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.1702T>C*

Version: 2.1

*CA400032350*

*953008 (ClinVar)*

**Gene**: ITGB3 (HGNC:3690)
**Condition**: Glanzmann thrombasthenia (MONDO:0100326)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 19f5e234-9525-4f78-8ce9-7c6fccaf0b73
**Approved on**: 2026/3/17
**Published on**: 2026/3/17

## *HGVS expressions*

**NM_000212.2:c.1702T>C**
NC_000017.11:g.47299319T>C
CM000679.2:g.47299319T>C
NC_000017.10:g.45376685T>C
CM000679.1:g.45376685T>C
NC_000017.9:g.42731684T>C
NG_008332.2:g.50478T>C
ENST00000696963.1:c.1702T>C
ENST00000559488.7:c.1702T>C
ENST00000559488.5:c.1702T>C
ENST00000560629.1:c.1667T>C
NM_000212.3:c.1702T>C

**Likely Pathogenic**

**Met criteria codes** 5

PS3_Moderate | PP4_Moderate | PM2_Supporting | PM3 | PP3

Evidence Links 2

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.1702T>C variant that results in the Cys568Arg amino acid change is reported homozygous in one individual in the literature (PMID: 10233432), meeting PP4_moderate criteria with mucocutaneous bleeding and absent aggregation with ADP, collagen, arachidonic acid but normal aggregation with ristocetin. Additionally, flow cytometry revealed minor amounts to absent GPIIb–IIIa complexes and Western blot confirmed trace amounts of GPIIb and IIIa. A second homozygous patient has been identified in unpublished data (PM3). It is absent in gnomADv4.1 (PM2_supporting) and is predicted damaging by in-silico tools (REVEL score of 0.977; PP3).**

**Experimental evidence shows reduced surface expression and defects in the maturation of GPIIb-IIIa complex (PMID: 12152649; 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, PP3 (VCEP specifications version 2).**

**Met criteria codes**

**PS3_Moderate** ✔

Flow cytometry on COS-7 cells transfected with the Cys568Arg variant showed strongly reduced (not absent) surface expression in the range of 15 - 20% of the GPIIb-IIIa complex. Western blotting also showed that expression was not completely abolished. Immunoprecipitation and Endo-H sensitivity assay showed accumulation of pro-αIIb, indicating that the mutation affects maturation of the integrin. The evidence of reduced expression, consistent with GT, meets criteria for PS3_Moderate.

Flow cytometry on COS-7 cells transfected with the Cys568Arg variant showed strongly reduced (not absent) surface expression in the range of 15 - 20% of the GPIIb-IIIa complex. Western blotting also showed that expression was not completely abolished. Immunoprecipitation and Endo-H sensitivity assay showed accumulation of pro-αIIb, indicating that the mutation affects maturation of the integrin. PubMed:12152649

**PP4_Moderate** ✔

1 published proband reported in PMID: 10233432 meets PP4_moderate criteria. 5yo female proband of Moroccan origin with numerous petechiae and hemorrhagic symptoms: erosive gastritis, epistaxis, traumatic bleeding since 5m of age. BT = 35 mins. Normal platelet count and morphology. Absent aggregation with ADP, collagen, arachidonic acid but normal aggregation with ristocetin. Clot retraction affected and required platelet transfusions. Other clinical findings include cardiac abnormalities, seizures and psychomotor developmental delay. Flow cytometry revealed minor amounts to absent GPIIb–IIIa complexes. Western blot confirmed trace amounts of GPIIb and IIIa. Variant detected by PCR-SSCP. 1 unpublished individual, from internal laboratory data, with petechiae and intracerebral, GI and nose bleeding, bleeding time >30 min, abnormal clot retraction, abnormal platelet aggregation with ADP, collagen, arachidonic acid, but normal aggregation to ristocetin, and <10% GPIIIa expression by flow cytometry.

5yo female proband of Moroccan origin with numerous petechiae and hemorrhagic symptoms: erosive gastritis, epistaxis, traumatic bleeding since 5m of age. BT = 35 mins. Normal platelet count and morphology. Absent aggregation with ADP, collagen, arachidonic acid but normal aggregation with ristocetin. Clot retraction affected and required platelet transfusions. Other clinical findings include cardiac abnormalities, seizures and psychomotor developmental delay. Flow cytometry revealed minor amounts to absent GPIIb–IIIa complexes. Western blot confirmed trace amounts of GPIIb and IIIa. Variant detected by PCR-SSCP. PubMed:10233432

**PM2_Supporting** ✔

Variant is absent from gnomADv4 (PM2_supporting).

**PM3** ✔

2 homozygous individuals (1 pt): 1 patient reported in PMID: 10233432 and 1 unpublished individual based on internal laboratory data meet criteria for PM3.

**PP3** ✔

REVEL score of 0.977 meets criteria for PP3 (>0.7 threshold).

Curation History

Showing 1 to 3 of 3 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.