

*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**

PP4\_Moderate

PP3

PM2

PM3\_Strong

**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 |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|--------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PP4_Moderate       |  |  | <div>P281S Identified in at least one patient with classic PKU. BH4 deficiency excluded.</div> <div>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. <a href="#">PubMed:15589814</a> </div>                        |
| PP3                |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline                                                                                                                                                                                                                                                                                                                                                                |
| PM2                |                                                                                   |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline                                                                                                                                                                                                                                                                                                                                                                |
| PM3_Strong         |  |  | <div>Detected with c.1315+1G&gt;A &amp; p.Arg243Ter, pathogenic in ClinVar</div> <div>Patient genotype: c. [841C&gt;T]; [1315+1G&gt;A] (VarID576, Pathogenic). <a href="#">PubMed:26666653</a> </div> <div>Patient genotype: p.[Arg243*];[Pro281Ser]. (VarID588, Pathogenic) <a href="#">PubMed:27121329</a> </div> |

Not Met criteria codes

|     |                                                                                     |                                                                                     |                                             |
|-----|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------|
| PM5 |  |  | P281L is Pathogenic in ClinVar, LP by PAHEP |
|-----|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------|

Curation History 



 

 

Showing 1 to 1 of 1 rows

|  |
|--|
|  |
|--|

