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.813T>G

CA16020865

619152 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 294f7fa4-2bba-4ea4-9bd0-32859d3e9ee3
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HGVS expressions

NM_000277.1:c.813T>G
NC_000012.12:g.102852844A>C
CM000674.2:g.102852844A>C
NC_000012.11:g.103246622A>C
CM000674.1:g.103246622A>C
NC_000012.10:g.101770752A>C
NG_008690.1:g.69759T>G
NG_008690.2:g.110567T>G
NM_000277.2:c.813T>G
NM_001354304.1:c.813T>G
NM_000277.3:c.813T>G
ENST00000307000.7:c.798T>G
ENST00000549247.6:n.572T>G
ENST00000553106.5:c.813T>G

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PM3 PP4_Moderate

Not Met criteria codes 1

PM5

Evidence Links 3

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.813T>G (p.His271Gln) variant in PAH has been reported in 3 individuals with PKU (BH4 deficiency excluded). (PP4_Moderate; PMID: 1829436, 18299955, 21307867). This variant is absent in population databases (PM2). This variant was detected with IVS10-11G>A, known pathogenic (PM3; PMID: 18299955). Computational evidence support 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, PP3.

Met criteria codes

PP3		✔	Deleterious effect predicted in SIFT, polyphen2, MutationTaster. REVEL=0.915
PM2		✔	Absent from ExAC, gnomAD, 1000G, ESP
PM3		✔	detected with IVS10-11G>A, known pathogenic PMID: 18299955 Patient genotype: IVS10-11G>A/H271Q PubMed:18299955
PP4_Moderate		✔	H271Q seen in 2 classic PKU patients in Israel (PMID: 1829436, 18299955) and 1 PKU patient in Japan. BH4 deficiency ruled out in Japanese patient. PMID: 21307867 Same patient as 18294361, and another patient (3 alleles): 1 patient w/classic PKU phenotype, homozygous. 2nd patient with classic PKU, IVS10-11G>A. PubMed:18299955 This study enrolled 203 Japanese residents with a serum phenylalanine level higher than 0.18mM. PAH deficiency was diagnosed at the participating institutions on the basis of absence of neurologic deterioration on a low phenylalanine diet, analysis of dihydropteridine reductase activity in red blood cells, biopterin loading test and/or pteridine analysis in urine. H271Q seen on 1 allele. PubMed:21307867 The present study is based on the 159 patients, who were Israeli citizens diagnosed through the newborn screening, either Jews, Arabs or Druze. H271Q was seen on 2 Non-Ashkenazi Jewish alleles. PubMed:18294361

Not Met criteria codes

PM5		✖	H271L LP in ClinVar

Curation History

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