Variant: NM_001126112.2(TP53):c.636del (p.Arg213fs)

Version: 1.0

CA248848

218342 (ClinVar)

Gene: TP53 (HGNC:7157)
Condition: Li-Fraumeni syndrome 1 (MONDO:0007903)
Inheritance Mode: Autosomal dominant inheritance
UUID: 43ea40bf-abe3-4125-8861-85030e6c815c
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HGVS expressions

NM_001126112.2:c.636del
NM_001126112.2(TP53):c.636del (p.Arg213fs)
NC_000017.11:g.7674898del
CM000679.2:g.7674898del
NC_000017.10:g.7578216del
CM000679.1:g.7578216del
NC_000017.9:g.7518941del
NG_017013.2:g.17656del
ENST00000503591.2:c.636del
ENST00000508793.6:c.636del
ENST00000509690.6:c.240del
ENST00000514944.6:c.357del
ENST00000604348.6:c.615del
ENST00000269305.9:c.636del
ENST00000269305.8:c.636del
ENST00000359597.8:c.636del
ENST00000413465.6:c.636del
ENST00000420246.6:c.636del
ENST00000445888.6:c.636del
ENST00000455263.6:c.636del
ENST00000504290.5:c.240del
ENST00000504937.5:c.240del
ENST00000505014.5:n.892del
ENST00000509690.5:c.240del
ENST00000510385.5:c.240del
ENST00000514944.5:c.357del
ENST00000574684.1:n.67+158del
ENST00000610292.4:c.519del
ENST00000610538.4:c.519del
ENST00000610623.4:c.159del
ENST00000615910.4:c.603del
ENST00000617185.4:c.636del
ENST00000618944.4:c.159del
ENST00000619186.4:c.159del
ENST00000619485.4:c.519del
ENST00000620739.4:c.519del
ENST00000622645.4:c.519del

ENST00000635293.1:c.519del
NM_000546.5:c.636del
NM_001126113.2:c.636del
NM_001126114.2:c.636del
NM_001126115.1:c.240del
NM_001126116.1:c.240del
NM_001126117.1:c.240del
NM_001126118.1:c.519del
NM_001276695.1:c.519del
NM_001276696.1:c.519del
NM_001276697.1:c.159del
NM_001276698.1:c.159del
NM_001276699.1:c.159del
NM_001276760.1:c.519del
NM_001276761.1:c.519del
NM_001276695.2:c.519del
NM_001276696.2:c.519del
NM_001276697.2:c.159del
NM_001276698.2:c.159del
NM_001276699.2:c.159del
NM_001276760.2:c.519del
NM_001276761.2:c.519del
NM_000546.6:c.636del
NM_001126112.3:c.636del
NM_001126113.3:c.636del
NM_001126114.3:c.636del
NM_001126115.2:c.240del
NM_001126116.2:c.240del
NM_001126117.2:c.240del
NM_001126118.2:c.519del
NM_001276695.3:c.519del
NM_001276696.3:c.519del
NM_001276697.3:c.159del
NM_001276698.3:c.159del
NM_001276699.3:c.159del
NM_001276760.3:c.519del
NM_001276761.3:c.519del

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PS4_Supporting

Not Met criteria codes 4

BA1 BS1 BS2 PP1

Evidence Links 0

Expert Panel

TP53 VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

TP53 VCEP

The p.R213fs 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 been reported in 2 probands meeting Chompret criteria (PS4_Supporting; PMID: 11370630, NIH). In summary, TP53 c.636del (p.R213fs) 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, PS4_Supporting.

Met criteria codes

PVS1	✔	Frameshift in exon 6 of 11 in core/DNA-binding domain
PM2_Supporting	✔	Absent from gnomAD (non-cancer). Supporting per VCEP
PS4_Supporting	✔	NIH cohort: Chompret (0.5 pts); PMID 11370630: Chompret (0.5 pts) Total = 1 pts.

Not Met criteria codes

BA1	✖	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
BS2	✖	Absent from FLOSSIES. Internal lab data not provided for evaluation.
PP1	✖	2 meioses in one family. Need 3+ to count.

Curation History

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