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Variant: NM_000419.5:c.727del

Version: 1.0

CA915940727

1330329 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6840e950-97da-47e6-8562-173e19221ad9
Approved on: 2021/7/14
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HGVS expressions

NM_000419.5:c.727del
NC_000017.11:g.44385021del
CM000679.2:g.44385021del
NC_000017.10:g.42462389del
CM000679.1:g.42462389del
NC_000017.9:g.39817915del
NG_008331.1:g.9486del
ENST00000262407.6:c.727del
ENST00000648408.1:c.158del
ENST00000262407.5:c.727del
ENST00000589645.5:n.178del
ENST00000591990.5:n.89del
ENST00000592075.5:n.96del
ENST00000592226.5:n.39+144del
ENST00000592253.5:n.235del
ENST00000592944.1:n.409del
NM_000419.3:c.727del
NM_000419.4:c.727del

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PP4_Moderate PM3_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 ITGA2B frameshift variant NM_000419.5:c.727del (p.Leu243PhefsTer136) introduces a frameshift in exon 7 of 30 total exons and premature termination codon in exon 12. The resulting mRNA product is predicted to undergo nonsense mediated decay, leading to loss of normal protein function. This variant has been observed in homozygosity in one individual with a phenotype specific for Glanzmann's thrombasthenia (GT) (GT41, PMID: 16463284). Furthermore, this variant is absent from population databases. In summary, this variant

meets criteria to be classified as pathogenic for GT. GT-specific criteria applied: PVS1, PM3_Supporting, PP4_Moderate, and PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from all population cohorts in gnomAD, ExAC, 1000 Genomes, and ESP.
PVS1	✔	This variant introduces a frameshift in exon 7/30, leading to a premature termination codon in exon 12, and producing an mRNA product expected to be susceptible to nonsense mediated decay.
PP4_Moderate	✔	All requirements for PP4_Moderate are met (GT41 in PMID: 16463284): history of bleeding and impaired aggregation to at least two agonists, but normal or only mildly reduced agglutination with ristocetin.
PM3_Supporting	✔	This variant was reported in homozygosity in one individual (GT41 in PMID: 16463284), sufficient to apply PM3_Supporting.

Curation History

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