

Variant: NM_000314.8(PTEN):c.181C>G (p.His61Asp)

CA000330 [↗](#)

7841 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 37398c37-6caa-4c1d-a1b1-3881be31e38b

Approved on: 2018-07-25

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HGVS expressions

NM_000314.8(PTEN):c.181C>G (p.His61Asp)

NM_000314.8:c.181C>G

NC_000010.11:g.87925529C>G

CM000672.2:g.87925529C>G

NC_000010.10:g.89685286C>G

CM000672.1:g.89685286C>G

NC_000010.9:g.89675266C>G

NG_007466.2:g.67091C>G

ENST00000700029.2:c.181C>G

ENST00000710265.1:c.181C>G

ENST00000472832.3:c.181C>G

ENST00000688158.2:n.916C>G

ENST00000688922.2:c.181C>G

ENST00000700021.1:c.165-5517C>G

ENST00000700022.1:c.181C>G

ENST00000700029.1:c.15C>G

ENST00000706954.1:c.181C>G

ENST00000706955.1:c.*216C>G

ENST00000686459.1:c.181C>G

ENST00000688158.1:c.*292C>G

ENST00000688308.1:c.181C>G

ENST00000688922.1:c.50C>G

ENST00000693560.1:c.700C>G

ENST00000371953.8:c.181C>G

ENST00000371953.7:c.181C>G

ENST00000498703.1:n.7C>G

ENST00000610634.1:c.79C>G

NM_000314.5:c.181C>G

NM_000314.6:c.181C>G

NM_001304717.2:c.700C>G

NM_001304718.1:c.-541-5517C>G

NM_000314.7:c.181C>G

NM_001304717.5:c.700C>G

NM_001304718.2:c.-541-5517C>G

Likely Pathogenic

Met criteria codes 5

- PS3_Moderate
- PP2
- PP3
- PM6
- PM2

Not Met criteria codes 21

- PVS1
- BA1
- BP5
- BP7
- BP2
- BP1
- BP4
- BP3
- BS2
- BS4
- BS3
- BS1
- PP4
- PP1
- PM3
- PM1
- PM5
- PM4
- PS2
- PS4
- PS1

Evidence Links 4

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.181C>G (p.His61Asp) meets criteria to be classified as likely 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). PS3: Phosphatase activity <50% of wild type (PMID 29706350, PMID 17942903, PMID 21828076) PM2: Absent in large sequenced populations (PMID 27535533). PM6: Assumed de novo, but without confirmation of paternity and maternity in a patient with the disease and no family history. (PMID 11748304) 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.

Met criteria codes

PS3_Moderate			Variant demonstrated loss of function when analyzed in vivo in yeast. Variant demonstrated no activity in vivo and demonstrated low protein expression levels in yeast. Variant was strongly destabilized in MCF-7cells. Per Felicia, I agree. Variant demonstrated no activity in vivo and demonstrated low protein expression levels in yeast. Variant was strongly destabilized in MCF-7cells. PubMed:17942903  score -3.85 PubMed:29706350  Variant demonstrated loss of function when analyzed in vivo in yeast. PubMed:21828076 
PP2			PP2 applied because of low rate of benign missense variation. Per Felicia, I agree.
PP3			Variant is the incorrect variant type to apply these criteria.
PM6			Reardon 2001. Case report of a male patient identified during gestation as probably having a tracheoesophageal fistula, owing to polyhydramnios and an absent stomach bubble on ultrasonography. Macrocephaly and bilateral hand malformations noted at birth. Mutation analysis showed a de novo germline mutation, H61D, not present in either parent and paternity is confirmed. PubMed:11748304 
PM2			Variant not present in population databases. Per Felicia, I agree.

Not Met criteria codes

PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			Variant not present in population databases. Per Felicia, I agree.
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
BP1		✖	PP2 applied because of low rate of benign missense variation. Per Felicia, I agree.
BP4		✖	Variant is the incorrect variant type to apply these criteria.
BP3		✖	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
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	Variant demonstrated loss of function when analyzed in vivo in yeast. Variant demonstrated no activity in vivo and demonstrated low protein expression levels in yeast. Variant was strongly destabilized in MCF-7cells. Per Felicia, I agree.
BS1		✖	Variant not present in population databases. Per Felicia, I agree.
PP4		✖	Patient phenotype information provided in paper does not meet a CC score or 4 or greater. Per Felicia, I agree. Patient phenotype information provided in paper does not meet a CC score or 4 or greater. PubMed:11748304 
PP1		✖	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
PM1		✖	Variant does not occur within specified residues.
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
PS2		✖	Case report of a male patient identified during gestation as probably having a tracheoesophageal fistula, owing to polyhydramnios and an absent stomach bubble on ultrasonography. Macrocephaly and bilateral hand malformations noted at birth. Mutation analysis showed a de novo germline mutation, H61D, not present in either parent and

paternity is confirmed. Per Felicia, I feel the the case in Reardon et al. should be PM6 since they didn't state whether maternity was confirmed. PM6 to be applied instead of PS2.

Case report of a male patient identified during gestation as probably having a tracheooesophageal fistula, owing to polyhydramnios and an absent stomach bubble on ultrasonography. Macrocephaly and bilateral hand malformations noted at birth. Mutation analysis showed a de novo germline mutation, H61D, not present in either parent and paternity is confirmed. [PubMed:11748304](#)

PS4			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

Curation History



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