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Variant: NM_000174.5(GP9):c.119del (p.Gly40fs)

Version: 1.0

CA658760376

2734558 (ClinVar)

Gene: GP9 (HGNC:2815)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5b958e6e-fc44-436d-bc99-f7c56b080539
Approved on: 2025/6/19
Published on: 2025/6/19

HGVS expressions

NM_000174.5(GP9):c.119del (p.Gly40fs)
NM_000174.5:c.119del
NC_000003.12:g.129061858del
CM000665.2:g.129061858del
NC_000003.11:g.128780701del
CM000665.1:g.128780701del
NC_000003.10:g.130263391del
NG_008715.1:g.6057del
ENST00000307395.5:c.119del
ENST00000307395.4:c.119del
NM_000174.4:c.119del

Likely Pathogenic

Met criteria codes 4

PM3_Supporting PM2_Supporting PP4 PVS1_Strong

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.119del (p.Gly40AlafsTer43) variant in GP9 is a frameshift variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong). At least one patient (Patient BS-4 in PMID: 21699652) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GP9 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 individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting). 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: PVS1_Strong, PP4, PM3_Supporting and PM2_Supporting (VCEP specifications version 2; date of approval xx/xx/xxxx).

Met criteria codes

PM3_Supporting	✔	This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (PMID: 21699652). This individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP4	✔	At least one patient (Patient BS-4 in PMID: 21699652) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GP9 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).
PVS1_Strong	✔	The c.119del (p.Gly40AlafsTer43) variant in GP9 is a frameshift variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong).

Curation History

Showing 1 to 1 of 1 rows

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