

Variant: NM_001126112.2(TP53):c.344A>G (p.His115Arg)

Version: 2.0

CA000126 [↗](#)

182925 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: aac8ac5a-a8b7-4651-9186-9267f2bbb3d5

Approved on: 2025/1/16

Published on: 2025/1/16

HGVS expressions

NM_001126112.2:c.344A>G

NM_001126112.2(TP53):c.344A>G (p.His115Arg)

NC_000017.11:g.7676025T>C

CM000679.2:g.7676025T>C

NC_000017.10:g.7579343T>C

CM000679.1:g.7579343T>C

NC_000017.9:g.7520068T>C

NG_017013.2:g.16526A>G

ENST00000503591.2:c.344A>G

ENST00000508793.6:c.344A>G

ENST00000509690.6:c.-21-789A>G

ENST00000514944.6:c.96+357A>G

ENST00000604348.6:c.344A>G

ENST00000269305.9:c.344A>G

ENST00000269305.8:c.344A>G

ENST00000359597.8:c.344A>G

ENST00000413465.6:c.344A>G

ENST00000420246.6:c.344A>G

ENST00000445888.6:c.344A>G

ENST00000455263.6:c.344A>G

ENST00000503591.1:c.344A>G

ENST00000505014.5:n.600A>G

ENST00000508793.5:c.344A>G

ENST00000509690.5:c.-21-789A>G

ENST00000514944.5:c.96+357A>G

ENST00000604348.5:c.344A>G

ENST00000610292.4:c.227A>G

ENST00000610538.4:c.227A>G

ENST00000615910.4:c.340A>G

ENST00000617185.4:c.344A>G

ENST00000619485.4:c.227A>G

ENST00000620739.4:c.227A>G

ENST00000622645.4:c.227A>G

ENST00000635293.1:c.227A>G

NM_000546.5:c.344A>G

NM_001126113.2:c.344A>G

NM_001126114.2:c.344A>G

NM_001126118.1:c.227A>G
NM_001276695.1:c.227A>G
NM_001276696.1:c.227A>G
NM_001276760.1:c.227A>G
NM_001276761.1:c.227A>G
NM_001276695.2:c.227A>G
NM_001276696.2:c.227A>G
NM_001276760.2:c.227A>G
NM_001276761.2:c.227A>G
NM_000546.6:c.344A>G
NM_001126112.3:c.344A>G
NM_001126113.3:c.344A>G
NM_001126114.3:c.344A>G
NM_001126118.2:c.227A>G
NM_001276695.3:c.227A>G
NM_001276696.3:c.227A>G
NM_001276760.3:c.227A>G
NM_001276761.3:c.227A>G

Likely Benign

Met criteria codes 3

PM2_Supporting BS3 BP4

Not Met criteria codes 11

BA1 PS1 PS3 PS4 PP3
PM1 PM5 PM6 BS2 BS1
BS4

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 2.2.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

NM_000546.6(TP53):c.344A>G variant in TP53 is a missense variant predicted to cause substitution of Histidine by Arginine at amino acid 115 (p.His115Arg). This variant has an allele frequency of 0.000003101 (5/1612276 alleles) across gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00003) 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 = 0.0464; 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 Likely Benign for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PM2_Supporting, BS3, BP4. (Bayesian Points: -4; VCEP specifications version 2.2; 1/16/2025).

Met criteria codes

PM2_Supporting  

This variant has an allele frequency of 0.000003101 (5/1612276 alleles) across gnomAD v4.1.0 which is lower than the ClinGen TP53 VCEP threshold (<0.00003) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

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(BS3; PMIDs: 12826609, 29979965, 30224644).
BP4			Computational predictor scores (BayesDel = 0.0464; 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).

Not Met criteria codes

BA1			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
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
PP3			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).
PM5			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			Invitae labs: 1 unaffected woman 60+ GeneDx: 1 unaffected woman 60+ Flossies: 1 case Not enough cases from any one data source to apply
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

Curation History [↗](#)

▾

▾

Showing 1 to 3 of 3 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.