The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000546.5(TP53):c.892G>T (p.Glu298Ter)

Version: 1.0

CA000484

93323 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome (MONDO:0018875)
Inheritance Mode: Autosomal dominant inheritance
UUID: 42caf4f2-7ef5-45d4-a593-271e92b9ca88
Approved on: 2019-08-28
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HGVS expressions

NM_000546.5:c.892G>T
NM_000546.5(TP53):c.892G>T (p.Glu298Ter)
NC_000017.11:g.7673728C>A
CM000679.2:g.7673728C>A
NC_000017.10:g.7577046C>A
CM000679.1:g.7577046C>A
NC_000017.9:g.7517771C>A
NG_017013.2:g.18823G>T
ENST00000503591.2:c.892G>T
ENST00000508793.6:c.892G>T
ENST00000509690.6:c.496G>T
ENST00000514944.6:c.613G>T
ENST00000604348.6:c.871G>T
ENST00000269305.9:c.892G>T
ENST00000269305.8:c.892G>T
ENST00000359597.8:c.892G>T
ENST00000413465.6:c.782+453G>T
ENST00000420246.6:c.892G>T
ENST00000445888.6:c.892G>T
ENST00000455263.6:c.892G>T
ENST00000504290.5:c.496G>T
ENST00000504937.5:c.496G>T
ENST00000509690.5:c.496G>T
ENST00000510385.5:c.496G>T
ENST00000610292.4:c.775G>T
ENST00000610538.4:c.775G>T
ENST00000610623.4:c.415G>T
ENST00000615910.4:c.859G>T
ENST00000617185.4:c.892G>T
ENST00000618944.4:c.415G>T
ENST00000619186.4:c.415G>T
ENST00000619485.4:c.775G>T
ENST00000620739.4:c.775G>T
ENST00000622645.4:c.775G>T
ENST00000635293.1:c.775G>T
NM_001126112.2:c.892G>T
NM_001126113.2:c.892G>T

NM_001126114.2:c.892G>T
NM_001126115.1:c.496G>T
NM_001126116.1:c.496G>T
NM_001126117.1:c.496G>T
NM_001126118.1:c.775G>T
NM_001276695.1:c.775G>T
NM_001276696.1:c.775G>T
NM_001276697.1:c.415G>T
NM_001276698.1:c.415G>T
NM_001276699.1:c.415G>T
NM_001276760.1:c.775G>T
NM_001276761.1:c.775G>T
NM_001276695.2:c.775G>T
NM_001276696.2:c.775G>T
NM_001276697.2:c.415G>T
NM_001276698.2:c.415G>T
NM_001276699.2:c.415G>T
NM_001276760.2:c.775G>T
NM_001276761.2:c.775G>T
NM_000546.6:c.892G>T
NM_001126112.3:c.892G>T
NM_001126113.3:c.892G>T
NM_001126114.3:c.892G>T
NM_001126115.2:c.496G>T
NM_001126116.2:c.496G>T
NM_001126117.2:c.496G>T
NM_001126118.2:c.775G>T
NM_001276695.3:c.775G>T
NM_001276696.3:c.775G>T
NM_001276697.3:c.415G>T
NM_001276698.3:c.415G>T
NM_001276699.3:c.415G>T
NM_001276760.3:c.775G>T
NM_001276761.3:c.775G>T

Pathogenic

Met criteria codes 4

PM2_Supporting PS4_Supporting PM1 PVS1

Evidence Links 1

Expert Panel

TP53 VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The p.Glu298* variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1). This variant is absent in the gnomAD cohort (PM2_Supporting; http://gnomad.broadinstitute.org). This variant has >10 observations as a somatic hotspot variant in tumors (PM1; cancerhotspots.org v(2)). Additionally, this variant has been reported in at least 2 probands meeting at least Chompret criteria (PS4_Supporting; PMID: 12610779, SCV000278127.5). In summary, TP53 c.892G>T; p.Glu298* meets criteria to be

classified as pathogenic for Li-Fraumeni syndrome. ACMG/AMP criteria applied, as specified by the TP53 Variant Curation Expert Panel: PVS1, PM2_Supporting, PM1, PS4_Supporting.

Met criteria codes

PM2_Supporting	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4_Supporting	✔	1 LFS classic proband (Hwang, et al) & 1 Chrompret proband (from EP member- SCV000278127.5 = 1.5 pts 32 family members w/33 tumors; authors state family meets LFS criteria. PubMed:12610779
PM1	✔	36 somatic observations in cancerhotspots.org
PVS1	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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