

Variant: *NM_000212.2(ITGB3):c.1299C>T (p.Pro433=)*

Version: 2.0

CA8623241 [↗](#)

323866 (ClinVar) [↗](#)

Gene: ITGB3 ([HGNC:3690](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 77c51cf2-073d-4123-9bca-809de4125661

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HGVS expressions

NM_000212.2(ITGB3):c.1299C>T (p.Pro433=)

NM_000212.2:c.1299C>T

NC_000017.11:g.47292177C>T

CM000679.2:g.47292177C>T

NC_000017.10:g.45369543C>T

CM000679.1:g.45369543C>T

NC_000017.9:g.42724542C>T

NG_008332.2:g.43336C>T

ENST00000696963.1:c.1299C>T

ENST00000559488.7:c.1299C>T

ENST00000559488.5:c.1299C>T

ENST00000560629.1:c.1264C>T

NM_000212.3:c.1299C>T

Likely Benign

Met criteria codes **3**

BP4 BP7 BS1

Not Met criteria codes **1**

BS2

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_000212.2(ITGB3):c.1299C>T (p.Pro433=) synonymous variant was observed by Illumina as part of a predisposition screen in an ostensibly healthy population and has been reported in the literature in a healthy cohort (PMID: 27965976) but has not been reported in a Glanzmann thrombasthenia patient. In gnomAD v4.0.0 the minor allele frequency is 0.001910 (174/91086 alleles) in the South Asian population, which meets the BS1 threshold (>0.00158). Splicing prediction algorithms (MaxEntScan, HSF, and SpliceAI) predict no impact

on splicing (BP4) and the nucleotide is not highly conserved (phyloP score 0.129449; BP7). In summary this variant meets criteria to be classified as likely benign. GT-specific criteria applied: BS1, BP4 and BP7.

Met criteria codes

BP4			Splicing prediction algorithms (MaxEntScan, HSF, and SpliceAI) predict no impact to the splice consensus sequence nor the creation of a new splice site. CADD RawScore 0.645923 and PHRED 10.70.
BP7			Splicing prediction algorithms (MaxEntScan, HSF, and SpliceAI) predict no impact to the splice consensus sequence nor the creation of a new splice site AND the nucleotide is not highly conserved (phyloP score 0.129449).
BS1			The highest population minor allele frequency in gnomAD v4.0.0 is 0.002969 (18/6062 alleles) in the Middle Eastern population, which is higher than the ClinGen PD VCEP BA1 threshold (>0.0024), due to this being a bottle-necked population this was downgraded to BS1. The next highest minor allele frequency in gnomAD v4.0.0 is 0.001910 (174/91086 alleles) in the South Asian population, which also meets the BS1 threshold (>0.00158).

Not Met criteria codes

BS2			One healthy native Chinese subject, in PMID: 27965976, was identified with this variant however the full genotype and phenotype was not provided for this individual.
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Curation History



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