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Variant: NM_001754.5(RUNX1):c.424del (p.Ala142fs)

Version: 1.0

CA645607374

2759299 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: a51923b3-48de-4c9b-b191-5561de3402a2
Approved on: 2024/9/10
Published on: 2024/9/10

HGVS expressions

NM_001754.5:c.424del
NM_001754.5(RUNX1):c.424del (p.Ala142fs)
NC_000021.9:g.34880642del
CM000683.2:g.34880642del
NC_000021.8:g.36252939del
CM000683.1:g.36252939del
NC_000021.7:g.35174809del
NG_011402.2:g.1109071del
ENST00000675419.1:c.424del
ENST00000300305.7:c.424del
ENST00000344691.8:c.343del
ENST00000358356.9:c.343del
ENST00000399237.6:c.388del
ENST00000399240.5:c.343del
ENST00000437180.5:c.424del
ENST00000455571.5:c.385del
ENST00000482318.5:c.*14del
NM_001001890.2:c.343del
NM_001122607.1:c.343del
NM_001754.4:c.424del
NM_001001890.3:c.343del
NM_001122607.2:c.343del

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PM5_Supporting

Not Met criteria codes 22

BS2 BS1 BS4 BS3 BP4 BP3 BP1 BP2 BP5 BP7 PS1 PS2 PS3 PM1 PM3 PM4 BA1 PM6 PP1 PP2 PP3 PP4

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 Version 2*
  - **PDF**
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.424del (p.Ala142LeufsTer3) is a frameshift variant which is predicted to undergo nonsense-mediated decay in a gene where loss-of-function is an established mechanism (PVS1). This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_supporting). This variant is downstream of c.98 (PM5_supporting). In summary, this variant meets 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

PVS1	✔	This variant is predicted to undergo nonsense mediated decay in a gene in which loss-of-function is an established mechanism (frameshift (-) c.98-c.758 as per VCEP specifications) (PVS1).
PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).
PM5_Supporting	✔	This variant is a nonsense/frameshift variants that is downstream of c.98 (PM5_Supporting).

Not Met criteria codes

BS2	✖	This rule is not applicable for MM-VCEP.
BS1	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	✖	nil data
BS3	✖	NMD predicted
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	✖	nil data
BP5	✖	This rule is not applicable for MM-VCEP.
BP7	✖	This variant is not a synonymous or intronic variant.

PS1	ℹ	✖	This variant is not a missense variant.
PS2		✖	nil data
PS3	ℹ	✖	NMD predicted
PM1		✖	This variant is not a missense variant.
PM3		✖	This rule is not applicable for MM-VCEP.
PM4	ℹ	✖	This variant is not an in-frame deletion/insertion.
BA1	ℹ	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PM6	ℹ	✖	nil data
PP1	ℹ	✖	nil data
PP2		✖	This rule is not applicable for MM-VCEP.
PP3	ℹ	✖	This variant does not have applicable in-silico data available.
PP4		✖	This rule is not applicable for MM-VCEP.

Curation History

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