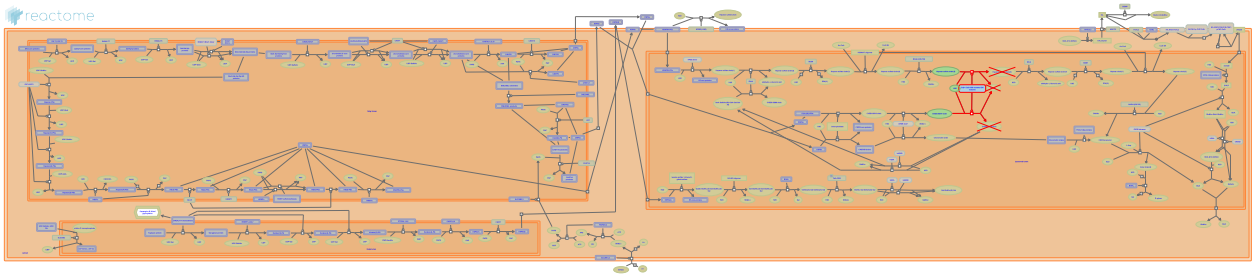
MPS II - Hunter syndrome



Alves, S., Coutinho, MF., Jassal, B., Matos, L.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

09/08/2021

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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

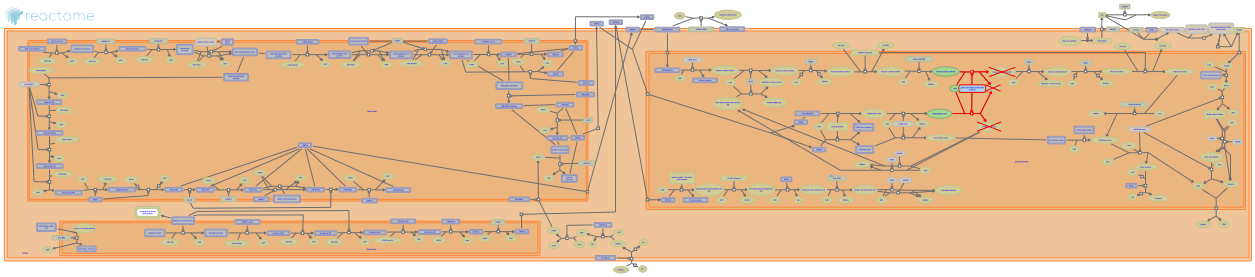
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 II - Hunter syndrome ↗

Stable identifier: R-HSA-2206296

Diseases: mucopolysaccharidosis II



Mucopolysaccharidosis II (MPS II, Hunter syndrome, MIM:309900) is an X-linked, recessive genetic disorder which therefore primarily affects males. MPS II was first described in 1917, by Major Charles Hunter (Hunter 1917) and is caused by a deficiency (or absence) of iduronate-2-sulfatase (IDS, MIM:300823), which would normally hydrolyse the 2-sulfate groups of the L-iduronate 2-sulfate units of dermatan sulfate, heparan sulfate and heparin. Without IDS, these GAGs accumulate in the body and are excessively excreted in urine. Although the disease was known since the early 1970s, being the first MPS to be defined clinically in humans, it wasn't until the 1990s that IDS was cloned. It is now known to be localized to Xq28 (Wilson et al. 1991) and contain 9 exons (Flomen et al. 1993) spanning approximately 24 kb (Wilson et al. 1993).

Build up can occur in the liver and spleen as well as in the walls and valves of the heart (reduced hepatic and cardiac function, liver/spleen hepatosplenomegaly), airways (leading to obstructive airway disease), all major joints and bones (joint stiffness and skeletal deformities) and in brain (severe mental retardation). The rate of progression and degree of severity of the disorder can be different for each person with MPS II. Severe forms of the disorder can result in death in childhood whereas those with a "milder" form can expect to live to their 20's or 30's. Some patients even survive into their fifth and sixth decades of life (Wraith et al. 2008, Beck 2011).

