

Variant: NM_000277.2(PAH):c.581T>C (p.Leu194Pro)

CA229633 [↗](#)

102742 (ClinVar) [↗](#)

Gene: PAH ([HGNC:5053](#))

Condition: phenylketonuria ([MONDO:0009861](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 434f1539-4967-4ff7-abc2-e2ff3ca9ecbe

Approved on: 2018-08-13

Published on: 2018-12-10

HGVS expressions

NM_000277.2(PAH):c.581T>C (p.Leu194Pro)

NM_000277.2:c.581T>C

NC_000012.12:g.102855261A>G

CM000674.2:g.102855261A>G

NC_000012.11:g.103249039A>G

CM000674.1:g.103249039A>G

NC_000012.10:g.101773169A>G

NG_008690.1:g.67342T>C

NG_008690.2:g.108150T>C

NM_000277.1:c.581T>C

NM_001354304.1:c.581T>C

NM_000277.3:c.581T>C

ENST00000307000.7:c.566T>C

ENST00000549111.5:n.677T>C

ENST00000553106.5:c.581T>C

Likely Pathogenic

Met criteria codes **4**

PP4_Moderate

PP3

PM2

PM3_Strong

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: PM2: Absent from 1000G, ESP. gnomAD MAF:0.00004.; PP3: Predicted deleterious in SIFT, Polyphen-2, MutationTaster. REVEL=0.899; PM3_Strong: Detected in trans with V245A and R261X, both pathogenic (PMID:7981714; PMID:16601866); PP4_Moderate: Detected in 3 patients (1 HPA, 1 PKU). BH4 deficiency excluded in 2 patients. (PMID:8533759; PMID:7981714; PMID:9012412; PMID:16601866). 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, PM3_Strong, PP4_Moderate).

Met criteria codes

PP4_Moderate			<p>Detected in 3 patients (1 HPA, 1 PKU). BH4 deficiency excluded in 2 patients.</p> <hr/> <p>L194P detected in 2 chromosomes of PKU patients from 4 centers in Great Britain. PubMed:9012412 </p> <p>Patient 28 detected w/L194L (Mild PKU). A defect in the synthesis or recycling of tetrahydrobiopterin was excluded by analysis of urinary pterins and dihydropteridine reductase activity in erythrocytes. PubMed:16601866 </p> <p>Likely same patient as Zschocke 1994. dihydrobiopterin reductase deficiency was excluded. HPA, 237 umol/L PubMed:8533759 </p> <p>Patient F had L194P. Phe levels 237 umol/L. PubMed:7981714 </p>
PP3			<p>Predicted deleterious in SIFT, Polyphen-2, MutationTaster. REVEL=0.899</p>
PM2			<p>Absent from 1000G, ESP. gnomAD MAF:0.00004.</p>
PM3_Strong			<p>Detected in trans with V245A and R261X, both pathogenic</p> <hr/> <p>Patient 28 genotype: L194P/R261X (VarID610, Path). All the mutations identified were confirmed by analysing parental DNA, which also enabled us to follow the segregation of the mutations. PubMed:16601866 </p> <p>Patient F: V245A (VarID632, Path) /L194P. The mutations identified were confirmed by restriction analysis of PCR products reamplified from genomic DNA in affected subjects and their parents. PubMed:7981714 </p>

Curation History



Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.