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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
Approved on: 2020/4/10
Published on: 2020/4/10

HGVS expressions

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

PM2 PM3 PP4_Moderate

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

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
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

Not Met criteria codes

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

Curation History

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