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Variant: NM_001354304.2:c.1271T>A

Version: 1.0

CA16020988

987757 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 79c72b03-7607-46a8-a596-c2c597940a6b
Approved on: 2020/8/7
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HGVS expressions

NM_001354304.2:c.1271T>A
NC_000012.12:g.102840444A>T
CM000674.2:g.102840444A>T
NC_000012.11:g.103234222A>T
CM000674.1:g.103234222A>T
NC_000012.10:g.101758352A>T
NG_008690.1:g.82159T>A
NG_008690.2:g.122967T>A
ENST00000553106.6:c.1271T>A
ENST00000307000.7:c.1256T>A
ENST00000551114.2:n.933T>A
ENST00000553106.5:c.1271T>A
ENST00000635477.1:c.375T>A
ENST00000635528.1:n.786T>A
NM_000277.1:c.1271T>A
NM_000277.2:c.1271T>A
NM_001354304.1:c.1271T>A
NM_000277.3:c.1271T>A

Pathogenic

Met criteria codes 3
PP4 PM2 PVS1

Not Met criteria codes 1
PM3

Evidence Links 1

Expert Panel
Phenylketonuria VCEP

Criteria Specification Information
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1271T>A (p.Leu424*) variant in PAH meets criteria to be classified as pathogenic. PAH-specific ACMG/AMP criteria applied: PM2: Absent from population databases (1000 Genomes, ExAC). PVS1: Nonsense mutation, causing early termination of exon 12. NMD is predicted to occur. PP4: Patient has classic PKU (PMID:24350308).PM3_Supporting: Found to co-occur with PAH EX5del4232ins268 in one

patient with classic PKU, but no additional studies to demonstrate phase of variants. No other PAH variants identified in patient (PMID:24350308). Not predicted to be responsive to BH4 (PMID:24350308)

Met criteria codes

PP4	✔	Patient has classic PKU PubMed:24350308
PM2	✔	Absent from population databases.
PVS1	✔	Nonsense mutation, variant is predicted to undergo NMD

Not Met criteria codes

PM3	✖	Co-occured with PAH EX5del4232ins268 (aka g.47563_51794del4232g.56161_56430ins268) in patient with classic PKU. This variant is currently unclassified. No additional testing to prove phase.

Curation History

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