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.1075_1078del

Version: 1.0

CA913184943

953001 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann's thrombasthenia (MONDO:0010119)
Inheritance Mode: Autosomal recessive inheritance
UUID: bd3b826a-5cd8-4c84-a916-054f34766f89
Approved on: 2020/9/6
Published on: 2021/1/28

HGVS expressions

NM_000419.4:c.1075_1078del
NC_000017.11:g.44383627_44383630del
CM000679.2:g.44383627_44383630del
NC_000017.10:g.42460995_42460998del
CM000679.1:g.42460995_42460998del
NC_000017.9:g.39816521_39816524del
NG_008331.1:g.10878_10881del
ENST00000262407.6:c.1075_1078del
ENST00000648408.1:c.506_509del
ENST00000262407.5:c.1075_1078del
ENST00000592226.5:n.315_318del
NM_000419.3:c.1075_1078del
NM_000419.5:c.1075_1078del

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PP4_Moderate

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 NM_000419.4:c.1075_1078del variant causes a frameshift and early termination of transcription, with predicted NMD of the mRNA. It is absent from population databases and is reported in one individual in the literature with a mild phenotype (PMID: 19172520). Based on the available evidence at this time, the c.1075_1078del variant is classified as pathogenic. GT-specific criteria met: PVS1, PM2_supporting, PP4_moderate.

Met criteria codes

PVS1	✔	The 4bp deletion in exon 12 causes a frameshift and premature stop at amino acid position 377. The resulting transcript is predicted to undergo NMD.
PM2_Supporting	✔	The variant is absent from gnomAD and other population databases.
PP4_Moderate	✔	Patient 8 from PMID: 19172520 meets the criteria for PP4_moderate; including mucocutaneous bleeding, impaired aggregation with all the agonists except ristocetin, and reduced surface expression of αIIbβ3. Patient 8 is a 3yo female from India, with occasional epistaxis, ecchymoses and gum bleeding. There was no family history of bleeding and parental consanguinity was reported. Platelet count was not reported but platelet aggregation was tested, using a lumi-aggregometer, with collagen, epinephrine, arachidonic acid and ristocetin. Impaired aggregation with all the agonists except ristocetin is not explicitly noted (but this is reported in the GT database entry 238). αIIbβ3 expression was analyzed by flow cytometry and patient classified as having Type I GT (GPIIB-IIIa < 5%). She was homozygous for the c.1075_1078del variant. PubMed:19172520

Not Met criteria codes

PM3	✖	Patient 8 in PMID: 19172520 is expected to be homozygous based on SSCP analysis and consanguinity. However, PM3_supporting is not applied since this has not been specified. Patient 8 is homozygous for the c.1075_1078del variant. PubMed:19172520

Curation History

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