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Variant: NM_000277.1(PAH):c.1184C>A (p.Ala395Asp)

Version: 1.0

CA229374

102548 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 02b4987f-4fbd-49c2-a11f-21ac92e69ecc
Approved on: 2022/7/30
Published on: 2022/7/30

HGVS expressions

NM_000277.1:c.1184C>A
NM_000277.1(PAH):c.1184C>A (p.Ala395Asp)
NC_000012.12:g.102843661G>T
CM000674.2:g.102843661G>T
NC_000012.11:g.103237439G>T
CM000674.1:g.103237439G>T
NC_000012.10:g.101761569G>T
NG_008690.1:g.78942C>A
NG_008690.2:g.119750C>A
ENST00000553106.6:c.1184C>A
ENST00000307000.7:c.1169C>A
ENST00000549247.6:n.943C>A
ENST00000551114.2:n.846C>A
ENST00000553106.5:c.1184C>A
ENST00000635477.1:c.288C>A
ENST00000635528.1:n.699C>A
NM_000277.2:c.1184C>A
NM_001354304.1:c.1184C>A
NM_000277.3:c.1184C>A
NM_001354304.2:c.1184C>A

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM5 PM2

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

This c.1184C>A (p.Ala395Asp) variant in PAH was reported in 1 patient with PAH deficiency (>1200 µmol/L Phe) (PMID 16256386). This variant was found at an amino acid residue where p.Ala395Pro, a pathogenic missense variant has been seen before. Computational

evidence for this missense variant is predicted to be damaging (SIFT), probably damaging (PolyPhen2), and disease-causing (MutationTaster). This variant is absent from population databases ExAC, gnomAD, 1000 Genomes, and ESP. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM5, PP3, PP4

Met criteria codes

PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster, REVEL=0.996
PP4	✔	PMID 16256386: p.Ala395Asp in one symptomatic patient (mental retardation between 6 months and 3 years old, classical PKU). PAH deficiency was diagnosed by conventional biochemical methods; classic PKU (Phe > 1200 umol/L). PMID 16256386: Table 1. p.Ala395Asp in one symptomatic patient. **PubMed:16256386**
PM5	✔	p.Ala395Pro pathogenic 2 submitters
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Curation History

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