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Variant: NM_000546.6(TP53):c.328C>G (p.Arg110Gly)

Version: 1.0

CA397844579

823452 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 25368fd9-d67d-4cc1-a726-ed149aced67e
Approved on: 2025/6/5
Published on: 2025/7/18

HGVS expressions

NM_000546.6(TP53):c.328C>G (p.Arg110Gly)
NM_000546.6:c.328C>G
NC_000017.11:g.7676041G>C
CM000679.2:g.7676041G>C
NC_000017.10:g.7579359G>C
CM000679.1:g.7579359G>C
NC_000017.9:g.7520084G>C
NG_017013.2:g.16510C>G
ENST00000503591.2:c.328C>G
ENST00000508793.6:c.328C>G
ENST00000509690.6:c.-21-805C>G
ENST00000514944.6:c.96+341C>G
ENST00000604348.6:c.328C>G
ENST00000269305.9:c.328C>G
ENST00000269305.8:c.328C>G
ENST00000359597.8:c.328C>G
ENST00000413465.6:c.328C>G
ENST00000420246.6:c.328C>G
ENST00000445888.6:c.328C>G
ENST00000455263.6:c.328C>G
ENST00000503591.1:c.328C>G
ENST00000505014.5:n.584C>G
ENST00000508793.5:c.328C>G
ENST00000509690.5:c.-21-805C>G
ENST00000514944.5:c.96+341C>G
ENST00000604348.5:c.328C>G
ENST00000610292.4:c.211C>G
ENST00000610538.4:c.211C>G
ENST00000615910.4:c.328C>G
ENST00000617185.4:c.328C>G
ENST00000619485.4:c.211C>G
ENST00000620739.4:c.211C>G
ENST00000622645.4:c.211C>G
ENST00000635293.1:c.211C>G
NM_000546.5:c.328C>G
NM_001126112.2:c.328C>G
NM_001126113.2:c.328C>G

NM_001126114.2:c.328C>G
NM_001126118.1:c.211C>G
NM_001276695.1:c.211C>G
NM_001276696.1:c.211C>G
NM_001276760.1:c.211C>G
NM_001276761.1:c.211C>G
NM_001276695.2:c.211C>G
NM_001276696.2:c.211C>G
NM_001276760.2:c.211C>G
NM_001276761.2:c.211C>G
NM_001126112.3:c.328C>G
NM_001126113.3:c.328C>G
NM_001126114.3:c.328C>G
NM_001126118.2:c.211C>G
NM_001276695.3:c.211C>G
NM_001276696.3:c.211C>G
NM_001276760.3:c.211C>G
NM_001276761.3:c.211C>G

Likely Pathogenic

Met criteria codes 4

BP4 PS3 PM2 PM5_Strong

Not Met criteria codes 9

BP2 BA1 PS4 PP1 PP3 PP4 PM1 BS2 BS1

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.328C>G variant in TP53 is a missense variant predicted to cause substitution of arginine by glycine at amino acid 110 (p.Arg110Gly). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). Although this variant has been observed in germline cases, to our knowledge, this variant has not been reported in individuals meeting classical LFS or Chompret criteria (PS4 not met; Internal lab contributors). In vitro assays performed in yeast and/or human cell lines showed non-functional transactivation and loss of growth suppression activity indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965). 2 different missense variants (p.Arg110Leu, p.Arg110Pro) (ClinVar Variation IDs: 406597, 233627), in the same codon have been classified as pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP's specifications. (PM5_Strong). Computational predictor scores (BayesDel = 0.056; Align GVGD Class C15) 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). In summary, this variant meets the criteria to be classified as Likely Pathogenic for Li Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PM2_Supporting, PS3, PM5_Strong, BP4. (Bayesian Points: 8; VCEP specifications version 2.3)

Met criteria codes

BP4	ℹ	✔	Computational predictor scores (BayesDel = 0.056; Align GVGD Class C15) 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).
PS3	ℹ	✔	In vitro assays performed in yeast and/or human cell lines showed non-functional transactivation and loss of growth suppression activity indicating that this variant impacts protein function (PS3; PMIDs: 12826609, 30224644, 29979965).
PM2		✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PM5_Strong	ℹ	✔	2 different missense variants (p.Arg110Leu, p.Arg110Pro) (ClinVar Variation IDs: 406597, 233627), in the same codon have been classified as pathogenic for Li-Fraumeni syndrome by the ClinGen TP53 VCEP's specifications. (PM5_Strong).

Not Met criteria codes

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
PS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	ℹ	✖	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
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).
BS2	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

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.328C>G (p.Arg1...	Likely Pathogenic	Li-Fraumeni Syndrome	2025-07-18	1.0	ClinGen TP53 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TP53 Version 2.3.0	TP53

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