Transport and synthesis of PAPS

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

16/11/2022
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: 82

This document contains 1 pathway and 4 reactions (see Table of Contents)
PAPS (3’-phosphoadenosine-5’-phosphosulfate), which functions as a sulfate donor in the cell, is synthesized from sulfate and two molecules of ATP in a two-step process (Robbins & Lipmann 1958) catalyzed in vertebrates by a bifunctional enzyme (Venkatachalam et al. 1998). PAPS synthesis takes place in the cytosol, and it is either consumed there in the sulfonation of a variety of hormones and xenobiotics, or it is transported to the Golgi apparatus and consumed in the synthesis of proteoglycans like chondroitin sulfate. Two isoforms of the human bifunctional enzyme are known, mutations in one of which are associated with defects in proteoglycan biosynthesis (Girard et al. 1998, ul Haque et al. 1998).

Literature references


The SLC26A1 and 2 genes encode proteins that facilitate sulfate (SO4(2-)) uptake into cells (Alper & Sharma 2013). The mechanism by which these transporters work is unclear but may be enhanced by extracellular halides or acidic pH environments, cotransporting protons electroneutrally. Both can transport SO4(2-) (as well as oxalate and Cl-) across the basolateral membrane of epithelial cells. SLC26A1 encodes the sulfate anion transporter 1 (SAT1) (Regeer et al. 2003) and is most abundantly expressed in the liver and kidney, with lower levels expressed in many other parts of the body. SLC26A2 is ubiquitously expressed and encodes a sulfate transporter (Diastrophic dysplasia protein, DTD, DTDST) (Hastbacka et al. 1994). This transporter provides sulfate for sulfation of glycosaminoglycan chains in proteoglycans needed for cartilage development. Defects in SLC26A2 are implicated in the pathogenesis of several human chondrodysplasias.

Followed by: PAPSS1,2 transfer SO4(2-) group to ATP to form APS

**Literature references**


**Editions**

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In the first step of PAPS biosynthesis, ATP and sulfate react to form adenylyl sulfate (APS) and pyrophosphate (PPI), catalyzed by the ATP sulfurylase domains of the bifunctional enzymes PAPS synthases 1 and 2 (PAPSS1 and 2). PAPSS2 is essential for the sulfation of glycosaminoglycan chains in proteoglycans, a necessary post translational modification. Defective PAPSS2 results in undersulfation of the glycosaminoglycan chains in proteoglycans which causes spondyloepimetaphyseal dysplasia Pakistani type (SEMD PA; MIM:612847), a bone disease characterized by epiphyseal dysplasia with mild metaphyseal abnormalities. Mutations resulting in SEMD PA include S438*, T48R and R329* (Ahmad et al. 1998, ul Haque et al. 1998, Noordam et al. 2009).

Preceded by: SLC26A1,2 cotransport SO4(2-), H+ from extracellular region to cytosol

Followed by: PAPSS1,2 transfer PO4(2-) group from ATP to APS to form PAPS

Literature references


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In the second step of PAPS biosynthesis, adenylyl sulfate (APS) is phosphorylated to 3'-phosphoadenylyl sulfate (PAPS), catalyzed by the APS kinase domains of the bifunctional enzymes PAPS synthases 1 and 2 (PAPSS1 and 2). PAPSS2 is essential for the sulfation of glycosaminoglycan chains of proteoglycans, a necessary post-translational modification. Defective PAPSS2 results in undersulfation of proteoglycans which causes spondyloepimetaphyseal dysplasia Pakistani type (SEMD-PA; MIM:612847), a bone disease characterized by epiphyseal dysplasia with mild metaphyseal abnormalities. Mutations resulting in SEMD-PA include S438*, T48R and R329* (Ahmad et al. 1998, ul Haque et al. 1998, Noordam et al. 2009).

**Preceded by:** PAPSS1,2 transfer SO4(2-) group to ATP to form APS

**Followed by:** SLC35B2,3 transport cytosolic PAPS to Golgi lumen

**Literature references**

SLC35B2,3 transport cytosolic PAPS to Golgi lumen

**Location:** Transport and synthesis of PAPS

**Stable identifier:** R-HSA-741449

**Type:** transition

**Compartments:** Golgi lumen, Golgi membrane, cytosol

The human gene SLC35B2 encodes the adenosine 3’-phospho 5’-phosphosulfate transporter 1 (PAPST1) (Ozeran et al. 1996, Kamiyama et al. 2003). In human tissues, PAPST1 is highly expressed in the placenta and pancreas and present at lower levels in the colon and heart. The human gene SLC35B3 encodes a human PAPS transporter gene that is closely related to PAPST1. Called PAPST2, it is predominantly expressed in the colon (Kamiyama et al. 2006). Both proteins can transport PAPS from the cytosol to the Golgi lumen.

**Preceded by:** PAPSS1,2 transfer PO4(2-) group from ATP to APS to form PAPS

**Literature references**


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