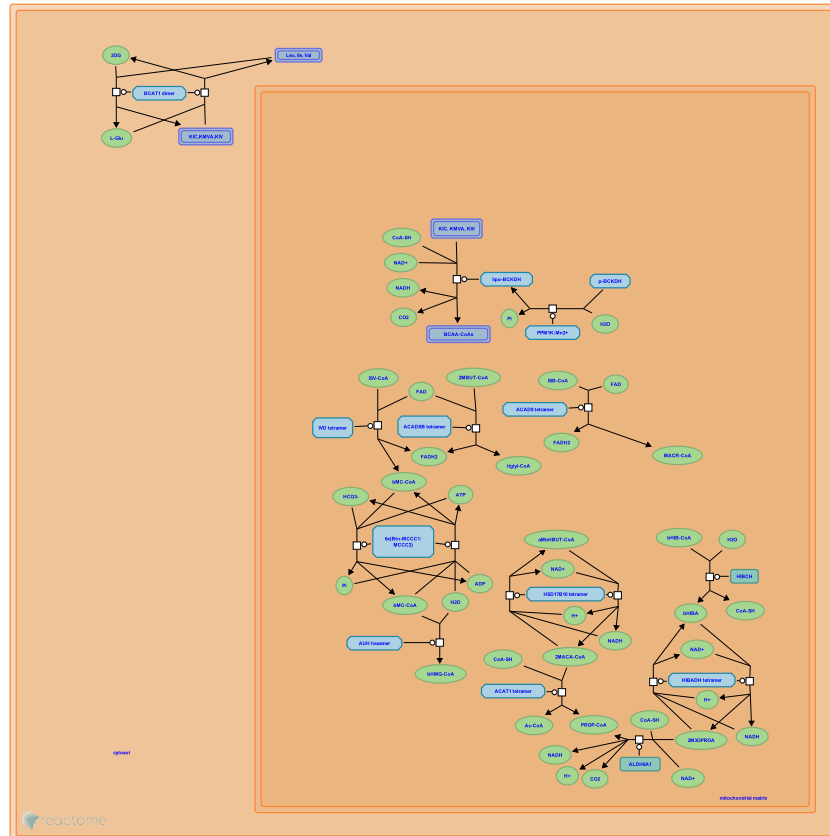


# Branched-chain amino acid catabolism



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

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

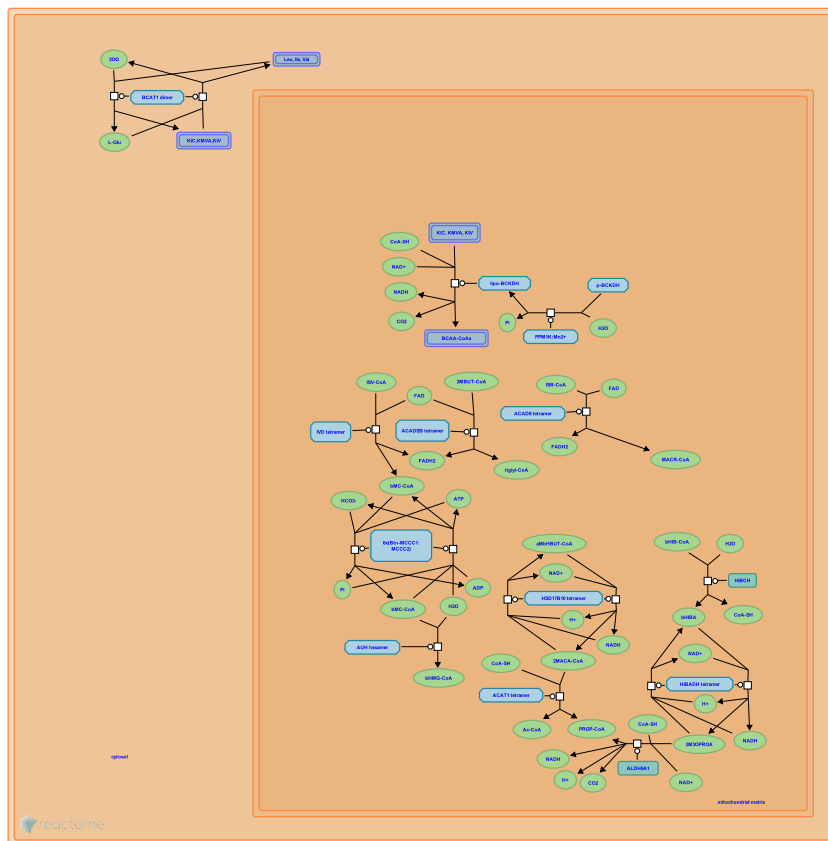
Reactome database release: 74

This document contains 1 pathway and 17 reactions ([see Table of Contents](#))

## Branched-chain amino acid catabolism ↗

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) 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] ↗**

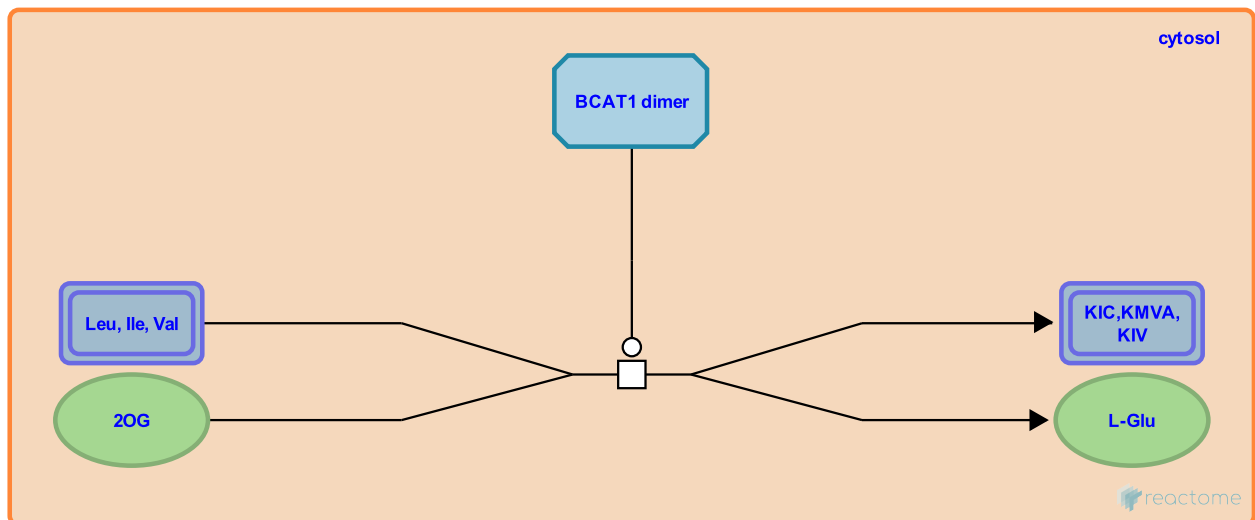
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) 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] ↗**

