

Variant: NM\_000314.7(PTEN):c.367C>G (p.His123Asp)

Version: 1.0

CA377482278 [↗](#)

428277 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 363d5223-feca-47e8-a3b8-115e05778f7f

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### HGVS expressions

**NM\_000314.7(PTEN):c.367C>G (p.His123Asp)**

**NM\_000314.7:c.367C>G**

NC\_000010.11:g.87933126C>G

CM000672.2:g.87933126C>G

NC\_000010.10:g.89692883C>G

CM000672.1:g.89692883C>G

NC\_000010.9:g.89682863C>G

NG\_007466.2:g.74688C>G

ENST00000700029.2:c.367C>G

ENST00000710265.1:c.367C>G

ENST00000472832.3:c.367C>G

ENST00000688158.2:n.1102C>G

ENST00000688922.2:c.\*197C>G

ENST00000700021.1:c.322C>G

ENST00000700022.1:c.367C>G

ENST00000700029.1:c.201C>G

ENST00000706954.1:c.367C>G

ENST00000706955.1:c.\*402C>G

ENST00000686459.1:c.367C>G

ENST00000688158.1:c.\*478C>G

ENST00000688308.1:c.367C>G

ENST00000688922.1:c.288C>G

ENST00000693560.1:c.886C>G

ENST00000371953.8:c.367C>G

ENST00000371953.7:c.367C>G

ENST00000498703.1:n.193C>G

ENST00000610634.1:c.265C>G

NM\_000314.5:c.367C>G

NM\_000314.6:c.367C>G

NM\_001304717.2:c.886C>G

NM\_001304718.1:c.-384C>G

NM\_001304717.5:c.886C>G

NM\_001304718.2:c.-384C>G

NM\_000314.8:c.367C>G

Pathogenic

Met criteria codes 5

PS3PP2PM2PM1PS4\_Supporting

Not Met criteria codes 1

PP4

Evidence Links 3

Expert Panel

PTEN VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                         |                                                                                                                                                                                                                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Evidence submitted by expert panel                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                         |                                                                                                                                                                                                                                          |
| <b>PTEN VCEP</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                         |                                                                                                                                                                                                                                          |
| <b>PTEN c.367C&gt;G (p.His123Asp) 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 &lt;50% of wild type OR RNA, mini-gene, or other assay shows impact on splicing. (PMID 29706350, 21828076) PM1: Located at a residue within a catalytic motif as defined by the ClinGen PTEN Expert Panel. PM2: Absent in large sequenced populations (PMID 27535533). 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 SCV000580072.3)</b> |                                                                                                                                                                         |                                                                                                                                                                                                                                          |
| <b>Met criteria codes</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                         |                                                                                                                                                                                                                                          |
| <b>PS3</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   | Comprehensive in vivo functional analysis of human PTEN using a heterologous yeast reconstitution system. Phosphatase activity was fully inactive (Rodríguez-Escudero I et al2011).                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                         | High-throughput functional assay testing PTEN lipid phosphatase activity score of -4.345802175 so this variant had truncation-like function and was 'TRUE'. <a href="#">PubMed:29706350</a>                                              |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                         | Comprehensive in vivo functional analysis of human PTEN using a heterologous yeast reconstitution system. Phosphatase activity was fully inactive. <a href="#">PubMed:21828076</a>                                                       |
| <b>PP2</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   | Missense                                                                                                                                                                                                                                 |
| <b>PM2</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                      | Not present in gnomAD (coverage >90X).                                                                                                                                                                                                   |
| <b>PM1</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   | This amino acid position, 123, is in a catalytic motif.                                                                                                                                                                                  |
| <b>PS4_Supporting</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |   | Teenager with fundic gland polyps diagnosed as a child with hamartomatous features, multiple lipomas, Hashimoto thyroiditis, right thigh hamartoma, macrocephaly, penile freckling. Pediatric CC score of 11 (1 point) (Ambry Genetics). |
| <b>Not Met criteria codes</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                         |                                                                                                                                                                                                                                          |
| <b>PP4</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                      | Teenager with fundic gland polyps diagnosed as a child with hamartomatous features, multiple lipomas, Hashimoto thyroiditis, right thigh hamartoma, macrocephaly, penile freckling. Pediatric CC score of 11 (1 point) (Ambry Genetics). |

PubMed:11918710 

Curation History 

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