

Variant: NM_000314.8(PTEN):c.209T>C (p.Leu70Pro)

CA000350 [↗](#)

7826 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 12985d15-e1e7-45ab-b3e5-48e082086d4d

Approved on: 2018-11-28

Published on: 2018-12-10

HGVS expressions

NM_000314.8:c.209T>C

NM_000314.8(PTEN):c.209T>C (p.Leu70Pro)

NC_000010.11:g.87925557T>C

CM000672.2:g.87925557T>C

NC_000010.10:g.89685314T>C

CM000672.1:g.89685314T>C

NC_000010.9:g.89675294T>C

NG_007466.2:g.67119T>C

ENST00000700029.2:c.209T>C

ENST00000710265.1:c.209T>C

ENST00000472832.3:c.209T>C

ENST00000688158.2:n.944T>C

ENST00000688922.2:c.209T>C

ENST00000700021.1:c.165-5489T>C

ENST00000700022.1:c.209T>C

ENST00000700029.1:c.43T>C

ENST00000706954.1:c.209T>C

ENST00000706955.1:c.*244T>C

ENST00000686459.1:c.209T>C

ENST00000688158.1:c.*320T>C

ENST00000688308.1:c.209T>C

ENST00000688922.1:c.78T>C

ENST00000693560.1:c.728T>C

ENST00000371953.8:c.209T>C

ENST00000371953.7:c.209T>C

ENST00000498703.1:n.35T>C

ENST00000610634.1:c.107T>C

NM_000314.5:c.209T>C

NM_000314.6:c.209T>C

NM_001304717.2:c.728T>C

NM_001304718.1:c.-541-5489T>C

NM_000314.7:c.209T>C

NM_001304717.5:c.728T>C

NM_001304718.2:c.-541-5489T>C

Likely Pathogenic

Met criteria codes 5

PS3_ModeratePP2PP3PM2_SupportingPS4_Supporting

Not Met criteria codes 21

PS2PS1BP5BP7BP2BP3BP1BP4PP1PP4PM6BA1PM3PM1PM4PM5BS4BS3BS1BS2PVS1

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.209T>C (p.Leu70Pro) 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). PS3: Phosphatase activity <50% of wild type (PMID 29706350) 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. PS4_P: Proband(s) with phenotype specificity score of 1-1.5. (internal laboratory contributor(s) ClinVar Organization ID: 26957)			
Met criteria codes			
PS3_Moderate			Mighell et al data is approved for moderate weight in the truncation-like range
PP2			Missense – PP2 met – Last NT but does not appear to impact splicing (low spliceAI scores)
PP3			REVEL score 0.988
PM2_Supporting			Absent gnomAD v2 and v4
PS4_Supporting			Internal lab case ClinVar Organization ID: 26957 1 phenotype specificity point. Pt also published in 33887726
Not Met criteria codes			
PS2			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
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
BP2		✖	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
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1		✖	1 meiosis internal lab case ClinVar Organization ID: 26957; proband infant F with macrocephaly, variant also present in brother with macro, lipoma, dev delay
PP4		✖	Moved to PS4. 3 internal lab cases: #1 Young adult F, eth unk, Macrocephaly, FTC dx late teens, goiter, lipoma dx 3. Min CC score = 21. #2: 40s Asian F, BrCA dx 40s, goiter dx late 20s. OFC not provided. CC score = 5. #3: Pediatric M, eth unk, Macrocephaly, lipoma, dev delay. Peds score = 5, 1 PP4 point. His baby sister with macrocephaly also positive: 1 meiosis
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	Absent gnomAD
PM3		✖	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
PM4		✖	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
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

