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Variant: NM_000212.3:c.118C>T

Version: 1.0

CA400031679

1879041 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 8b8dc150-3ac0-4be6-90f0-e037ecfc22b1
Approved on: 2022/4/7
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HGVS expressions

NM_000212.3:c.118C>T
NC_000017.11:g.47274457C>T
CM000679.2:g.47274457C>T
NC_000017.10:g.45351823C>T
CM000679.1:g.45351823C>T
NC_000017.9:g.42706822C>T
NG_008332.2:g.25616C>T
ENST00000696963.1:c.118C>T
ENST00000559488.7:c.118C>T
ENST00000559488.5:c.118C>T
ENST00000560629.1:c.83C>T
ENST00000571680.1:c.118C>T
NM_000212.2:c.118C>T

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PP4_Strong

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.118C>T (p.Gln40Ter) variant in exon 2/15 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). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). At least one patient (Patient GT8 in PMID:25373348) 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 severely reduced, as measured by flow cytometry and Western blot. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries (PP4_strong). In summary this variant meets 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: PP4_strong, PVS1, PM2_supporting. (VCEP specifications version 2; date of approval 02/03/2022)

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1	✔	The c.118C>T (p.Gln40Ter) variant in exon 2/15 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 (Patient GT8 in PMID:25373348) 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 severely reduced, as measured by flow cytometry and Western blot. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries (PP4_strong).

Curation History

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