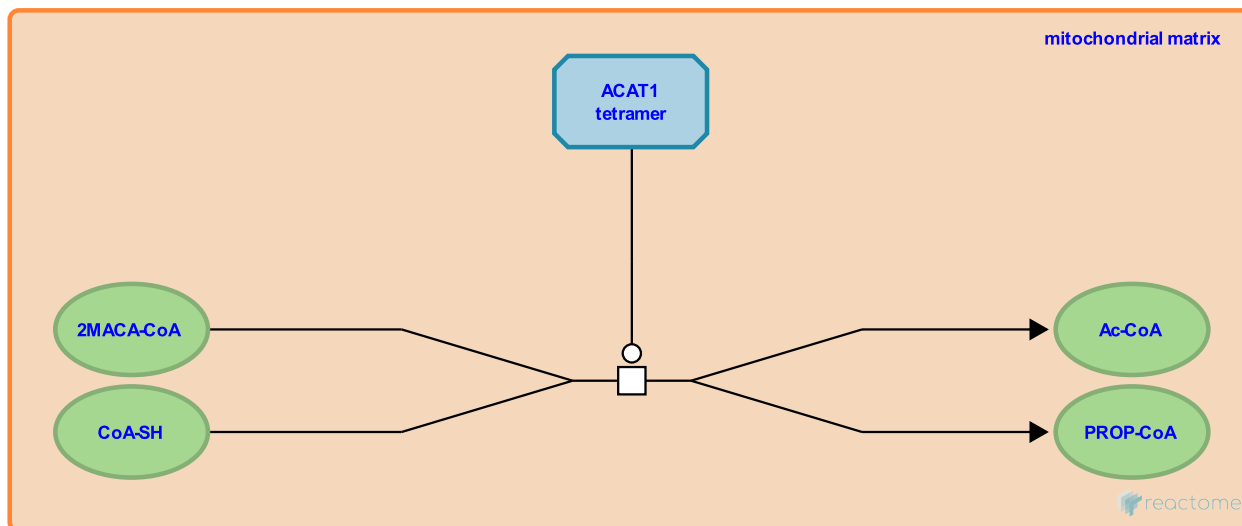
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: alpha-methyl-beta-hydroxybutyryl-CoA + NAD+ <=> alpha-methylacetoacetyl-CoA + NADH + H+

isobutyryl-CoA + FAD => methacrylyl-CoA + FADH2 ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70859

Type: transition

Compartments: mitochondrial matrix

Inferred from: isobutyryl-CoA + FAD => methacrylyl-CoA + FADH2 (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: BCKDH synthesizes BCAA-CoA from KIC, KMVA, KIV

Followed by: ECHS1 hydrates methacrylyl-CoA

## ECHS1 hydrates methacrylyl-CoA ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70870

Type: transition

Compartments: mitochondrial matrix

Inferred from: ECHS1 hydrates methacrylyl-CoA (Homo sapiens)
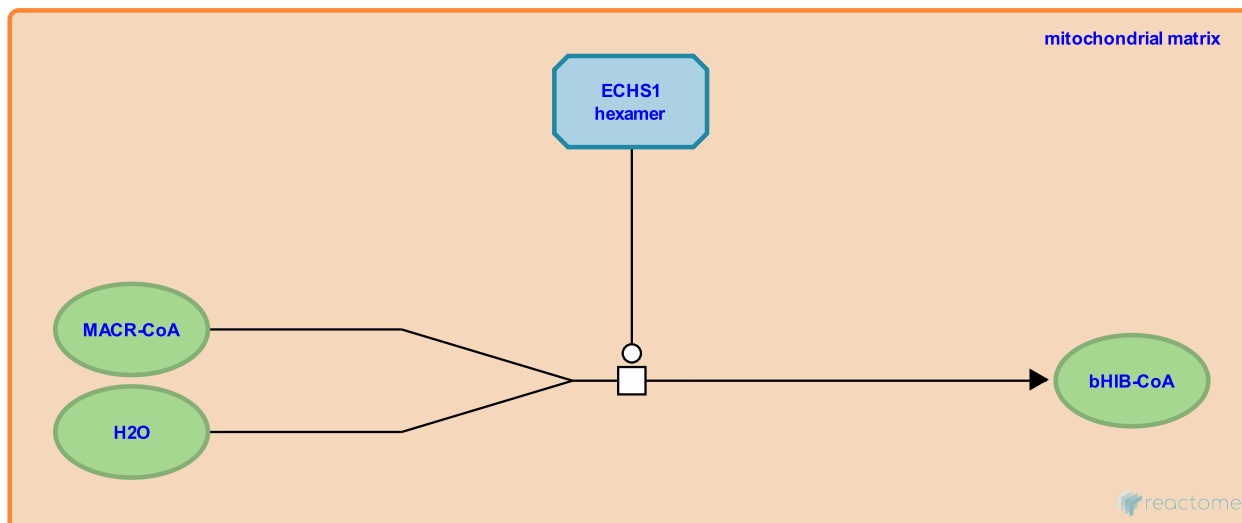
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: isobutyryl-CoA + FAD => methacrylyl-CoA + FADH2

