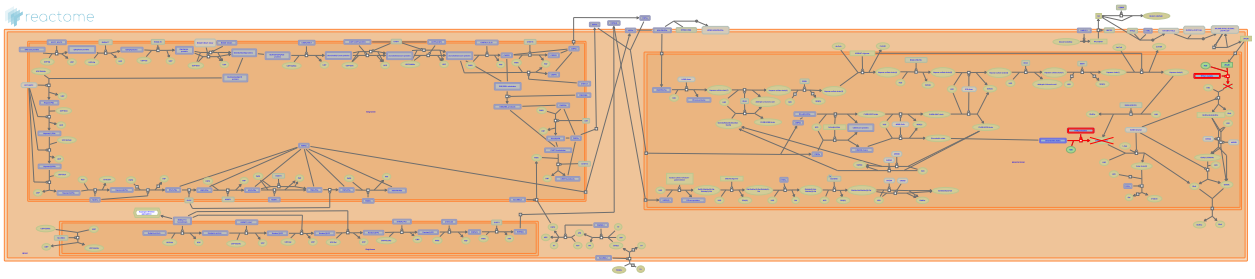
MPS IX - Natowicz syndrome



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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. ↗

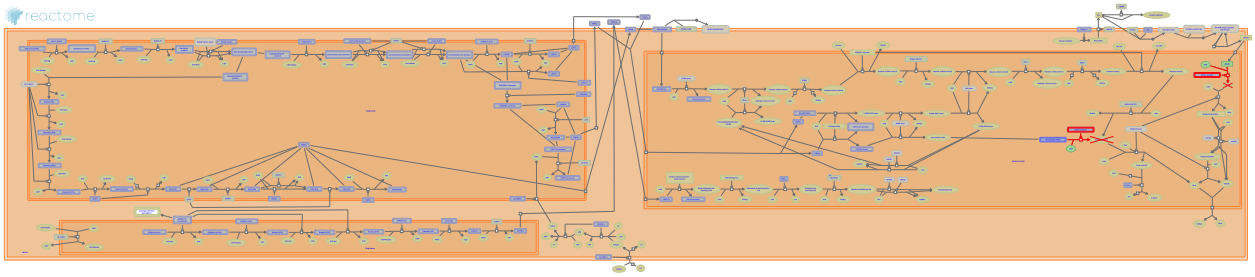
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 IX - Natowicz syndrome ↗

Stable identifier: R-HSA-2206280

Diseases: mucopolysaccharidosis



Mucopolysaccharidosis type IX (MPS IX, Natowicz syndrome, Hyaluronidase deficiency, MIM:601492) is a rare lysosomal storage disease characterized by high hyaluronan (HA) concentration in the serum resulting from deficiency in hyaluronidase 1 (HYAL1, MIM:607071) which normally hydrolyses 1-4 linkages between N-acetylglucosamine (GlcNAc) and D-glucuronate (GlcA) residues. Symptoms of MPS IX are periodically painful soft tissue masses around the joints, acquired short stature and erosion of the hip joint, although joint movement and intelligence are normal (Natowicz et al. 1996, Triggs-Raine et al. 1999).

Literature references

Salo, TJ., Natowicz, MR., Triggs-Raine, B., Wicklow, BA., Zhang, H. (1999). Mutations in HYAL1, a member of a tandemly distributed multigene family encoding disparate hyaluronidase activities, cause a newly described lysosomal disorder, mucopolysaccharidosis IX. *Proc. Natl. Acad. Sci. U.S.A., 96*, 6296-300. ↗

Short, MP., Gebhardt, MC., Natowicz, MR., Rosenthal, DI., Dickersin, GR., Sims, KB. et al. (1996). Clinical and biochemical manifestations of hyaluronidase deficiency. *N. Engl. J. Med., 335*, 1029-33. ↗

