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# *Variant: NM_000419.5:c.2338del*

Version: 1.0

*CA915940686*

*1691468 (ClinVar)*

**Gene**: ITGA2B (HGNC:3674)
**Condition**: Glanzmann thrombasthenia (MONDO:0100326)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** f28f1fac-9f0c-4f6c-b95c-6e7711948e9b
**Approved on**: 2022/5/17
**Published on**: 2022/6/12

## *HGVS expressions*

**NM_000419.5:c.2338del**
NC_000017.11:g.44376319del
CM000679.2:g.44376319del
NC_000017.10:g.42453687del
CM000679.1:g.42453687del
NC_000017.9:g.39809213del
NG_008331.1:g.18188del
ENST00000262407.6:c.2338del
ENST00000648408.1:c.1769del
ENST00000262407.5:c.2338del
ENST00000592462.5:n.1133del
NM_000419.3:c.2338del
NM_000419.4:c.2338del

**Pathogenic**

**Met criteria codes** 3

PM2_Supporting PVS1 PP4_Moderate

**Not Met criteria codes** 1

PM3

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_000419.5:c.2338del (p.Glu780SerfsTer46) variant in ITGA2B exon 23 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon 25/30 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been detected in at least one proband with Glanzmann thrombasthenia. However, it is unclear if the reported proband (GT38, PMID: 19691478) was homozygous for this variant or if a second ITGA2B variant was identified. At least one patient (Patient GT38 in PMID: 19691478) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_Moderate). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). In summary, this variant meets the criteria to be classified as pathogenic for autosomal recessive Glanzmann**

**Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1, PM2_Supporting, PP4_Moderate. (VCEP specifications version 2; date of approval 05/17/2022)**

**Met criteria codes**

| | | |
|---|---|---|
| **PM2_Supporting** | ✔ | This variant is absent from gnomAD v2.1.1 (PM2_Supporting). |
| **PVS1** | ✔ | The c.2338del (p.Glu780SerfsTer46) variant in exon 23 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon 25/30 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). |
| **PP4_Moderate** | ✔ | At least one patient (Patient GT38 in PMID: 19691478) with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_Moderate). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PM3** | ✖ | This variant has been detected in at least one proband with Glanzmann thrombasthenia. However, it is unclear if the reported proband (GT38, PMID: 19691478) was homozygous for this variant or if a second ITGA2B variant was identified (0 points). |

Curation History

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