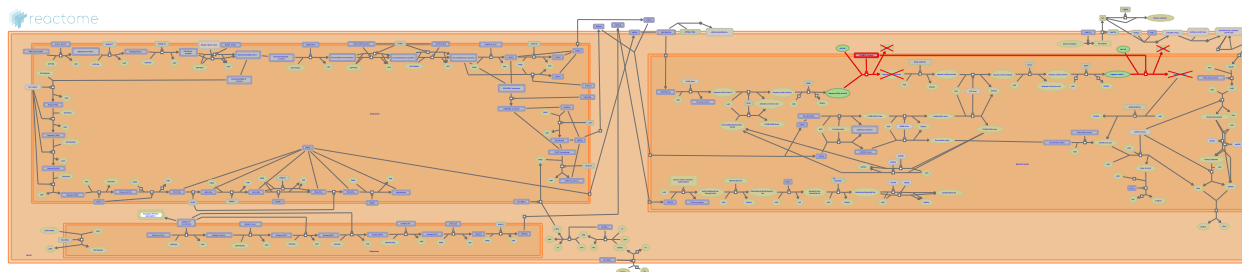


# MPS IIIC - Sanfilippo syndrome C



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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](https://reactome.org/textbook/).

30/04/2024

## 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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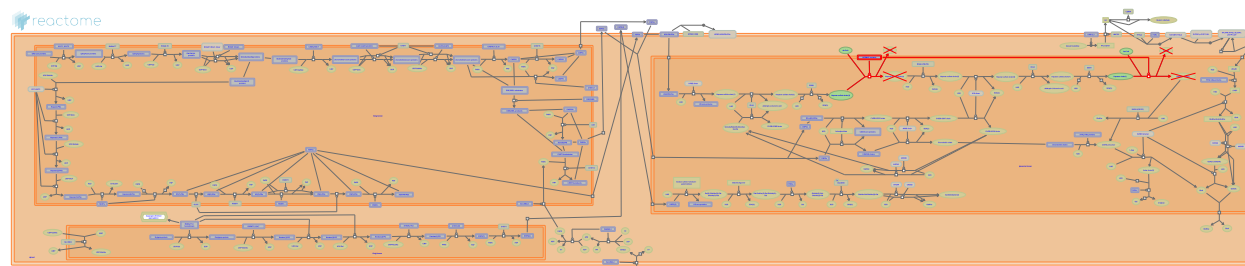
Reactome database release: 88

This document contains 1 pathway and 2 reactions ([see Table of Contents](#))

## MPS IIIC - Sanfilippo syndrome C [↗](#)

**Stable identifier:** R-HSA-2206291

**Diseases:** mucopolysaccharidosis III



Mucopolysaccharidosis III (Sanfilippo syndrome) was described in 1963 by a pediatrician named Sylvester Sanfilippo (*J. Pediat.* 63: 837838, 1963, no reference). Mucopolysaccharidosis type IIIC (MPS IIIC, Sanfilippo syndrome C; MIM:252930) is an autosomal recessive genetic disorder due to the loss of heparan alpha-glucosaminide N-acetyltransferase (HGSNAT; MIM:610453) that normally acetylates the non-reducing terminal alpha-glucosamine residue of heparan sulfate. The molecular defects underlying MPS IIIC remained unknown for almost three decades due to the low tissue content and instability of HGSNAT. But, during the last decade, the gene was cloned in parallel by two different groups and shown to contain 18 exons and span approximately 62Kb (Fan et al. 2006, Hrebicek et al. 2006). Loss of HGSNAT results in build up of this glycosaminoglycan (GAG) in cells and tissues and is characterized by severe central nervous system degeneration but only with mild somatic disease and death occurs typically during the second or third decade of life (Kresse et al. 1978, Klein et al. 1978, Feldhammer et al. 2009, de Ruijter et al. 2011).

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### Editions

2012-04-26	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Matos, L., Alves, S.

## Defective HGSNAT does not acetylate Heparan chain(1) ↗

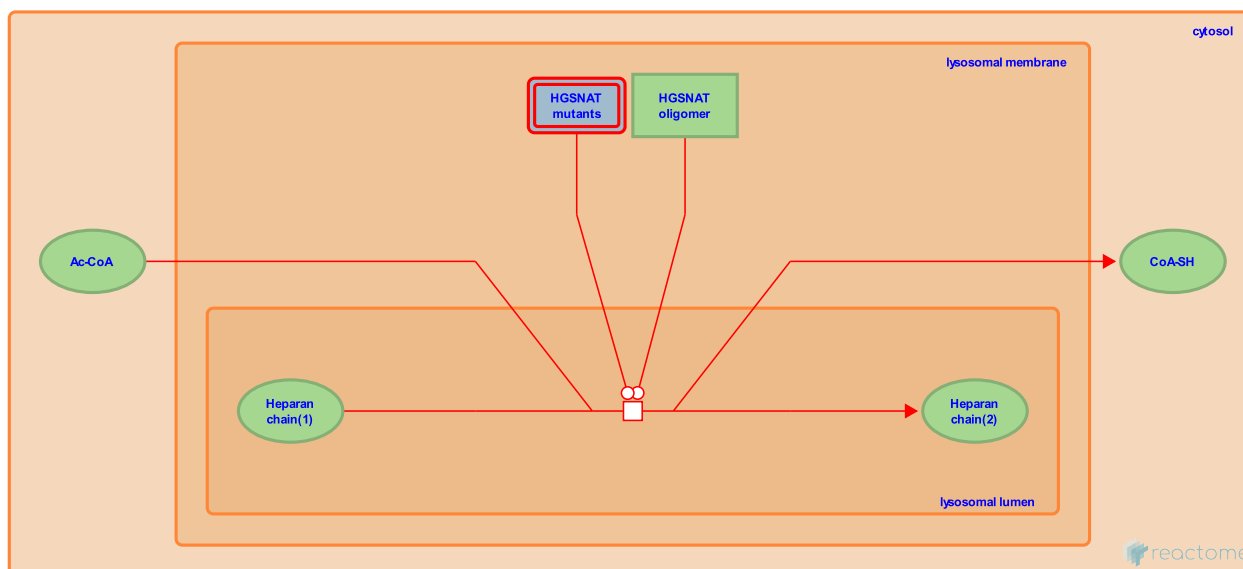
**Location:** MPS IIIC - Sanfilippo syndrome C

