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Variant: NM_000277.1(PAH):c.841C>T (p.Pro281Ser)

CA220587

92749 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4bb0b9e5-fa14-4fb0-bac1-1bcae3cc23b8
Approved on: 2018-08-10
Published on: 2018-12-10

HGVS expressions

NM_000277.1(PAH):c.841C>T (p.Pro281Ser)
NM_000277.1:c.841C>T
NC_000012.12:g.102852816G>A
CM000674.2:g.102852816G>A
NC_000012.11:g.103246594G>A
CM000674.1:g.103246594G>A
NC_000012.10:g.101770724G>A
NG_008690.1:g.69787C>T
NG_008690.2:g.110595C>T
NM_000277.2:c.841C>T
NM_001354304.1:c.841C>T
NM_000277.3:c.841C>T
ENST00000307000.7:c.826C>T
ENST00000549247.6:n.600C>T
ENST00000553106.5:c.841C>T
ENST00000635477.1:n.2C>T

Likely Pathogenic

Met criteria codes 4

PM2 PM3_Strong PP3 PP4_Moderate

Not Met criteria codes 1

PM5

Evidence Links 3

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: 1 allele in ExAC ; PP3: tools predict damaging ; PP4_Moderate: P281S Identified in at least one patient with classic PKU. BH4 deficiency excluded. (PMID:15589814); PM3_Strong: Detected with c.1315+1G>A & p.Arg243Ter, pathogenic in ClinVar (PMID:26666653; PMID:27121329). 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_Strong).

Met criteria codes

PM2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3_Strong	✔	Detected with c.1315+1G>A & p.Arg243Ter, pathogenic in ClinVar Patient genotype: c. [841C>T]; [1315+1G>A] (VarID576, Pathogenic). PubMed:26666653 Patient genotype: p.[Arg243*];[Pro281Ser]. (VarID588, Pathogenic) PubMed:27121329
PP3	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4_Moderate	✔	P281S Identified in at least one patient with classic PKU. BH4 deficiency excluded. known mutations in the PAH gene, and pterin profile and dihydropteridine reductase activity excluding a primary defect in BH4 metabolism. Patient 54 with Classic PKU was homozygous for P281S. Phe before BH4 loading: 1145 umol/L. PubMed:15589814

Not Met criteria codes

PM5	✖	P281L is Pathogenic in ClinVar, LP by PAHEP

Curation History

Showing 1 to 1 of 1 rows

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