Variant: NM_000277.1(PAH):c.842C>T (p.Pro281Leu)

Version: 1.0

CA220589

589 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: c12aac5a-a84d-4ecc-b66a-d375bf2deb7b
Approved on: 2018-08-27
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HGVS expressions

NM_000277.1:c.842C>T
NM_000277.1(PAH):c.842C>T (p.Pro281Leu)
NC_000012.12:g.102852815G>A
CM000674.2:g.102852815G>A
NC_000012.11:g.103246593G>A
CM000674.1:g.103246593G>A
NC_000012.10:g.101770723G>A
NG_008690.1:g.69788C>T
NG_008690.2:g.110596C>T
ENST00000553106.6:c.842C>T
ENST00000307000.7:c.827C>T
ENST00000549247.6:n.601C>T
ENST00000553106.5:c.842C>T
ENST00000635477.1:c.3C>T
NM_000277.2:c.842C>T
NM_001354304.1:c.842C>T
NM_000277.3:c.842C>T
NM_001354304.2:c.842C>T

Likely Pathogenic

Met criteria codes 4

PM3 PP4_Moderate PS3 PP3

Not Met criteria codes 2

PM1 PM2

Evidence Links 4

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: PP3: ; PS3: 2% activity in bioPKU (PAH0309) (PMID:25596310; PMID:17935162); PP4_Moderate: 2 patients with moderate or classical PKU; patients with severe PKU. BH4 deficiency ruled out. (PMID:15503242; PMID:12655553); PM3: IVS4-1G>A (P/LP) (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: (PP3, PS3, PP4_Moderate, PM3).

Met criteria codes

PM3	✔	IVS4-1G>A (P/LP) Table 1 showed two patients with either moderate (IVS4-1G>A and P281L) or classical PKU (G239S and P281L). PubMed:15503242
PP4_Moderate	✔	2 patients with moderate or classical PKU; patients with severe PKU. BH4 deficiency ruled out. Table 1 showed two patients with either moderate (IVS4-1G>A and P281L) or classical PKU (G239S and P281L). Urinary pterin analysis and dihydropteridine reductase (DHPR) assay were performed to exclude 6-pyruvoyl-tetrahydropterin synthase (PTPS) deficiencies. PubMed:15503242 In Table 2, found in patients with severe PKU PubMed:12655553
PS3	✔	2% activity in bioPKU (PAH0309) 1% activity of wild-type. PubMed:17935162 0.9% activity of WT (Table S4) PubMed:25596310
PP3	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Not Met criteria codes

PM1	✖	Locates in the co-factor binding domain 2
PM2	✖	gnomAD MAF =0.00021

Curation History

Showing 1 to 1 of 1 rows