**Stable identifier:** R-HSA-2263492

**Type:** transition

**Compartments:** lysosomal lumen, cytosol, lysosomal membrane

**Diseases:** mucopolysaccharidosis III



Enzyme misfolding due to missense mutations results in incorrect glycosylation therefore HGSNAT is not targeted to the lysosome and stays in the ER (Feldhammer et al. 2009). This, together with mutations giving rise to nonsense-mediated mRNA decay (Fedele & Hopwood 2010), appear to be the major molecular mechanisms underlying MPSIIIC. More than 50 mutations are known in the HGSNAT gene. Some of them drastically reduce enzyme activity; W403C/A615T double mutant (Fedele & Hopwood 2010), R344C, S518F and R384X (Fedele et al. 2007, Ruijter et al.2008).

### Literature references

- Hopwood, JJ., Fedele, AO. (2010). Functional analysis of the HGSNAT gene in patients with mucopolysaccharidosis IIIC (Sanfilippo C Syndrome). *Hum Mutat*, 31, E1574-86. ↗
- Pshezhetsky, AV., Valstar, MJ., Van Diggelen, OP., van der Helm, RM., van de Kamp, JM., Ruijter, GJ. et al. (2008). Clinical and genetic spectrum of Sanfilippo type C (MPS IIIC) disease in The Netherlands. *Mol Genet Metab*, 93, 104-11. ↗
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### Editions

2012-05-21	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Matos, L., Alves, S.

## Defective HGSNAT does not acetylate Heparan sulfate chain(3) ↗

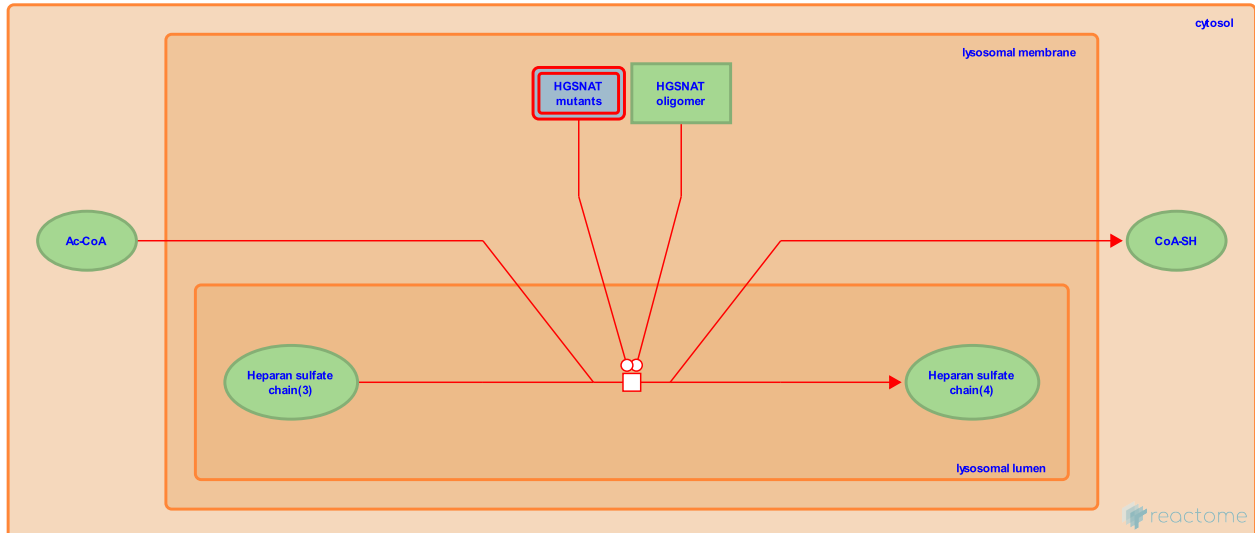
**Location:** MPS IIIC - Sanfilippo syndrome C

**Stable identifier:** R-HSA-9036056

**Type:** transition

**Compartments:** lysosomal lumen, cytosol, lysosomal membrane

**Diseases:** mucopolysaccharidosis III



Enzyme misfolding due to missense mutations results in incorrect glycosylation therefore HGSNAT is not targeted to the lysosome and stays in the ER (Feldhammer et al. 2009). This, together with mutations giving rise to nonsense-mediated mRNA decay (Fedele & Hopwood 2010), appear to be the major molecular mechanisms underlying MPSIIIC. More than 50 mutations are known in the HGSNAT gene. Some of them drastically reduce enzyme activity; W403C/A615T double mutant (Fedele & Hopwood 2010), R344C, S518F and R384X (Fedele et al. 2007, Ruijter et al.2008).

### Literature references

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