

Variant: NM_000277.2(PAH):c.311C>A (p.Ala104Asp)

CA229515 [↗](#)

102650 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 86ce59a8-cc5a-46f9-9b96-2254638db653

Approved on: 2018-08-07

Published on: 2018-12-10

HGVS expressions

NM_000277.2:c.311C>A

NM_000277.2(PAH):c.311C>A (p.Ala104Asp)

NC_000012.12:g.102894776G>T

CM000674.2:g.102894776G>T

NC_000012.11:g.103288554G>T

CM000674.1:g.103288554G>T

NC_000012.10:g.101812684G>T

NG_008690.1:g.27827C>A

NG_008690.2:g.68635C>A

NM_000277.1:c.311C>A

NM_001354304.1:c.311C>A

NM_000277.3:c.311C>A

ENST00000307000.7:c.296C>A

ENST00000546844.1:c.311C>A

ENST00000548928.1:n.233C>A

ENST00000549111.5:n.407C>A

ENST00000550978.6:n.295C>A

ENST00000551337.5:c.311C>A

ENST00000551988.5:n.400C>A

ENST00000553106.5:c.311C>A

Pathogenic

Met criteria codes **3**

PS3

PM2

PM3_Strong

Not Met criteria codes **1**

PP3

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: Extremely low frequency: 0.00009 in gnomAD; PS3: 26% PAH enzyme activity; PM3_Strong: Detected with Y414C, pathogenic in ClinVar and V245L (P/LP) (PMID:9429153; PMID:24368688). In summary this variant meets criteria to be classified as pathogenic for phenylketonuria in an autosomal recessive manner based on the ACMG/AMP criteria applied as specified by the PAH Expert Panel: (PM2, PS3, PM3_Strong).

Met criteria codes

PS3	✓	26% PAH enzyme activity
PM2	✓	Extremely low frequency: 0.00009 in gnomAD
PM3_Strong	 ✓	Detected with Y414C, pathogenic in ClinVar and V245L (P/LP)
Patient genotype: A104D/D222G (VarID 102775, clinical significance not provided). Patient genotype: Y414C (VarID 593, Pathogenic)/A104D. PubMed:9429153 		
ID #72: p.A104D/p.V245L (VarID 102810, Pathogenic/ likely pathogenic) PubMed:24368688 		

Not Met criteria codes

PP3	 ✗	Conflicting predictions for pathogenicity: benign in Polyphen-2, disease causing in MutationTaster
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Curation History

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