

Variant: NM_000419.5:c.962G>T

Version: 2.0

CA399804765 [↗](#)

996169 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: cc73bafa-1187-4229-9a07-413bf2550bd8

Approved on: 2024/3/7

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HGVS expressions

NM_000419.5:c.962G>T

NC_000017.11:g.44383930C>A

CM000679.2:g.44383930C>A

NC_000017.10:g.42461298C>A

CM000679.1:g.42461298C>A

NC_000017.9:g.39816824C>A

NG_008331.1:g.10576G>T

ENST00000262407.6:c.962G>T

ENST00000648408.1:c.393G>T

ENST00000262407.5:c.962G>T

ENST00000589645.5:n.413G>T

ENST00000591990.5:n.507G>T

ENST00000592226.5:n.202G>T

NM_000419.3:c.962G>T

NM_000419.4:c.962G>T

Likely Pathogenic

Met criteria codes **4**

PP4_Strong

PP3

PM5_Supporting

PM2_Supporting

Not Met criteria codes **1**

PM3

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.962G>T (p.Gly321Val) missense variant has been reported in at least two compound heterozygous probands (PMID: 29675921 and GT database patient 437). GT40 of PMID: 29675921 meets the criteria for PP4_Strong; including mucocutaneous

bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of $\alpha\text{IIb}\beta\text{3}$ measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. The variant is absent from all population database cohorts, including gnomADv2.1.1 (PM2_supporting) and is predicted deleterious (REVEL score 0.907; PP3). The Gly321Val variant occurs at the same residue as Gly321Trp (classified Likely Pathogenic by the PD-EP; PM5_supporting). In summary this variant meets criteria to be classified as likely pathogenic for GT. GT-specific criteria applied: PM2_supporting, PM5_supporting, PP3, and PP4_strong.

Met criteria codes

PP4_Strong			GT40 of PMID: 29675921 meets the criteria for PP4_Strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of $\alpha\text{IIb}\beta\text{3}$ measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries.
PP3			REVEL score of 0.907 is above the >.0.7 threshold to support a deleterious effect.
PM5_Supporting			The Gly321Val variant occurs at the same residue as Gly321Trp (classified Likely Pathogenic by the PD-EP).
PM2_Supporting			This variant is absent from all population cohorts in gnomAD, ExAC, 1000 Genomes, and ESP.

Not Met criteria codes

PM3			One compound heterozygote has been reported, GT40 in PMID: 29675921. However the second variant, Arg584Ter, has an allele frequency exceeding the PM2 threshold so is not considered. An additional compound heterozygous patient was reported in the GT database with Gly321Val and Ala341Val (classified VUS by the PD-EP) and is not considered here to avoid circularity.
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Curation History

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