The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Approved on: 2020/8/7
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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 PM3 PM2

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
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
PM2	✔	Absent from ExAC, gnomAD, 1000G, ESP

Not Met criteria codes

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

Curation History

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