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

PM2_Supporting PP1 PVS1_Strong PS4_Supporting

Not Met criteria codes 20

PP3 PP4 BA1 PM6 PM1 PM3 PM5 PM4 BS1 BS4 BS3 BS2 PS1 PS2 PS3 BP5 BP7 BP4 BP3 BP2

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.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

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP1	✔	This variant has been reported to segregate with LFS-associated cancers in 3-4 meioses in 1 family (PP1; 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).
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).

Not Met criteria codes

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
BA1	✖	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
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	ℹ	✖	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
BS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	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

Curation History

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