

Variant: NM_000546.5(TP53):c.814G>A (p.Val272Met)

Version: 1.1

CA000427 [↗](#)

185814 (ClinVar) [↗](#)

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

Condition: Li-Fraumeni syndrome 1 ([MONDO:0007903](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: f3006a48-5b31-4ef1-8f3d-575a86c78f1b

Approved on: 2022/3/18

Published on: 2022/3/18

HGVS expressions

NM_000546.5(TP53):c.814G>A (p.Val272Met)

NM_000546.5:c.814G>A

NC_000017.11:g.7673806C>T

CM000679.2:g.7673806C>T

NC_000017.10:g.7577124C>T

CM000679.1:g.7577124C>T

NC_000017.9:g.7517849C>T

NG_017013.2:g.18745G>A

ENST00000503591.2:c.814G>A

ENST00000508793.6:c.814G>A

ENST00000509690.6:c.418G>A

ENST00000514944.6:c.535G>A

ENST00000604348.6:c.793G>A

ENST00000269305.9:c.814G>A

ENST00000269305.8:c.814G>A

ENST00000359597.8:c.814G>A

ENST00000413465.6:c.782+375G>A

ENST00000420246.6:c.814G>A

ENST00000445888.6:c.814G>A

ENST00000455263.6:c.814G>A

ENST00000504290.5:c.418G>A

ENST00000504937.5:c.418G>A

ENST00000509690.5:c.418G>A

ENST00000510385.5:c.418G>A

ENST00000610292.4:c.697G>A

ENST00000610538.4:c.697G>A

ENST00000610623.4:c.337G>A

ENST00000615910.4:c.781G>A

ENST00000617185.4:c.814G>A

ENST00000618944.4:c.337G>A

ENST00000619186.4:c.337G>A

ENST00000619485.4:c.697G>A

ENST00000620739.4:c.697G>A

ENST00000622645.4:c.697G>A

ENST00000635293.1:c.697G>A

NM_001126112.2:c.814G>A

NM_001126113.2:c.814G>A

NM_001126114.2:c.814G>A
NM_001126115.1:c.418G>A
NM_001126116.1:c.418G>A
NM_001126117.1:c.418G>A
NM_001126118.1:c.697G>A
NM_001276695.1:c.697G>A
NM_001276696.1:c.697G>A
NM_001276697.1:c.337G>A
NM_001276698.1:c.337G>A
NM_001276699.1:c.337G>A
NM_001276760.1:c.697G>A
NM_001276761.1:c.697G>A
NM_001276695.2:c.697G>A
NM_001276696.2:c.697G>A
NM_001276697.2:c.337G>A
NM_001276698.2:c.337G>A
NM_001276699.2:c.337G>A
NM_001276760.2:c.697G>A
NM_001276761.2:c.697G>A
NM_000546.6:c.814G>A
NM_001126112.3:c.814G>A
NM_001126113.3:c.814G>A
NM_001126114.3:c.814G>A
NM_001126115.2:c.418G>A
NM_001126116.2:c.418G>A
NM_001126117.2:c.418G>A
NM_001126118.2:c.697G>A
NM_001276695.3:c.697G>A
NM_001276696.3:c.697G>A
NM_001276697.3:c.337G>A
NM_001276698.3:c.337G>A
NM_001276699.3:c.337G>A
NM_001276760.3:c.697G>A
NM_001276761.3:c.697G>A

Pathogenic

Met criteria codes 4

- PS4_Moderate
- PM6_Strong
- PS3
- PM1

Not Met criteria codes 9

- PS1
- BP4
- PP3
- BA1
- PM5
- PM2
- BS2
- BS1
- BS3

Evidence Links 0

Expert Panel

TP53 VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

This variant has >10 observations as a somatic hotspot variant in tumors (PM1; cancerhotspots.org v(2)). Transactivation assays show a low functioning allele according to Kato, et al. and there is evidence of a dominant negative effect and loss of function according to Giacomelli, et al. (PS3; PMID: 12826609, 30224644). This variant has been reported in 4 probands meeting Chompret criteria (PS4_Moderate; PMID: 25584008, 23175693, IARC, NIH). There are de novo observations in 2 probands with childhood rhabdomyosarcoma, osteosarcoma, without parental confirmation (PM6_Strong; PMID: IARC, NIH). In summary, TP53 c.814G>A (p.Val272Met) meets criteria to be classified as pathogenic for Li-Fraumeni syndrome. ACMG/AMP criteria applied, as specified by the TP53 Variant Curation Expert Panel: PM1, PS3, PS4_Moderate, PM6_Strong.

Met criteria codes

PS4_Moderate			2 phenotype points; 1 case of Chompret from NIH cohort, 1 case of Chompret from IARC, 2 cases of Chompret from literature (PMID: 25584008, 23175693)
PM6_Strong			2 de novo points (Strong) for highest-weighted cancers in probands (NIH cohort and IARC)
PS3			Kato non-functional; Kotler LOF; Giacomelli DNE and LOF
PM1			Yes, 34/66 samples on cancerhotspots.com

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			aGVGD = C15; BayesDel = 0.5009
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			V272A (ClinVar: 565884, 1x VUS); V272E (ClinVar: 376673, LP somatic only); V272G (ClinVar: 233323, 1x VUS); V272L (1) (ClinVar: 574679, 1x VUS); V272L (2) (ClinVar: 12358, 1x LP); None evaluated by VCEP
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			Absent from FLOSSIES. Internal cases in 60+ women are at low VAF and suspicious for CHIP
BS1			1 allele in European non-Finnish in gnomAD (non-cancer) (AF = 0.000009756)
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History ↗	
Showing 1 to 2 of 2 rows	

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.