

Variant: NM_000546.6(TP53):c.332T>G (p.Leu111Arg)

Version: 2.0

CA16603050 [↗](#)

376631 (ClinVar) [↗](#)

Gene: TP53 ([HGNC:7157](#))

Condition: Li-Fraumeni syndrome ([MONDO:0018875](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 96ab2334-8f49-48fc-a973-aa806a4567a1

Approved on: 2026/1/6

Published on: 2026/1/14

HGVS expressions

NM_000546.6(TP53):c.332T>G (p.Leu111Arg)

NM_000546.6:c.332T>G

NC_000017.11:g.7676037A>C

CM000679.2:g.7676037A>C

NC_000017.10:g.7579355A>C

CM000679.1:g.7579355A>C

NC_000017.9:g.7520080A>C

NG_017013.2:g.16514T>G

ENST00000503591.2:c.332T>G

ENST00000508793.6:c.332T>G

ENST00000509690.6:c.-21-801T>G

ENST00000514944.6:c.96+345T>G

ENST00000604348.6:c.332T>G

ENST00000269305.9:c.332T>G

ENST00000269305.8:c.332T>G

ENST00000359597.8:c.332T>G

ENST00000413465.6:c.332T>G

ENST00000420246.6:c.332T>G

ENST00000445888.6:c.332T>G

ENST00000455263.6:c.332T>G

ENST00000503591.1:c.332T>G

ENST00000505014.5:n.588T>G

ENST00000508793.5:c.332T>G

ENST00000509690.5:c.-21-801T>G

ENST00000514944.5:c.96+345T>G

ENST00000604348.5:c.332T>G

ENST00000610292.4:c.215T>G

ENST00000610538.4:c.215T>G

ENST00000615910.4:c.332T>G

ENST00000617185.4:c.332T>G

ENST00000619485.4:c.215T>G

ENST00000620739.4:c.215T>G

ENST00000622645.4:c.215T>G

ENST00000635293.1:c.215T>G

NM_000546.5:c.332T>G

NM_001126112.2:c.332T>G

NM_001126113.2:c.332T>G

NM_001126114.2:c.332T>G
NM_001126118.1:c.215T>G
NM_001276695.1:c.215T>G
NM_001276696.1:c.215T>G
NM_001276760.1:c.215T>G
NM_001276761.1:c.215T>G
NM_001276695.2:c.215T>G
NM_001276696.2:c.215T>G
NM_001276760.2:c.215T>G
NM_001276761.2:c.215T>G
NM_001126112.3:c.332T>G
NM_001126113.3:c.332T>G
NM_001126114.3:c.332T>G
NM_001126118.2:c.215T>G
NM_001276695.3:c.215T>G
NM_001276696.3:c.215T>G
NM_001276760.3:c.215T>G
NM_001276761.3:c.215T>G

Pathogenic

Met criteria codes 5

- PS3
- PM1_Supporting
- PP3_Moderate
- PM5
- PM2_Supporting

Not Met criteria codes 20

- BP5
- BP7
- BP4
- BP3
- BP1
- BP2
- PS1
- PS2
- PS4
- PP1
- PP2
- PP4
- PM6
- PM3
- PM4
- BA1
- PVS1
- BS1
- BS4
- BS3

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 2.4.0

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6: c.332T>G variant in TP53 is a missense variant predicted to cause substitution of leucine by arginine at amino acid 111 (p.Leu111Arg). To our knowledge, this variant has not been reported in individuals meeting classical LFS or Chompret criteria (PS4 not met). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In vitro assays performed in yeast and/or human cell lines showed non-functional transactivation and loss of growth suppression activity indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965). Computational predictor scores (BayesDel = 0.4821; Align GVGD = Class 65) are above recommended thresholds (BayesDel > 0.16 and an Align GVGD Class of 65), evidence that correlates with impact to TP53 via protein change (PP3_Moderate). This variant has 6 somatic occurrences for the same amino acid change in cancerhotspots.org (v2) sufficient to be defined as a mutational hotspot by the Clingen TP53 VCEP (2-9 somatic occurrences, PMID: 30311369) (PM1_Supporting). Another missense variant (c.332T>C, p.Leu111Pro) (ClinVar Variation ID: 376630), in the same codon has been classified as pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP’s specifications.(PM5). In summary, this variant meets the criteria to be classified as likely pathogenic for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PS3, PP3_moderate, PM1_supporting, PM5, PM2_supporting. (Bayesian Points: 10; VCEP specifications version 2.4)

Met criteria codes			
PS3		✓	In vitro assays performed in yeast and/or human cell lines showed non-functional transactivation and loss of growth suppression activity indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965).
PM1_Supporting		✓	This variant has 6 somatic occurrences for the same amino acid change in cancerhotspots.org (v2) sufficient to be defined as a mutational hotspot by the Clingen TP53 VCEP (2-9 somatic occurrences, PMID: 30311369) (PM1_Supporting).
PP3_Moderate		✓	Computational predictor scores (BayesDel = 0.4821; Align GVGD = Class 65) are above recommended thresholds (BayesDel > 0.16 and an Align GVGD Class of 65), evidence that correlates with impact to TP53 via protein change (PP3_Moderate).
PM5		✓	Another missense variant (c.332T>C, p.Leu111Pro) (ClinVar Variation ID: 376630), in the same codon has been classified as pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP’s specifications.(PM5).
PM2_Supporting		✓	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

BP5		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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

PS4			To our knowledge, this variant has not been reported in individuals meeting classical LFS or Chompret criteria (PS4 not met).
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2			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
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

	▼	▼
--	---	---

Showing 1 to 2 of 2 rows

[illegible]

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.