

Variant: *NM_000212.3:c.940G>T*

Version: 2.0

CA400025612 [↗](#)

996176 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5925bffc-2d34-408f-8a71-55c2fd81f0cf

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HGVS expressions

NM_000212.3:c.940G>T

NC_000017.11:g.47289681G>T

CM000679.2:g.47289681G>T

NC_000017.10:g.45367047G>T

CM000679.1:g.45367047G>T

NC_000017.9:g.42722046G>T

NG_008332.2:g.40840G>T

ENST00000696963.1:c.940G>T

ENST00000559488.7:c.940G>T

ENST00000559488.5:c.940G>T

ENST00000560629.1:c.905G>T

ENST00000571680.1:c.940G>T

NM_000212.2:c.940G>T

Likely Pathogenic

Met criteria codes 4

PP4_Strong

PP3

PM3_Supporting

PM2_Supporting

Not Met criteria codes 1

PM5

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

NM_000212.3(ITGB3):c.940G>T (p.Asp314Tyr) is a missense variant that has been reported in one patient (GT6) who presented with significant mucocutaneous bleeding, platelet aggregation was absent with three physiological agonists (normal with ristocetin) and flowcytometry demonstrated reduced (<5%) surface expression of $\alpha\text{IIb}\beta 3$ (PMID: 25728920; PP4_strong). The variant in homozygous state in this individual (PM3_supporting). It is absent from all major population cohorts in gnomAD v2.1.1 (PM2_supporting). REVEL score (0.977)

predicts this missense variant to have a deleterious effect on gene product (PP3). This variant meets GT specific criteria for PP4_strong , PP3, PM2_Supporting, and PM3_supporting and has therefore been classified as Likely Pathogenic for autosomal recessive Glanzmann thrombasthenia.

Met criteria codes

PP4_Strong			PMID: 25728920 reported a proband (GT6) who presented with significant mucocutaneous bleeding, platelet aggregation was absent with three physiological agonists (normal with ristocetin) and flowcytometry demonstrated reduced (<5%) surface expression of αIIbβ3.Sanger sequencing ensured coverage of exons and splice sites of the ITGA2B and ITGB3 genes as well as untranslated regions (UTR). PP4_strong applied.
PP3			REVEL score = 0.977 which is above the impact threshold of 0.70. Multiple insilico splicing tools such as SpliceAI and MaxEntScan predict a splice site acceptor loss.
PM3_Supporting			PMID: 25728920 reported this variant to be homozygous in one proband. (0.5 points) Therefore, PM3 is applied at supporting strength.
PM2_Supporting			Absent from all major population cohorts (gnomAD, ExAC, 1000 Genomes and ESP)

Not Met criteria codes

PM5			A missense change, Asp314Ala, has been reported at position that has been classified as Likely Pathogenic by ClinGen platelet disorder VCEP. This evidence is not considered here to avoid circularity.
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Curation History

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