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.240_241del (p.Glu80fs)

Version: 1.1

CA658824422

561230 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: e51a9323-787c-4449-b2e7-f05afb4a89ed
Approved on: 2024/3/26
Published on: 2024/3/26

HGVS expressions

NM_001754.5:c.240_241del
NM_001754.5(RUNX1):c.240_241del (p.Glu80fs)
NC_000021.9:g.34886953_34886954del
CM000683.2:g.34886953_34886954del
NC_000021.8:g.36259250_36259251del
CM000683.1:g.36259250_36259251del
NC_000021.7:g.35181120_35181121del
NG_011402.2:g.1102758_1102759del
ENST00000675419.1:c.240_241del
ENST00000300305.7:c.240_241del
ENST00000344691.8:c.159_160del
ENST00000358356.9:c.159_160del
ENST00000399237.6:c.204_205del
ENST00000399240.5:c.159_160del
ENST00000437180.5:c.240_241del
ENST00000455571.5:c.201_202del
ENST00000482318.5:c.59-6241_59-6240del
NM_001001890.2:c.159_160del
NM_001122607.1:c.159_160del
NM_001754.4:c.240_241del
NM_001001890.3:c.159_160del
NM_001122607.2:c.159_160del

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PM5_Supporting PS4_Moderate

Not Met criteria codes 22

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

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.240_241del (p.Glu80fs) 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). Two unpublished probands meeting the RUNX1 phenotype criteria are noted (PS4_Moderate; SCV000807768.1). In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PVS1, PM2_supporting, PM5_supporting, PS4_Moderate.

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 variant causes a frameshift that introduces a premature termination codon. The resulting transcript is expected to undergo NMD.
PM5_Supporting	✔	This variant is a nonsense/frameshift variants that is downstream of c.98 (PM5_Supporting).
PS4_Moderate	✔	Proband from PMID: 28933735 has a different nucleotide change. From internal laboratory data (SCV000807768.1): 2 unrelated patients with thrombocytopenia and family history of thrombocytopenia and hematologic malignancy.

Not Met criteria codes

PP1	✖	No data currently available
PP2	✖	MM-VCEP deemed N/A for RUNX1
PP3	✖	This variant does not have applicable in-silico data available.
PP4	✖	MM-VCEP deemed N/A for RUNX1
PM1	✖	This variant is not a missense variant.
PM3	✖	MM-VCEP deemed N/A for RUNX1
BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PM4	✖	This variant is not an in-frame deletion/insertion.
PM6	✖	No data currently available
BS2	✖	MM-VCEP deemed N/A for RUNX1

BS1	ℹ	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	ℹ	✖	No data currently available
BS3	ℹ	✖	No data currently available
PS1	ℹ	✖	This variant is not a missense, or synonymous variant.
PS2		✖	No data currently available
PS3	ℹ	✖	No data currently available
BP4	ℹ	✖	This variant does not have applicable in-silico data available.
BP3		✖	MM-VCEP deemed N/A for RUNX1
BP1		✖	MM-VCEP deemed N/A for RUNX1
BP2	ℹ	✖	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.
BP5		✖	MM-VCEP deemed N/A for RUNX1
BP7	ℹ	✖	This variant is not a synonymous or intronic variant.

Curation History

Showing 1 to 2 of 2 rows

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