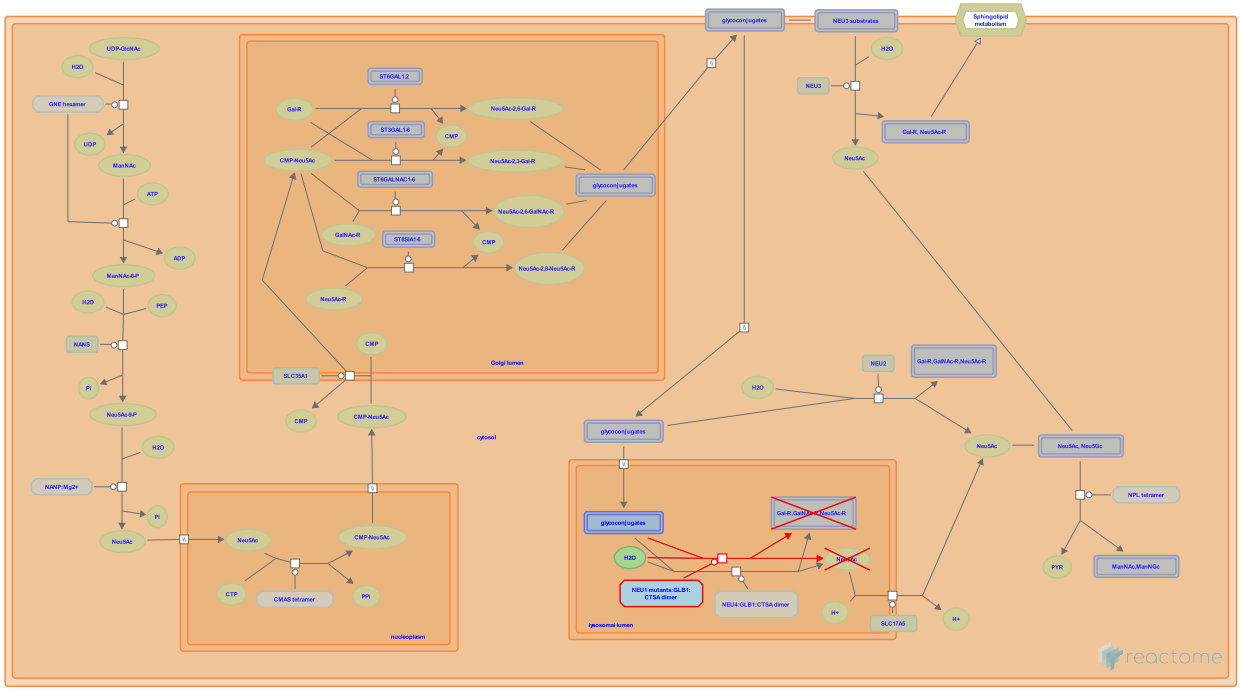
Defective NEU1 causes sialidosis



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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.

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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.

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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. ↗

