

Variant: *NM_000407.5(GP1BB):c.406G>T (p.Glu136Ter)*

Version: 1.0

CA322080037 [↗](#)

1679210 (ClinVar) [↗](#)

Gene: GP1BB ([HGNC:2812](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 8ea2064e-3b97-47af-aef1-194ab06ebdf3

Approved on: 2025/2/11

Published on: 2025/2/14

HGVS expressions

NM_000407.5(GP1BB):c.406G>T (p.Glu136Ter)

NM_000407.5:c.406G>T

NC_000022.11:g.19724249G>T

CM000684.2:g.19724249G>T

NC_000022.10:g.19711772G>T

CM000684.1:g.19711772G>T

NC_000022.9:g.18091772G>T

NG_007974.1:g.5707G>T

ENST00000366425.4:c.406G>T

ENST00000366425.3:c.406G>T

ENST00000431044.5:c.*1491G>T

NM_000407.4:c.406G>T

NR_037611.1:n.4146G>T

NR_037612.1:n.2650G>T

Likely Pathogenic

Met criteria codes **4**

PVS1_Strong

PP4

PM3_Supporting

PM2_Supporting

Not Met criteria codes **1**

PS4

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 GP1BB Version 1.0.0*

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

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

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.406G>T (p.Glu136Ter) variant in GP1BB is a nonsense variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove 34% (>10%) of the protein (PVS1_Strong). At least one patient (Patient 2 in PMID: 33217855) with this variant had impaired aggregation for ristocetin (aggregation in response to other agonists is not specifically mentioned). Additionally, this patient showed less than 10% expression of GPIba (0%) measured by flow cytometry, which is highly specific

for Bernard-Soulier syndrome (PP4). Full gene sequencing of all BSS genes was also performed for this patient by WES. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with Bernard-Soulier syndrome. The patient is homozygous for the variant (PM3_Supporting). The Grpmax filtering allele frequency in gnomADv4.1 is 0.000002920 (based on 7/997364 alleles) in the European (non-Finnish) population, which is below the <0.0000651678 threshold for 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 1).

Met criteria codes

PVS1_Strong			The c.406G>T (p.Glu136Ter) variant in GP1BB is a nonsense variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove 34% (>10%) of the protein (PVS1_Strong).
PP4			At least one patient (Patient 2 in PMID: 33217855) with this variant had impaired aggregation for ristocetin (aggregation in response to other agonists is not specifically mentioned). Additionally, this patient showed less than 10% expression of GPIba (0%) measured by flow cytometry, which is highly specific for Bernard-Soulier syndrome. Full gene sequencing of all BSS genes was also performed for this patient by WES but analysis for structural variants was not performed. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with Bernard-Soulier syndrome (PP4).
PM3_Supporting			This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (Patient 2 in PMID: 33217855) who was homozygous for the variant (0.5 PM3 points, PM3_Supporting).
PM2_Supporting			The Grpmax filtering allele frequency in gnomADv4.1 is 0.000002920 (based on 7/997364 alleles) in the European (non-Finnish) population, which is below the <0.0000651678 threshold for PM2_supporting.

Not Met criteria codes

PS4			One patient heterozygous for Glu136Ter variant was reported (PMID: 36430862) with Thrombocytopenia (platelet count <150 × 109/L), platelet size = macro (MPV >12.8fl), 0.25pt
-----	--	---	---

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.](#)