Variant: NM_000173.7(GP1BA):c.1232C>T (p.Pro411Leu)

Version: 1.0

CA8314930

255464 (ClinVar)

Gene: GP1BA (HGNC:2811)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 690785fc-52f7-46da-8aaf-ac302a947877
Approved on: 2025-02-11
Published on: 2025-02-12

HGVS expressions

NM_000173.7:c.1232C>T
NM_000173.7(GP1BA):c.1232C>T (p.Pro411Leu)
NC_000017.11:g.4933836C>T
CM000679.2:g.4933836C>T
NC_000017.10:g.4837131C>T
CM000679.1:g.4837131C>T
NC_000017.9:g.4777911C>T
NG_008767.2:g.6542C>T
ENST00000329125.6:c.1232C>T
ENST00000649830.1:c.-888+506G>A
ENST00000329125.5:c.1232C>T
ENST00000611961.1:c.1232C>T
NM_000173.6:c.1232C>T

Benign

Met criteria codes 2

BA1 **BP4**

Not Met criteria codes 4

PP4 **PM3** **PM2** **BS1**

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 NM_000173.7(GP1BA):c.1232C>T variant in GP1BA is a missense variant predicted to cause substitution of Proline by Leucine at amino acid 411 (p.Pro411Leu). The Grpmax filtering allele frequency in gnomAD v4.1 is 0.007836 (based on 54/5424) in the Middle Eastern population, which is higher than the ClinGen PD VCEP threshold (>0.001), and therefore meets BA1. The computational predictor REVEL gives a score of 0.223, which is below the ClinGen PD VCEP threshold of <0.290 and predicts no damaging effect on GP1BA function and the SpliceAI score is zero (BP4). In summary, this variant meets the criteria to be classified as Benign for autosomal recessive Bernard-

Soulier syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: BA1 and BP4 (VCEP specifications version 1).

Met criteria codes

BA1	✓	The Grpmax filtering allele frequency in gnomAD v4.1 is 0.007836 (based on 54/5424) in the Middle Eastern population, which is higher than the ClinGen PD VCEP threshold (>0.001), and therefore meets this criterion (BA1).
BP4	✓	The computational predictor REVEL gives a score of 0.223, which is below the ClinGen PD VCEP threshold of <0.290 and predicts no damaging effect on GP1BA function and the SpliceAI score is zero (BP4).

Not Met criteria codes

PP4	✗	Internal patient also carries the GP1BB c. 127G>T Gly43Trp, GP1BB c.176A>C Glu59Ala variants. Multiple CBC studies have identified mild thrombocytopenia, with testing on 9/28/2016, 10/25/2016, and 9/23/2021 showing platelet counts of 113 K/CUMM, 98 K /CUMM and 104 K/CUMM and MPV of 12.3 fL, 12.1 fL, and 14.1 fL respectively. On a sample from 1/18/22 there was normal platelet aggregation and ATP release. Testing on a sample from 10/21/21 showed normal platelet glycoprotein testing with GPIIb of 143%, GPIIIa of 134%, GPIX of 80% and GPIb-alpha of 110% and platelet TEM showed a normal mean dense body count of 3.0 dense granules/platelet with increased large and round platelets
PM3	✗	Internal patient also carries the GP1BB c. 127G>T Gly43Trp and GP1BB c.176A>C Glu59Ala variants, but no other GP1BA variant.
PM2	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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