

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

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HGVS expressions

NM_000314.6:c.370T>C

NM_000314.6(PTEN):c.370T>C (p.Cys124Arg)

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

PS4_SupportingPM6_StrongPS3PP2PM2PM1

Not Met criteria codes 20

BA1BS1BS4BS3BS2BP5BP7BP4BP3BP1BP2PVS1PS1PS2PP1PP3PP4PM3PM5PM4

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

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

PM6_Strong

2 internal GDx cases (SCV000568254.4)

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)
PM2			absent gnomAD, good coverage. I agree (FH)
PM1			I Agree (FH)

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

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

Curation History 		
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