Defective EXT2 (in EXT1:EXT2) does not transfer GlcA to heparan

Jassal, B., Spillmann, D.

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

04/03/2021

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. ↗

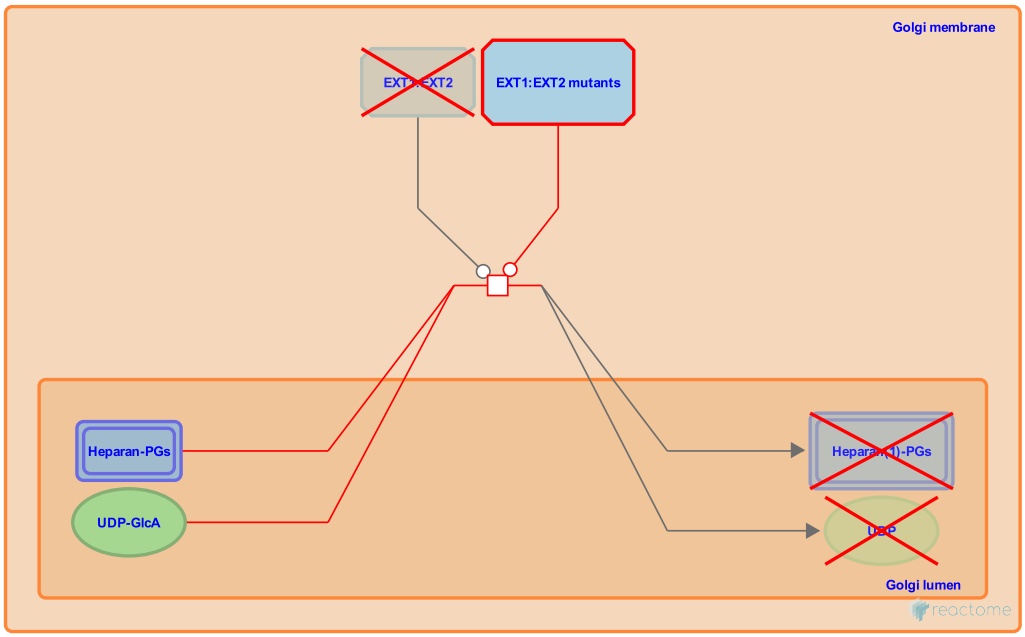
Defective EXT2 (in EXT1:EXT2) does not transfer GlcA to heparan ↗

Stable identifier: R-HSA-9036289

Type: transition

Compartments: Golgi membrane, Golgi lumen

Diseases: hereditary multiple exostoses



Exostosin 1 and 2 (EXT1 and 2) are dual-specific glycosyltransferases required to form heparan sulfate (HS) which is involved in regulating various body functions during development, homeostasis and pathology including blood clotting, angiogenesis and metastasis of cancer cells. They are able to transfer N-acetylglucosamine (GlcNAc) and glucuronate (GlcA) to HS during its synthesis. Defects in EXT2 cause exostoses 2 (MIM:133701), an autosomal dominant disorder characterised by multiple projections of bone capped by cartilage resulting in deformed legs, forearms and hands. Mutations causing exostoses 2 are V187Pfs*115, 404fs*, D227N, G172*, Q258* and Y222* (Stickens et al. 1996, Wyuts et al. 1996, Philippe et al. 1997, Heinritz et al. 2009).

Literature references

Heinritz, W., Hüffmeier, U., Strenge, S., Miterski, B., Zweier, C., Leinung, S. et al. (2009). New mutations of EXT1 and EXT2 genes in German patients with Multiple Osteochondromas. *Ann. Hum. Genet., 73*, 283-91. ↗

Philippe, C., Porter, DE., Emerton, ME., Wells, DE., Simpson, AH., Monaco, AP. (1997). Mutation screening of the EXT1 and EXT2 genes in patients with hereditary multiple exostoses. *Am. J. Hum. Genet., 61*, 520-8. ↗

Stickens, D., Clines, G., Burbee, D., Ramos, P., Thomas, S., Hogue, D. et al. (1996). The EXT2 multiple exostoses gene defines a family of putative tumour suppressor genes. *Nat. Genet., 14*, 25-32. ↗

Wuyts, W., Van Hul, W., Wauters, J., Nemtsova, M., Reyniers, E., Van Hul, EV. et al. (1996). Positional cloning of a gene involved in hereditary multiple exostoses. *Hum. Mol. Genet., 5*, 1547-57. ↗

Editions

2013-05-31	Authored, Edited	Jassal, B.
2014-07-09	Reviewed	Spillmann, D.