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Variant: NM_001354304.2:c.364C>T

Version: 1.0

CA16020780

987906 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 052ffdf9-0a02-44a0-84c1-9b0a9f729be4
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HGVS expressions

NM_001354304.2:c.364C>T
NC_000012.12:g.102877539G>A
CM000674.2:g.102877539G>A
NC_000012.11:g.103271317G>A
CM000674.1:g.103271317G>A
NC_000012.10:g.101795447G>A
NG_008690.1:g.45064C>T
NG_008690.2:g.85872C>T
ENST00000553106.6:c.364C>T
ENST00000307000.7:c.349C>T
ENST00000549111.5:n.460C>T
ENST00000550978.6:c.348C>T
ENST00000551337.5:c.364C>T
ENST00000551988.5:n.453C>T
ENST00000553106.5:c.364C>T
NM_000277.1:c.364C>T
NM_000277.2:c.364C>T
NM_001354304.1:c.364C>T
NM_000277.3:c.364C>T

Likely Pathogenic

Met criteria codes 4

PM3 PM2 PP3 PP4_Moderate

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.364C>T (p.Pro122Ser) missense variant in PAH was reported in a Spanish patient with Mild HPA. A defect in the synthesis or regeneration in the pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels and measuring dihydropteridine reductase activity. This variant was detected in trans with pathogenic variant p.Asp415Asn (PMID 27121329). It was found at extremely low

frequency in gnomAD (MAF=0.00003) and predicted deleterious using in silico data. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM3, PP4 moderate, and PP3.

Met criteria codes

PM3	✔	Detected in trans with pathogenic variant p. Asp415Asn. Segregation analysis was done (PMID 27121329). PubMed:30459323
PM2	✔	Extremely low frequency in gnomAD (MAF=0.00003).
PP3	✔	Predicted deleterious in SIFT, PolyPhen2, Mutation Taster, REVEL= 0.983
PP4_Moderate	✔	Reported in a Spanish patient with Mild HP-NT. A defect in the synthesis or regeneration in the pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels as well as by measuring the dihydropteridine reductase activity (PMID 27121329).

Curation History

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