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Variant: NM_000419.5:c.527C>T

Version: 2.0

CA399805789

953018 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5f6c2e98-4031-47f6-883a-5354adebb7c9
Approved on: 2023/10/17
Published on: 2023/10/17

HGVS expressions

NM_000419.5:c.527C>T
NC_000017.11:g.44385598G>A
CM000679.2:g.44385598G>A
NC_000017.10:g.42462966G>A
CM000679.1:g.42462966G>A
NC_000017.9:g.39818492G>A
NG_008331.1:g.8908C>T
ENST00000262407.6:c.527C>T
ENST00000262407.5:c.527C>T
ENST00000592944.1:n.212C>T
NM_000419.3:c.527C>T
NM_000419.4:c.527C>T

Likely Pathogenic

Met criteria codes 5

PM5 PP4_Moderate PM3_Supporting PP3 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_000419.4:c.527C>T (p.Pro176Leu) variant has been reported (PMID: 1060770) in at least one compound heterozygous (with pathogenic variant c.1545-1del) proband with a phenotype highly specific to GT (PP4_Moderate, PM3_supporting). It is absent from gnomADv2.1.1)PM2_supporting0 and multiple lines of computational evidence support a deleterious effect (REVEL score of 0.855; PP3). The pathogenic variant Pro176Ala occurs at the same amino acid residue (PM5). In summary, this variant meets criteria to be classified as likely pathogenic for GT. GT-specific criteria applied: PM2_Supporting, PM3_Supporting, PM5, PP3, and PP4_Moderate.

Met criteria codes

PM5	✔	The Pro176Leu variant occurs at the same residue as the previously classified Pathogenic Pro176Ala variant and the Likely Pathogenic Pro176His variant.
PP4_Moderate	✔	At least one proband from PMID: 1060770 meets the criteria for PP4; including mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin.
PM3_Supporting	✔	PMID: 10607701 Patient Chinese-14 is compound heterozygous for Pro176Leu and pathogenic variant c.1545-1del, without confirmation of trans phase.
PP3	✔	SIFT (Damaging), Polyphen2-HDIV 1 (probably Damaging), and Mutation Taster (disease causing) agree that this variant has a deleterious effect and the REVEL score is 0.855, above the >0.7 threshold.
PM2_Supporting	✔	This variant is absent from all population cohorts in gnomAD, ExAC, 1000 Genomes, and ESP.

Curation History

Showing 1 to 2 of 2 rows

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