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_000277.2(PAH):c.511G>A (p.Gly171Arg)

Version: 1.0

CA229598

102716 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 0dbfb1dc-9c9b-4fbe-b1a1-37b190aafe51
Approved on: 2018-08-10
Published on: 2019-05-04

HGVS expressions

NM_000277.2:c.511G>A
NM_000277.2(PAH):c.511G>A (p.Gly171Arg)
NC_000012.12:g.102855331C>T
CM000674.2:g.102855331C>T
NC_000012.11:g.103249109C>T
CM000674.1:g.103249109C>T
NC_000012.10:g.101773239C>T
NG_008690.1:g.67272G>A
NG_008690.2:g.108080G>A
NM_000277.1:c.511G>A
NM_001354304.1:c.511G>A
NM_000277.3:c.511G>A
ENST00000307000.7:c.496G>A
ENST00000549111.5:n.607G>A
ENST00000551988.5:n.532G>A
ENST00000553106.5:c.511G>A

Likely Pathogenic

Met criteria codes 4

PP3 PM2 PM3_Strong PP4_Moderate

Evidence Links 2

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

PAH-specific ACMG/AMP criteria applied: PM2: Absent from ExAC, gnomAD, 1000G, ESP; PP3: Deleterious effect predicted in SIFT, Polyphen-2, MutationTaster. REVEL=0.966; PP4_Moderate: Detected in PKU patients. BH4 deficiency assessed. Upgraded per ClinGen PAH EP. (PMID:26600521; PMID:23430918); PM3_Strong: Detected with c.611A>G (P/LP) and R408W (P). Upgraded per ClinGen SVI workgroup. (PMID:23430918; PMID:26600521). In summary this variant meets criteria to be classified as likely pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PM2, PP3, PP4_Moderate, PM3_Strong).

Met criteria codes

PP3	✔	Deleterious effect predicted in SIFT, Polyphen-2, MutationTaster. REVEL=0.966
PM2	✔	Absent from ExAC, gnomAD, 1000G, ESP
PM3_Strong	✔	Detected with c.611A>G (P/LP) and R408W (P). Upgraded per ClinGen SVI workgroup. EX6-96G>A (c.611A>G) (P/LP) maternal, G171R paternal PubMed:26600521 Patient Genotype: p.G171R/ p.R408W PubMed:23430918
PP4_Moderate	✔	Detected in PKU patients. BH4 deficiency assessed. Upgraded per ClinGen PAH EP. Detected in 1 PKU patient: PKU (>450 umol/L). PubMed:23430918 Phe>120 uM, no BH4 defect, in trans with EX6-96G>A PubMed:26600521

Curation History

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