

Variant: NM_000546.5(TP53):c.245C>T (p.Pro82Leu)

Version: 1.1

CA000080 [↗](#)

182946 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 9c16efaa-0151-4cfa-a50b-acebbb823912

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HGVS expressions

NM_000546.5(TP53):c.245C>T (p.Pro82Leu)

NM_000546.5:c.245C>T

NC_000017.11:g.7676124G>A

CM000679.2:g.7676124G>A

NC_000017.10:g.7579442G>A

CM000679.1:g.7579442G>A

NC_000017.9:g.7520167G>A

NG_017013.2:g.16427C>T

ENST00000503591.2:c.245C>T

ENST00000508793.6:c.245C>T

ENST00000509690.6:c.-21-888C>T

ENST00000514944.6:c.96+258C>T

ENST00000604348.6:c.245C>T

ENST00000269305.9:c.245C>T

ENST00000269305.8:c.245C>T

ENST00000359597.8:c.245C>T

ENST00000413465.6:c.245C>T

ENST00000420246.6:c.245C>T

ENST00000445888.6:c.245C>T

ENST00000455263.6:c.245C>T

ENST00000503591.1:c.245C>T

ENST00000505014.5:n.501C>T

ENST00000508793.5:c.245C>T

ENST00000509690.5:c.-21-888C>T

ENST00000514944.5:c.96+258C>T

ENST00000604348.5:c.245C>T

ENST00000610292.4:c.128C>T

ENST00000610538.4:c.128C>T

ENST00000615910.4:c.245C>T

ENST00000617185.4:c.245C>T

ENST00000619485.4:c.128C>T

ENST00000620739.4:c.128C>T

ENST00000622645.4:c.128C>T

ENST00000635293.1:c.128C>T

NM_001126112.2:c.245C>T

NM_001126113.2:c.245C>T

NM_001126114.2:c.245C>T

NM_001126118.1:c.128C>T
NM_001276695.1:c.128C>T
NM_001276696.1:c.128C>T
NM_001276760.1:c.128C>T
NM_001276761.1:c.128C>T
NM_001276695.2:c.128C>T
NM_001276696.2:c.128C>T
NM_001276760.2:c.128C>T
NM_001276761.2:c.128C>T
NM_000546.6:c.245C>T
NM_001126112.3:c.245C>T
NM_001126113.3:c.245C>T
NM_001126114.3:c.245C>T
NM_001126118.2:c.128C>T
NM_001276695.3:c.128C>T
NM_001276696.3:c.128C>T
NM_001276760.3:c.128C>T
NM_001276761.3:c.128C>T

Likely Benign

Met criteria codes 4

BS3 BS2 BP4 PM2_Supporting

Not Met criteria codes 12

BS1 BS4 PS1 PS2 PS3 PS4
BA1 PP1 PP3 PP4 PM1
PM5

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.245C>T variant in TP53 is a missense variant predicted to cause substitution of proline by leucine at amino acid 82 (p.Pro82Leu). This variant has been observed in 4-7 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_Moderate; Internal Lab Contributors: SCV000215716.6). This variant has an allele frequency of 0.00003335 (5/59976 alleles) in the Admixed American population in gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00004) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). 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 (BS3; PMIDs: 12826609, 29979965, 30224644). Computational predictor scores (BayesDel = 0.0708; Align GVGD Class C0) are below the recommended thresholds (BayesDel < 0.16 and an Align GVGD Class ≤ 55), evidence that does not predict a damaging effect on TP53 via protein change. SpliceAI predictor score of [0.01] predicts that the variant has no impact on splicing (score threshold <0.210) (BP4). In summary, this variant meets the criteria to be classified as Likely Benign for Li Fraumeni Syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: BS2_moderate, PM2_Supporting BS3, BP4, (Bayesian Points: -6; VCEP specifications version 2.0; 7/24/2024).

Met criteria codes

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			BS2_MODERATE This variant has been observed in 4-7 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_Moderate; Internal Lab Contributors: SCV000215716.6).
BP4			Computational predictor scores (BayesDel = 0.0708; Align GVGD Class C0) are below the recommended thresholds (BayesDel < 0.16 and an Align GVGD Class ≤ 55), evidence that does not predict a damaging effect on TP53 via protein change. SpliceAI predictor score of [0.01] predicts that the variant has no impact on splicing (score threshold <0.210) (BP4).
PM2_Supporting			This variant has an allele frequency of 0.00003335 (5/59976 alleles) in the Admixed American population in gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00004) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

Not Met criteria codes

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
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
BA1			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

