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(PAH):c.266dupC (p.Ala90Cysfs)

Version: 1.0

CA229503

102642 (ClinVar)

Gene: PAH
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 576bbc2e-c3f8-4d05-8b80-899d55eae361
Approved on: 2020/5/8
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HGVS expressions

NM_000277.1:c.266dupC
NM_000277.1:c.264_265insC
NM_000277.1(PAH):c.266dupC (p.Ala90Cysfs)
NM_000277.1:c.266_267insC
NC_000012.12:g.102894822dup
CM000674.2:g.102894822dup
NC_000012.11:g.103288600dup
CM000674.1:g.103288600dup
NC_000012.10:g.101812730dup
NG_008690.1:g.27782dup
NG_008690.2:g.68590dup
ENST00000553106.6:c.266dup
ENST00000307000.7:c.251dup
ENST00000546844.1:c.266dup
ENST00000548677.2:n.353dup
ENST00000548928.1:n.188dup
ENST00000549111.5:n.362dup
ENST00000550978.6:c.250dup
ENST00000551337.5:c.266dup
ENST00000551988.5:n.355dup
ENST00000553106.5:c.266dup
NM_000277.1:c.266dup
NM_000277.2:c.266dup
NM_001354304.1:c.266dup
NM_000277.3:c.266dup
NM_001354304.2:c.266dup

Pathogenic

Met criteria codes 4

PM3 PM2 PVS1 PP4_Moderate

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

Variant classified as Pathogenic using the following criteria: PVS1; PM2; PM3; PP4_Moderate. PVS1: frameshift variant in exon 2 of 13, predicted to result in PTC with removal of >10% of the protein and NMD; PM2: absent from ExAC, gnomAD, 1000G, ESP. PP4_Moderate; PM3: c.266_267insC seen on 2 PKU alleles, with BH4 deficiency ruled out (PMID: 21147011). Detected with pathogenic variants IVS12+1G>A and p.I65T (PMID: 9452062); and p.Pro281Leu (Likely Pathogenic per ClinGen PAH VCEP, PMID: 26666653).

Met criteria codes

PM3	✓	found in with IVS12+1G>A (Pathogenic per ClinGen PAH VCEP) and p.I65T (P 10 submitters) parental analysis not reported (PMID: 9452062); with p.Pro281Leu (Likely Pathogenic per ClinGen PAH VCEP) in one French PKU case parental analysis not reported (PMID: 26666653). p.P281R in 2 patients, parental analysis not reported PMID: 21147011 PubMed:21147011
PM2	✓	absent from ExAC, gnomAD, 1000G, ESP
PVS1	✓	PVS1: frameshift variant in exon 2 of 13, predicted to result in PTC with removal of >10% of the protein and NMD
PP4_Moderate	✓	c.266_267insC seen on 2 PKU alleles. BH4 deficiency ruled out. Upgraded per ClinGen Metabolic workgroup 588 hyperphenylalaninemic patients were investigated. Assessment included PAH gene and genes of the BH4 synthesis/recycling pathways (PTS and QDPR). c.266_267insC seen in 2 alleles. PubMed:21147011

Curation History

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