

Variant: *NM_000314.8(PTEN):c.599T>C (p.Phe200Ser)*

Version: 2.0

CA000532 [↗](#)

189414 (ClinVar) [↗](#)

Gene: PTEN ([HGNC:5728](#))

Condition: PTEN hamartoma tumor syndrome ([MONDO:0017623](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 633ec420-0afb-4647-b05d-ed0a118f2469

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HGVS expressions

NM_000314.8(PTEN):c.599T>C (p.Phe200Ser)

NM_000314.8:c.599T>C

NC_000010.11:g.87952224T>C

CM000672.2:g.87952224T>C

NC_000010.10:g.89711981T>C

CM000672.1:g.89711981T>C

NC_000010.9:g.89701961T>C

NG_007466.2:g.93786T>C

ENST00000700029.2:c.599T>C

ENST00000710265.1:c.599T>C

ENST00000472832.3:c.599T>C

ENST00000688158.2:n.1334T>C

ENST00000688922.2:c.*429T>C

ENST00000700021.1:c.554T>C

ENST00000700022.1:c.493-5629T>C

ENST00000700023.1:n.1757T>C

ENST00000700024.1:n.1991T>C

ENST00000700025.1:n.1368T>C

ENST00000700029.1:c.433T>C

ENST00000706954.1:c.599T>C

ENST00000706955.1:c.*634T>C

ENST00000686459.1:c.*185T>C

ENST00000688158.1:c.*710T>C

ENST00000688308.1:c.599T>C

ENST00000688922.1:c.520T>C

ENST00000693560.1:c.1118T>C

ENST00000371953.8:c.599T>C

ENST00000371953.7:c.599T>C

ENST00000472832.2:c.26T>C

NM_000314.5:c.599T>C

NM_000314.6:c.599T>C

NM_001304717.2:c.1118T>C

NM_001304718.1:c.8T>C

NM_000314.7:c.599T>C

NM_001304717.5:c.1118T>C

NM_001304718.2:c.8T>C

Likely Pathogenic

Met criteria codes 4

PS4_Moderate PP2 PP3 PM2

Not Met criteria codes 22

BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP4 BP3 BP1 BP2
PVS1 PS1 PS2 PS3 PP1
PP4 PM6 PM1 PM3 PM5
PM4

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

Evidence submitted by expert panel

PTEN VCEP

PTEN c.599T>C (p.Phe200Ser) is currently classified as a variant of uncertain significance 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). PM2_P: Absent in gnomad v4. PS4_M: Probands with phenotype specificity score of 2-3.5. (internal laboratory contributor SCV000222124.11) 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 of 0.857, > 0.7 threshold.

Met criteria codes

PS4_Moderate			GDX1: child with extreme macrocephaly, DD, other neuro features, peds score = 5 = 1 PS4 point. GDX2: child with non-extreme macrocephaly, dev delay, lipoma vs. AVM, hemangioma, peds score minimum = 6 = 1 PS4 point. GDX3: child with autism, inherited from father, no other information available. No weight added.
PP2			PTEN is a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease.
PP3			REVEL score of 0.857, > 0.7 threshold.
PM2			Variant absent gnomAD v4.

Not Met criteria codes

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			Score -3.25 BUT not high confidence - no criteria can apply. PubMed:29706350 
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
PVS1			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
PS3			Low confidence for cummulative functional score in Mighell et al. 2018 (PMID: 29706350).
			Score -3.25 BUT not high confidence - no criteria can apply. PubMed:29706350 
PP1			GDX1/Invitae/Eng lab shared family: variant present in proband with macrocephaly, dev delay, penile freck; father with macrocephaly, lipomas, hemangioma, oral papillomas, polyps and pat uncle with lipomas and polyps. Also unaffected PGM and her mother with breast cancer dx 80. Per VCEP review count 2 meioses (proband, dad, pat uncle).
PP4			

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM6			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			Phe200Val at same codon, no VCEP curation, cannot apply PM5.
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



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