

Variant: *NM_000277.2(PAH):c.169_171delGAG (p.Glu57del)*

Version: 1.0

CA229461 [↗](#)

102613 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 322ad14d-14cd-4966-a70d-b6f5fb632418

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HGVS expressions

NM_000277.2:c.169_171del

NM_000277.2(PAH):c.169_171delGAG (p.Glu57del)

NC_000012.12:g.102894918_102894920del

CM000674.2:g.102894918_102894920del

NC_000012.11:g.103288696_103288698del

CM000674.1:g.103288696_103288698del

NC_000012.10:g.101812826_101812828del

NG_008690.1:g.27685_27687del

NG_008690.2:g.68493_68495del

ENST00000553106.6:c.169_171del

ENST00000307000.7:c.154_156del

ENST00000546844.1:c.169_171del

ENST00000548677.2:n.256_258del

ENST00000548928.1:n.91_93del

ENST00000549111.5:n.265_267del

ENST00000550978.6:c.153_155del

ENST00000551337.5:c.169_171del

ENST00000551988.5:n.258_260del

ENST00000553106.5:c.169_171del

ENST00000635500.1:n.137_139del

NM_000277.1:c.169_171del

NM_001354304.1:c.169_171del

NM_000277.3:c.169_171del

NM_001354304.2:c.169_171del

Likely Pathogenic

Met criteria codes **4**

PM3_Strong

PP4

PM2

PM4

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.169_171del in-frame deletion variant has been identified in at least 2 probands with phenotypes of mild to classic PKU (PMIDs: 18299955, 22106832). It has been detected in trans with pathogenic variants Ala403Val (PMID: 18299955) and c.1066-11G>A (PMID: 22106832). This variant is absent from 1000G, ESP, and gnomAD databases. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM3_Strong, PM2, PM4, PP4.

Met criteria codes

PM3_Strong			This variant has been reported in two compound heterozygotes, in trans with Ala403Val (ClinVar 92731, Pathogenic) and c.1066-11G>A (ClinVar 607, Pathogenic). A compound heterozygous patient is described with this c.169_171del variant and the c.1066-11G>A (ClinVar 607, Pathogenic) variant. PubMed:22106832  A mild PKU patient is reported to be heterozygous for this variant and Ala403Val (ClinVar 92731, Pathogenic). This c.169_171del variant is referred to as "IVS2 - 2 del" in this article but this is in fact the intended variant as this paper is the reference provided in BIOPKU and HGMD has confirmed, by personal communication with the authors, that this is the c.169_171del variant. PubMed:18299955 
PP4			One proband has been described with PHE levels of 6.5–10 mg/dl. It was unclear if a defect of BH4 cofactor metabolism was excluded. PHE levels were not provided for the compound heterozygous patient described with this c.169_171del variant and the c.1066-11G>A . PubMed:22106832  A mild PKU patient is reported to be heterozygous for this variant and Ala403Val (ClinVar 92731, Pathogenic). Mild PKU was defined as having plasma phenylalanine concentrations of 6.5–10 mg/dl. Most patients were tested for the exclusion of lacking the cofactor BH4 but it was not specified if that included this patient. PubMed:18299955 
PM2			This variant is absent from gnomAD, ExAC, 1000 Genomes, and ESP.
PM4			The in-frame deletion removes one amino acid (Glu57).

Curation History

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