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Variant: NM_000277.2(PAH):c.1033G>A (p.Ala345Thr)

CA229291

102483 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: e8f41b26-818c-4003-b73f-0be5c4dcd234
Approved on: 2018-08-10
Published on: 2018-12-10

HGVS expressions

NM_000277.2(PAH):c.1033G>A (p.Ala345Thr)
NM_000277.2:c.1033G>A
NC_000012.12:g.102844368C>T
CM000674.2:g.102844368C>T
NC_000012.11:g.103238146C>T
CM000674.1:g.103238146C>T
NC_000012.10:g.101762276C>T
NG_008690.1:g.78235G>A
NG_008690.2:g.119043G>A
NM_000277.1:c.1033G>A
NM_001354304.1:c.1033G>A
NM_000277.3:c.1033G>A
ENST00000307000.7:c.1018G>A
ENST00000549247.6:n.792G>A
ENST00000551114.2:n.695G>A
ENST00000553106.5:c.1033G>A
ENST00000635477.1:n.137G>A
ENST00000635528.1:n.548G>A

Likely Pathogenic

Met criteria codes 5

PP3 PM2 PM5 PM3 PP4_Moderate

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 controls in ExaC, 100 Genomes, ESP, and gnomAD; PP3: Deleterious effected predicted by SIFT, Polyphen2, and MutationTaster; PM5: A345S (Variant ID 102484) predicted pathogenic in ClinVar; PP4_Moderate: Found in two individuals with Classic PKU on exon 10.Urinary pterin analysis and dihydropteridine reductase (DHPR) assay were performed t (PMID:15503242); PM3: Found in trans with R243Q (pathogenic in ClinVar). (PMID:15503242). 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, PM5, PP4_Moderate, PM3).

Met criteria codes

PP3	✔	Deleterious effected predicted by SIFT, Polyphen2, and MutationTaster
PM2	✔	Absent from controls in ExaC, 100 Genomes, ESP, and gnomAD
PM5	✔	A345S (Variant ID 102484) predicted pathogenic in ClinVar
PM3	✔	Found in trans with R243Q (pathogenic in ClinVar). Found in trans with R243Q (pathogenic in ClinVar) in Patients 53 and 65, and G332V (not in ClinVar). PubMed:15503242
PP4_Moderate	✔	Found in two individuals with Classic PKU on exon 10.Urinary pterin analysis and dihydropteridine reductase (DHPR) assay were performed t Found in two individuals with Classic PKU on exon 10. Found in trans with G332V in a individual with classic PKU. Found in trans with R243Q in two individuals, one with Classic PKU and one NA. Urinary pterin analysis and dihydropteridine reductase (DHPR) assay were performed t PubMed:15503242

Curation History

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