

Variant: *NM_000212.3:c.1728del*

Version: 1.0

CA915940253 [↗](#)

1330331 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 12180185-5824-4aa1-9378-3110470434b7

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HGVS expressions

NM_000212.3:c.1728del

NC_000017.11:g.47299345del

CM000679.2:g.47299345del

NC_000017.10:g.45376711del

CM000679.1:g.45376711del

NC_000017.9:g.42731710del

NG_008332.2:g.50504del

ENST00000696963.1:c.1728del

ENST00000559488.7:c.1728del

ENST00000559488.5:c.1728del

ENST00000560629.1:c.1693del

NM_000212.2:c.1728del

Pathogenic

Met criteria codes **4**

PM3_Supporting

PP4_Strong

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 NM_000212.3(ITGB3):c.1728del variant results in a frameshift (p.Ser577ProfsTer92) with a premature stop codon in exon 12/15 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). At least two probands has been reported with this variant, including GT28 of PMID: 29675921 who meets the criteria for PP4_strong. GT28 is compound heterozygous for c.1728del and Gln298Ter (Classified Pathogenic by the PD-VCEP; PM3_supporting). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1, PM2_supporting, PM3_supporting, PP4_strong. (VCEP specifications version 2; date of approval xx/xx/xxxx)

Met criteria codes

PM3_Supporting			GT28 of PMID: 29675921 is compound heterozygous for c.1728del and Gln298Ter (Classified Pathogenic by the PD-VCEP). Confirmation of trans phase was not reported. 0.5pt (PM3_supporting).
PP4_Strong			GT28 of PMID: 29675921 meets the criteria for PP4_strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of α IIb β 3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries.
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1			The c.1728del variant results in a frameshift (p.p.Ser577ProfsTer92) with a premature stop codon in exon 12/15 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Curation History 		
 Showing 1 to 1 of 1 rows		

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