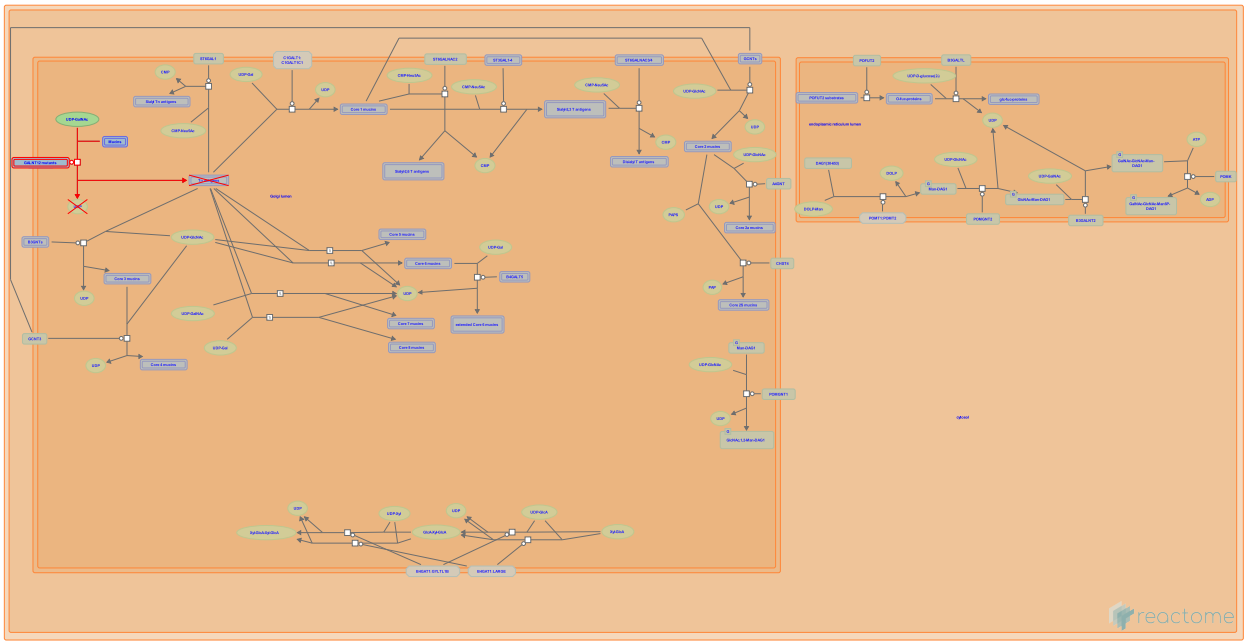
Defective GALNT12 causes CRCS1



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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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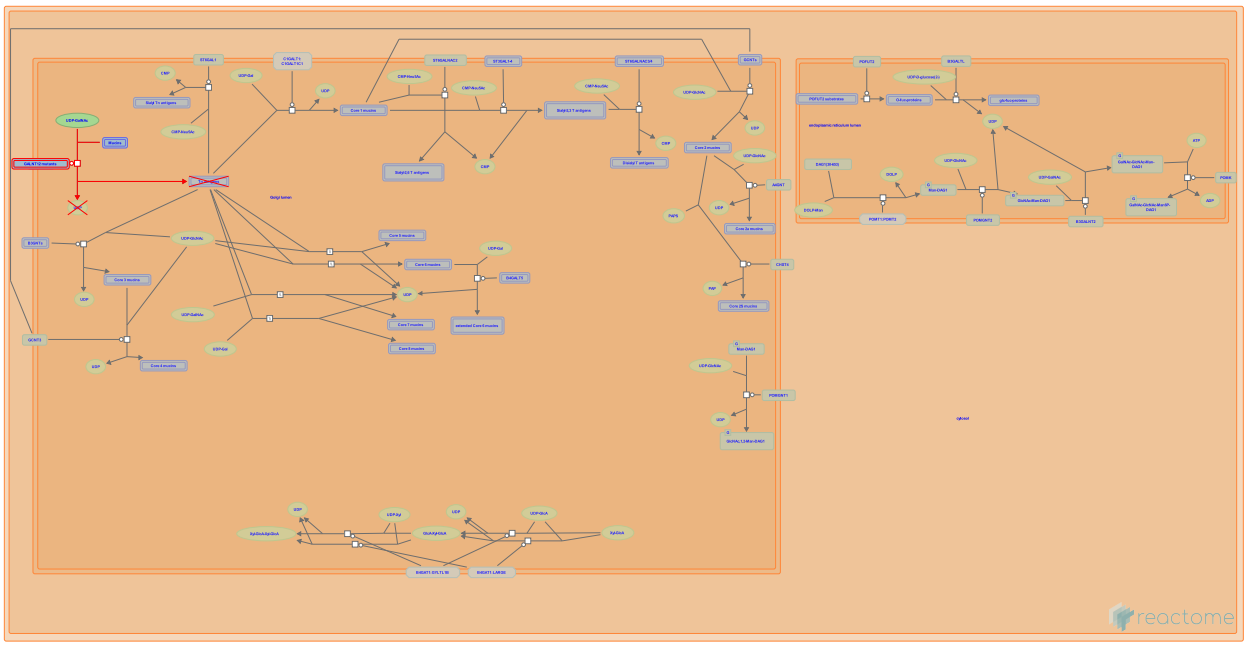
Defective GALNT12 causes CRCS1

Stable identifier: R-HSA-5083636

Diseases: colorectal cancer



The family of UDP GalNAc:polypeptide N acetylgalactosaminyltransferases (GalNAc transferases, GALNTs) carry out the addition of N acetylgalactosamine on serine, threonine or possibly tyrosine residues on a wide variety of proteins, and most commonly associated with mucins (Wandall et al. 1997). This reaction takes place in the Golgi apparatus (Rottger et al. 1998). There are 20 known members of the GALNT family, 15 of which have been characterised and 5 candidate members which are thought to belong to this family based on sequence similarity (Bennett et al. 2012). The GALNT-family is classified as belonging to CAZy family GT27. Defects in one of the GALNT family, GALNT12 (Guo et al. 2002) (MIM: 610290) can result in decreased glycosylation of mucins, mainly expressed in the digestive organs such as the stomach, small intestine and colon, and may play a role in colorectal cancer 1 (CRCS1; MIM:608812). CRCS1 is a complex disease characterised by malignant lesions arising from the inner walls of the colon and rectum (Guda et al. 2009, Clarke et al. 2012).

