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_000314.6(PTEN):c.370T>C (p.Cys124Arg)

Version: 1.0

CA000422

7817 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: b3d1af7f-63db-40b7-9bb6-1937661a6003
Approved on: 2019/6/25
Published on: 2019/7/23

HGVS expressions

NM_000314.6(PTEN):c.370T>C (p.Cys124Arg)
NM_000314.6:c.370T>C
NC_000010.11:g.87933129T>C
CM000672.2:g.87933129T>C
NC_000010.10:g.89692886T>C
CM000672.1:g.89692886T>C
NC_000010.9:g.89682866T>C
NG_007466.2:g.74691T>C
ENST00000700029.2:c.370T>C
ENST00000710265.1:c.370T>C
ENST00000472832.3:c.370T>C
ENST00000688158.2:n.1105T>C
ENST00000688922.2:c.*200T>C
ENST00000700021.1:c.325T>C
ENST00000700022.1:c.370T>C
ENST00000700029.1:c.204T>C
ENST00000706954.1:c.370T>C
ENST00000706955.1:c.*405T>C
ENST00000686459.1:c.370T>C
ENST00000688158.1:c.*481T>C
ENST00000688308.1:c.370T>C
ENST00000688922.1:c.291T>C
ENST00000693560.1:c.889T>C
ENST00000371953.8:c.370T>C
ENST00000371953.7:c.370T>C
ENST00000498703.1:n.196T>C
ENST00000610634.1:c.268T>C
NM_000314.5:c.370T>C
NM_001304717.2:c.889T>C
NM_001304718.1:c.-381T>C
NM_000314.7:c.370T>C
NM_001304717.5:c.889T>C
NM_001304718.2:c.-381T>C
NM_000314.8:c.370T>C

Pathogenic

Met criteria codes 6

PS3 PP2 PM1 PM6_Strong PM2 PS4_Supporting

Not Met criteria codes 20

PS1 PS2 PP1 PP3 PP4 PM3 PM5 PM4 BA1 BS1 BS4 BS3 BS2 PVS1 BP5 BP7 BP4 BP3 BP1 BP2

Evidence Links 8

Expert Panel

PTEN VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

PTEN VCEP

PTEN c.370T>C (p.Cys124Arg) meets criteria to be classified as pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (PMID 30311380). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PS3: Phosphatase activity <50% of wild type (PMID 10866302, PMID 29706350) PM6_S: Two probands with presumed de novo occurrence (maternity/paternity not confirmed) in a patient with the disease and no family history. (internal laboratory contributor SCV000568254.4) PM1: Located at a residue within a catalytic motif as defined by the ClinGen PTEN Expert Panel. PM2: Absent in large sequenced populations (PMID 27535533). PP2: PTEN is defined by the PTEN Expert Panel as a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease. PS4_P: Proband(s) with phenotype specificity score of 1-1.5. (internal laboratory contributor SCV000568254.4)

Met criteria codes

PS3	✔	I agree (FH) Appears to show decreased stability (score 0.28) but EP still figuring out cutoff for this publication, and PS3 already applied for other literature. PubMed:29785012 Y2H assay, no interaction with LKB1. Not relevant for criteria. PubMed:15987703 Knock-in mouse model; HOM mice embryonic lethal, HOM mouse fetuses displayed multiple anomalies. PS3 already applied for other literature. PubMed:20194734 Phosphatase activity in truncation-like range (-4.45) - PS3 applies per EP. PubMed:29706350 Complete loss of phosphatase activity, similar to null. PubMed:10866302
PP2	✔	I agree (FH)
PM1	✔	I Agree (FH)
PM6_Strong	✔	2 internal GDx cases (SCV000568254.4)
PM2	✔	absent gnomAD, good coverage. I agree (FH)
PS4_Supporting	✔	1 internal GDx case (SCV000568254.4)

Same pt as Nelen 1997. PubMed:10234502

Identified in pt n130, female with macrocephaly, benign thyroid disease, and CS-related skin findings NOS. Minimum CC score = 11. PubMed:9259288

Reported in two families with "CS". Family 1.) Macrocephaly, benign findings of skin, thyroid, GI and breast Family 2.) Head size not documented, malignant and benign GI findings, benign findings thyroid, skin, and breast. Unsure which features present in which individuals, unable to apply criteria. PubMed:9467011

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
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
PP4	✖	Tied into PS4.
PM3	✖	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
PM4	✖	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
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

BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1		✖	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		✖	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
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	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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