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.512dup (p.Arg172Glufs)

Version: 1.0

CA645369422

428206 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: df053db0-9ad9-48ee-aea1-550cda8b3586
Approved on: 2019/3/5
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HGVS expressions

NM_000314.6:c.512dup
NM_000314.6(PTEN):c.512dup (p.Arg172Glufs)
NC_000010.11:g.87952137dup
CM000672.2:g.87952137dup
NC_000010.10:g.89711894dup
CM000672.1:g.89711894dup
NC_000010.9:g.89701874dup
NG_007466.2:g.93699dup
ENST00000700029.2:c.512dup
ENST00000710265.1:c.512dup
ENST00000472832.3:c.512dup
ENST00000688158.2:n.1247dup
ENST00000688922.2:c.*342dup
ENST00000700021.1:c.467dup
ENST00000700022.1:c.493-5716dup
ENST00000700023.1:n.1670dup
ENST00000700024.1:n.1904dup
ENST00000700025.1:n.1281dup
ENST00000700029.1:c.346dup
ENST00000706954.1:c.512dup
ENST00000706955.1:c.*547dup
ENST00000686459.1:c.*98dup
ENST00000688158.1:c.*623dup
ENST00000688308.1:c.512dup
ENST00000688922.1:c.433dup
ENST00000693560.1:c.1031dup
ENST00000371953.8:c.512dup
ENST00000371953.7:c.512dup
NM_000314.5:c.512dup
NM_001304717.2:c.1031dup
NM_001304718.1:c.-80dup
NM_000314.7:c.512dup
NM_001304717.5:c.1031dup
NM_001304718.2:c.-80dup
NM_000314.8:c.512dup

Pathogenic

Met criteria codes 3

PM2 PS4_Supporting PVS1

Not Met criteria codes 22

PM6 PM1 PM3 PM5 PM4
BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP4 BP3 BP1 BP2 PS1
PS2 PS3 PP1 PP2 PP3

Evidence Links 10

Expert Panel

PTEN VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

PTEN VCEP

PTEN c.512dup (p.R172Efs) 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). PVS1: Null variant predicted to result in nonsense-mediated decay or causing truncation/frameshift at or 5' to c.1121 (NM_000314.4). PM2: Absent in large sequenced populations (PMID 27535533). PS4_P: Proband(s) with phenotype specificity score of 1-1.5. (PMID 17526801)

Met criteria codes

PM2	✔	Absent in gnomAD. (JM agree)
PS4_Supporting	✔	Per K. Sesock: At least 2 patients (please see notes below). A patient with CC score = at least 10, and a pediatric patient with a peds score = 11. Per J. Mester: agree PS4_supporting; strongly suspect pt reported in CCF and Boston publications is the same individual.

Author overlap and likely patient overlap with PMIDs 21194675, 20600018, 21956414, 22261759. Variant listed identified in this study in Supplementary Table 4. PubMed:25669429

Variant referred to as c.514dupA in Table 2, and 4 patients with variant are reported. No additional patient specific information reported. PubMed:21659347

Author overlap and possible patient overlap with PMIDs 21194675, 20600018, 21956414, 22261759, 25669429. This study reports a 21-year-old female with Cowden syndrome and lymphoid hyperplasia. This could be the same patient as the 19.4-year-old patient reported in PMID 21194675, however there is limited information to confirm if this is the same patient or not. PubMed:27477328

Author overlap and likely patient overlap with PMIDs 21194675, 20600018, 21956414. PubMed:22261759

Patient 3349: Multiple hamartomas. No additional patient specific information reported. CC score = 10 (at least) PubMed:20600018

Author overlap and likely patient overlap with PMIDs 21194675, 20600018. PubMed:21956414

Institution overlap, author overlap, and likely patient overlap with PMID 20600018. Patient age of 19.4 is listed in Table S2, however no additional patient specific information reported. PubMed:21194675

Likely patient overlap with PMIDs 17526801, 20962022. PubMed:21190448

Institution overlap (no author overlap) and patient overlap with PMID 17526801. Authors further characterize thyroid findings to include 2.0-cm nodule in left thyroid lobe, thyroidectomy revealed multiple follicular adenomas with a papillary microcarcinoma in the largest adenoma PubMed:20962022

Reviewed by K. Sesock: Patient 16: Variant referred to as c.513insA. Female, 8.5 years at diagnosis, GI polyps. Maternal uncle with PTEN mutation. 7 years at first PHTS symptom of multiple GI polyps. OFC = >97%. None of the following present: mental retardation/global developmental delay, pervasive developmental disorder. Normal brain MRI performed for the indication of macrocephaly, large anterior fontanelle at 23 months. Also, diagnosed with non-medullary thyroid cancer, solitary thyroid nodule, genitourinary malformation, lipomas. Peds score = 11. (JM agree 1 phenotype specificity point) PubMed:17526801

PVS1		✔	Premature termination codon (frameshift) subject to nonsense-mediated decay. (JM agree)

Not Met criteria codes

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
BA1		✖	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
BS3		✖	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
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
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
PP1		✖	Patient from PMID 17526801 has a maternal uncle with PTEN mutation, however not enough meioses to meet criteria.
PP2		✖	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

Curation History

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