

Variant: NM_000546.6(TP53):c.414C>T (p.Ala138=)

Version: 1.0

CA497925710 [↗](#)

482234 (ClinVar) [↗](#)

Gene: TP53 ([HGNC:7157](#))
Condition: Li-Fraumeni syndrome ([MONDO:0018875](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 0fbddfff-af44-44e7-8fc8-ba584e35fc96
Approved on: 2025/6/5
Published on: 2025/7/18

HGVS expressions

NM_000546.6:c.414C>T
NM_000546.6(TP53):c.414C>T (p.Ala138=)
NC_000017.11:g.7675198G>A
CM000679.2:g.7675198G>A
NC_000017.10:g.7578516G>A
CM000679.1:g.7578516G>A
NC_000017.9:g.7519241G>A
NG_017013.2:g.17353C>T
ENST00000503591.2:c.414C>T
ENST00000508793.6:c.414C>T
ENST00000509690.6:c.18C>T
ENST00000514944.6:c.135C>T
ENST00000604348.6:c.393C>T
ENST00000269305.9:c.414C>T
ENST00000269305.8:c.414C>T
ENST00000359597.8:c.414C>T
ENST00000413465.6:c.414C>T
ENST00000420246.6:c.414C>T
ENST00000445888.6:c.414C>T
ENST00000455263.6:c.414C>T
ENST00000504290.5:c.18C>T
ENST00000504937.5:c.18C>T
ENST00000505014.5:n.670C>T
ENST00000508793.5:c.414C>T
ENST00000509690.5:c.18C>T
ENST00000510385.5:c.18C>T
ENST00000514944.5:c.135C>T
ENST00000604348.5:c.393C>T
ENST00000610292.4:c.297C>T
ENST00000610538.4:c.297C>T
ENST00000610623.4:c.-64C>T
ENST00000615910.4:c.381C>T
ENST00000617185.4:c.414C>T
ENST00000618944.4:c.-64C>T
ENST00000619186.4:c.-64C>T
ENST00000619485.4:c.297C>T
ENST00000620739.4:c.297C>T

ENST00000622645.4:c.297C>T
ENST00000635293.1:c.297C>T
NM_000546.5:c.414C>T
NM_001126112.2:c.414C>T
NM_001126113.2:c.414C>T
NM_001126114.2:c.414C>T
NM_001126115.1:c.18C>T
NM_001126116.1:c.18C>T
NM_001126117.1:c.18C>T
NM_001126118.1:c.297C>T
NM_001276695.1:c.297C>T
NM_001276696.1:c.297C>T
NM_001276697.1:c.-64C>T
NM_001276698.1:c.-64C>T
NM_001276699.1:c.-64C>T
NM_001276760.1:c.297C>T
NM_001276761.1:c.297C>T
NM_001276695.2:c.297C>T
NM_001276696.2:c.297C>T
NM_001276697.2:c.-64C>T
NM_001276698.2:c.-64C>T
NM_001276699.2:c.-64C>T
NM_001276760.2:c.297C>T
NM_001276761.2:c.297C>T
NM_001126112.3:c.414C>T
NM_001126113.3:c.414C>T
NM_001126114.3:c.414C>T
NM_001126115.2:c.18C>T
NM_001126116.2:c.18C>T
NM_001126117.2:c.18C>T
NM_001126118.2:c.297C>T
NM_001276695.3:c.297C>T
NM_001276696.3:c.297C>T
NM_001276697.3:c.-64C>T
NM_001276698.3:c.-64C>T
NM_001276699.3:c.-64C>T
NM_001276760.3:c.297C>T
NM_001276761.3:c.297C>T

Likely Benign

Met criteria codes 3

PM2_Supporting BP4 BP7

Not Met criteria codes 21

BA1 PS2 PS3 PS4 PP1 PP2
PP3 PP4 PM1 PM3 PM4
PM6 BS2 BS1 BS4 BS3
BP3 BP1 BP2 PVS1 BP5

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

TP53 VCEP

The c.414C>T (p.Ala138=) variant is a synonymous (silent) variant outside of the core splice motif, and BP4 code is met for splicing prediction (BP4, BP7). To our knowledge, this variant has not been reported in individuals meeting classical LFS or Chompret criteria (PS4 not met). This variant has an allele frequency of 6.195e-7 (1/1614158 alleles) across gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00003) for PM2_Supporting and has no more than one allele per non-bottleneck subpopulation (PM2_Supporting). To our knowledge, functional assays have not been reported for this variant (PS3/BS3 not met). The computational splicing predictor SpliceAI gives a score of [0.01], predicting that the variant has no impact on splicing (score threshold ≤ 0.10) (BP4). 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: BP4, BP7, PM2_Supporting. (Bayesian Points: -1; VCEP specifications version 2.3)

Met criteria codes

PM2_Supporting			This variant has an allele frequency of 6.195e-7 (1/1614158 alleles) across gnomAD v4.1.0 which is lower than the Clingen TP53 VCEP threshold (<0.00003) for PM2_Supporting and has no more than one allele per non-bottleneck subpopulation (PM2_Supporting).
BP4			The computational splicing predictor SpliceAI gives a score of [0.01], predicting that the variant has no impact on splicing (score threshold ≤ 0.10) (BP4).
BP7			The c.414C>T (p.Ala138=) variant is a synonymous (silent) variant outside of the core splice motif, and BP4 code is met for splicing prediction (BP4, BP7).

Not Met criteria codes

BA1			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
PP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PP3			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
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).
PM3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
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
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 



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