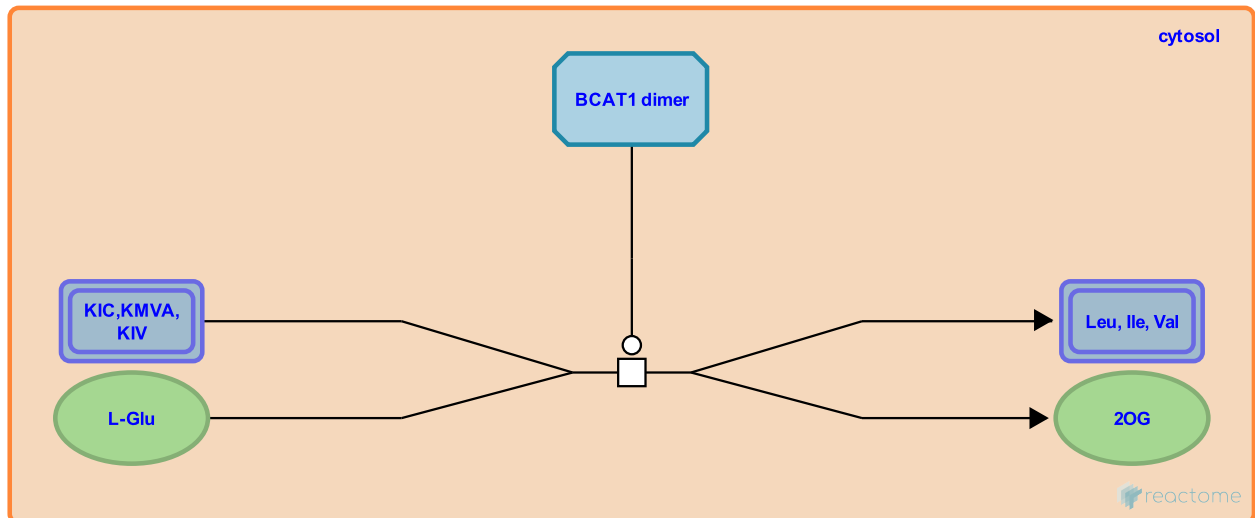
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

## BCKDH transfers CoA group from CoA-SH to BCAAs ↗

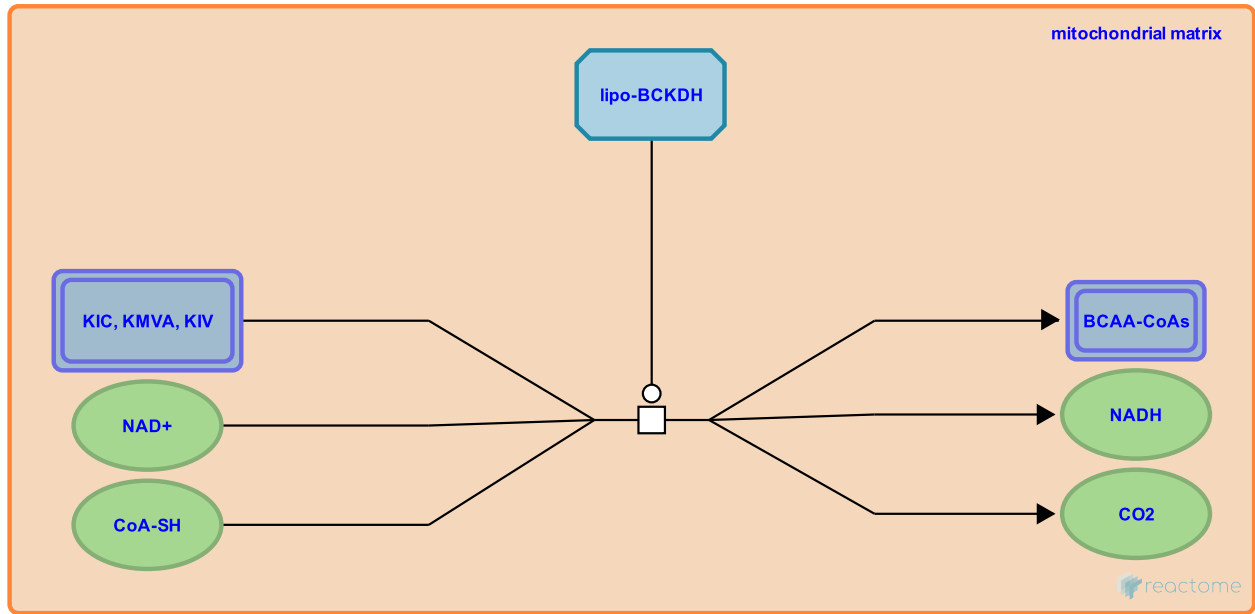
**Location:** Branched-chain amino acid catabolism

**Stable identifier:** R-GGA-70713

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** BCKDH transfers CoA group from CoA-SH to BCAAs (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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Followed by:** [isovaleryl-CoA + FAD => beta-methylcrotonyl-CoA + FADH2](#), [isobutyryl-CoA + FAD => methacrylyl-CoA + FADH2](#), [alpha-methylbutyryl-CoA + FAD => tiglyl-CoA + FADH2](#)

