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Variant: NM_001276761.2:c.749T>C

Version: 1.0

CA397836609

1172923 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome 1 (MONDO:0007903)
Inheritance Mode: Autosomal dominant inheritance
UUID: 6dab48cd-422d-4d98-9cea-3e99b23c6a4b
Approved on: 2021/6/16
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HGVS expressions

NM_001276761.2:c.749T>C
NC_000017.11:g.7673754A>G
CM000679.2:g.7673754A>G
NC_000017.10:g.7577072A>G
CM000679.1:g.7577072A>G
NC_000017.9:g.7517797A>G
NG_017013.2:g.18797T>C
ENST00000503591.2:c.866T>C
ENST00000508793.6:c.866T>C
ENST00000509690.6:c.470T>C
ENST00000514944.6:c.587T>C
ENST00000604348.6:c.845T>C
ENST00000269305.9:c.866T>C
ENST00000269305.8:c.866T>C
ENST00000359597.8:c.866T>C
ENST00000413465.6:c.782+427T>C
ENST00000420246.6:c.866T>C
ENST00000445888.6:c.866T>C
ENST00000455263.6:c.866T>C
ENST00000504290.5:c.470T>C
ENST00000504937.5:c.470T>C
ENST00000509690.5:c.470T>C
ENST00000510385.5:c.470T>C
ENST00000610292.4:c.749T>C
ENST00000610538.4:c.749T>C
ENST00000610623.4:c.389T>C
ENST00000615910.4:c.833T>C
ENST00000617185.4:c.866T>C
ENST00000618944.4:c.389T>C
ENST00000619186.4:c.389T>C
ENST00000619485.4:c.749T>C
ENST00000620739.4:c.749T>C
ENST00000622645.4:c.749T>C
ENST00000635293.1:c.749T>C
NM_000546.5:c.866T>C
NM_001126112.2:c.866T>C
NM_001126113.2:c.866T>C

NM_001126114.2:c.866T>C
NM_001126115.1:c.470T>C
NM_001126116.1:c.470T>C
NM_001126117.1:c.470T>C
NM_001126118.1:c.749T>C
NM_001276695.1:c.749T>C
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NM_001276698.1:c.389T>C
NM_001276699.1:c.389T>C
NM_001276760.1:c.749T>C
NM_001276761.1:c.749T>C
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NM_001276760.2:c.749T>C
NM_000546.6:c.866T>C
NM_001126112.3:c.866T>C
NM_001126113.3:c.866T>C
NM_001126114.3:c.866T>C
NM_001126115.2:c.470T>C
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NM_001126117.2:c.470T>C
NM_001126118.2:c.749T>C
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NM_001276698.3:c.389T>C
NM_001276699.3:c.389T>C
NM_001276760.3:c.749T>C
NM_001276761.3:c.749T>C

Likely Benign

Met criteria codes 3

BP4 PM2_Supporting BS3

Not Met criteria codes 14

BP2 PS1 PS2 PS3 PS4 PP1 PP3 PM6 PM1 PM5 BA1 BS2 BS1 BS4

Evidence Links 0

Expert Panel

TP53 VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

This variant is absent in the gnomAD cohort (PM2_Supporting; http://gnomad.broadinstitute.org). Transactivation assays show retained function according to Kato, et al. and there is no evidence of a dominant negative effect or loss of function according to Giacomelli, et al. (BS3; PMID: 12826609, 30224644). This variant has a BayesDel score < 0.16 and Align GVGD (Zebrafish) is Class C0 (BP4). In summary, TP53 c.866T>C (p.Leu289Pro) meets criteria to be classified as likely benign for Li-Fraumeni syndrome. ACMG/AMP criteria applied, as specified by the TP53 Variant Curation Expert Panel: PM2_Supporting, BS3, BP4. PM2_Supporting should not be considered conflicting evidence as there is sufficient evidence for classification as Likely Benign

Met criteria codes

BP4	✔	AGVGD of C0 and BayesDel of -0.0138
PM2_Supporting	✔	Variant absent from gnomAD (not filtered)
BS3	✔	Kato just functional at 75.45%. Giacomelli retained function with no DNE or LOF.

Not Met criteria codes

BP2	✖	No cases in literature or internal data
PS1	✖	Two other variants in ClinVar: one benign, one VUS
PS2	✖	No cases in literature or internal data
PS3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	✖	Not observed in literature or internal data
PP1	✖	No cases in literature or internal data
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	✖	No cases in literature or internal data
PM1	✖	Not a hotspot codon and not in cancer hotspots
PM5	✖	Two other variants in ClinVar: one benign, one VUS
BA1	✖	Not present in gnomAD
BS2	✖	Not in FLOSSIES

BS1		✖	Not present in gnomAD
BS4		✖	No cases in literature or internal data

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001276761.2:c.749T>C	Likely Benign	Li-Fraumeni Syndrome 1	2021-06-16	1.0	-	TP53

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