

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

NM_000174.5:c.212T>G

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**

PM5

BP4

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 GPIIb 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 GPIIb 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			
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.
BP4			The computational predictor REVEL gives a score of 0.623, which is above the ClinGen PD VCEP PP3 threshold of <0.290.
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 [↗](#)



▼

▼

Showing 1 to 2 of 2 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.