

Variant: NM_000277.2(PAH):c.829T>G (p.Tyr277Asp)

CA251534 [↗](#)

603 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: ac3ebdc5-43ab-403b-8ef9-27fff7d691ba

Approved on: 2018-08-05

Published on: 2018-12-10

HGVS expressions

NM_000277.2(PAH):c.829T>G (p.Tyr277Asp)

NM_000277.2:c.829T>G

NC_000012.12:g.102852828A>C

CM000674.2:g.102852828A>C

NC_000012.11:g.103246606A>C

CM000674.1:g.103246606A>C

NC_000012.10:g.101770736A>C

NG_008690.1:g.69775T>G

NG_008690.2:g.110583T>G

NM_000277.1:c.829T>G

NM_001354304.1:c.829T>G

NM_000277.3:c.829T>G

ENST00000307000.7:c.814T>G

ENST00000549247.6:n.588T>G

ENST00000553106.5:c.829T>G

Pathogenic

Met criteria codes **5**

PP4_Moderate

PP3

PM2

PM3

PS3

Not Met criteria codes **1**

PM5

Evidence Links **2**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.829T>G (p.Tyr277Asp) variant in PAH has been reported in 2 individuals with Classic PKU (BH4 deficiency excluded). (PP4_Moderate; PMID: 8268925; PMID: 23500595). This variant has an extremely low allele frequency (1/121400) in ExAC (PM2; <http://exac.broadinstitute.org>). This variant has 0% enzyme activity (PS3; <http://www.biopku.org/centralStore/biopku/PAH%20activity.pdf>). This variant was detected in trans with L48S (Pathogenic in ClinVar) (PM3; PMID: 23500595). Computational prediction tools and

conservation analysis suggest that the c.829T>G 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

Met criteria codes

PP4_Moderate			Found in 2 individuals with Classic PKU with BH4 deficiency excluded. PMID: 8268925; PMID: 23500595.
			Found in 2 individuals with Classic PKU with BH4 deficiency excluded. PubMed:23500595 
			One individual reported with PKU. PubMed:8268925 
PP3			Deleterious affected predicted by SIFT and PolyPhen. Predicted A,A (damaging) by MutationTaster.
PM2			1/121400 reported in ExAC. Absent in 1000 genomes, gnomAD, and ESP.
PM3			Found in trans with L48S, pathogenic in ClinVar PMID: 23500595
			Found in trans with L48S in two individual with Classic PKU. PubMed:23500595 
PS3			PAH activity is 0% from BioPKU

Not Met criteria codes

PM5			Y277C (likely pathogenic in ClinVar)
-----	---	---	--------------------------------------

Curation History

▼

▼

Showing 1 to 1 of 1 rows

--

