

Variant: NM_000314.6(PTEN):c.545T>C (p.Leu182Ser)

Version: 1.1

CA000177 [↗](#)

187827 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 37c0f7de-70de-4f9e-93c7-c0ada6770ecc

Approved on: 2023/12/1

Published on: 2023/12/14

HGVS expressions

NM_000314.6:c.545T>C

NM_000314.6(PTEN):c.545T>C (p.Leu182Ser)

NC_000010.11:g.87952170T>C

CM000672.2:g.87952170T>C

NC_000010.10:g.89711927T>C

CM000672.1:g.89711927T>C

NC_000010.9:g.89701907T>C

NG_007466.2:g.93732T>C

ENST00000700029.2:c.545T>C

ENST00000710265.1:c.545T>C

ENST00000472832.3:c.545T>C

ENST00000688158.2:n.1280T>C

ENST00000688922.2:c.*375T>C

ENST00000700021.1:c.500T>C

ENST00000700022.1:c.493-5683T>C

ENST00000700023.1:n.1703T>C

ENST00000700024.1:n.1937T>C

ENST00000700025.1:n.1314T>C

ENST00000700029.1:c.379T>C

ENST00000706954.1:c.545T>C

ENST00000706955.1:c.*580T>C

ENST00000686459.1:c.*131T>C

ENST00000688158.1:c.*656T>C

ENST00000688308.1:c.545T>C

ENST00000688922.1:c.466T>C

ENST00000693560.1:c.1064T>C

ENST00000371953.8:c.545T>C

ENST00000371953.7:c.545T>C

NM_000314.5:c.545T>C

NM_001304717.2:c.1064T>C

NM_001304718.1:c.-47T>C

NM_000314.7:c.545T>C

NM_001304717.5:c.1064T>C

NM_001304718.2:c.-47T>C

NM_000314.8:c.545T>C

Uncertain Significance

Met criteria codes3

PP2PP3PM2_Supporting

Not Met criteria codes22

PM1PM3PM5PM4PM6BS2BS1BS4BS3PVS1PS1PS2PS4BP5BP7BP4BP3BP1BP2BA1PP1PP4

Evidence Links4

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

PTEN c.545T>C (p.Leu182Ser) 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 3.0.0). Please see a summary of the rules and criteria codes in the “PTEN ACMG Specifications Summary” document (assertion method column). Of note, this variant may be disease-causing when present in the homozygous state (PMID: 26443266), but this expert panel curation is based on presence in the heterozygous state. 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. PP3: REVEL score > 0.7 (score of this variant =0.972)

Met criteria codes

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 is 0.972
PM2_Supporting			Absent in gnomAD.

Not Met criteria codes

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

PM6			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
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			Mighell results in WT-like range (-0.22) which is not >0, so no longer meets BS3 due to updated classification rules. HOM and HET pt cells appeared to show increase in S6 phosphorylation, but not as dramatic as R130Q. "Mitochondrial depolarization" also reported as increased, esp in HOM and 1 HET sample, but no pos control used and unclear relevance for criteria application. PubMed:26443266  Phosphatase activity in WT-like range (score -0.22). Value is < 0.0 so no longer meets criteria for BS3 due to updated classification criteria. PubMed:29706350 
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
PS4			HET parents unaffected so no criteria being applied as curating based on AD inheritance. KS agrees. Variant HOM in Turkish brother and sister from consanguineous parents. Both children had PHTS features (both with extreme macrocephaly, mild DD, hypotonia, absence seizures; boy also with penile freckles; girl also with dolicocephaly and adenoid hypertrophy). HET parents normal - no features and normal OFCs. PubMed:26443266  Appears to be same family as described in Schwerd 2016. PubMed:28097321  Variant identified in a pt with features of PHTS, but no details provided. PubMed:21194675 
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
BA1		×	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

Curation History 		
		
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