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Variant: NM_000419.5:c.2702C>A

Version: 1.0

CA399792888

1879058 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2a757eaa-34b1-4cd7-809d-7974e950ee53
Approved on: 2022/11/15
Published on: 2022/12/7

HGVS expressions

NM_000419.5:c.2702C>A
NC_000017.11:g.44375616G>T
CM000679.2:g.44375616G>T
NC_000017.10:g.42452984G>T
CM000679.1:g.42452984G>T
NC_000017.9:g.39808510G>T
NG_008331.1:g.18890C>A
ENST00000262407.6:c.2702C>A
ENST00000648408.1:c.2133C>A
ENST00000262407.5:c.2702C>A
ENST00000587295.5:c.253+217C>A
ENST00000592462.5:n.1497C>A
NM_000419.3:c.2702C>A
NM_000419.4:c.2702C>A

Pathogenic

Met criteria codes 4

PM2_Supporting PM3 PVS1 PP4_Moderate

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

NM_000419.5(ITGA2B):c.2702C>A (p.Ser901Ter) found in three unrelated homozygous probands from Tunisia (PMID:30325339; PM3) causes a premature stop codon at exon 26 and is predicted to undergo nonsense mediated decay (PVS1). At least one patient with this variant displayed abnormal bleeding and an impaired response to agonists, with a normal response to ristocetin, which is characteristic of

Glanzmann thrombasthenia (PMID:30325339; PP4_moderate). The variant was not found in 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_moderate, and PM3.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v[2.1.1] (PM2_Supporting).
PM3	✔	This variant has been detected in at least 3 probands with Glanzmann thrombasthenia. Three probands were reportedly unrelated from different parts of Tunisia and were homozygous for the variant (PMID: 30325339. Total points: 1) (PM3).
PVS1	✔	The c.2702C>A (p.Ser901Ter) variant in exon 26 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 26/30 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Moderate	✔	At least one patient (Patient F3P1 in PMID: 30325339) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann Thrombasthenia (PP4_moderate). However, ITGA2B and ITGB3 were not reported to be sequenced across all exons and intron/exon boundaries.

Curation History

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