The tricarboxylic acid cycle

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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.

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Literature references


Reactome database release: 78

This document contains 1 pathway and 14 reactions (see Table of Contents)
The reactions of the tricarboxylic acid (TCA cycle) mediate the complete oxidation of two carbon atoms from acetyl CoA, derived from catabolism of glucose and long chain fatty acids, to CO2, and the generation of NADH + H+ and FADH2. Carbon skeletons derived from catabolism of amino acids enter the TCA cycle as oxaloacetate, 2-oxoglutarate, and succinyl CoA. The TCA cycle thus plays a central role in the generation of energy by catabolism of energy-rich molecules from the diet, but also plays a critical role in the interconversions of metabolic intermediates needed to maintain pools of amino acids and other metabolites at physiological levels.
**acetyl-CoA + H2O + oxaloacetate => citrate + CoA**

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-373006

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial citrate synthase catalyzes the reaction of acetyl-CoA, H2O, and oxaloacetate to form citrate and CoA. The active enzyme is a homodimer (Liao et al. 1991).

**Preceded by:** malate + NAD+ <=> oxaloacetate + NADH + H+

**Followed by:** citrate <=> isocitrate

**Literature references**


**Editions**

2008-09-10 Authored, Edited D'Eustachio, P.
citrate <=> isocitrate

Location: The tricarboxylic acid cycle

Stable identifier: R-GGA-373015

Type: transition

Compartments: mitochondrial matrix

Mitochondrial aconitase catalyzes the reversible isomerization of citrate to form isocitrate (Shimogiri et al. 2002).

Preceded by: acetyl-CoA + H2O + oxaloacetate => citrate + CoA

Followed by: isocitrate + NAD+ => 2-oxoglutarate (alpha-ketoglutarate) + CO2 + NADH + H+

Literature references


Editions

2008-09-10 Authored, Edited D'Eustachio, P.
isocitrate $\leftrightarrow$ citrate

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-373140

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial aconitase catalyzes the reversible isomerization of isocitrate to form citrate (Shimogiri et al. 2002).

**Literature references**

isocitrate + NAD+ => 2-oxoglutarate (alpha-ketoglutarate) + CO2 + NADH + H+ →

Location: The tricarboxylic acid cycle

Stable identifier: R-GGA-373024

Type: transition

Compartments: mitochondrial matrix

Inferred from: isocitrate + NAD+ => alpha-ketoglutarate + CO2 + NADH + H+ [IDH3] (Homo sapiens)

Mitochondrial isocitrate dehydrogenase (IDH3-like) catalyzes the reaction of isocitrate and NAD+ to form 2-oxoglutarate (alpha-ketoglutarate), CO2, and NADH + H+. No chicken enzyme capable of catalyzing this reaction has been identified, although an open reading frame capable of encoding a protein closely similar to authentic human mitochondrial isocitrate dehydrogenase (IDH3) has been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

Preceded by: citrate <-> isocitrate

Followed by: 2-oxoglutarate (alpha-ketoglutarate) + CoASH + NAD+ => succinylCoA + CO2 + NADH + H+

Editions

2008-09-10  Authored, Edited  D'Eustachio, P.
2-oxoglutarate (alpha-ketoglutarate) + CoASH + NAD+ => succinylCoA + CO2 + NADH + H+

Location: The tricarboxylic acid cycle

Stable identifier: R-GGA-373042

Type: transition

Compartments: mitochondrial matrix

Inferred from: alpha-ketoglutarate + CoASH + NAD+ => succinyl-CoA + CO2 + NADH + H+ (Homo sapiens)

Mitochondrial 2-oxoglutarate (alpha-ketoglutarate) dehydrogenase complex catalyzes the reaction of 2-oxoglutarate, CoASH, and NAD+ to form succinylCoA, CO2, and NADH + H+. No chicken enzyme complex capable of catalyzing this reaction has been identified, although open reading frames capable of encoding proteins closely similar to each of the three authentic human 2-oxoglutarate dehydrogenase E1, E2, and E3 subunits have been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

