

Variant: *NM_001354304.2:c.169-1G>A*

Version: 1.0

CA386304277 [↗](#)

987775 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 644dc10b-d8fe-4691-a94b-a62d358ef02b

Approved on: 2020/10/15

Published on: 2020/10/15

HGVS expressions

NM_001354304.2:c.169-1G>A

NC_000012.12:g.102894919C>T

CM000674.2:g.102894919C>T

NC_000012.11:g.103288697C>T

CM000674.1:g.103288697C>T

NC_000012.10:g.101812827C>T

NG_008690.1:g.27684G>A

NG_008690.2:g.68492G>A

ENST00000553106.6:c.169-1G>A

ENST00000307000.7:c.154-1G>A

ENST00000546844.1:c.169-1G>A

ENST00000548677.2:n.256-1G>A

ENST00000548928.1:n.91-1G>A

ENST00000549111.5:n.265-1G>A

ENST00000550978.6:c.153-1G>A

ENST00000551337.5:c.169-1G>A

ENST00000551988.5:n.258-1G>A

ENST00000553106.5:c.169-1G>A

ENST00000635500.1:n.137-1G>A

NM_000277.1:c.169-1G>A

NM_000277.2:c.169-1G>A

NM_001354304.1:c.169-1G>A

NM_000277.3:c.169-1G>A

Pathogenic

Met criteria codes **4**

PP4 PM2 PM3 PVS1

Evidence Links **1**

Expert Panel

Phenylketonuria VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

This c.169-1G>A (aka IVS2-1G>A) variant in PAH has been observed in at least two patients with PAH deficiency (PMID: 18294361 and 30159852) in trans with pathogenic variant c.168+5G>C. One patient was homozygous for this variant (PMID: 30159852). This variant is absent in controls from population databases. This variant in the -1 splice acceptor site of intron 2 results in exon skipping or use of a cryptic splice site. The variant disrupts the reading frame and is predicted to undergo nonsense mediated decay. This variant breaks the splice site in intron 2 according to computational models. In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PM3, and PP4.

Met criteria codes

PP4			This variant is observed in at least two patients, one with classical PKU and the other with unspecified Phe levels. BH4 deficiency was not ruled out in this study. PMID: 30159852
PubMed:30159852 			
PM2			This variant is absent in controls in gnomAD, ExAC, and 1000 Genomes population databases.
PM3			[c.169-1G>A; c.168+5G>C] and [c.169-1G>A; c.169-1G>A]. Segregation analysis was done. PMID: 30159852
PVS1			This variant in the -1 splice acceptor site of IVS2 results in exon skipping or use of a cryptic splice site. The variant disrupts the reading frame and is predicted to undergo nonsense mediated decay (NMD). This variant breaks the splice site in IVS2 according to Splice AI (1- splice altering) and TraP (0.558, >99%ile, probably damaging).

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.