Editions

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

Defective HYAL1 does not hydrolyse Chondroitin chains ↗

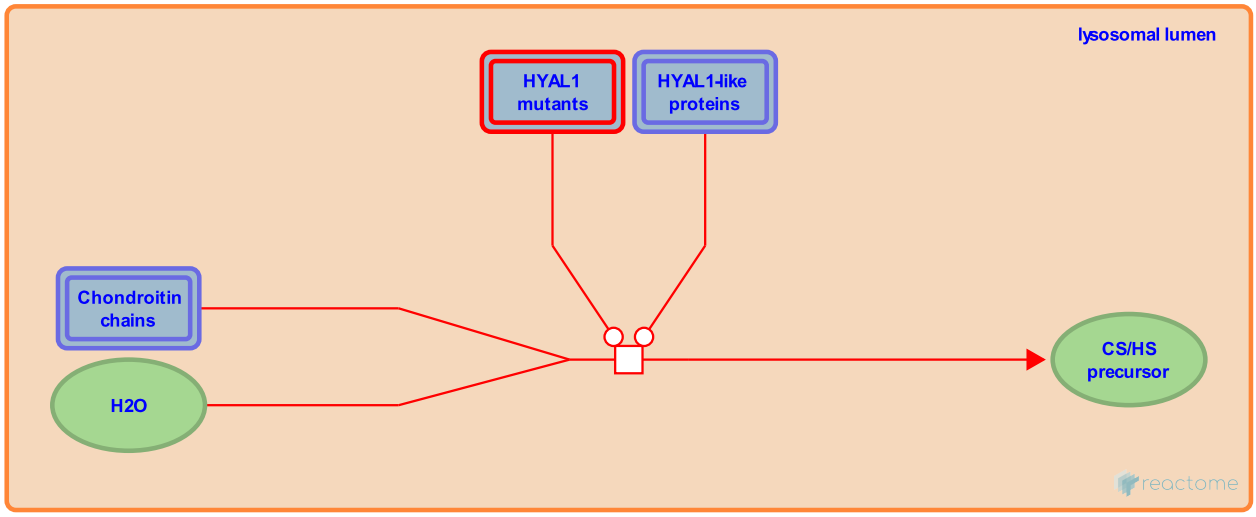
Location: MPS IX - Natowicz syndrome

Stable identifier: R-HSA-2318585

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis



Hyaluronidase 1 (HYAL1) hydrolyses 1-4 linkages between GalNAc and D-glucuronate residues in chondroitin (or dermatan). It also hydrolyses this linkage in hyaluronate, another glycosaminoglycan (GAG) composed of repeating disaccharide units but the only one which is non-sulfated. Defects in HYAL1 (MIM:607071) cause mucopolysaccharidosis type IX (MPS IX, Natowicz syndrome, Hyaluronidase deficiency, MIM:601492), a rare lysosomal storage disease. Triggs-Raine et al. identified a patient with two mutations in HYAL1 alleles, a nonconservative amino acid substitution (Glu268Lys) and a complex intragenic rearrangement (1361del37ins14) that results in a premature termination codon (Triggs-Raine et al. 1999).

Literature references

Salo, TJ., Natowicz, MR., Triggs-Raine, B., Wicklow, BA., Zhang, H. (1999). Mutations in HYAL1, a member of a tandemly distributed multigene family encoding disparate hyaluronidase activities, cause a newly described lysosomal disorder, mucopolysaccharidosis IX. *Proc. Natl. Acad. Sci. U.S.A., 96*, 6296-300. ↗

Editions

2012-06-14	Authored, Edited	Jassal, B.
2012-08-27	Reviewed	Coutinho, MF., Alves, S.

Defective HYAL1 does not hydrolyse (HA)50

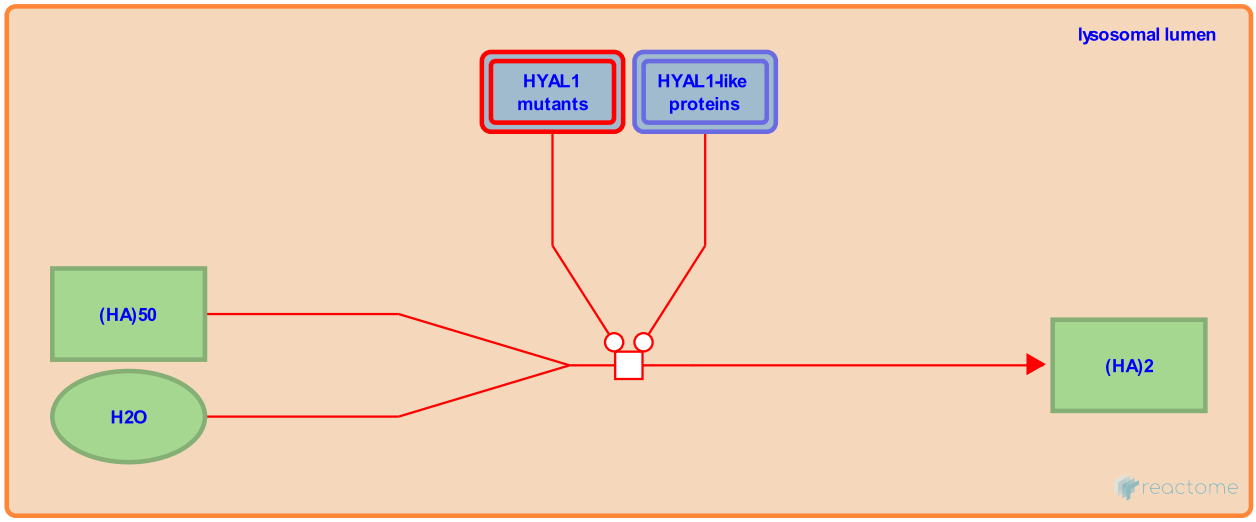
Location: MPS IX - Natowicz syndrome

Stable identifier: R-HSA-9036077

Type: transition

Compartments: lysosomal lumen

Diseases: mucopolysaccharidosis



In the acidic environment of the lysosome, hyaluronidase 1 (HYAL1) is able to hydrolyse large 20kDa HA fragments (approximately 50 disaccharide units) to 800 Da fragments (2 disaccharide units). Defects in HYAL1 (MIM:607071) cause mucopolysaccharidosis type IX (MPS IX, Natowicz syndrome, Hyaluronidase deficiency, MIM:601492), a rare lysosomal storage disease. Triggs-Raine et al. identified a patient with two mutations in HYAL1 alleles, a nonconservative amino acid substitution (Glu268Lys, that is HYAL1 E268K) and a complex intragenic rearrangement (1361del37ins14, that is HYAL1 V251Ffs*20) that results in a premature termination codon (Triggs-Raine et al. 1999).

Literature references

Salo, TJ., Natowicz, MR., Triggs-Raine, B., Wicklow, BA., Zhang, H. (1999). Mutations in HYAL1, a member of a tandemly distributed multigene family encoding disparate hyaluronidase activities, cause a newly described lysosomal disorder, mucopolysaccharidosis IX. *Proc. Natl. Acad. Sci. U.S.A., 96*, 6296-300.

Editions

2012-06-14	Authored, Edited	Jassal, B.
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