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.80A>G (p.Tyr27Cys)

Version: 1.1

CA16613238

404160 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: d78c91f0-0265-4f61-9c40-6a7bc3309acb
Approved on: 2023/10/11
Published on: 2023/10/18

HGVS expressions

NM_000314.8(PTEN):c.80A>G (p.Tyr27Cys)
NM_000314.8:c.80A>G
NC_000010.11:g.87894025A>G
CM000672.2:g.87894025A>G
NC_000010.10:g.89653782A>G
CM000672.1:g.89653782A>G
NC_000010.9:g.89643762A>G
NG_007466.2:g.35587A>G
ENST00000700029.2:c.80A>G
ENST00000710265.1:c.80A>G
ENST00000472832.3:c.80A>G
ENST00000688158.2:n.899+13587A>G
ENST00000688922.2:c.80A>G
ENST00000700021.1:c.80A>G
ENST00000700022.1:c.80A>G
ENST00000706954.1:c.80A>G
ENST00000706955.1:c.*115A>G
ENST00000686459.1:c.80A>G
ENST00000688158.1:c.*275+13587A>G
ENST00000688308.1:c.80A>G
ENST00000693560.1:c.599A>G
ENST00000371953.8:c.80A>G
ENST00000371953.7:c.80A>G
ENST00000462694.1:n.82A>G
ENST00000610634.1:c.-23A>G
NM_000314.5:c.80A>G
NM_000314.6:c.80A>G
NM_001304717.2:c.599A>G
NM_001304718.1:c.-626A>G
NM_000314.7:c.80A>G
NM_001304717.5:c.599A>G
NM_001304718.2:c.-626A>G

Likely Pathogenic

Met criteria codes 5

PS3_Moderate PP2 PP3 PM6_Strong PM2_Supporting

Not Met criteria codes 20

BP5 BP7 BP4 BP3 BP1 BP2 PS1 PS2 PP1 PP4 PM1 PM3 PM5 PM4 PVS1 BA1 BS1 BS4 BS3 BS2

Evidence Links 3

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.80A>G (p.Tyr27Cys) 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 3.0.0). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PM6_S: Assumed de novo, but without confirmation of paternity and maternity in a patient with the disease and no family history in a proband(s) with phenotype specificity score of 1-1.5 (PMID: 24375884). PS3_M: Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -1.648 (≤ -1.11) on a high throughput phosphatase assay (PMID:29706350). PM2_P: 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 > 0.7 (score of this variant = 0.991)

Met criteria codes

PS3_Moderate	✔	Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -1.648 (≤ -1.11) on a high throughput phosphatase assay (PMID:29706350). Note: discussed with team, decided to not apply criteria to Mingo given lack of positive control. Mighell et al (2018): High confidence variant, cum_score = -1.648 Low (score 0.35) protein abundance PubMed:29785012 Hypomorphic score -1.65. Score now below threshold (-1.11) for application of PS3_Moderate evidence per updated assessment guidelines. PubMed:29706350 Study appears to show loss of phosphatase activity and protein localization in nucleus or nucleus/cytoplasm. However, no positive control provided. PubMed:29706633
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 = 0.991)
PM6_Strong	✔	One proband with presumed de novo occurrence (maternity/paternity not confirmed) for a patient with highly specific phenotype. (PMID: 24375884) Vanderver 2014 (PMID: 24375884): Per v3 guidelines (released 3/27/23), can bump PM6 to PM6_S for de novo occurrence with highly specific phenotype (meets criteria to count towards PS4).

PM2_Supporting		✔	Absent in gnomAD

Not Met criteria codes

BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	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
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
PP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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

PVS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1		✖	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
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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