Synthesis of UDP-N-acetyl-glucosamine

D'Eustachio, P., Dall'Olio, GM., Gagneux, P., Jassal, B.

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21/06/2022
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.

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: 81

This document contains 1 pathway and 7 reactions (see Table of Contents)

https://reactome.org
Synthesis of UDP-N-acetyl-glucosamine

Stable identifier: R-HSA-446210

UDP-acetylglucosamine acts as a donor for the first two steps of the N-glycan precursor biosynthesis pathway, and is later used as a substrate for further modifications after the precursor has been attached to the protein. It is synthesized from fructose 6-phosphate, glutamine, acetyl-CoA, and UTP in four steps.

Editions

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Humans are not able to catalyse the formation of N-glycolylneuraminic acid (Neu5Gc) due to an inactive CMAHP enzyme. Neu5Gc can be obtained from dietary sources and must be degraded to avoid accumulation and resultant chronic inflammation known as xenosialitis (Varki et al. 2011). Degradation of excess Neu5Gc results in the formation of two ubiquitous metabolites involved in asparagine N-linked glycolylation; glycolate and glucosamine 6-phosphate. In the Neu5Gc degradation pathway, N-acylglucosamine 2-epimerase (RENBP) dimer catalyses the reversible isomerisation of N-acetylmannosamine (ManNAc) to N-acetylglucosamine (GlcNAc) and of N-glycolylymannosamine (ManNGc) to N-glycolylglucosamine (GlcNGc) (Takahashi et al. 1999, 2001).

Followed by: NAGK dimer phosphorylates GlcNAc, GlcNGc to GlcNAc-6-P, GlcNGc-6-P

**Literature references**


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**Preceded by:** RENBP isomerises ManNAc, ManNGc to GlcNAc, GlcNGc

**Followed by:** AMDHD2 hydrolyses GlcNGc-6-P to GlcN6P and CCA

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AMDHD2 hydrolyses GlcNGc-6-P to GlcN6P and CCA

Location: Synthesis of UDP-N-acetyl-glucosamine

Stable identifier: R-HSA-6803789

Type: transition

Compartments: cytosol

Humans are not able to catalyse the formation of N-glycolylneuraminic acid (Neu5Gc) due to an inactive CMAHP enzyme. Neu5Gc can be obtained from dietary sources and must be degraded to avoid accumulation and resultant chronic inflammation known as xenosialitis (Varki et al. 2011). In the Neu5Gc degradation pathway, the putative N-acetylglucosamine-6-phosphate deacetylase (AMDHD2) is thought to irreversibly hydrolyse N-glycolylglucosamine 6-phosphate (GlcNGc-6-P), resulting in the ubiquitous metabolites glycolate (CCA) and glucosamine 6-phosphate (GlcN6P) (Bergfeld et al. 2012).

Preceded by: NAGK dimer phosphorylates GlcNAc, GlcNGc to GlcNAc-6-P, GlcNGc-6-P

Followed by: Acetylation of glucosamine 6-phosphate to GlcNAc6P

Literature references


Editions

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2016-01-11 Reviewed D’Eustachio, P.
GFPT1,2 transfer an amino group from L-Gln to F6P to form GlcN6P

Location: Synthesis of UDP-N-acetyl-glucosamine

Stable identifier: R-HSA-449715

Type: transition

Compartments: cytosol

Glucosamine-fructose 6-phosphate aminotransferases 1 and 2 (GFPT1,2) are the first and rate-limiting enzymes in the hexosamine synthesis pathway, and thus formation of hexosamines like N-acetylglucosamine (GlcNAc). These enzymes probably play a role in limiting the availability of substrates for the N- and O-linked glycosylation of proteins (McKnight et al. 1992, Oki et al. 1999). GFPT1 and 2 are required for normal functioning of neuromuscular synaptic transmission. Defects in GFPT1 lead to altered muscle fibre morphology and impaired neuromuscular junction development (Senderek et al. 2011).

Followed by: Acetylation of glucosamine 6-phosphate to GlcNAc6P

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**Acetylation of glucosamine 6-phosphate to GlcNAc6P**

**Location:** Synthesis of UDP-N-acetyl-glucosamine

**Stable identifier:** R-HSA-449734

**Type:** transition

**Compartments:** cytosol

Cytosolic GNPNAT1 catalyzes the reaction of glucosamine 6-phosphate and acetyl-CoA to form N-acetyl-glucosamine 6-phosphate (GlcNAc6P) and CoA-SH. Structural studies indicate that the active form of the enzyme is a dimer (Wang J et al, 2008).

**Preceded by:** AMDHD2 hydrolyses GlcNGc-6-P to GlcN6P and CCA, GFPT1,2 transfer an amino group from L-Gln to F6P to form GlcN6P

**Followed by:** Isomerization of GlcNAc6P to GlcNAc1P

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Isomerization of GlcNAc6P to GlcNAc1P

**Location:** Synthesis of UDP-N-acetyl-glucosamine

**Stable identifier:** R-HSA-446185

**Type:** transition

**Compartments:** cytosol

Cytosolic PGM3 catalyzes the isomerization of N-acetyl-D-glucosamine 6-phosphate (GlcNAc6P) to form N-acetyl-D-glucosamine 1-phosphate (GlcNAc1P) (Pang H et al, 2002).

**Preceded by:** Acetylation of glucosamine 6-phosphate to GlcNAc6P

**Followed by:** GlcNAc1P is dephosphorylated to UDP-N-acetyl-glucosamine

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GlcNAc1P is dephosphorylated to UDP-N-acetyl-glucosamine

**Location:** Synthesis of UDP-N-acetyl-glucosamine

**Stable identifier:** R-HSA-446204

**Type:** transition

**Compartments:** cytosol

Cytosolic UAP1 catalyzes the reaction of N-acetyl-D-glucosamine 1-phosphate (GlcNAc1P) and UTP to UDP-N-acetyl-D-glucosamine and pyrophosphate. Structural studies indicate that the active form of the enzyme is a dimer (Peneff C et al, 2001).

**Preceded by:** Isomerization of GlcNAc6P to GlcNAc1P

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