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_000173.7(GP1BA):c.1077G>A (p.Trp359Ter)

Version: 1.0

CA116657

4151 (ClinVar)

Gene: GP1BA (HGNC:2811)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: d8a22472-b2b9-48f1-a1ac-21cf7211b306
Approved on: 2026/3/17
Published on: 2026/3/17

HGVS expressions

NM_000173.7:c.1077G>A
NM_000173.7(GP1BA):c.1077G>A (p.Trp359Ter)
NC_000017.11:g.4933681G>A
CM000679.2:g.4933681G>A
NC_000017.10:g.4836976G>A
CM000679.1:g.4836976G>A
NC_000017.9:g.4777756G>A
NG_008767.2:g.6387G>A
ENST00000329125.6:c.1077G>A
ENST00000649830.1:c.-888+661C>T
ENST00000329125.5:c.1077G>A
ENST00000611961.1:c.1077G>A
NM_000173.6:c.1077G>A

Likely Pathogenic

Met criteria codes 4

PP1 PP4 PVS1_Strong PM2_Supporting

Not Met criteria codes 1

PM3

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 GP1BA Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.1077G>A (p.Trp359Ter) variant in GP1BA is a nonsense 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 (Proband in PMID: 2308962) with this variant had absent expression of GPIba measured by flow cytometry or Western blot, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with Bernard-Soulier syndrome (PP4). The variant has been reported to segregate in the proband plus 2 heterozygous children and the

heterozygous mother, all had significantly reduced surface expression of GP1BA (PP1). The largest MAF allele frequency in gnomAD v4.0.1 is 0.0000008476 (based on 1/1179860 alleles) in the European (non-Finnish) population, which is lower than the ClinGen PD VCEP threshold (<0.0001114; 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, PP1, and PM2_Supporting (VCEP specifications version 1.1).

Met criteria codes

PP1	✔	The variant has been reported to segregate in the proband plus 2 additional heterozygous children and the heterozygous mother, all had significantly reduced surface expression of GP1BA by immunoblot (PP1).
PP4	✔	At least one patient (Proband in PMID: 2308962) with this variant had absent expression of GPIba measured by flow cytometry or Western blot, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with Bernard-Soulier syndrome (PP4).
PVS1_Strong	✔	The c.1077G>A (p.Trp359Ter) variant in GP1BA is a nonsense 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).
PM2_Supporting	✔	The largest MAF allele frequency in gnomAD v4.0.1 is 0.0000008476 (based on 1/1179860 alleles) in the European (non-Finnish) population, which is lower than the ClinGen PD VCEP threshold (<0.0001114; PM2_Supporting).

Not Met criteria codes

PM3	✖	Proband in PMID: 2308962 is compound heterozygous for the c.1077G>A (p.Trp359Ter) and another variant that the authors were unable to detect

Curation History

Showing 1 to 1 of 1 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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.