

Variant: *NM_000277.3:c.134T>C*

Version: 1.0

CA16020730 [↗](#)

805809 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: b21b61c5-295c-4c84-9398-395bfe6b5da3

Approved on: 2019/4/4

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HGVS expressions

NM_000277.3:c.134T>C

NC_000012.12:g.102912825A>G

CM000674.2:g.102912825A>G

NC_000012.11:g.103306603A>G

CM000674.1:g.103306603A>G

NC_000012.10:g.101830733A>G

NG_008690.1:g.9778T>C

NG_008690.2:g.50586T>C

ENST00000553106.6:c.134T>C

ENST00000307000.7:c.119T>C

ENST00000546844.1:c.134T>C

ENST00000548677.2:n.221T>C

ENST00000548928.1:n.56T>C

ENST00000549111.5:n.230T>C

ENST00000550978.6:c.118T>C

ENST00000551337.5:c.134T>C

ENST00000551988.5:n.223T>C

ENST00000553106.5:c.134T>C

ENST00000635500.1:n.102T>C

NM_000277.1:c.134T>C

NM_000277.2:c.134T>C

NM_001354304.1:c.134T>C

NM_001354304.2:c.134T>C

Uncertain Significance

Met criteria codes **2**

PM2 PP4

Not Met criteria codes **2**

PM3 PP3

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.134T>C (p.Val45Ala) PAH variant has been reported in a patient with mild hyperphenylalaninemia (PMID: 22513348). This variant is absent from 1000G, ESP, and gnomAD databases. It is a missense variant with conflicting predictions of pathogenicity: SIFT: Tolerated, PolyPhen: Benign, MutationTaster: Disease causing, REVEL=0.697. In summary, this variant meets criteria to be classified as uncertain significance for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PP4.

Met criteria codes

PM2		Absent from ExAC, gnomAD, 1000G, ESP.
PP4		Detected in a patient with MHP, BH4 deficiency not reported to be ruled out PMID: 22513348
p.V45A was detected in a patient with MHP (Phe < 0.6 mmol/L on a normal diet). PubMed:22513348		

Not Met criteria codes

PM3		detected with p.P281L, but segregation studies not reported
Patient 62 genotype: p.V45A p.P281L, but no segregation studies reported PubMed:22513348		
PP3		Conflicting predictions of pathogenicity: SIFT: Tolerated, PolyPhen: Benign, MutationTaster: Disease causing; REVEL=0.697.

Curation History

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