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Variant: NM_000277.2(PAH):c.719T>C (p.Phe240Ser)

Version: 1.0

CA229715

102802 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 40c992e0-e990-4d77-850d-2ded8efbba8f
Approved on: 2020/11/9
Published on: 2022/2/20

HGVS expressions

NM_000277.2(PAH):c.719T>C (p.Phe240Ser)
NM_000277.2:c.719T>C
NC_000012.12:g.102852938A>G
CM000674.2:g.102852938A>G
NC_000012.11:g.103246716A>G
CM000674.1:g.103246716A>G
NC_000012.10:g.101770846A>G
NG_008690.1:g.69665T>C
NG_008690.2:g.110473T>C
ENST00000553106.6:c.719T>C
ENST00000307000.7:c.704T>C
ENST00000549247.6:n.478T>C
ENST00000553106.5:c.719T>C
NM_000277.1:c.719T>C
NM_001354304.1:c.719T>C
NM_000277.3:c.719T>C
NM_001354304.2:c.719T>C

Likely Pathogenic

Met criteria codes 4
PM2 PM3 PP3 PP4

Not Met criteria codes 1
PM5

Evidence Links 1

Expert Panel
Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.719T>C (p.Phe240Ser) variant in PAH has been reported in 1 individual with classic PKU detected with pathogenic variant p.R261Q (PMID: 11139255). This variant is absent in population databases. Computational evidence supports a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP3, PP4.

Met criteria codes

PM2	✔	Absent from ExAC, gnomAD, 1000G, ESP
PM3	✔	Detected with R261Q, Path/LP, maternally inherited PMID: 11139255 F240S seen in trans with R261Q (VarID 582, Pathogenic/Likely Pathogenic). IVS2+19T>C polymorphism (VarID 92736, benign) occurred in cis to the F240S mutation, as the mother had these substitutions in the same status. PubMed:11139255
PP3	✔	Predicted deleterious in SIFT, Polyphen2, MutationTaster. REVEL=0.969.
PP4	✔	c.719T>C seen in 1 patient with classic PKU. BH4 deficiency not excluded. PMID: 11139255 These mutations were detected during the characterization of the PAH genotypes of 115 patients with PKU from the southeast region of Brazil. The patients were identified by a neonatal screening program and were considered to have PKU when the phenylalanine levels were above 4 mg/dl. c.719T>C was seen in 1 patient with classic PKU. PubMed:11139255

Not Met criteria codes

PM5	✖	F240V, no clnical significance provided in ClinVar, US by PAH VCEP

Curation History

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