

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

UID: 2c368255-4933-4361-8189-bf9f960f5fed

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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**

PP4_Moderate PP3 PM3_Supporting

PM2 PM5

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

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
PM2	✓	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP
PM5	✓	A309M (Pathogenic, 4 submitters), A309D (LP, 1 submitter)

Curation History [↗](#)



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