

Variant: *NM_000419.4:c.2951C>A*

Version: 2.0

CA399790180 [↗](#)

952998 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 6a7fde6e-8154-4494-85af-3ead01f92afe

Approved on: 2023/9/7

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HGVS expressions

NM_000419.4:c.2951C>A

NC_000017.11:g.44374463G>T

CM000679.2:g.44374463G>T

NC_000017.10:g.42451831G>T

CM000679.1:g.42451831G>T

NC_000017.9:g.39807357G>T

NG_008331.1:g.20043C>A

ENST00000262407.6:c.2951C>A

ENST00000648408.1:c.2374+196C>A

ENST00000262407.5:c.2951C>A

ENST00000587295.5:c.253+1370C>A

ENST00000588098.1:c.37+196C>A

ENST00000592462.5:n.2650C>A

NM_000419.3:c.2951C>A

NM_000419.5:c.2951C>A

Likely Pathogenic

Met criteria codes **4**

PM3_Supporting

PP3

PP4_Strong

PM2_Supporting

Evidence Links **1**

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 missense variant NM_000419.5(ITGA2B):c.2951C>A (p.Thr984Lys) has been reported in one homozygous proband (PM3_supporting) who meets the criteria for PP4_strong, including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and

<5% surface expression of αIIbβ3 measured by flow cytometry (PMID: 25728920). The variant is absent from population databases, including gnomADv2.1.1 (PM2_supporting). Multiple lines of computational evidence support a deleterious effect with a REVEL score of 0.774 (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for GT. GT-specific criteria applied: PM2_supporting, PP3, PM3_supporting, PP4_strong.

Met criteria codes

PM3_Supporting			One homozygous individual has been reported with the Thr984Lys variant. 0.5pt
			One homozygous individual, patient GT72, has been reported with the Thr984Lys variant. PubMed:25728920 
PP3			Multiple lines of computational evidence support a deleterious effect with a REVEL score of 0.774 (above the >0.7 threshold).
PP4_Strong			One patient has been described with the Arg169Ter variant who meets the criteria for PP4, including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and <5% surface expression of αIIbβ3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries.
			Patient GT72, homozygous for Thr984Lys, had a history of mucocutaneous bleeding (marked bleeding syndrome with epistaxis, ecchymoses, gingivorrhagia, menorrhagia) and a WHO bleeding score of 3. There was absent platelet aggregation with ADP and severely reduced with at least two additional agonists but normal ristocetin-induced aggregation. There was <5% αIIbβ3 platelet surface expression confirmed by flow cytometry. PubMed:25728920 
PM2_Supporting			This variant is absent from gnomAD, ExAC and 1000 Genomes.

Curation History

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