

Variant: *NM_000173.7:c.1457C>A*

Version: 1.0

CA397321949 [↗](#)

Gene: GP1BA ([HGNC:2811](#))

Condition: Bernard-Soulier syndrome ([MONDO:0009276](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 0c2ff5be-05f7-4b40-b32b-719a5bd93322

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HGVS expressions

NM_000173.7:c.1457C>A

NC_000017.11:g.4934061C>A

CM000679.2:g.4934061C>A

NC_000017.10:g.4837356C>A

CM000679.1:g.4837356C>A

NC_000017.9:g.4778097C>A

NG_008767.2:g.6767C>A

ENST00000329125.6:c.1457C>A

ENST00000649830.1:c.-888+281G>T

ENST00000329125.5:c.1457C>A

ENST00000611961.1:c.1379C>A

NM_000173.6:c.1457C>A

Likely Pathogenic

Met criteria codes **4**

PVS1_Strong

PM3_Supporting

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 GP1BA Version 1.0.0

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

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

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.1457C>A (p.Ser486Ter) variant in GP1BA 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). At least one patient (Patient 1 in PMID: 7949089) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GPIba 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 individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting). The highest MAF is 0.00001335 (based on 1/74904 alleles) in the African/African American population, which

is lower than the ClinGen PD VCEP threshold (<0.0001114; 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_Supporting and PM2_Supporting (VCEP specifications version 1).

Met criteria codes

PVS1_Strong			The c.1457C>A (p.Ser486Ter) variant in GP1BA 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).
PM3_Supporting			This variant has been detected in at least 1 probands with Bernard-Soulier syndrome (PMID: 7949089). This individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting).
PP4			At least one patient (Patient 1 in PMID: 7949089) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GPIba 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			The highest MAF is 0.00001335 (based on 1/74904 alleles) in the African/African American population, which is lower than the ClinGen PD VCEP threshold (<0.0001114; PM2_Supporting).

Curation History

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