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_001126112.2(TP53):c.907A>G (p.Ser303Gly)*

Version: 2.0

*CA000491*

*142332 (ClinVar)*

**Gene**: TP53 (HGNC:7157)
**Condition**: Li-Fraumeni syndrome (MONDO:0018875)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 481b1f30-a3cc-4e41-8fac-e657737c7811
**Approved on**: 2025/1/16
**Published on**: 2025/1/16

## *HGVS expressions*

**NM_001126112.2(TP53):c.907A>G (p.Ser303Gly)**
**NM_001126112.2:c.907A>G**
NC_000017.11:g.7673713T>C
CM000679.2:g.7673713T>C
NC_000017.10:g.7577031T>C
CM000679.1:g.7577031T>C
NC_000017.9:g.7517756T>C
NG_017013.2:g.18838A>G
ENST00000503591.2:c.907A>G
ENST00000508793.6:c.907A>G
ENST00000509690.6:c.511A>G
ENST00000514944.6:c.628A>G
ENST00000604348.6:c.886A>G
ENST00000269305.9:c.907A>G
ENST00000269305.8:c.907A>G
ENST00000359597.8:c.907A>G
ENST00000413465.6:c.782+468A>G
ENST00000420246.6:c.907A>G
ENST00000445888.6:c.907A>G
ENST00000455263.6:c.907A>G
ENST00000504290.5:c.511A>G
ENST00000504937.5:c.511A>G
ENST00000509690.5:c.511A>G
ENST00000510385.5:c.511A>G
ENST00000610292.4:c.790A>G
ENST00000610538.4:c.790A>G
ENST00000610623.4:c.430A>G
ENST00000615910.4:c.874A>G
ENST00000617185.4:c.907A>G
ENST00000618944.4:c.430A>G
ENST00000619186.4:c.430A>G
ENST00000619485.4:c.790A>G
ENST00000620739.4:c.790A>G
ENST00000622645.4:c.790A>G
ENST00000635293.1:c.790A>G
NM_000546.5:c.907A>G
NM_001126113.2:c.907A>G

NM_001126114.2:c.907A>G
NM_001126115.1:c.511A>G
NM_001126116.1:c.511A>G
NM_001126117.1:c.511A>G
NM_001126118.1:c.790A>G
NM_001276695.1:c.790A>G
NM_001276696.1:c.790A>G
NM_001276697.1:c.430A>G
NM_001276698.1:c.430A>G
NM_001276699.1:c.430A>G
NM_001276760.1:c.790A>G
NM_001276761.1:c.790A>G
NM_001276695.2:c.790A>G
NM_001276696.2:c.790A>G
NM_001276697.2:c.430A>G
NM_001276698.2:c.430A>G
NM_001276699.2:c.430A>G
NM_001276760.2:c.790A>G
NM_001276761.2:c.790A>G
NM_000546.6:c.907A>G
NM_001126112.3:c.907A>G
NM_001126113.3:c.907A>G
NM_001126114.3:c.907A>G
NM_001126115.2:c.511A>G
NM_001126116.2:c.511A>G
NM_001126117.2:c.511A>G
NM_001126118.2:c.790A>G
NM_001276695.3:c.790A>G
NM_001276696.3:c.790A>G
NM_001276697.3:c.430A>G
NM_001276698.3:c.430A>G
NM_001276699.3:c.430A>G
NM_001276760.3:c.790A>G
NM_001276761.3:c.790A>G

**Likely Benign**

**Met criteria codes** 3

BP4 PM2_Supporting BS3

**Not Met criteria codes** 22

PS1 PS2 PS3 PS4 BP5 BP7
BP3 BP1 BP2 BA1 PP1 PP2
PP3 PP4 PM6 PM1 PM5
PM4 BS1 BS4 PVS1 BS2

## Evidence Links 1

## 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.907A>G variant in TP53 is a missense variant predicted to cause substitution of serine by glycine at amino acid 303 (p.Ser303Gly). This variant has an allele frequency of 0.000002542 (3/1180040 alleles) in the European (non-Finnish) population in gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00004) 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 = -0.0726; Align GVGD Class C0) are below the recommended thresholds (BayesDel ≤ -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_Moderate). 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_Moderate. (Bayesian Points: -5; VCEP specifications version 2.2; 1/16/2025).**

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**Met criteria codes**

| | | |
|---|---|---|
| **BP4** | ✔ | BP4_MODERATE Computational predictor scores (BayesDel = -0.0726; Align GVGD Class C0) are below the recommended thresholds (BayesDel ≤ -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_Moderate). |
| **PM2_Supporting** | ✔ | This variant has an allele frequency of 0.000002542 (3/1180040 alleles) in the European (non-Finnish) population in gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00004) 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). |

No Kotler data for variant **PubMed:29979965**

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**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** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS4** | ✖ | Observed 9+ times across clinical laboratories with no informative cases. |
| **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 |

| | | | |
|---|---|---|---|
| **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 |
| **BA1** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP1** | ℹ | ✖ | Observed 9+ times across clinical laboratories with no informative cases. |
| **PP2** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP3** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP4** | ℹ | ✖ | 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 |
| **PM1** | ℹ | ✖ | 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** | ℹ | ✖ | Two different missense variants (p.Ser303Arg, p.Ser303Asn) in the same codon have been reported (ClinVar Variation ID 1024359, 230695). However, the variants have not yet been curated to determine if they would be classified as pathogenic or likely pathogenic by the ClinGen TP53 VCEP’s specifications (PM5 not evaluated). |
| **PM4** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS1** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS4** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PVS1** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

| | | | |
|---|---|---|---|
| **BS2** | | ✖ | Observed 9+ times across clinical laboratories with no informative cases. |

## Curation History

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| See Report | Preferred Variant Title | Classification | Condition | Published Date | Version | Criteria Specification | Gene |
|---|---|---|---|---|---|---|---|
| View | NM_001126112.2(TP53):c.907A>G (p.S... | 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_001126112.2(TP53):c.907A>G (p.S... | Likely Benign | Li-Fraumeni Syndrome 1 | 2021-06-16 | 1.0 | - | TP53 |

Showing 1 to 2 of 2 rows

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