

Variant: *NM_000277.3:c.1154T>C*

Version: 1.0

CA16020951 [↗](#)

2682167 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 11e1322e-9388-417b-aa8f-2016b206fa5a

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HGVS expressions

NM_000277.3:c.1154T>C

NC_000012.12:g.102843691A>G

CM000674.2:g.102843691A>G

NC_000012.11:g.103237469A>G

CM000674.1:g.103237469A>G

NC_000012.10:g.101761599A>G

NG_008690.1:g.78912T>C

NG_008690.2:g.119720T>C

ENST00000553106.6:c.1154T>C

ENST00000307000.7:c.1139T>C

ENST00000549247.6:n.913T>C

ENST00000551114.2:n.816T>C

ENST00000553106.5:c.1154T>C

ENST00000635477.1:c.258T>C

ENST00000635528.1:n.669T>C

NM_000277.1:c.1154T>C

NM_000277.2:c.1154T>C

NM_001354304.1:c.1154T>C

NM_001354304.2:c.1154T>C

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate PP3 PM3 PM2

Not Met criteria codes **2**

PM5 PS3

Evidence Links **0**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1154T>C (p.Leu385Pro) variant in PAH has been reported in at least 3 Chinese patients with Phe > 120umol/L (BH4 deficiency excluded) (PP4_Moderate; PMIDs:29499199, 23932990). This variant was detected in the homozygous state in two patients (PM3;

PMID:23932990). This variant is absent in population databases (PM2). This variant is predicted deleterious by SIFT, PolyPhen, MutationTaster, and REVEL = 0.817 (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PP4_Moderate, PM3, PP3.

Met criteria codes

PP4_Moderate			At least 2 classic PKU patients are reported in PMID: 23932990 with Phe >1200umol/L and BH4 deficiency ruled out via urinary pterin analysis with HPLC and DHPR activity assay.
PP3			Variant predicted deleterious by SIFT, PolyPhen, MutationTaster, and REVEL = 0.817.
PM3			PMID: 23932990 2 Patients are reported to be homozygous for Leu385Pro - 1.0 points
PM2			Variant absent from population databases

Not Met criteria codes

PM5			c.1155G>C (p.L385L) reported in PAH database, but absent in ClinVar and ClinGen Allele Registry, predicted benign by in silico models
PS3			PMID: 23932990 - predicted null based on identification in patient with classic PKU in homoallelic state

Curation History

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