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Variant: NM_000212.3(ITGB3):c.749A>G (p.Asp250Gly)

Version: 1.1

CA16043530

374016 (ClinVar)

Gene: ITGB3 (HGNC:3690)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5cfe055c-97a2-4530-9287-d69b13220702
Approved on: 2025/11/6
Published on: 2025/11/7

HGVS expressions

NM_000212.3(ITGB3):c.749A>G (p.Asp250Gly)
NM_000212.3:c.749A>G
NC_000017.11:g.47286394A>G
CM000679.2:g.47286394A>G
NC_000017.10:g.45363760A>G
CM000679.1:g.45363760A>G
NC_000017.9:g.42718759A>G
NG_008332.2:g.37553A>G
ENST00000696963.1:c.749A>G
ENST00000559488.7:c.749A>G
ENST00000559488.5:c.749A>G
ENST00000560629.1:c.714A>G
ENST00000571680.1:c.749A>G
NM_000212.2:c.749A>G

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PM3 PP4_Moderate

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 c.749A>G variant in ITGB3 is a missense variant predicted to cause substitution of aspartic acid by glycine at amino acid 250. The variant has been reported in at least one patient (Glanzmann Patient, "HEMOSTAZA SKOZI KLINIČNE PRIMERE" August 2022) who displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann

thrombasthenia (PP4_moderate). This individual is compound heterozygous for this variant and pathogenic variant c.1699C>T (p.Gln567Ter) (PM3). The variant is absent from gnomADv4.1 (PM2_supporting). The computational predictor REVEL gives a score of 0.988, which is above the ClinGen PD VCEP PP3 threshold of >0.7 and predicts a damaging effect on ITGB3 function. In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PM2_Supporting, PP3, PP4_moderate, and PM3. (VCEP specifications version 2.1)

Met criteria codes

PM2_Supporting ✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).
PP3 ✔	The computational predictor REVEL gives a score of .988, which is above the ClinGen PD VCEP threshold of >0.7 and predicts a damaging effect on function (PP3).
PM3 ✔	This variant has been detected in at least 1 proband with Glanzmann thrombasthenia. For 1 of those individuals, 1 was compound heterozygous for this variant and a pathogenic variant c.1699C>T (p.Gln567Ter), confirmed in trans by parental testing ("HEMOSTAZA SKOZI KLINIČNE PRIMERE").
PP4_Moderate ✔	At least one patient (Glanzmann Patient Patient from "HEMOSTAZA SKOZI KLINIČNE PRIMERE") with this variant displayed mucocutaneous bleeding and impaired aggregation with all agonists except ristocetin, which is highly specific for Glanzmann thrombasthenia (PP4_moderate). Additionally, αIIbβ3 surface expression was reduced to 0% (<25%), as measured by flow cytometry/Western blot. However, ITGA2B and ITGB3 were not reported to be sequenced across all exons and intron/exon boundaries.

Curation History

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