

Variant: NM_000419.5:c.2489T>G

Version: 1.1

CA8602667 [↗](#)

1879014 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 8383e80f-14d2-4c1e-8dd9-7bc707c6f685

Approved on: 2025/4/15

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HGVS expressions

NM_000419.5:c.2489T>G

NC_000017.11:g.44375945A>C

CM000679.2:g.44375945A>C

NC_000017.10:g.42453313A>C

CM000679.1:g.42453313A>C

NC_000017.9:g.39808839A>C

NG_008331.1:g.18561T>G

ENST00000262407.6:c.2489T>G

ENST00000648408.1:c.1920T>G

ENST00000262407.5:c.2489T>G

ENST00000587295.5:c.141T>G

ENST00000592462.5:n.1284T>G

NM_000419.3:c.2489T>G

NM_000419.4:c.2489T>G

Uncertain Significance

Met criteria codes **2**

PM3_Supporting

PM2_Supporting

Not Met criteria codes **2**

PP3

PP4

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.2489T>G (p.Leu830Arg) missense variant has been reported in at least one homozygous patient (UPN 9 in PMID: 16879215; PM3_supporting). The highest population minor allele frequency in gnomAD v4.1 is 0.00001098 (1/91048 alleles) in the South Asian 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 uncertain significance for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PM2_supporting, PM3_supporting.			
Met criteria codes			
PM3_Supporting			UPN 9 is homozygous for this variant (PM3_supporting; PMID: 16879215).
PM2_Supporting			The highest population minor allele frequency in gnomAD v4.1 is 0.00001098 (1/91048 alleles) in the South Asian genetic ancestry group, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting).
Not Met criteria codes			
PP3			The computational predictor REVEL gives a score of 0.568, 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 is not likely to have an impact on splicing (though a possible acceptor site gain is reported with a score of 0.23).
PP4			UPN 9 (PMID: 16879215) has a history of mucocutaneous bleeding as well as absent platelet aggregation in response to ADP, epinephrine, and collagen but also has a poor ristocetin response. Additionally, α IIb β 3 surface expression was reduced to 10%, as measured by flow cytometry.

Curation History



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