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Variant: NM_000419.5:c.212C>G

Version: 1.1

CA399806497

2506413 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1d7393bb-e854-4e1d-a9a0-36a72f7d1c3b
Approved on: 2026/2/5
Published on: 2026/2/5

HGVS expressions

NM_000419.5:c.212C>G
NC_000017.11:g.44386108G>C
CM000679.2:g.44386108G>C
NC_000017.10:g.42463476G>C
CM000679.1:g.42463476G>C
NC_000017.9:g.39819002G>C
NG_008331.1:g.8398C>G
ENST00000262407.6:c.212C>G
ENST00000262407.5:c.212C>G
NM_000419.3:c.212C>G
NM_000419.4:c.212C>G

Likely Pathogenic

Met criteria codes 3

PP3 PP4_Strong PM2_Supporting

Not Met criteria codes 1

PM3

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.212C>G (p.Pro71Arg) missense variant has been reported in at least one Glanzmann thrombasthenia patient (PMID: 21113249). Patient GE displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia . Additionally, αIIbβ3 surface expression was reduced to <1%, as measured by flow cytometry, and there was<1% binding to PAC-1. (PP4_strong). The full genotype of Patient GE was reported later in Pilgrimm-Thorp (2012) Haemophilia 18S3 157 and a PhD dissertation from D. Pillitteri, the patient is compound heterozygous for this variant and Leu684Arg (classified VUS by the PD VCEP; PM3_NotMet). The Pro71Arg variant is absent from gnomAD v4.1 (PM2_Supporting) and the computational

predictor REVEL gives a score of 0.809, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on 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: PP4_strong, PM2_supporitng, PP3_supporting.

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.809, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3).
PP4_Strong	✔	Patient GE displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, αIIbβ3 surface expression was reduced to <1%, as measured by flow cytometry, and there was <1% binding to PAC-1. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries (PP4_strong; PMID: 21113249).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).

Not Met criteria codes

PM3	✖	Patient GE is presumed compound heterozygous. The patient is heterozygous for the maternally inherited Leu684Arg variant (classified VUS by the PD-EP), however a second variant was not identified and the father was not reported. A later abstract from the authors (Pilgrimm-Thorp (2012) Haemophilia 18S3 157) reported the second variant as Pro71Arg. Confirmation of trans phase was not reported. Not considered here to avoid circularity.

Curation History

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