

Variant: *NM_000419.5:c.423G>T*

Version: 1.1

CA399806022 [↗](#)

1691484 (ClinVar) [↗](#)

Gene: ITGA2B ([HGNC:3674](#))

Condition: Glanzmann thrombasthenia ([MONDO:0100326](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: dbf139ea-99d4-4741-aec7-223bc87d713a

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HGVS expressions

NM_000419.5:c.423G>T

NC_000017.11:g.44385702C>A

CM000679.2:g.44385702C>A

NC_000017.10:g.42463070C>A

CM000679.1:g.42463070C>A

NC_000017.9:g.39818596C>A

NG_008331.1:g.8804G>T

ENST00000262407.6:c.423G>T

ENST00000262407.5:c.423G>T

ENST00000592944.1:n.108G>T

NM_000419.3:c.423G>T

NM_000419.4:c.423G>T

Likely Pathogenic

Met criteria codes **4**

PM2_Supporting

PP4_Strong

PP3

PM3_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 missense variant NM_000419.5(ITGA2B):c.423G>T (p.Trp141Cys) has been reported in at least one patient (GT14 in PMID: 25728920), with mucocutaneous bleeding and impaired aggregation against all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, α IIb β 3 surface expression was reduced to <5%, as measured by flow cytometry (PP4_strong). GT14 of PMID: 25728920 is compound heterozygous for Trp141Cys and c.2902del (classified as Pathogenic by the PD-EP), confirmation of trans phase was not reported (PM3_supporting). This variant is absent from gnomAD v4.1 (PM2_Supporting). The computational predictor REVEL gives a

score of 0.879, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3). In summary this variant meets 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, PM3_supporting, PP3. (VCEP specifications version 2.1)

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP4_Strong			At least one patient (GT14 in PMID: 25728920) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, α IIb β 3 surface expression was reduced to<5%, as measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. (PP4_strong)
PP3			The computational predictor REVEL gives a score of 0.879, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3).
PM3_Supporting			GT14 of PMID: 25728920 is compound heterozygous for Trp141Cys and c.2902del (classified as Pathogenic by the PD-EP), confirmation of trans phase was not reported (0.5pt; PM3_supporting).

Curation History

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