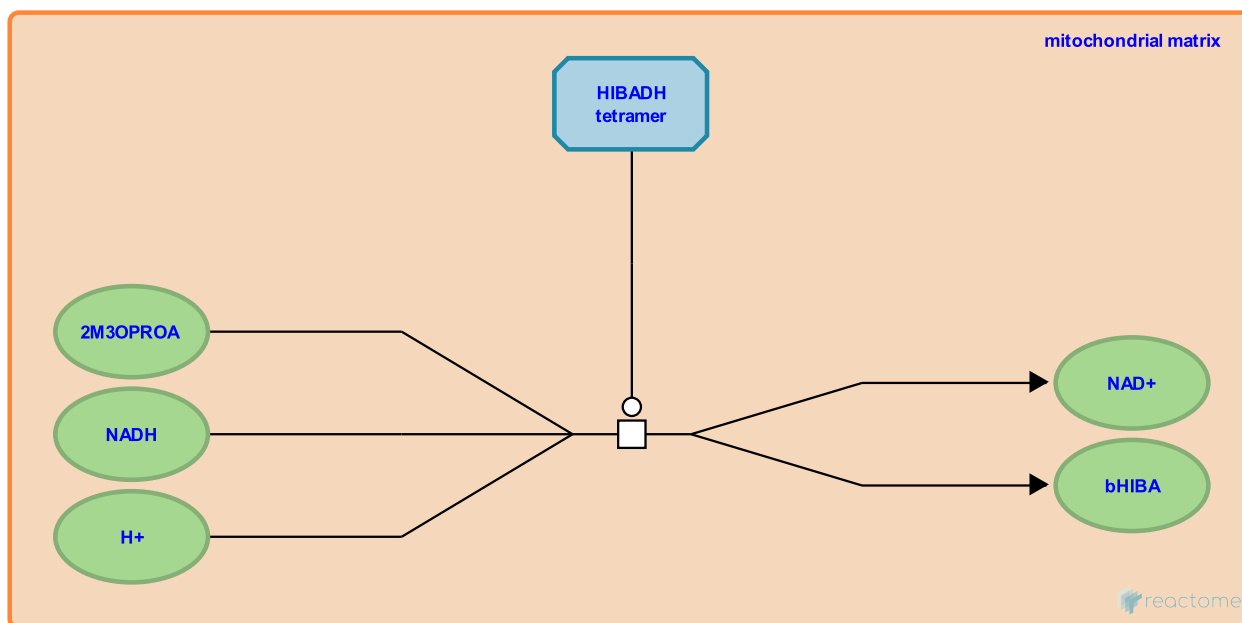**beta-hydroxyisobutyrate + NAD+ <=> methylmalonyl semialdehyde + NADH + H+** ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70885