Literature references

Fritz, TA., Mandel, U., Bennett, EP., Tabak, LA., Gerken, TA., Clausen, H. (2012). Control of mucin-type O-glycosylation: a classification of the polypeptide GalNAc-transferase gene family. *Glycobiology, 22*, 736-56.

Whitehouse, C., White, J., Bennett, EP., Olivo, JC., Röttger, S., Berger, EG. et al. (1998). Localization of three human polypeptide GalNAc-transferases in HeLa cells suggests initiation of O-linked glycosylation throughout the Golgi apparatus. *J Cell Sci, 111*, 45-60.

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Papadopoulos, N., Lowe, JB., Lawrence, E., Wiesner, GL., Willis, J., Moinova, H. et al. (2009). Inactivating germ-line and somatic mutations in polypeptide N-acetylgalactosaminyltransferase 12 in human colon cancers. *Proc. Natl. Acad. Sci. U.S.A., 106*, 12921-5.

Burchell, J., Bennett, EP., Hassan, H., Taylor-Papadimitriou, J., Roepstorff, P., Hollingsworth, MA. et al. (1997). Substrate specificities of three members of the human UDP-N-acetyl-alpha-D-galactosamine:Polypeptide N-acetylgalactosaminyltransferase family, GalNAc-T1, -T2, and -T3. *J Biol Chem, 272*, 23503-14.

