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# *Variant: NM_000419.5:c.531T>A*

Version: 1.0

*CA290955739*

*996195 (ClinVar)*

**Gene**: ITGA2B (HGNC:3674)
**Condition**: Glanzmann's thrombasthenia (MONDO:0010119)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 590bab7e-2dad-47cc-9986-0645b00b30e5
**Approved on**: 2020/9/8
**Published on**: 2021/1/22

## *HGVS expressions*

**NM_000419.5:c.531T>A**
NC_000017.11:g.44385594A>T
CM000679.2:g.44385594A>T
NC_000017.10:g.42462962A>T
CM000679.1:g.42462962A>T
NC_000017.9:g.39818488A>T
NG_008331.1:g.8912T>A
ENST00000262407.6:c.531T>A
ENST00000262407.5:c.531T>A
ENST00000592944.1:n.216T>A
NM_000419.3:c.531T>A
NM_000419.4:c.531T>A

**Pathogenic**

**Met criteria codes** 4

PM3_Supporting PVS1 PP4_Moderate PM2_Supporting

Evidence Links 2

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.531T>A (p.Cys177Ter) 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 heterozygosity in a proband with a phenotype specific for Glanzmann's thrombasthenia (GT) and in homozygosity in an additional individual with 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, PM3_supporting, and PP4_moderate.**

**Met criteria codes**

**PM3_Supporting** ✔

This variant was reported in homozygosity in one individual (CabGT-1, PMID: 20020534). This homozygous occurrence earns 0.5 points and is sufficient to apply PM3_supporting. This variant has also been observed in combination with a second ITGA2B variant (c.435C>A, p.Asn145Lys) without confirmation of variant phase (PMID: 26096001, Patient A). However, this evidence contributed to PM3 in the classification of p.Asn145Lys and was not counted for p.Cys177Ter to avoid circularity.

PubMed:20020534

| | | |
|---|---|---|
| **PVS1** | ✔ | This variant introduces a termination codon at amino acid position 177 in exon 4/30. The resulting mRNA product is predicted to undergo nonsense mediated decay, leading to loss of normal protein function. |
| **PP4_Moderate** | ✔ | All requirements for PP4 are met (PMID: 26096001, Patient A): easy bruising and gastrointestinal bleeding; total lack of platelet aggregation in response to physiologic agonists except normal response to ristocetin; direct sequencing of all coding regions of ITGA2B and ITGB3.<br>PubMed:26096001 |
| **PM2_Supporting** | ✔ | Variant not observed in gnomAD v2.1.1 or v3. |

Curation History

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