

Variant: *NM_001754.5(RUNX1):c.593A>C (p.Asp198Ala)*

Version: 1.1

CA410207974 [↗](#)

561251 (ClinVar) [↗](#)

Gene: RUNX1 ([HGNC:861](#))

Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome ([MONDO:0011071](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 9e51dbad-5cbe-4a99-8a12-f7daf29fd7ab

Approved on: Fri, 02 Oct 2026 00:00:00 +0000

Published on: Fri, 02 Oct 2026 00:00:00 +0000

HGVS expressions

NM_001754.5(RUNX1):c.593A>C (p.Asp198Ala)

NM_001754.5:c.593A>C

NC_000021.9:g.34859494T>G

CM000683.2:g.34859494T>G

NC_000021.8:g.36231791T>G

CM000683.1:g.36231791T>G

NC_000021.7:g.35153661T>G

NG_011402.2:g.1130218A>C

ENST00000675419.1:c.593A>C

ENST00000300305.7:c.593A>C

ENST00000344691.8:c.512A>C

ENST00000358356.9:c.512A>C

ENST00000399237.6:c.557A>C

ENST00000399240.5:c.512A>C

ENST00000437180.5:c.593A>C

ENST00000467577.1:n.85A>C

ENST00000482318.5:c.*183A>C

NM_001001890.2:c.512A>C

NM_001122607.1:c.512A>C

NM_001754.4:c.593A>C

NM_001001890.3:c.512A>C

NM_001122607.2:c.512A>C

Likely Pathogenic

Met criteria codes 4

PM1_Strong

PP3

PS4_Supporting

PM2_Supporting

Not Met criteria codes 22

BP4

BP3

BP1

BP2

BP5

BP7

BS2

BS1

BS4

BS3

PP1

PP2

PP4

PM3

PM5

PM4

PS1

PS2

PS3

BA1

PM6

PVS1

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**

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.593A>C (p.Asp198Ala) 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 (0.96) (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, internal data from PreventionGenetics). 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

PM1_Strong			This variant affects the following hotspot residue within the RHD: D198 (PM1_strong).
PP3			This missense variant has a REVEL score ≥ 0.88 (0.962) (PP3). SpliceAI score is null.
PS4_Supporting			Answer from the lab who submitted the variant in Clinvar (PreventionGenetics) : Our patient had AML, a personal and family history of familial thrombocytopenia, easy bruising, and hypocellular marrow at diagnosis. The individual's mother also carried the variant and had thrombocytopenia. Although they were unavailable for testing, the maternal grandmother and great-grandfather also were reported to have easy bruising. The maternal great-grandfather died of leukemia in his 60s.
PM2_Supporting			This variant is completely absent from all population databases with at least 20x coverage for RUNX1 in gnomAD v2.1.1 and v3.1.2 (PM2_supporting).

Not Met criteria codes

BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			This rule is not applicable to the MMVCEP.
BP1			This rule is not applicable to the MMVCEP.
BP2			To our knowledge, no publication has reported this variant to date.
BP5			This rule is not applicable to the MMVCEP.
BP7			This is a missense variant.
BS2			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
BS4			Clinvar has one entry for this variant but the affected status is unknown. To our knowledge, no publication has reported this variant to date.
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			Answer from the lab who submitted the variant in Clinvar (PreventionGenetics) : Our patient had AML, a personal and family history of familial thrombocytopenia, easy bruising, and hypocellular marrow at diagnosis. The individual's mother also carried the variant and had thrombocytopenia. Although they were unavailable for testing, the maternal grandmother and great-grandfather also were reported to have easy bruising. The maternal great-grandfather died of leukemia in his 60s. ==> 2 meioses with positive genotype instead of 3.
PP2			This rule is not applicable to the MMVCEP.
PP4			This rule is not applicable to the MMVCEP.
PM3			This rule is not applicable to the MMVCEP.
PM5			PM1_strong met.
PM4			This variant is a missense.
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			To our knowledge, no publication has reported this variant to date.
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6			To our knowledge, no publication has reported this variant to date.
PVS1			This is a missense variant.

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.