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Variant: NM_000212.3:c.1697G>A

Version: 1.0

CA400032338

977132 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann's thrombasthenia (MONDO:0010119)
Inheritance Mode: Autosomal recessive inheritance
UUID: 35e048e3-fc85-4711-aaa6-3c21d109e705
Approved on: 2020/9/8
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HGVS expressions

NM_000212.3:c.1697G>A
NC_000017.11:g.47299314G>A
CM000679.2:g.47299314G>A
NC_000017.10:g.45376680G>A
CM000679.1:g.45376680G>A
NC_000017.9:g.42731679G>A
NG_008332.2:g.50473G>A
ENST00000696963.1:c.1697G>A
ENST00000559488.7:c.1697G>A
ENST00000559488.5:c.1697G>A
ENST00000560629.1:c.1662G>A
NM_000212.2:c.1697G>A

Pathogenic

Met criteria codes 5

PM3_Supporting PP4_Strong PM2_Supporting PS3 PP3

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_000212.3:c.1697G>A variant in ITGB3 resulting in a missense change, Gly566Asp, is absent from gnomAD v2.1.1 and v3 . It has a very high REVEL score of 0.99. It is reported in at least two unrelated probands, one of them homozygous and the other compound heterozygous with the Arg119Gln variant (PMID: 25728920, 27098940). Experimental studies show that the variant leads to complete absence of cell-surface expression of αIIbβ3, when expressed in CHO cells (PMID: 27098940). In summary, the variant meets criteria to be classified as pathogenic. GT-specific criteria met: PS3, PP4_Strong, PP3, PM2_Supporting, PM3_Supporting.

Met criteria codes

PM3_Supporting	✔	1 homozygous proband reported in PMID: 27098940 meets criteria for PM3_Supporting

PP4_Strong	ℹ	✔	Probands from PMID: 25728920 and PMID: 27098940 meet criteria for PP4_Strong including bleeding phenotype, abnormal platelet aggregation in response to >2 agonists and normal aggregation to ristocetin, reduced αIIbβ3 integrin expression on flow cytometry and full sequencing of ITGA2B and ITGB3 both genes.
PM2_Supporting	ℹ	✔	The variant is absent from gnomAD v2.1.1 and v3 and meets criteria for PM2_Supporting
PS3	ℹ	✔	Evidence from PMID: 27098940 meets PS3 criteria with mutant-expressing CHO cells showing complete absence of cell-surface expression of αIIbβ3
PP3	ℹ	✔	The variant meets PP3 with a REVEL score of 0.99 (threshold: >0.7)

Curation History

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