

Variant: *NM_000212.3:c.1801T>G*

Version: 2.0

CA400032570 [↗](#)

996182 (ClinVar) [↗](#)

Gene: ITGB3 ([HGNC:3690](#))

Condition: Glanzmann thrombasthenia ([MONDO:0100326](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 72cebe41-4367-4953-81a8-fb42ba7bc4c6

Approved on: 2023/11/2

Published on: 2023/11/3

HGVS expressions

NM_000212.3:c.1801T>G

NC_000017.11:g.47299418T>G

CM000679.2:g.47299418T>G

NC_000017.10:g.45376784T>G

CM000679.1:g.45376784T>G

NC_000017.9:g.42731783T>G

NG_008332.2:g.50577T>G

ENST00000696963.1:c.1801T>G

ENST00000559488.7:c.1801T>G

ENST00000559488.5:c.1801T>G

ENST00000560629.1:c.1766T>G

NM_000212.2:c.1801T>G

Likely Pathogenic

Met criteria codes **5**

PP4_Moderate

PP3

PM3_Supporting

PM5

PM2_Supporting

Evidence Links **0**

Expert Panel

Platelet Disorders VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Platelet Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2.1*

[↗](#) **PDF**

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Platelet Disorders VCEP

The NM_000212.3:c.1801T>G in ITGB3 results in the missense change, Cys601Gly. The variant is absent from gnomAD v2.1.1 and v3 and meets criteria for PM2. The variant is reported in a homozygous (PM3_supporting) GT patient meeting the GT phenotype criteria (PMID: 16879215; PP4_moderate). The REVEL score for this variant is high (0.985), meeting PP3. The variant occurs at the same residue at which another missense variant, Cys601Arg, which has been classified as pathogenic by the Platelet Disorders VCEP (PM5). In summary, this

variant meets criteria to be classified as likely pathogenic. GT-specific criteria met: PM2_Supporting, PP4_Moderate, PP3, PM3_Supporting, PM5.

Met criteria codes

PP4_Moderate			Proband from PMID: 16879215 meets criteria for PP4_Moderate including mucocutaneous bleeding, absent aggregometry with >2 agonists, <25% integrin expression on WB and flow cytometry. However ITGA2B and ITGB3 were not fully sequenced.
PP3			REVEL score of 0.985 meets criteria for PP3 (threshold: >0.7)
PM3_Supporting			1 homozygous proband from PMID: 16879215 meets criteria for PM3_Supporting.
PM5			Cys601Arg is a pathogenic variant (as classified by the PD-EP) at the same residue due to the nucleotide change c.1801T>C.
PM2_Supporting			Cys601Gly is absent from gnomAD v2.1.1 and v3, meeting criteria for PM2_Supporting.

Curation History

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