

Variant: *NM_000546.6(TP53):c.634T>A (p.Phe212Ile)*

Version: 1.0

CA16620624 [↗](#)

422414 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 316a4c4a-ff7a-4b9e-89e6-c92af23915b9

Approved on: 2026/2/5

Published on: 2026/2/10

HGVS expressions

NM_000546.6(TP53):c.634T>A (p.Phe212Ile)

NM_000546.6:c.634T>A

NC_000017.11:g.7674897A>T

CM000679.2:g.7674897A>T

NC_000017.10:g.7578215A>T

CM000679.1:g.7578215A>T

NC_000017.9:g.7518940A>T

NG_017013.2:g.17654T>A

ENST00000503591.2:c.634T>A

ENST00000508793.6:c.634T>A

ENST00000509690.6:c.238T>A

ENST00000514944.6:c.355T>A

ENST00000604348.6:c.613T>A

ENST00000269305.9:c.634T>A

ENST00000269305.8:c.634T>A

ENST00000359597.8:c.634T>A

ENST00000413465.6:c.634T>A

ENST00000420246.6:c.634T>A

ENST00000445888.6:c.634T>A

ENST00000455263.6:c.634T>A

ENST00000504290.5:c.238T>A

ENST00000504937.5:c.238T>A

ENST00000505014.5:n.890T>A

ENST00000509690.5:c.238T>A

ENST00000510385.5:c.238T>A

ENST00000514944.5:c.355T>A

ENST00000574684.1:n.67+156T>A

ENST00000610292.4:c.517T>A

ENST00000610538.4:c.517T>A

ENST00000610623.4:c.157T>A

ENST00000615910.4:c.601T>A

ENST00000617185.4:c.634T>A

ENST00000618944.4:c.157T>A

ENST00000619186.4:c.157T>A

ENST00000619485.4:c.517T>A

ENST00000620739.4:c.517T>A

ENST00000622645.4:c.517T>A

ENST00000635293.1:c.517T>A

NM_000546.5:c.634T>A

NM_001126112.2:c.634T>A

NM_001126113.2:c.634T>A

NM_001126114.2:c.634T>A

NM_001126115.1:c.238T>A

NM_001126116.1:c.238T>A

NM_001126117.1:c.238T>A

NM_001126118.1:c.517T>A

NM_001276695.1:c.517T>A

NM_001276696.1:c.517T>A

NM_001276697.1:c.157T>A

NM_001276698.1:c.157T>A

NM_001276699.1:c.157T>A

NM_001276760.1:c.517T>A

NM_001276761.1:c.517T>A

NM_001276695.2:c.517T>A

NM_001276696.2:c.517T>A

NM_001276697.2:c.157T>A

NM_001276698.2:c.157T>A

NM_001276699.2:c.157T>A

NM_001276760.2:c.517T>A

NM_001276761.2:c.517T>A

NM_001126112.3:c.634T>A

NM_001126113.3:c.634T>A

NM_001126114.3:c.634T>A

NM_001126115.2:c.238T>A

NM_001126116.2:c.238T>A

NM_001126117.2:c.238T>A

NM_001126118.2:c.517T>A

NM_001276695.3:c.517T>A

NM_001276696.3:c.517T>A

NM_001276697.3:c.157T>A

NM_001276698.3:c.157T>A

NM_001276699.3:c.157T>A

NM_001276760.3:c.517T>A

NM_001276761.3:c.517T>A

Uncertain Significance

Met criteria codes 3

BP4

PM2_Supporting

PS4_Supporting

Not Met criteria codes 23

PS1

PS2

PS3

BP3

BP1

BP2

BP5

BP7

PP1

PP2

PP3

PP4

BA1

PM1

PM3

PM5

PM4

PM6

BS2

BS1

BS4

BS3

PVS1

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](#)

TP53 VCEP

The NM_000546.6: c.634T>A variant in TP53 is a missense variant predicted to cause substitution of phenylalanine by isoleucine at amino acid 212 (p.Phe212Ile). This variant has been reported in 2 unrelated proband smeeeting Revised Chompret criteria and reported in 1 individual under the age of 40 diagnosed with a HER2+ breast cancer. Based on this evidence, this variant scores 1.5 total points meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; Internal lab contributors). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In vitro assays performed in yeast and/or human cell lines showed conflicting results with respect to transactivation, growth suppression activity, and/or tetramer formation (PS3/BS3 not met; PMIDs: 12826609, 16007150, 29979965, 30224644). Computational predictor scores (BayesDel = -0.00674022; Align GVGD Class C0) are below the recommended thresholds (BayesDel < 0.16 and > -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). In summary, this variant meets the criteria to be classified as of uncertain significance for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PS4_Supporting, BP4, PM2_supporting. (Bayesian Points: 1; VCEP specifications version 2.4)

Met criteria codes

BP4			Computational predictor scores (BayesDel = -0.00674022; Align GVGD Class C0) are below the recommended thresholds (BayesDel < 0.16 and > -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).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PS4_Supporting			This variant has been reported in 2 unrelated probandscsmeeting Revised Chompret criteria and reported in 1 individual under the age of 40 diagnosed with a HER2+ breast cancer. Based on this evidence, this variant scores 1.5 total points meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; Internal lab contributors).

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			In vitro assays performed in yeast and/or human cell lines showed conflicting results with respect to transactivation, growth suppression activity, and/or tetramer formation (PS3/BS3 not met; PMIDs: 12826609, 16007150, 29979965, 30224644).
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			
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
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
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
BA1		✖	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).
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	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
PM6		✖	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
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			In vitro assays performed in yeast and/or human cell lines showed conflicting results with respect to transactivation, growth suppression activity, and/or tetramer formation (PS3/BS3 not met; PMIDs: 12826609, 16007150, 29979965, 30224644).
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
  ▾  ▾		
Showing 1 to 1 of 1 rows		

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.