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_000546.6(TP53):c.784G>A (p.Gly262Ser)

Version: 2.0

CA000416

141228 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8466fc33-68c8-4faa-b8de-23f1b6417e6d
Approved on: 2025/4/3
Published on: 2025/6/23

HGVS expressions

NM_000546.6(TP53):c.784G>A (p.Gly262Ser)
NM_000546.6:c.784G>A
NC_000017.11:g.7673836C>T
CM000679.2:g.7673836C>T
NC_000017.10:g.7577154C>T
CM000679.1:g.7577154C>T
NC_000017.9:g.7517879C>T
NG_017013.2:g.18715G>A
ENST00000503591.2:c.784G>A
ENST00000508793.6:c.784G>A
ENST00000509690.6:c.388G>A
ENST00000514944.6:c.505G>A
ENST00000604348.6:c.763G>A
ENST00000269305.9:c.784G>A
ENST00000269305.8:c.784G>A
ENST00000359597.8:c.784G>A
ENST00000413465.6:c.782+345G>A
ENST00000420246.6:c.784G>A
ENST00000445888.6:c.784G>A
ENST00000455263.6:c.784G>A
ENST00000504290.5:c.388G>A
ENST00000504937.5:c.388G>A
ENST00000509690.5:c.388G>A
ENST00000510385.5:c.388G>A
ENST00000610292.4:c.667G>A
ENST00000610538.4:c.667G>A
ENST00000610623.4:c.307G>A
ENST00000615910.4:c.751G>A
ENST00000617185.4:c.784G>A
ENST00000618944.4:c.307G>A
ENST00000619186.4:c.307G>A
ENST00000619485.4:c.667G>A
ENST00000620739.4:c.667G>A
ENST00000622645.4:c.667G>A
ENST00000635293.1:c.667G>A
NM_000546.5:c.784G>A
NM_001126112.2:c.784G>A

NM_001126113.2:c.784G>A
NM_001126114.2:c.784G>A
NM_001126115.1:c.388G>A
NM_001126116.1:c.388G>A
NM_001126117.1:c.388G>A
NM_001126118.1:c.667G>A
NM_001276695.1:c.667G>A
NM_001276696.1:c.667G>A
NM_001276697.1:c.307G>A
NM_001276698.1:c.307G>A
NM_001276699.1:c.307G>A
NM_001276760.1:c.667G>A
NM_001276761.1:c.667G>A
NM_001276695.2:c.667G>A
NM_001276696.2:c.667G>A
NM_001276697.2:c.307G>A
NM_001276698.2:c.307G>A
NM_001276699.2:c.307G>A
NM_001276760.2:c.667G>A
NM_001276761.2:c.667G>A
NM_001126112.3:c.784G>A
NM_001126113.3:c.784G>A
NM_001126114.3:c.784G>A
NM_001126115.2:c.388G>A
NM_001126116.2:c.388G>A
NM_001126117.2:c.388G>A
NM_001126118.2:c.667G>A
NM_001276695.3:c.667G>A
NM_001276696.3:c.667G>A
NM_001276697.3:c.307G>A
NM_001276698.3:c.307G>A
NM_001276699.3:c.307G>A
NM_001276760.3:c.667G>A
NM_001276761.3:c.667G>A

Likely Benign

Met criteria codes 3

BS2 PM2_Supporting PP3

Not Met criteria codes 14

BS1 BS4 BS3 BP4 BP2
PM1 PM5 PS1 PS2 PS3
PS4 PP1 PP4 BA1

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.784G>A variant in TP53 is a missense variant predicted to cause substitution of glycine by serine at amino acid 262 (p.Gly262Ser). This variant received a total of 0.5 points in one individual (PS4 not met; Internal lab contributors). This variant has been observed in at least 8 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; Internal lab contributor). This variant has an allele frequency of 0.00002358 (38/1611646 alleles) across gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00003) for PM2_Supporting and has a subpopulation allele frequency of <0.00004 in all non-bottleneck populations with 2 or more alleles present (PM2_Supporting). The computational splicing predictor SpliceAI gives a score of 0.52, predicting that the variant has an impact on splicing (score threshold > 0.20) (PP3). 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, PM2_Supporting, PP3. (Bayesian Points: -2; VCEP specifications version 2.2; date of approval)

Met criteria codes

BS2	✔	This variant has been observed in at least 8 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; Internal lab contributor).
PM2_Supporting	✔	This variant has an allele frequency of 0.00002358 (38/1611646 alleles) across gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00003) for PM2_Supporting and has a subpopulation allele frequency of <0.00004 in all non-bottleneck populations with 2 or more alleles present (PM2_Supporting).
PP3	✔	The computational splicing predictor SpliceAI gives a score of 0.52, predicting that the variant has an impact on splicing (score threshold > 0.20) (PP3)

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
BP4	✖	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
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	✖	

3 different missense variants (p.Gly262Asp, p.Gly262Val, p.Gly262Arg) in the same codon have been reported (ClinVar Variation IDs: 2993845, 428889, 1760888). However, these variants do not meet criteria for PM5 code application (PM5 not met).

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	✖	Functional codes not to be used when PP3 is applied for based on SpliceAI
PS4	✖	This variant received a total of 0.5 points in one individual (PS4 not met; Internal lab contributors).
PP1	✖	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
BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000546.6(TP53):c.784G>A (p.Gly2…	Likely Benign	Li-Fraumeni Syndrome	2025-06-23	2.0	ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.3.0	TP53
View	NM_001126112.2(TP53):c.784G>A (p.…	Uncertain Significance	Li-Fraumeni Syndrome	2020-09-04	1.0	-	TP53

Showing 1 to 2 of 2 rows

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