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Variant: NM_000212.3:c.1980C>A

Version: 1.0

CA400032983

1330334 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 184c3689-ab69-40b9-8f76-205700d2d0ae
Approved on: 2021/6/30
Published on: 2021/12/23

HGVS expressions

NM_000212.3:c.1980C>A
NC_000017.11:g.47300544C>A
CM000679.2:g.47300544C>A
NC_000017.10:g.45377910C>A
CM000679.1:g.45377910C>A
NC_000017.9:g.42732909C>A
NG_008332.2:g.51703C>A
ENST00000696963.1:c.1980C>A
ENST00000559488.7:c.1980C>A
ENST00000559488.5:c.1980C>A
ENST00000560629.1:c.1945C>A
NM_000212.2:c.1980C>A

Pathogenic

Met criteria codes 3

PP4_Strong PVS1 PM2_Supporting

Not Met criteria codes 1

PM3

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.1980C>A (p.Tyr660Ter) nonsense variant creates 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, GT23 of PMID: 29675921 meets the criteria for PP4_strong. 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, PP4_strong. (VCEP specifications version 2; date of approval xx/xx/xxxx)

Met criteria codes

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.
PVS1	✔	The NM_000212.3(ITGB3):c.1980C>A (p.Tyr660Ter) is a nonsense 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 v2.1.1 (PM2_Supporting).

Not Met criteria codes

PM3	✖	GT23 is compound heterozygous for Tyr660Ter and Gly716Val (not yet classified by the PD-VCEP). Confirmation of trans phase was not reported. Not counted here to avoid circularity. 0pt

Curation History

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