

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

**UID:** 0dbfb1dc-9c9b-4fbe-b1a1-37b190aafe51

**Approved on:** 2018-08-10

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### 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**

PP4\_Moderate

PM3\_Strong

PP3

PM2

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

#### 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](#)

#### 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](#)

#### PP3



Deleterious effect predicted in SIFT, Polyphen-2, MutationTaster. REVEL=0.966

#### PM2



Absent from ExAC, gnomAD, 1000G, ESP

### Curation History [↗](#)

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