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_000174.5(GP9):c.236C>T (p.Thr79Ile)

Version: 2.0

CA2602667

900152 (ClinVar)

Gene: GP9 (HGNC:2815)
Condition: Bernard-Soulier syndrome (MONDO:0009276)
Inheritance Mode: Autosomal recessive inheritance
UUID: d11db64b-6ccb-4f2e-a5dd-705bcea48e56
Approved on: 2025-02-11
Published on: 2025-02-17

HGVS expressions

NM_000174.5:c.236C>T
NM_000174.5(GP9):c.236C>T (p.Thr79Ile)
NC_000003.12:g.129061975C>T
CM000665.2:g.129061975C>T
NC_000003.11:g.128780818C>T
CM000665.1:g.128780818C>T
NC_000003.10:g.130263508C>T
NG_008715.1:g.6174C>T
ENST00000307395.5:c.236C>T
ENST00000307395.4:c.236C>T
NM_000174.4:c.236C>T

Benign

Met criteria codes 1

BA1

Not Met criteria codes 2

PP4 BP4

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 GP9 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.236C>T variant in GP9 is a missense variant predicted to cause substitution of threonine by isoleucine at amino acid 79. The Grpmax Filtering allele frequency in gnomAD v4.1 is 0.001800 (based on 126/60030 alleles) in Admixed American population, which is higher than the ClinGen PD VCEP threshold (>0.001 for GP9), and therefore meets this criterion (BA1). 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. (VCEP specifications version 1)

Met criteria codes

BA1	✔	The Grpmax Filtering allele frequency in gnomAD v4.1 is 0.001800 (based on 126/60030 alleles) in Admixed American population, which is higher than the ClinGen PD VCEP threshold (>0.001 for GP9), and therefore meets this criterion (BA1).

Not Met criteria codes

PP4	✖	2 patients (cases 3 and 6 in PMID:35349645) with this variant and with macrothrombocytopenia have been observed in the literature. Aggregation analysis was not consistent with BSS for these cases (reduced to Arachidonic acid, CRP, ADP, and TRAP), so PP4 was not met.
BP4	✖	The computational predictor REVEL gives a score of 0.18, which is below the ClinGen PD VCEP threshold of <0.290 and predicts no damaging effect on GP9 function; SpliceAI predicts no impact on splicing but has an Acceptor Gain delta score of 0.09 (BP4_NotMet).

Curation History

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