

Variant: NM_000546.5(TP53):c.214C>G (p.Pro72Ala)

Version: 2.0

CA000070 [↗](#)

142854 (ClinVar) [↗](#)

Gene: TP53 ([HGNC:7157](#))
Condition: Li-Fraumeni syndrome ([MONDO:0018875](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 3a7347e6-77f5-4cc5-a6d2-555e45cc238b
Approved on: 2025/2/6
Published on: 2025/2/7

HGVS expressions

NM_000546.5:c.214C>G
NM_000546.5(TP53):c.214C>G (p.Pro72Ala)
NC_000017.11:g.7676155G>C
CM000679.2:g.7676155G>C
NC_000017.10:g.7579473G>C
CM000679.1:g.7579473G>C
NC_000017.9:g.7520198G>C
NG_017013.2:g.16396C>G
ENST00000503591.2:c.214C>G
ENST00000508793.6:c.214C>G
ENST00000509690.6:c.-21-919C>G
ENST00000514944.6:c.96+227C>G
ENST00000604348.6:c.214C>G
ENST00000269305.9:c.214C>G
ENST00000269305.8:c.214C>G
ENST00000359597.8:c.214C>G
ENST00000413465.6:c.214C>G
ENST00000420246.6:c.214C>G
ENST00000445888.6:c.214C>G
ENST00000455263.6:c.214C>G
ENST00000503591.1:c.214C>G
ENST00000505014.5:n.470C>G
ENST00000508793.5:c.214C>G
ENST00000509690.5:c.-21-919C>G
ENST00000514944.5:c.96+227C>G
ENST00000604348.5:c.214C>G
ENST00000610292.4:c.97C>G
ENST00000610538.4:c.97C>G
ENST00000615910.4:c.214C>G
ENST00000617185.4:c.214C>G
ENST00000619485.4:c.97C>G
ENST00000620739.4:c.97C>G
ENST00000622645.4:c.97C>G
ENST00000635293.1:c.97C>G
NM_001126112.2:c.214C>G
NM_001126113.2:c.214C>G
NM_001126114.2:c.214C>G

NM_001126118.1:c.97C>G
NM_001276695.1:c.97C>G
NM_001276696.1:c.97C>G
NM_001276760.1:c.97C>G
NM_001276761.1:c.97C>G
NM_001276695.2:c.97C>G
NM_001276696.2:c.97C>G
NM_001276760.2:c.97C>G
NM_001276761.2:c.97C>G
NM_000546.6:c.214C>G
NM_001126112.3:c.214C>G
NM_001126113.3:c.214C>G
NM_001126114.3:c.214C>G
NM_001126118.2:c.97C>G
NM_001276695.3:c.97C>G
NM_001276696.3:c.97C>G
NM_001276760.3:c.97C>G
NM_001276761.3:c.97C>G

Likely Benign

Met criteria codes 2

BS2 BP4

Not Met criteria codes 19

BA1 BS1 BS4 BS3 BP1 BP2
PS1 PS2 PS3 PS4 PP1 PP2
PP3 PP4 PM1 PM3 PM5
PM6 PM2

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 2.2.0
- Criteria Specification Approval History
- Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6: c.214C>G variant in TP53 is a missense variant predicted to cause substitution of proline by alanine at amino acid 72 (p.Pro72Ala). This is a polymorphic residue (alternate nomenclature: p.Arg72). This variant received a total of 0.5 points in one individual. (PS4 not met; Internal lab contributors). 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 contributor). In vitro assays performed in yeast and/or human cell lines showed conflicting results with respect to transactivation, growth suppression activity, and/or tetramer formation (PS3/BS3 not met; PMIDs: 12826609, 30224644). Computational predictor scores (BayesDel = -0.215412; Align GVGD Class C0) are below the recommended thresholds (BayesDel < 0.16 and > -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: BS2_Moderate, BP4_Moderate. (Bayesian Points: -4; VCEP specifications version 2.2; 2/6/2025)

Met criteria codes

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 contributor).
BP4			BP4_MODERATE Computational predictor scores (BayesDel = -0.215412; Align GVGD Class C0) are below the recommended thresholds (BayesDel < 0.16 and > -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).
Not Met criteria codes			
BA1			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			In vitro assays performed in yeast and/or human cell lines showed conflicting results with respect to transactivation, growth suppression activity, and/or tetramer formation (PS3/BS3 not met; PMIDs: 12826609, 30224644)
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
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			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
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
PM5			10 different missense variants in the same codon have been reported (ClinVar Variation IDs: 2176025, 232750, 485023, 12351, 182953, 185120, 1786573, 3328172, 237944, 864652) although all are B/LB/VUS and none are suspicious for pathogenicity (PM5 not met).
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			The highest population minor allele frequency in gnomAD v4.1.0 is 0.0001337 (6/44892 alleles) in the East Asian population (PM2, BS1, and BA1 are not met).

Curation History



Showing 1 to 2 of 2 rows

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