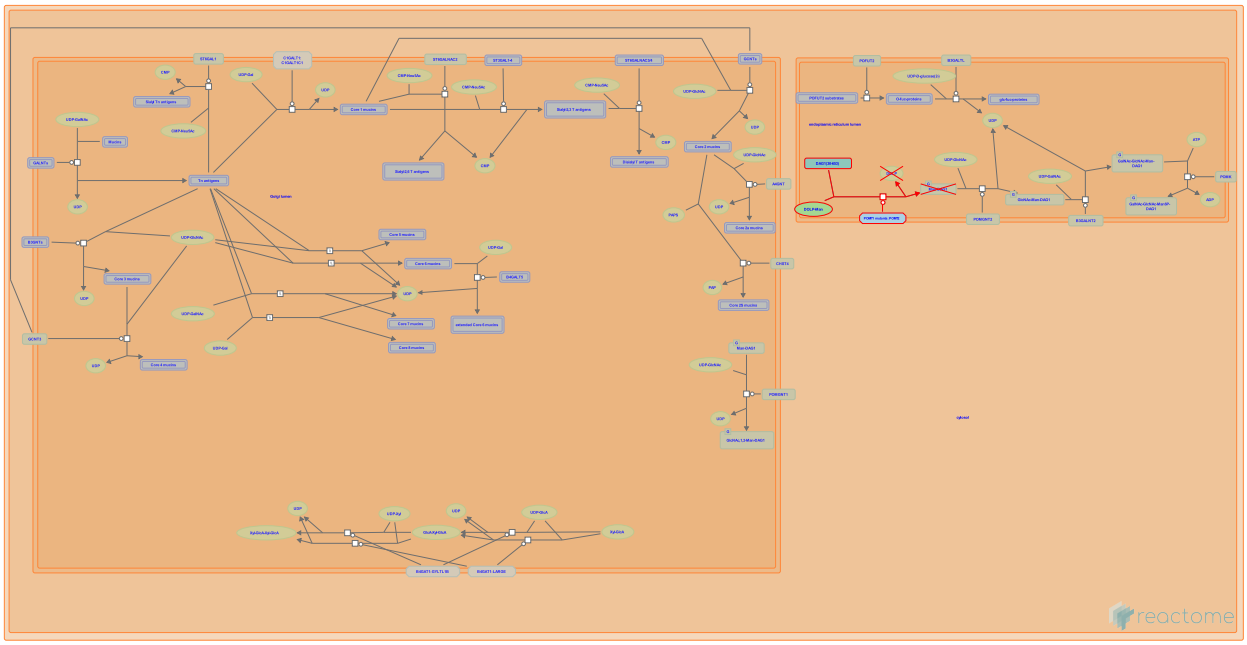
Defective POMT1 causes MDDGA1, MDDGB1 and MDDGC1



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04/05/2024

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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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. ↗

