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Variant: NM_000277.3(PAH):c.1021A>T (p.Lys341Ter)

Version: 1.0

CA229272

102470 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 83a0c192-3b59-4e0d-95de-e711ebb17cde
Approved on: 2022/6/12
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HGVS expressions

NM_000277.3(PAH):c.1021A>T (p.Lys341Ter)
NM_000277.3:c.1021A>T
NC_000012.12:g.102844380T>A
CM000674.2:g.102844380T>A
NC_000012.11:g.103238158T>A
CM000674.1:g.103238158T>A
NC_000012.10:g.101762288T>A
NG_008690.1:g.78223A>T
NG_008690.2:g.119031A>T
ENST00000553106.6:c.1021A>T
ENST00000307000.7:c.1006A>T
ENST00000549247.6:n.780A>T
ENST00000551114.2:n.683A>T
ENST00000553106.5:c.1021A>T
ENST00000635477.1:c.125A>T
ENST00000635528.1:n.536A>T
NM_000277.1:c.1021A>T
NM_000277.2:c.1021A>T
NM_001354304.1:c.1021A>T
NM_001354304.2:c.1021A>T

Pathogenic

Met criteria codes 4

PVS1 PM2 PP4 PM3_Supporting

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1021A>T (p.Lys341Ter) nonsense variant occurs in exon 10 of 13 and is predicted to result in NMD. It absent from population databases, including gnomAD. It has been reported in at least one patient with cPKU (PMID: 9452062), compound heterozygous with

R408W c.1315+1G>A (ClinVar 576, Pathogenic reviewed by PAH VCEP). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PM3_supporting, PP4.

Met criteria codes

PVS1	✔	The c.1021A>T (p.Lys341Ter) nonsense variant occurs in exon 10 of 13 and is predicted to result in NMD.
PM2	✔	The variant is absent from population databases, including gnomAD, ExAC, 1000 Genomes, and ESP.
PP4	✔	Patient 429 of PMID: 9452062 has classical PKU with PHE >1,200 µmol/L.
PM3_Supporting	✔	Patient 429 of PMID: 9452062 is compound heterozygous for K341X and c.1315+1G>A (ClinVar 576, Pathogenic reviewed by PAH expert panel). Confirmation of trans phase was not reported.

Curation History

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