The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000212.2:c.115T>G

Version: 2.1

CA400031666

953043 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4c19257d-2ea0-4ff6-9dc1-e00dd5628fd8
Approved on: 2026/2/5
Published on: 2026/2/5

HGVS expressions

NM_000212.2:c.115T>G
NC_000017.11:g.47274454T>G
CM000679.2:g.47274454T>G
NC_000017.10:g.45351820T>G
CM000679.1:g.45351820T>G
NC_000017.9:g.42706819T>G
NG_008332.2:g.25613T>G
ENST00000696963.1:c.115T>G
ENST00000559488.7:c.115T>G
ENST00000559488.5:c.115T>G
ENST00000560629.1:c.80T>G
ENST00000571680.1:c.115T>G
NM_000212.3:c.115T>G

Likely Pathogenic

Met criteria codes 5

PM2_Supporting PP3 PS3_Moderate PP4_Moderate PM3_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 NM_000212.3(ITGB3):c.115T>G variant that results in the Cys39Gly amino acid change is reported in one homozygous individual in the literature (PMID: 16463284; PM3_supporting). Proband from PMID: 1646328 meets the criteria for PP4_Moderate; including mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin. It is absent in population database gnomADv4.1 (PM2_supporting) and is predicted damaging by in-silico tools (REVEL score of 0.939; PP3). Experimental evidence shows reduced surface expression of

integrin αIIbβ3 PMID: 16463284; PS3_moderate). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PP4_moderate, PM2_supporting, PM3_supporting, PP3, PS3_moderate. (VCEP specifications version 2).

Met criteria codes

PM2_Supporting	✔	Variant is absent from gnomADv4.1 (PM2_supporting).
PP3	✔	REVEL score of 0.939 meets PP3 criteria (threshold: >0.7)
PS3_Moderate	✔	Greatly reduced surface expression of integrin αIIbβ3 on BHK cells shown in PMID: 16463284 meets PS3_Moderate Wildtype β3, Cys39Gly and artificial mutation, Cys13Ser, expression vectors were constructed and cotransfected into baby hamster kidney cells along with wildtype αIIb vector. FACS and Immunoblot analyses (Figure 5) detected trace amounts of αIIbβ3 protein. PubMed:16463284
PP4_Moderate	✔	Proband from PMID: 1646328 meets the criteria for PP4_Moderate; including mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin.
PM3_Supporting	✔	One homozygous individual, GT11, from PMID: 16463284 meets criteria for PM3_Supporting. Individual GT11 was predicted to be homozygous based on haplotype analysis and consanguinity status. PubMed:16463284

Curation History

Showing 1 to 3 of 3 rows

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