Variant: NM_000314.8(PTEN):c.1061C>A (p.Pro354Gln)

Version: 1.1

CA000275

143020 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: e75a40b0-8e18-418e-b6c7-079646958d18
Approved on: 2026-03-18
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HGVS expressions

NM_000314.8:c.1061C>A
NM_000314.8(PTEN):c.1061C>A (p.Pro354Gln)
NC_000010.11:g.87965321C>A
CM000672.2:g.87965321C>A
NC_000010.10:g.89725078C>A
CM000672.1:g.89725078C>A
NC_000010.9:g.89715058C>A
NG_007466.2:g.106883C>A
ENST00000700029.2:c.1154C>A
ENST00000710265.1:c.*90C>A
ENST00000688158.2:n.1796C>A
ENST00000688922.2:c.*891C>A
ENST00000700021.1:c.1016C>A
ENST00000700022.1:c.*400C>A
ENST00000700023.1:n.2219C>A
ENST00000700024.1:n.2453C>A
ENST00000706954.1:c.1061C>A
ENST00000706955.1:c.*1096C>A
ENST00000686459.1:c.*647C>A
ENST00000688158.1:c.*1172C>A
ENST00000688308.1:c.1061C>A
ENST00000688922.1:c.982C>A
ENST00000693560.1:c.1580C>A
ENST00000371953.8:c.1061C>A
ENST00000371953.7:c.1061C>A
NM_000314.5:c.1061C>A
NM_000314.6:c.1061C>A
NM_001304717.2:c.1580C>A
NM_001304718.1:c.470C>A
NM_000314.7:c.1061C>A
NM_001304717.5:c.1580C>A
NM_001304718.2:c.470C>A

Likely Benign

Met criteria codes 4

BS1 BP4 PP2 BS3_Supporting

Not Met criteria codes 22

BA1 BS2 BS4 BP5 BP7 BP3 BP1 BP2 PVS1 PS1 PS2 PS3 PS4 PP1 PP3 PP4 PM1 PM3 PM5 PM4 PM6 PM2

Evidence Links 7

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

NM_000314.8(PTEN):c.1061C>A (p.Pro354Gln) variant meets criteria to be classified as likely benign 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). BS1: To be applied for variants with filtering allele frequency (FAF) of 0.000043 up to 0.00056 (0.0043% up to 0.056%) in gnomAD. Popmax FAF of this variant=0.0001051. BS3_P: In vitro or in vivo functional study or studies showing no damaging effect on protein function. This variant: score of 0.09 (WT-like range) on high throughput phosphatase assay (PMID:29706350). BP4: REVEL score < 0.5 (score=0.497). 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. Using the Bayesian point system (PMID: 29300386) for this variant with conflicting evidence: 1 benign strong and 2 benign supporting = -6. 1 pathogenic supporting = 1. Total = – 5 (likely benign).

Met criteria codes

BS1	✔	gnomAD v2.1.1: 19/125384 (.0115%) European/non-Finnish pop (.00011515). Popmax Filtering AF is .0001051 which meets BS1 criteria [gnomAD Filtering allele frequency from 0.000043 (0.0043%) up to 0.00056 (0.056%)].
BP4	✔	REVEL score < 0.5 (score=0.497)
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.
BS3_Supporting	✔	In vitro or in vivo functional study or studies showing no damaging effect on protein function. Score of 0.09 (WT-like range) on high throughput phosphatase assay (PMID:29706350). Score of 0.09 (WT-like range) on high throughput phosphatase assay PubMed:29706350 WT-like abundance on high-throughput VAMP-seq assay, indicating stable protein PubMed:29785012

Not Met criteria codes

BA1	✖	0.015% (19/122,896) European (Non-Finnish) alleles in gnomAD; 3/1886 alleles in GME variome.

BS2		✖	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
BP5		✖	Some cases suggestive, but overlapping phenotypes with PHTS
BP7		✖	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
PS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4		✖	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		✖	Germline finding in a pt with neuroblastoma PubMed:26580448 Eng lab paper, same pts in other lab publications. Identified in two sisters. The first being a 49 year old woman with normal head circumference and a history of breast cancer, fibrocystic breast disease and uterine fibroids. Reported to NOT meet ICC criteria. The second being a 56 year old female (head circumference unknown) with a history of

fibrocystic breast disease and a genitourinary tumor. This patient also did NOT meet ICC criteria. PubMed:21343951
Identified in a pt undergoing clinical testing; no phenotype info provided. PubMed:21659347
Identified in a pt with BrCA dx 57 who had a FDR with BrCA. PubMed:26898890
Seen in a pt with a Lynch-related cancer and/or polyps who also harbored an MSH2 PATH, but no phenotype provided. PubMed:25980754

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	✖	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
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2	✖	0.015% (19/122,896) European (Non-Finnish) alleles in gnomAD; 3/1886 alleles in GME variome.

Curation History

Showing 1 to 2 of 2 rows