

Variant: NM_000277.1:c.697T>A

CA16020843 [↗](#)

619163 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: b990f0f7-2c1b-428d-bfec-28ed05f717f4

Approved on: 2018-12-10

Published on: 2018-12-10

HGVS expressions

NM_000277.1:c.697T>A

NC_000012.12:g.102855145A>T

CM000674.2:g.102855145A>T

NC_000012.11:g.103248923A>T

CM000674.1:g.103248923A>T

NC_000012.10:g.101773053A>T

NG_008690.1:g.67458T>A

NG_008690.2:g.108266T>A

NM_000277.2:c.697T>A

NM_001354304.1:c.697T>A

NM_000277.3:c.697T>A

ENST00000307000.7:c.682T>A

ENST00000549111.5:n.793T>A

ENST00000553106.5:c.697T>A

Pathogenic

Met criteria codes **5**

PP4_Moderate

PM3_Strong

PS3

PP3

PM2

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.697T>A (p.Phe233Ile) variant in PAH has been reported in 2 unrelated patients with PKU (BH4 deficiency excluded) and was detected with known pathogenic variants p.R408W and p.V245A. (PP4_Moderate, PM3_Strong; PMID: 23764561). This variant is absent in population databases (PM2). This variant showed no specific activity in functional assay and no response to chaperone co-expression (PS3; PMID: 28653649). Computational prediction tools and conservation analysis suggest this variant may impact the protein (PP3). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PP4_Moderate, PS3, PM3_strong, PM2, PP3.

Met criteria codes

PP4_Moderate			p.F233I was detected in two unrelated PKU patients. BH4 deficiency was excluded. PMID: 23764561 We investigated the mutation spectrum of the phenylalanine hydroxylase gene (PAH) in a cohort of patients from 135 Slovak PKU families. We identified the novel missense mutation: p.F233I. Patients with BH4 deficiency were excluded from molecular analysis. PubMed:23764561 
PM3_Strong			p.F233I was detected in two apparently unrelated patients in compound heterozygosity with p.R408W (VarID 577, Pathogenic) and p.V245A (Pathogenic) PMID: 23764561 Mutation p.F233I was detected in two apparently unrelated patients in compound heterozygosity with p.R408W (VarID 577, Pathogenic) and p.V245A (Pathogenic) respectively. PubMed:23764561 
PS3			Showed no specific activity in functional assay and no response to chaperone co-expression. PMID: 28653649 In this study, in silico prediction and in vitro prokaryotic and eukaryotic expression systems were used to functionally characterize five PAH missense variants (including p.F233I). p.F233I was classified as deleterious mutations since it showed no specific activity in functional assay and no response to chaperone co-expression. Protein levels of the PAH variant was very low when expressed in HepG2 cells. PubMed:28653649 
PP3			Deleterious effect predicted in SIFT, Polyphen2, MutationTaster. REVEL=0.92
PM2			Absent from ExAC, gnomAD, 1000G, ESP

Curation History



 

 

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.