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: 1.1

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: 2024-08-05
Published on: 2024-08-05

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 PP4 PVS1 PS4_Supporting

Not Met criteria codes 14

PS1 PS2 PS3 PP1 PP3 PM1 PM5 BA1 BS2 BS1 BS4 BS3 BP7 BP4

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.892G>T (p.Glu298Ter) is a TP53 nonsense variant inducing a premature termination codon upstream of p.Lys351. The variant is predicted to undergo nonsense-mediated decay (PVS1). This variant has been observed in 1 family meeting Revised Chompret criteria. This proband was under the age of 40 diagnosed with a HER2+ breast cancer. Based on this evidence, this variant scores 1 total point meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; Internal lab contributors: SCV000278127.7). At least one individual with this variant was found to have a variant allele fraction 25-35%, which is a significant predictor of variant pathogenicity (PP4, PMID: 34906512, SCV000278127.7). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as pathogenic for Li Fraumeni Syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen TP53 VCEP: PVS1, PS4_Supporting, PP4, PM2_Supporting. (Bayesian Points: 11; VCEP specifications version 2.0; 7/24/2024)

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP4	✔	At least one individual with this variant was found to have a variant allele fraction 25-35%, which is a significant predictor of variant pathogenicity (PP4, PMID: 34906512, SCV000278127.7).
PVS1	✔	The NM_000546.6 c.892C>T (p.Glu298Ter) is a TP53 nonsense varianti upstream of p.Lys351. The variant is predicted to undergo nonsense-mediated decay (PVS1).
PS4_Supporting	✔	This variant has been observed in 1 family meeting Revised Chompret criteria. This proband was under the age of 40 diagnosed with a HER2+ breast cancer. Based on this evidence, this variant scores 1 total point meeting the TP53 VCEP phenotype scoring criteria of 1-1.5 points. (PS4_Supporting; Internal lab contributors: SCV000278127.7).

Not Met criteria codes

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
PP1	✖	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
PM1	✖	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

BA1		✖	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
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

Curation History

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