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_000314.6(PTEN):c.395G>A (p.Gly132Asp)

CA000444

92822 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 9c15b246-ef9f-4f55-a246-126b49710717
Approved on: 2018-04-06
Published on: 2018-12-10

HGVS expressions

NM_000314.6:c.395G>A
NM_000314.6(PTEN):c.395G>A (p.Gly132Asp)
NC_000010.11:g.87933154G>A
CM000672.2:g.87933154G>A
NC_000010.10:g.89692911G>A
CM000672.1:g.89692911G>A
NC_000010.9:g.89682891G>A
NG_007466.2:g.74716G>A
ENST00000371953.8:c.395G>A
ENST00000371953.7:c.395G>A
ENST00000498703.1:n.221G>A
ENST00000610634.1:c.293G>A
NM_000314.5:c.395G>A
NM_001304717.2:c.914G>A
NM_001304718.1:c.-356G>A
NM_000314.7:c.395G>A
NM_001304717.5:c.914G>A
NM_001304718.2:c.-356G>A
NM_000314.8:c.395G>A
NM_000314.8(PTEN):c.395G>A (p.Gly132Asp)

Pathogenic

Met criteria codes 5

PM6 PM2 PS3 PS4 PP2

Evidence Links 5

Expert Panel

PTEN VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

PTEN VCEP

PTEN c.395G>A (p.Gly132Asp) 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). PS3: Phosphatase activity <50% of wild type (PMID 29706350, PMID

32350270) PS4: Probands with phenotype specificity score of 4-15.5 (PMID 25288137, PMID 23335809, PMID 23470840, internal laboratory contributor(s) SCV000279163) 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. (Internal laboratory contributor(s) SCV000279163) 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

PM6	✔	Internal laboratory case.
PM2	✔	Absent in gnomAD
PS3	✔	LOF for multiple assays c/w Mighell results PubMed:32350270 Score -3.36, truncation-like range PubMed:29706350
PS4	✔	2.5 phenotype specificity points from literature, additional 1.5 points from internal laboratory case. 4yo M with autism and OFC +5.9SD. Peds score = 5 = 1 phenotype specificity point. PubMed:25288137 Adult pt in Eng lab publications (Busch 2013, Hobert 2012, Heindl 2012, Heald 2010, Tan 2011) – conservative CC score = 50 = 1 phenotype specificity point. PubMed:23470840 3 probands in Bubien 2013: #1: minimum CC score = 15; #2: also likely the pt in Derrey 2013, minimum CC score = 25 = 0.5 phenotype specificity point; #3: minimum CC score = 16. PubMed:23335809
PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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