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.48G>A

Version: 1.1

CA399807046

1879030 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4f031968-cbb7-4531-ae38-579af7ff6b20
Approved on: 2025/5/1
Published on: 2025/5/2

HGVS expressions

NM_000419.5:c.48G>A
NC_000017.11:g.44389426C>T
CM000679.2:g.44389426C>T
NC_000017.10:g.42466794C>T
CM000679.1:g.42466794C>T
NC_000017.9:g.39822320C>T
NG_008331.1:g.5080G>A
ENST00000262407.6:c.48G>A
ENST00000262407.5:c.48G>A
NM_000419.3:c.48G>A
NM_000419.4:c.48G>A

Likely Pathogenic

Met criteria codes 4

PM3_Supporting | PVS1_Moderate | PM2_Supporting | PP4_Moderate

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.48G>A (p.Trp16Ter) variant in exon 1 is a nonsense variant in biologically-relevant-exon 1/30. Premature termination codons within exon 1/ first 100 nucleotides may not cause NMD and instead may lead to translation re-initiation (PMID: 27618451). Therefore, PVS1 is downgraded to PVS1_Moderate. At least one patient (UPN 1 in PMID: 16879215) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_moderate). Additionally, αIIbβ3 surface expression was reduced to 5.6%, as measured by flow cytometry. UPN 1 is homozygous for this variant (PM3_supporting; PMID: 16879215). This variant is absent from gnomAD v4.1 (PM2_Supporting). 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: PVS1_moderate, PM2_supporting, PM3_supporting, PP4_moderate.

Met criteria codes

PM3_Supporting	✔	UPN 1 is homozygous for this variant (PM3_supporting; PMID: 16879215).
PVS1_Moderate	✔	The NM_000419.5(ITGA2B):c.48G>A (p.Trp16Ter) variant in exon 1 is a nonsense variant in biologically-relevant-exon 1/30. Premature termination codon within exon 1/ first 100 nucleotides may not cause NMD and instead may lead to translation re-initiation (PMID: 27618451). Therefore, PVS1 is downgraded to PVS1_moderate.
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP4_Moderate	✔	At least one patient (UPN 1 in PMID: 16879215) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_moderate). Additionally, αIIbβ3 surface expression was reduced to 5.6%, as measured by flow cytometry. However, ITGA2B and ITGB3 were not sequenced across all exons and intron/exon boundaries.

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.