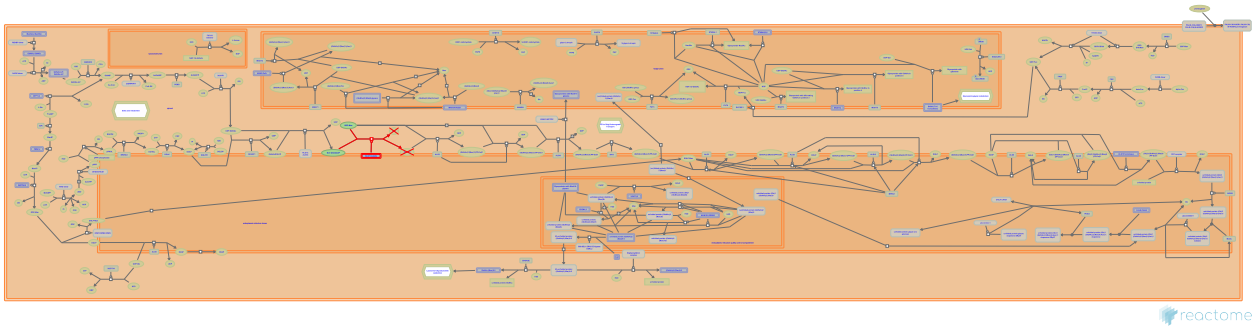
Defective ALG1 causes ALG1-CDG (CDG-1k)



Belaya, K., Jassal, B.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

27/09/2020

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. ↗

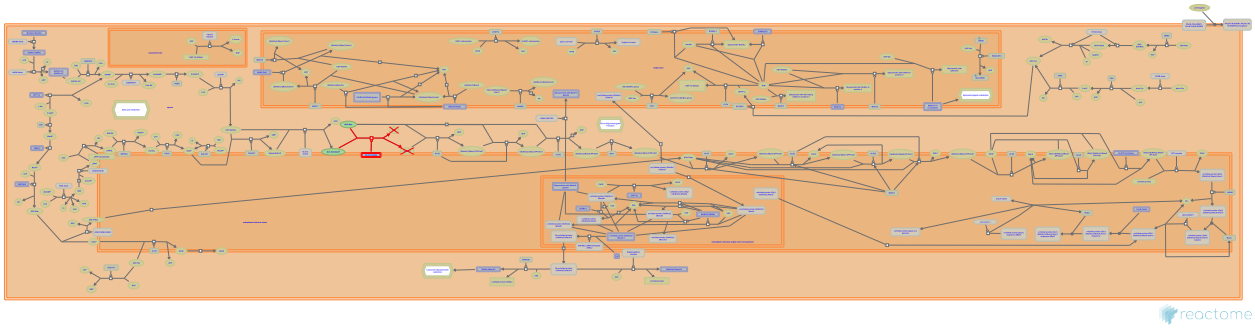
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Defective ALG1 causes ALG1-CDG (CDG-1k)

Stable identifier: R-HSA-4549380

Diseases: congenital disorder of glycosylation type I



Chitobiosyldiphosphodolichol beta-mannosyltransferase (ALG1) normally tranfers a mannose moiety to the lipid-linked oligosaccharide (LLO aka N-glycan precursor) which is required for subsequent N-glycosylation of proteins. Defects in ALG1 can cause congenital disorder of glycosylation 1k (ALG1-CDG, previously known as CDG1k; MIM:608540), a multisystem disorder characterised by under-glycosylated serum glycoproteins. CDG type 1 diseases result in a wide variety of clinical features, such as defects in the nervous system development, psychomotor retardation, dysmorphic features, hypotonia, coagulation disorders, and immunodeficiency. Compared to other CDGs, ALG1-CDG has a very severe phenotype, which can result in an early death (Schwarz et al. 2004, Kranz et al. 2004, Dupre et al. 2010).

Literature references

Dupré, T., Vuillaumier-Barrot, S., Chantret, I., Yayé, HS., Le Bizec, C., Afenjar, A. et al. (2010). Guanosine diphosphate-mannose:GlcNAc2-PP-dolichol mannosyltransferase deficiency (congenital disorders of glycosylation type Ik): five new patients and seven novel mutations. *J. Med. Genet., 47*, 729-35.

Schwarz, M., Thiel, C., Lübbehusen, J., Dorland, B., de Koning, T., von Figura, K. et al. (2004). Deficiency of GDP-Man:GlcNAc2-PP-dolichol mannosyltransferase causes congenital disorder of glycosylation type Ik. *Am J Hum Genet, 74*, 472-81.

Kranz, C., Denecke, J., Lehle, L., Sohlbach, K., Jeske, S., Meinhardt, F. et al. (2004). Congenital disorder of glycosylation type Ik (CDG-Ik): a defect of mannosyltransferase I. *Am J Hum Genet, 74*, 545-51.

Editions

2013-09-12	Authored, Edited	Jassal, B.
2014-10-31	Reviewed	Belaya, K.

