The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000212.3:c.842A>C

Version: 1.1

CA400024802

1330335 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: ef63c97b-506b-488b-ae9e-6d8a57a0d655
Approved on: 2024/8/20
Published on: 2024/8/20

HGVS expressions

NM_000212.3:c.842A>C
NC_000017.11:g.47287134A>C
CM000679.2:g.47287134A>C
NC_000017.10:g.45364500A>C
CM000679.1:g.45364500A>C
NC_000017.9:g.42719499A>C
NG_008332.2:g.38293A>C
ENST00000696963.1:c.842A>C
ENST00000559488.7:c.842A>C
ENST00000559488.5:c.842A>C
ENST00000560629.1:c.807A>C
ENST00000571680.1:c.842A>C
NM_000212.2:c.842A>C

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PP3 PP4_Strong PM2_Supporting

Evidence Links 0

Expert Panel

Platelet Disorders VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Platelet Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2.1*
PDF
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The NM_000212.3(ITGB3):c.842A>C (p.His281Pro) missense variant has been identified in at least 1 probands, GT11 of PMID: 29675921 meeting the criteria for PP4_strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of αIIbβ3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. GT11 of PMID: 29675921 is compound heterozygous for His281Pro and Cys400Tyr (classified Pathogenic by the PD-VCEP;

PM3_Supporting) without confirmation of phasing . This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.988, which predicts a damaging effect on ITGB3 function (PP3). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PM2_supporting, PP3, PP4_strong, PM3_supporting. (VCEP specifications version 2; date of approval xx/xx/xxxx)

Met criteria codes

PM3_Supporting	✔	GT11 of PMID: 29675921 is compound heterozygous for His281Pro and Cys400Tyr (Classified Pathogenic by the PD-VCEP). Confirmation of trans phase was not reported. 0.5pt (PM3_Supporting)
PP3	✔	The computational predictor REVEL gives a score of 0.988, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on ITGB3 function (PP3).
PP4_Strong	✔	GT11 of PMID: 29675921 meets the criteria for PP4_strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of αIIbβ3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries.
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.