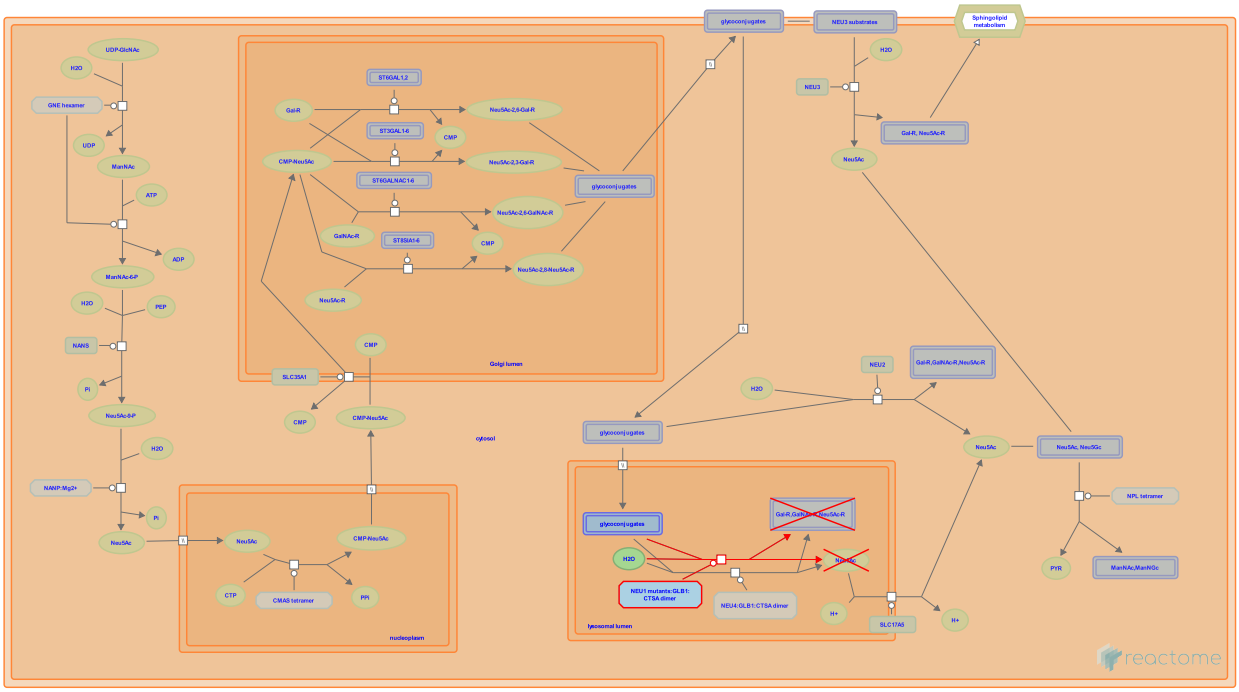
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Defective NEU1 causes sialidosis ↗

Stable identifier: R-HSA-4341670

Diseases: lysosomal storage disease



Sialidases have important roles in the degradation of glycoconjugates by removing terminal sialic acid residues. Defects in sialidase 1 (NEU1) cause sialidosis, a lysosomal storage disease characterised by the progressive lysosomal storage of sialidated glycopeptides and oligosaccharides and the accumulation and excretion of N-acetylneuraminic acid (Neu5Ac) covalently-linked ('bound') glycoconjugates (Lowden & O'Brien 1979). The sialidoses are distinct from the sialurias in which there is storage and excretion of 'free' Neu5Ac. Sialidosis manifests into types I and II forms. Type I is the milder form, also known as the 'normosomatic' type or the cherry red spot-myoclonus syndrome. Sialidosis type II is the more severe form with an earlier onset, and is also known as the 'dysmorphic' type.

Literature references

Lowden, JA., O'Brien, JS. (1979). Sialidosis: a review of human neuraminidase deficiency. *Am. J. Hum. Genet., 31*, 1-18 . ↗

Editions

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2015-04-30	Reviewed	Spillmann, D.

