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# *Variant: NM_000173.7(GP1BA):c.987G>A (p.Trp329Ter)*

Version: 1.0

*CA397319477*

*3251584 (ClinVar)*

**Gene**: GP1BA (HGNC:2811)
**Condition**: Bernard-Soulier syndrome (MONDO:0009276)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** 1018b1ce-9d8a-4366-87fe-6b0ac2fef6f7
**Approved on**: 2025/11/6
**Published on**: 2025/11/7

## *HGVS expressions*

**NM_000173.7:c.987G>A**
**NM_000173.7(GP1BA):c.987G>A (p.Trp329Ter)**
NC_000017.11:g.4933591G>A
CM000679.2:g.4933591G>A
NC_000017.10:g.4836886G>A
CM000679.1:g.4836886G>A
NC_000017.9:g.4777666G>A
NG_008767.2:g.6297G>A
ENST00000329125.6:c.987G>A
ENST00000649830.1:c.-888+751C>T
ENST00000329125.5:c.987G>A
ENST00000611961.1:c.987G>A
NM_000173.6:c.987G>A

**Likely Pathogenic**

**Met criteria codes** 5

PM3_Supporting PP4 PVS1_Strong PM2_Supporting PS3_Supporting

Evidence Links 1

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.987G>A (p.Trp329Ter) 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: 26133172) with this variant had aggregation absent for ristocetin and present for all other agonists, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had macrothrombocytopenia which is consistent with Bernard-Soulier syndrome (PP4). This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (Case 1 in PMID: 26133172). This individual was homozygous for the**

**variant (0.5 PM3 points, PM3_Supporting). Surface expression of GP1a and GP9 measured by flow cytometry and Western blot in CHO cells transiently co-transfected with c.987G>A (p.Trp329Ter) variant GP1a and wild type GP1b, and GP9 showed decreased expression at 1% WT levels, indicating that this variant impacts protein function (PMID: 26133172, PS3_supporting). The Grpmax Filtering allele frequency in gnomAD v4.1.0 is absent (based on 1/1179858 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, PM3_Supporintg, PS3_Supporting, and PM2_Supporting (VCEP specifications version 1).**

**Met criteria codes**

| | |
|---|---|
| **PM3_Supporting** ✔ | This variant has been detected in at least 1 proband with Bernard-Soulier syndrome (Case 1 in PMID: 26133172). This individual was homozygous for the variant (0.5 PM3 points, PM3_Supporting). |
| **PP4** ✔ | At least one patient (Patient 1 in PMID: 26133172) with this variant had aggregation absent for ristocetin and present for all other agonists, which is highly specific for Bernard-Soulier syndrome. Additionally, the patient had macrothrombocytopenia which is consistent with Bernard-Soulier syndrome (PP4). |
| **PVS1_Strong** ✔ | The c.987G>A (p.Trp329Ter) 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 Grpmax Filtering allele frequency in gnomAD v4.1.0 is absent (based on 1/1179858 alleles) in the European (non Finnish) population, which is lower than the ClinGen PD VCEP threshold (<0.0001114; PM2_Supporting). |
| **PS3_Supporting** ✔ | Surface expression of GP1a and GP9 measured by flow cytometry and Western blot in CHO cells transiently co-transfected with c.987G>A (p.Trp329Ter) variant GP1a and wild type GP1b, and GP9 showed decreased expression at 1% WT levels, indicating that this variant impacts protein function (PMID: 26133172, PS3_supporting). |

Surface expression of GP1a and GP9 measured by flow cytometry and Western blot in CHO cells transiently co-transfected with c.987G>A (p.Trp329Ter) variant GP1a and wild type GP1b, and GP9 showed decreased expression at 1% WT levels, indicating that this variant impacts protein function (PMID: 26133172, PS3_supporting).

PubMed:26133172

Curation History

Showing 1 to 1 of 1 rows

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