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Variant: NM_000173.7:c.800C>G

Version: 1.0

CA397318711

Gene: GP1BA (HGNC:2811)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 29b19bc3-8379-4423-8080-4ea3ee272741
Approved on: 2025/5/1
Published on: 2025/5/2

HGVS expressions

NM_000173.7:c.800C>G
NC_000017.11:g.4933404C>G
CM000679.2:g.4933404C>G
NC_000017.10:g.4836699C>G
CM000679.1:g.4836699C>G
NC_000017.9:g.4777479C>G
NG_008767.2:g.6110C>G
ENST00000329125.6:c.800C>G
ENST00000649830.1:c.-888+938G>C
ENST00000329125.5:c.800C>G
ENST00000611961.1:c.800C>G
NM_000173.6:c.800C>G

Likely Pathogenic

Met criteria codes 5

PVS1_Strong | PM3_Supporting | PP4 | PP1_Moderate | 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 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.800C>G (p.Ser267Ter) 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 3 in PMID: 26044173) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GPIba 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 (PP4). This individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting). The variant has been reported to segregate in the proband plus 2 additional homozygous BSS affected

siblings (2 PP1 points, PP1_Moderate). 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, PP1_Moderate, PP4, PM2_Supporting and PM3_Supporting (VCEP specifications version 1.0.0).

Met criteria codes

PVS1_Strong	✔	The c.800C>G (p.Ser267Ter) 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).
PM3_Supporting	✔	This variant has been detected in at least 1 probands with Bernard-Soulier syndrome (PMID: 26044173). This individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting).
PP4	✔	At least one patient (Patient 3 in PMID: 26044173) with this variant had aggregation absent for ristocetin and present for all other agonists and less than 10% expression of GPIba 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 (PP4).
PP1_Moderate	✔	* parents were consanguineous The variant has been reported to segregate in the proband plus 2 additional homozygous BSS affected siblings (2 PP1 points, PP1_Moderate).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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