Literature references

Hunter, C. (1917). A Rare Disease in Two Brothers. *Proc. R. Soc. Med., 10*, 104-16. ↗

Beck, M. (2011). Mucopolysaccharidosis Type II (Hunter Syndrome): clinical picture and treatment. *Curr Pharm Biotechnol, 12*, 861-6. ↗

Wilson, PJ., Meaney, CA., Hopwood, JJ., Morris, CP. (1993). Sequence of the human iduronate 2-sulfatase (IDS) gene. *Genomics, 17*, 773-5. ↗

Wraith, JE., Scarpa, M., Beck, M., Bodamer, OA., De Meirleir, L., Guffon, N. et al. (2008). Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. *Eur J Pediatr, 167*, 267-77. ↗

Wilson, PJ., Suthers, GK., Callen, DF., Baker, E., Nelson, PV., Cooper, A. et al. (1991). Frequent deletions at Xq28 indicate genetic heterogeneity in Hunter syndrome. *Hum. Genet., 86*, 505-8. ↗

Editions

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

Defective IDS does not hydrolyse dermatan sulfate (Chebi:63517 chain) ↗

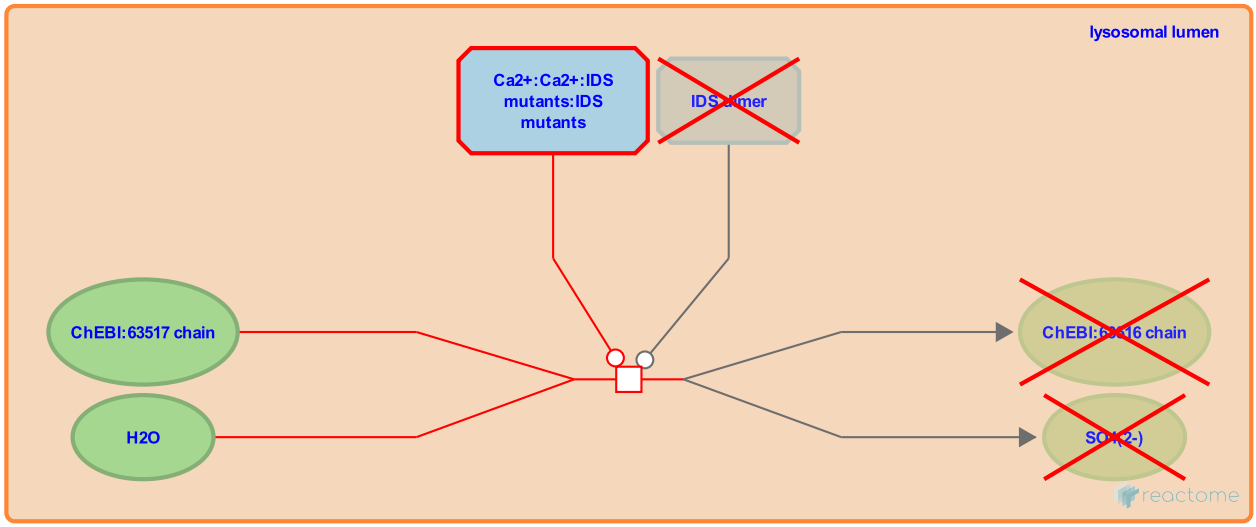
Location: MPS II - Hunter syndrome

Stable identifier: R-HSA-2262743

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis II



Mucopolysaccharidosis II (MPS II, Hunter syndrome, MIM:309900) is an X-linked genetic disorder caused by defects in the gene encoding the enzyme iduronate 2-sulfatase (IDS, MIM:300823). This causes an accumulation of the GAGs dermatan sulfate and heparan sulfate and their excessive excretion in urine. MPS II has a broad range of severity with variable mental retardation and life expectancy. This disease has a prevelence of approximately 1 in 170,000 male births (Muenzer et al. 2009). The R468 codon may be a mutational hot-spot, as it has been noted in patients with diverse ethnic origins: R468W (Crotty et al. 1992), R468L and R468Q (Isogai et al. 1998). R443X is also a frequent mutation (Froissart et al. 1998).

Literature references

Crotty, PL., Braun, SE., Anderson, RA., Whitley, CB. (1992). Mutation R468W of the iduronate-2-sulfatase gene in mild Hunter syndrome (mucopolysaccharidosis type II) confirmed by in vitro mutagenesis and expression. *Hum Mol Genet, 1*, 755-7. ↗

Isogai, K., Sukegawa, K., Tomatsu, S., Fukao, T., Song, XQ., Yamada, Y. et al. (1998). Mutation analysis in the iduronate-2-sulphatase gene in 43 Japanese patients with mucopolysaccharidosis type II (Hunter disease). *J Inherit Metab Dis, 21*, 60-70. ↗

Froissart, R., Maire, I., Millat, G., Cudry, S., Birot, AM., Bonnet, V. et al. (1998). Identification of iduronate sulfatase gene alterations in 70 unrelated Hunter patients. *Clin Genet, 53*, 362-8. ↗

Muenzer, J., Beck, M., Eng, CM., Escolar, ML., Giugliani, R., Guffon, NH. et al. (2009). Multidisciplinary management of Hunter syndrome. *Pediatrics, 124*, e1228-39. ↗

Editions

2012-05-20	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Matos, L., Alves, S.

