

Variant: *NM_000419.5(ITGA2B):c.857T>A (p.Val286Asp)*

Version: 2.0

CA399805011 [↗](#)

1210210 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5289ffc6-3f4b-45c1-b8b2-471eff1a1312

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HGVS expressions

NM_000419.5(ITGA2B):c.857T>A (p.Val286Asp)

NM_000419.5:c.857T>A

NC_000017.11:g.44384345A>T

CM000679.2:g.44384345A>T

NC_000017.10:g.42461713A>T

CM000679.1:g.42461713A>T

NC_000017.9:g.39817239A>T

NG_008331.1:g.10161T>A

ENST00000262407.6:c.857T>A

ENST00000648408.1:c.288T>A

ENST00000262407.5:c.857T>A

ENST00000589645.5:n.308T>A

ENST00000591990.5:n.402T>A

ENST00000592075.5:n.226T>A

ENST00000592226.5:n.97T>A

ENST00000592253.5:n.365T>A

ENST00000592944.1:n.539T>A

NM_000419.3:c.857T>A

NM_000419.4:c.857T>A

Likely Pathogenic

Met criteria codes **5**

PM3_Supporting

PP1

PP3

PP4_Strong

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**

Platelet Disorders VCEP

The NM_000419.5(ITGA2B):c.857T>A (p.Val286Asp) missense variant is absent from large population databases, including gnomADv2.1.1 (PM2_supporting). This variant has been reported in the homozygous state (PM3_supporting) in at least one proband who meets criteria for the GT phenotype, which includes history of significant mucocutaneous bleeding, absent platelet aggregation with three physiological agonists, normal with ristocetin. Flow cytometry demonstrated reduced (<5%) αIIbβ3 surface expression (PMID: 25728920; PP4_strong). The variant segregated with disease in two homozygous siblings (PMID: 36672149; PP1). In silico tools (REVEL score = 0.825) predict deleterious effects on gene function (PP3). In summary, this variant meets criteria for PP4_strong, PM2_supporting, PP3, PP1 and PM3_supporting; and is therefore classified as Likely Pathogenic for GT.

Met criteria codes

PM3_Supporting			The p.Val286Asp variant has been reported in homozygous state in one proband by PMID:25728920 [0.5 points]
PP1			The variant segregated with disease in two homozygous siblings (PMID: 36672149; PP1)
PP3			REVEL score=0.825, which is above the threshold of >0.70 for PP3_supporting.
PP4_Strong			The p.Val286Asp variant has been reported in at least one proband who meets GT specific criteria for PP4_strong - which includes history of significant mucocutaneous bleeding, absent platelet aggregation with three physiological agonists, normal with ristocetin. Flowcytometry demonstrated reduced (<5%) αIIbβ3 surface expression. Sanger sequencing was performed to ensure coverage of all exons and UTRs of ITGA2B and ITGB3 genes.
PM2_Supporting			p.Val286Asp is absent from large population cohorts (gnomAD).

Curation History

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Showing 1 to 2 of 2 rows

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