

Variant: *NM_000277.1:c.656T>C*

Version: 1.0

CA16020831 [↗](#)

932275 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: a5edbcce-d479-4336-b5c0-84590d81afac

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HGVS expressions

NM_000277.1:c.656T>C

NC_000012.12:g.102855186A>G

CM000674.2:g.102855186A>G

NC_000012.11:g.103248964A>G

CM000674.1:g.103248964A>G

NC_000012.10:g.101773094A>G

NG_008690.1:g.67417T>C

NG_008690.2:g.108225T>C

ENST00000553106.6:c.656T>C

ENST00000307000.7:c.641T>C

ENST00000549111.5:n.752T>C

ENST00000553106.5:c.656T>C

NM_000277.2:c.656T>C

NM_001354304.1:c.656T>C

NM_000277.3:c.656T>C

NM_001354304.2:c.656T>C

Uncertain Significance

Met criteria codes **3**

PP4_Moderate

PP3

PM2

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.656T>C (p.Phe219Ser) variant in PAH has been reported in a Chinese patient with PAH deficiency (referred to as P219S, BH4 deficiency excluded, PMID 21307867). This variant is absent from population databases. Multiple lines of computational evidence support a deleterious effect. In summary, this variant meets criteria to be classified as uncertain significance for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PP3.

Met criteria codes			
PP4_Moderate			PMID 21307867: (referred to as P219S) c.656T>C in a patient cohort with Phe level higher than 0.18mM. analysis of dihydropteridine reductase activity in red blood cells, biopterin loading test and/or pteridine analysis in urine performed.
PMID 21307867: listed as P219S c.656T>C in Table 2. A patient cohort with Phe level higher than 0.18mM PubMed:21307867 			
PP3			Predicted deleterious in SIFT, PolyPhen2, MutationTaster. REVEL=0.901
PM2			Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Curation History 	
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