

Variant: NM_000546.6(TP53):c.379T>C (p.Ser127Pro)

Version: 1.0

CA397843917 [↗](#)

934410 (ClinVar) [↗](#)

Gene: TP53 ([HGNC:7157](#))
Condition: Li-Fraumeni syndrome ([MONDO:0018875](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 130cd553-8ab6-4a2a-8452-d95fd366c6e5
Approved on: 2026/3/4
Published on: 2026/4/22

HGVS expressions

NM_000546.6:c.379T>C
NM_000546.6(TP53):c.379T>C (p.Ser127Pro)
NC_000017.11:g.7675233A>G
CM000679.2:g.7675233A>G
NC_000017.10:g.7578551A>G
CM000679.1:g.7578551A>G
NC_000017.9:g.7519276A>G
NG_017013.2:g.17318T>C
ENST00000503591.2:c.379T>C
ENST00000508793.6:c.379T>C
ENST00000509690.6:c.-18T>C
ENST00000514944.6:c.100T>C
ENST00000604348.6:c.376-18T>C
ENST00000269305.9:c.379T>C
ENST00000269305.8:c.379T>C
ENST00000359597.8:c.379T>C
ENST00000413465.6:c.379T>C
ENST00000420246.6:c.379T>C
ENST00000445888.6:c.379T>C
ENST00000455263.6:c.379T>C
ENST00000503591.1:c.379T>C
ENST00000504290.5:c.-18T>C
ENST00000504937.5:c.-18T>C
ENST00000505014.5:n.635T>C
ENST00000508793.5:c.379T>C
ENST00000509690.5:c.-18T>C
ENST00000510385.5:c.-18T>C
ENST00000514944.5:c.100T>C
ENST00000604348.5:c.376-18T>C
ENST00000610292.4:c.262T>C
ENST00000610538.4:c.262T>C
ENST00000610623.4:c.-99T>C
ENST00000615910.4:c.346T>C
ENST00000617185.4:c.379T>C
ENST00000618944.4:c.-99T>C
ENST00000619186.4:c.-99T>C
ENST00000619485.4:c.262T>C

ENST00000620739.4:c.262T>C
ENST00000622645.4:c.262T>C
ENST00000635293.1:c.262T>C
NM_000546.5:c.379T>C
NM_001126112.2:c.379T>C
NM_001126113.2:c.379T>C
NM_001126114.2:c.379T>C
NM_001126115.1:c.-18T>C
NM_001126116.1:c.-18T>C
NM_001126117.1:c.-18T>C
NM_001126118.1:c.262T>C
NM_001276695.1:c.262T>C
NM_001276696.1:c.262T>C
NM_001276697.1:c.-99T>C
NM_001276698.1:c.-99T>C
NM_001276699.1:c.-99T>C
NM_001276760.1:c.262T>C
NM_001276761.1:c.262T>C
NM_001276695.2:c.262T>C
NM_001276696.2:c.262T>C
NM_001276697.2:c.-99T>C
NM_001276698.2:c.-99T>C
NM_001276699.2:c.-99T>C
NM_001276760.2:c.262T>C
NM_001276761.2:c.262T>C
NM_001126112.3:c.379T>C
NM_001126113.3:c.379T>C
NM_001126114.3:c.379T>C
NM_001126115.2:c.-18T>C
NM_001126116.2:c.-18T>C
NM_001126117.2:c.-18T>C
NM_001126118.2:c.262T>C
NM_001276695.3:c.262T>C
NM_001276696.3:c.262T>C
NM_001276697.3:c.-99T>C
NM_001276698.3:c.-99T>C
NM_001276699.3:c.-99T>C
NM_001276760.3:c.262T>C
NM_001276761.3:c.262T>C

Likely Pathogenic

Met criteria codes 5

- PM1_Supporting
- PP3_Moderate
- PM2_Supporting
- PS3
- PP4

Not Met criteria codes 11

- BS1
- BS4
- BS3
- BS2
- BP4
- PS1
- PS2
- PS4
- BA1
- PP1
- PM5

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(TP53):c.379T>C variant in TP53 is a missense variant predicted to cause substitution of serine by proline at amino acid 127 (p.Ser127Pro). Although this variant has been observed in germline cases, to our knowledge, this variant has not been reported in individuals meeting classical LFS or Chompret criteria (PS4 not met; Internal lab contributors). At least one individual with this variant was found to have a variant allele fraction of 5-35%, which is a significant predictor of variant pathogenicity (PP4, PMID: 34906512, 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 = 0.58628; Align GVGD = Class C65) are above recommended thresholds (BayesDel > 0.16 and an Align GVGD Class of 65), evidence that correlates with impact to TP53 via protein change (PP3_Moderate). 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). 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, PS3, PP3_moderate, PM1_supporting, PM2_supporting. (Bayesian Points: 9; VCEP specifications version 2.4)

Met criteria codes

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).
PP3_Moderate			Computational predictor scores (BayesDel = 0.58628; Align GVGD = Class C65) are above recommended thresholds (BayesDel > 0.16 and an Align GVGD Class of 65), evidence that correlates with impact to TP53 via protein change (PP3_Moderate).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
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).
PP4			At least one individual with this variant was found to have a variant allele fraction of 5-35%, which is a significant predictor of variant pathogenicity (PP4, PMID: 34906512, Internal lab contributor).

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
BS3			

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
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
PS4			Although this variant has been observed in germline cases, to our knowledge, this variant has not been reported in individuals meeting classical LFS or Chompret criteria (PS4 not met; Internal lab contributors).
BA1			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
PM5			Another missense variant (p.Ser127Thr) (ClinVar Variation ID: 824232), with Grantham score equal to or less than the current variant in the same codon has been classified as likely pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP’s specifications. However, this variant does not meet criteria for PM5 code application as it does not have clinical data that counts towards pathogenicity (PM5 not met).

Curation History [↗](#)



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