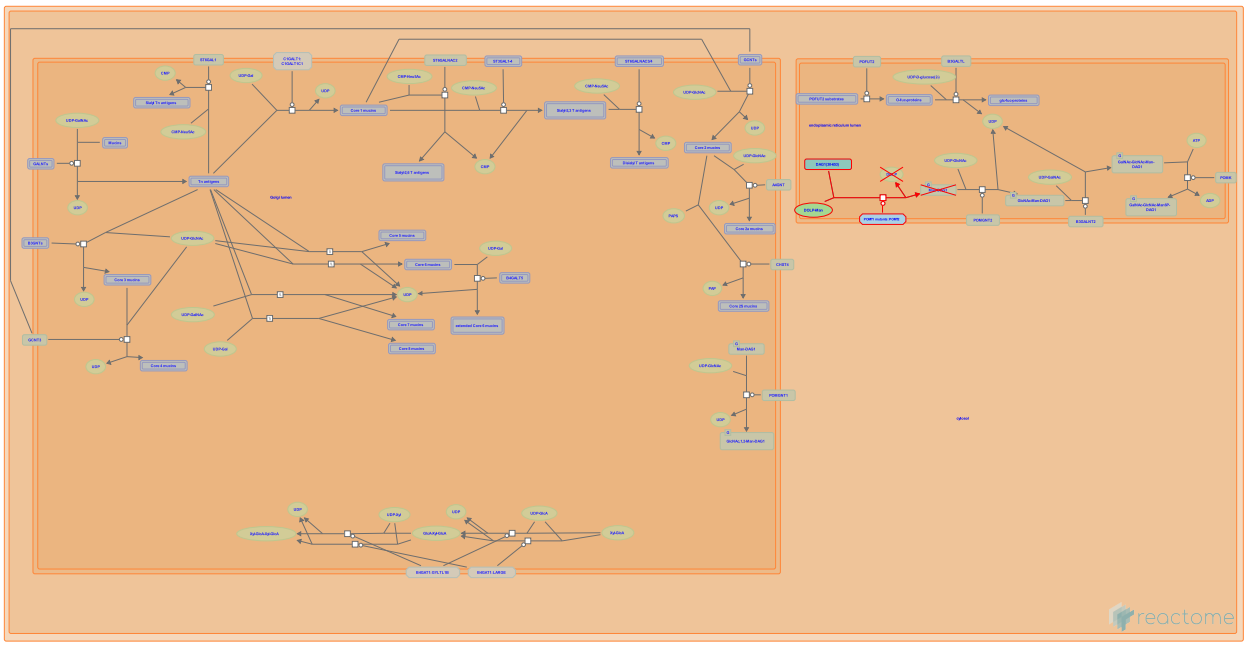
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 POMT1 causes MDDGA1, MDDGB1 and MDDGC1 ↗

Stable identifier: R-HSA-5083633

Diseases: muscular dystrophy-dystroglycanopathy



Co-expression of both protein O-mannosyl-transferases 1 and 2 (POMT1 and POMT2; CAZy family GT39) is necessary for enzyme activity, that is mediating the transfer of mannosyl residues to the hydroxyl group of serine or threonine residues of proteins such as alpha-dystroglycan (DAG1; MIM:128239). DAG1 is a cell surface protein that plays an important role in the assembly of the extracellular matrix in muscle, brain, and peripheral nerves by linking the basal lamina to cytoskeletal proteins. Defects in POMT1 (MIM:607423) results in defective glycosylation of DAG1 and can cause severe congenital muscular dystrophy-dystroglycanopathies ranging from a severe type A, MDDGA1 (brain and eye abnormalities; MIM:236670), through a less severe type B, MDDGB1 (congenital form with mental retardation; MIM:613155) to a milder type C, MDDGC1 (limb girdle form; MIM:609308) (Bertini et al. 2011, Wells 2013).

Literature references

Wells, L. (2013). The o-mannosylation pathway: glycosyltransferases and proteins implicated in congenital muscular dystrophy. *J. Biol. Chem., 288*, 6930-5. ↗

Gualandi, F., D'Amico, A., Petrini, S., Bertini, E. (2011). Congenital muscular dystrophies: a brief review. *Semin Pediatr Neurol, 18*, 277-88. ↗

Editions

2013-11-07	Authored, Edited	Jassal, B.
2015-12-18	Reviewed	Joshi, HJ., Hansen, L.