## PPM1K dephosphorylates p-BCKDH ↗

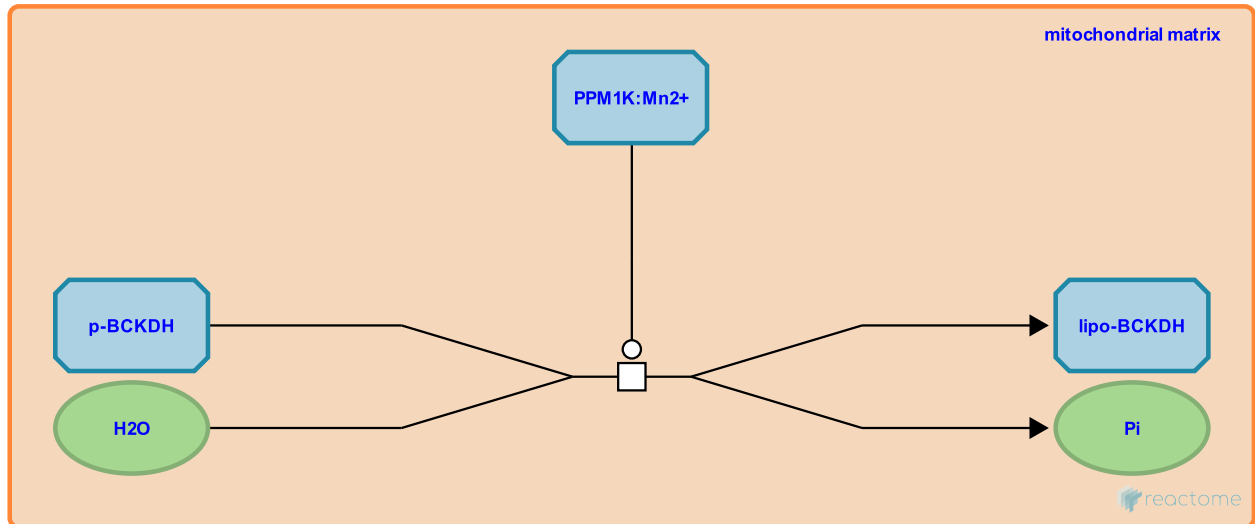
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-5693153

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** [PPM1K dephosphorylates p-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

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

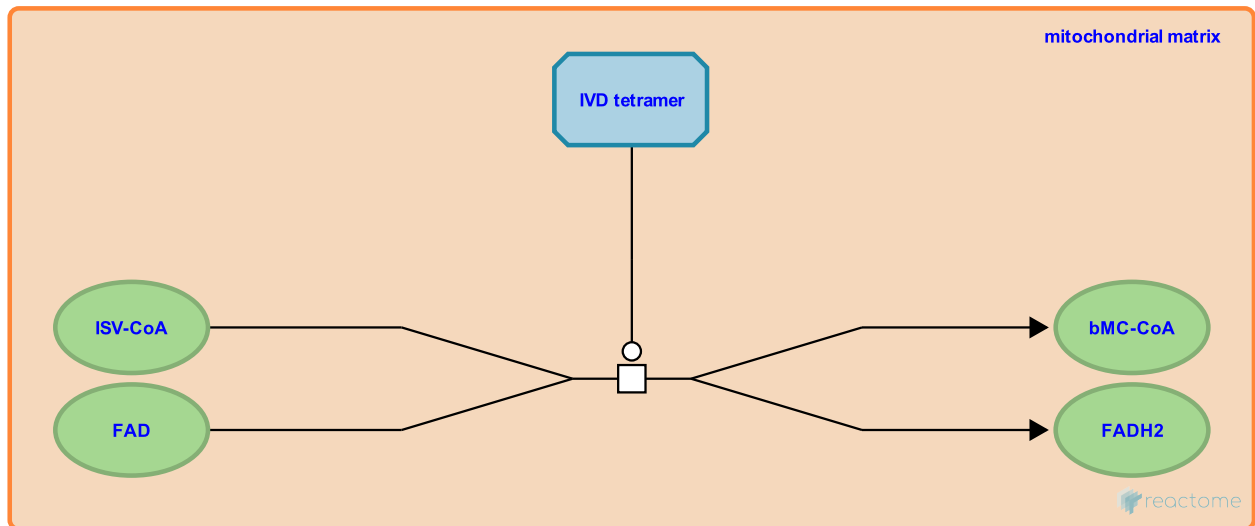
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [BCKDH transfers CoA group from CoA-SH to BCAAs](#)

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



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

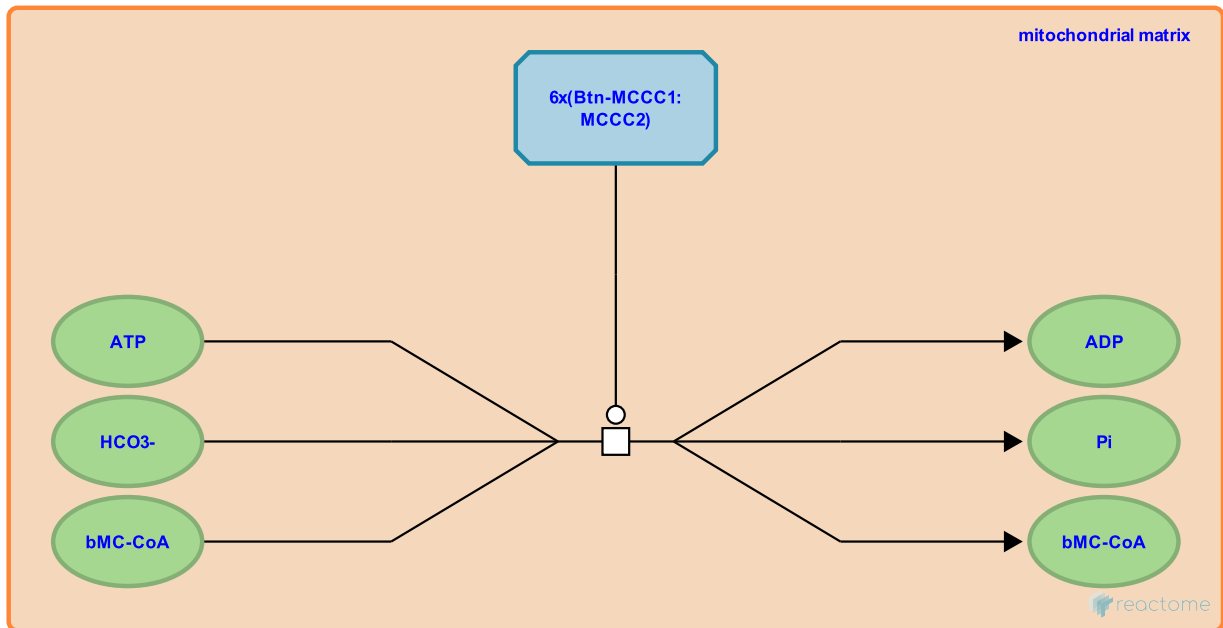
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-70773

