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_000546.6(TP53):c.*1175A>C*

Version: 1.0

CA000049

35555 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2430f17c-bc66-400f-85de-64e4101ea804
Approved on: 2025/12/5
Published on: 2025/12/5

HGVS expressions

NM_000546.6(TP53):c.*1175A>C
NM_000546.6:c.*1175A>C
NC_000017.11:g.7668434T>G
CM000679.2:g.7668434T>G
NC_000017.10:g.7571752T>G
CM000679.1:g.7571752T>G
NC_000017.9:g.7512477T>G
NG_017013.2:g.24117A>C
ENST00000503591.2:c.*1175A>C
ENST00000508793.6:c.*1175A>C
ENST00000509690.6:c.*1175A>C
ENST00000514944.6:c.*1175A>C
ENST00000604348.6:c.*1175A>C
ENST00000269305.9:c.*1175A>C
ENST00000269305.8:c.*1175A>C
ENST00000359597.8:c.994-2190A>C
ENST00000413465.6:c.782+5747A>C
ENST00000420246.6:c.*1464A>C
ENST00000445888.6:c.*1175A>C
ENST00000455263.6:c.*1376A>C
ENST00000504290.5:c.*1376A>C
ENST00000504937.5:c.*1175A>C
ENST00000510385.5:c.*1464A>C
ENST00000610292.4:c.*1175A>C
ENST00000610538.4:c.*1376A>C
ENST00000610623.4:c.*1376A>C
ENST00000617185.4:c.*1464A>C
ENST00000618944.4:c.*1464A>C
ENST00000619186.4:c.*1175A>C
ENST00000619485.4:c.*1175A>C
ENST00000620739.4:c.*1175A>C
ENST00000622645.4:c.*1464A>C
ENST00000635293.1:c.984-1009A>C
NM_000546.5:c.*1175A>C
NM_001126112.2:c.*1175A>C
NM_001126113.2:c.*1376A>C
NM_001126114.2:c.*1464A>C

NM_001126115.1:c.*1175A>C
NM_001126116.1:c.*1464A>C
NM_001126117.1:c.*1376A>C
NM_001126118.1:c.*1175A>C
NM_001276695.1:c.*1376A>C
NM_001276696.1:c.*1464A>C
NM_001276697.1:c.*1175A>C
NM_001276698.1:c.*1464A>C
NM_001276699.1:c.*1376A>C
NM_001276760.1:c.*1175A>C
NM_001276761.1:c.*1175A>C
NM_001276695.2:c.*1376A>C
NM_001276696.2:c.*1464A>C
NM_001276697.2:c.*1175A>C
NM_001276698.2:c.*1464A>C
NM_001276699.2:c.*1376A>C
NM_001276760.2:c.*1175A>C
NM_001276761.2:c.*1175A>C
NM_001126112.3:c.*1175A>C
NM_001126113.3:c.*1376A>C
NM_001126114.3:c.*1464A>C
NM_001126115.2:c.*1175A>C
NM_001126116.2:c.*1464A>C
NM_001126117.2:c.*1376A>C
NM_001126118.2:c.*1175A>C
NM_001276695.3:c.*1376A>C
NM_001276696.3:c.*1464A>C
NM_001276697.3:c.*1175A>C
NM_001276698.3:c.*1464A>C
NM_001276699.3:c.*1376A>C
NM_001276760.3:c.*1175A>C
NM_001276761.3:c.*1175A>C

Benign

Met criteria codes 1

BA1

Not Met criteria codes 3

PM2 BS2 BS1

Evidence Links 0

Expert Panel

TP53 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.3.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6 c.*1175A>C variant resides in the 3’UTR of TP53. Because the variant is located in the 3’UTR, it is not expected to alter the amino acid sequence. The filtering allele frequency is 0.01138 in the European non-Finnish population in gnomAD v4.1.0, which is

higher than the ClinGen TP53 VCEP threshold (≥0.001) for BA1, and therefore meets this criterion (BA1). In summary, this variant meets the criteria to be classified as Benign for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: BA1. Of note, this variant has been identified as a potential risk allele for glioma in multiple GWAS studies. This variant is also reported to have TP53 functional impact in a homozygous individual in PMID: 33051313. This data is outside the scope of the VCEP which focuses on curation for Li Fraumeni syndrome and was not factored into variant curation.(Bayesian Points: N/A; VCEP specifications version 2.3)

Met criteria codes

BA1	✔	**Gnomad warning** The filtering allele frequency is 0.01138 in the European non-Finnish population in gnomAD v4.1.0, which is higher than the ClinGen TP53 VCEP threshold (≥0.001) for BA1, and therefore meets this criterion (BA1).

Not Met criteria codes

PM2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	✖	This variant has been observed in at least 8 heterozygous unrelated females from the same data source with no personal history of cancer prior to age 60 years and no personal history of sarcoma at any age (BS2; FLOSSIES Database).
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000546.6(TP53):c.*1175A>C	Benign	Li-Fraumeni Syndrome	2025-12-05	1.0	ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.3.0	TP53

Showing 1 to 1 of 1 rows

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