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Variant: NM_000419.5:c.1429G>C

Version: 1.1

CA399803370

2506407 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 9c5d7371-edaf-46f4-a59c-faad98839c61
Approved on: 2026/1/20
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HGVS expressions

NM_000419.5:c.1429G>C
NC_000017.11:g.44380610C>G
CM000679.2:g.44380610C>G
NC_000017.10:g.42457978C>G
CM000679.1:g.42457978C>G
NC_000017.9:g.39813504C>G
NG_008331.1:g.13896G>C
ENST00000262407.6:c.1429G>C
ENST00000648408.1:c.860G>C
ENST00000262407.5:c.1429G>C
ENST00000592226.5:n.902G>C
ENST00000592462.5:n.224G>C
NM_000419.3:c.1429G>C
NM_000419.4:c.1429G>C

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PS3_Moderate PM3_Supporting PM2_Supporting

Not Met criteria codes 1

PP3

Evidence Links 1

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_000419.5(ITGA2B):c.1429G>C (p.Ala477Pro) missense variant was detected in a patient with GT (PMID 15946231) with epistaxis, gingival bleeding, and purpura. This variant is absent from the gnomAD database v2.1.1 (PM2_Supporting). This variant was detected in the homozygous state in a patient with GT (PMID 15946231; PM3_supporting). Transfected CHO cells were used to measure the surface

expression of normal and mutant αIIbβ3 receptors was performed using MoAb SZ22; only 14% expression was noted (PS3_Moderate). This variant was identified in a patient (PMID 15946231) with recurrent epistaxis, gingival hemorrhage, and purpura. They demonstrated a normal platelet count, prolonged bleeding time, and absence of platelet aggregation in response to adenosine diphosphate (ADP), epinephrine, and collagen; he had a normal response to ristocetin and decreased αIIbβ3 expression (PP4_Moderate). 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: PP4_Moderate, PS3_Moderate, PM2_supporting, PM3_supporting.

Met criteria codes

PP4_Moderate	✔	This variant was identified in a patient (PMID 15946231) with recurrent epistaxis, gingival hemorrhage, and purpura. They demonstrated a a normal platelet count, prolonged bleeding time, and absence of platelet aggregation in response to adenosine diphosphate (ADP), epinephrine, and collagen; he had a normal response to ristocetin and decreased αIIbβ3 expression.
PS3_Moderate	✔	Transfected CHO cells were used to measure the surface expression of normal and mutant αIIbβ3 receptors was performed using MoAb SZ22; only 14% expression was noted. Similar results to Fu et al., Flow cytometry demonstrated that the expression of alphaIIbA477P (A446P)beta3 on the membrane was only 12.95% of the normal alphaIIbbeta3 complex. PubMed:19734576
PM3_Supporting	✔	This variant was detected in the homozygous state in a patient with GT (PMID 15946231).
PM2_Supporting	✔	This variant is absent from the gnomAD database v2.1.1 (PM2_Supporting).

Not Met criteria codes

PP3	✖	This variant has a REVEL score of 0.576 that does not meet with threshold established by the PD VCEP of >/= 0.7 (PP3_NotMet).

Curation History

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