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_001754.5(RUNX1):c.593A>G (p.Asp198Gly)

Version: 1.1

CA410207973

3342374 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 3f28fc37-8920-46d9-b79f-2a5be9bd3642
Approved on: Mon, 05 Oct 2026 00:00:00 +0000
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HGVS expressions

NM_001754.5(RUNX1):c.593A>G (p.Asp198Gly)
NM_001754.5:c.593A>G
NC_000021.9:g.34859494T>C
CM000683.2:g.34859494T>C
NC_000021.8:g.36231791T>C
CM000683.1:g.36231791T>C
NC_000021.7:g.35153661T>C
NG_011402.2:g.1130218A>G
ENST00000675419.1:c.593A>G
ENST00000300305.7:c.593A>G
ENST00000344691.8:c.512A>G
ENST00000358356.9:c.512A>G
ENST00000399237.6:c.557A>G
ENST00000399240.5:c.512A>G
ENST00000437180.5:c.593A>G
ENST00000467577.1:n.85A>G
ENST00000482318.5:c.*183A>G
NM_001001890.2:c.512A>G
NM_001122607.1:c.512A>G
NM_001754.4:c.593A>G
NM_001001890.3:c.512A>G
NM_001122607.2:c.512A>G

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PM1_Strong PS4_Supporting

Not Met criteria codes 22

BA1 PP1 PP2 PP4 PM6 PVS1 PM3 PM5 PM4 BS1 BS4 BS3 BS2 PS1 PS2 PS3 BP5 BP7 BP4 BP3 BP1 BP2

Evidence Links 0

Expert Panel

Myeloid Malignancy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RUNX1 Version 3.1*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.593A>G (p.Asp198Gly) is a missense variant which affects one of the hotspot residues (Asp198) within the RHD (amino acids 89-204; PM1_Strong). This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting) and has been reported in one proband meeting at least one of the RUNX1-phenotypic criteria (PS4_Supporting; PMID: 28855357). In summary, this variant meets the criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PM1_Strong, PM2_Supporting, PS4_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).
PP3	✔	This variant does not have an available REVEL score, but multiple other predictors (SIFT,PolyPhen2-HDIV, PolyPhen2-HVAR, LRT, MutationTaster, MutationAssessor, FATHMM, PROVEAN, MetaSVM, MetaLR, FATHMM-MKL) predict a deleterious impact, but this variant does NOT have a SpliceAI score ≥ 0.38 (0.01) (PP3).
PM1_Strong	✔	This variant affects the following hotspot residue within the RHD: D198 (PM1_strong).
PS4_Supporting	✔	This variant has been reported in one proband meeting at least one of the RUNX1-phenotypic criteria (PS4_Supporting; PMID: 28855357, SCV005332537.1).

Not Met criteria codes

BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PP1	✖	Segregation data for this variant has not been reported in literature.
PP2	✖	This rule is not applicable for MM-VCEP
PP4	✖	This rule is not applicable for MM-VCEP
PM6	✖	De novo data for this variant has not been reported in literature.
PVS1	✖	This variant is not a null variant.
PM3	✖	This rule is not applicable for MM-VCEP
PM5	✖	This variant is a missense change at the same residue (p.Asp198) where a different missense change has been previously established as a pathogenic variant (ClinVar ID 627342) based on MM-VCEP rules for RUNX1 and RNA data. Not met because PM1_strong is met.

PM4	ℹ	✖	This variant is not an in-frame deletion/insertion.
BS1	ℹ	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	ℹ	✖	Segregation data for this variant has not been reported in literature.
BS3	ℹ	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
BS2		✖	This rule is not applicable for MM-VCEP
PS1	ℹ	✖	There has not yet been a missense change resulting in the same change in protein which has been determined to be pathogenic at this amino acid residue.
PS2		✖	De novo data for this variant has not been reported in literature.
PS3	ℹ	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
BP5		✖	This rule is not applicable for MM-VCEP
BP7	ℹ	✖	This variant does not have a phyloP score < 2.0. (Score 7.69457)
BP4	ℹ	✖	This variant does not have applicable in-silico data available.
BP3		✖	This rule is not applicable for MM-VCEP
BP1		✖	This rule is not applicable for MM-VCEP
BP2	ℹ	✖	This variant has not been observed in trans with a pathogenic variant for a fully penetrant dominant gene/disorder or observed in cis with a pathogenic variant in any inheritance pattern.

Curation History

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