Vitamin C (ascorbate) metabolism

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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: 76

This document contains 1 pathway and 9 reactions (see Table of Contents)
Vitamin C (ascorbate) is an antioxidant and a cofactor in reactions catalyzed by Cu+-dependent monooxygenases and Fe++-dependent dioxygenases. Many mammals can synthesize ascorbate de novo; humans and other primates cannot due to an evolutionarily recent mutation in the gene catalyzing the last step of the biosynthetic pathway. Reactions annotated here mediate the uptake of ascorbate and its fully oxidized form, dehydroascorbate (DHA) by cells, and the reduction of DHA and monodehydroascorbate to regenerate ascorbate (Linster and Van Schaftingen 2007).

**Literature references**


**Editions**

2007-04-24 Authored Jassal, B.
SLC2A1,3 transports DeHA from extracellular region to cytosol

**Location:** Vitamin C (ascorbate) metabolism

**Stable identifier:** R-HSA-198818

**Type:** transition

**Compartments:** plasma membrane

The uptake of extracellular dehydroascorbate (DeHA) into the cytosol is mediated by GLUT1 and GLUT3 (encoded by SLC2A1 and SLCA3 respectively) associated with the plasma membrane (Rumsey et al. 1997, 2000). This process may play a significant role in ascorbate utilization in the central nervous system (Agus et al. 1997). The process is efficiently competitively inhibited by glucose, leading to the suggestion that inhibited dehydroascorbate uptake may contribute to the pathology of diabetes (Liang et al. 2001, Rumsey et al. 2000).

**Followed by:** DeHA hydrolyses to 2,3-DKG, GSTO dimers reduce DeHA to AscH-, DeHA hydrolyses to threonate and oxalate

**Literature references**


**Editions**

2007-07-05 Authored D'Eustachio, P.
SLC23A1,2 cotransports AscH-, 2Na+ from extracellular region to cytosol

Location: Vitamin C (ascorbate) metabolism

Stable identifier: R-HSA-198870

Type: transition

Compartments: plasma membrane

The plasma membrane-associated transport proteins SVCT1 and SVCT2 (encoded by SLC23A1 and SLC23A2 respectively) are each capable of mediating the uptake of one molecule of ascorbate (AscH-) and two sodium ions from the extracellular space to the cytosol (Daruwala et al. 1999, Rajan et al. 1999, Wang et al. 1999). In the body SVCT2 is expressed in most tissues, while SVCT1 is largely confined to epithelial cells (Liang et al. 2001). SVCT2 may mediate fetal uptake of ascorbate from the maternal circulation (Rajan et al. 1999). The transporters responsible for its uptake from the small intestine and for its release from enterocytes into the circulation have not been identified, although both SVCT1 and 2 are expressed in intestinal cells.

Literature references


Editions

2007-07-05 Authored D'Eustachio, P.
Asc.- radical dissociates to AscH- and DeHA

**Location:** Vitamin C (ascorbate) metabolism

**Stable identifier:** R-HSA-9640302

**Type:** transition

**Compartments:** cytosol

The ascorbate radical (Asc.-) easily donates an electron, forming a stable radical which dissociates into ascorbate (AscH-), the dominant form at physiological pH, and dehydroascorbate (DeHA). This reaction is the basis for its antioxidant properties (Du et al. 2013).

**Followed by:** DeHA hydrolyses to threonate and oxalate, DeHA hydrolyses to 2,3-DKG

**Literature references**


**Editions**

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DeHA hydrolyses to 2,3-DKG

Location: Vitamin C (ascorbate) metabolism

Stable identifier: R-HSA-9640307

Type: transition

Compartments: cytosol

If peroxide is not present, dehydroascorbate (DeHA) quickly hydrolyses to 2,3-diketogulonate (2,3-DKG) (Simpson & Ortwerth 2000).

