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Variant: NM_000277.3(PAH):c.617A>G (p.Tyr206Cys)

Version: 1.0

CA229660

102762 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 00b21724-fa72-4baa-ae3e-4292390ade23
Approved on: 2022/6/12
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HGVS expressions

NM_000277.3(PAH):c.617A>G (p.Tyr206Cys)
NM_000277.3:c.617A>G
NC_000012.12:g.102855225T>C
CM000674.2:g.102855225T>C
NC_000012.11:g.103249003T>C
CM000674.1:g.103249003T>C
NC_000012.10:g.101773133T>C
NG_008690.1:g.67378A>G
NG_008690.2:g.108186A>G
ENST00000553106.6:c.617A>G
ENST00000307000.7:c.602A>G
ENST00000549111.5:n.713A>G
ENST00000553106.5:c.617A>G
NM_000277.1:c.617A>G
NM_000277.2:c.617A>G
NM_001354304.1:c.617A>G
NM_001354304.2:c.617A>G

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 NM_000277.3(PAH):c.617A>G (p.Tyr206Cys) missense variant has been reported in 1 patient with mild phenylketonuria (Phe = 914 umol/liter, BH4 deficiency excluded) (PP4_moderate; PMID: 29499199). This variant is absent from population databases (PM2), and is predicted deleterious by SIFT, Polyphen2, Mutation Taster. REVEL= 0.96 (PP3). This variant has been detected with pathogenic variants: p.Y204C (PMID: 16256386) and R241C (PMID: 26322415) (PM3). 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	✔	PMID: 29499199 - Y206C detected in 1 patient with mild phenylketonuria (Phe = 914 umol/liter), BH4 deficiency excluded via urinary pterin analysis
PM3	✔	PMID: 16256386 - Y206C detected with Y204C (reported as pathogenic in ClinVar; ClinVarID:590) in 1 Chinese patient with mild PKU; phase not confirmed, 0.5 points; PMID: 26322415 - Y206C detected with R241C in with Chinese patient (reported as pathogenic in ClinVar, VarID: 102803); parental DNA analyzed - Phase confirmed, 1.0 point
PM2	✔	Variant absent from population databases.
PP3	✔	Predicted deleterious in SIFT, Polyphen2, Mutation Taster. REVEL= 0.96.

Curation History

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