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Variant: NM_000546.6(TP53):c.337T>A (p.Phe113Ile)

Version: 1.0

CA397844510

1469551 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 454d1e83-d15f-4d8a-b020-b002fddfb132
Approved on: Thu, 06 Aug 2026 00:00:00 +0000
Published on: Tue, 22 Sep 2026 00:00:00 +0000

HGVS expressions

NM_000546.6(TP53):c.337T>A (p.Phe113Ile)
NM_000546.6:c.337T>A
NC_000017.11:g.7676032A>T
CM000679.2:g.7676032A>T
NC_000017.10:g.7579350A>T
CM000679.1:g.7579350A>T
NC_000017.9:g.7520075A>T
NG_017013.2:g.16519T>A
ENST00000503591.2:c.337T>A
ENST00000508793.6:c.337T>A
ENST00000509690.6:c.-21-796T>A
ENST00000514944.6:c.96+350T>A
ENST00000604348.6:c.337T>A
ENST00000269305.9:c.337T>A
ENST00000269305.8:c.337T>A
ENST00000359597.8:c.337T>A
ENST00000413465.6:c.337T>A
ENST00000420246.6:c.337T>A
ENST00000445888.6:c.337T>A
ENST00000455263.6:c.337T>A
ENST00000503591.1:c.337T>A
ENST00000505014.5:n.593T>A
ENST00000508793.5:c.337T>A
ENST00000509690.5:c.-21-796T>A
ENST00000514944.5:c.96+350T>A
ENST00000604348.5:c.337T>A
ENST00000610292.4:c.220T>A
ENST00000610538.4:c.220T>A
ENST00000615910.4:c.334-1T>A
ENST00000617185.4:c.337T>A
ENST00000619485.4:c.220T>A
ENST00000620739.4:c.220T>A
ENST00000622645.4:c.220T>A
ENST00000635293.1:c.220T>A
NM_000546.5:c.337T>A
NM_001126112.2:c.337T>A
NM_001126113.2:c.337T>A

NM_001126114.2:c.337T>A
NM_001126118.1:c.220T>A
NM_001276695.1:c.220T>A
NM_001276696.1:c.220T>A
NM_001276760.1:c.220T>A
NM_001276761.1:c.220T>A
NM_001276695.2:c.220T>A
NM_001276696.2:c.220T>A
NM_001276760.2:c.220T>A
NM_001276761.2:c.220T>A
NM_001126112.3:c.337T>A
NM_001126113.3:c.337T>A
NM_001126114.3:c.337T>A
NM_001126118.2:c.220T>A
NM_001276695.3:c.220T>A
NM_001276696.3:c.220T>A
NM_001276760.3:c.220T>A
NM_001276761.3:c.220T>A

Likely Pathogenic

Met criteria codes 4

PS3 PP4_Moderate BS2_Supporting PM2_Supporting

Not Met criteria codes 13

PS1 PS2 PS4 PP1 PP3 PM1 PM5 BA1 BS1 BS4 BS3 BP5 BP4

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*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6: c.337T>A variant in TP53 is a missense variant predicted to cause substitution of phenylalanine by isoleucine at amino acid 113 (p.Phe113Ile). At least two individuals with this variant were found to have a variant allele fraction of 5-25%, which is a significant predictor of variant pathogenicity (PP4_Moderate, PMID: 34906512, Internal lab contributors). This variant received a total of 0.5 points in one proband (PS4 not met; Internal lab contributor). This variant has been observed in 2-3 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_Supporting; Internal lab contributor). 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 by the majority of available assays indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965, 39774325). 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: PM2_Supporting, PS3, PP4_Moderate, BS2_Supporting. (Bayesian Points: 6; 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 by the majority of available assays indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965, 39774325).
PP4_Moderate	✔	At least two individuals with this variant were found to have a variant allele fraction of 5-25%, which is a significant predictor of variant pathogenicity (PP4_Moderate, PMID: 34906512, Internal lab contributors).
BS2_Supporting	✔	This variant has been observed in 2-3 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_Supporting; Internal lab contributor).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

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
PS4	✖	This variant received a total of 0.5 points in one proband (PS4 not met; Internal lab contributor).
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	The results from the computational predictors BayesDel and AlignGVGD do not agree, providing no evidence that correlates with a damaging or benign impact on TP53 function via protein change. Additionally, SpliceAI predicts that the variant has no impact on splicing (score threshold ≤ 0.10) (PP3 and BP4 not met).
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	✖	Six different missense variants affecting the same codon have been reported (c.337T>C, p.Phe113Leu; c.337T>G, p.Phe113Val; c.338T>C, p.Phe113Ser; c.338T>G, p.Phe113Cys; c.339C>A, p.Phe113Leu; c.339C>G, p.Phe113Leu) (ClinVar Variation IDs: 3634432, 141302, 823709, 634690, 2125367, 2702402). However, these variants do not meet the criteria for PM5 code application as the Grantham scores are all higher than this variant (PM5 not met).
BA1	✖	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
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	The results from the computational predictors BayesDel and AlignGVGD do not agree, providing no evidence that correlates with a damaging or benign impact on TP53 function via protein change. Additionally, SpliceAI predicts that the variant has no impact on splicing (score threshold ≤ 0.10) (PP3 and BP4 not met).

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.337T>A (p.Phe1…	Likely Pathogenic	Li-Fraumeni Syndrome	2026-09-22	1.0	ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.4	TP53

Showing 1 to 1 of 1 rows

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