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_000546.5(TP53):c.779C>A (p.Ser260Tyr)

Version: 2.0

CA10580921

231033 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4cd6d688-6774-41c7-b590-7f3359f7d34c
Approved on: 2025/1/16
Published on: 2025/1/16

HGVS expressions

NM_000546.5:c.779C>A
NM_000546.5(TP53):c.779C>A (p.Ser260Tyr)
NC_000017.11:g.7674184G>T
CM000679.2:g.7674184G>T
NC_000017.10:g.7577502G>T
CM000679.1:g.7577502G>T
NC_000017.9:g.7518227G>T
NG_017013.2:g.18367C>A
ENST00000503591.2:c.779C>A
ENST00000508793.6:c.779C>A
ENST00000509690.6:c.383C>A
ENST00000514944.6:c.500C>A
ENST00000604348.6:c.758C>A
ENST00000269305.9:c.779C>A
ENST00000269305.8:c.779C>A
ENST00000359597.8:c.779C>A
ENST00000413465.6:c.779C>A
ENST00000420246.6:c.779C>A
ENST00000445888.6:c.779C>A
ENST00000455263.6:c.779C>A
ENST00000504290.5:c.383C>A
ENST00000504937.5:c.383C>A
ENST00000509690.5:c.383C>A
ENST00000510385.5:c.383C>A
ENST00000610292.4:c.662C>A
ENST00000610538.4:c.662C>A
ENST00000610623.4:c.302C>A
ENST00000615910.4:c.746C>A
ENST00000617185.4:c.779C>A
ENST00000618944.4:c.302C>A
ENST00000619186.4:c.302C>A
ENST00000619485.4:c.662C>A
ENST00000620739.4:c.662C>A
ENST00000622645.4:c.662C>A
ENST00000635293.1:c.662C>A
NM_001126112.2:c.779C>A
NM_001126113.2:c.779C>A

NM_001126114.2:c.779C>A
NM_001126115.1:c.383C>A
NM_001126116.1:c.383C>A
NM_001126117.1:c.383C>A
NM_001126118.1:c.662C>A
NM_001276695.1:c.662C>A
NM_001276696.1:c.662C>A
NM_001276697.1:c.302C>A
NM_001276698.1:c.302C>A
NM_001276699.1:c.302C>A
NM_001276760.1:c.662C>A
NM_001276761.1:c.662C>A
NM_001276695.2:c.662C>A
NM_001276696.2:c.662C>A
NM_001276697.2:c.302C>A
NM_001276698.2:c.302C>A
NM_001276699.2:c.302C>A
NM_001276760.2:c.662C>A
NM_001276761.2:c.662C>A
NM_000546.6:c.779C>A
NM_001126112.3:c.779C>A
NM_001126113.3:c.779C>A
NM_001126114.3:c.779C>A
NM_001126115.2:c.383C>A
NM_001126116.2:c.383C>A
NM_001126117.2:c.383C>A
NM_001126118.2:c.662C>A
NM_001276695.3:c.662C>A
NM_001276696.3:c.662C>A
NM_001276697.3:c.302C>A
NM_001276698.3:c.302C>A
NM_001276699.3:c.302C>A
NM_001276760.3:c.662C>A
NM_001276761.3:c.662C>A

Likely Benign

Met criteria codes 3

BS2_Supporting BS3 PM2_Supporting

Not Met criteria codes 14

BS1 BS4 BP4 BP2 PS1 PS2 PS3 PS4 PP1 PP3 BA1 PM1 PM5 PM6

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

The NM_000546.6: c.779C>A variant in TP53 is a missense variant predicted to cause substitution of serine by tyrosine at amino acid 260 (p.Ser260Tyr). 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; ClinVar SCV000830817.4, Internal lab contributors). This variant has an allele frequency of 0.000001864 (3/1609760 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). 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: BS2_Supporting, PM2_Supporting, BS3. (Bayesian Points: -4; VCEP specifications version 2.2; 1/16/2025).

Met criteria codes

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; ClinVar SCV000830817.4, Internal lab contributors).
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).
PM2_Supporting	✔	This variant has an allele frequency of 0.000001864 (3/1609760 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).

Not Met criteria codes

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
BP4	✖	Align-GVGD Class C0, BayesDel 0.229798. No splicing effect: varSEAK class 1, SpliceAI acceptor loss 0.0, donor loss 0.0, acceptor gain 0.0, donor gain 0.0
BP2	✖	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
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
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).
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).
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

Curation History

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000546.5(TP53):c.779C>A (p.Ser2...	Likely Benign	Li-Fraumeni Syndrome	2025-01-16	2.0	ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.2.0	TP53
View	NM_000546.5(TP53):c.779C>A (p.Ser2...	Likely Benign	Li-Fraumeni Syndrome 1	2021-09-24	1.0	-	TP53

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.