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.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
Approved on: 2018-11-28
Published on: 2018-12-10

HGVS expressions

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

PP2 PP3 PM2 PM6_Strong PS3_Moderate PS4_Moderate

Not Met criteria codes 20

PP4 PP1 PM5 PM3 PM1 PM4 BA1 BS2 BS4 BS3 BS1 PS1 PS2 BP2 BP3 BP1 BP4 PVS1 BP5 BP7

Evidence Links 0

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

PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✔	REVEL = 0.961
PM2	✔	Absent in gnomAD
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).
PS3_Moderate	✔	Mighell = -4.1
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

Not Met criteria codes

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
PP1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	Absent in gnomAD
BS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	Absent in gnomAD
PS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2	ℹ	✖	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
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

Curation History

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