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Variant: NM_000407.5:c.143C>A

Version: 1.0

CA322079870

627237 (ClinVar)

Gene: GP1BB (HGNC:2812)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7d6fb538-f15c-4acb-9bb6-bcae957c61e9
Approved on: 2026/6/4
Published on: 2026/6/5

HGVS expressions

NM_000407.5:c.143C>A
NC_000022.11:g.19723986C>A
CM000684.2:g.19723986C>A
NC_000022.10:g.19711509C>A
CM000684.1:g.19711509C>A
NC_000022.9:g.18091509C>A
NG_007974.1:g.5444C>A
ENST00000366425.4:c.143C>A
ENST00000366425.3:c.143C>A
ENST00000431044.5:c.*1228C>A
ENST00000455843.5:c.*1228C>A
ENST00000470814.1:n.2115C>A
NM_000407.4:c.143C>A
NR_037611.1:n.3883C>A
NR_037612.1:n.2387C>A

Likely Pathogenic

Met criteria codes 4

PM3 PVS1_Strong PP4 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 for GP1BB Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.143C>A (p.Ser48Ter) variant in GP1BB is a nonsense variant that is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong). At least one patient (Patient II:1 in PMID: 18825380) with this variant had aggregation absent for ristocetin and present for all other agonists as well as less than 10% expression of GPIba and GP9 measured by flow cytometry, which is highly

specific for Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with Bernard-Soulier syndrome (PP4). This variant has been detected in at least two unrelated probands with Bernard-Soulier syndrome (PMID: 19484238). Both of these probands were homozygous for the variant (PM3). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive Bernard-Soulier syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1_Strong, PP4, PM3 and PM2_Supporting (VCEP specifications version 1).

Met criteria codes

PM3	✔	This variant has been detected in at least two unrelated probands with Bernard-Soulier syndrome (PMID: 19484238). Both of these probands were homozygous for the variant (1 PM3 point, PM3).
PVS1_Strong	✔	The c.143C>A (p.Ser48Ter) variant in GP1BB is a nonsense variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong).
PP4	✔	At least one patient (Patient II:1 in PMID: 18825380) with this variant had aggregation absent for ristocetin and present for all other agonists as well as less than 10% expression of GPIba and GP9 measured by flow cytometry, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with Bernard-Soulier syndrome (PP4).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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