

Variant: *NM_000277.3(PAH):c.1229T>G (p.Phe410Cys)*

Version: 1.0

CA229406 [↗](#)

102572 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: e9257609-957e-41b4-95ab-02e30f8c924c

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HGVS expressions

NM_000277.3(PAH):c.1229T>G (p.Phe410Cys)

NM_000277.3:c.1229T>G

NC_000012.12:g.102840486A>C

CM000674.2:g.102840486A>C

NC_000012.11:g.103234264A>C

CM000674.1:g.103234264A>C

NC_000012.10:g.101758394A>C

NG_008690.1:g.82117T>G

NG_008690.2:g.122925T>G

ENST00000553106.6:c.1229T>G

ENST00000307000.7:c.1214T>G

ENST00000551114.2:n.891T>G

ENST00000553106.5:c.1229T>G

ENST00000635477.1:c.333T>G

ENST00000635528.1:n.744T>G

NM_000277.1:c.1229T>G

NM_000277.2:c.1229T>G

NM_001354304.1:c.1229T>G

NM_001354304.2:c.1229T>G

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PP3 PM2 PM3

Not Met criteria codes 1

PM5

Evidence Links 1

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information !

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1229T>G (p.Phe410Cys) variant in PAH has been detected in two Portuguese patients with moderate PKU (serum Phe = 6.6mg/dL and 15.0mg/dL); BH4 deficiency excluded via urinary pterin analysis (PMID N/A - linked article; PP4_Moderate). This variant was detected

with L249F (reported as Pathogenic in ClinVar; VarID:102821; 7 submitters) and R270K (reported as Pathogenic in ClinVar; VarID:102846; 5 submitters) - phase not confirmed - 1.0 points (PMID N/A - linked article; PM3). This variant is absent from population databases (PM2). This variant is predicted deleterious by SIFT, PolyPhen2, MutationTaster, and REVEL = 0.99. 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			Linked article - F410C detected in two Portuguese patients with moderate PKU (serum Phe = 6.6mg/dL and 15.0mg/dL); BH4 deficiency excluded via urinary pterin analysis
<div>PubMed:18798839 </div>			
PP3			Variant predicted deleterious by SIFT, PolyPhen2, MutationTaster, and REVEL = 0.99.
PM2			Variant absent from population databases.
PM3			Linked article - F410C detected with L249F (reported as Pathogenic in ClinVar; VarID:102821; 7 submitters) and R270K (reported as Pathogenic in ClinVar; VarID:102846; 5 submitters) - phase not confirmed - 1.0 points

Not Met criteria codes

PM5			Variant as same amino acid residue as NM_000277.3(PAH):c.1229T>C (p.Phe410Ser) (ClinVarID:102571, VUS, 2 submitters, not yet curated by ClinGen PAH VCEP) and c.1228T>A (p.Phe410Ile) which is not reported in ClinVar and has been curated as Likely Pathogenic by ClinGen PAH VCEP
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Curation History

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