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** [beta-methylcrotonyl-CoA + ATP + CO2 <=> beta-methylglutaconyl-CoA + ADP + orthophosphate + 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.](/electronic_inference_compara.html) 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] ↗**

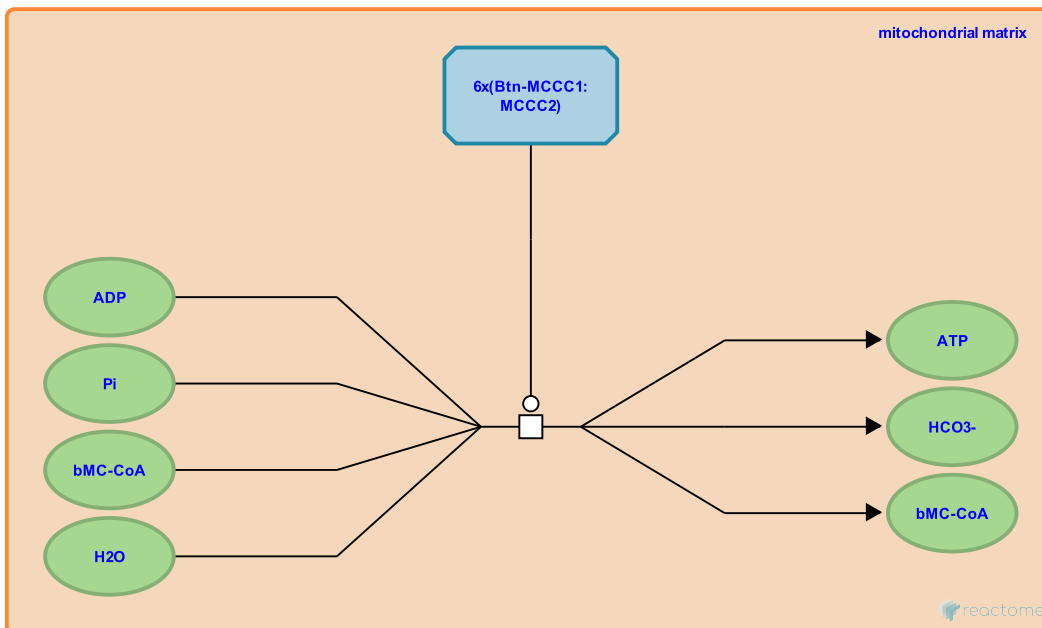
**Location:** Branched-chain amino acid catabolism

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

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

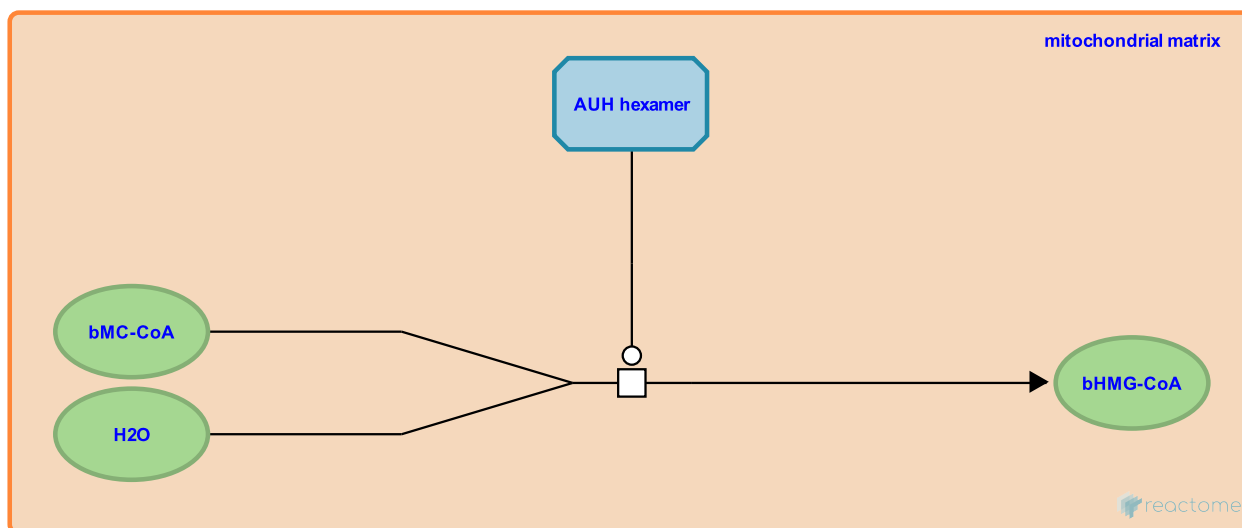
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) 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 ↗**

