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Variant: NM_000212.3:c.1784_1802delinsGTCACA

Version: 1.0

CA915940255

1330323 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 66d12cfa-7b48-4f33-8217-e25f30d77f68
Approved on: 2021/11/4
Published on: 2021/12/23

HGVS expressions

NM_000212.3:c.1784_1802delinsGTCACA
NC_000017.11:g.47299401_47299419delinsGTCACA
CM000679.2:g.47299401_47299419delinsGTCACA
NC_000017.10:g.45376767_45376785delinsGTCACA
CM000679.1:g.45376767_45376785delinsGTCACA
NC_000017.9:g.42731766_42731784delinsGTCACA
NG_008332.2:g.50560_50578delinsGTCACA
ENST00000696963.1:c.1784_1802delinsGTCACA
ENST00000559488.7:c.1784_1802delinsGTCACA
ENST00000559488.5:c.1784_1802delinsGTCACA
ENST00000560629.1:c.1749_1767delinsGTCACA
NM_000212.2:c.1784_1802delinsGTCACA

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PM3_Supporting PP4_Strong

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.1784_1802delinsGTCACA variant results in a frameshift (p.Ser595CysfsTer70) 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 one proband has been reported with this variant, GT41 of PMID: 29675921 who meets the criteria for PP4_strong. GT41 is comopund heterozygous for this variant and Trp579Ter (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 11/04/2021)

Met criteria codes

PM2_Supporting	ℹ	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1	ℹ	✔	The c.1784_1802delinsGTCACA variant results in a frameshift (p.Ser595CysfsTer70) 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).
PM3_Supporting	ℹ	✔	GT41 of PMID: 29675921 is compound heterozygous for c.1784_1802delinsGTCACA and Trp579Ter (classified Pathogenic by the PD-VCEP). Confirmation of trans phase was not reported. 0.5pt
PP4_Strong	ℹ	✔	GT41 of PMID: 29675921 meets the criteria for PP4_strong; including mucocutaneous bleeding, impaired aggregation with all agonists except ristocetin, and reduced surface expression of αIIbβ3 measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries.

Curation History

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See Report	Preferred Variant Title	Classification ℹ	Condition	Published Date	Version ℹ	Criteria Specification	Gene
View	NM_000212.3:c.1784_1802delinsGTCACA	Pathogenic	Glanzmann Thrombasthenia	2021-12-23	1.0	-	ITGB3

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