

Variant: *NM_000212.3(ITGB3):c.1986dup (p.Asp663Ter)*

Version: 1.0

CA915940608 [↗](#)

1684418 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: f81fbd7c-7f4b-4cb6-a8a7-e42d88347d32

Approved on: 2022/12/1

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HGVS expressions

NM_000212.3(ITGB3):c.1986dup (p.Asp663Ter)

NM_000212.3:c.1986dup

NC_000017.11:g.47300550dup

CM000679.2:g.47300550dup

NC_000017.10:g.45377916dup

CM000679.1:g.45377916dup

NC_000017.9:g.42732915dup

NG_008332.2:g.51709dup

ENST00000696963.1:c.1986dup

ENST00000559488.7:c.1986dup

ENST00000559488.5:c.1986dup

ENST00000560629.1:c.1951dup

NM_000212.2:c.1986dup

Pathogenic

Met criteria codes **4**

PP4_Strong

PM3_Supporting

PVS1

PM2_Supporting

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

NM_000212.3(ITGB3):c.1986dup (p.Asp663Ter) found in a homozygous proband (PMID: 29084015; PM3_supporting) causes a premature stop codon at exon 12 and is predicted to undergo nonsense mediated decay (PVS1). The affected individual displayed abnormal bleeding and an impaired response to agonists, with a normal response to ristocetin, which is characteristic of GT. Additionally, α IIb β 3 surface expression was absent (<25%), as measured by flow cytometry (PP4_strong). The variant was not found in gnomAD v2.1.1

(PM2_supporting). In summary the criteria PVS1, PP4_strong, PM2_supporting, and PM3_supporting, were applied to reach a classification of pathogenic.

Met criteria codes			
PP4_Strong			At least one patient (Patient 8 in PMID:29084015) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, αIIbβ3 surface expression was reduced to 0% (<25%), as measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. (PP4_strong)
PM3_Supporting			This variant has been detected in at least 1 proband with Glanzmann thrombasthenia. One proband was homozygous for the variant (PMID:29084015). Total points: .5 (PM3_Supporting).
PVS1			The c.1986dup (p.Asp663Ter) variant in exon 12 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant exon 12/15 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting			This variant is absent from gnomAD v[2.1.1] (PM2_Supporting).

Curation History

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