Defective IDS does not hydrolyse Heparan sulfate chain(5) ↗

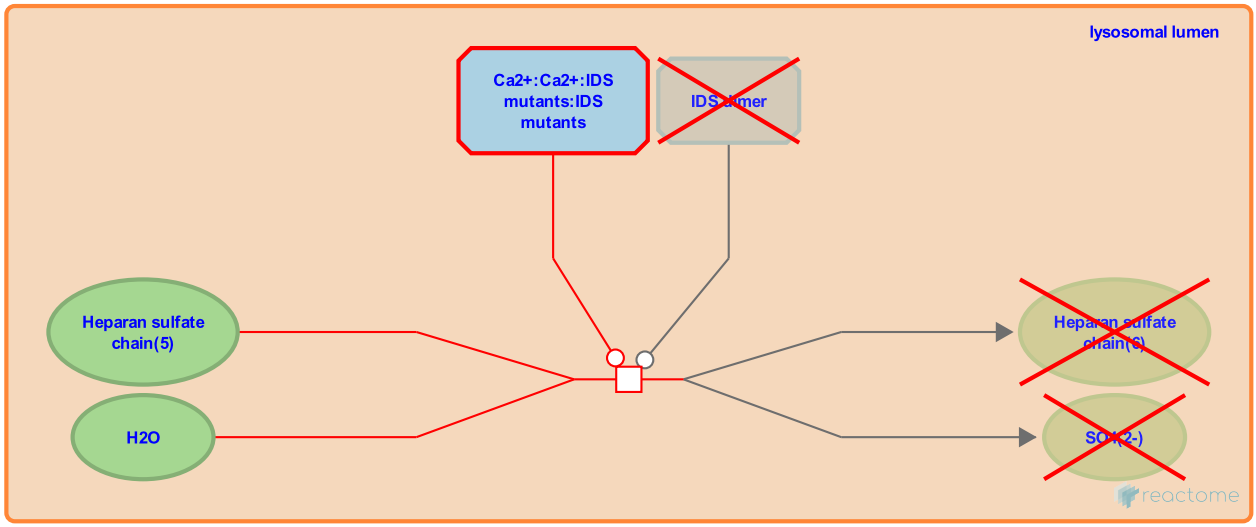
Location: MPS II - Hunter syndrome

Stable identifier: R-HSA-9036046

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis II



Mucopolysaccharidosis II (MPS II, Hunter syndrome, MIM:309900) is an X-linked genetic disorder caused by defects in the gene encoding the enzyme iduronate 2-sulfatase (IDS, MIM:300823). This causes an accumulation of the GAGs dermatan sulfate and heparan sulfate and their excessive excretion in urine. MPS II has a broad range of severity with variable mental retardation and life expectancy. This disease has a prevelence of approximately 1 in 170,000 male births (Muenzer et al. 2009). The R468 codon may be a mutational hot-spot, as it has been noted in patients with diverse ethnic origins: R468W (Crotty et al. 1992), R468L and R468Q (Isogai et al. 1998). R443X is also a frequent mutation (Froissart et al. 1998).

Literature references

Crotty, PL., Braun, SE., Anderson, RA., Whitley, CB. (1992). Mutation R468W of the iduronate-2-sulfatase gene in mild Hunter syndrome (mucopolysaccharidosis type II) confirmed by in vitro mutagenesis and expression. *Hum Mol Genet, 1*, 755-7. ↗

Isogai, K., Sukegawa, K., Tomatsu, S., Fukao, T., Song, XQ., Yamada, Y. et al. (1998). Mutation analysis in the iduronate-2-sulphatase gene in 43 Japanese patients with mucopolysaccharidosis type II (Hunter disease). *J Inherit Metab Dis, 21*, 60-70. ↗

Froissart, R., Maire, I., Millat, G., Cudry, S., Birot, AM., Bonnet, V. et al. (1998). Identification of iduronate sulfatase gene alterations in 70 unrelated Hunter patients. *Clin Genet, 53*, 362-8. ↗

Muenzer, J., Beck, M., Eng, CM., Escolar, ML., Giugliani, R., Guffon, NH. et al. (2009). Multidisciplinary management of Hunter syndrome. *Pediatrics, 124*, e1228-39. ↗

Editions

2012-05-20	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Matos, L., Alves, S.

Table of Contents

Introduction 1

MPS II - Hunter syndrome 2

Defective IDS does not hydrolyse dermatan sulfate (Chebi:63517 chain) 3

Defective IDS does not hydrolyse Heparan sulfate chain(5) 4

Table of Contents 5