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(ITGB3):c.1641C>A (p.Cys547Ter)

Version: 1.0

CA400030168

977131 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 08d055ef-9deb-4c6a-bd3b-7d6bc0b854f4
Approved on: 2022/9/20
Published on: 2022/12/7

HGVS expressions

NM_000212.3(ITGB3):c.1641C>A (p.Cys547Ter)
NM_000212.3:c.1641C>A
NC_000017.11:g.47292519C>A
CM000679.2:g.47292519C>A
NC_000017.10:g.45369885C>A
CM000679.1:g.45369885C>A
NC_000017.9:g.42724884C>A
NG_008332.2:g.43678C>A
ENST00000696963.1:c.1641C>A
ENST00000559488.7:c.1641C>A
ENST00000559488.5:c.1641C>A
ENST00000560629.1:c.1606C>A
NM_000212.2:c.1641C>A

Pathogenic

Met criteria codes 4

PM3_Supporting PVS1 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.1641C>A (p.Cys547Ter) variant in exon 10/15 is a nonsense variant predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). It has been reported homozygous (PM3_supporting) in at least one GT proband (P18 in PMID: 34275420) who displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, αIIbβ3 surface expression was absent, as measured

by flow cytometry (PP4_strong). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). In summary, based on the available evidence at this time, the variant is classified as pathogenic for GT. GT-specific criteria applied: PVS1, PM2_Supporting, PM3_supporting, PP4_strong.

Met criteria codes

PM3_Supporting	✔	P18 is homozygous for this variant (PMID: 34275420; PM3_supporting)
PVS1	✔	The c.1641C>A (p.Cys547Ter) variant in exon 10/15 is a nonsense variant predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Strong	✔	At least one patient (P18 in PMID: 34275420) 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 <5%, as measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. (PP4_strong)
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History

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