The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

# *Variant: NM_001354304.2:c.543_545del*

Version: 1.0

*CA1139532590*

*987763 (ClinVar)*

**Gene**: PAH (HGNC:5053)
**Condition**: phenylketonuria (MONDO:0009861)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** bbdff8c0-4e9b-4d1f-aa34-07027c9399eb
**Approved on**: 2020/10/16
**Published on**: 2020/10/16

## *HGVS expressions*

**NM_001354304.2:c.543_545del**
NC_000012.12:g.102855300_102855302del
CM000674.2:g.102855300_102855302del
NC_000012.11:g.103249078_103249080del
CM000674.1:g.103249078_103249080del
NC_000012.10:g.101773208_101773210del
NG_008690.1:g.67304_67306del
NG_008690.2:g.108112_108114del
ENST00000553106.6:c.543_545del
ENST00000307000.7:c.528_530del
ENST00000549111.5:n.639_641del
ENST00000551988.5:n.564_566del
ENST00000553106.5:c.543_545del
NM_000277.1:c.543_545del
NM_000277.2:c.543_545del
NM_001354304.1:c.543_545del
NM_000277.3:c.543_545del

**Likely Pathogenic**

**Met criteria codes** 4

PM3_Supporting PM2 PM4 PP4_Moderate

Evidence Links 1

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Phenylketonuria VCEP***

**This c.543_545del (p.Glu182del) variant in PAH was reported in a patient with moderate PKU. BH4 enzyme deficiency was ruled out by analysis of urinary pterins and DHPR activity. This variant is observed with pathogenic variant c.611A>G, phase is unknown (PMID: 28754886). The variant is absent from controls in population databases. This in-frame deletion changes the protein length in a non-repeat region. In summary, this variant meets criteria to be classified as likely pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PM2, PM4, PP4_moderate, and PM3_supporting.**

**Met criteria codes**

| | | |
|---|---|---|
| **PM3_Supporting** | ✔ | c.[611A>G];[541-543delGAG]. Phase is unknown. PMID:28754886 |
| **PM2** | ✔ | This variant is absent from controls in ExAC, 1000 Genomes, and gnomAD population databases. |
| **PM4** | ✔ | This in-frame deletion changes the protein length in a non-repeat region. |
| **PP4_Moderate** | ✔ | This variant was observed in one patient with moderate PKU (Phe=900 µmol/L). Patients with defect in the synthesis and recycling of BH4 were excluded by analysis of urinary pterins and dihydropteridine reductase activity in erythrocytes. PMID: 28754886 |

PubMed:28754886

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.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.