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Variant: NM_000277.3:c.925G>A

Version: 1.0

CA16021003

1327567 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2c368255-4933-4361-8189-bf9f960f5fed
Approved on: 2019/12/14
Published on: 2021/9/6

HGVS expressions

NM_000277.3:c.925G>A
NC_000012.12:g.102846939C>T
CM000674.2:g.102846939C>T
NC_000012.11:g.103240717C>T
CM000674.1:g.103240717C>T
NC_000012.10:g.101764847C>T
NG_008690.1:g.75664G>A
NG_008690.2:g.116472G>A
ENST00000553106.6:c.925G>A
ENST00000307000.7:c.910G>A
ENST00000549247.6:n.684G>A
ENST00000551114.2:n.587G>A
ENST00000553106.5:c.925G>A
ENST00000635477.1:c.74-2508G>A
ENST00000635528.1:n.440G>A
NM_000277.1:c.925G>A
NM_000277.2:c.925G>A
NM_001354304.1:c.925G>A
NM_001354304.2:c.925G>A

Likely Pathogenic

Met criteria codes 5

PM2 PM5 PP4_Moderate PP3 PM3_Supporting

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.925G>A (p.Ala309Thr) variant in PAH has been reported a Danish patient with mild PKU (PMID: 26542770) and a Chinese patient with moderate PKU (BH4 deficiency excluded PMID: 30747360) (PP4_Moderate). This variant is absent in population databases (PM2). This variant was detected with pathogenic variant c.1241A>G, p.Y414C (PM3_supporting). Computational evidence supports a deleterious

effect. A different pathogenic missense change has been seen at the same amino acid residue (A309M). In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM5, PM3_supporting, PP3.

Met criteria codes

PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PM5	✔	A309M (Pathogenic, 4 submitters), A309D (LP, 1 submitter)
PP4_Moderate	✔	reported in a Danish patient with mild PKU (PMID: 26542770) and a Chinese patient with moderate PKU (BH4 deficiency excluded PMID: 30747360)
PP3	✔	Deleterious effect predicted in SIFT, PolyPhen2, MutationTaster. REVEL=0.949
PM3_Supporting	✔	detected with c.1241A>G, p.Y414C (P, 14 submitters). parental analysis not reported

Curation History

Showing 1 to 1 of 1 rows

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