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Variant: NM_001754.5(RUNX1):c.891_904del (p.Pro298fs)

Version: 1.2

CA2739267612

2839740 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 25352593-9a9f-44c1-9037-0e4eb472ac58
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.891_904del
NM_001754.5(RUNX1):c.891_904del (p.Pro298fs)
NC_000021.9:g.34799366_34799379del
CM000683.2:g.34799366_34799379del
NC_000021.8:g.36171663_36171676del
CM000683.1:g.36171663_36171676del
NC_000021.7:g.35093533_35093546del
NG_011402.2:g.1190335_1190348del
ENST00000675419.1:c.891_904del
ENST00000300305.7:c.891_904del
ENST00000344691.8:c.810_823del
ENST00000399240.5:c.618_631del
ENST00000437180.5:c.891_904del
ENST00000482318.5:c.*481_*494del
NM_001001890.2:c.810_823del
NM_001754.4:c.891_904del
NM_001001890.3:c.810_823del

Likely Pathogenic

Met criteria codes 3

PVS1_Strong PM5_Supporting PM2_Supporting

Not Met criteria codes 23

PS1 PS2 PS3 PS4 BA1 PP1 PP2 PP3 PP4 PM6 PM1 PM3 PM4 BS2 BS1 BS4 BS3 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.891_904del (p.Pro298Phefs*297) is a frameshift variant which is not predicted to undergo NMD (PVS1_Strong). This variant is downstream of c.98 (PM5_Supporting) and is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the ClinGen Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PVS1_Strong, PM5_Supporting, PM2_Supporting.

Met criteria codes

PVS1_Strong	✔	This variant is not predicted to undergo NMD, and the truncated/altered region is critical for protein function (frameshift (-) c.759-c.1440 as per VCEP specifications) (PVS1_Strong).
PM5_Supporting	✔	Other nonsense/frameshift variants have been reported as pathogenic/likely pathogenic in exon 8 (PMID: 35764482).
PM2_Supporting	✔	Completely absent from gnomAD v2+v3+v4 with a mean coverage of at least 20X.

Not Met criteria codes

PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PS3	✖	No relevant literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PS4	✖	Proband data for this variant has not been reported in literature.
BA1	✖	Completely absent from gnomAD v2+v3+v4 with a mean coverage of at least 20X.
PP1	✖	Segregation data for this variant has not been reported in literature.
PP2	✖	This rule is not applicable for MM-VCEP.
PP3	✖	This variant does not have applicable in-silico data available.
PP4	✖	Not applicable
PM6	✖	No literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
PM1	✖	This variant is not a missense variant.
PM3	✖	This rule is not applicable for MM-VCEP.

PM4		✖	This variant is not an in-frame deletion/insertion.
BS2		✖	This rule is not applicable for MM-VCEP.
BS1		✖	Completely absent from gnomAD v2+v3+v4 with a mean coverage of at least 20X.
BS4		✖	Segregation data for this variant has not been reported in literature.
BS3		✖	No relevant literature was found in LOVD, HGMD, ClinVar, COSMIC, Mastermind, and Google/Google Scholar searches.
BP5		✖	This rule is not applicable for MM-VCEP.
BP7		✖	This variant is not a synonymous or intronic variant.
BP4		✖	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		✖	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

Showing 1 to 3 of 3 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001754.5(RUNX1):c.891_904del (p...	Likely Pathogenic	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2026-10-05	1.2	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RUNX1 Version 3.1	RUNX1
View	NM_001754.5(RUNX1):c.891_904del (p...	Likely Pathogenic	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2025-01-15	1.1	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1
View	NM_001754.5(RUNX1):c.891_904del (p...	Likely Pathogenic	Hereditary Thrombocytopenia And Hematologic Cancer Predisposition Syndrome	2024-11-04	1.0	ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2	RUNX1

Showing 1 to 3 of 3 rows

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