Vitamin B2 (riboflavin) 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: 75

This document contains 1 pathway and 5 reactions (see Table of Contents)
Vitamin B2 (riboflavin) metabolism

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

SLC52A1,2,3 transport RIB from extracellular region to cytosol

**Location:** Vitamin B2 (riboflavin) metabolism

**Stable identifier:** R-HSA-3165230

**Type:** transition

**Compartments:** cytosol, extracellular region, plasma membrane

The water-soluble vitamin riboflavin (RIB, vitamin B2) is essential for normal cellular functions. Three human riboflavin transporters mediate the transport of RIB into cells and play an important role in RIB homeostasis. The transporters are assigned to a new sub-family of the SLC superfamily; SLC52A1, SLC52A2 and SLC52A3 (aka RFVT1, RFVT2 and RFVT3 respectively). Solute carrier family 52, riboflavin transporter, member 1 (SLC52A1, RFVT1) is widely expressed with highest expression in the testis, placenta and small intestine (Yonezawa et al. 2008). Solute carrier family 52, riboflavin transporter, member 2 (SLC52A2, RFVT2) is highly expressed in brain, foetal brain and salivary gland (Yao et al. 2010). Solute carrier family 52, riboflavin transporter, member 3 (SLC52A3, RFVT3) transports riboflavin (RIB) from the lumen into small intestine epithelial cells (Yoshimatsu et al. 2014). Activity is inhibited by riboflavin analogues such as flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) (Yao et al. 2010). Defects in SLC52A3 cause Brown-Vialetto-Van Laere syndrome type 1 (BVVLS1; MIM:211530). BVVLS1 is a rare autosomal recessive neurologic disorder characterised by sensorineural hearing loss and a variety of cranial nerve palsies (Green et al. 2010). Defects in SLC52A3 also cause Fazio-Londe disease (FALOND; MIM:211500), a rare neurological disease characterised by progressive weakness of the muscles innervated by cranial nerves located at the lower brain stem (Bosch et al. 2011).

**Literature references**


**Editions**

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Phosphorylation of riboflavin (RIB) results in the formation of the first cofactor, flavin mononucleotide (FMN). This reaction is catalyzed by riboflavin kinase (RFK), a cytosolic enzyme existing as a monomer. It utilizes either zinc or magnesium ions in the reaction.

**Preceded by:** 2xTRAP hydrolyzes FMN to RIB

**Followed by:** FLAD1 phosphorylates FMN

**Literature references**

**FLAD1 phosphorylates FMN**

**Location:** Vitamin B2 (riboflavin) metabolism

**Stable identifier:** R-HSA-196929

**Type:** transition

**Compartments:** cytosol

FMN can be phosphorylated and adenylated to produce the second cofactor from riboflavin origins, flavin adenine dinucleotide (FAD). The enzyme responsible, FMN adenylyltransferase (FLAD1 aka FAD synthase), is cytosolic and transfers a phosphate and an adenyl group from ATP to form FAD.

**Preceded by:** RFK:Mg2+ phosphorylates RIB, 2xENPP1 hydrolyzes FAD to FMN

**Followed by:** 2xENPP1 hydrolyzes FAD to FMN

**Literature references**

**2xENPP1 hydrolyzes FAD to FMN**

**Location:** Vitamin B2 (riboflavin) metabolism

**Stable identifier:** R-HSA-196955

**Type:** transition

**Compartments:** cytosol, plasma membrane

Phosphatase action on flavin adenine dinucleotide (FAD) can reform flavin mononucleotide (FMN). The enzyme performing the reaction is nucleotide pyrophosphatase (ENPP1) and it exists as a homodimer on the plasma membrane.

**Preceded by:** FLAD1 phosphorylates FMN

**Followed by:** 2xTRAP hydrolyzes FMN to RIB, FLAD1 phosphorylates FMN

**Literature references**

**2xTRAP hydrolyzes FMN to RIB**

**Location:** Vitamin B2 (riboflavin) metabolism

**Stable identifier:** R-HSA-196950

**Type:** transition

**Compartments:** cytosol

Cytosolic, homodimeric tartrate-resistant acid phosphatase type 5 (TRAP) catalyzes the hydrolysis of flavin mononucleotide (FMN) to yield riboflavin (RIB) and orthophosphate.

**Preceded by:** 2xENPP1 hydrolyzes FAD to FMN

**Followed by:** RFK:Mg2+ phosphorylates RIB

**Literature references**

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