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_000407.5(GP1BB):c.1A>T (p.Met1Leu)

Version: 1.0

CA410676172

1691253 (ClinVar)

Gene: GP1BB (HGNC:2812)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3ed97f3b-9c25-4bb1-be4c-64d4e6f5baa3
Approved on: 2025/2/11
Published on: 2025/2/14

HGVS expressions

NM_000407.5:c.1A>T
NM_000407.5(GP1BB):c.1A>T (p.Met1Leu)
NC_000022.11:g.19723570A>T
CM000684.2:g.19723570A>T
NC_000022.10:g.19711093A>T
CM000684.1:g.19711093A>T
NC_000022.9:g.18091093A>T
NG_007974.1:g.5028A>T
ENST00000366425.4:c.1A>T
ENST00000366425.3:c.1A>T
ENST00000431044.5:c.*1086A>T
ENST00000455843.5:c.*1086A>T
ENST00000470814.1:n.1973A>T
NM_000407.4:c.1A>T
NR_037611.1:n.3741A>T
NR_037612.1:n.2245A>T

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 2

PM5 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 NM_000407.5:c.1A>T (p.Met1Leu) variant in GP1BB may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein. There is no alternative in-frame methionine in GP1BB

(PVS1). The Grpmax filtering allele frequency in gnomaDv4.1is 6.800e-7 (based on 3/1176548 alleles) in the European (non-Finnish) population, which is below the <0.0000651678 threshold for PM2_supporting. One heterozygous macrothrombocytopenia patient has been reported with this variant (PMID: 28983057; PS4_NotMet). 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 and PM2_Supporting (VCEP specifications 1).

Met criteria codes

PVS1	✔	The NM_000407.5:c.1A>T (p.Met1Leu) variant in GP1BB may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein. There is no alternative in-frame methionine in GP1BB (PVS1)
PM2_Supporting	✔	The Grpmax filtering allele frequency in gnomaDv4.1is 6.800e-7 (based on 3/1176548 alleles) in the European (non-Finnish) population, which is below the <0.0000651678 threshold for PM2_supporting.

Not Met criteria codes

PM5	✖	Met1Ile has also been reported in this gene but in heterozygous occurrence in macrothrombocytopenia (PMID: 28064200) so it is not considered here.
PS4	✖	One heterozygous macrothrombocytopenia (platelet count = 101 X 10^9 /, MPV = 15 fL) patient (PMID: 28983057) has been reported 0.25pt

Curation History

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