The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000212.3:c.2147G>T

Version: 1.1

CA400033923

1330333 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: ea96a10a-ffb9-4798-9c3f-ae0c2393f5e8
Approved on: 2024/8/20
Published on: 2024/8/20

HGVS expressions

NM_000212.3:c.2147G>T
NC_000017.11:g.47307483G>T
CM000679.2:g.47307483G>T
NC_000017.10:g.45384849G>T
CM000679.1:g.45384849G>T
NC_000017.9:g.42739848G>T
NG_008332.2:g.58642G>T
ENST00000696963.1:c.2147G>T
ENST00000559488.7:c.2147G>T
ENST00000559488.5:c.2147G>T
ENST00000560629.1:c.2112G>T
NM_000212.2:c.2147G>T
NR_110880.1:n.363-3701C>A
NR_110881.1:n.227-3701C>A

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PP3 PP4_Strong 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

The NM_000212.3(ITGB3):c.2147G>T (p.Gly716Val) missense has been identified in at least 1 proband, GT23 of PMID: 29675921 meeting 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.

This variant is absent from gnomAD v4.1.0 (PM2_Supporting). GT23 of PMID: 29675921 is compound heterozygous for Gly716Val and Tyr660Ter (classified Pathogenic by the PD-VCEP; PM3_supporting). The computational predictor REVEL gives a score of 0.802, which predicts a damaging effect on ITGB3 function (PP3). In summary, this variant meets the 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_supporting, PP3, PP4_strong. (VCEP specifications version 2; date of approval xx/xx/xxxx)

Met criteria codes

PM3_Supporting	✔	GT23 of PMID: 29675921 is compound heterozygous for Gly716Val and Tyr660Ter (classified Pathogenic by the PD-VCEP). Confirmation of trans phase was no reported. 0.5pt (PM3_supporting).
PP3	✔	The computational predictor REVEL gives a score of 0.802, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on ITGB3 function (PP3).
PP4_Strong	✔	GT23 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.
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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