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Variant: NM_000419.5:c.1672C>T

Version: 1.0

CA290949843

996196 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann's thrombasthenia (MONDO:0010119)
Inheritance Mode: Autosomal recessive inheritance
UUID: 27432f6c-0a8e-4dd5-abdc-e3aeb530dae4
Approved on: 2020/8/27
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HGVS expressions

NM_000419.5:c.1672C>T
NC_000017.11:g.44380082G>A
CM000679.2:g.44380082G>A
NC_000017.10:g.42457450G>A
CM000679.1:g.42457450G>A
NC_000017.9:g.39812976G>A
NG_008331.1:g.14424C>T
ENST00000262407.6:c.1672C>T
ENST00000648408.1:c.1103C>T
ENST00000262407.5:c.1672C>T
ENST00000592226.5:n.1145C>T
ENST00000592462.5:n.467C>T
NM_000419.3:c.1672C>T
NM_000419.4:c.1672C>T

Pathogenic

Met criteria codes 3

PM3_Supporting PVS1 PM2_Supporting

Not Met criteria codes 1

PP4

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 ITGA2B nonsense variant NM_000419.4:c.1672C>T (p.Gln558Ter) introduces a premature termination codon 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 an individual with a platelet aggregation phenotype consistent with Glanzmann's thrombasthenia (GT), however sufficient bleeding phenotype information was not provided to determine if the individual's phenotype is specific for GT. This variant has not been reported in population databases. In summary, this variant meets criteria to be classified as pathogenic for GT. GT-specific criteria applied: PVS1, PM2_Supporting, and PM3_supporting.

Met criteria codes

PM3_Supporting	✔	This variant was reported in homozygosity in one individual (CabGT-8 in PMID: 20020534). This homozygous occurrence earns 0.5 points and is sufficient to apply PM3_supporting. PubMed:20020534
PVS1	✔	This variant introduces a termination codon at amino acid position 558 in exon 17/30. The resulting mRNA product is predicted to undergo nonsense mediated decay, leading to loss of normal protein function.
PM2_Supporting	✔	Variant not observed in gnomAD v2.1.1 or v3.

Not Met criteria codes

PP4	✖	This variant was reported in homozygosity in one individual (originally reported as CabGT-8 in PMID: 20020534, additional information reported as 279 — Patient 8 in Glanzmann's Thrombasthenia Database) with a platelet aggregation phenotype consistent with Glanzmann's Thrombasthenia (abnormal response to multiple agonists and normal response to ristocetin). However, sufficient phenotypic information (bleeding phenotype, surface expression, etc.) to meet PP4 were not provided.

Curation History

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