

Variant: *NM_000174.5(GP9):c.20T>C (p.Leu7Pro)*

Version: 1.0

CA123183 [↗](#)

13534 (ClinVar) [↗](#)

Gene: GP9 ([HGNC:2815](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 6d4e983d-0fd7-4362-b71c-a2e4fc24d230

Approved on: 2025/9/4

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HGVS expressions

NM_000174.5(GP9):c.20T>C (p.Leu7Pro)

NM_000174.5:c.20T>C

NC_000003.12:g.129061759T>C

CM000665.2:g.129061759T>C

NC_000003.11:g.128780602T>C

CM000665.1:g.128780602T>C

NC_000003.10:g.130263292T>C

NG_008715.1:g.5958T>C

ENST00000307395.5:c.20T>C

ENST00000307395.4:c.20T>C

NM_000174.4:c.20T>C

Likely Pathogenic

Met criteria codes **5**

PP4_Moderate

PM3_Supporting

PM2_Supporting

PS3_Supporting

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 1.0.0

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

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

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.20T>C variant in GP9 is a missense variant predicted to cause substitution of Leucine by Proline at amino acid 7 (p.Leu7Pro). At least one patient (Patient 1 in PMID: 12100158) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GPIba, GP1bb 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. Functional evidence meeting PS3_supporting is accepted in lieu of del/dup analysis, as it addresses concerns about misattribution of phenotypic effects to the variant due to an undetected CNV(PP4_Moderate). This individual was homozygous for the variant (0.5 points, PM3_Supporting). Surface expression of GP1a, GP1b, and GP9 measured by flow cytometry in CHO cells transiently co-

transfected with c.20T>C (p.Leu7Pro) variant GP9 and wild type GP1a and GP1b showed absent expression, indicating that this variant impacts protein function (PMID: 12100158)(PS3_supporting). The computational predictor REVEL gives a score of 0.731, which is above the ClinGen PD VCEP threshold of >0.644 and predicts a damaging effect on GP9 function (PP3). 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: PP4_Moderate, PM3_Supporting, PS3_Supporting, PP3 and PM2_Supporting (VCEP specifications version 2; date of approval 09/04/2025).

Met criteria codes

PP4_Moderate			At least one patient (Patient 1 in PMID: 12100158) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GPIba, GP1bb 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. Functional evidence meeting PS3_supporting is accepted in lieu of del/dup analysis, as it addresses concerns about misattribution of phenotypic effects to the variant due to an undetected CNV(PP4_Moderate).
PM3_Supporting			This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (PMID: 12100158). This individual was homozygous for the variant (0.5 points, PM3_Supporting).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PS3_Supporting			Surface expression of GP1a, GP1b, and GP9 measured by flow cytometry in CHO cells transiently co-transfected with c.20T>C (p.Leu7Pro) variant GP9 and wild type GP1a and GP1b showed absent expression, indicating that this variant impacts protein function (PMID: 12100158)(PS3_supporting).
PP3			The computational predictor REVEL gives a score of 0.731, which is above the ClinGen PD VCEP threshold of >0.644 and predicts a damaging effect on GP9 function (PP3).

Curation History



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