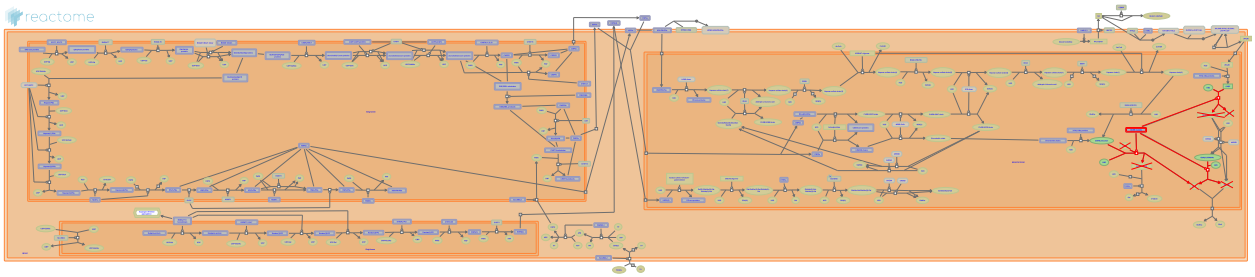
MPS VII - Sly syndrome



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29/04/2024

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.
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).

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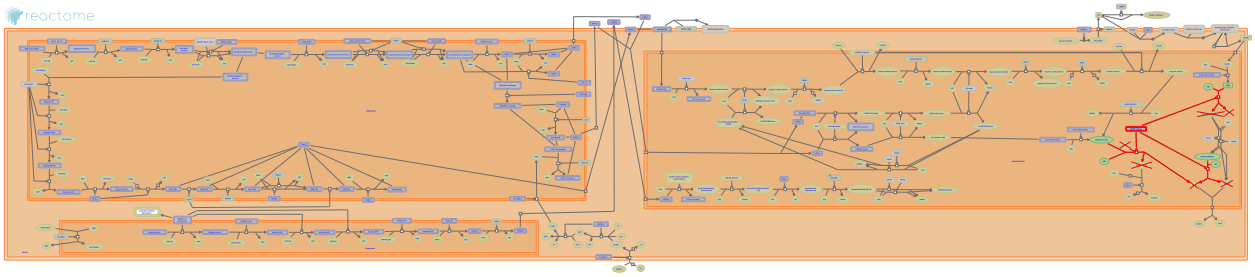
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

MPS VII - Sly syndrome ↗

Stable identifier: R-HSA-2206292

Diseases: mucopolysaccharidosis VII



Mucopolysaccharidosis type VII (MPS VII, Sly syndrome, beta-glucuronidase deficiency; MIM:253220) is an autosomal recessive lysosomal storage disease characterized by a deficiency of the enzyme beta-glucuronidase (GUSB; MIM:611499) which would normally cleave glucuronide residues from dematan sulphate, keratan sulphate and chondroitin sulphate, resulting in build up of these GAGs in cells and tissues (Sly et al. 1973). The gene encoding GUSB is 21 kb long, contains 12 exons and gives rise to two different types of cDNAs, through an alternate splicing mechanism (Miller et al. 1990). It maps to 7q11.21-q11.22 (Speleman et al. 1996). The phenotype is highly variable, ranging from severe causing death, non-immune hydrops fetalis (Vervoort et al. 1996) to mild forms with survival into adulthood (Storch et al. 2003). Most patients with the intermediate phenotype show hepatomegaly, skeletal anomalies, coarse facies, and variable degrees of mental impairment (Shipley et al. 1993, Tomatsu et al. 2009).

Literature references

Bachinsky, DR., Grubb, JH., Sly, WS., Klinkenberg, M., Wu, BM., Shipley, JM. (1993). Mutational analysis of a patient with mucopolysaccharidosis type VII, and identification of pseudogenes. *Am. J. Hum. Genet., 52*, 517-26. ↗

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Editions

2012-04-26	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Alves, S.
2012-08-28	Reviewed	Ashworth, J.

