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.289_299delinsCTCCTTCCGCTG (p.Phe97fs)

Version: 1.0

CA915952644

647118 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2d0a0109-82ce-4d95-b775-93c4312cc6a3
Approved on: 2023/12/9
Published on: 2023/12/9

HGVS expressions

NM_001754.5(RUNX1):c.289_299delinsCTCCTTCCGCTG (p.Phe97fs)
NM_001754.5:c.289_299delinsCTCCTTCCGCTG
NC_000021.9:g.34886895_34886905delinsCAGCGGAAGGAG
CM000683.2:g.34886895_34886905delinsCAGCGGAAGGAG
NC_000021.8:g.36259192_36259202delinsCAGCGGAAGGAG
CM000683.1:g.36259192_36259202delinsCAGCGGAAGGAG
NC_000021.7:g.35181062_35181072delinsCAGCGGAAGGAG
NG_011402.2:g.1102807_1102817delinsCTCCTTCCGCTG
ENST00000675419.1:c.289_299delinsCTCCTTCCGCTG
ENST00000300305.7:c.289_299delinsCTCCTTCCGCTG
ENST00000344691.8:c.208_218delinsCTCCTTCCGCTG
ENST00000358356.9:c.208_218delinsCTCCTTCCGCTG
ENST00000399237.6:c.253_263delinsCTCCTTCCGCTG
ENST00000399240.5:c.208_218delinsCTCCTTCCGCTG
ENST00000437180.5:c.289_299delinsCTCCTTCCGCTG
ENST00000455571.5:c.250_260delinsCTCCTTCCGCTG
ENST00000482318.5:c.59-6192_59-6182delinsCTCCTTCCGCTG
NM_001001890.2:c.208_218delinsCTCCTTCCGCTG
NM_001122607.1:c.208_218delinsCTCCTTCCGCTG
NM_001754.4:c.289_299delinsCTCCTTCCGCTG
NM_001001890.3:c.208_218delinsCTCCTTCCGCTG
NM_001122607.2:c.208_218delinsCTCCTTCCGCTG

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PM5_Supporting

Not Met criteria codes 23

PP1 PP2 PP3 PP4 PM1 PM3 BA1 PM4 PM6 BS2 BS1 BS4 BS3 PS1 PS2 PS3

Expert Panel

Myeloid Malignancy VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2*
PDF

PS4 BP4 BP3 BP1 BP2 BP5 BP7

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence Links 0

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.289_299delinsCTCCTTCCGCTG (p.Phe97fs) is a frameshift variant. The transcript product is predicted to undergo NMD (PVS1). 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). This variant was reported in ClinVar in 2018 by Invitae but the affected status of the proband is unknown (Variation ID 647118). This variant is a frameshift change or agreement in splicing predictors (SSF and MES) showing no splicing effects (PM5_Supporting). In summary, this variant meets the criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PVS1, PM2_supporting, PM5_supporting.

Met criteria codes

PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting).
PVS1	✔	The transcript product of this frameshift variant is predicted to undergo NMD.
PM5_Supporting	✔	This is a frameshift variants that are downstream of c.98 (in transcript NM_001754.4)

Not Met criteria codes

PP1	✖	This rule is not applicable because there is no information on segregation in affected individuals with this variant.
PP2	✖	This rule is not applicable for MM-VCEP
PP3	✖	This rule is not applicable because this is a loss of function variant.
PP4	✖	This rule is not applicable for MM-VCEP.
PM1	✖	This is a frameshift variant
PM3	✖	This rule is not applicable for MM-VCEP.
BA1	✖	This rule is not applicable because the variant is completely absent from all population databases.
PM4	✖	This rule is not applicable because this is a loss of function variant.

PM6	ℹ	✖	This rule is not applicable because there is no information on affected individuals nor the family.
BS2		✖	This rule is not applicable for MM-VCEP
BS1	ℹ	✖	This rule is not applicable because the variant is completely absent from all population databases.
BS4	ℹ	✖	This rule is not applicable because there is no information on segregation in affected individuals with this variant.
BS3	ℹ	✖	This rule does not apply because there are no functional studies for this variant.
PS1	ℹ	✖	This rule is not applicable because this is a loss of function variant.
PS2		✖	This rule is not applicable because there are no affected individuals with this variant.
PS3	ℹ	✖	This rule does not apply because there are no functional studies for this variant.
PS4	ℹ	✖	This rule is not applicable because there is no published information on affected individuals nor a RUNX1 case control study. This variant was reported in ClinVar in 2018 by Invitae but the affected status of the proband is unknown (Variation ID 647118).
BP4	ℹ	✖	This rule is not applicable because this is a loss of function variant.
BP3		✖	This rule is not applicable for MM-VCEP
BP1		✖	This rule is not applicable for MM-VCEP
BP2	ℹ	✖	This rule is not applicable because we have no phase information in affected individuals for this variant.
BP5		✖	This rule is not applicable for MM-VCEP.
BP7	ℹ	✖	This rule is not applicable because this is a loss of function variant.

Curation History

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