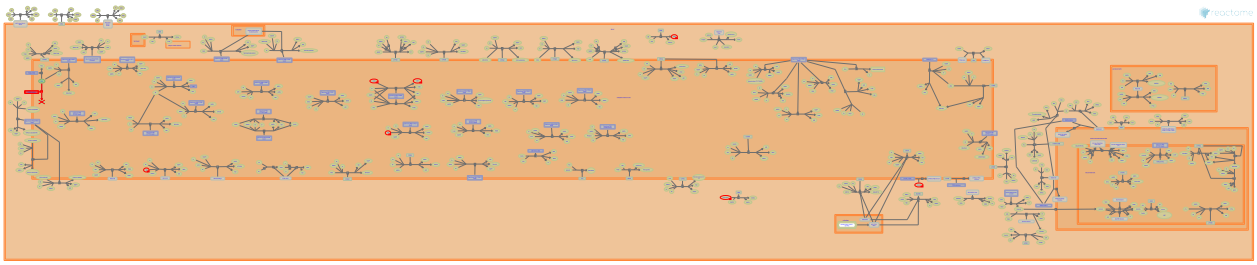
Defective TBXAS1 causes GHDD



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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.

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. ↗

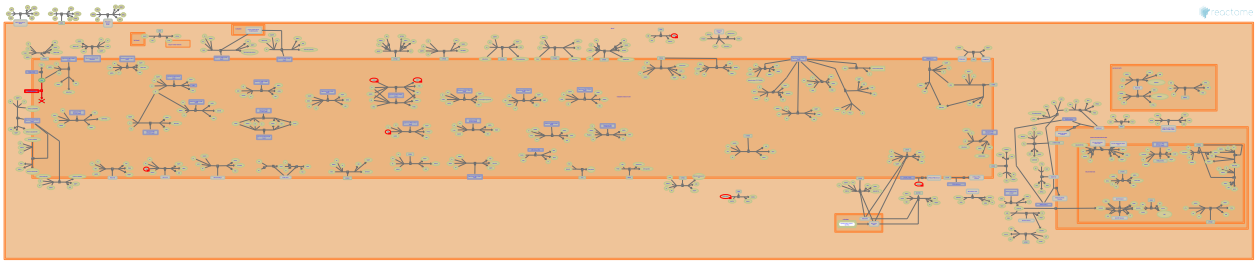
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 TBXAS1 causes GHDD

Stable identifier: R-HSA-5579032

Diseases: bone disease, anemia



Thromboxane-A synthase (TBXAS1), an enzyme of the arachidonic acid cascade, produces thromboxane A2 (TXA2) from prostaglandin H2 (PGH2). Together with prostacyclin (PGI2), TXA2 plays a key role in the maintenance of haemostasis. It is also a constrictor of vascular and respiratory smooth muscle and implicated in the induction of osteoclast differentiation and activation. Defects in TBXAS1 can cause Ghosal hematodiaphyseal dysplasia (GHDD; MIM:231095), a rare autosomal recessive disorder characterised by increased bone density with predominant diaphyseal involvement and aregenerative anemia, a bone marrow failure where functional marrow cells are regenerated slowly or not at all (Genevieve et al. 2008).

Literature references

Munnich, A., Isidor, B., Serre, V., Bellais, S., Dreyfus, M., de Vernejoul, MC. et al. (2008). Thromboxane synthase mutations in an increased bone density disorder (Ghosal syndrome). *Nat. Genet., 40*, 284-6.

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2014-11-03	Reviewed	Nakaki, T.

Defective TBXAS1 does not isomerise PGH2 to TXA2 ↗

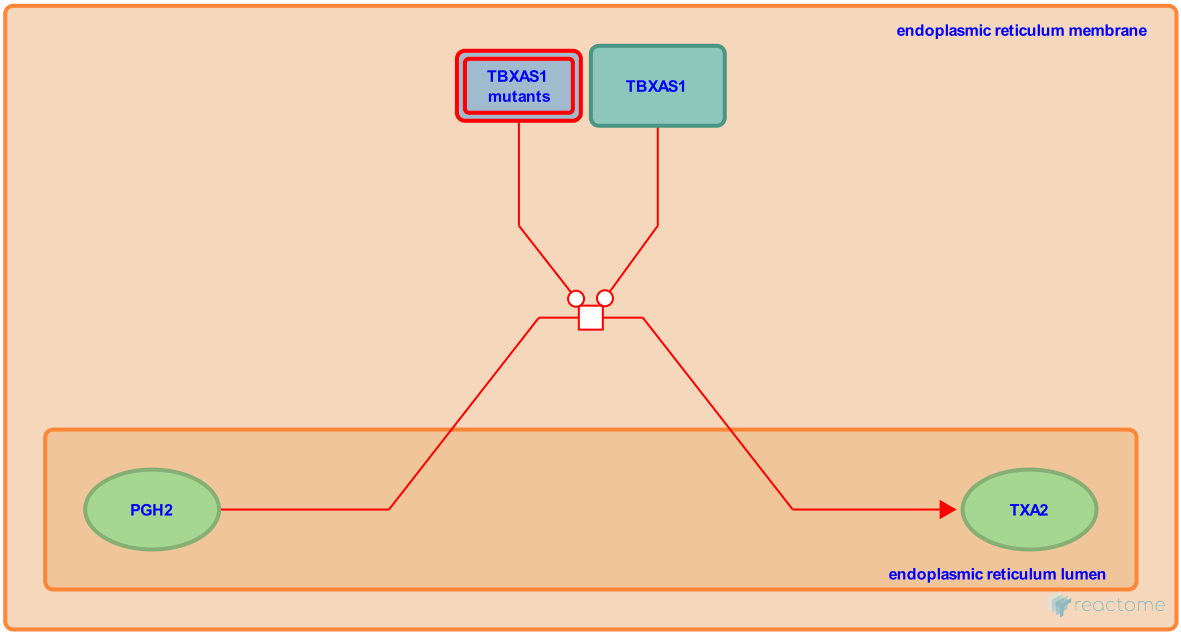
Location: Defective TBXAS1 causes GHDD

Stable identifier: R-HSA-5603275

Type: transition

Compartments: endoplasmic reticulum membrane, endoplasmic reticulum lumen

Diseases: bone disease, anemia



Thromboxane-A synthase (TBXAS1), an enzyme of the arachidonic acid cascade, produces thromboxane A2 (TXA2) from prostaglandin H2 (PGH2). Together with prostacyclin (PGI2), TXA2 plays a key role in the maintenance of haemostasis. It is also a constrictor of vascular and respiratory smooth muscle and implicated in the induction of osteoclast differentiation and activation. Defects in TBXAS1 can cause Ghosal hematodiaphyseal dysplasia (GHDD; MIM:231095), a rare autosomal recessive disorder characterised by increased bone density with predominant diaphyseal involvement and aregenerative anemia, a bone marrow failure where functional marrow cells are regenerated slowly or not at all. Mutations that can cause GHDD are L488P, L83P, G482W and R413E (Genevieve et al. 2008).

Literature references

Munnich, A., Isidor, B., Serre, V., Bellais, S., Dreyfus, M., de Vernejoul, MC. et al. (2008). Thromboxane synthase mutations in an increased bone density disorder (Ghosal syndrome). *Nat. Genet., 40*, 284-6. ↗

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