Defective ALG1 does not transfer the first Man to the N-glycan precursor ↗

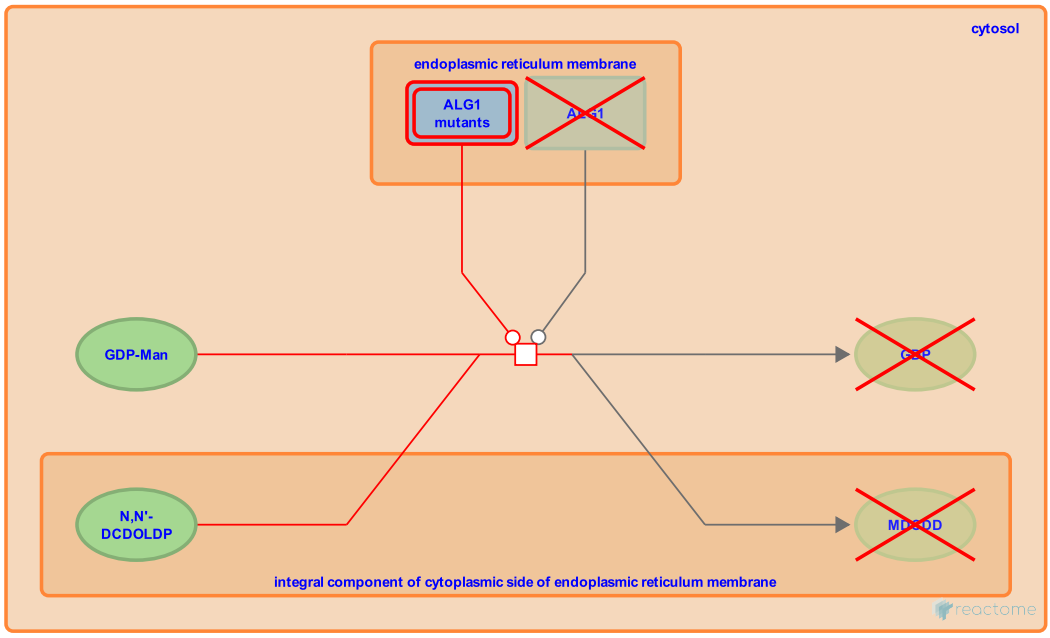
Location: Defective ALG1 causes ALG1-CDG (CDG-1k)

Stable identifier: R-HSA-4549382

Type: transition

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

Diseases: congenital disorder of glycosylation type I



Chitobiosyldiphosphodolichol beta-mannosyltransferase (ALG1) normally tranfers a mannose moiety to the lipid-linked oligosaccharide (LLO aka N-glycan precursor) which is required for subsequent N-glycosylation of proteins. Defects in ALG1 can cause congenital disorder of glycosylation 1k (ALG1-CDG, previously known as CDG1k; MIM:608540), a multisystem disorder characterised by under-glycosylated serum glycoproteins. CDG type 1 diseases result in a wide variety of clinical features, such as defects in the nervous system development, psychomotor retardation, dysmorphic features, hypotonia, coagulation disorders, and immunodeficiency. Compared to other CDGs, ALG1-CDG has a very severe phenotype, which can result in an early death. Mutations in ALG1 causing ALG1-CDG include S258L, G342P, S150R, M377V, G145D, C396* and R276W (Schwarz et al. 2004, Kranz et al. 2004, Grubenmann et al. 2004, Dupre et al. 2010).

Literature references

Kranz, C., Denecke, J., Lehle, L., Sohlbach, K., Jeske, S., Meinhardt, F. et al. (2004). Congenital disorder of glycosylation type Ik (CDG-Ik): a defect of mannosyltransferase I. *Am J Hum Genet, 74*, 545-51. ↗

Schwarz, M., Thiel, C., Lübbehusen, J., Dorland, B., de Koning, T., von Figura, K. et al. (2004). Deficiency of GDP-Man:GlcNAc2-PP-dolichol mannosyltransferase causes congenital disorder of glycosylation type Ik. *Am J Hum Genet, 74*, 472-81. ↗

Dupré, T., Vuillaumier-Barrot, S., Chantret, I., Yayé, HS., Le Bizec, C., Afenjar, A. et al. (2010). Guanosine diphosphate-mannose:GlcNAc2-PP-dolichol mannosyltransferase deficiency (congenital disorders of glycosylation type Ik): five new patients and seven novel mutations. *J. Med. Genet., 47*, 729-35. ↗

Grubenmann, CE., Frank, CG., Hülsmeier, AJ., Schollen, E., Matthijs, G., Mayatepek, E. et al. (2004). Deficiency of the first mannosylation step in the N-glycosylation pathway causes congenital disorder of glycosylation type Ik. *Hum Mol Genet, 13*, 535-42. ↗

Editions

2013-09-12	Authored, Edited	Jassal, B.
2014-10-31	Reviewed	Belaya, K.

Table of Contents