Preceded by: isocitrate + NAD+ => 2-oxoglutarate (alpha-ketoglutarate) + CO2 + NADH + H+

Followed by: succinylCoA + ADP + Pi <=> succinate + CoASH + ATP, succinylCoA + GDP + Pi <=> succinate + CoASH + GTP

Editions

2008-09-10 Authored, Edited D'Eustachio, P.
\[
\text{succinylCoA + GDP + Pi} \leftrightarrow \text{succinate + CoASH + GTP}
\]

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-372980

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial succinyl-CoA synthetase catalyzes the reversible reaction of succinyl-CoA, GDP, and orthophosphate to form succinate, CoASH, and GTP. The enzyme is a heterodimer consisting of an alpha chain and a beta chain that determines whether the reaction involves adenine nucleotides or guanine nucleotides (as here). The biochemical properties of the chicken enzyme have been studied in detail (Hamilton and Ottaway 1981) but the genes encoding its component proteins have not been cloned. The molecular properties of these proteins are inferred from those of their pigeon homologues (Johnson et al. 1998).

**Preceded by:** 2-oxoglutarate (alpha-ketoglutarate) + CoASH + NAD+ \rightarrow succinylCoA + CO2 + NADH + H+

**Followed by:** succinate + FAD \leftrightarrow fumarate + FADH2

**Literature references**


**Editions**

2008-09-10 Authored, Edited D'Eustachio, P.
succinate + CoASH + GTP <=> succinylCoA + GDP + Pi

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-373148

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial succinyl-CoA synthetase catalyzes the reversible reaction of succinate, CoASH, and GTP to form succinylCoA, GDP, and orthophosphate. The enzyme is a heterodimer consisting of an alpha chain and a beta chain that determines whether the reaction involves adenine nucleotides or guanine nucleotides (as here). The biochemical properties of the chicken enzyme have been studied in detail (Hamilton and Ottaway 1981) but the genes encoding its component proteins have not been cloned. The molecular properties of these proteins are inferred from those of their pigeon homologues (Johnson et al. 1998).

**Literature references**


**succinylCoA + ADP + Pi <=> succinate + CoASH + ATP**

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-372977

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial succinyl-CoA synthetase catalyzes the reversible reaction of succinylCoA, ADP, and orthophosphate to form succinate, CoASH, and ATP. The enzyme is a heterodimer consisting of an alpha chain and a beta chain that determines whether the reaction involves adenine nucleotides (as here) or guanine nucleotides. The biochemical properties of the chicken enzyme have been studied in detail (Hamilton and Ottaway 1981) but the genes encoding its component proteins have not been cloned. The molecular properties of these proteins are inferred from those of their pigeon homologues (Johnson et al. 1998).

**Preceded by:** 2-oxoglutarate (alpha-ketoglutarate) + CoASH + NAD+ => succinylCoA + CO2 + NADH + H+

**Followed by:** succinate + FAD <=> fumarate + FADH2

**Literature references**


**Editions**

2008-09-10 Authored, Edited D'Eustachio, P.
succinate + CoASH + ATP ⇌ succinylCoA + ADP + Pi

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-373134

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial succinyl-CoA synthetase catalyzes the reversible reaction of succinate, CoASH, and ATP to form succinylCoA, ADP, and orthophosphate. The enzyme is a heterodimer consisting of an alpha chain and a beta chain that determines whether the reaction involves adenine nucleotides (as here) or guanine nucleotides. The biochemical properties of the chicken enzyme have been studied in detail (Hamilton and Ottaway 1981) but the genes encoding its component proteins have not been cloned. The molecular properties of these proteins are inferred from those of their pigeon homologues (Johnson et al. 1998).

