The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000277.1:c.788T>C

CA16020857

619150 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: ff16e9ce-c14a-43a3-9502-03a9763729f0
Approved on: 2018-12-10
Published on: 2018-12-10

HGVS expressions

NM_000277.1:c.788T>C
NC_000012.12:g.102852869A>G
CM000674.2:g.102852869A>G
NC_000012.11:g.103246647A>G
CM000674.1:g.103246647A>G
NC_000012.10:g.101770777A>G
NG_008690.1:g.69734T>C
NG_008690.2:g.110542T>C
NM_000277.2:c.788T>C
NM_001354304.1:c.788T>C
NM_000277.3:c.788T>C
ENST00000307000.7:c.773T>C
ENST00000549247.6:n.547T>C
ENST00000553106.5:c.788T>C

Pathogenic

Met criteria codes 5

PM3 PM2 PS3 PP3 PP4

Evidence Links 2

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.788T>C (p.Phe263Ser) variant in PAH has been reported in 1 patient with hyperphenylalaninemia (BH4 deficiency not excluded) and was detected with known pathogenic variant c.1066-11G>A (PP4, PM3; PMID: 23357515). This variant is absent in population databases (PM2). This variant has 4% enzyme activity (PS3; PMID:20179079). Computational prediction tools and conservation analysis suggest that 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: PS3, PM2, PM3, PP3, PP4.

Met criteria codes

PM3		✔	Detected with c.1066-11G>A. PMID: 23357515
			Based on our analysis, we predict that p.(Phe263Ser) causes significant impairment of the protein structure and function, and that patients carrying this mutation have the classical PKU phenotype (like our patient with the genotype p.[Phe263Ser];[c.1066-11 G > A]). PubMed:23357515
PM2		✔	Absent from ExAC, gnomAD, 1000G, ESP
PS3		✔	COS-7 cells expressing a recombinant PAH protein carrying p.Phe263Ser show almost no PAH activity (4+/-17 % of w.t.). PMID: 20179079
			mouse model of HPA with in vitro analysis of murine recombinant PAH proteins; the Pahenu mouse carries p.Phe263Ser on both alleles and is characterized by the classical PKU phenotype, and COS-7 cells expressing a recombinant murine protein carrying p.Phe263Ser show almost no PAH activity (4+/-17 % of w.t.). PubMed:20179079
PP3		✔	Predicted deleterious in SIFT, Polyphen2, MutationTaster
PP4		✔	F263 seen on 1 allele in a Czech HPA patient. PMID: 23357515
			665 unrelated Czech HPA patients. F263S seen on 1 allele. PubMed:23357515

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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.