The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000419.4:c.2153dup

Version: 1.0

CA913189170

953023 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann's thrombasthenia (MONDO:0010119)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7a03816f-303b-4f16-97b4-1c93db27ee90
Approved on: 2020/9/4
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HGVS expressions

NM_000419.4:c.2153dup
NC_000017.11:g.44377732dup
CM000679.2:g.44377732dup
NC_000017.10:g.42455100dup
CM000679.1:g.42455100dup
NC_000017.9:g.39810626dup
NG_008331.1:g.16774dup
ENST00000262407.6:c.2153dup
ENST00000648408.1:c.1584dup
ENST00000262407.5:c.2153dup
ENST00000592462.5:n.948dup
NM_000419.3:c.2153dup
NM_000419.5:c.2153dup

Pathogenic

Met criteria codes 3

PP4_Moderate PM2_Supporting PVS1

Not Met criteria codes 1

PM3

Evidence Links 1

Expert Panel

Platelet Disorders VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.2153dup (p.Cys718Trpfs) frameshift variant has been reported in at least one compound heterozygous proband (PMID: 11798398) with a phenotype highly specific to GT. It is predicted to undergo NMD due to creation of a premature stop codon in exon 21. This variant is absent from controls in gnomAD, ExAC, and 1000 genomes. In summary, this variant meets criteria to be classified as Pathogenic for GT. GT-specific criteria applied: PVS1, PM2_supporting, and PP4_moderate.

Met criteria codes

PP4_Moderate	✔	Patient FO, a compound heterozygote, was reported to have type I GT with a lack of GpIIb-GPIIIa at the platelet surface (by Western blot and flow cytometry). With information available in the GT database this patient meets PP4_moderate criteria with a bleeding phenotype, absent aggregation with ADP and collagen but normal with ristocetin, and lack of protein expression on the platelet surface. Patient FO, a compound heterozygote, was reported to have type I GT with a lack of GpIIb-GPIIIa at the platelet surface (by Western blot and flow cytometry). GT diagnosis was reportedly evoked on clinical presentation and platelet aggregation analysis. Platelet aggregation, reported in the Glanzmann Thrombasthenia database entry 185, was absent in response to collagen and ADP but normal for ristocetin and the patient was noted to have a bleeding time >10 min. PubMed:11798398
PM2_Supporting	✔	This variant is absent from all population cohorts in gnomAD, ExAC, 1000 Genomes, and ESP.
PVS1	✔	This frameshift variant c.2153dup (p.Cys718TrpfsTer2) generates a stop codon two residues downstream in exon 21 of 30 and as such is expected to undergo NMD.

Not Met criteria codes

PM3	✖	Patient FO is compound heterozygous for c.2153dupG (p.Cys718Trpfs*2) and pathogenic variant c.1234G>A (p.Gly412Arg). The trans phase of the variants was not confirmed. To avoid circularity the proband was counted only towards the classification Gly412Arg not c.2153dup. 0pt. PubMed:11798398

Curation History

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