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Variant: NM_001354304.2:c.253A>T

Version: 1.0

CA16020757

932263 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: eef3b853-ba5c-4908-86b9-3bd943cd2361
Approved on: 2020/5/8
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HGVS expressions

NM_001354304.2:c.253A>T
NC_000012.12:g.102894834T>A
CM000674.2:g.102894834T>A
NC_000012.11:g.103288612T>A
CM000674.1:g.103288612T>A
NC_000012.10:g.101812742T>A
NG_008690.1:g.27769A>T
NG_008690.2:g.68577A>T
ENST00000553106.6:c.253A>T
ENST00000307000.7:c.238A>T
ENST00000546844.1:c.253A>T
ENST00000548677.2:n.340A>T
ENST00000548928.1:n.175A>T
ENST00000549111.5:n.349A>T
ENST00000550978.6:c.237A>T
ENST00000551337.5:c.253A>T
ENST00000551988.5:n.342A>T
ENST00000553106.5:c.253A>T
NM_000277.1:c.253A>T
NM_000277.2:c.253A>T
NM_001354304.1:c.253A>T
NM_000277.3:c.253A>T

Pathogenic

Met criteria codes 4

PM3 PM2 PVS1 PP4

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

Variant c.253A>T (p.Lys85Ter) in PAH was found in 3 Moroccan patients with Phe levels >600 umol/L (PMID: 19786003) (PP4). This is a nonsense variant in exon 3 out of 13 coding exons, predicted to undergo nonsense mediated mRNA decay, as it is not located in the 3'-most exon or the 3'-most 50 bp of the penultimate exon. The exon is present in biologically-relevant transcripts (PVS1). Three patients were homozygous for p.K85X (PMID: 19786003) (PM3). Parental and familial DNA were sequenced. The variant was absent from controls in gnomAD, PAGE, 100 Genomes or ESP (PM2). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied:PVS1, PM3, PP4, PM2.

Met criteria codes

PM3	✔	3 patients were found to be homozygous for p.K85X (PMID: 19786003). Parental and familial DNA were sequenced.
PM2	✔	Absent from controls in gnomAD, PAGE, 1000 Genomes or ESP.
PVS1	✔	This is a nonsense variant in exon 3 out of 13 coding exons. The variant is predicted to undergo nonsense mediated mRNA decay (NMD), as it is not located in the 3'-most exon or the 3'-most 50 bp of the penultimate exon. The exon is present in biologically-relevant transcripts.
PP4	✔	Variant p.K85X was found in 3 Moroccan patients with Phe levels >600 umol/L (PMID: 19786003).

PubMed:19786003

Curation History

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