Preceded by: SLC2A1,3 transports DeHA from extracellular region to cytosol, Asc.- radical dissociates to AscH- and DeHA

Followed by: 2,3-DKG hydrolyses to ERU and oxalate

Literature references
2,3-DKG hydrolyses to ERU and oxalate

**Location:** Vitamin C (ascorbate) metabolism

**Stable identifier:** R-HSA-9640321

**Type:** transition

**Compartments:** cytosol

2,3-Diketogulonate (2,3-DKG) further hydrolyses into erythrulose (ERU) and oxalate (Simpson & Ortwerth 2000).

**Preceded by:** DeHA hydrolyses to 2,3-DKG

**Literature references**


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DeHA hydrolyses to threonate and oxalate

**Location:** Vitamin C (ascorbate) metabolism

**Stable identifier:** R-HSA-9640316

**Type:** transition

**Compartments:** cytosol

Ascorbate can autoxidise, generating superoxide and its dismutation product H2O2. The resulting dehydroascorbate (DeHA) gets oxidised by H2O2 and hydrolyses to threonate and oxalate (Simpson & Ortwerth 2000).

**Preceded by:** Asc.- radical dissociates to AscH- and DeHA, SLC2A1,3 transports DeHA from extracellular region to cytosol

**Literature references**


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**CYB5A:heme reduces Asc.- to AscH-**

**Location:** Vitamin C (ascorbate) metabolism

**Stable identifier:** R-HSA-198845

**Type:** transition

**Compartments:** cytosol, mitochondrial outer membrane

The reduction of cytosolic semidehydroascorbate (SDA) to ascorbate (AscH-) is catalyzed by cytochrome B5 (CYB5A) associated with the mitochondrial outer membrane. In the course of the reaction, the heme iron of the cytochrome is oxidized (Linster & Van Schaftingen 2007, Shirabe et al. 1995).

**Preceded by:** CYB5R3:FAD reduces CYB5A:ferriheme to CYB5A:heme

**Followed by:** CYB5R3:FAD reduces CYB5A:ferriheme to CYB5A:heme

**Literature references**


**Editions**

2007-07-05 Authored D'Eustachio, P.
**CYB5R3:FAD reduces CYB5A:ferriheme to CYB5A:heme**

**Location:** Vitamin C (ascorbate) metabolism

**Stable identifier:** R-HSA-198824

**Type:** transition

**Compartments:** cytosol, mitochondrial outer membrane

Cytochrome b5 reductase (CYB5R3) catalyzes the reduction of cytosolic ferric CYB5A (CYB5A:ferriheme) to ferrous CYPB5A (CYB5A:heme), coupled to the conversion of NADH to NAD+ (Shirabe et al. 1995). CYB5R3 is associated with the outer mitochondrial membrane via a myristoyl group added post-translationally to glycine residue 2 of the protein (Borgese et al. 1993).

**Preceded by:** CYB5A:heme reduces Asc.- to AscH-

**Followed by:** CYB5A:heme reduces Asc.- to AscH-

**Literature references**


**Editions**

2007-07-05 Authored D'Eustachio, P.
GSTO dimers reduce DeHA to Asch-

Location: Vitamin C (ascorbate) metabolism

Stable identifier: R-HSA-198813

Type: transition

Compartments: cytosol

Cytosolic omega class glutathione transferases (GSTO1 and GSTO2) catalyze the reaction of dehydroascorbate (DeHA) and glutathione (GSH) to form ascorbate (Asch-) and oxidized glutathione (GSSG). The GSTO enzymes occur as homodimers (Board et al. 2000), and while both have dehydroascorbate reductase activity in vitro, that of GSTO2 is much greater than that of GSTO1 (Schmuck et al. 2005). Polymorphisms affecting the activities of the two enzymes have been described (Whitbread et al. 2005).

Preceded by: SLC2A1,3 transports DeHA from extracellular region to cytosol

Literature references


Editions

2007-07-05 Authored D'Eustachio, P.
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