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Variant: NM_000277.3(PAH):c.850T>C (p.Cys284Arg)

Version: 1.0

CA229822

102878 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: f2c506ad-64eb-4609-9b6b-1f13c72a3465
Approved on: 2019/12/8
Published on: 2021/4/9

HGVS expressions

NM_000277.3(PAH):c.850T>C (p.Cys284Arg)
NM_000277.3:c.850T>C
NC_000012.12:g.102851749A>G
CM000674.2:g.102851749A>G
NC_000012.11:g.103245527A>G
CM000674.1:g.103245527A>G
NC_000012.10:g.101769657A>G
NG_008690.1:g.70854T>C
NG_008690.2:g.111662T>C
ENST00000553106.6:c.850T>C
ENST00000307000.7:c.835T>C
ENST00000549247.6:n.609T>C
ENST00000551114.2:n.512T>C
ENST00000553106.5:c.850T>C
ENST00000635477.1:c.11T>C
NM_000277.1:c.850T>C
NM_000277.2:c.850T>C
NM_001354304.1:c.850T>C
NM_001354304.2:c.850T>C

Likely Pathogenic

Met criteria codes 4

PP4_Moderate PM3 PM2 PP3

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.850T>C (p.Cys284Arg) variant in PAH has been reported in 1 individual with classic PKU (BH4 deficiency excluded). (PP4_Moderate; PMID: 30050108). This variant is absent in population databases (PM2). This variant was detected in trans with pathogenic variant p.EX6-

96A>G (VarID590; PM3). Computational evidence predicts a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3, PP3.

Met criteria codes

PP4_Moderate	✔	reported in a patient with classic PKU, BH4 deficiency ruled out PMID: 30050108
PM3	✔	detected in trans with p.EX6-96A>G (VarID590, P, 4 submitters)
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PP3	✔	Predicted deleterious in SIFT, PolyPhen2, MutationTaster. REVEL=0.903

Curation History

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