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.16A>G (p.Lys6Glu)

Version: 1.0

CA377781810

644390 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 42dd26e4-54dd-4c3b-abdc-5f9f3dac0795
Approved on: 2021/6/4
Published on: 2022/9/30

HGVS expressions

NM_000314.8(PTEN):c.16A>G (p.Lys6Glu)
NM_000314.8:c.16A>G
NC_000010.11:g.87864485A>G
CM000672.2:g.87864485A>G
NC_000010.10:g.89624242A>G
CM000672.1:g.89624242A>G
NC_000010.9:g.89614222A>G
NG_007466.2:g.6047A>G
NG_033079.1:g.3953T>C
ENST00000700029.2:c.16A>G
ENST00000710265.1:c.16A>G
ENST00000472832.3:c.16A>G
ENST00000688922.2:c.16A>G
ENST00000700021.1:c.16A>G
ENST00000700022.1:c.16A>G
ENST00000706954.1:c.16A>G
ENST00000706955.1:c.16A>G
ENST00000686459.1:c.16A>G
ENST00000688158.1:c.16A>G
ENST00000688308.1:c.16A>G
ENST00000693560.1:c.535A>G
ENST00000371953.8:c.16A>G
ENST00000371953.7:c.16A>G
ENST00000462694.1:n.18A>G
ENST00000487939.1:n.37A>G
ENST00000610634.1:c.-87A>G
NM_000314.5:c.16A>G
NM_000314.6:c.16A>G
NM_001304717.2:c.535A>G
NM_001304718.1:c.-690A>G
NM_000314.7:c.16A>G
NM_001304717.5:c.535A>G
NM_001304718.2:c.-690A>G

Met criteria codes 5

Expert Panel

Pathogenic

PM2 PP2 PS2_Very Strong PS4_Moderate PS3_Supporting

Evidence Links 4

PTEN VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.16A>G (p.Lys6Glu) 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). PS2_VS: One proven plus two assumed de novo observations in a patient with the disease and no family history. (internal laboratory contributor(s) SCV001369131.2, SCV001819316.1) PS4_M: Probands with phenotype specificity score of 2-3.5. (internal laboratory contributor(s) SCV001819316.1) 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. PS3_P: Abnormal in vitro cellular assay or transgenic model with phenotype different from wild type that does not meet PS3. (PMID 32366478, PMID 32350270, PMID 29706350)

Met criteria codes

PM2	✔	absent
PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2_Very Strong	✔	Internal lab cases SCV001369131.2, SCV001819316.1
PS4_Moderate	✔	Internal lab cases, 3 total phenotype specificity points (SCV001819316.1)
PS3_Supporting	✔	VCEP approved criteria based on combined published evidence suggesting some functional impact, but not strong enough for full PS3 score -1.62 (hypomorphic range) PubMed:29706350 WT-like abundance, indicating protein stability PubMed:29785012 no impact on stability, but LOF with respect to lipid phosphatase and some additional studies PubMed:32350270 partial LOF on spheroid formation and yeast assays, slight instability PubMed:32366478

Curation History

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