

Variant: *NM_000277.3(PAH):c.1304A>T (p.Asp435Val)*

Version: 1.0

CA386492936 [↗](#)

625291 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5f40c3bc-a96c-4619-bf95-57c324cff700

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HGVS expressions

NM_000277.3(PAH):c.1304A>T (p.Asp435Val)

NM_000277.3:c.1304A>T

NC_000012.12:g.102840411T>A

CM000674.2:g.102840411T>A

NC_000012.11:g.103234189T>A

CM000674.1:g.103234189T>A

NC_000012.10:g.101758319T>A

NG_008690.1:g.82192A>T

NG_008690.2:g.123000A>T

ENST00000553106.6:c.1304A>T

ENST00000307000.7:c.1289A>T

ENST00000551114.2:n.966A>T

ENST00000553106.5:c.1304A>T

ENST00000635477.1:c.408A>T

ENST00000635528.1:n.819A>T

NM_000277.1:c.1304A>T

NM_000277.2:c.1304A>T

NM_001354304.1:c.1304A>T

NM_001354304.2:c.1304A>T

Likely Pathogenic

Met criteria codes **3**

PP4_Moderate **PM2** **PM3**

Not Met criteria codes **1**

PP3

Evidence Links **2**

Expert Panel

[Phenylketonuria VCEP](#) [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1304A>T (p.Asp435Val) variant in PAH has been reported in a Uygur patient with moderate PKU (BH4 deficiency ruled out) (PP4_Moderate; PMID: 31355225). This variant was detected with p.Ala434Asp (Likely pathogenic in ClinVar) (PM3; PMID: 31355225). The

variant is absent from population databases (PM2). Computational evidence is conflicting. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP4_Moderate.

Met criteria codes

PP4_Moderate			PMID: 31355225 - PCR and Sanger sequencing detected D435V in an Uygur patient with moderate PKU (Phe = 360-1200umol/L), BH4 deficiency ruled out
PubMed:31355225 			
PM2			Variant absent from population databases
PM3			PMID: 31355225 - Patient 108 carried the previously described variant p.Ala434Asp (VarID 102586, LP, 2 submitters), parents were tested - variants confirmed in trans - 1.0 points
PubMed:31332730 			

Not Met criteria codes

PP3			Variant predicted to be tolerated by SIFT, benign by PolyPhen2, disease causing by MutationTaster, and REVEL = 0.707.
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Curation History



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