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_000419.5:c.266G>A

Version: 1.0

CA399806384

996185 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann's thrombasthenia (MONDO:0010119)
Inheritance Mode: Autosomal recessive inheritance
UUID: a54a6b68-6293-4cc7-a82a-06f6cc2515b7
Approved on: 2020/10/14
Published on: 2021/1/19

HGVS expressions

NM_000419.5:c.266G>A
NC_000017.11:g.44386054C>T
CM000679.2:g.44386054C>T
NC_000017.10:g.42463422C>T
CM000679.1:g.42463422C>T
NC_000017.9:g.39818948C>T
NG_008331.1:g.8452G>A
ENST00000262407.6:c.266G>A
ENST00000262407.5:c.266G>A
NM_000419.3:c.266G>A
NM_000419.4:c.266G>A

Pathogenic

Met criteria codes 5

PM3_Supporting | PP1 | PP4_Moderate | PVS1 | PM2_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 nonsense variant NM_000419.5:c.266G>A (p.Trp89Ter) is expected to introduce a premature termination and 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) (GT-13, PMID: 25539746; reported as p.Trp51Stop in the publication, but determined to be p.Trp58Ter/p.Trp89Ter through personal communication with the corresponding author, Dr. José Rivera) and an affected relative (also homozygous for this variant). 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, PM2_supporting, PP1.

Met criteria codes

PM3_Supporting		✔	This variant has been observed in homozygosity in one individual (GT-13, PMID: 25539746), sufficient to apply PM3_supporting. This variant was reported as p.Trp51Stop (without signal peptide) in the publication, but was determined to be p.Trp58Ter/p.Trp89Ter through personal communication with the corresponding author, Dr. José Rivera.
PP1		✔	This variant was observed in homozygosity in the original proband (GT-13, reported in PMID: 25539746) and an affected family member (also in homozygosity), as well as multiple unaffected heterozygous family members (personal communication from Dr. José Rivera, Universidad de Murcia, corresponding author of PMID: 25539746).
PP4_Moderate		✔	All requirements for PP4_moderate are met (GT-13, PMID: 25539746): history of bleeding; impaired aggregation to at least two agonists, but normal or only mildly reduced agglutination with ristocetin; flow cytometry showed <5% expression of αIIbβ3.
PVS1		✔	This variant introduces a termination codon at amino acid position 89 in exon 2/30. The resulting mRNA product is predicted to undergo nonsense mediated decay, leading to loss of normal protein function.
PM2_Supporting		✔	This is a rare variant not reported in control population databases, including gnomAD v2.1.1, gnomAD v3, PAGE, 1000 Genomes, and ESP, meeting the criterion to apply PM2_supporting.

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.