The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000174.5(GP9):c.212T>G (p.Phe71Cys)

Version: 1.1

CA2602666

1491487 (ClinVar)

Gene: GP9 (HGNC:2815)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 0ff7deb4-f87f-4d5e-95c1-a7ad1a5bfa8d
Approved on: 2026/1/20
Published on: 2026/1/23

HGVS expressions

NM_000174.5:c.212T>G
NM_000174.5(GP9):c.212T>G (p.Phe71Cys)
NC_000003.12:g.129061951T>G
CM000665.2:g.129061951T>G
NC_000003.11:g.128780794T>G
CM000665.1:g.128780794T>G
NC_000003.10:g.130263484T>G
NG_008715.1:g.6150T>G
ENST00000307395.5:c.212T>G
ENST00000307395.4:c.212T>G
NM_000174.4:c.212T>G

Likely Pathogenic

Met criteria codes 3

PM3_Strong | PM2_Supporting | PP4

Not Met criteria codes 3

BP4 | PM5 | PP3

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 GP9 Version 1.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.212T>G variant in GP9 is a missense variant predicted to cause substitution of Phenylalanine by Cysteine at amino acid 71 (p.Phe71Cys). At least one patient (Patient BS-23 in PMID:21699652) with this variant had aggregation absent for ristocetin and present for all other agonists, as well as 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 is consistent with Bernard-Soulier syndrome (PP4). This variant has been detected in at least three unrelated probands with Bernard-Soulier syndrome. Two of these individuals were homozygous for the variant (PMID:21699652, 1 PM3 point). One individual was compound heterozygous for this variant and the NM_000174.5(GP9):c.182A>G (p.Asn61Ser) which has been classified as Pathogenic by the PD VCEP. (1 PM3 point). These variants were

confirmed in trans by family testing (2 PM3 points, PM3_Strong). The Grpmax filtering allele frequency in gnomaDv4.1 is 0 (based on 1/1179890 alleles) in the European (non-Finnish) population, which is below the <0.0000329 threshold for 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: PP4, PM3, PM2_Supporting, PM3_Strong (VCEP specifications version 1).

Met criteria codes

PM3_Strong	✔	This variant has been detected in at least three unrelated probands with Bernard-Soulier syndrome. Two of these individuals were homozygous for the variant (PMID:21699652, 1 PM3 point). One individual was compound heterozygous for this variant and the NM_000174.5(GP9):c.182A>G (p.Asn61Ser) which has been classified as Pathogenic by the PD VCEP. (1 PM3 point). These variants were confirmed in trans by family testing (2 PM3 points, PM3_Strong).
PM2_Supporting	✔	The Grpmax filtering allele frequency in gnomaDv4.1 is 0 (based on 1/1179890 alleles) in the European (non-Finnish) population, which is below the <0.0000329 threshold for PM2_supporting.
PP4	✔	At least one patient (Patient BS-23 in PMID:21699652) with this variant had aggregation absent for ristocetin and present for all other agonists, as well as 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 is consistent with Bernard-Soulier syndrome (PP4).

Not Met criteria codes

BP4	✖	The computational predictor REVEL gives a score of 0.623, which is above the ClinGen PD VCEP PP3 threshold of <0.290.
PM5	✖	Another missense variant in the same codon has been reported in a patient with Bernard-Soulier syndrome c.212T>C (p.Phe71Ser) classified as likely pathogenic by the ClinGen PD VCEP, not considered here to avoid circularity.
PP3	✖	The computational predictor REVEL gives a score of 0.623, which is below the ClinGen PD VCEP PP3 threshold of >0.644 and does not predict a damaging effect on GP9 function. And the computational splicing predictor SpliceAI indicated that the variant has no predicted impact on splicing.

Curation History

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