

Variant: NM_000277.1:c.176A>T

CA16020736 [↗](#)

619154 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: cfee7c8b-e49c-474a-bebe-719a67c0306e

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HGVS expressions

NM_000277.1:c.176A>T

NC_000012.12:g.102894911T>A

CM000674.2:g.102894911T>A

NC_000012.11:g.103288689T>A

CM000674.1:g.103288689T>A

NC_000012.10:g.101812819T>A

NG_008690.1:g.27692A>T

NG_008690.2:g.68500A>T

NM_000277.2:c.176A>T

NM_001354304.1:c.176A>T

NM_000277.3:c.176A>T

ENST00000307000.7:c.161A>T

ENST00000546844.1:c.176A>T

ENST00000548677.2:n.263A>T

ENST00000548928.1:n.98A>T

ENST00000549111.5:n.272A>T

ENST00000550978.6:n.160A>T

ENST00000551337.5:c.176A>T

ENST00000551988.5:n.265A>T

ENST00000553106.5:c.176A>T

ENST00000635500.1:n.144A>T

Uncertain Significance

Met criteria codes **3**

PP4

PM2

PM3

Not Met criteria codes **1**

PP3

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.176A>T (p.Asp59Val) variant in PAH has been reported in an Italian patient with mild PKU (BH4 deficiency not totally excluded) with pathogenic variant p.R261Q (PP4, PM3; PMID: 25003100) This variant is absent from 1000G, ESP, ExAC and gnomAD. computational evidence is conflicting. In summary, this variant meets criteria to be classified as uncertain significance for PAH. PAH-specific ACMG/AMP criteria applied: PP4, PM2, PP3.

Met criteria codes

PP4			Identified in Italian mild PKU patient. Phe, Tyr levels, and Phe/Tyr ratio were assessed. PMID: 25003100
Seventeen subjects were sampled among the PKU patients in charge of the Department of Paediatrics and Child Neurology and Psychiatry in Rome, according to the following criteria: (a) genetically confirmed defect of PAH; (e) availability of biochemical data covering the patient’s history from the diagnosis up to the study; (f) absence of medical condition, other than PKU. Patient 5: D59V, mild PKU, Phe: 313 uM. Phe, Tyr levels, and Phe/Tyr ratio were assessed on dry blood spot on the day of neuropsychological assessment, and before T1 and T2 examinations.			
PubMed:25003100 			
PM2			Absent from ExAC, gnomAD, 1000G, ESP
PM3			Detected with R261Q, P/LP in ClinVar
Patient 8 genotype: D59V/R261Q (P/LP in ClinVar) PubMed:25003100 			

Not Met criteria codes

PP3			Conflicting predictions of pathogenicity. SIFT:T,D; Polyphen2:B, MutationTaster:D. REVEL=0.747
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Curation History



 

 

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