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_000546.5(TP53):c.139C>T (p.Pro47Ser)

Version: 1.1

CA000053

43588 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: d9f1afe3-5f5c-4af4-8f96-d83399ee9404
Approved on: 2024-08-05
Published on: 2024-08-05

HGVS expressions

NM_000546.5:c.139C>T
NM_000546.5(TP53):c.139C>T (p.Pro47Ser)
NC_000017.11:g.7676230G>A
CM000679.2:g.7676230G>A
NC_000017.10:g.7579548G>A
CM000679.1:g.7579548G>A
NC_000017.9:g.7520273G>A
NG_017013.2:g.16321C>T
ENST00000503591.2:c.139C>T
ENST00000508793.6:c.139C>T
ENST00000509690.6:c.-21-994C>T
ENST00000514944.6:c.96+152C>T
ENST00000604348.6:c.139C>T
ENST00000269305.9:c.139C>T
ENST00000269305.8:c.139C>T
ENST00000359597.8:c.139C>T
ENST00000413465.6:c.139C>T
ENST00000420246.6:c.139C>T
ENST00000445888.6:c.139C>T
ENST00000455263.6:c.139C>T
ENST00000503591.1:c.139C>T
ENST00000505014.5:n.395C>T
ENST00000508793.5:c.139C>T
ENST00000509690.5:c.-21-994C>T
ENST00000514944.5:c.96+152C>T
ENST00000604348.5:c.139C>T
ENST00000610292.4:c.22C>T
ENST00000610538.4:c.22C>T
ENST00000615910.4:c.139C>T
ENST00000617185.4:c.139C>T
ENST00000619485.4:c.22C>T
ENST00000620739.4:c.22C>T
ENST00000622645.4:c.22C>T
ENST00000635293.1:c.22C>T
NM_001126112.2:c.139C>T
NM_001126113.2:c.139C>T
NM_001126114.2:c.139C>T

NM_001126118.1:c.22C>T
NM_001276695.1:c.22C>T
NM_001276696.1:c.22C>T
NM_001276760.1:c.22C>T
NM_001276761.1:c.22C>T
NM_001276695.2:c.22C>T
NM_001276696.2:c.22C>T
NM_001276760.2:c.22C>T
NM_001276761.2:c.22C>T
NM_000546.6:c.139C>T
NM_001126112.3:c.139C>T
NM_001126113.3:c.139C>T
NM_001126114.3:c.139C>T
NM_001126118.2:c.22C>T
NM_001276695.3:c.22C>T
NM_001276696.3:c.22C>T
NM_001276760.3:c.22C>T
NM_001276761.3:c.22C>T

Benign

Met criteria codes 4

BA1 BS3 BS2 BP4

Not Met criteria codes 12

PS1 PS2 PS3 PS4 PP1 PP3 PP4 PM2 PM1 PM5 BS1 BS4

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 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6: c.139C>T variant in TP53 is a missense variant predicted to cause substitution of Proline by Serine at amino acid 47 (p.Pro47Ser). The filtering allele frequency of the c.139C>T variant in the TP53 gene is 0.01560 for African/African American population by 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 (Bayesian Points: N/A; VCEP specifications version 2.0; 7/24/2024).

Met criteria codes

BA1	✔	The filtering allele frequency of the c.139C>T variant in the TP53 gene is 0.01560 for African/African American population by gnomAD v4.1.0, which is higher than the ClinGen TP53 VCEP threshold (≥0.001) for BA1, and therefore meets this criterion (BA1).
BS3	✔	In vitro assays performed in yeast and/or human cell lines showed functional transactivation and retained growth suppression activity indicating that this variant does not impact protein function (PMIDs: 12826609, 29979965,

30224644) (BS3)

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 and Internal Lab Contributors: SCV000186571.8).
BP4	✔	BP4_MODERATE. Computational predictor scores (BayesDel = -0.2146; Align GVGD Class C0) are below the recommended thresholds (BayesDel ≤ -0.008 and an Align GVGD Class ≤ 55), evidence that does not predict a damaging effect on TP53 via protein change. SpliceAI predicts that the variant has no impact on splicing (BP4_Moderate)

Not Met criteria codes

PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	This variant does not reside within a region of TP53 that is defined as a mutational hotspot by the ClinGen TP53 VCEP (PM1 not met).
PM5	✖	3 different missense variants (c.140C>G; p.Pro47Arg, .139C>G; p.Pro47Ala, c.139C>A; p.Pro47Thr) in the same codon have been reported (ClinVar Variation ID 819145, 1721838, 406608). However, the variants have not yet been curated to determine if they would be classified as pathogenic or likely pathogenic by the ClinGen TP53 VCEP's specifications (PM5 not evaluated).

BS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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