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:c.1036C>T

Version: 1.0

CA397319681

Gene: GP1BA (HGNC:2811)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 8a0d9655-c2f5-46ca-8bcd-e030daadb9fb
Approved on: 2025/12/16
Published on: 2025/12/16

HGVS expressions

NM_000173.7:c.1036C>T
NC_000017.11:g.4933640C>T
CM000679.2:g.4933640C>T
NC_000017.10:g.4836935C>T
CM000679.1:g.4836935C>T
NC_000017.9:g.4777715C>T
NG_008767.2:g.6346C>T
ENST00000329125.6:c.1036C>T
ENST00000649830.1:c.-888+702G>A
ENST00000329125.5:c.1036C>T
ENST00000611961.1:c.1036C>T
NM_000173.6:c.1036C>T

Likely Pathogenic

Met criteria codes 5

PVS1_Strong | PP1 | PP4 | PM3 | PM2_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 GP1BA Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.1036C>T (p.Gln346Ter) 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 (Patient 1 in PMID:33553065) with this variant had less than 10% expression of GPIba and GP9 measured by flow cytometry, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding is consistent with Bernard-Soulier syndrome (PP4). This individual was compound heterozygous for this variant and the NM_000173.7:c.1601_1602del (p.Tyr534CysfsTer82) variant, which was classified as Pathogenic by the Clingen PD VCEP. The variants were confirmed in trans through parental testing (1 point, PM3). 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, PM3, PP1, PP4 and PM2_Supporting (VCEP specifications version 1).

Met criteria codes

PVS1_Strong	✔	The c.1036C>T (p.Gln346Ter) 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).
PP1	✔	The variant has been reported to segregate in the proband plus 1 additional compound heterozygous BSS affected family members (1 point, PP1).
PP4	✔	At least one patient (Patient 1 in PMID:33553065) with this variant had less than 10% expression of GPIba and GP9 measured by flow cytometry, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding is consistent with Bernard-Soulier syndrome (PP4).
PM3	✔	This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (Patient 1 in PMID: 33553065). This individual was compound heterozygous for this variant and the NM_000173.7:c.1601_1602del (p.Tyr534CysfsTer82) variant, which was classified as Pathogenic by the Clingen PD VCEP. The variants were confirmed in trans through parental testing (1 point, PM3).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

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.