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Variant: NM_000277.3:c.171_172del

Version: 1.0

CA16020735

805810 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: a03eef36-3bab-4f4c-ba0b-6914a0fd44a7
Approved on: 2019/4/3
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HGVS expressions

NM_000277.3:c.171_172del
NC_000012.12:g.102894917_102894918del
CM000674.2:g.102894917_102894918del
NC_000012.11:g.103288695_103288696del
CM000674.1:g.103288695_103288696del
NC_000012.10:g.101812825_101812826del
NG_008690.1:g.27687_27688del
NG_008690.2:g.68495_68496del
ENST00000553106.6:c.171_172del
ENST00000307000.7:c.156_157del
ENST00000546844.1:c.171_172del
ENST00000548677.2:n.258_259del
ENST00000548928.1:n.93_94del
ENST00000549111.5:n.267_268del
ENST00000550978.6:c.155_156del
ENST00000551337.5:c.171_172del
ENST00000551988.5:n.260_261del
ENST00000553106.5:c.171_172del
ENST00000635500.1:n.139_140del
NM_000277.1:c.171_172del
NM_000277.2:c.171_172del
NM_001354304.1:c.171_172del
NM_001354304.2:c.171_172del

Pathogenic

Met criteria codes 3

PVS1 PM2 PP4

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.169_170delGA variant in PAH has been previously reported as a single (heterozygous) mutation in 1 Chinese PKU case (PMID: 26503515; PP4). The variant is a frameshift variant occurring 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, PP4.

Met criteria codes

PVS1	✔	The variant is a frameshift variant occurring 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).
PM2	✔	It is absent from control databases including ethnically matched individuals, including gnomAD/ExAC, 1000 Genomes, and ESP (PM2).
PP4	✔	The c.169_170delGA variant in PAH has been previously reported as a single (heterozygous) mutation in 1 Chinese PKU case (PMID: 26503515); patient-specific information was not provided regarding the type of PKU, but methods indicate all patients had plasma Phe > 120umol/L and DHPR and urinary biopterin and neopterin studies. The c.169_170delGA variant in PAH has been previously reported as a single (heterozygous) mutation in 1 Chinese PKU case (PMID: 26503515); no further information appears to be provided regarding the type of PKU and/or the proband's genotype (PP4). These patients were diagnosed at birth either through a neonatal screening program or based on clinical presentation. Biochemical testing data, including plasma phenylalanine (Phe) levels, dihydropteridine reductase activity, urinary biopterin and neopterin ratio, and tetrahydrobiopterin loading, were collected. These patients were classified into one of three separate phenotype categories according to their pretreatment plasma Phe levels, including mild hyperphenylalaninaemia (Phe 120–600umol/L), mild PKU(Phe 600-1200µmol/L), and classic PKU (Phe>1200µmol/L)47. PubMed:26503515

Curation History

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