

Variant: NM_000212.3:c.1595G>T

Version: 1.1

CA400029961 [↗](#)

1879032 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 1a1de21d-c6a1-42e4-bd6a-fa8b296a1d99

Approved on: 2025/6/19

Published on: 2025/6/19

HGVS expressions

NM_000212.3:c.1595G>T

NC_000017.11:g.47292473G>T

CM000679.2:g.47292473G>T

NC_000017.10:g.45369839G>T

CM000679.1:g.45369839G>T

NC_000017.9:g.42724838G>T

NG_008332.2:g.43632G>T

ENST00000696963.1:c.1595G>T

ENST00000559488.7:c.1595G>T

ENST00000559488.5:c.1595G>T

ENST00000560629.1:c.1560G>T

NM_000212.2:c.1595G>T

Likely Pathogenic

Met criteria codes **4**

PP3

PM5

PM2_Supporting

PP4_Moderate

Not Met criteria codes **1**

PM3

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_000212.3(ITGB3):c.1595G>T (p.Cys532Phe) missense variant has been reported in at least one patient (Case 10 in PMID: 34066320) who displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_moderate). This variant is absent from gnomAD v4.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.965, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3). Two different missense variants, Cys532Tyr and Cys532Arg, in the same codon as Cys532Phe, have been classified as likely pathogenic for

Glanzmann thrombasthenia by the ClinGen PD VCEP (PM5). 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: PM2_supporting, PM5, PP3, PP4_moderate.

Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.965, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3).
PM5			Two different missense variants, Cys532Tyr and Cys532Arg, in the same codon as Cys532Phe, have been classified as likely pathogenic for Glanzmann thrombasthenia by the ClinGen PD VCEP (PM5).
PM2_Supporting			This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP4_Moderate			At least one patient (Case 10 in PMID: 34066320) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_moderate). Additionally, α IIb β 3 surface expression was reduced but the value was not provided.

Not Met criteria codes

PM3			Case 10 (PMID: 34066320) is compound heterozygous for Cys532Phe and c.1913+5G>T (classified Likely Pathogenic by the PD-EP; does not meet PM2). The variants were confirmed in trans by Sanger sequencing in family 10. Opt
-----	---	---	---

Curation History

▼

▼

Showing 1 to 2 of 2 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.