

Variant: *NM_001354304.2:c.1228T>A*

Version: 1.0

CA16020973 [↗](#)

932279 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: c902ca40-4683-4efb-bbf2-b066017fac3b

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HGVS expressions

NM_001354304.2:c.1228T>A
NC_000012.12:g.102840487A>T
CM000674.2:g.102840487A>T
NC_000012.11:g.103234265A>T
CM000674.1:g.103234265A>T
NC_000012.10:g.101758395A>T
NG_008690.1:g.82116T>A
NG_008690.2:g.122924T>A
ENST00000553106.6:c.1228T>A
ENST00000307000.7:c.1213T>A
ENST00000551114.2:n.890T>A
ENST00000553106.5:c.1228T>A
ENST00000635477.1:c.332T>A
ENST00000635528.1:n.743T>A
NM_000277.1:c.1228T>A
NM_000277.2:c.1228T>A
NM_001354304.1:c.1228T>A
NM_000277.3:c.1228T>A

Likely Pathogenic

Met criteria codes 4

PP3 PP4 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 variant c.1228T>A (p.Phe410Ile) in PAH has been reported in 1 Danish patient with mild/moderate PKU (BH4 deficiency not excluded) (PMID: 26542770; PP4). This same patient carried this variant in trans with the previously reported c.1315+1G>A variant which has been reported as Pathogenic in ClinVar (PMID: 26542770; PM3). This variant is absent from population databases (PM2) and is predicted

deleterious by SIFT, PolyPhen2, MutationTaster, and REVEL = 0.969 (PP3). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP3, PP4.

Met criteria codes

PP3			Variant predicted deleterious by SIFT, PolyPhen2, MutationTaster, and REVEL = 0.969.
PP4			PMID: 26542770 - F410I detected in 1 Danish patient with moderate/mild PKU (Phe = 600-1200umol/L), BH4 deficiency not excluded. <div>PubMed:26542770 </div>
PM2			Variant absent from population databases
PM3			PMID: 26542770 - F410I detected in trans in with c.1315+1G>A, reported as Pathogenic in ClinVar, confirmed in trans (VarID:576, 19 submitters) - 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.1229T>G (p.Phe410Cys) (ClinVarID: 102572, no interpretation, 1 submitter) and has been curated by the ClinGen PAH VCEP as VUS.
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Curation History

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