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Variant: NM_000419.5(ITGA2B):c.240_241del (p.Glu80fs)

Version: 2.0

CA1139654962

977125 (ClinVar)

Gene: ITGA2B
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: cf37ba1d-7bdf-406c-91aa-6a6acdd669a6
Approved on: 2022/6/8
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HGVS expressions

NM_000419.5:c.240_241del
NM_000419.5(ITGA2B):c.240_241del (p.Glu80fs)
NC_000017.11:g.44386081_44386082del
CM000679.2:g.44386081_44386082del
NC_000017.10:g.42463449_42463450del
CM000679.1:g.42463449_42463450del
NC_000017.9:g.39818975_39818976del
NG_008331.1:g.8426_8427del
ENST00000262407.6:c.240_241del
ENST00000262407.5:c.240_241del
NM_000419.3:c.240_241del
NM_000419.4:c.240_241del

Pathogenic

Met criteria codes 4

PM3_Supporting PP4_Strong PVS1 PM2_Supporting

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_000419.5(ITGA2B):c.240_241del (p.Glu80fs) frameshift variant occurs in exon 2 of 30 where it creates a premature stop codon and is predicted to result in NMD. At least one patient (P1 in PMID: 34275420) is homozygous for this variant (PM3_supporting) and displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia. Additionally, αIIbβ3 surface expression was reduced to <5%, as measured by flow cytometry (PP4_strong). It is absent from gnomAD, ExAC, 1000 Genomes, and ESP. In summary, this variant meets criteria to be classified as pathogenic for GT. GT-specific criteria applied: PP4_Strong, PM2_Supporting, PM3_supporting, and PVS1.

Met criteria codes

PM3_Supporting		✔	P1 (PMID: 34275420) is homozygous for this variant. 0.5pt (PM3_supporting)
PP4_Strong		✔	At least one patient (P1 in PMID: 34275420) 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 reduced to <5%, as measured by flow cytometry. ITGA2B and ITGB3 were sequenced across all exons and intron/exon boundaries. (PP4_strong)
PVS1		✔	The frameshift variant occurs in exon 2 of 30 where it creates a premature stop codon and is predicted to result in NMD.
PM2_Supporting		✔	This variant is absent from all population cohorts in gnomAD, ExAC, 1000 Genomes, and ESP.

Curation History

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