

Variant: *NM_000419.5(ITGA2B):c.1063G>A (p.Glu355Lys)*

Version: 1.0

CA115844 [↗](#)

2899 (ClinVar) [↗](#)

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

Condition: Glanzmann's thrombasthenia ([MONDO:0010119](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 4fb9bbea-ef5f-4224-a74d-fbf5b546f159

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HGVS expressions

NM_000419.5(ITGA2B):c.1063G>A (p.Glu355Lys)

NM_000419.5:c.1063G>A

NC_000017.11:g.44383640C>T

CM000679.2:g.44383640C>T

NC_000017.10:g.42461008C>T

CM000679.1:g.42461008C>T

NC_000017.9:g.39816534C>T

NG_008331.1:g.10866G>A

ENST00000262407.6:c.1063G>A

ENST00000648408.1:c.494G>A

ENST00000262407.5:c.1063G>A

ENST00000592226.5:n.303G>A

NM_000419.3:c.1063G>A

NM_000419.4:c.1063G>A

Pathogenic

Met criteria codes **5**

PM2_Supporting

PP4_Moderate

PS3

PP3

PM3

Evidence Links **0**

Expert Panel

[Platelet Disorders VCEP](#) [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Platelet Disorders VCEP

The NM_000419.5(ITGA2B):c.1063G>A (p.Glu355Lys) missense variant has been reported in several patients (PMIDs: 11122161, 9722314, 9215749, 22250950, 9734640) with a phenotype highly specific to GT. It occurs at a very low allele frequency of 0.00001978 (2/101,102 alleles) in the non-Finnish European gnomAD population. The variant is predicted to have a deleterious effect (REVEL score 0.793). The functional impact has been assessed by transfection in CHO cells, showing lack of $\alpha IIb\beta 3$ surface expression with the Glu355Lys mutant (PMIDs: 11122161, 12362239). In summary this variant meets criteria to be classified as Pathogenic for GT. GT-specific criteria applied: PS3, PM2_Supporting, PM3, PP3, and PP4_Moderate.

Met criteria codes			
PM2_Supporting			This variant is at an extremely low frequency (below the <1/10,000 threshold) with an overall allele frequency from gnomAD of 0.000008807 and MAF of 0.00001978 (2/101,102 alleles) in the non-Finnish European population.
PP4_Moderate			The patient in PMID: 11122161 meets criteria for PP4_moderate; including mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin. Additionally, there was an absence of platelet GPIIb, as measured by flow cytometry and Western blot.
PS3			In PMID: 11122161 and PMID: 12362239, surface expression, in transfected CHO cells expressing normal β 3, was measured by flow cytometry, finding that the Glu355Lys variant prevented the surface expression of the α IIb β 3.
PP3			REVEL score of 0.793 is above the >.0.7 threshold, in support of a deleterious effect.
PM3			At least four homozygous patients have been reported (PMIDs: 11122161, 9722314, 9215749, 22250950) for Glu355Lys. An additional compound heterozygous case has been reported (in PMID: 9734640) with Ile596Thr, which is not considered here as Ile596Thr has an allele frequency above the threshold for PM2.

Curation History 	
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