

Variant: *NM_000314.6(PTEN):c.314G>A (p.Cys105Tyr)*

Version: 2.0

CA000393 [↗](#)

142261 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: dce7b398-e447-420b-8da1-a51cbf6a8e69

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HGVS expressions

NM_000314.6(PTEN):c.314G>A (p.Cys105Tyr)

NM_000314.6:c.314G>A

NC_000010.11:g.87933073G>A

CM000672.2:g.87933073G>A

NC_000010.10:g.89692830G>A

CM000672.1:g.89692830G>A

NC_000010.9:g.89682810G>A

NG_007466.2:g.74635G>A

ENST00000700029.2:c.314G>A

ENST00000710265.1:c.314G>A

ENST00000472832.3:c.314G>A

ENST00000688158.2:n.1049G>A

ENST00000688922.2:c.*144G>A

ENST00000700021.1:c.269G>A

ENST00000700022.1:c.314G>A

ENST00000700029.1:c.148G>A

ENST00000706954.1:c.314G>A

ENST00000706955.1:c.*349G>A

ENST00000686459.1:c.314G>A

ENST00000688158.1:c.*425G>A

ENST00000688308.1:c.314G>A

ENST00000688922.1:c.235G>A

ENST00000693560.1:c.833G>A

ENST00000371953.8:c.314G>A

ENST00000371953.7:c.314G>A

ENST00000498703.1:n.140G>A

ENST00000610634.1:c.212G>A

NM_000314.5:c.314G>A

NM_001304717.2:c.833G>A

NM_001304718.1:c.-437G>A

NM_000314.7:c.314G>A

NM_001304717.5:c.833G>A

NM_001304718.2:c.-437G>A

NM_000314.8:c.314G>A

Pathogenic

Met criteria codes 6

PS3_Moderate

PP2

PP3

PM2

PS2

PM6_Strong

Not Met criteria codes 20

BP5

BP7

BP4

BP3

BP1

BP2

BS2

BS1

BS4

BS3

PP1

PP4

PM1

PM3

PM5

PM4

PS1

PS4

BA1

PVS1

Evidence Links 3

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			
<p>PTEN c.314G>A (p.Cys105Tyr) meets criteria to be classified as pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (PMID 30311380). Please see a summary of the rules and criteria codes in the “PTEN ACMG Specifications Summary” document (assertion method column). PM2_P: Absent in large sequenced populations (PMID 27535533). PM6_S: Assumed de novo, but without confirmation of paternity and maternity in a patient with the disease and no family history and highly specific phenotype. (internal laboratory contributor ClinVar Organization ID 26957) 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 =0.9) PS3_M: Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -2.06 (≤ -1.11) on a high throughput phosphatase assay (PMID:29706350). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. (internal laboratory contributor ClinVar Organization ID: 26957)</p>			
Met criteria codes			
PS3_Moderate	<div><div></div><div></div></div>	✓	<p>Mighell = -2.06, in hypomorphic range.</p> <p>Variant scored in "hypomorphic" range on high-throughput phosphatase assay. No criteria applies.</p> <div>PubMed:29706350</div> <p>Variant disrupts interaction with LKB1 in Y2H assay. <div>PubMed:15987703</div></p>
PP2	<div><div></div><div></div></div>	✓	<p>I agree (FH)</p>
PP3	<div><div></div><div></div></div>	✓	<p>REVEL = 0.9</p>
PM2		✓	<p>Absent in gnomAD I agree (FH)</p>
PS2	<div><div></div><div></div></div>	✓	<p>Internal case ClinVar Organization ID 26957, de novo via WES trio in pt with NDD, macrocephaly NOS, skin tags, cortical dysplasia, seizures.</p>
PM6_Strong	<div><div></div><div></div></div>	✓	<p>Internal case ClinVar Organization ID 26957, peds score =8. I agree (FH)</p>

Not Met criteria codes			
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		✖	I agree (FH)
BP2		✖	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		✖	Absent in gnomAD I agree (FH)
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	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		✖	<p>GDx internal case with peds score = 8. I agree (FH) Criteria moved to PS4 section.</p> <hr/> <p>Reported in "sporadic" BRR case with GI polyps, lipoma, penile freckling. If adult, CC score minimum = 7. If child, peds score minimum = 4. PubMed:10400993 </p>
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		✖	Could curate C105F if needed to help this get to PATH.

PM4			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
PS4			GDx internal case with peds score = 8; assumed de novo case, PS4_P met but used to bump PM6 to PM6_S.
BA1			Absent in gnomAD I agree (FH)
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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Showing 1 to 3 of 3 rows		
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