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Variant: NM_000212.3:c.415G>C

Version: 2.0

CA400021843

1691483 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 0ac2ce25-1af9-4a5b-aee3-cae3ef88564e
Approved on: 2025/4/15
Published on: 2025/5/13

HGVS expressions

NM_000212.3:c.415G>C
NC_000017.11:g.47284496G>C
CM000679.2:g.47284496G>C
NC_000017.10:g.45361862G>C
CM000679.1:g.45361862G>C
NC_000017.9:g.42716861G>C
NG_008332.2:g.35655G>C
ENST00000696963.1:c.415G>C
ENST00000559488.7:c.415G>C
ENST00000559488.5:c.415G>C
ENST00000560629.1:c.380G>C
ENST00000571680.1:c.415G>C
NM_000212.2:c.415G>C

Likely Pathogenic

Met criteria codes 4

PP3 PM3 PP4_Moderate 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:c.415G>C variant in ITGB3 is a missense variant predicted to cause substitution of aspartic acid by histidine at amino acid 139 (p.Asp139His). This variant has been observed in compound heterozygosity in one individual (GT53 in PMID: 19691478) in trans (phase confirmed) with ITGB3 variant c.422A>G (p.Tyr141Cys, classified by the Platelet Disorders VCEP as a Pathogenic; PM3). This individual displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for

Glanzmann thrombasthenia (PP4_Moderate). This variant is absent from gnomAD v4.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.986, which is above the ClinGen Platelet Disorders VCEP threshold of >0.7 and predicts a damaging effect on function (PP3). In summary, this variant is 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, PM3 PP3, PP4_Moderate. (VCEP specifications version 2)

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.986, which is above the ClinGen Platelet Disorders VCEP threshold of >0.7 and predicts a damaging effect on function (PP3).
PM3	✔	Patient GT53 reported in PMID: 19691478 is compound heterozygous for this variant and the ITGB3 variant c.422A>G (p.Tyr141Cys, classified by the Platelet Disorders VCEP as a Pathogenic, trans phase confirmed) (1 point; PM3)
PP4_Moderate	✔	At least one patient (Patient GT53 in PMID: 19691478) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_moderate).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).

Curation History

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