Variant: NM_000314.8(PTEN):c.530A>G (p.Tyr177Cys)

Version: 1.0

CA377484342

580948 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: d54df80d-a2f1-4e6b-88d4-e3884ce1c395
Approved on: 2025-12-05
Published on: 2025-12-17

HGVS expressions

NM_000314.8:c.530A>G
NM_000314.8(PTEN):c.530A>G (p.Tyr177Cys)
NC_000010.11:g.87952155A>G
CM000672.2:g.87952155A>G
NC_000010.10:g.89711912A>G
CM000672.1:g.89711912A>G
NC_000010.9:g.89701892A>G
NG_007466.2:g.93717A>G
ENST00000700029.2:c.530A>G
ENST00000710265.1:c.530A>G
ENST00000472832.3:c.530A>G
ENST00000688158.2:n.1265A>G
ENST00000688922.2:c.*360A>G
ENST00000700021.1:c.485A>G
ENST00000700022.1:c.493-5698A>G
ENST00000700023.1:n.1688A>G
ENST00000700024.1:n.1922A>G
ENST00000700025.1:n.1299A>G
ENST00000700029.1:c.364A>G
ENST00000706954.1:c.530A>G
ENST00000706955.1:c.*565A>G
ENST00000686459.1:c.*116A>G
ENST00000688158.1:c.*641A>G
ENST00000688308.1:c.530A>G
ENST00000688922.1:c.451A>G
ENST00000693560.1:c.1049A>G
ENST00000371953.8:c.530A>G
ENST00000371953.7:c.530A>G
NM_000314.5:c.530A>G
NM_000314.6:c.530A>G
NM_001304717.2:c.1049A>G
NM_001304718.1:c.-62A>G
NM_000314.7:c.530A>G
NM_001304717.5:c.1049A>G
NM_001304718.2:c.-62A>G

Likely Pathogenic

Met criteria codes 4

PS4 PP3 PM2_Supporting PS3_Moderate

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 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.530 (p.Tyr177Cys) 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). 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_M: Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -2.19 (≤ -1.11) on a high throughput phosphatase assay (PMID:29706350). PS4_P: Proband(s) with phenotype specificity score of 1-1.5. (internal laboratory contributor(s): SCV002643107.2, SCV005439375.1, SCV000833590.5) PM2_P: Absent in large sequenced populations

Met criteria codes

PS4	✔	Ambry 1 - male proband with sebaceous carcinoma, previous skin cancer (NOS) x2 in 30s. FHx: Mother with skin cancer NOS and history of 2-5 polyps; Father with prostate cancer in 60s and hx of 2-5 polyps. Sebaceous carcinoma is rare and highly specific for PHTS. Gene DX- Observed via exome (no parents tested though) in a kid with autism, seizures, dural AV fistules (counts as AVM), and macrocephaly. LabCorp We have observed this variant in approximately 5 individuals none of whom were counted as clinical evidence. Clinical indications for testing included epilepsy and macrocephaly, coarse facies, delays.
PP3	✔	REVEL score > 0.7. The REVEL score is .97
PM2_Supporting	✔	Ultra-rare in population databases (allele frequency < 0.001%)
PS3_Moderate	✔	study demonstrates impaired lipid phosphatase activity (PMID: 29706350 & 29785012);

Curation History

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