The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001276761.2:c.892C>A

Version: 2.0

CA397832787

1019612 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 94981547-1bc0-489e-8b9a-b5963be2d6de
Approved on: 2025/5/7
Published on: 2025/12/5

HGVS expressions

NM_001276761.2:c.892C>A
NC_000017.11:g.7670700G>T
CM000679.2:g.7670700G>T
NC_000017.10:g.7574018G>T
CM000679.1:g.7574018G>T
NC_000017.9:g.7514743G>T
NG_017013.2:g.21851C>A
ENST00000503591.2:c.1009C>A
ENST00000508793.6:c.1009C>A
ENST00000509690.6:c.613C>A
ENST00000514944.6:c.730C>A
ENST00000604348.6:c.988C>A
ENST00000269305.9:c.1009C>A
ENST00000269305.8:c.1009C>A
ENST00000359597.8:c.993+2835C>A
ENST00000413465.6:c.782+3481C>A
ENST00000420246.6:c.*116C>A
ENST00000445888.6:c.1009C>A
ENST00000455263.6:c.*28C>A
ENST00000504290.5:c.*28C>A
ENST00000504937.5:c.613C>A
ENST00000510385.5:c.*116C>A
ENST00000576024.1:c.54-1010C>A
ENST00000610292.4:c.892C>A
ENST00000610538.4:c.*28C>A
ENST00000610623.4:c.*28C>A
ENST00000615910.4:c.976C>A
ENST00000617185.4:c.*116C>A
ENST00000618944.4:c.*116C>A
ENST00000619186.4:c.532C>A
ENST00000619485.4:c.892C>A
ENST00000620739.4:c.892C>A
ENST00000622645.4:c.*116C>A
ENST00000635293.1:c.892C>A
NM_000546.5:c.1009C>A
NM_001126112.2:c.1009C>A
NM_001126113.2:c.*28C>A

NM_001126114.2:c.*116C>A
NM_001126115.1:c.613C>A
NM_001126116.1:c.*116C>A
NM_001126117.1:c.*28C>A
NM_001126118.1:c.892C>A
NM_001276695.1:c.*28C>A
NM_001276696.1:c.*116C>A
NM_001276697.1:c.532C>A
NM_001276698.1:c.*116C>A
NM_001276699.1:c.*28C>A
NM_001276760.1:c.892C>A
NM_001276761.1:c.892C>A
NM_001276695.2:c.*28C>A
NM_001276696.2:c.*116C>A
NM_001276697.2:c.532C>A
NM_001276698.2:c.*116C>A
NM_001276699.2:c.*28C>A
NM_001276760.2:c.892C>A
NM_000546.6:c.1009C>A
NM_001126112.3:c.1009C>A
NM_001126113.3:c.*28C>A
NM_001126114.3:c.*116C>A
NM_001126115.2:c.613C>A
NM_001126116.2:c.*116C>A
NM_001126117.2:c.*28C>A
NM_001126118.2:c.892C>A
NM_001276695.3:c.*28C>A
NM_001276696.3:c.*116C>A
NM_001276697.3:c.532C>A
NM_001276698.3:c.*116C>A
NM_001276699.3:c.*28C>A
NM_001276760.3:c.892C>A
NM_001276761.3:c.892C>A

Likely Pathogenic

Met criteria codes 6

PS4_Supporting PM1_Supporting BP4 PM5_Supporting PS3 PM2_Supporting

Not Met criteria codes 10

BA1 BS2 BS1 BS4 BS3 PS1 PS2 PP1 PP3 PP4

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 2.3.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6:c.1009C>A variant in TP53 is a missense variant predicted to cause substitution of arginine by serine at amino acid 337 (p.Arg337Ser). This variant has been reported in 2 unrelated probands meeting Revised Chompret criteria. Based on this evidence, this variant scores 1 total point meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; PMIDs, ClinVar SCVs, 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 non-functional transactivation and loss of growth suppression activity indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965). This variant has 4 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). Two missense variants (p.Arg337Pro, p.Arg337Leu) in the same codon have been classified as likely pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP's specifications.(PM5_Supporting). Computational predictor scores (BayesDel = 0.154096; Align GVGD Class C35) 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 Pathogenic for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PS3, BP4, PM1_Supporting, PM2_Supporting, PM5_Supporting, PS4_Supporting. (Bayesian Points: 7; VCEP specifications version 2.3)

Met criteria codes

PS4_Supporting	✔	This variant has been reported in 2 unrelated probands meeting Revised Chompret criteria. Based on this evidence, this variant scores 1 total point meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; PMIDs, ClinVar SCVs, Internal lab contributors).
PM1_Supporting	✔	This variant has 4 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).
BP4	✔	Computational predictor scores (BayesDel = 0.154096; Align GVGD Class C35) 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).
PM5_Supporting	✔	Two missense variants (p.Arg337Pro, p.Arg337Leu) in the same codon have been classified as likely pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP's specifications.(PM5_Supporting).
PS3	✔	In vitro assays performed in yeast and/or human cell lines showed non-functional transactivation and loss of growth suppression activity indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

BA1	✖	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		✖	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
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
PP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 2 of 2 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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.