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Variant: NM_000277.3:c.206dup

Version: 1.0

CA16020746

805815 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 0185d46f-b8fb-42ca-8749-6ee669523777
Approved on: 2019/4/4
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HGVS expressions

NM_000277.3:c.206dup
NC_000012.12:g.102894882dup
CM000674.2:g.102894882dup
NC_000012.11:g.103288660dup
CM000674.1:g.103288660dup
NC_000012.10:g.101812790dup
NG_008690.1:g.27722dup
NG_008690.2:g.68530dup
ENST00000553106.6:c.206dup
ENST00000307000.7:c.191dup
ENST00000546844.1:c.206dup
ENST00000548677.2:n.293dup
ENST00000548928.1:n.128dup
ENST00000549111.5:n.302dup
ENST00000550978.6:c.190dup
ENST00000551337.5:c.206dup
ENST00000551988.5:n.295dup
ENST00000553106.5:c.206dup
ENST00000635500.1:n.174dup
NM_000277.1:c.206dup
NM_000277.2:c.206dup
NM_001354304.1:c.206dup
NM_001354304.2:c.206dup

Pathogenic

Met criteria codes 4

PP4 PM2 PM3 PVS1

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.206dupC variant in PAH has been previously reported as a heterozygous variant detected in trans with the known pathogenic c.1066-11G>A variant in a single Caucasian proband with classic PKU; BH4 deficiency was not formally excluded (PMID: 23430918) (PM3, PP4). The variant is a 1bp insertion leading to a nonsense variant which occurs in exon 3 of 13 in the in the canonical transcript of PAH, a gene fulfilling the most recent criteria for LOF being a known disease mechanism (see PMID: 30192042) (PVS1). It is absent from control databases including ethnically matched individuals, including gnomAD/ExAC, 1000 Genomes, and ESP (PM2). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PM3, PP4.

Met criteria codes

PP4	✔	The c.206dupC variant in PAH has been previously reported as a heterozygous variant detected in trans with the known pathogenic c.1066-11G>A variant in a single Caucasian proband with classic PKU; BH4 deficiency was not formally excluded (PMID: 23430918) (PM3) (PP4).
		The c.206dupC variant in PAH has been previously reported as a heterozygous variant detected in trans with the known pathogenic c.1066-11G>A variant in a single Caucasian proband with classic PKU; BH4 deficiency was not formally excluded (PMID: 23430918) (PM3) (PP4). PubMed:23430918
PM2	✔	It is absent from control databases including ethnically matched individuals, including gnomAD/ExAC, 1000 Genomes, and ESP (PM2).
PM3	✔	The c.206dupC variant in PAH has been previously reported as a heterozygous variant detected in trans with the known pathogenic c.1066-11G>A variant in a single Caucasian proband with classic PKU; BH4 deficiency was not formally excluded (PMID: 23430918) (PM3) (PP4).
		The c.206dupC variant in PAH has been previously reported as a heterozygous variant detected in trans with the known pathogenic c.1066-11G>A variant in a single Caucasian proband with classic PKU; BH4 deficiency was not formally excluded (PMID: 23430918) (PM3) (PP4). PubMed:23430918
PVS1	✔	The variant is a 1bp insertion leading to a nonsense variant which occurs in exon 3 of 13 in the in the canonical transcript of PAH, a gene fulfilling the most recent criteria for LOF being a known disease mechanism (see PMID: 30192042) (PVS1).

Curation History

Showing 1 to 1 of 1 rows

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