

Variant: NM_000546.5(TP53):c.993+1delG

Version: 2.1

CA645369685 [↗](#)

428898 (ClinVar) [↗](#)

Gene: TP53 ([HGNC:7157](#))
Condition: Li-Fraumeni syndrome ([MONDO:0018875](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: a608c703-2232-4c79-86dd-00844776434d
Approved on: 2025/6/24
Published on: 2025/6/24

HGVS expressions

NM_000546.5(TP53):c.993+1delG
NM_000546.5:c.993+1delG
NC_000017.11:g.7673535del
CM000679.2:g.7673535del
NC_000017.10:g.7576853del
CM000679.1:g.7576853del
NC_000017.9:g.7517578del
NG_017013.2:g.19017del
ENST00000503591.2:c.993+1del
ENST00000508793.6:c.993+1del
ENST00000509690.6:c.597+1del
ENST00000514944.6:c.714+1del
ENST00000604348.6:c.972+1del
ENST00000269305.9:c.993+1del
ENST00000269305.8:c.993+1del
ENST00000359597.8:c.993+1del
ENST00000413465.6:c.782+647del
ENST00000420246.6:c.993+1del
ENST00000445888.6:c.993+1del
ENST00000455263.6:c.993+1del
ENST00000504290.5:c.597+1del
ENST00000504937.5:c.597+1del
ENST00000510385.5:c.597+1del
ENST00000576024.1:c.53+1del
ENST00000610292.4:c.876+1del
ENST00000610538.4:c.876+1del
ENST00000610623.4:c.516+1del
ENST00000615910.4:c.960+1del
ENST00000617185.4:c.993+1del
ENST00000618944.4:c.516+1del
ENST00000619186.4:c.516+1del
ENST00000619485.4:c.876+1del
ENST00000620739.4:c.876+1del
ENST00000622645.4:c.876+1del
ENST00000635293.1:c.876+1del
NM_000546.5:c.993+1del
NM_001126112.2:c.993+1del

NM_001126113.2:c.993+1del
NM_001126114.2:c.993+1del
NM_001126115.1:c.597+1del
NM_001126116.1:c.597+1del
NM_001126117.1:c.597+1del
NM_001126118.1:c.876+1del
NM_001276695.1:c.876+1del
NM_001276696.1:c.876+1del
NM_001276697.1:c.516+1del
NM_001276698.1:c.516+1del
NM_001276699.1:c.516+1del
NM_001276760.1:c.876+1del
NM_001276761.1:c.876+1del
NM_001276695.2:c.876+1del
NM_001276696.2:c.876+1del
NM_001276697.2:c.516+1del
NM_001276698.2:c.516+1del
NM_001276699.2:c.516+1del
NM_001276760.2:c.876+1del
NM_001276761.2:c.876+1del
NM_000546.6:c.993+1del
NM_001126112.3:c.993+1del
NM_001126113.3:c.993+1del
NM_001126114.3:c.993+1del
NM_001126115.2:c.597+1del
NM_001126116.2:c.597+1del
NM_001126117.2:c.597+1del
NM_001126118.2:c.876+1del
NM_001276695.3:c.876+1del
NM_001276696.3:c.876+1del
NM_001276697.3:c.516+1del
NM_001276698.3:c.516+1del
NM_001276699.3:c.516+1del
NM_001276760.3:c.876+1del
NM_001276761.3:c.876+1del

Likely Pathogenic

Met criteria codes 4

- PS4_Supporting
- PVS1_Strong
- PP1
- PM2_Supporting

Not Met criteria codes 20

- PM1
- PM3
- PM5
- PM4
- PM6
- BS2
- BS1
- BS4
- BS3
- PS1
- PS2
- PS3
- BP5
- BP7
- BP4
- BP3
- BP2
- BA1
- PP3
- 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](#)

TP53 VCEP

The NM_000546.6:c.993+1del is a deletion of a single G nucleotide within the canonical donor site of exon 9 of TP53. Through exon 9 skipping, the variant is observed in an RT-PCR assay to produce multiple aberrant transcripts encoding frameshift alterations predicted to induce nonsense-mediated decay. Since the assay does not fully account for leakiness, code weight downgraded to Strong (PVS1_Strong (RNA); PMID: 10980596). This variant has been reported in 1 proband meeting Classic LFS criteria. Based on this evidence, this variant scores 1 total points meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; PMID: 10980596). This variant has been reported to segregate with LFS-associated cancers in 3-4 meioses in 1 family (PP1; PMID: 10980596). This variant is absent from gnomAD v4.1.0 (PM2_Supporting).. In summary, this variant meets criteria to be classified as likely pathogenic for Li-Fraumeni syndrome based on the ACMG/AMP criteria applied, as specified by the TP53 Variant Curation Expert Panel: PVS1_Strong(RNA), PS4_Supporting, PP1, PM2_Supporting (Bayesian Points: 7; VCEP specifications version 2.0; 7/24/2024).

Met criteria codes

PS4_Supporting			This variant has been reported in 1 proband meeting Classic LFS criteria. Based on this evidence, this variant scores 1 total points meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; PMID: 10980596).
PVS1_Strong			The NM_000546.6:c.993+1del is a deletion of a single G nucleotide within the canonical donor site of exon 9 of TP53. Through exon 9 skipping, the variant is observed in an RT-PCR assay to produce multiple aberrant transcripts encoding frameshift alterations predicted to induce nonsense-mediated decay. Since the assay does not fully account for leakiness, code weight downgraded to Strong (PVS1_Strong (RNA); PMID: 10980596).
PP1			This variant has been reported to segregate with LFS-associated cancers in 3-4 meioses in 1 family (PP1; PMID: 10980596).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			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
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
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	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
BP3		✖	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
BA1		✖	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

Curation History	
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