The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000277.1:c.1171_1172del

Version: 1.0

CA16020956

553594 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: f10c8ee8-5a9e-49ac-82f1-d14021ad1340
Approved on: 2020/6/19
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HGVS expressions

NM_000277.1:c.1171_1172del
NC_000012.12:g.102843677_102843678del
CM000674.2:g.102843677_102843678del
NC_000012.11:g.103237455_103237456del
CM000674.1:g.103237455_103237456del
NC_000012.10:g.101761585_101761586del
NG_008690.1:g.78929_78930del
NG_008690.2:g.119737_119738del
ENST00000553106.6:c.1171_1172del
ENST00000307000.7:c.1156_1157del
ENST00000549247.6:n.930_931del
ENST00000551114.2:n.833_834del
ENST00000553106.5:c.1171_1172del
ENST00000635477.1:c.275_276del
ENST00000635528.1:n.686_687del
NM_000277.2:c.1171_1172del
NM_001354304.1:c.1171_1172del
NM_000277.3:c.1171_1172del
NM_001354304.2:c.1171_1172del

Pathogenic

Met criteria codes 4

PVS1 PP4_Moderate PM3 PM2

Evidence Links 3

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1171_1172del (p.Ser391PhefsTer2) variant in PAH has been reported in an individual with Classic PKU (BH4 deficiency excluded). (PMID: 8268925, 11708866, 27121329) in trans with pathogenic variant p.Ser349Pro. It is a frameshift variant in exon 11 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function. This variant has an extremely low

allele frequency (MAF=0.000008799) in gnomAD. In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PM3, PP4_Moderate,

Met criteria codes

PVS1	✔	frameshift variant in exon 11 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function
PP4_Moderate	✔	Seen in an individual with Classic PKU. PMID: 8268925, PMID: 11708866 A defect in the synthesis or regeneration pathways of 6R-BH4 was ruled out by analyzing urinary pterin levels as well as by measuring the dihydropteridine reductase activity. PMID: 27121329 Seen in an individual with Classic PKU. PubMed:11708866 Seen in individual with Classic PKU. PubMed:8268925
PM3	✔	detected in trans with p.[Ser349Pro] (P/LP). Segregation analysis was done to rule out the presence of large genomic rearrangements. PMID: 27121329 PubMed:27121329
PM2	✔	Absent from controls in ExAC, 1000 Genomes, and ESP. MAF=0.000008799 in gnomAD

Curation History

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