Editions

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

Defective GALNT12 does not transfer GalNAc to mucins ↗

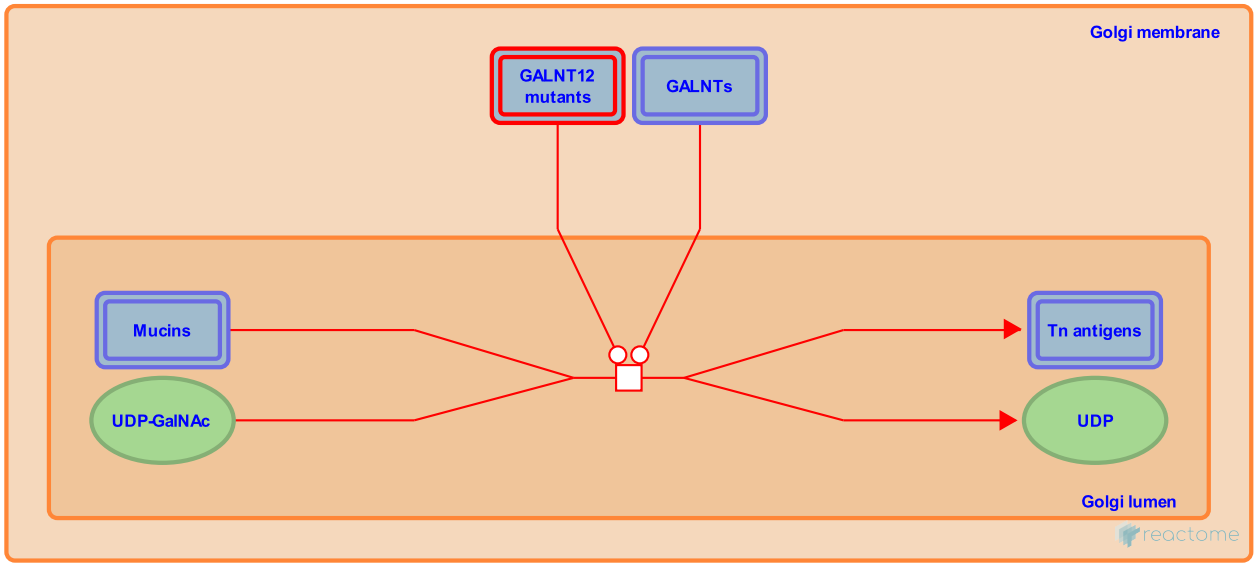
Location: Defective GALNT12 causes CRCS1

Stable identifier: R-HSA-5096532

Type: transition

Compartments: Golgi lumen, Golgi membrane

Diseases: colorectal cancer



The family of UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferases (GalNAc-transferases, GALNTs) carry out the addition of N-acetylgalactosamine (GalNAc) on serine or threonine residues of proteins, especially mucins. This is the initial reaction in the formation of O-linked oligosaccharide biosynthesis (Guo et al. 2002). Defects in one of the GALNT family, GALNT12, can result in decreased glycosylation of mucins, mainly expressed in the digestive organs such as the stomach, small intestine and colon, and may play a role in colorectal cancer 1 (CRCS1; MIM:608812). CRCS1 is a complex disease characterised by malignant lesions arising from the inner walls of the colon and rectum. Mutations implicated in CRCS1 are M1I, T491M, Y395* (Guda et al. 2009), D303N and Y396C (Clarke et al. 2012).

Literature references

Fritz, TA., Mandel, U., Bennett, EP., Tabak, LA., Gerken, TA., Clausen, H. (2012). Control of mucin-type O-glycosylation: a classification of the polypeptide GalNAc-transferase gene family. *Glycobiology, 22*, 736-56. ↗

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Papadopoulos, N., Lowe, JB., Lawrence, E., Wiesner, GL., Willis, J., Moinova, H. et al. (2009). Inactivating germ-line and somatic mutations in polypeptide N-acetylgalactosaminyltransferase 12 in human colon cancers. *Proc. Natl. Acad. Sci. U.S.A., 106*, 12921-5. ↗

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Editions

2013-11-11	Authored, Edited	Jassal, B.
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