

Variant: *NM_000314.6(PTEN):c.284C>T (p.Pro95Leu)*

Version: 1.0

CA000383 [↗](#)

189403 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 43eee6bc-e0e1-4ce0-8d9a-b838428c1884

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HGVS expressions

NM_000314.6(PTEN):c.284C>T (p.Pro95Leu)

NM_000314.6:c.284C>T

NC_000010.11:g.87933043C>T

CM000672.2:g.87933043C>T

NC_000010.10:g.89692800C>T

CM000672.1:g.89692800C>T

NC_000010.9:g.89682780C>T

NG_007466.2:g.74605C>T

ENST00000700029.2:c.284C>T

ENST00000710265.1:c.284C>T

ENST00000472832.3:c.284C>T

ENST00000688158.2:n.1019C>T

ENST00000688922.2:c.*114C>T

ENST00000700021.1:c.239C>T

ENST00000700022.1:c.284C>T

ENST00000700029.1:c.118C>T

ENST00000706954.1:c.284C>T

ENST00000706955.1:c.*319C>T

ENST00000686459.1:c.284C>T

ENST00000688158.1:c.*395C>T

ENST00000688308.1:c.284C>T

ENST00000688922.1:c.205C>T

ENST00000693560.1:c.803C>T

ENST00000371953.8:c.284C>T

ENST00000371953.7:c.284C>T

ENST00000498703.1:n.110C>T

ENST00000610634.1:c.182C>T

NM_000314.5:c.284C>T

NM_001304717.2:c.803C>T

NM_001304718.1:c.-467C>T

NM_000314.7:c.284C>T

NM_001304717.5:c.803C>T

NM_001304718.2:c.-467C>T

NM_000314.8:c.284C>T

Pathogenic

Met criteria codes5

PS4_SupportingPS3PP2PM6PM2

Not Met criteria codes21

BA1BS1BS4BS3BS2BP5BP7BP4BP3BP1BP2PVS1PS1PS2PP1PP3PP4PM1PM3PM5PM4

Evidence Links7

Expert Panel

Criteria Specification Information ⓘ Criteria Specifications for this VCEP ⓘ

Evidence submitted by expert panel

PTEN VCEP

PTEN c.284C>T (p.Pro95Leu) 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 21828076, PMID 29706350) PM2: Absent in large sequenced populations (PMID 27535533). PM6: Assumed de novo, but without confirmation of paternity and maternity in a patient with the disease and no family history. (internal laboratory contributor ClinVar Organization ID 26957) 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 ClinVar Organization ID 26957)

Met criteria codes

PS4_Supporting ⓘ ✓

Heald B et al. in a prospective series of PTEN mutation carriers reported subject 1515 has having > 50 hamartomas. The Herman Laboratory Nationwide Children's Hospital reported clinical data into Clinvar. The patient had macrocephaly (+6.4 SD) and > 40 colon polyps and 15 were > 1cm and all were juvenile polyps. It is unclear whether this patient is the same as the patient reported in Heald B et al. Tan et. al reported individual 20 as meeting relaxed International Consortium operational criteria for PTHS. Could meet PS4_S but need more phenotype information. Entry by MPerpich. KS: GeneDx internal data: male child with macrocephaly, penile freckling, developmental delay and pediatric proband score = 7. This case is also de novo, and reaches 1 phenotype specificity point. A second case of a female in her 40's with breast cancer and 3 colon polyps (adenomatous and hyperplastic). PTEN study data: Very likely this is the same patient as Heald et al., OFC = 60 cm, GI hamartomas (6), and GI polyps NOS (44), and CC score = 22.

PubMed:21194675 ⓘ

Macrocephaly (+6.4 SD); Colonoscopy with >40 polyps throughout the colon, 15 were >1cm, all were juvenile type.

PubMed:28526761 ⓘ

Likely is the same patient as Heald et al. and Tan et al.

PubMed:25669429 ⓘ

Variant identified in 2 individuals in study.

PubMed:21659347 ⓘ

PubMed:20600018 ⓘ

PS3 ⓘ ✓

Escudero et al. (2011) demonstrated a high percentage of PIP3+ cells (similar to vector), no growth rescue and reduced PTEN activity in figure 4. Miguel et al. (2018) classified variant as truncation-like with a G score of -3.414242736. MPerpich entry. KS agrees. Matreyek results not available.

PP2			KS agrees.
PM6			Internal case from GeneDx: male child with macrocephaly, developmental delay and penile freckling (pediatric proband specificity score = 7).
PM2			Variant is not present in gnomAD. KS agrees.

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			Included under PS4.
PM1			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
PM5			ClinVar entry for Pro95Thr, however that variant not is reported in the literature. Likely will not meet likely pathogenic/pathogenic at this time. May be reasonable to re-evaluate in future.
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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