Type: transition

Compartments: mitochondrial matrix

Inferred from: beta-hydroxyisobutyrate + NAD+ <=> methylmalonyl semialdehyde + NADH + H+ (Homo sapiens)
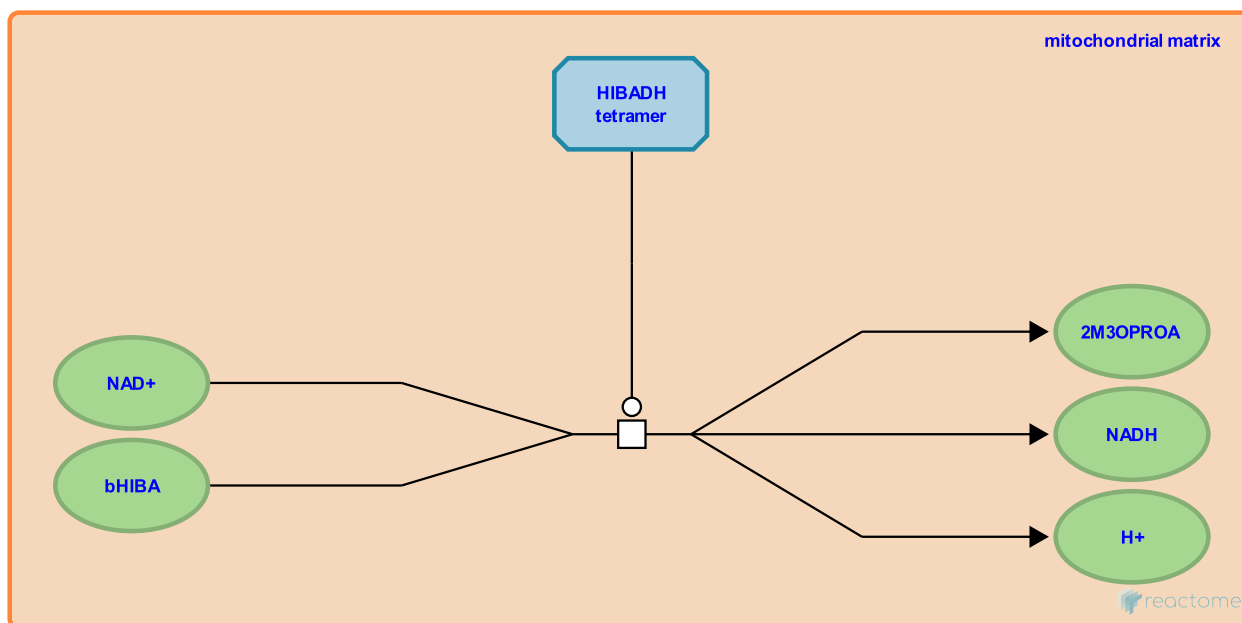
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: methylmalonate semialdehyde + NAD+ + CoA => propionyl-CoA + CO2 + NADH + H+

methylmalonyl semialdehyde + NADH + H+ <=> beta-hydroxyisobutyrate + NAD+ ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-508473

Type: transition

Compartments: mitochondrial matrix

Inferred from: methylmalonyl semialdehyde + NADH + H+ <=> beta-hydroxyisobutyrate + NAD+ (Homo sapiens)

This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

methylmalonate semialdehyde + NAD+ + CoA => propionyl-CoA + CO2 + NADH + H+ ↗

Location: Branched-chain amino acid catabolism

Stable identifier: R-XTR-70893

Type: transition

Compartments: mitochondrial matrix

Inferred from: methylmalonate semialdehyde + NAD+ + CoA => propionyl-CoA + CO2 + NADH + H+ (Homo sapiens)
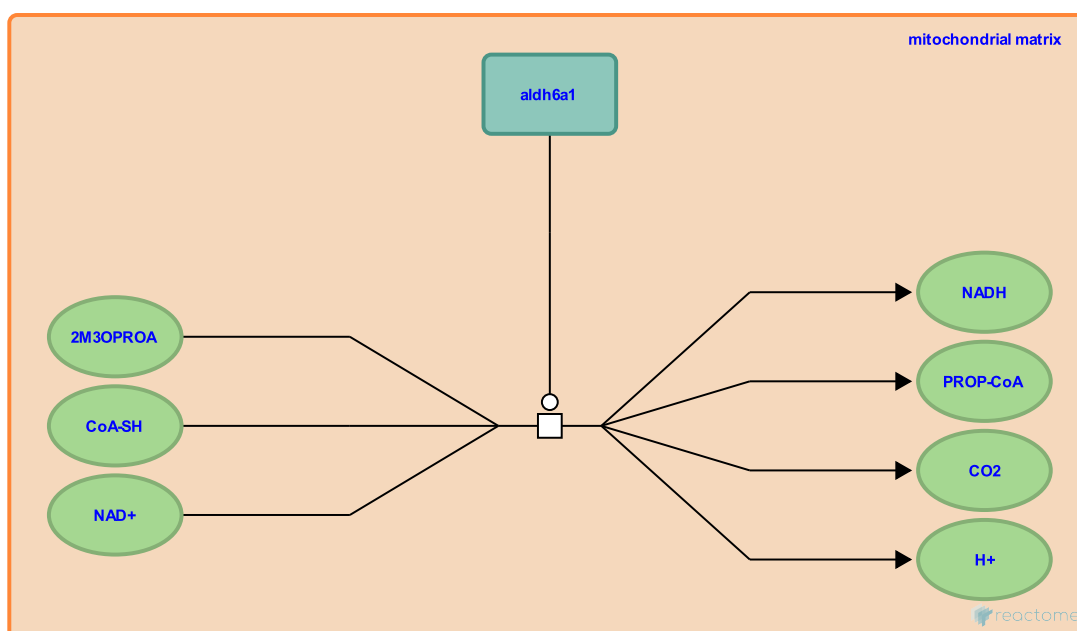
This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: beta-hydroxyisobutyrate + NAD+ <=> methylmalonyl semialdehyde + NADH + H+

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