

Variant: *NM_001354304.2:c.690_691insG*

Version: 1.0

CA16020841 [↗](#)

987779 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: effe9fc1-41ac-418a-84bb-15deca118a02

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HGVS expressions

NM_001354304.2:c.690_691insG

NC_000012.12:g.102855151_102855152insC

CM000674.2:g.102855151_102855152insC

NC_000012.11:g.103248929_103248930insC

CM000674.1:g.103248929_103248930insC

NC_000012.10:g.101773059_101773060insC

NG_008690.1:g.67451_67452insG

NG_008690.2:g.108259_108260insG

ENST00000553106.6:c.690_691insG

ENST00000307000.7:c.675_676insG

ENST00000549111.5:n.786_787insG

ENST00000553106.5:c.690_691insG

NM_000277.1:c.690_691insG

NM_000277.2:c.690_691insG

NM_001354304.1:c.690_691insG

NM_000277.3:c.690_691insG

Pathogenic

Met criteria codes **3**

PP4

PM2

PVS1

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Phenylketonuria VCEP

This c.690_691insG (p.Ser231ValfsTer?) variant in PAH was reported in one patient with Hyperphenylalaninemia (PMID: 28982351). This variant is absent from controls in population databases. This is a frameshift variant in exon 6 out of 13 coding exons. The variant is predicted to undergo nonsense mediated mRNA decay (NMD), as it is not located in the 3'-most exon or the 3'-most 50 bp of the penultimate exon. In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, and PP4.

Met criteria codes

PP4			Observed in a patient with HPA (Phe > 120 μmol/L). Patients with BH4 cofactor deficiency were ruled out using urinary pterin analysis. There is no mention of DHPR being assessed. PMID: 28982351
PubMed:28982351 			
PM2			This variant is absent from controls in gnomAD and ExAC.
PVS1			This is a frameshift variant in exon 6 out of 13 coding exons. The variant is predicted to undergo nonsense mediated mRNA decay (NMD), as it is not located in the 3'-most exon or the 3'-most 50 bp of the penultimate exon. The exon is present in biologically-relevant transcripts. Loss of function is a known mechanism of disease: 175 pathogenic null variants reported in Clinvar across 13 different exons, 22 of which are in exon 6.

Curation History



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