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.1163A>C (p.Glu388Ala)

Version: 2.0

CA000047

141425 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4ef47921-0407-4ece-a6d2-91823363a565
Approved on: Thu, 06 Aug 2026 00:00:00 +0000
Published on: Tue, 22 Sep 2026 00:00:00 +0000

HGVS expressions

NM_000546.5:c.1163A>C
NM_000546.5(TP53):c.1163A>C (p.Glu388Ala)
NC_000017.11:g.7669628T>G
CM000679.2:g.7669628T>G
NC_000017.10:g.7572946T>G
CM000679.1:g.7572946T>G
NC_000017.9:g.7513671T>G
NG_017013.2:g.22923A>C
ENST00000503591.2:c.1163A>C
ENST00000508793.6:c.1163A>C
ENST00000509690.6:c.767A>C
ENST00000514944.6:c.884A>C
ENST00000604348.6:c.1142A>C
ENST00000269305.9:c.1163A>C
ENST00000269305.8:c.1163A>C
ENST00000359597.8:c.994-3384A>C
ENST00000413465.6:c.782+4553A>C
ENST00000420246.6:c.*270A>C
ENST00000445888.6:c.1163A>C
ENST00000455263.6:c.*182A>C
ENST00000504290.5:c.*182A>C
ENST00000504937.5:c.767A>C
ENST00000510385.5:c.*270A>C
ENST00000576024.1:c.116A>C
ENST00000610292.4:c.1046A>C
ENST00000610538.4:c.*182A>C
ENST00000610623.4:c.*182A>C
ENST00000615910.4:c.1130A>C
ENST00000617185.4:c.*270A>C
ENST00000618944.4:c.*270A>C
ENST00000619186.4:c.686A>C
ENST00000619485.4:c.1046A>C
ENST00000620739.4:c.1046A>C
ENST00000622645.4:c.*270A>C
ENST00000635293.1:c.983+981A>C
NM_001126112.2:c.1163A>C
NM_001126113.2:c.*182A>C

NM_001126114.2:c.*270A>C
NM_001126115.1:c.767A>C
NM_001126116.1:c.*270A>C
NM_001126117.1:c.*182A>C
NM_001126118.1:c.1046A>C
NM_001276695.1:c.*182A>C
NM_001276696.1:c.*270A>C
NM_001276697.1:c.686A>C
NM_001276698.1:c.*270A>C
NM_001276699.1:c.*182A>C
NM_001276760.1:c.1046A>C
NM_001276761.1:c.1046A>C
NM_001276695.2:c.*182A>C
NM_001276696.2:c.*270A>C
NM_001276697.2:c.686A>C
NM_001276698.2:c.*270A>C
NM_001276699.2:c.*182A>C
NM_001276760.2:c.1046A>C
NM_001276761.2:c.1046A>C
NM_000546.6:c.1163A>C
NM_001126112.3:c.1163A>C
NM_001126113.3:c.*182A>C
NM_001126114.3:c.*270A>C
NM_001126115.2:c.767A>C
NM_001126116.2:c.*270A>C
NM_001126117.2:c.*182A>C
NM_001126118.2:c.1046A>C
NM_001276695.3:c.*182A>C
NM_001276696.3:c.*270A>C
NM_001276697.3:c.686A>C
NM_001276698.3:c.*270A>C
NM_001276699.3:c.*182A>C
NM_001276760.3:c.1046A>C
NM_001276761.3:c.1046A>C

Benign

Met criteria codes 4

BP4 BS2 PM2_Supporting BS3

Not Met criteria codes 19

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

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

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6: c.1163A>C variant in TP53 is a missense variant predicted to cause substitution of glutamic acid by alanine at amino acid 388 (p.Glu388Ala). This variant has been observed in 4-7 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_Moderate; Internal lab contributors). This variant has an allele frequency of 0.000008054 (13/1614128 alleles) across gnomAD v4.1.1 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). In vitro assays performed in yeast and/or human cell lines showed functional transactivation and retained growth suppression activity by the majority of available assays indicating that this variant does not impact protein function (BS3; PMIDs: 12826609, 30224644). Computational predictor scores (BayesDel = -0.0336; Align GVGD Class 0) 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). 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). In summary, this variant meets the criteria to be classified as Benign for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: BS2_Moderate, PM2_Supporting, BS3, BP4_Moderate. (Bayesian Points: -7; VCEP specifications version 2.4).

Met criteria codes

BP4	✔	BP4_MODERATE Computational predictor scores (BayesDel = -0.0336; Align GVGD Class 0) 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).
BS2	✔	BS2_MODERATE This variant has been observed in 4-7 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_Moderate; Internal lab contributors).
PM2_Supporting	✔	This variant has an allele frequency of 0.000008054 (13/1614128 alleles) across gnomAD v4.1.1 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).
BS3	✔	In vitro assays performed in yeast and/or human cell lines showed functional transactivation and retained growth suppression activity by the majority of available assays indicating that this variant does not impact protein function (BS3; PMIDs: 12826609, 30224644).

Not Met criteria codes

PS1	✖	The current variant is the only variant found in this codon in ClinVar.
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

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	✖	The current variant is the only variant found in this codon in ClinVar.
PM4		✖	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
BA1	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
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
BP7	ℹ	✖	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	✖	Li et al. 2016 (PMID: 26534844): Figure 1, family 71, 2 individuals with a personal history of BC (no LFS criteria or Chompret), in 4 unaffected individuals, and absent in 1 individual with a personal history of BC
PP1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000546.5(TP53):c.1163A>C (p.Glu...	Benign	Li-Fraumeni Syndrome	2026-09-22	2.0	ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.4	TP53
View	NM_000546.5(TP53):c.1163A>C (p.Glu...	Likely Benign	Li-Fraumeni Syndrome	2022-01-10	1.2	-	TP53
View	NM_000546.5(TP53):c.1163A>C (p.Glu...	Likely Benign	Li-Fraumeni Syndrome	2020-08-24	1.1	-	TP53
View	NM_000546.5(TP53):c.1163A>C (p.Glu...	Likely Benign	Li-Fraumeni Syndrome	2020-08-14	1.0	-	TP53

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