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.592G>A (p.Asp198Asn)

Version: 1.1

CA410207977

3340076 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: eb5fc630-4965-4523-93d0-363dbe915adf
Approved on: Mon, 05 Oct 2026 00:00:00 +0000
Published on: Mon, 05 Oct 2026 00:00:00 +0000

HGVS expressions

NM_001754.5:c.592G>A
NM_001754.5(RUNX1):c.592G>A (p.Asp198Asn)
NC_000021.9:g.34859495C>T
CM000683.2:g.34859495C>T
NC_000021.8:g.36231792C>T
CM000683.1:g.36231792C>T
NC_000021.7:g.35153662C>T
NG_011402.2:g.1130217G>A
ENST00000675419.1:c.592G>A
ENST00000300305.7:c.592G>A
ENST00000344691.8:c.511G>A
ENST00000358356.9:c.511G>A
ENST00000399237.6:c.556G>A
ENST00000399240.5:c.511G>A
ENST00000437180.5:c.592G>A
ENST00000467577.1:n.84G>A
ENST00000482318.5:c.*182G>A
NM_001001890.2:c.511G>A
NM_001122607.1:c.511G>A
NM_001754.4:c.592G>A
NM_001001890.3:c.511G>A
NM_001122607.2:c.511G>A

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PM1_Strong PS4_Supporting

Not Met criteria codes 20

BA1 PP1 PP2 PP4 PM6 PVS1 PM3 PM5 PM4 BS1 BS4 BS2 PS1 PS2 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.592G>A (p.Asp198Asn) is a missense variant which affects one of the hotspot residues (Asp198) within the RHD (amino acids 89-204; PM1_Strong). This variant has a REVEL score ≥ 0.88 (0.93) (PP3) and is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). This variant has been reported in one proband meeting at least one of the RUNX1-phenotypic criteria (PS4_Supporting; PMID: 26175287). 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, PP3, 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 missense variant has a REVEL score ≥ 0.88 (0.93) (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: 26175287).

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	✖	This variant does not have two or more (only 1 reported) assumed de novo occurrences in the literature.
PVS1	✖	This variant is not a null variant.
PM3	✖	This rule is not applicable for MM-VCEP.
PM5	✖	PM1_strong met.
PM4	✖	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.
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		✖	This variant does not have a proven de novo occurrence in the literature.
BP5		✖	This rule is not applicable for MM-VCEP.
BP7	ℹ	✖	This variant is not a synonymous or intronic variant.
BP4	ℹ	✖	This missense variant does not have a REVEL score < 0.50.
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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