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.59G>T (p.Gly20Val)

Version: 1.0

CA377781994

428266 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: fcbc972e-ad73-404c-ae8e-7cedfd4ec264
Approved on: 2023/8/4
Published on: 2023/10/19

HGVS expressions

NM_000314.8:c.59G>T
NM_000314.8(PTEN):c.59G>T (p.Gly20Val)
NC_000010.11:g.87864528G>T
CM000672.2:g.87864528G>T
NC_000010.10:g.89624285G>T
CM000672.1:g.89624285G>T
NC_000010.9:g.89614265G>T
NG_007466.2:g.6090G>T
NG_033079.1:g.3910C>A
ENST00000700029.2:c.59G>T
ENST00000710265.1:c.59G>T
ENST00000472832.3:c.59G>T
ENST00000688922.2:c.59G>T
ENST00000700021.1:c.59G>T
ENST00000700022.1:c.59G>T
ENST00000706954.1:c.59G>T
ENST00000706955.1:c.59G>T
ENST00000686459.1:c.59G>T
ENST00000688158.1:c.59G>T
ENST00000688308.1:c.59G>T
ENST00000693560.1:c.578G>T
ENST00000371953.8:c.59G>T
ENST00000371953.7:c.59G>T
ENST00000462694.1:n.61G>T
ENST00000487939.1:n.80G>T
ENST00000610634.1:c.-44G>T
ENST00000618586.1:n.28G>T
NM_000314.5:c.59G>T
NM_000314.6:c.59G>T
NM_001304717.2:c.578G>T
NM_001304718.1:c.-647G>T
NM_000314.7:c.59G>T
NM_001304717.5:c.578G>T
NM_001304718.2:c.-647G>T

Likely Pathogenic

Met criteria codes 5

PM2_Supporting | PS2 | PP2 | PP3 | PS4_Supporting

Not Met criteria codes 3

PS3 | PM1 | PM5

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 3.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

NM_000314.8(PTEN):c.59G>T (p.Gly20Val) meets criteria to be classified as likely 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). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history (Internal laboratory contributor(s) SCV001393771.3). PS4_P: Proband(s) with phenotype specificity score of 1-1.5 Internal laboratory contributor(s) SCV001393771.3). PM2_Supporting: 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. PP3: REVEL score = 0.931.

Met criteria codes

PM2_Supporting	✔	Absent in gnomAD. Updated from moderate to supporting level of evidence.
PS2	✔	From Invitae: This variant has been observed to be de novo in an individual with features consistent with a PTEN-related condition (Invitae). ClinVar contains an entry for this variant (Variation ID: 428266). INTERNAL OBSERVATION: a child reported to have macrocephaly, lipoma, and gross motor delays. Parental testing done at Invitae confirmed relatedness and de novo status.
PP2	✔	This is a missense variant.
PP3	✔	REVEL score = 0.931 (>0.75). From the REVEL home page, I downloaded the genome segment file "Chromosome 10: 074894550 - 094291662" to check/get the REVEL score (Matt J.).
PS4_Supporting	✔	Invitae: A child (< 10 yo) reported to have macrocephaly, lipoma, and gross motor delays (Ped score = 5).

Not Met criteria codes

PS3	✖	Mighell et al (2018) {29706350}: High confidence variant, cum_score = -0.9465 (> -1.11 threshold).
PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM5		✖	G20E: 1 ClinVar entry (VUS - GeneDx). Not curated by EP at this time, functional evidence found, possible cases; even if G20E was pathogenic, then G20V would still not meet likely pathogenic with applying PM5. BLOSUM = -2 (greater than G20E BLOSUM: -3). G20A: 1 ClinVar entry (VUS - Invitae). Not curated by EP at this time, functional evidence suggests this variant to impact function; even if G20E was pathogenic, then G20V would still not meet likely pathogenic with applying PM5. BLOSUM = 0 (greater than G20E BLOSUM: -3).

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.