Keratan sulfate biosynthesis

D'Eustachio, P., He, L., Jassal, B.
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: 73

This document contains 1 pathway and 9 reactions (see Table of Contents)
Keratan sulfate biosynthesis

Stable identifier: R-HSA-2022854

Keratan sulfate (KSI) is the best characterised keratan sulfate. It is 10 times more abundant in cornea than cartilage. KSI is attached to an asparagine (Asn) residue on the core protein via an N-linked branched oligosaccharide (an N-glycan core structure used as a precursor in N-glycan biosynthesis). KSI is elongated by the alternate additions of galactose (Gal) and N-acetylglucosamine (GlcNAc), mediated by glycosyltransferases. Elongation is terminated by the addition of a single N-acetyleneuraminic acid (sialyl) residue. KSI is also sulfated on Gal and GlcNAc residues by at least two sulfotransferases (Funderburgh 2000, Funderburgh 2002, Quantock et al. 2010). KSI can be attached to asparagine residues on core proteins, creating so called proteoglycans (PGs). Seven common core proteins found in corneal and skeletal tissues are used as examples here.

Literature references


Editions

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<td>2012-03-28</td>
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SLC35D2 exchanges UDP-sugars for UMP

Location: Keratan sulfate biosynthesis

Stable identifier: R-HSA-744231

Type: transition

Compartments: Golgi membrane

The human gene SLC35D2 encodes the UDP-N-acetylglucosamine/UDP-glucose/GDP-mannose transporter (UGTREL8; homolog of Fringe connection protein 1, HFRC1). It resides on the Golgi membrane where it mediates the transport of nucleotide sugars such as UDP-GlcNAc and UDP-glucose into the Golgi lumen in exchange for UMP (Suda et al. 2004, Ishida et al. 2005).

Followed by: B3GNT1,2,3,4,7 add GlcNAc to form Keratan-PG

Literature references


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<td>2010-05-17</td>
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The family of beta 4-galactosyltransferases (B4GALTs) is composed of at least six known members with different Km and acceptor specificities (Guo et al. 2001) that probably originated by gene duplication (Lo et al. 1998). They mediate the transfer of galactose to N-glycan structures which initiate the beginning of keratan sulfate (KS) biosynthesis. B4GALT1 is associated with Congenital Disorder of Glycosylation of type IId (MIM:607091) (Hansske et al. 2002), and is expressed as two splicing isoforms of which only one is localized in the Golgi system (Lopez et al. 1991, Schaub et al. 2006).

Followed by: B3GNT1,2,3,4,7 add GlcNAc to form Keratan-PG

Literature references


Editions

2011-12-15 Authored, Edited Jassal, B.

2012-03-28 Reviewed D'Eustachio, P.
B3GNT1,2,3,4,7 add GlcNAc to form Keratan-PG

Location: Keratan sulfate biosynthesis

Stable identifier: R-HSA-2025724

Type: transition

Compartments: Golgi membrane, Golgi lumen

The UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase family (B3GNTs) consists of 9 members in humans (Kolbinger et al, 1998; Shiraishi et al, 2001; Togayachi et al, 2001; Iwai et al, 2002; Huang et al, 2004; Ishida et al, 2005; Zheng et al, 2004). Members 1,2,3,4 and 7 can catalyse the addition of N-acetylglucosamine (GlcNAc) to the galactosyl residue of the saccharide chain in a beta-1,3 linkage to form a structure called Keratan-proteoglycan (PG).

Preceded by: B4GALTs transfer Gal to the N-glycan precursor, SLC35D2 exchanges UDP-sugars for UMP

Followed by: B4GALTs transfer Gal to the keratan chain

Literature references


## Editions

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**B4GALTs transfer Gal to the keratan chain**

**Location:** Keratan sulfate biosynthesis

**Stable identifier:** R-HSA-2046265

**Type:** transition

**Compartments:** Golgi membrane, Golgi lumen

The family of beta 4-galactosyltransferases (B4GALTs) is composed by at least six known members with different Km and acceptor specificities (Guo et al. 2001) and probably originated by duplication (Lo et al. 1998). They mediate the transfer of galactose to N-glycan structures, either to begin, or in this case, to elongate keratan chains. B4GALT1 is associated with Congenital Disorder of Glycosylation of type IId (MIM:607091) (Hansske et al. 2002), and is expressed as two splicing isoforms of which only one is localized in the Golgi system (Lopez et al. 1991, Schaub et al. 2006).

**Preceded by:** B3GNT1,2,3,4,7 add GlcNAc to form Keratan-PG

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The family of beta 4-galactosyltransferases (B4GALTs) is composed by at least six known members with different Km and acceptor specificities (Guo et al. 2001) that probably originated by gene duplication (Lo et al. 1998). They mediate the transfer of galactose to N-glycan structures, in this case, to elongate an antenna with a keratan chain. B4GALT1 is associated with Congenital Disorder of Glycosylation of type IIId (MIM:607091) (Hansske et al. 2002), and is expressed as two splicing isoforms of which only one is localized in the Golgi system (Lopez et al. 1991, Schaub et al. 2006).

Followed by: The keratan chain can be capped by N-acetylneuraminic acid

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The keratan chain can be capped by N-acetylneuraminic acid

**Location:** Keratan sulfate biosynthesis

**Stable identifier:** R-HSA-2046285

**Type:** transition

**Compartments:** Golgi membrane, Golgi lumen


**Preceded by:** B4GALTs transfer Gal to a branch of keratan

**Followed by:** CHST2,5,6 transfer SO4(2-) to GlcNAc residues on keratan-PG to form KSPG

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CHST2,5,6 transfer SO4(2-) to GlcNAc residues on keratan-PG to form KSPG

**Location:** Keratan sulfate biosynthesis

**Stable identifier:** R-HSA-2046222

**Type:** transition

**Compartments:** Golgi membrane, Golgi lumen

Carbohydrate sulfotransferases 2, 5 and 6 (CHST2, 5 and 6) catalyze the transfer of sulfate to position 6 of non-reducing ends of N-acetylglucosamine (GlcNAc) residues within keratan-like molecules (Sakaguchi et al. 2000, Lee et al. 1999, Akama et al. 2002). Keratan(4)-PG represents keratan before sulfation has occurred.

**Preceded by:** The keratan chain can be capped by N-acetylneuraminic acid

**Followed by:** Further sulfation on galactose residues produces KSPG

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https://reactome.org
Further sulfation on galactose residues produces KSPG

**Location:** Keratan sulfate biosynthesis

**Stable identifier:** R-HSA-2046175

**Type:** transition

**Compartments:** Golgi membrane, Golgi lumen

Carbohydrate sulfotransferase 1 (CHST1, keratan sulfate Gal-6 sulfotransferase) mediates the sulfation of galactose (Gal) on position 6 in keratan sulfate proteoglycans (KSPGs) (Fukuta et al. 1997).

**Preceded by:** CHST2,5,6 transfer SO4(2-) to GlcNAc residues on keratan-PG to form KSPG

**Followed by:** KSPG is secreted from the cell

**Literature references**


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KSPG is secreted from the cell

Location: Keratan sulfate biosynthesis

Stable identifier: R-HSA-2046180

Type: omitted

Compartments: Golgi lumen, extracellular region

Once formed, keratan sulfate proteoglycans (KSPGs) are secreted from the cell into the extracellular matrix (ECM) by an unknown translocation mechanism (Funderburgh 2000). KSPG can bind with many cell surface and extracellular proteins.

Precended by: Further sulfation on galactose residues produces KSPG

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