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.526C>T (p.Arg176Ter)

Version: 1.0

CA275338

102723 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 08d51386-af9e-4de1-8e7b-0dc6c2252c91
Approved on: 2018-08-13
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HGVS expressions

NM_000277.2:c.526C>T
NM_000277.2(PAH):c.526C>T (p.Arg176Ter)
NC_000012.12:g.102855316G>A
CM000674.2:g.102855316G>A
NC_000012.11:g.103249094G>A
CM000674.1:g.103249094G>A
NC_000012.10:g.101773224G>A
NG_008690.1:g.67287C>T
NG_008690.2:g.108095C>T
NM_000277.1:c.526C>T
NM_001354304.1:c.526C>T
NM_000277.3:c.526C>T
ENST00000307000.7:c.511C>T
ENST00000549111.5:n.622C>T
ENST00000551988.5:n.547C>T
ENST00000553106.5:c.526C>T

Pathogenic

Met criteria codes 4

PP4_Moderate PVS1 PM3_Strong 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: PVS1: Nonsense variant; PM2: ExAC MAF: 0.00010; PP4_Moderate: BH4 defect excluded in all patients in Liu 2015. Identified in 6 patients in this study (PMID:10394930; PMID:26600521); PM3_Strong: Identified in 6 patients, in trans with R243Q and R241C (both pathogenic) (PMID:26600521). 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: (PVS1, PM2, PP4_Moderate, PM3_Strong).

Met criteria codes

PP4_Moderate	✔	BH4 defect excluded in all patients in Liu 2015. Identified in 6 patients in this study
		Patients with PAH-deficient hyperphenylalaninaemia in 272 independent families (248 PKU and 24 MHP) living in Germany were investigated. R176X was detected on 1 chromosome. PubMed:10394930 BH4 defect excluded in all patients PubMed:26600521
PVS1	✔	Nonsense variant
PM3_Strong	✔	Identified in 6 patients, in trans with R243Q and R241C (both pathogenic)
		Identified in 6 patients, in trans with R243Q and R241C (both pathogenic) PubMed:26600521
PM2	✔	ExAC MAF: 0.00010

Curation History

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