

Variant: NM_000314.7(PTEN):c.838A>G (p.Ile280Val)

Version: 1.1

CA377485551 [↗](#)

468719 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d625033c-bcc2-4e6c-ad5d-f0259d0cf8d7

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HGVS expressions

NM_000314.7(PTEN):c.838A>G (p.Ile280Val)

NM_000314.7:c.838A>G

NC_000010.11:g.87960930A>G

CM000672.2:g.87960930A>G

NC_000010.10:g.89720687A>G

CM000672.1:g.89720687A>G

NC_000010.9:g.89710667A>G

NG_007466.2:g.102492A>G

ENST00000700029.2:c.931A>G

ENST00000710265.1:c.838A>G

ENST00000472832.3:c.838A>G

ENST00000688158.2:n.1573A>G

ENST00000688922.2:c.*668A>G

ENST00000700021.1:c.793A>G

ENST00000700022.1:c.*177A>G

ENST00000700023.1:n.1996A>G

ENST00000700024.1:n.2230A>G

ENST00000700025.1:n.1607A>G

ENST00000700026.1:n.475A>G

ENST00000700029.1:c.765A>G

ENST00000706954.1:c.838A>G

ENST00000706955.1:c.*873A>G

ENST00000686459.1:c.*424A>G

ENST00000688158.1:c.*949A>G

ENST00000688308.1:c.838A>G

ENST00000688922.1:c.759A>G

ENST00000693560.1:c.1357A>G

ENST00000371953.8:c.838A>G

ENST00000371953.7:c.838A>G

ENST00000472832.2:c.265A>G

NM_000314.5:c.838A>G

NM_000314.6:c.838A>G

NM_001304717.2:c.1357A>G

NM_001304718.1:c.247A>G

NM_001304717.5:c.1357A>G

NM_001304718.2:c.247A>G

NM_000314.8:c.838A>G

Uncertain Significance

Met criteria codes 3

PP2 PM2 BS3

Not Met criteria codes 23

PS1 PS2 PS3 PS4 BA1 PP1
PP3 PP4 PM6 PM1 PM3
PM5 PM4 BS2 BS1 BS4
PVS1 BP5 BP7 BP4 BP3
BP1 BP2

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 3.2.0

Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

PTEN VCEP

PTEN c.838A>G (p.Ile280Val) is currently classified as a variant of uncertain significance 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: present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (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. BS3: Missense variants with both lipid phosphatase activity AND results from a second assay appropriate to the protein domain demonstrating no statistically significant difference from wild type. (PMID 29706350, PMID 29785012)

Met criteria codes

PP2		✓	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2		✓	Allele frequency reported: 1/112924 in Finnish ancestry in gnomAD and 1/249790 in total population, or <0.00001 (0.001%) allele frequency.
BS3		✓	Matreyek et al. lists variant as having a cumulative score of 1.012413 which is in the WT-like range. Miguell et al. lists variant as -0.063958094 which is in the WT-like range meeting BS3/BS3_supporting)

Not Met criteria codes

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			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4			Gene Dx internal case: proband Cauc M child with hypotonia, macrocephaly +3SD, motor delay, no GU exam. Mom POSITIVE, has asthma and hypoglycemia, she has a mat half-brother with RCC dx 30s but no other cancers. Ped proband specificity score = 4 only (no point).
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
PP3			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
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			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
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
PVS1			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

Curation History 		
		
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