

Variant: NM_000314.6(PTEN):c.331T>C (p.Trp111Arg)

CA000401 [↗](#)

92820 (ClinVar) [↗](#)

Gene: PTEN ([HGNC:5728](#))

Condition: PTEN hamartoma tumor syndrome ([MONDO:0017623](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 59486401-1daa-48dc-813f-bde6605d8cfd

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HGVS expressions

NM_000314.6:c.331T>C

NM_000314.6(PTEN):c.331T>C (p.Trp111Arg)

NC_000010.11:g.87933090T>C

CM000672.2:g.87933090T>C

NC_000010.10:g.89692847T>C

CM000672.1:g.89692847T>C

NC_000010.9:g.89682827T>C

NG_007466.2:g.74652T>C

ENST00000700029.2:c.331T>C

ENST00000710265.1:c.331T>C

ENST00000472832.3:c.331T>C

ENST00000688158.2:n.1066T>C

ENST00000688922.2:c.*161T>C

ENST00000700021.1:c.286T>C

ENST00000700022.1:c.331T>C

ENST00000700029.1:c.165T>C

ENST00000706954.1:c.331T>C

ENST00000706955.1:c.*366T>C

ENST00000686459.1:c.331T>C

ENST00000688158.1:c.*442T>C

ENST00000688308.1:c.331T>C

ENST00000688922.1:c.252T>C

ENST00000693560.1:c.850T>C

ENST00000371953.8:c.331T>C

ENST00000371953.7:c.331T>C

ENST00000498703.1:n.157T>C

ENST00000610634.1:c.229T>C

NM_000314.5:c.331T>C

NM_001304717.2:c.850T>C

NM_001304718.1:c.-420T>C

NM_000314.7:c.331T>C

NM_001304717.5:c.850T>C

NM_001304718.2:c.-420T>C

NM_000314.8:c.331T>C

Pathogenic

Met criteria codes6

PM6_StrongPS4_ModeratePP2PP3PS3_ModeratePM2

Not Met criteria codes20

BA1BS4BS3BS1BS2BP5BP7BP2BP3BP1BP4PVS1PS1PS2PP4PP1PM5PM3PM1PM4

Evidence Links0

Expert Panel

PTEN VCEP

Criteria Specification Information

Criteria Specification:

ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.1.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

PTEN VCEP

PTEN c.331T>C (p.Trp111Arg) 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_M: Functional studies showing a damaging effect on protein function. Phosphatase activity ≤ -1.11 per Mighell et al. 2018 (PMID: 29706350). This variant: score of -4.10 PM2_P: Absent in large sequenced populations (PMID 27535533). PS4_M: Probands with phenotype specificity score of 2-3.5. (internal laboratory contributor(s) ClinVar Organization ID: 61756, ClinVar Organization ID: 19864) 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. PP3: REVEL score > 0.7 (score of this variant =0.961) PM6_S: Assumed de novo, but without confirmation of paternity and maternity in a patient with the disease and no family history and high phenotype specificity (PMID 35102303)

Met criteria codes

PM6_Strong		✓	Constitutional mosaicism in PMID 35102303, adult with CC score = 36. Parents not tested but VAF 29-34% and mosaic on Sanger. Criteria approved for use by the VCEP given constitutional mosaicism indicates variant arose during embryogenesis (de novo).
PS4_Moderate		✓	Internal lab submitters Ambry (Organization ID: 61756) case with 1 phenotype specificity point; Eng lab (Organization ID: 19864) case with 1 phenotype specificity point
PP2		✓	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3		✓	REVEL = 0.961
PS3_Moderate		✓	Mighell = -4.1
PM2		✓	Absent in gnomAD

Not Met criteria codes

BA1			Absent in gnomAD
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
BS1			Absent in gnomAD
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
BP2			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
BP4			REVEL = 0.961
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
PP4			Internal lab case: F proband in 50s endometrial ca in late 20s, IDC in 50s, nodular thyroid goiter in 30s, lung carcinoid in 50s, >10 hamartomatous colon polyps in 30s (no head circumference mentioned) - added under PS4_M Cleveland Clinic (CC) score of 31 (1 point/PP4_supporting) FHx: Sister- ADD/ADHD, redundant colon/no motility; Mother- CRC in 70s; Mat aunt- lung; MGF- CRC; MGM- lung; Father- prostate in 60s; Pat gr aunt- breast

