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

Version: 2.0

CA658824419

561238 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: 9a538152-2ada-41e8-9f16-2172b1c46648
Approved on: 2024/3/26
Published on: 2024/3/26

HGVS expressions

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

Pathogenic

Met criteria codes 3

PVS1 PM5_Supporting PM2_Supporting

Not Met criteria codes 23

PM6 PM1 PM3 PM4 BA1 BS1 BS4 BS3 BS2 BP5 BP7 BP4 BP3 BP1 BP2 PS1 PS2 PS3 PS4 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

The NM_001754.4:c.424dup (p.Ala142fs) variant is a frameshift variant that is predicted to introduce a premature stop codon and expected to result in nonsense-mediated mRNA decay (PVS1). This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). This variant is a nonsense/frameshift variants that is downstream of c.98 (PM5_Supporting). The variant has not been reported as germ-line in patients with familial platelet disorder with predisposition to hematologic malignancies in the literature, to the best of our knowledge. 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	✔	The variant causes a frameshift and early termination of translation. The resulting transcript is predicted to undergo NMD.
PM5_Supporting	✔	This variant is a nonsense/frameshift variants that is downstream of c.98 (PM5_Supporting).
PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting).

Not Met criteria codes

PM6	✖	No data currently available
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.
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
BS1	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	✖	No data currently available
BS3	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
BS2	✖	This rule is not applicable for MM-VCEP.
BP5	✖	This rule is not applicable for MM-VCEP.
BP7	✖	This variant is not a synonymous or intronic variant.

BP4	ℹ	✖	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	ℹ	✖	No data currently available
PS1	ℹ	✖	This variant is not a missense, or synonymous variant.
PS2		✖	No data currently available
PS3	ℹ	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
PS4	ℹ	✖	The variant has not been reported germ line in patients with familial platelet disorder with predisposition to hematologic malignancies in the literature, to the best of our knowledge. PMID: 28933735 reports a patient with AML in whom the variant is somatic - not counted towards PS4. From internal laboratory data (SCV000807781.1): In the absence of phenotype information on the individual, they were not included in PS4 scoring.
PP1	ℹ	✖	No data currently available
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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