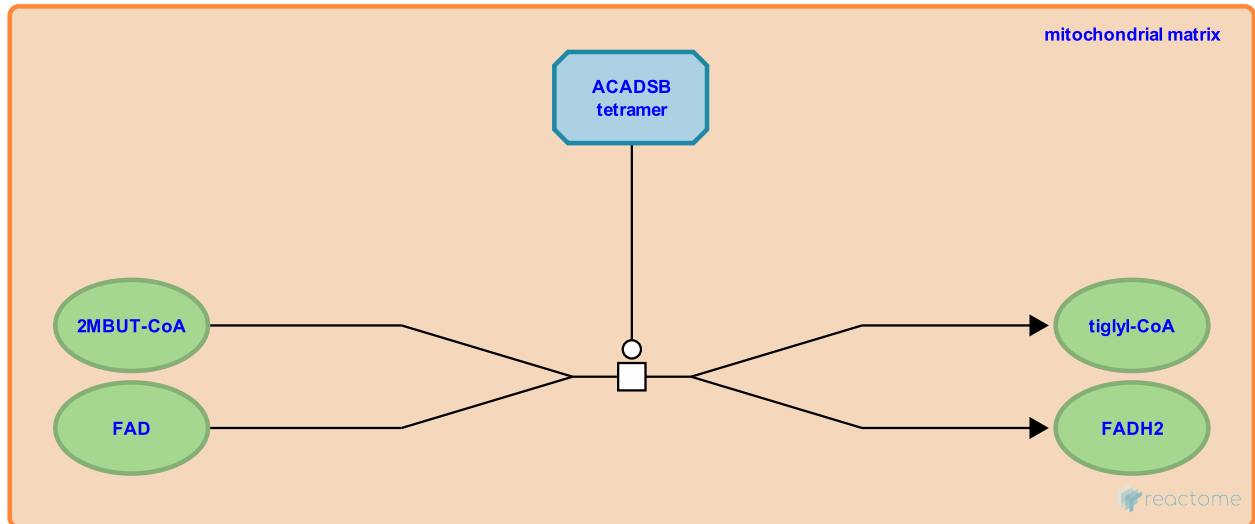
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [BCKDH transfers CoA group from CoA-SH to BCAAs](#)

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

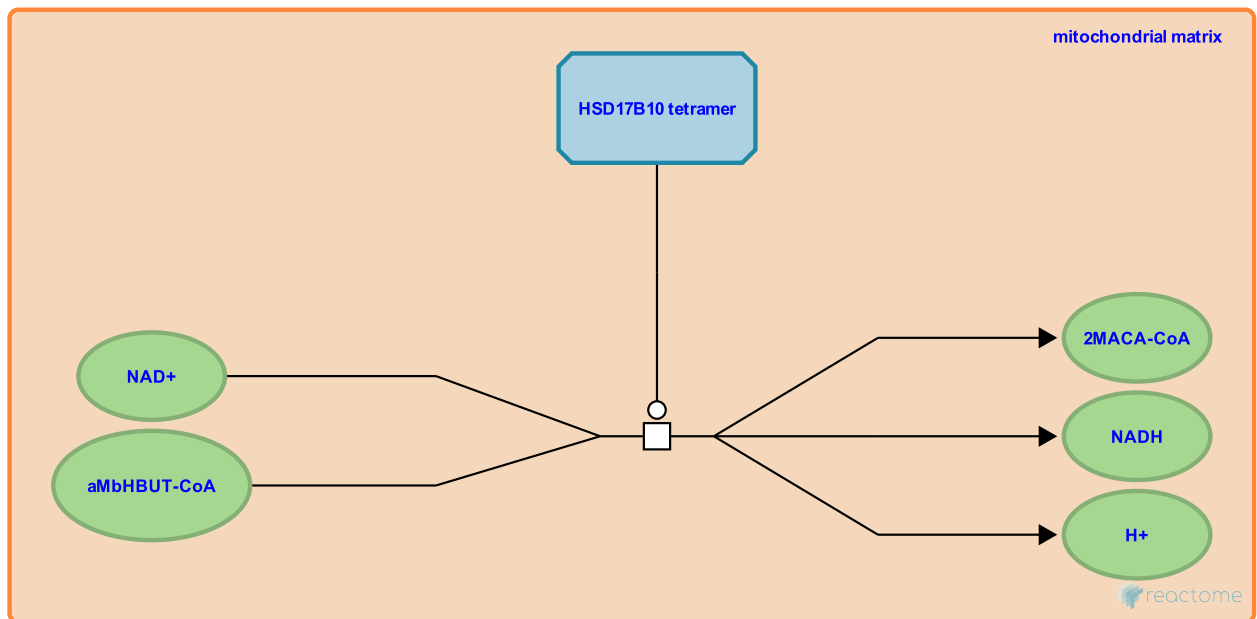
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) 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+ ↗**

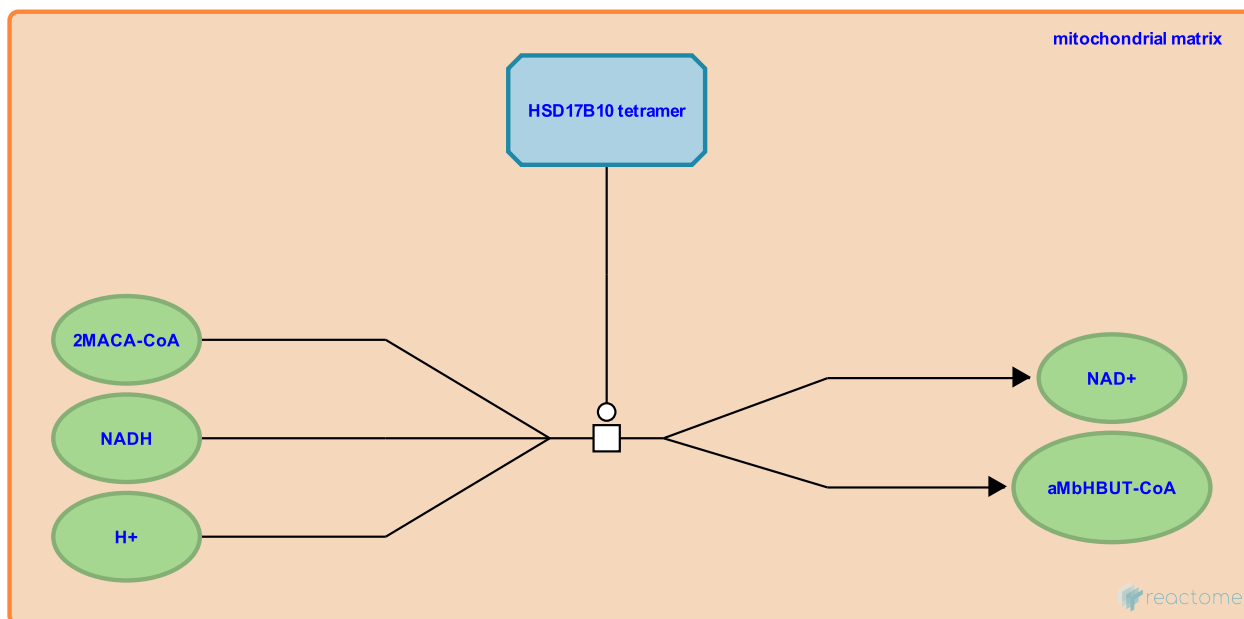
**Location:** Branched-chain amino acid catabolism

