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Variant: NM_000277.2(PAH):c.827T>A (p.Met276Lys)

CA229795

102857 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: b816d0d3-13ff-424f-a001-bf9ec73622e4
Approved on: 2018-12-09
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HGVS expressions

NM_000277.2:c.827T>A
NM_000277.2(PAH):c.827T>A (p.Met276Lys)
NC_000012.12:g.102852830A>T
CM000674.2:g.102852830A>T
NC_000012.11:g.103246608A>T
CM000674.1:g.103246608A>T
NC_000012.10:g.101770738A>T
NG_008690.1:g.69773T>A
NG_008690.2:g.110581T>A
NM_000277.1:c.827T>A
NM_001354304.1:c.827T>A
NM_000277.3:c.827T>A
ENST00000307000.7:c.812T>A
ENST00000549247.6:n.586T>A
ENST00000553106.5:c.827T>A

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PM3 PM5 PM2

Not Met criteria codes 1

PP3

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.827T>A (p.Met276Lys) variant in PAH is absent from population databases, and found in the same codon as a previously reported pathogenic variant (p.Met276Val). It has been identified in trans with a known pathogenic variant (I95del), in which a defect of BH4 metabolism was excluded as a cause of elevated phenylalanine (PMID: 25894915).

Met criteria codes

PP4_Moderate		✔	BH4 defect excluded in all patients PMID: 25894915
			Variant in trans with a variant reported as pathogenic in clinvar (I95del). Single patient with MHP (Phe 278umol/L) PubMed:25894915
PM3		✔	in trans with I95del (pathogenic in clinvar)(Chen, 2015)
			single patient in trans with I95del (pathogenic in clinvar) PubMed:25894915
PM5		✔	p.Met276Val is LP
PM2		✔	Absent from population databases

Not Met criteria codes

PP3		✖	SIFT = tolerated Provean = damaging REVEL = 0.783

Curation History

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