Defective GUSB does not hydrolyse (HA)2

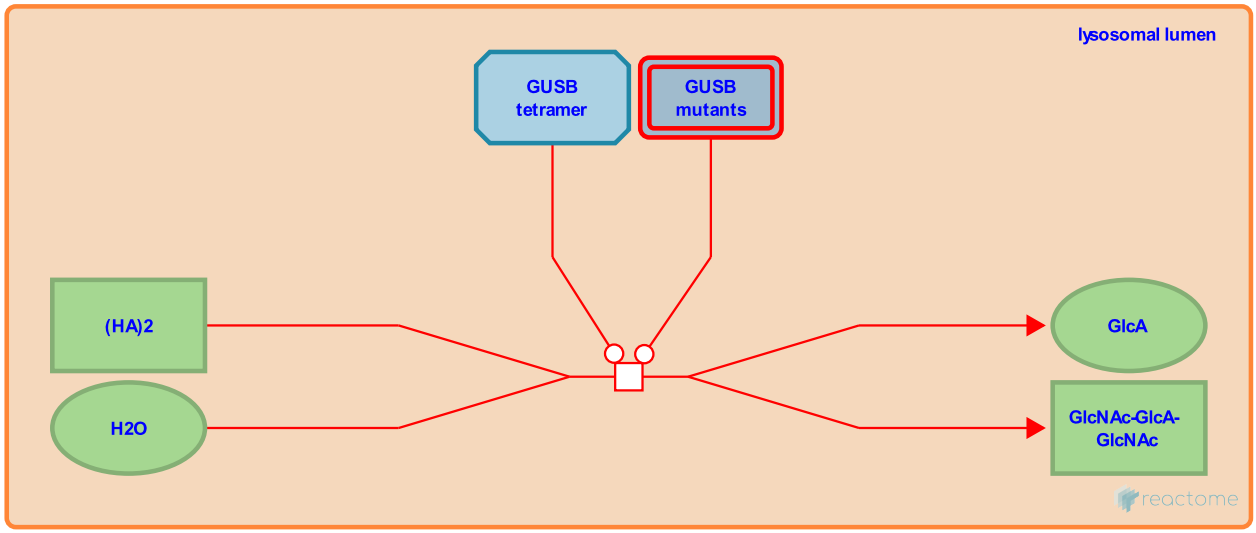
Location: MPS VII - Sly syndrome

Stable identifier: R-HSA-2318373

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis VII



Tetrameric lysosomal enzyme beta-glucuronidase (GUSB tetramer) hydrolyses glucuronate from the HA tetrasaccharide (HA(2)) resulting in the single sugars glucuronic acid and N-acetylglucosamine. Defects in beta-glucuronidase (GUSB; MIM:611499) cause mucopolysaccharidosis type VII (MPS VII, Sly syndrome, beta-glucuronidase deficiency; MIM:253220), an autosomal recessive lysosomal storage disease. Mutations causing severe forms of the disease are R356* (Shipley et al. 1993), A354V and R611W (Wu & Sly 1993), S52F (Vervoot et al. 1997) and R216W (Vervoort et al. 1996).

Literature references

Bachinsky, DR., Grubb, JH., Sly, WS., Klinkenberg, M., Wu, BM., Shipley, JM. (1993). Mutational analysis of a patient with mucopolysaccharidosis type VII, and identification of pseudogenes. *Am. J. Hum. Genet., 52*, 517-26.

Fryns, JP., Liebaers, I., Lissens, W., Kleijer, WJ., Vervoort, R., Wevers, R. et al. (1997). Molecular analysis of the beta-glucuronidase gene: novel mutations in mucopolysaccharidosis type VII and heterogeneity of the polyadenylation region. *Hum. Genet., 99*, 462-8.

Zabot, MT., Young, EP., Liebaers, I., Lissens, W., Chabas, A., Islam, MR. et al. (1996). Molecular analysis of patients with beta-glucuronidase deficiency presenting as hydrops fetalis or as early mucopolysaccharidosis VII. *Am. J. Hum. Genet., 58*, 457-71.

Sly, WS., Wu, BM. (1993). Mutational studies in a patient with the hydrops fetalis form of mucopolysaccharidosis type VII. *Hum. Mutat., 2*, 446-57.

Editions

2012-06-13	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Alves, S.

