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Variant: NM_000419.5(ITGA2B):c.842C>T (p.Thr281Ile)

Version: 2.0

CA399805055

1210182 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: db73dca4-48dc-46f7-aade-c0a32a8c7e2b
Approved on: 2024/5/2
Published on: 2024/5/3

HGVS expressions

NM_000419.5(ITGA2B):c.842C>T (p.Thr281Ile)
NM_000419.5:c.842C>T
NC_000017.11:g.44384543G>A
CM000679.2:g.44384543G>A
NC_000017.10:g.42461911G>A
CM000679.1:g.42461911G>A
NC_000017.9:g.39817437G>A
NG_008331.1:g.9963C>T
ENST00000262407.6:c.842C>T
ENST00000648408.1:c.273C>T
ENST00000262407.5:c.842C>T
ENST00000589645.5:n.293C>T
ENST00000591990.5:n.204C>T
ENST00000592075.5:n.211C>T
ENST00000592226.5:n.82C>T
ENST00000592253.5:n.350C>T
ENST00000592944.1:n.524C>T
NM_000419.3:c.842C>T
NM_000419.4:c.842C>T

Likely Pathogenic

Met criteria codes 3

PM3_Supporting PP4_Strong PM2_Supporting

Not Met criteria codes 2

BP4 PP3

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 missense variant NM_000419.5(ITGA2B):c.842C>T (p.Thr281Ile) is absent from gnomADv4.o (PM2_supporting). It is reported in one compound heterozygous individual (PMID: 25373348) with c.2602-3C>A and c.2602-2A>G (classified Likely Pathogenic by the PD-VCEP; SCV001809877.2) and one homozygous individual (PMID: 31029159; PM3_supporting). GT16 of PMID: 25373348 meets bleeding phenotype, aggregometry criteria, and integrin expression is reported to be <5% reduced by flow cytometry, and all exons of ITGA2B and ITGB3 genes as well as surrounding intron regions were sequenced. (PP4_Strong). In summary, this variant meets criteria to be classified as Likely Pathogenic for GT. GT-specific criteria applied: PP4_Strong, PM2_Supporting, PM3_Supporting.

Met criteria codes

PM3_Supporting	✔	Case 12 of PMID: 31029159 is homozygous for Thr281Ile.
PP4_Strong	✔	GT16 of PMID: 25373348 meets bleeding phenotype, aggregometry criteria, and integrin expression is reported to be <5% reduced by flow cytometry, and all exons of ITGA2B and ITGB3 genes as well as surrounding intron regions were sequenced.
PM2_Supporting	✔	This variant is absent from gnomADv4.0

Not Met criteria codes

BP4	✖	The c.842C>T (p.Thr281Ile) variant has a REVEL score of 0.211, this is below the threshold of <0.25 for BP4 however MaxEntScan identifies a new acceptor site (2.55 > 3.69 => 44.71%) and the phyloP score of 2.981 suggests high conservation at this site so BP4 is not applied.
PP3	✖	MaxEntScan identifies a new weak acceptor site (2.55 > 3.69 => 44.71%) however this is not identified by other predictors (Splice AI delta score 0.02).

Curation History

Showing 1 to 2 of 2 rows

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