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

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

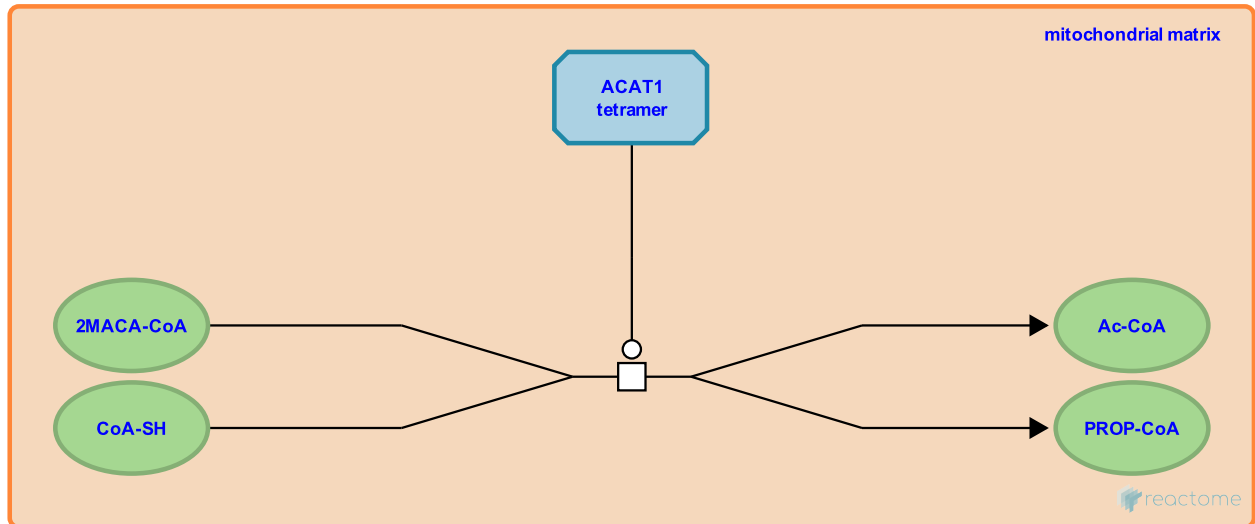
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) 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 ↗**

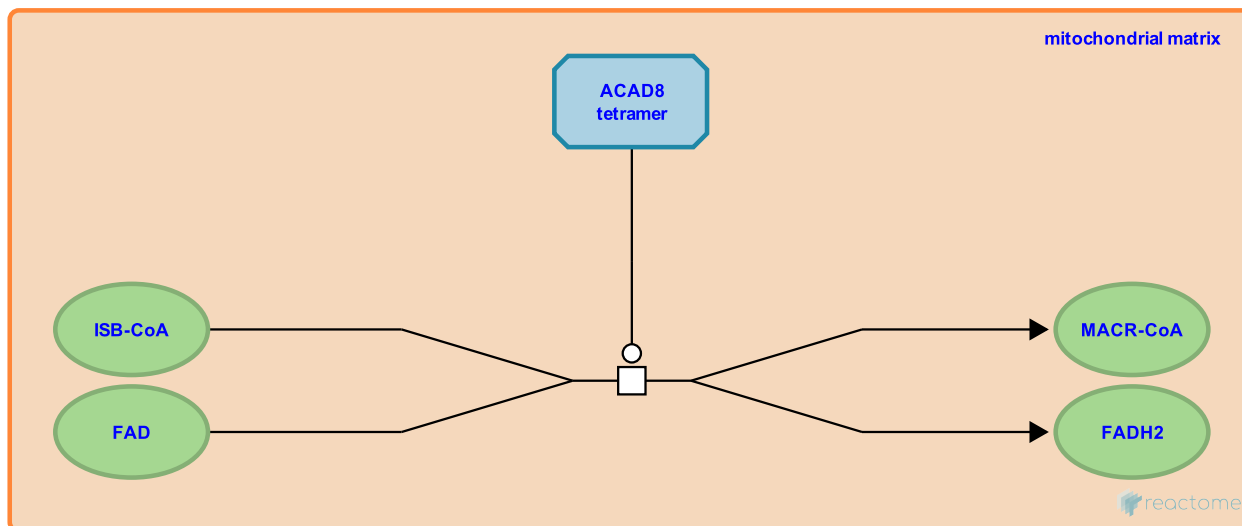
**Location:** Branched-chain amino acid catabolism

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** BCKDH transfers CoA group from CoA-SH to BCAAs



