The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000314.8(PTEN):c.520T>A (p.Tyr174Asn)

CA000501

142220 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 58b7be5a-c98e-4344-9f4f-cff2dd70911d
Approved on: 2018-04-06
Published on: 2018-12-10

HGVS expressions

NM_000314.8(PTEN):c.520T>A (p.Tyr174Asn)
NM_000314.8:c.520T>A
NC_000010.11:g.87952145T>A
CM000672.2:g.87952145T>A
NC_000010.10:g.89711902T>A
CM000672.1:g.89711902T>A
NC_000010.9:g.89701882T>A
NG_007466.2:g.93707T>A
ENST00000700029.2:c.520T>A
ENST00000710265.1:c.520T>A
ENST00000472832.3:c.520T>A
ENST00000688158.2:n.1255T>A
ENST00000688922.2:c.*350T>A
ENST00000700021.1:c.475T>A
ENST00000700022.1:c.493-5708T>A
ENST00000700023.1:n.1678T>A
ENST00000700024.1:n.1912T>A
ENST00000700025.1:n.1289T>A
ENST00000700029.1:c.354T>A
ENST00000706954.1:c.520T>A
ENST00000706955.1:c.*555T>A
ENST00000686459.1:c.*106T>A
ENST00000688158.1:c.*631T>A
ENST00000688308.1:c.520T>A
ENST00000688922.1:c.441T>A
ENST00000693560.1:c.1039T>A
ENST00000371953.8:c.520T>A
ENST00000371953.7:c.520T>A
NM_000314.5:c.520T>A
NM_000314.6:c.520T>A
NM_001304717.2:c.1039T>A
NM_001304718.1:c.-72T>A
NM_000314.7:c.520T>A
NM_001304717.5:c.1039T>A
NM_001304718.2:c.-72T>A

Likely Pathogenic

Met criteria codes 5

PM5 PS3_Moderate PM2_Supporting PP2 PP3

Not Met criteria codes 2

PS4 PP1

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.520T>A (p.Tyr174Asn) meets criteria to be classified as likely pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria v3.1.0 (PMID 30311380). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PM5: Missense change at the same amino acid position and equal BLOSUM62 score (Henikoff et al. 1992 (PMID: 1438297)). c.521A>G (p.Tyr174Cys), has been identified and characterized by PTEN VCEP as likely pathogenic. PS3_M: Truncation-like score of -2.92 in Massively parallel functional assay interrogating phosphatase activity Mighell et al. 2018 (PMID: 29706350). Additionally, mutated protein found to have greater than 50% reduction in phosphatase activity in Han et al. 2000 (PMID: 10866302). PP2: PTEN classified 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 (.946) greater than 0.7. PM2_P: Variant absent from gnomad v4.

Met criteria codes

PM5	✔	Missense change at the same amino acid position and equal BLOSUM62 score (Henikoff et al. 1992 (PMID: 1438297)). c.521A>G (p.Tyr174Cys), has been identified and characterized by PTEN VCEP as likely pathogenic.
PS3_Moderate	✔	Truncation-like score of -2.92 in Massively parallel functional assay interrogating phosphatase activity Mighell et al. 2018 (PMID: 29706350). Additionally, mutated protein found to have greater than 50% reduction in phosphatase activity in Han et al. 2000 (PMID: 10866302). Score -2.92 truncation-like range PubMed:29706350
PM2_Supporting	✔	Variant absent from gnomad v4.
PP2	✔	PTEN classified 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 (.946) greater than 0.7.

Not Met criteria codes

PS4	✖	Internal laboratory submission of proband and two sons positive for p.Y174N. Proband presented with more than 5 gastrointestinal polyps, both sons had macrocephaly, one with extreme macrocephaly. Cleavand clinic scores not

high enough to apply weight.

PP1		✖	Co-segregation in two -meioses

Curation History

Showing 1 to 2 of 2 rows

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