Defective GUSB does not hydrolyse GlcA-β1,3-GlcNAc ↗

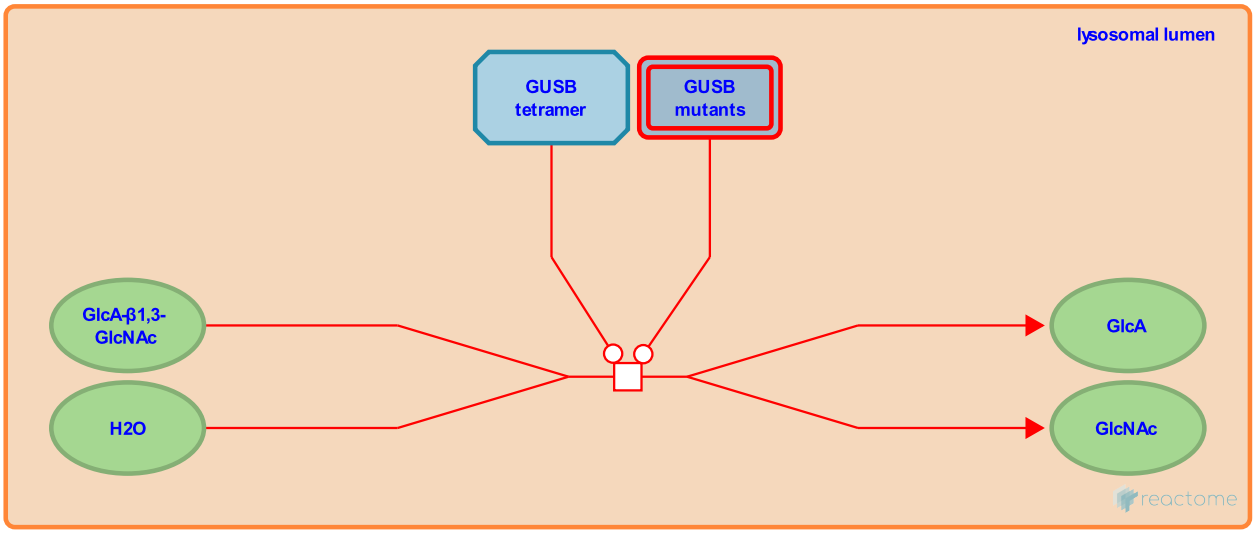
Location: MPS VII - Sly syndrome

Stable identifier: R-HSA-9036068

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis VII



Tetrameric lysosomal enzyme beta-glucuronidase (GUSB tetramer) hydrolyses glucuronate from the HA disaccharide GlcA-β1,3-GlcNAc resulting in the single sugars glucuronic acid and N-acetylglucosamine. Defects in beta-glucuronidase (GUSB; MIM:611499) cause mucopolysaccharidosis type VII (MPS VII, Sly syndrome, beta-glucuronidase deficiency; MIM:253220), an autosomal recessive lysosomal storage disease. Mutations causing severe forms of the disease are R356* (Shipley et al. 1993), A354V and R611W (Wu & Sly 1993), S52F (Vervoot et al. 1997) and R216W (Vervoort et al. 1996).

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Sly, WS., Wu, BM. (1993). Mutational studies in a patient with the hydrops fetalis form of mucopolysaccharidosis type VII. *Hum. Mutat., 2*, 446-57. ↗

Editions

2012-06-13	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Alves, S.

Defective GUSB does not hydrolyse CS/HS precursor ↗

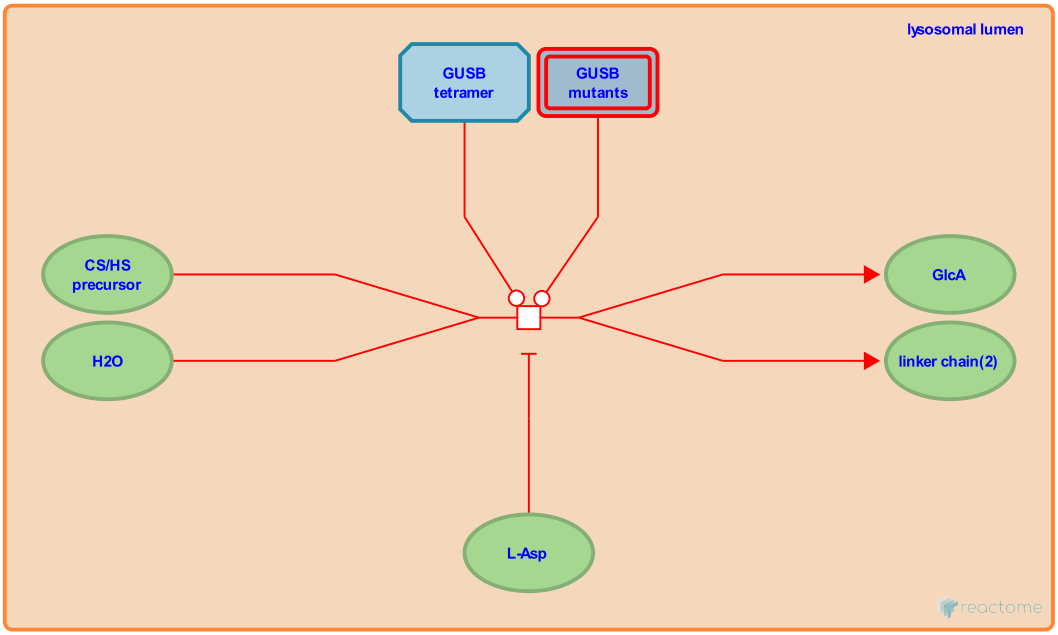
Location: MPS VII - Sly syndrome

Stable identifier: R-HSA-9036070

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis VII



Tetrameric lysosomal enzyme beta-glucuronidase (GUSB tetramer) hydrolyses glucuronate from heparan or the linker chain. Defects in beta-glucuronidase (GUSB; MIM:611499) cause mucopolysaccharidosis type VII (MPS VII, Sly syndrome, beta-glucuronidase deficiency; MIM:253220), an autosomal recessive lysosomal storage disease. Mutations causing severe forms of the disease are R356* (Shipley et al. 1993), A354V and R611W (Wu & Sly 1993), S52F (Vervoot et al. 1997) and R216W (Vervoort et al. 1996).

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Sly, WS., Wu, BM. (1993). Mutational studies in a patient with the hydrops fetalis form of mucopolysaccharidosis type VII. *Hum. Mutat., 2*, 446-57. ↗

Editions

2012-06-13	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Alves, S.

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