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Variant: NM_000277.3(PAH):c.941del (p.Pro314fs)

Version: 1.0

CA229866

102906 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: e27280b9-e470-4ae1-a0ea-56e2782d634d
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HGVS expressions

NM_000277.3(PAH):c.941del (p.Pro314fs)
NM_000277.3:c.941del
NC_000012.12:g.102846924del
CM000674.2:g.102846924del
NC_000012.11:g.103240702del
CM000674.1:g.103240702del
NC_000012.10:g.101764832del
NG_008690.1:g.75680del
NG_008690.2:g.116488del
ENST00000553106.6:c.941del
ENST00000307000.7:c.926del
ENST00000549247.6:n.700del
ENST00000551114.2:n.603del
ENST00000553106.5:c.941del
ENST00000635477.1:c.74-2492del
ENST00000635528.1:n.456del
NM_000277.1:c.941del
NM_000277.2:c.941del
NM_001354304.1:c.941del
NM_001354304.2:c.941del

Pathogenic

Met criteria codes 4

PVS1 PM3 PM2 PP4

Evidence Links 0

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The frameshift variant c.941del (HGVS nomenclature c.940del) occurs in exon 9 of 13 and is predicted to result in NMD. The variant is absent from population databases, including gnomAD. One classical PKU patient has been reported (PMID: 9600453) with this variant in

trans with c.1066-11G>A (ClinVar 607, Pathogenic with expert panel review). 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

PVS1	✔	The c.941del variant in exon 9 results in the p.Pro314LeufsTer27 frameshift which creates a premature stop codon in exon 10 of 13. This is predicted to result in NMD.
PM3	✔	Patient F536 of PMID: 9600453 is compound heterozygous for c.941del and c.1066-11G>A (ClinVar 607, Pathogenic with expert panel review).
PM2	✔	Variant is absent from population databases including gnomAD, ExAC, 1000 Genomes, and ESP.
PP4	✔	Patient F536 of PMID: 9600453 has a classical PKU phenotype with Phe levels at diagnosis higher than 20 mg/dl.

Curation History

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