

Variant: NM_000314.8(PTEN):c.1003C>T (p.Arg335Ter)

Version: 1.0

CA000245 [↗](#)

7833 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d8f603d6-ea02-46e0-aba3-29f60f0b30b6

Approved on: 2025/12/15

Published on: 2026/6/26

HGVS expressions

NM_000314.8:c.1003C>T

NM_000314.8(PTEN):c.1003C>T (p.Arg335Ter)

NC_000010.11:g.87961095C>T

CM000672.2:g.87961095C>T

NC_000010.10:g.89720852C>T

CM000672.1:g.89720852C>T

NC_000010.9:g.89710832C>T

NG_007466.2:g.102657C>T

ENST00000700029.2:c.1096C>T

ENST00000710265.1:c.1003C>T

ENST00000472832.3:c.1003C>T

ENST00000688158.2:n.1738C>T

ENST00000688922.2:c.*833C>T

ENST00000700021.1:c.958C>T

ENST00000700022.1:c.*342C>T

ENST00000700023.1:n.2161C>T

ENST00000700024.1:n.2395C>T

ENST00000700025.1:n.1772C>T

ENST00000700026.1:n.640C>T

ENST00000706954.1:c.1003C>T

ENST00000706955.1:c.*1038C>T

ENST00000686459.1:c.*589C>T

ENST00000688158.1:c.*1114C>T

ENST00000688308.1:c.1003C>T

ENST00000688922.1:c.924C>T

ENST00000693560.1:c.1522C>T

ENST00000371953.8:c.1003C>T

ENST00000371953.7:c.1003C>T

ENST00000472832.2:c.430C>T

NM_000314.5:c.1003C>T

NM_000314.6:c.1003C>T

NM_001304717.2:c.1522C>T

NM_001304718.1:c.412C>T

NM_000314.7:c.1003C>T

NM_001304717.5:c.1522C>T

NM_001304718.2:c.412C>T

Pathogenic

Met criteria codes 5

PS4PP1PS2_Very StrongPM2_SupportingPVS1

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.1003C>T (p.Arg335Ter) meets criteria to be classified as Pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (ACMG Classification Rules Specified for PTEN Variant Curation version 3.1.0). Please see a summary of the rules and criteria codes in the “PTEN ACMG Specifications Summary” document (assertion method column). PVS1: Null variant predicted to result in nonsense-mediated decay or causing truncation/frameshift at or 5’ to c.1121 (NM_000314.8). PS4: Probands with phenotype specificity score of 4-15.5 PM2_Supporting: Present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533). PP1: Co-segregation with disease in multiple affected family members, with 3 or 4 meioses observed. (PMID 10353779) PS2_VS: One proven plus two assumed de novo observations in a patient with the disease and no family history. (PMID 40407579, PMID 22595938, PMID 30233642)		
Met criteria codes		
PS4		Probands with total specificity score of 5. Probands are as follows: Pediatric patient with macrocephaly, developmental delay, and penile freckling. Phenotype score +7, +1 proband point (PMID 10353779). Pediatric patient presumed de novo with macrocephaly, developmental delay, arteriovenous hemangioma, acral keratoses, and a lipoma. Phenotype score +7, +1 proband point (PMID 22595938). Pediatric patient presumed de novo with macrocephaly, developmental delay, and multiple lipomas. Phenotype score +5, +1 proband point (PMID 10232405). Pediatric patient presumed de novo with macrocephaly, hemangiomas, increased perivascular space, and hamartomatous polyps. Phenotype Score +9, +1 proband point (PMID 24052722). Pediatric patient presumed de novo with extreme macrocephaly, developmental delay and autism, thyroid nodules, and a vascular malformation. Phenotype Score +9, +1 proband point (PMID 28526761).
PP1		Co-segregation with disease in multiple affected family members, with 3 family members affected (PMID: 10353779).
PS2_Very Strong		Adult patient presumed de novo with macrocephaly, developmental delay, lipoma, Hashimoto's thyroiditis, arteriovenous malformation, and breast fibroadenomas (Phenotype score +19, does not meet PS4; meets PM6) (PMID 40407579). Pediatric patient presumed de novo with macrocephaly and autism (Phenotype score +4 (including autism), does not meet PS4; meets PM6) (PMID 22595938). Adult patient confirmed de novo (WES trio +sibling) with RC, Hashimoto's Thyroiditis, and thyroid cancer (dx 20-49). (Phenotype score +9, does not meet PS4; meets PS2) (PMID 30233642).
PM2_Supporting		Variant is present at <0.00001 allele frequency and <0.00002 in a subpopulation with multiple alleles in gnomAD (v4).

PVS1



This nonsense mutation causes a truncation 5' to c.1121 in a biologically-relevant transcript (NM_000314.8).

Curation History [↗](#)

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.