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_000419.5:c.961G>T

Version: 2.0

CA399804768

996170 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5738e7ef-8f53-4bd1-960e-21c223060287
Approved on: 2024/2/20
Published on: 2024/2/20

HGVS expressions

NM_000419.5:c.961G>T
NC_000017.11:g.44383931C>A
CM000679.2:g.44383931C>A
NC_000017.10:g.42461299C>A
CM000679.1:g.42461299C>A
NC_000017.9:g.39816825C>A
NG_008331.1:g.10575G>T
ENST00000262407.6:c.961G>T
ENST00000648408.1:c.392G>T
ENST00000262407.5:c.961G>T
ENST00000589645.5:n.412G>T
ENST00000591990.5:n.506G>T
ENST00000592226.5:n.201G>T
NM_000419.3:c.961G>T
NM_000419.4:c.961G>T

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PP3 PP4_Strong

Not Met criteria codes 2

PM3 PM5

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_000419.5(ITGA2B):c.962G>T (p.Gly321Trp) missense variant has been reported in at least one compound heterozygous GT57 proband (PMID:25728920). GT57 of PMID:25728920 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. The variant is absent from all population database cohorts, including gnomADv4.0 (PM2_supporting) and is predicted deleterious (REVEL score 0.95; PP3). In summary this variant meets criteria to be classified as likely pathogenic for GT. GT-specific criteria applied: PM2_Supporting, PP3, and PP4_Strong.

Met criteria codes

PM2_Supporting	✔	This variant is absent from all population cohorts in gnomADv4.0 (PM2_supporting).
PP3	✔	REVEL score of 0.95 is above the >.0.7 threshold to support a deleterious effect.
PP4_Strong	✔	GT57 of PMID:25728920 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.

Not Met criteria codes

PM3	✖	GT57 of PMID: 25728920 is compound heterozygous for Gly321Trp and Phe191Val (classified Likely Pathogenic by the PD-EP). Confirmation of the trans relationship was not reported. 0.25pt
PM5	✖	The Gly321Trp variant occurs at the same residue as Gly321Val (classified likely pathogenic by the PD-EP). Not considered here to avoid circularity.

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.