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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
Published on: 2025/12/10

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

PM3_Supporting | PP3 | PP4_Moderate | PM2_Supporting | PS3_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 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

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).
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).
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).
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).

Curation History

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