

Variant: NM_000277.2(PAH):c.823C>T (p.Pro275Ser)

CA229789 [↗](#)

102853 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 85ea4e16-15ba-4de1-88b7-46e398122a6e

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HGVS expressions

NM_000277.2:c.823C>T

NM_000277.2(PAH):c.823C>T (p.Pro275Ser)

NC_000012.12:g.102852834G>A

CM000674.2:g.102852834G>A

NC_000012.11:g.103246612G>A

CM000674.1:g.103246612G>A

NC_000012.10:g.101770742G>A

NG_008690.1:g.69769C>T

NG_008690.2:g.110577C>T

NM_000277.1:c.823C>T

NM_001354304.1:c.823C>T

NM_000277.3:c.823C>T

ENST00000307000.7:c.808C>T

ENST00000549247.6:n.582C>T

ENST00000553106.5:c.823C>T

Pathogenic

Met criteria codes **5**

PP3

PM2

PM5

PP4_Moderate

PM3_Strong

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.823C>T (p.Pro275Ser) variant in PAH is absent from all population databases, and is in the same codon as two other likely pathogenic variants. In silico algorithms agree on a damaging effect. It has been identified in trans with two independent pathogenic variants (R408W and c.669delC; PMID: 20123475, 24705691), and a defect in BH4 metabolism was excluded as a cause of elevated phenylalanine in multiple patients. In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM3_strong, PM2, PP4_Moderate, PM5, PP3.

Met criteria codes

PP3			In silico agree damaging. REVEL=0.954
PM2			not found in any population databases
PM5			p.Pro275Leu and p.Pro275Arg, both LP in ClinVar
PP4_Moderate			BH4 defect excluded in all patients (PMID: 24705691, PMID: 20123475). Phe = 380umol/L (Gassio 2010) BH4 defect excluded in all patients PubMed:24705691  BH4 defect excluded in all patients PubMed:20123475 
PM3_Strong			R408W (Cassio, 2010) c.669delC (Gu, 2014) in trans with c.669delC PubMed:24705691  in trans with R408W PubMed:20123475 

Curation History



 

 

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