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Variant: NM_000173.7(GP1BA):c.673T>C (p.Cys225Arg)

Version: 1.0

CA397318014

1031446 (ClinVar)

Gene: GP1BA (HGNC:2811)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 42cd378a-1c69-4e17-921c-a6d05ff77a09
Approved on: 2026/2/5
Published on: 2026/2/5

HGVS expressions

NM_000173.7:c.673T>C
NM_000173.7(GP1BA):c.673T>C (p.Cys225Arg)
NC_000017.11:g.4933277T>C
CM000679.2:g.4933277T>C
NC_000017.10:g.4836572T>C
CM000679.1:g.4836572T>C
NC_000017.9:g.4777352T>C
NG_008767.2:g.5983T>C
ENST00000329125.6:c.673T>C
ENST00000649830.1:c.-888+1065A>G
ENST00000329125.5:c.673T>C
ENST00000611961.1:c.673T>C
NM_000173.6:c.673T>C

Likely Pathogenic

Met criteria codes 6

PM3_Supporting PP3 PP4 PM1 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 for GP1BA Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.673T>C variant in GP1BA is a missense variant predicted to cause substitution of Cysteine by Arginine at amino acid 225 (p.Cys225Arg). At least one patient (internal case from Versiti) with this variant had less than 10% expression of GPIba measured by flow cytometry, which is highly specific for Bernard-Soulier syndrome, the patient also had excessive mucocutaneous bleeding consistent with Bernard-Soulier syndrome (PP4). This individual was compound heterozygous for this variant and the NM_000173.7(GP1BA):c.1601_1602del (p.Tyr534CysfsTer?) variant which was classified as Pathogenic by the PD VCEP. The phase of the

variants in this patient is unknown (0.5 points, PM3_Supporting). This variant resides at a disulfide bond residue, Cys225 GP1BA that is defined as a critical functional domain by the ClinGen PD VCEP (PM1). The largest population MAF allele frequency in gnomAD v4.1.0 is 0.000001695 (based on 2/1179886 alleles) in the European (non-Finnish) population, which is lower than the ClinGen PD VCEP threshold (<0.0001114; PM2_Supporting). The computational predictor REVEL gives a score of 0.653, which is above the ClinGen PD VCEP threshold of >0.644 and predicts a damaging effect on function (PP3). Another missense variant (c.673T>A, p.Cys225Ser) in the same codon has been classified as Pathogenic for Bernard-Soulier syndrome by the ClinGen PD VCEP (PM5). 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: PP4, PM1, PM5, PM2_Supporting, PM3_supporting and PP3 (VCEP specifications version 1).

Met criteria codes

PM3_Supporting	✔	This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (internal case from Versiti). This individual was compound heterozygous for this variant and the NM_000173.7(GP1BA):c.1601_1602del (p.Tyr534CysfsTer?) variant which was classified as Pathogenic by the PD VCEP. These phase in this variants is unknown (0.5 points, PM3_Supporting).
PP3	✔	The computational predictor REVEL gives a score of 0.653, which is above the ClinGen PD VCEP threshold of >0.644 and predicts a damaging effect on function (PP3).
PP4	✔	At least one patient (internal case from Versiti) with this variant had 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 which are consistent with Bernard-Soulier syndrome (PP4).
PM1	✔	This variant resides at a disulfide bond residue, Cys225 GP1BA that is defined as a critical functional domain by the ClinGen PD VCEP (PM1).
PM5	✔	Another missense variant (c.673T>A, p.Cys225Ser) in the same codon has been classified as Pathogenic for Bernard-Soulier syndrome by the ClinGen PD VCEP (PM5).
PM2_Supporting	✔	The largest population MAF allele frequency in gnomAD v4.1.0 is 0.000001695 (based on 2/1179886 alleles) in the European (non-Finnish) population, which is lower than the ClinGen PD VCEP threshold (<0.0001114; PM2_Supporting).

Curation History

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