Defective POMT1 does not transfer Man from Dol-P-Man to DAG1 ↗

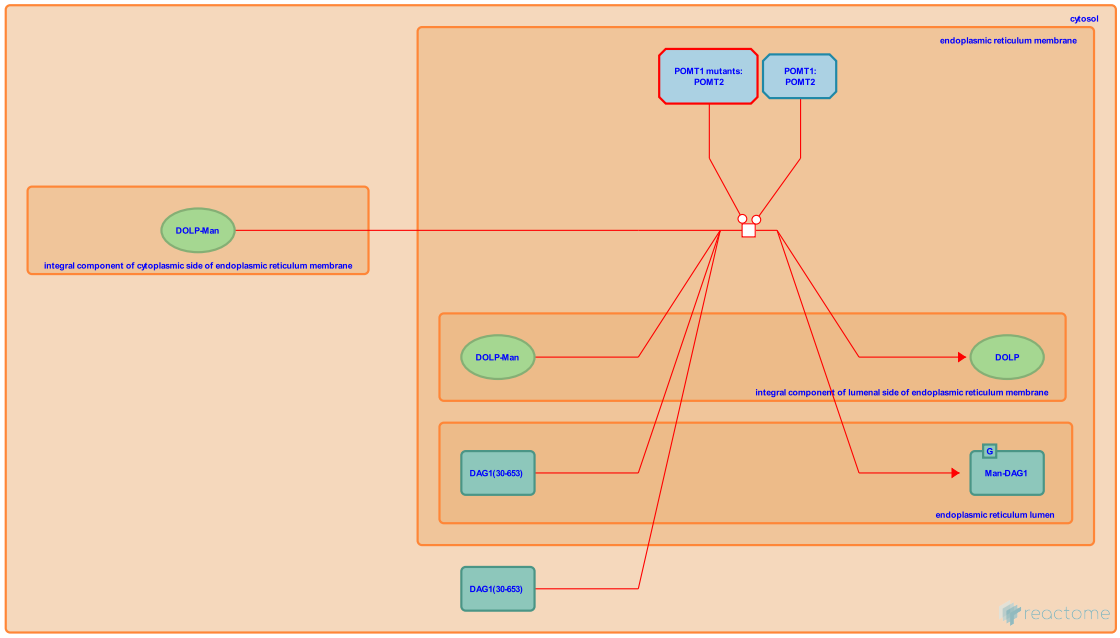
Location: Defective POMT1 causes MDDGA1, MDDGB1 and MDDGC1

Stable identifier: R-HSA-5615604

Type: transition

Compartments: endoplasmic reticulum membrane, integral component of cytoplasmic side of endoplasmic reticulum membrane, cytosol

Diseases: muscular dystrophy-dystroglycanopathy



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Several mutations are known and mutations causing the severest type A1 form include G76R, Q303*, S727Afs*3, W705Lfs*26 and D723Efs*8 (Beltran-Valero de Bernabe et al. 2002, Godfrey et al. 2007, Mercuri et al. 2009).

Literature references

Talim, B., Smith, J., Abbs, S., Brown, SC., Clement, E., Godfrey, C. et al. (2007). Refining genotype phenotype correlations in muscular dystrophies with defective glycosylation of dystroglycan. *Brain, 130*, 2725-35. ↗

Scuderi, C., Mottarelli, E., Morandi, L., Laverda, A., Saredi, S., Moggio, M. et al. (2009). Congenital muscular dystrophies with defective glycosylation of dystroglycan: a population study. *Neurology, 72*, 1802-9. ↗

Wells, L. (2013). The o-mannosylation pathway: glycosyltransferases and proteins implicated in congenital muscular dystrophy. *J. Biol. Chem., 288*, 6930-5. ↗

Merlini, L., Brunner, HG., van Bokhoven, H., Chitayat, D., van Beusekom, E., Celli, J. et al. (2002). Mutations in the O-mannosyltransferase gene POMT1 give rise to the severe neuronal migration disorder Walker-Warburg syndrome. *Am. J. Hum. Genet., 71*, 1033-43. ↗

Gualandi, F., D'Amico, A., Petrini, S., Bertini, E. (2011). Congenital muscular dystrophies: a brief review. *Semin Pediatr Neurol, 18*, 277-88. ↗

Editions

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2015-12-18	Reviewed	Joshi, HJ., Hansen, L.

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