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_000314.8(PTEN):c.380G>A (p.Gly127Glu)

Version: 1.0

CA377482305

428225 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: e6e5c29e-1f51-4e2a-b97a-72ee191e7c2b
Approved on: 2026/6/17
Published on: 2026/6/24

HGVS expressions

NM_000314.8(PTEN):c.380G>A (p.Gly127Glu)
NM_000314.8:c.380G>A
NC_000010.11:g.87933139G>A
CM000672.2:g.87933139G>A
NC_000010.10:g.89692896G>A
CM000672.1:g.89692896G>A
NC_000010.9:g.89682876G>A
NG_007466.2:g.74701G>A
ENST00000700029.2:c.380G>A
ENST00000710265.1:c.380G>A
ENST00000472832.3:c.380G>A
ENST00000688158.2:n.1115G>A
ENST00000688922.2:c.*210G>A
ENST00000700021.1:c.335G>A
ENST00000700022.1:c.380G>A
ENST00000700029.1:c.214G>A
ENST00000706954.1:c.380G>A
ENST00000706955.1:c.*415G>A
ENST00000686459.1:c.380G>A
ENST00000688158.1:c.*491G>A
ENST00000688308.1:c.380G>A
ENST00000688922.1:c.301G>A
ENST00000693560.1:c.899G>A
ENST00000371953.8:c.380G>A
ENST00000371953.7:c.380G>A
ENST00000498703.1:n.206G>A
ENST00000610634.1:c.278G>A
NM_000314.5:c.380G>A
NM_000314.6:c.380G>A
NM_001304717.2:c.899G>A
NM_001304718.1:c.-371G>A
NM_000314.7:c.380G>A
NM_001304717.5:c.899G>A
NM_001304718.2:c.-371G>A

Likely Pathogenic

Met criteria codes 6

PM1 PS3_Moderate PS4_Moderate PM2_Supporting PP2 PP3

Not Met criteria codes 1

PP1

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 3.2.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.380G>A (p.Gly127Glu or NC_000010.10:g.89692896G>A) meets criteria to be classified as Likely 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). PM1: Located at a residue within a catalytic motif as defined by the ClinGen PTEN Expert Panel. PS3_M: Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -2.68 (≤ -1.11) on a high throughput phosphatase assay (PMID:29706350). PS4: Proband(s) with phenotype specificity score of 2-3.5. (PMID 40564777). 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 =0.954). PM2_P: Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533).

Met criteria codes

PM1	✔	Located at a residue within a catalytic motif as defined by the ClinGen PTEN Expert Panel.
PS3_Moderate	✔	Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -2.68 (≤ -1.11) on a high throughput phosphatase assay (PMID:29706350).
PS4_Moderate	✔	Proband(s) with phenotype specificity score of 2-3.5. (PMID 40564777). Proband #1: 15 yr old F born with postnatal macrosomia (4350 g/54 cm) and macrocephaly. Seen by cardiologist until the age 11 yrs due to interventricular septal defect,. Mixed germ cell tumor consisting of mature teratoma and yolk salk tumor on right ovary (age =7). Follicular adenoma on left lobe of thyroid gland (age =10). +5 Pediatric phenotype points, + 1 proband point. Proband #2: Younger brother of Proband #1. Macrosomia, macrocephaly, papillomatosis of the palatine tonsils, right-sided cryptochidism, aplasia of right testis, macular pigmentation of the penis. +9 Pediatric phenotype points, +1 proband point. Total proband points for Proband #1 and #2 = 1. Due to probands being related. Proband #3: Father of Proband #1 and #2, has macrocephaly and penile lentiginosis. CC score of +12, no weight added. (PMID 40564777) Ambry #1: 4yo male with CAL spots, macrocephaly, scoliosis, penile freckling, leg weakness, and hypertrichosis. +5 Pedistric phenotype score, +1 proband point.
PM2_Supporting	✔	Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (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.

PP3		✔	REVEL score > 0.7 (score of this variant =0.954)

Not Met criteria codes

PP1		✖	PP1 requires co-segregation with disease in multiple affected family members, with 3 or 4 meioses, only two meiosis observed in PMID 40564777.

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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.