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.535T>A (p.Tyr179Asn)

Version: 1.0

CA229613

102729 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1530f57a-9096-4f98-a934-15ce8f576c73
Approved on: 2018-08-10
Published on: 2019-08-17

HGVS expressions

NM_000277.2:c.535T>A
NM_000277.2(PAH):c.535T>A (p.Tyr179Asn)
NC_000012.12:g.102855307A>T
CM000674.2:g.102855307A>T
NC_000012.11:g.103249085A>T
CM000674.1:g.103249085A>T
NC_000012.10:g.101773215A>T
NG_008690.1:g.67296T>A
NG_008690.2:g.108104T>A
ENST00000553106.6:c.535T>A
ENST00000307000.7:c.520T>A
ENST00000549111.5:n.631T>A
ENST00000551988.5:n.556T>A
ENST00000553106.5:c.535T>A
NM_000277.1:c.535T>A
NM_001354304.1:c.535T>A
NM_000277.3:c.535T>A
NM_001354304.2:c.535T>A

Likely Pathogenic

Met criteria codes 4

PP3 PP4_Moderate PM2 PM3

Evidence Links 1

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=0.929; PP4_Moderate: Detected in 1 PKU patient, primary BH4 deficiency excluded. Upgraded per ClinGen PAH EP. (PMID:23430918); PM3: Detected with c.1066-11G>A (P) (PMID:23430918). 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).

Met criteria codes

PP3	✔	Deleterious effect predicted in SIFT, Polyphen-2, MutationTaster. REVEL=0.929
PP4_Moderate	✔	Detected in 1 PKU patient, primary BH4 deficiency excluded. Upgraded per ClinGen PAH EP. Detected in 1 PKU patient: previously documented Phe level >360 umol/L and a Phe level >450 umol/L at the screening visit. Patients with a diagnosis of primary BH4 deficiency were excluded from the study. PubMed:23430918
PM2	✔	Absent from ExAC, gnomAD, 1000G, ESP
PM3	✔	Detected with c.1066-11G>A (P) Patient genotype: p.Y179N: c.1066-11G>A PubMed:23430918

Curation History

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