

Variant: *NM_000277.1:c.835_836delinsTG*

Version: 1.0

CA645372267 [↗](#)

1693227 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: a3e440b0-140d-43fb-9d30-ac885cc5f588

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HGVS expressions

NM_000277.1:c.835_836delinsTG

NC_000012.12:g.102852821_102852822delinsCA

CM000674.2:g.102852821_102852822delinsCA

NC_000012.11:g.103246599_103246600delinsCA

CM000674.1:g.103246599_103246600delinsCA

NC_000012.10:g.101770729_101770730delinsCA

NG_008690.1:g.69781_69782delinsTG

NG_008690.2:g.110589_110590delinsTG

ENST00000553106.6:c.835_836delinsTG

ENST00000307000.7:c.820_821delinsTG

ENST00000549247.6:n.594_595delinsTG

ENST00000553106.5:c.835_836delinsTG

NM_000277.2:c.835_836delinsTG

NM_001354304.1:c.835_836delinsTG

NM_000277.3:c.835_836delinsTG

NM_001354304.2:c.835_836delinsTG

Likely Pathogenic

Met criteria codes **4**

PM3_Supporting

PP4_Moderate

PP3

PM2

Not Met criteria codes **1**

PM5

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.835_836delinsTG (p.Pro279Cys) variant in PAH has been reported in 1 individual with hyperphenylalaninemia (BH4 deficiency excluded), detected with pathogenic variant p.R408W (PMID: 21147011). This variant is absent in population databases. Computational evidence supports a deleterious effect. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PM2, PM3_supporting, PP3.

Met criteria codes

PM3_Supporting			Seen with R408W in 1 patient. Parental testing not reported. PMID: 21147011
			P279C seen with R408W (VarID 577, Pathogenic in ClinVar) in 1 patient PubMed:21147011 
PP4_Moderate			P279C seen in 1 patient with hyperphenylalaninemia. BH4 deficiency excluded by assessment of the PAH gene and genes of the BH4 synthesis/recycling pathways (PTS and QDPR). PMID: 21147011
			588 hyperphenylalaninemic patients were investigated. Assessment included PAH gene and genes of the BH4 synthesis/recycling pathways (PTS and QDPR). P279C seen on 1 allele. PubMed:21147011 
PP3			Deleterious effect predicted in SIFT, Polyphen2, MutationTaster
PM2			Absent from ExAC, 1000G, ESP, gnomAD

Not Met criteria codes

PM5			P279L and P279A are likely pathogenic in ClinVar
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Curation History



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