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Variant: NM_000212.3:c.1814G>A

Version: 1.1

CA400032596

1691461 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 66d35f45-73aa-4a34-a3a0-c1772f0556ee
Approved on: 2025/3/6
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HGVS expressions

NM_000212.3:c.1814G>A
NC_000017.11:g.47299431G>A
CM000679.2:g.47299431G>A
NC_000017.10:g.45376797G>A
CM000679.1:g.45376797G>A
NC_000017.9:g.42731796G>A
NG_008332.2:g.50590G>A
ENST00000696963.1:c.1814G>A
ENST00000559488.7:c.1814G>A
ENST00000559488.5:c.1814G>A
ENST00000560629.1:c.1779G>A
NM_000212.2:c.1814G>A

Likely Pathogenic

Met criteria codes 5

PM2_Supporting | PP3 | PP4_Strong | PM5_Supporting | PM3_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

The NM_000212.3(ITGB3):c.1814G>A (p.Gly605Asp) missense variant is absent from gnomAD v4.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.966, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3). Another missense variant c.1813G>A (p.Gly605Ser) in the same codon has been classified as likely pathogenic for Glanzmann thrombasthenia by the ClinGen PD VCEP (PM5_supporting). This variant has been reported in one GT patient (PMID: 29615672), this patient displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for

Glanzmann thrombasthenia. Additionally, αIIbβ3 surface expression was severely reduced to 6-7%, as measured by flow cytometry (PP4_strong). This patient is compound heterozygous for Gly605Asp and Asn470Ter (classified Pathogenic by the PD-EP; confirmation of trans phase was not reported, PM3_supporting). In summary this variant meets 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, PM3_supporitng, PM5_supporting, PP3, PP4_strong. (VCEP specifications version 2)

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP3	✔	The computational predictor REVEL gives a score of 0.966, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3).
PP4_Strong	✔	One GT patient has been reported with this variant in PMID: 29615672, this patient displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, αIIbβ3 surface expression was severely reduced to 6-7%, as measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries (PP4_strong).
PM5_Supporting	✔	Another missense variant c.1813G>A (p.Gly605Ser) in the same codon has been classified as likely pathogenic for Glanzmann thrombasthenia by the ClinGen PD VCEP (PM5_supporting).
PM3_Supporting	✔	The patient in PMID: 29615672 is compound heterozygous for Gly605Asp and Asn470Ter (classified Pathogenic by the PD-EP). Confirmation of trans phase was not reported (0.5pt; PM3_supporting).

Curation History

Showing 1 to 2 of 2 rows

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