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.847A>G

Version: 1.0

CA16020876

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: deb05865-1cb0-4972-95ae-59e2da8df3a4
Approved on: 2018-12-10
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HGVS expressions

NM_000277.1:c.847A>G
NC_000012.12:g.102851752T>C
CM000674.2:g.102851752T>C
NC_000012.11:g.103245530T>C
CM000674.1:g.103245530T>C
NC_000012.10:g.101769660T>C
NG_008690.1:g.70851A>G
NG_008690.2:g.111659A>G
NM_000277.2:c.847A>G
NM_001354304.1:c.847A>G
NM_000277.3:c.847A>G
ENST00000307000.7:c.832A>G
ENST00000549247.6:n.606A>G
ENST00000551114.2:n.509A>G
ENST00000553106.5:c.847A>G
ENST00000635477.1:n.8A>G

Likely Pathogenic

Met criteria codes 4

PM3 PM5 PM2 PP4_Moderate

Not Met criteria codes 1

PP3

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.847A>G (p.Ile283Val) variant in PAH is absent from all population databases, and is at the same amino acid as a previously established pathogenic variant (c.847A>T (p.Ile283Phe)). It has been identified in a patient with classic PKU (BH4 defect excluded), and in trans with a known pathogenic variant (c.1045T>C, p.Ser349Pro) PMID: 27121329. Summary evidence using PAH specific ACMG/AMP guidelines :PM2, PM5, PM3, PP4_Moderate.

Met criteria codes

PM3	✔	In trans with c.1045T>C (p.Ser349Pro) (pathogenic in ClinVar)
		In trans with c.1045T>C (p.Ser349Pro) (pathogenic in ClinVar) PubMed:27121329
PM5	✔	NM_000277.2(PAH):c.847A>T (p.Ile283Phe) is LP/P in ClinVar
PM2	✔	Absent from all population databases
PP4_Moderate	✔	Single patient with Classic PKU (>1200umol/L), BH4 non-responder. PMID: 27121329
		Single patient with BH4 non-responsive Classic PKU PubMed:27121329

Not Met criteria codes

PP3	✖	in silico predictors do not agree. REVEL=0.438

Curation History

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