

Variant: NM_000546.5(TP53):c.372C>A (p.Cys124Ter)

Version: 1.1

CA397844214 [↗](#)

458537 (ClinVar) [↗](#)

Gene: TP53 ([HGNC:7157](#))

Condition: Li-Fraumeni syndrome ([MONDO:0018875](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: a9d7558a-f941-4cec-95c8-682dafc6ca40

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HGVS expressions

NM_000546.5:c.372C>A

NM_000546.5(TP53):c.372C>A (p.Cys124Ter)

NC_000017.11:g.7675997G>T

CM000679.2:g.7675997G>T

NC_000017.10:g.7579315G>T

CM000679.1:g.7579315G>T

NC_000017.9:g.7520040G>T

NG_017013.2:g.16554C>A

ENST00000503591.2:c.372C>A

ENST00000508793.6:c.372C>A

ENST00000509690.6:c.-21-761C>A

ENST00000514944.6:c.96+385C>A

ENST00000604348.6:c.372C>A

ENST00000269305.9:c.372C>A

ENST00000269305.8:c.372C>A

ENST00000359597.8:c.372C>A

ENST00000413465.6:c.372C>A

ENST00000420246.6:c.372C>A

ENST00000445888.6:c.372C>A

ENST00000455263.6:c.372C>A

ENST00000503591.1:c.372C>A

ENST00000505014.5:n.628C>A

ENST00000508793.5:c.372C>A

ENST00000509690.5:c.-21-761C>A

ENST00000514944.5:c.96+385C>A

ENST00000604348.5:c.372C>A

ENST00000610292.4:c.255C>A

ENST00000610538.4:c.255C>A

ENST00000615910.4:c.340+28C>A

ENST00000617185.4:c.372C>A

ENST00000619485.4:c.255C>A

ENST00000620739.4:c.255C>A

ENST00000622645.4:c.255C>A

ENST00000635293.1:c.255C>A

NM_001126112.2:c.372C>A

NM_001126113.2:c.372C>A

NM_001126114.2:c.372C>A

NM_001126118.1:c.255C>A
NM_001276695.1:c.255C>A
NM_001276696.1:c.255C>A
NM_001276760.1:c.255C>A
NM_001276761.1:c.255C>A
NM_001276695.2:c.255C>A
NM_001276696.2:c.255C>A
NM_001276760.2:c.255C>A
NM_001276761.2:c.255C>A
NM_000546.6:c.372C>A
NM_001126112.3:c.372C>A
NM_001126113.3:c.372C>A
NM_001126114.3:c.372C>A
NM_001126118.2:c.255C>A
NM_001276695.3:c.255C>A
NM_001276696.3:c.255C>A
NM_001276760.3:c.255C>A
NM_001276761.3:c.255C>A

Pathogenic

Met criteria codes 3

PVS1 PS2 PM2_Supporting

Not Met criteria codes 6

PM1 PM6 BS3 PS3 PS4
PP4

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 2.0.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The NM_000546.6 c.372C>A (p.Cys124Ter) is a TP53 nonsense variant upstream of p.Lys351. The variant is predicted to undergo nonsense-mediated decay (PVS1; PMID: 22233476). This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 2 individuals with LFS-associated cancers totaling 4 phenotype points (PS2; PMID: 22233476, 32658383). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as pathogenic for Li Fraumeni Syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PVS1, PS2, PM2_Supporting. (Bayesian Points: 13; VCEP specifications version 2.0; 7/24/2024).

Met criteria codes

PVS1



The NM_000546.6 c.372C>A (p.Cys124Ter) is a TP53 nonsense variant upstream of p.Lys351. The variant is predicted to undergo nonsense-mediated decay (PVS1; PMID: 22233476).

PS2



This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 2 individual(s) with an LFS-associated cancer totaling 4 phenotype points (PS2; PMID: 22233476, 32658383).

PM2_Supporting  

This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PM1			This variant does not reside within a region of TP53 that is defined as a mutational hotspot or critical functional domain by the ClinGen TP53 VCEP (PM1 not met).
PM6			This evidence code is not currently applicable for TP53 VCEP curations.
BS3			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 1 point across 2 unrelated probands. However, PS4 cannot be applied because individuals are counted towards de novo code PS2. (PS4 not met; PMIDs: 22233476, 32658383).
PP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



 

 

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