**beta-hydroxyisobutyryl-CoA + H2O => beta-hydroxyisobutyrate + CoA ↗**

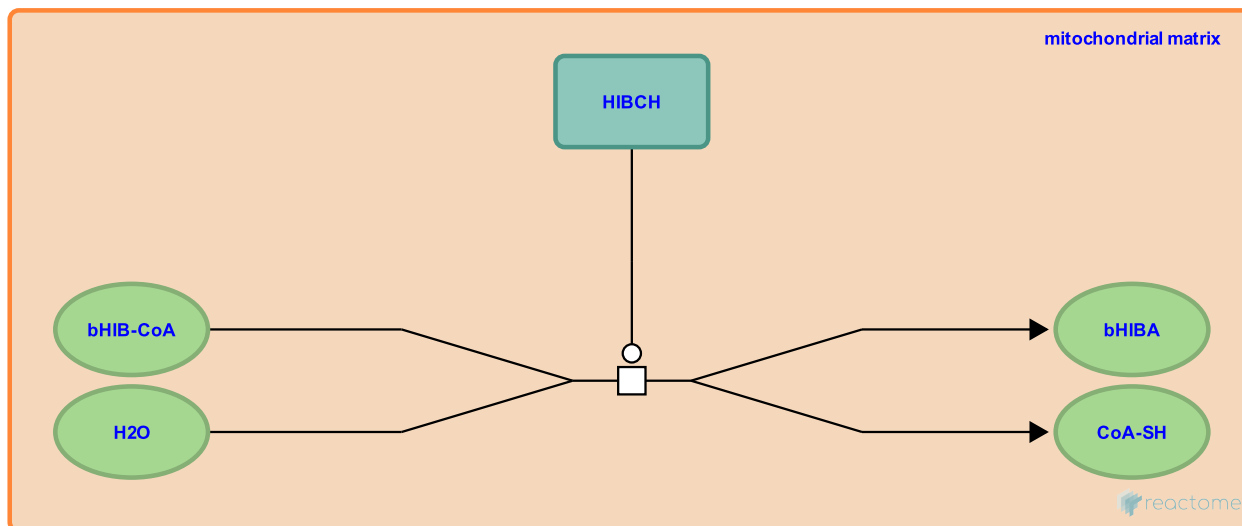
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-70881

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** [beta-hydroxyisobutyryl-CoA + H2O => beta-hydroxyisobutyrate + 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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Followed by:** [beta-hydroxyisobutyrate + NAD+ <=> methylmalonyl semialdehyde + NADH + H+](#)

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

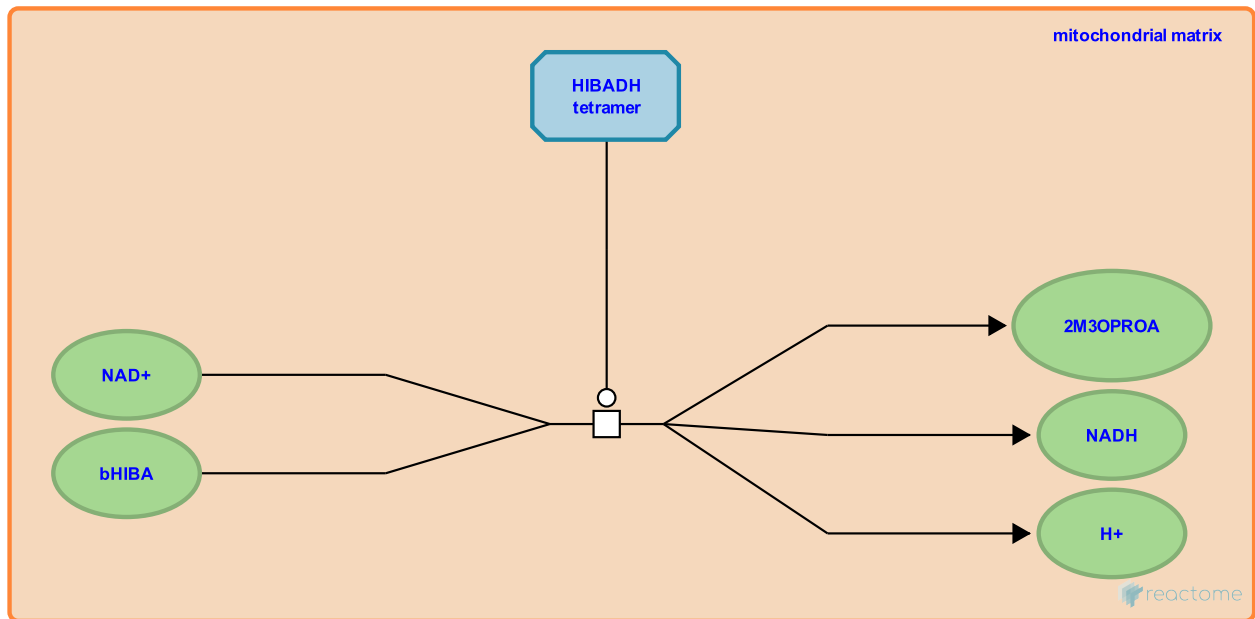
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [beta-hydroxyisobutyryl-CoA + H2O => beta-hydroxyisobutyrate + CoA](#)