**Literature references**


succinate + FAD <=> fumarate + FADH2

Location: The tricarboxylic acid cycle

Stable identifier: R-GGA-373147

Type: transition

Compartments: mitochondrial matrix, mitochondrial inner membrane

Inferred from: Succinate <=> Fumarate (with FAD redox reaction on enzyme) (Homo sapiens)

The SDH (succinate dehydrogenase) complex, embedded in the inner mitochondrial membrane, catalyzes the reversible oxidation of succinate to fumarate, coupled to the reduction of SDH-associated FAD to FADH2. No chicken enzyme capable of catalyzing this reaction has been characterized, although open reading frames capable of encoding three of the four proteins predicted from characterization of authentic human mitochondrial succinate dehydrogenase has been identified computationally in the ENSEMBL chicken gene set or in large-scale screens of cDNA clones. This reaction is inferred from its human counterpart.

Preceded by: succinylCoA + ADP + Pi <=> succinate + CoASH + ATP, succinylCoA + GDP + Pi <=> succinate + CoASH + GTP

Followed by: fumarate + H2O <=> malate

Editions

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fumarate + FADH2 ⇌ succinate + FAD

Location: The tricarboxylic acid cycle

Stable identifier: R-GGA-373129

Type: transition

Compartments: mitochondrial matrix, mitochondrial inner membrane

Inferred from: Succinate ⇌ Fumarate (with FAD redox reaction on enzyme) (Homo sapiens)

The SDH (succinate dehydrogenase) complex, embedded in the inner mitochondrial membrane, catalyzes the reversible reduction of fumarate to succinate, coupled to the oxidation of SDH-associated FADH2 to FADH. No chicken enzyme capable of catalyzing this reaction has been characterized, although open reading frames capable of encoding three of the four proteins predicted from characterization of authentic human mitochondrial succinate dehydrogenase has been identified computationally in the ENSEMBL chicken gene set or in large-scale screens of cDNA clones. This reaction is inferred from its human counterpart.
fumarate + H2O <=> malate

Location: The tricarboxylic acid cycle

Stable identifier: R-GGA-373145

Type: transition

Compartments: mitochondrial matrix

Inferred from: Fumarate + H2O <=> (S)-Malate (Homo sapiens)

Mitochondrial FH (fumarate hydratase) catalyzes the reversible reaction of fumarate and H2O to form malate. No chicken enzyme capable of catalyzing this reaction has been identified, although an open reading frame capable of encoding a protein closely similar to authentic human mitochondrial FH has been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

Preceded by: succinate + FAD <=> fumarate + FADH2

Followed by: malate + NAD+ <=> oxaloacetate + NADH + H+

Editions

2008-09-10 Author, Edited D'Eustachio, P.
**malate \leftrightarrow fumarate + H2O**

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-373141

**Type:** transition

**Compartments:** mitochondrial matrix

Mitochondrial FH (fumarate hydratase) catalyzes the reversible reaction of malate to form fumarate and H2O. No chicken enzyme capable of catalyzing this reaction has been identified, although an open reading frame capable of encoding a protein closely similar to authentic human mitochondrial FH has been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart (Sudarshan et al. 2007, Tomlinson et al. 2002).

**Literature references**


\[
\text{malate} + \text{NAD}^+ \rightleftharpoons \text{oxaloacetate} + \text{NADH} + \text{H}^+
\]

**Location:** The tricarboxylic acid cycle

**Stable identifier:** R-GGA-373047

**Type:** transition

**Compartments:** mitochondrial matrix

**Inferred from:** (S)-Malate + NAD+ \rightleftharpoons Oxaloacetate + NADH + H+ (Homo sapiens)

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MDH2 (mitochondrial malate dehydrogenase) catalyzes the reversible reaction of malate and NAD+ to form oxaloacetate and NADH + H+. No chicken enzyme capable of catalyzing this reaction has been identified, although an open reading frame capable of encoding a protein closely similar to authentic human mitochondrial malate dehydrogenase (MDH2) has been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

**Preceded by:** fumarate + H2O \rightleftharpoons malate

**Followed by:** acetyl-CoA + H2O + oxaloacetate \rightarrow citrate + CoA

**Editions**

2008-09-10  Authored, Edited  D'Eustachio, P.
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