

Variant: NM_000277.1(PAH):c.926C>T (p.Ala309Val)

CA220592 [↗](#)

92753 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: db2881e3-3790-4e61-95e9-4ee16b4291d4

Approved on: 2018-08-10

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HGVS expressions

NM_000277.1(PAH):c.926C>T (p.Ala309Val)

NM_000277.1:c.926C>T

NC_000012.12:g.102846938G>A

CM000674.2:g.102846938G>A

NC_000012.11:g.103240716G>A

CM000674.1:g.103240716G>A

NC_000012.10:g.101764846G>A

NG_008690.1:g.75665C>T

NG_008690.2:g.116473C>T

NM_000277.2:c.926C>T

NM_001354304.1:c.926C>T

NM_000277.3:c.926C>T

ENST00000307000.7:c.911C>T

ENST00000549247.6:n.685C>T

ENST00000551114.2:n.588C>T

ENST00000553106.5:c.926C>T

ENST00000635477.1:n.74-2507C>T

ENST00000635528.1:n.441C>T

Pathogenic

Met criteria codes **5**

PS3

PP3

PP4

PM2

PM3

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

PAH-specific ACMG/AMP criteria applied: PM2: Low frequency. 1.0e-5; PP3: All databases agree on damaging effect. REVEL=0.921; PS3: Enzyme activity = 30% (Ho, 2008) (PMID:18590700); PM3: Single patient with classic PKU, c.842C>T (pathogenic in ClinVar) / c.926C>T (PMID:26666653); PP4: Single patient with classic PKU (>1200umol/L), BH4 defect not excluded (PMID:26666653). In summary this variant meets criteria to be classified as pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PM2, PP3, PS3, PM3, PP4).

Met criteria codes

PS3		Enzyme activity = 30% (Ho, 2008)
PAH activity analysis. Site directed mutagenesis, transfected COS-1 cells. Enzyme activity measured as conversion of L-[14C]phe to L-[14C]tyr. Use both standard cDNA expression system and a new Intinac plasmid system which incorporates intronic sequences. Standard cDNA method demonstrates 30% and intinac system demonstrates 14% residual enzyme activity. PubMed:18590700		
PP3		All databases agree on damaging effect. REVEL=0.921
PP4		Single patient with classic PKU (>1200umol/L), BH4 defect not excluded
Genotype-phenotype association in French patients with PKU. 364 patients, 24hr BH4 loading test. PubMed:26666653		
PM2		Low frequency. 1.0e-5
PM3		Single patient with classic PKU, c.842C>T (pathogenic in ClinVar) / c.926C>T
Genotype-phenotype association in French patients with PKU. 364 patients, 24hr BH4 loading test. PubMed:26666653		

Curation History

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