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Variant: NM_000546.6(TP53):c.337T>G (p.Phe113Val)

Version: 1.0

CA000124

141302 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: bc642d79-0efb-4f57-9ae3-177a7515c323
Approved on: Wed, 01 Jul 2026 00:00:00 +0000
Published on: Tue, 22 Sep 2026 00:00:00 +0000

HGVS expressions

NM_000546.6(TP53):c.337T>G (p.Phe113Val)
NM_000546.6:c.337T>G
NC_000017.11:g.7676032A>C
CM000679.2:g.7676032A>C
NC_000017.10:g.7579350A>C
CM000679.1:g.7579350A>C
NC_000017.9:g.7520075A>C
NG_017013.2:g.16519T>G
ENST00000503591.2:c.337T>G
ENST00000508793.6:c.337T>G
ENST00000509690.6:c.-21-796T>G
ENST00000514944.6:c.96+350T>G
ENST00000604348.6:c.337T>G
ENST00000269305.9:c.337T>G
ENST00000269305.8:c.337T>G
ENST00000359597.8:c.337T>G
ENST00000413465.6:c.337T>G
ENST00000420246.6:c.337T>G
ENST00000445888.6:c.337T>G
ENST00000455263.6:c.337T>G
ENST00000503591.1:c.337T>G
ENST00000505014.5:n.593T>G
ENST00000508793.5:c.337T>G
ENST00000509690.5:c.-21-796T>G
ENST00000514944.5:c.96+350T>G
ENST00000604348.5:c.337T>G
ENST00000610292.4:c.220T>G
ENST00000610538.4:c.220T>G
ENST00000615910.4:c.334-1T>G
ENST00000617185.4:c.337T>G
ENST00000619485.4:c.220T>G
ENST00000620739.4:c.220T>G
ENST00000622645.4:c.220T>G
ENST00000635293.1:c.220T>G
NM_000546.5:c.337T>G
NM_001126112.2:c.337T>G
NM_001126113.2:c.337T>G

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

Likely Pathogenic

Met criteria codes 5

PS3 PP3 PM2_Supporting PM1_Supporting PP4_Moderate

Not Met criteria codes 11

PS1 PS2 PS4 PP1 PM6 PM5 BA1 BS1 BS4 BS2 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>G variant in TP53 is a missense variant predicted to cause substitution of phenylalanine by valine at amino acid 113 (p.Phe113Val). 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, ClinVar SCV000754598.8, SCV000184579.8). This variant received a total of 0.5 points across 1 proband. (PS4 not met; 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). Computational predictor scores (BayesDel =0.3138; Align GVGD = Class C45) are above recommended thresholds (BayesDel > 0.16 and an Align GVGD Class of > 15), evidence that correlates with impact to TP53 via protein change (PP3). 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). 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: PP4_Moderate, BS2_Moderate, PM2_Supporting, PS3, PP3, PM1_Supporting (Bayesian Points: 7; 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).
PP3	✔	Computational predictor scores (BayesDel =0.3138; Align GVGD = Class C45) are above recommended thresholds (BayesDel > 0.16 and an Align GVGD Class of > 15), evidence that correlates with impact to TP53 via protein change (PP3).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
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).
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, ClinVar SCV000754598.8, SCV000184579.8).

Not Met criteria codes

PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	GeneDx case of female with breast in 20s and VAF of 35% is highly suspicious for constitutional mosaicism, but as fibroblasts are negative PS2 was not counted. The VCEP feels this case evidence is supportive of the LP classification of this variant as appropriate, even if clinical codes are not actually applied.
PS4	✖	This variant received a total of 0.5 points across 1 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
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	2 different missense variants (p.Phe113Leu, p.Phe113Ile) with Grantham scores equal to or less than the current variant in the same codon have been reported. However, these variants do not meet criteria for PM5 code application (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
BS2	✖	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

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>G (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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