**Followed by:** [methylmalonate semialdehyde + NAD+ + CoA => propionyl-CoA + CO2 + NADH + H+](#)

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

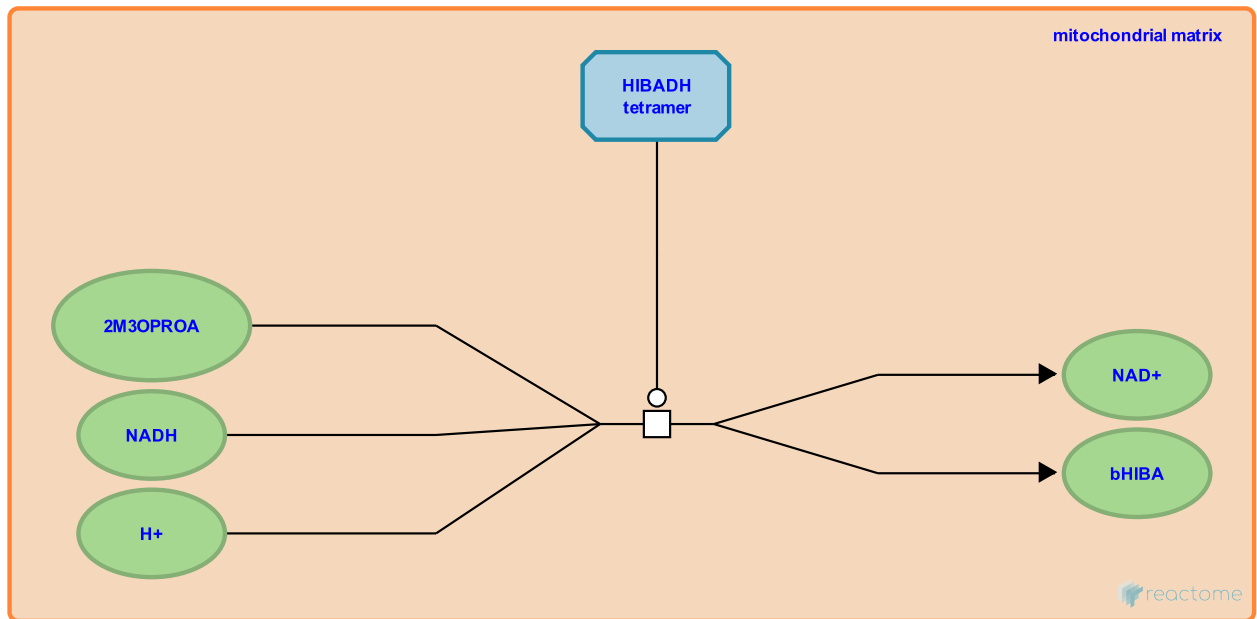
**Location:** [Branched-chain amino acid catabolism](#)

**Stable identifier:** R-GGA-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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**methyImalonate semialdehyde + NAD<sup>+</sup> + CoA => propionyl-CoA + CO<sub>2</sub> + NADH + H<sup>+</sup>** ↗

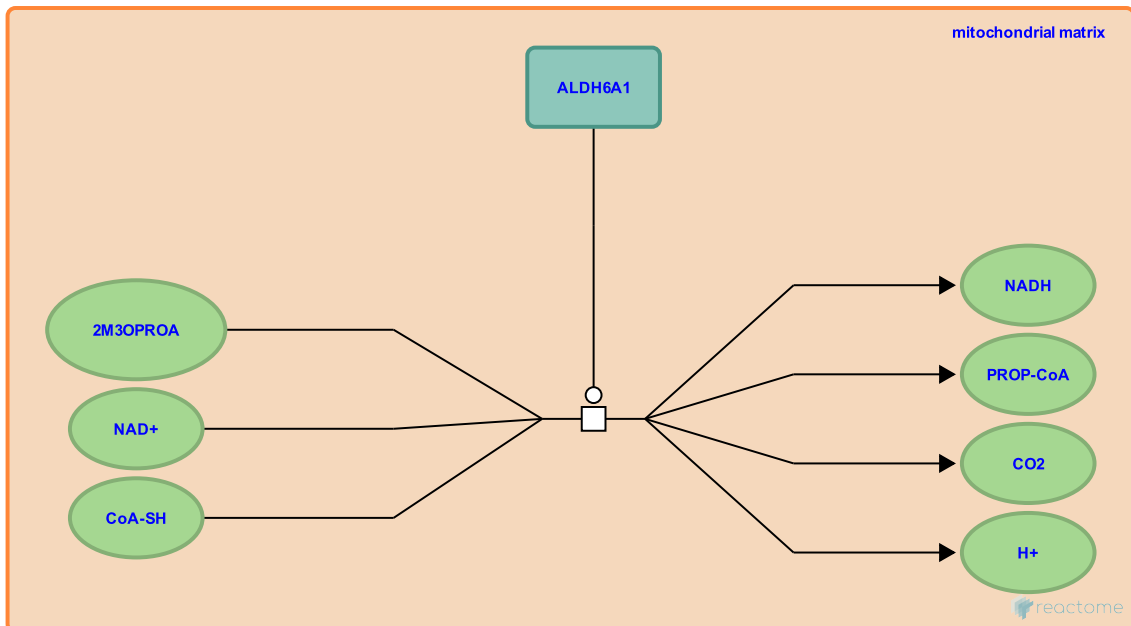
**Location:** Branched-chain amino acid catabolism

**Stable identifier:** R-GGA-70893

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** methyImalonate semialdehyde + NAD<sup>+</sup> + CoA => propionyl-CoA + CO<sub>2</sub> + NADH + H<sup>+</sup>  
(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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** beta-hydroxyisobutyrate + NAD<sup>+</sup> <=> methyImalonyl semialdehyde + NADH + H<sup>+</sup>

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↗ alpha-methylacetoacetyl-CoA + NADH + H <sup>+</sup> $\rightleftharpoons$ alpha-methyl-beta-hydroxybutyryl-CoA + NAD <sup>+</sup>	13
↗ alpha-methyl-acetoacetyl-CoA + CoA $\Rightarrow$ propionyl-CoA + acetyl-CoA	14
↗ isobutyryl-CoA + FAD $\Rightarrow$ methacrylyl-CoA + FADH <sub>2</sub>	15
↗ beta-hydroxyisobutyryl-CoA + H <sub>2</sub> O $\Rightarrow$ beta-hydroxyisobutyrate + CoA	16
↗ beta-hydroxyisobutyrate + NAD <sup>+</sup> $\rightleftharpoons$ methylmalonyl semialdehyde + NADH + H <sup>+</sup>	17
↗ methylmalonyl semialdehyde + NADH + H <sup>+</sup> $\rightleftharpoons$ beta-hydroxyisobutyrate + NAD <sup>+</sup>	18
↗ methylmalonate semialdehyde + NAD <sup>+</sup> + CoA $\Rightarrow$ propionyl-CoA + CO <sub>2</sub> + NADH + H <sup>+</sup>	19
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