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Variant: NM_000277.3:c.190_194del

Version: 1.0

CA16020742

805814 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 537c252b-458c-4470-b4cf-41cce415c4bf
Approved on: 2019/4/4
Published on: 2019/8/16

HGVS expressions

NM_000277.3:c.190_194del
NC_000012.12:g.102894893_102894897del
CM000674.2:g.102894893_102894897del
NC_000012.11:g.103288671_103288675del
CM000674.1:g.103288671_103288675del
NC_000012.10:g.101812801_101812805del
NG_008690.1:g.27706_27710del
NG_008690.2:g.68514_68518del
ENST00000553106.6:c.190_194del
ENST00000307000.7:c.175_179del
ENST00000546844.1:c.190_194del
ENST00000548677.2:n.277_281del
ENST00000548928.1:n.112_116del
ENST00000549111.5:n.286_290del
ENST00000550978.6:c.174_178del
ENST00000551337.5:c.190_194del
ENST00000551988.5:n.279_283del
ENST00000553106.5:c.190_194del
ENST00000635500.1:n.158_162del
NM_000277.1:c.190_194del
NM_000277.2:c.190_194del
NM_001354304.1:c.190_194del
NM_001354304.2:c.190_194del

Pathogenic

Met criteria codes 4

PM3 PM2 PP4_Moderate 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.190_194delCACAT variant in PAH has been previously reported as a single variant, found in trans with the Likely Pathogenic (per internal PAH ClinGen Working Group classification -see PAH0095) p.Ala156Pro variant in a female Chinese proband with classic PKU (PM3) (PMID: 28754886); the authors report that BH4 deficiency was excluded by “analysis of urinary pterins and dihydropteridine reductase activity in erythrocytes” (PP4_Moderate) (PMID: 28754886). The sequence change results in 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, PP4_Moderate, PM3.

Met criteria codes

PM3	✔	The c.190_194delCACAT variant in PAH has been previously reported as a single variant, found in trans with the Likely Pathogenic (per internal PAH ClinGen Working Group classification -see PAH0095) p.Ala156Pro variant in a female Chinese proband with classic PKU (PM3) (PMID: 28754886) The c.190_194delCACAT variant in PAH has been previously reported as a single variant, found in trans with the Likely Pathogenic (per internal PAH ClinGen Working Group classification -see PAH0095) p.Ala156Pro variant in a female Chinese proband with classic PKU (PM3) (PMID: 28754886) PubMed:28754886
PM2	✔	It is absent from control databases including ethnically matched individuals, including gnomAD/ExAC, 1000 Genomes, and ESP (PM2).
PP4_Moderate	✔	The c.190_194delCACAT variant in PAH has been previously reported as a single variant, found in trans with the Likely Pathogenic (per internal PAH ClinGen Working Group classification -see PAH0095) p.Ala156Pro variant in a female Chinese proband with classic PKU (PM3) (PMID: 28754886); the authors report that BH4 deficiency was excluded by “analysis of urinary pterins and dihydropteridine reductase activity in erythrocytes” (PP4_Moderate) (PMID: 28754886). The c.190_194delCACAT variant in PAH has been previously reported as a single variant, found in trans with the Likely Pathogenic (per internal PAH ClinGen Working Group classification -see PAH0095) p.Ala156Pro variant in a female Chinese proband with classic PKU (PM3) (PMID: 28754886); the authors report that BH4 deficiency was excluded by “analysis of urinary pterins and dihydropteridine reductase activity in erythrocytes” (PP4_Moderate) (PMID: 28754886). PubMed:28754886
PVS1	✔	The sequence change results in 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

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