Metabolism of water-soluble vitamins and cofactors

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13/06/2019
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


Reactome database release: 69

This document contains 11 pathways (see Table of Contents)
Metabolism of water-soluble vitamins and cofactors

Stable identifier: R-HSA-196849

Vitamins are a diverse group of organic compounds, required in small amounts in the diet. They have distinct biochemical roles, often as coenzymes, and are either not synthesized or synthesized only in limited amounts by human cells. Vitamins are classified according to their solubility, either fat-soluble or water-soluble. The physiological processes dependent on vitamin-requiring reactions include many aspects of intermediary metabolism, vision, bone formation, and blood coagulation, and vitamin deficiencies are associated with a correspondingly diverse and severe group of diseases.

Water-soluble vitamins include ascorbate (vitamin C) and the members of the B group: thiamin (vitamin B1), riboflavin (B2), niacin (B3), pantothenate (B5), pyridoxine (B6), biotin (B7), folate (B9), and cobalamin (B12). Metabolic processes annotated here include the synthesis of thiamin pyrophosphate (TPP) from thiamin (B1), the synthesis of FMN and FAD from riboflavin (B2), the synthesis of nicotinic acid (niacin - B3) from tryptophan, the synthesis of Coenzyme A from pantothenate (B5), and features of the metabolism of folate (B9).

Editions

2007-04-24  Authored  Jassal, B.
Vitamin C (ascorbate) metabolism

**Location:** Metabolism of water-soluble vitamins and cofactors

**Stable identifier:** R-HSA-196836

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.
Vitamin B1 (thiamin) metabolism

**Location:** Metabolism of water-soluble vitamins and cofactors

**Stable identifier:** R-HSA-196819

Vitamin B1 (thiamin) is found naturally in certain foodstuffs such as green peas, spinach, liver, bananas, whole grains and legumes. Human diseases associated with thiamin deficiency include beriberi, due to a thiamin-deficient diet, TMRA, due to defects in the SLC19A2 transport protein, and Wernicke-Korsakoff Syndrome, associated with thiamin deficiency in alcoholism (Haas 1988). Thiamin is water-soluble so is not stored in the body. When pyrophosphorylated, thiamin is converted into the coenzyme thiamin pyrophosphate (ThPP, codecarboxylase) which plays an essential role in oxidative decarboxylation and group transfer reactions.

**Literature references**


**Editions**

2007-04-24 Authored Jassal, B.
Vitamin B2 (riboflavin) metabolism

Location: Metabolism of water-soluble vitamins and cofactors

Stable identifier: R-HSA-196843

Riboflavin (vitamin B2, E101) is an essential component for the cofactors FAD (flavin-adenine dinucleotide) and FMN (flavin mononucleotide). Together with NAD+ and NADP+, FAD and FMN are important hydrogen carriers and take part in more than 100 redox reactions involved in energy metabolism. Riboflavin is present in many vegetables and meat and during digestion, various flavoproteins from food are degraded and riboflavin is resorbed. The major degradation and excretion product in humans is riboflavin (Rivlin 1970).

Literature references

Vitamin B5 (pantothenate) metabolism

Location: Metabolism of water-soluble vitamins and cofactors

Stable identifier: R-HSA-199220

Panthenate (vitamin B5) is the precursor of coenzyme A (Robishaw and Neely 1985) and is the prosthetic group of acyl carrier protein (ACP) (Joshi et al. 2003). Its name is derived from the Greek pantothen meaning "from everywhere" and small quantities of pantothenic acid are found in nearly every foodstuff.

Literature references


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Animals cannot synthesize pyridoxal 5′-phosphate (PLP) which is a ligand in aminotransferases and other enzymes. PLP's accessible derivatives pyridoxine, pyridoxal, and pyridoxamine are traditionally called vitamins B6. They are taken up nutritionally from bacteria and plants, but also created from PLP in the body. The pathways used to recycle PLP from these three compounds can therefore be called vitamin B6 activation as well as PLP salvage. Because of the close similarity of the molecules, only two enzymes are needed for the task (McCormick & Chen, 1999).

**Literature references**

Vitamin B₁₂ (cobalamin, Cbl) is a water-soluble vitamin with a key role in blood formation and normal functioning of the brain and nervous system. Cbl consists of a planar corrin ring coordinating with a cobalt atom through four nitrogen atoms. A 5,6-dimethylbenzamidizole base coordinates with the cobalt atom in the lower axial position while a number of different species can coordinate with the cobalt atom in the upper axial position. It is the cobalt-corrin ring complex that gives all Cbls a deep red colour. Only bacteria and archaea are able to synthesise Cbl thus humans need a dietary intake to prevent deficiency (Green 2010, Quadros 2010, Watkins & Rosenblatt 2011). A common semi-synthetic form of the vitamin, cyanocobalamin (CNCbl, where a cyanide group is in the upper axial position), is produced from bacterial hydroxocobalamin and used in many pharmaceuticals, supplements and as a food additive. In mammalian cells, Cbl or CNCbl is converted to two active coenzyme derivatives; methylcobalamin (MetCbl) and adenosylcobalamin (AdoCbl). MetCbl is required for activity of the cytoplasmic enzyme methionine synthase, which converts homocysteine to methionine. AdoCbl is required for activity of the mitochondrial enzyme methylmalonyl CoA mutase, which converts L-methylmalonyl-CoA to succinyl-CoA (Seetharam 1999). This pathway outlines the intake, transport and metabolism of Cbl and is assumed to be equally applicable to CNCbl.

Literature references


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Biotin transport and metabolism

Location: Metabolism of water-soluble vitamins and cofactors

Stable identifier: R-HSA-196780

Biotin (Btn) is an essential cofactor in a variety of carboxylation reactions (Zempleni et al. 2009). Humans cannot synthesize Btn but it is abundant in the human diet and can be taken up from the intestinal lumen by the SLC5A6 transporter. Its uptake, intracellular translocation, covalent conjugation to apoenzymes, and salvage are described here.

Literature references


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Nicotinate (niacin) and nicotinamide are precursors of the coenzymes nicotinamide-adenine dinucleotide (NAD+) and nicotinamide-adenine dinucleotide phosphate (NADP+). When NAD+ and NADP+ are interchanged in a reaction with their reduced forms, NADH and NADPH respectively, they are important cofactors in several hundred redox reactions. Nicotinate is synthesized from 2-amino-3-carboxymuconate semialdehyde, an intermediate in the catabolism of the essential amino acid tryptophan (Magni et al. 2004).

**Literature references**


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Folates are essential cofactors that provide one-carbon moieties in various states of reduction for biosynthetic reactions. Processes annotated here include transport reactions by which folates are taken up by cells and moved intracellularly, folate conjugation with glutamate (required for folate retention within a cell), and some of the key reactions in the generation of reduced folates and one-carbon derivatives of folate.

**Literature references**


Molybdenum cofactor biosynthesis

Location: Metabolism of water-soluble vitamins and cofactors

Stable identifier: R-HSA-947581

Compartments: cytosol

Molybdenum cofactor (MoCo) is needed by three enzymes in humans: sulfite oxidase, xanthine oxidase and aldehyde oxidase. The pathway of its synthesis is so conserved that plants and bacteria can readily use human enzymes. Bacteria, however, diverge after the first three steps from this path and their final MoCo differs from that of the eukaryotes. Plants and animals have also developed a refinement of their MoCo which is needed for the function of their xanthine and aldehyde oxidases. This means, in humans we find sulfurated instead of desulfurated molybdenum cofactor on these two enzymes (Schwarz 2005; Schwarz, Mendel, Ribbe 2009).

Literature references


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