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Variant: NM_000277.2(PAH):c.839_840insT (p.Glu280Aspfs)

Version: 1.0

CA229810

102867 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 44b9a940-234d-4ed7-911c-55dac5f90d77
Approved on: 2023/10/15
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HGVS expressions

NM_000277.2:c.839_840insT
NM_000277.2(PAH):c.839_840insT (p.Glu280Aspfs)
NC_000012.12:g.102852817_102852818insA
CM000674.2:g.102852817_102852818insA
NC_000012.11:g.103246595_103246596insA
CM000674.1:g.103246595_103246596insA
NC_000012.10:g.101770725_101770726insA
NG_008690.1:g.69785_69786insT
NG_008690.2:g.110593_110594insT
ENST00000553106.6:c.839_840insT
ENST00000307000.7:c.824_825insT
ENST00000549247.6:n.598_599insT
ENST00000553106.5:c.839_840insT
NM_000277.1:c.839_840insT
NM_001354304.1:c.839_840insT
NM_000277.3:c.839_840insT
NM_001354304.2:c.839_840insT

Pathogenic

Met criteria codes 3

PM2_Supporting PP4 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.839_840insT (p.Glu280Aspfs) variant in PAH has been reported in an individual with PKU (PP4; 15300621). This variant has is absent from ExAC and gnomAD (PM2_supporting). It is a null variant (frameshift) in exon 7/13 with NMD predicted (PVS1). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2_supporting, PP4.

Met criteria codes

PM2_Supporting	✔	Absent from controls in ExAC and gnomAD v2.1.1
PP4	✔	280insT was detected in a PKU patient. PMID: 15300621 The PAH genes from 40 phenylketonuria (PKU) patients and 30 normal controls were screened by PCR-single strand conformation polymorphism (SSCP) and further sequencing. 280insT was detected. No abnormalities in the PAH gene from 30 controls were detected. PubMed:15300621
PVS1	✔	Null variant (frameshift) in exon 7/13. This variant is an insertion of a T between coding positions 839 and 840. This leads to a change from glutamic acid to aspartic acid at position 280, followed by a threonine and then premature stop codon. NMD predicted.

Curation History

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