

Variant: *NM_000277.1:c.730C>T*

Version: 1.0

CA16020848 [↗](#)

1327557 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5699cad9-8be5-43c0-83a9-176d13cbcfa5

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HGVS expressions

NM_000277.1:c.730C>T

NC_000012.12:g.102852927G>A

CM000674.2:g.102852927G>A

NC_000012.11:g.103246705G>A

CM000674.1:g.103246705G>A

NC_000012.10:g.101770835G>A

NG_008690.1:g.69676C>T

NG_008690.2:g.110484C>T

ENST00000553106.6:c.730C>T

ENST00000307000.7:c.715C>T

ENST00000549247.6:n.489C>T

ENST00000553106.5:c.730C>T

NM_000277.2:c.730C>T

NM_001354304.1:c.730C>T

NM_000277.3:c.730C>T

NM_001354304.2:c.730C>T

Likely Pathogenic

Met criteria codes 4

PP3

PP4

PM2

PM3

Not Met criteria codes 1

PM5

Evidence Links 1

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.730C>T (p.Pro244Ser) variant in PAH has been reported in 1 individual with classic PKU, detected in trans with pathogenic variant p.R158Q (PMID: 26542770). This variant is absent in population databases. Computational evidence supports a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PM3, PP3.

Met criteria codes

PP3			Deleterious effect predicted in SIFT, Polyphen2, MutationTaster. REVEL=0.964
PP4			Seen in 1 patient with classic PKU. BH4 deficiency not ruled out. PMID: 26542770
			We describe the genotypes of the complete cohort of PKU patients in Denmark, 376 patients. All patients had PKU according to biochemical criteria. c.730C>T (p.P244S) was found in Patient 6. PubMed:26542770 
PM2			Absent from ExAC, gnomAD, 1000G, ESP
PM3			In trans with R158Q, known pathogenic. PMID: 26542770
			P244S in trans with R158Q (VarID 587, Pathogenic). Parental testing confirmed that the two mutations identified in the 368 patients all were present in trans. PubMed:26542770 

Not Met criteria codes

PM5			P244L (VarID 621) is likely pathogenic by PAH VCEP
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Curation History



 

 

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