Defective NEU1 does not hydrolyse Neu5Ac from glycoconjugates ↗

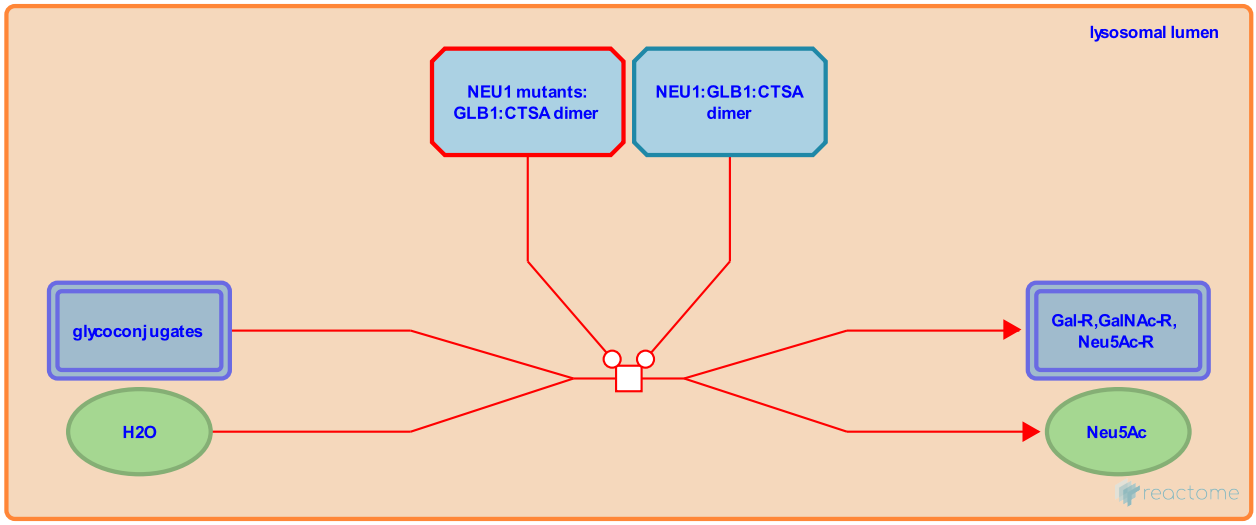
Location: Defective NEU1 causes sialidosis

Stable identifier: R-HSA-4341669

Type: transition

Compartments: lysosomal lumen

Diseases: lysosomal storage disease



NEU1 Sialidase 1 (NEU1, neuraminidase, receptor-destroying enzyme, RDE) normally hydrolyses N-acetylneuraminic acid (Neu5Ac) from glycoconjugates with alpha2,3-, alpha2,6- or alpha2,8-linked terminal sialated residues in the lysosomal lumen, a step in the degradation process of glycoproteins and gangliosides. NEU1 is active in a multienzyme complex comprising cathepsin A protective protein (CTSA) and beta-galactosidase (Bonten et al. 1996, Rudenko et al. 1995). Defects in NEU1 cause Sialidosis (MIM:256550), a lysosomal storage disorder manifesting as type I (late-onset) or type II (earlier-onset) (Bonten et al. 1996). Generally, patients with the more severe type II disease have catalytically inactive enzymes whereas patients with the milder type I disease have some residual activity. Mutations causing the severest type II disease include E377*, L303P, W29*, R225P and W23* (Bonten et al. 1996, Pshezhetsky et al. 1997, Sergi et al. 2001, Pattison et al. 2004).

Literature references

Pankarican, M., Igdoura, SA., Rupar, CA., Graham, FL., Pattison, S. (2004). Five novel mutations in the lysosomal sialidase gene (NEU1) in type II sialidosis patients and assessment of their impact on enzyme activity and intracellular targeting using adenovirus-mediated expression. *Hum. Mutat., 23*, 32-9. ↗

Sergi, C., Zoubaa, S., Rieger, P., Otto, HF., Dietrich, H., Cantz, M. et al. (2001). Prenatal diagnosis and fetal pathology in a Turkish family harboring a novel nonsense mutation in the lysosomal alpha-N-acetyl-neuraminidase (sialidase) gene. *Hum. Genet., 109*, 421-8. ↗

Igdoura, S., Dallaire, L., Elsliger, MA., Qu, J., Wang, S., Richard, C. et al. (1997). Cloning, expression and chromosomal mapping of human lysosomal sialidase and characterization of mutations in sialidosis. *Nat. Genet., 15*, 316-20. ↗

van der Spoel, A., Grosveld, G., d'Azzo, A., Fornerod, M., Bonten, E. (1996). Characterization of human lysosomal neuraminidase defines the molecular basis of the metabolic storage disorder sialidosis. *Genes Dev, 10*, 3156-69. ↗

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