

Variant: *NM_000419.4:c.889G>C*

Version: 3.0

CA8603305 [↗](#)

953005 (ClinVar) [↗](#)

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

Condition: Glanzmann thrombasthenia ([MONDO:0010119](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 0e2ba47d-6962-4167-a1df-def62f5aa041

Approved on: 2024/9/5

Published on: 2024/9/30

HGVS expressions

NM_000419.4:c.889G>C

NC_000017.11:g.44384313C>G

CM000679.2:g.44384313C>G

NC_000017.10:g.42461681C>G

CM000679.1:g.42461681C>G

NC_000017.9:g.39817207C>G

NG_008331.1:g.10193G>C

ENST00000262407.6:c.889G>C

ENST00000648408.1:c.320G>C

ENST00000262407.5:c.889G>C

ENST00000589645.5:n.340G>C

ENST00000591990.5:n.434G>C

ENST00000592075.5:n.258G>C

ENST00000592226.5:n.129G>C

ENST00000592253.5:n.397G>C

NM_000419.3:c.889G>C

NM_000419.5:c.889G>C

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PP1

PM2_Supporting

PM3

Not Met criteria codes **2**

BP4

PP3

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_000419.4:c.889G>C variant that results in the Ala297Pro amino acid change is seen in one unpublished homozygous GT individual with mild mucocutaneous bleeding symptoms and lack of platelet aggregation in response to ADP, collagen, U46619, AA and TRAP, but normal response to ristocetin (PP4_moderate). As well as their affected homozygous sibling (PP1). A second homozygous individual has also been reported (PM3; PMID: 32089034). The variant is reported in gnomADv4.1 at a frequency of 0.00004392 (4/91080 alleles) in the South Asian population, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting). In summary, based on the available evidence at this time, the variant is classified as likely pathogenic for GT. GT-specific criteria applied: PM2_Supporting, PM3, PP1, and PP4_Moderate.

Met criteria codes

PP4_Moderate			One unpublished homozygous individual (from internal laboratory data) has mild mucocutaneous bleeding symptoms and lack of platelet aggregation in response to ADP, collagen, U46619, AA and TRAP, but normal response to ristocetin (PP4_moderate).
PP1			The homozygous individual from internal laboratory data has a similarly affected sibling who is also homozygous for the variant. Segregation in 1 affected relative with phase confirmation meets criteria for PP1.
PM2_Supporting			The variant is reported in gnomADv4.1 at a frequency of 0.00004392 (4/91080 alleles) in the South Asian population, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting).
PM3			1 homozygous individual from internal laboratory data, with parents tested and found to be heterozygous for the variant and a second homozygote reported in PMID: 32089034 (1pt; PM3).

Not Met criteria codes

BP4			The computational predictor REVEL gives a score of 0.369, which is above the ClinGen PD VCEP PP3 threshold of <0.25.
PP3			The computational predictor REVEL gives a score of 0.369, which is below the ClinGen PD VCEP PP3 threshold of >0.7 and does not predict a damaging effect on ITGA2B function. And the computational splicing predictor SpliceAI indicated that the variant has no predicted impact on splicing.

Curation History



Showing 1 to 4 of 4 rows

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