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_000419.4:c.460_462del

Version: 2.1

CA8603457

953044 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: d96f1014-4193-4a0e-ab30-935705d7b081
Approved on: 2026/8/18
Published on: 2026/8/19

HGVS expressions

NM_000419.4:c.460_462del
NC_000017.11:g.44385663_44385665del
CM000679.2:g.44385663_44385665del
NC_000017.10:g.42463031_42463033del
CM000679.1:g.42463031_42463033del
NC_000017.9:g.39818557_39818559del
NG_008331.1:g.8841_8843del
ENST00000262407.6:c.460_462del
ENST00000262407.5:c.460_462del
ENST00000592944.1:n.145_147del
NM_000419.3:c.460_462del
NM_000419.5:c.460_462del

Likely Pathogenic

Met criteria codes 3

PM4 PP4_Strong PM2_Supporting

Not Met criteria codes 1

PM3

Evidence Links 1

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.460_462del deletion variant results in the in-frame deletion of Glu154 (PM4). It has been observed, in at least one case (PMID: 29675921) meeting the clinical and laboratory criteria of Glanzmann thrombasthenia, including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of αIIbβ3 measured by flow cytometry (PP4_strong). The highest population minor allele frequency in gnomAD v4.1.1 is 0.000001695 (2/1180028 alleles) in the European non-Finnish genetic ancestry group, which is lower than the ClinGen PD VCEP threshold (<0.0001; 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: PP4_strong, PM2_supporting, PM4, PP4_strong. (VCEP specifications version 2).

Met criteria codes

PM4	✔	The deletion of c.460_462 results in an in-frame deletion of Glu154.
PP4_Strong	✔	Patient GT32 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. Patient GT32 has a bleeding score of 2 with epistaxis and has a normal platelet count. Platelet aggregation is absent in response to ADP and collagen but normal to ristocetin. αIIbβ3 expression, measured by flow cytometry is 10-20%. PubMed:29675921
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.1 is 0.000001695 (2/1180028 alleles) in the European non-Finnish genetic ancestry group, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting).

Not Met criteria codes

PM3	✖	This variant has been reported once in the compound heterozygous state, with likely pathogenic variant Gly296Arg (GT32 in PMID: 29675921, not considered here to avoid circularity) and once from PMID: 38103590 in a compound heterozygous GT patient also carrying the c.2852_2853delinsC variant without confirmation of trans phase (classified as VUS by the ClinGen Platelet Disorders VCEP, not included here to avoid circularity).

Curation History

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