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Variant: NM_000212.3:c.941A>C

Version: 2.0

CA400025615

996159 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 96a290ca-2034-477d-82dd-a8e62c4c5ce8
Approved on: 2023/12/19
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HGVS expressions

NM_000212.3:c.941A>C
NC_000017.11:g.47289682A>C
CM000679.2:g.47289682A>C
NC_000017.10:g.45367048A>C
CM000679.1:g.45367048A>C
NC_000017.9:g.42722047A>C
NG_008332.2:g.40841A>C
ENST00000696963.1:c.941A>C
ENST00000559488.7:c.941A>C
ENST00000559488.5:c.941A>C
ENST00000560629.1:c.906A>C
ENST00000571680.1:c.941A>C
NM_000212.2:c.941A>C

Likely Pathogenic

Met criteria codes 5

PM3_Supporting PP4_Moderate PM5_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_000212.3(ITGB3):c.941A>C (p.Asp314Ala) missense variant has been reported at least once in literature, in a homozygous patient (PMID:20514620; PM3_supporting). The patient was demonstrated to have lack of platelet aggregation with three physiological agonists (normal with ristocetin) and this was confirmed by flow cytometry. Personal communication with the authors revealed the patient was treated for multiple mucocutaneous bleeding phenotypes (PP4_moderate). The variant is absent from all population database cohorts,

including gnomAD (PM2_supporting) and is predicted deleterious (REVEL score 0.974; PP3). The Asp314Alal variant occurs at the same residue as Asp314Tyr (classified Likely Pathogenic by the PD-EP; PM5_supporting). In summary this variant meets criteria to be classified as likely pathogenic for GT. GT-specific criteria applied: PM2_supporting, PM3_supporitng, PM5_supporting, PP3, and PP4_moderate.

Met criteria codes

PM3_Supporting	✔	This variant has been reported in homozygous state in one proband. (PMID: 20514620)) 0.5 points
PP4_Moderate	✔	PMID:20514620 reported a 7.5 year old male child who was demonstrated to have lack of platelet aggregation with three physiological agonists (normal with ristocetin) and this was confirmed by flow cytometry. Personal communication with the authors revealed the patient was treated for multiple mucocutaneous bleeding phenotypes. Unknown if there was full sequencing of the ITGB3 and ITGA2B genes.
PM5_Supporting	✔	Another missense change (Asp314Tyr) has been reported at this position, which has been classified as likely pathogenic by Clingen platelet VCEP. Therefore, PM5_supporting applied.
PP3	✔	REVEL score of 0.974 is above the impact threshold of 0.70 , Therefore PP3 is met.
PM2_Supporting	✔	This variant is absent from large population databases including gnomAD, ExAC, 1000Genomes

Curation History

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