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# *Variant: NM_000212.3:c.1456del*

Version: 1.0

*CA915940376*

*1210187 (ClinVar)*

**Gene**: ITGB3 (HGNC:3690)
**Condition**: Glanzmann thrombasthenia (MONDO:0100326)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 156ca3cf-d423-482c-9bdc-648db7c5bf10
**Approved on**: 2021/8/17
**Published on**: 2021/8/20

## *HGVS expressions*

**NM_000212.3:c.1456del**
NC_000017.11:g.47292334del
CM000679.2:g.47292334del
NC_000017.10:g.45369700del
CM000679.1:g.45369700del
NC_000017.9:g.42724699del
NG_008332.2:g.43493del
ENST00000696963.1:c.1456del
ENST00000559488.7:c.1456del
ENST00000559488.5:c.1456del
ENST00000560629.1:c.1421del
NM_000212.2:c.1456del

**Pathogenic**

**Met criteria codes** 4

PM3_Supporting PP4_Moderate PM2_Supporting PVS1

Evidence Links 0

Expert Panel

Platelet Disorders VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Platelet Disorders VCEP***

**The p.Cys486Alafs*183 variant in exon 10 of ITGB3 gene is predicted to introduce a premature stop codon 183 amino acids downstream and result in NMD. This variant is absent from large population databases including gnomAD. It has been reported previously in compound heterozygous state with another pathogenic variant (p.Arg287Serfs*34) in one proband who meets the ClinGen PD-VCEP criteria for the GT phenotype. The variant meets criteria for PVS1, PP4_moderate, PM3_supporting and PM2_supporting and is classified as pathogenic.**

**Met criteria codes**

**PM3_Supporting** ✔ The p.Cys486Alafs variant was reported to occur in compound heterozygous state in one proband with another frameshift variant, p.Arg287Serfs, which has been classified as pathogenic by ClinGen PD-VCEP. 0.5 points.

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|---|---|---|---|
| **PP4_Moderate** | ℹ | ✔ | One individual with the p.Cys486Alafs variant in compound heterozygous state presented with significant mucocutaneous bleeding. Platelet aggregometry demonstrated absence of platelet aggregation with 3 platelet agonists and normal aggregation with ristocetin. Flowcytometry for surface expression of glycoproteins was not performed. Sanger sequencing ensured coverage of exons and splice sites of the ITGA2B and ITGB3 genes as well as untranslated regions (UTR). PMID:25728920 PP4_moderate applied. |
| **PM2_Supporting** | ℹ | ✔ | The p.Cys486Alafs variant is absent from large population databases including gnomAD. |
| **PVS1** | ℹ | ✔ | The p.Cys486Alafs variant located in exon 10 is predicted to introduce a premature stop codon 183 amino acids downstream, resulting in NMD. |

Curation History

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