

Variant: NM_000419.5:c.2029G>A

Version: 2.0

CA399800002 [↗](#)

1210172 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: e3a228d9-41c8-4d47-8882-5e80827c815e

Approved on: 2024/6/6

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HGVS expressions

NM_000419.5:c.2029G>A

NC_000017.11:g.44378427C>T

CM000679.2:g.44378427C>T

NC_000017.10:g.42455795C>T

CM000679.1:g.42455795C>T

NC_000017.9:g.39811321C>T

NG_008331.1:g.16079G>A

ENST00000262407.6:c.2029G>A

ENST00000648408.1:c.1460G>A

ENST00000262407.5:c.2029G>A

ENST00000592462.5:n.824G>A

NM_000419.3:c.2029G>A

NM_000419.4:c.2029G>A

Likely Pathogenic

Met criteria codes **3**

PM2_Supporting

PP4_Strong

PM3_Supporting

Not Met criteria codes **1**

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_000419.5(ITGA2B):c.2029G>A (p.Glu677Lys) missense variant has a highest population minor allele frequency in gnomAD v4.0 of 0.000002625 (2/761904 alleles) in the European (non-Finnish)population, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting). It has been reported in two patients with GT (PMID: 29675921, Patient 439 of the Glanzmann Thrombasthenia Database). GT1 of PMID: 29675921 is compound heterozygous for Glu677Lys and Arg351Ter (classified Pathogenic by the PD-EP

SCV001809862.1; PM3_supporting). GT1 of PMID: 29675921 meets the criteria for PP4_strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and <5% expression of α IIb β 3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. In summary, based on the evidence available at this time, the variant is classified as likely pathogenic. GT-specific criteria applied: PM2_supporting, PM3_supporting, and PP4_strong.

Met criteria codes

PM2_Supporting			The highest population minor allele frequency in gnomAD v4.0 is 0.000002625 (2/761904 alleles) in the European (non-Finnish)population, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting).
PP4_Strong			GT1 of PMID: 29675921 meets the criteria for PP4_strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and <5% expression of α IIb β 3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries.
PM3_Supporting			GT1 of PMID: 29675921 is compound heterozygous for Glu677Lys and Arg351Ter (classified Pathogenic by the PD-EP). Confirmation of trans phase was not reported. 0.5pt

Not Met criteria codes

PP3			The REVEL score for this variant is 0.415, which does not meet the VCEP-established threshold of >0.7 to support a deleterious effect (PP3_NotMet) of <0.25 to support no impact (BP4_NotMet). Additionally, no impact on splicing is predicted (SpliceAI delta scores 0.00-0.01).
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Curation History





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