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Variant: NM_000314.8(PTEN):c.80A>C (p.Tyr27Ser)

Version: 1.0

CA10603162

280724 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1d6c53d1-6cb2-4e76-a5e8-dcc135e646ff
Approved on: 2023/8/4
Published on: 2023/10/19

HGVS expressions

NM_000314.8:c.80A>C
NM_000314.8(PTEN):c.80A>C (p.Tyr27Ser)
NC_000010.11:g.87894025A>C
CM000672.2:g.87894025A>C
NC_000010.10:g.89653782A>C
CM000672.1:g.89653782A>C
NC_000010.9:g.89643762A>C
NG_007466.2:g.35587A>C
ENST00000700029.2:c.80A>C
ENST00000710265.1:c.80A>C
ENST00000472832.3:c.80A>C
ENST00000688158.2:n.899+13587A>C
ENST00000688922.2:c.80A>C
ENST00000700021.1:c.80A>C
ENST00000700022.1:c.80A>C
ENST00000706954.1:c.80A>C
ENST00000706955.1:c.*115A>C
ENST00000686459.1:c.80A>C
ENST00000688158.1:c.*275+13587A>C
ENST00000688308.1:c.80A>C
ENST00000693560.1:c.599A>C
ENST00000371953.8:c.80A>C
ENST00000371953.7:c.80A>C
ENST00000462694.1:n.82A>C
ENST00000610634.1:c.-23A>C
NM_000314.5:c.80A>C
NM_000314.6:c.80A>C
NM_001304717.2:c.599A>C
NM_001304718.1:c.-626A>C
NM_000314.7:c.80A>C
NM_001304717.5:c.599A>C
NM_001304718.2:c.-626A>C

Likely Pathogenic

Met criteria codes 6

PS4_Supporting PP2 PP3 PS2 PM2_Supporting PS3_Supporting

Not Met criteria codes 1

BS3

Evidence Links 1

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>C (p.Tyr27Ser) 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). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. [internal laboratory contributor(s)] PS3_P: Other studies demonstrating lipid phosphatase activity <50% of wild-type or abnormal in vitro cellular assay or transgenic model with phenotype different from wild-type that does not meet PS3_moderate. Hans, et al. PMID: 10866302: demonstrated low phosphatase activity. PS4_P: Proband(s) with phenotype specificity score of 1-1.5. [internal laboratory contributor(s)] PM2_P: 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: in silico REVEL score of 0.966 (>0.7)

Met criteria codes

PS4_Supporting	✔	Gene Dx Case de novo case: child with extreme macrocephaly +5.5SD, autism, overgrowth, hypotonia; was de novo via WES. Gets PS2 and 1 point towards PS4_P.
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: .966 (>0.7).
PS2	✔	GeneDx de novo case via exome trio in child with extreme macrocephaly, hydrocephalus, GI polyps, motor delay, brain venous anomaly. Gets PS2
PM2_Supporting	✔	Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533).
PS3_Supporting	✔	Hans, et al. PMID: 10866302: demonstrated low phosphatase activity. VCEP agreed with applying PS3_Supporting. Demonstrates low phosphatase activity. PubMed:10866302

Not Met criteria codes

BS3		✖	Miguell PMID: 29706350; (- 0.778782855) WT-like, not > 0, so cannot apply BS3_supp

Curation History

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