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Variant: NM_000212.3:c.122_125dup

Version: 1.0

CA915940804

953030 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann's thrombasthenia (MONDO:0010119)
Inheritance Mode: Autosomal recessive inheritance
UUID: f6a5ee90-18f2-4c37-8ef2-253611169962
Approved on: 2020/6/4
Published on: 2021/1/23

HGVS expressions

NM_000212.3:c.122_125dup
NC_000017.11:g.47274461_47274464dup
CM000679.2:g.47274461_47274464dup
NC_000017.10:g.45351827_45351830dup
CM000679.1:g.45351827_45351830dup
NC_000017.9:g.42706826_42706829dup
NG_008332.2:g.25620_25623dup
ENST00000696963.1:c.122_125dup
ENST00000559488.7:c.122_125dup
ENST00000559488.5:c.122_125dup
ENST00000560629.1:c.87_90dup
ENST00000571680.1:c.122_125dup
NM_000212.2:c.122_125dup

Pathogenic

Met criteria codes 3

PM3_Supporting PM2_Supporting PVS1

Not Met criteria codes 1

PP4

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_000212.2:c.122_125dup variant results in premature termination of translation at Cys42 in exon 2/15. The resulting transcript is predicted to undergo NMD. The variant is absent from all population databases including gnomAD. The variant is reported in one homozygous individual who does not meet criteria for PP4 (PMID: 12353082). In summary, based on the evidence available at this time, the variant is classified as pathogenic. GT-specific criteria applied: PVS1, PM2_Supporting, PM3_Supporting.

Met criteria codes

PM3_Supporting	✔	One GT patient has been identified with this homozygous variant in PMID: 12353082 (Patient 2).
PM2_Supporting	✔	This variant is absent from all population cohorts in gnomAD, ExAC, 1000 Genomes, and ESP.
PVS1	✔	The c.122_125dup variant immediately generates the Cys42Ter premature stop codon in exon 2 of 15. This is predicted to result in NMD.

Not Met criteria codes

PP4	✖	One patient has been identified with this variant in PMID: 12353082. Patient 2 was diagnosed with GT based on absence of platelet aggregation in response to ADP and <1% of normal levels of platelet surface expression measured by radio-electroimmunoassay. Additionally, under nonreduced immunoblot conditions, beta3 subunits were undetectable. This patient does not meet PP4 because only one agonist was reported with impaired aggregation and ristocetin response was not reported (although it was noted to be normal in the GT database), and surface expression was not measured by either flow cytometry or Western blot.

Curation History

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