

Variant: *NM_000284.4(PDHA1):c.795A>G (p.Ala265=)*

Version: 1.0

CA285340 [↗](#)

92772 (ClinVar) [↗](#)

Gene: PDHA1 ([HGNC:5160](#))

Condition: pyruvate dehydrogenase deficiency ([MONDO:0019169](#))

Inheritance Mode: X-linked inheritance

UUID: 85d56eda-9660-4049-967d-93d797bab503

Approved on: 2021/5/5

Published on: 2021/5/6

HGVS expressions

NM_000284.4:c.795A>G

NM_000284.4(PDHA1):c.795A>G (p.Ala265=)

NC_000023.11:g.19355721A>G

CM000685.2:g.19355721A>G

NC_000023.10:g.19373839A>G

CM000685.1:g.19373839A>G

NC_000023.9:g.19283760A>G

NG_016781.1:g.16829A>G

ENST00000355808.10:c.816A>G

ENST00000379805.4:c.*487A>G

ENST00000417819.6:c.879A>G

ENST00000423505.6:c.909A>G

ENST00000481733.2:n.590A>G

ENST00000696704.1:c.*127A>G

ENST00000696705.1:c.*250A>G

ENST00000422285.7:c.795A>G

ENST00000379804.1:c.-49A>G

ENST00000379806.9:c.909A>G

ENST00000422285.6:c.795A>G

ENST00000481733.1:n.223A>G

ENST00000540249.5:c.702A>G

ENST00000545074.5:c.816A>G

NM_000284.3:c.795A>G

NM_001173454.1:c.909A>G

NM_001173455.1:c.816A>G

NM_001173456.1:c.702A>G

NM_001173454.2:c.909A>G

NM_001173455.2:c.816A>G

NM_001173456.2:c.702A>G

Benign

Met criteria codes **3**

BP7

BA1

BS2

Evidence Links **0**

Expert Panel

Mitochondrial Diseases VCEP [↗](#)

Criteria Specification Information **!**

Evidence submitted by expert panel

Mitochondrial Diseases VCEP

The allele frequency of the c.795A>G variant in the PDHA1 gene is 13.1% in gnomAD, including more than 9,000 hemizygotes. This allele frequency, and the frequency with which it is seen in hemizygotes in the general population are high enough to be classified as benign based on thresholds defined by the ClinGen PDHA1 Variant Curation Expert Panel (>0.092%; gnomAD- BA1; >16 hemizygotes- BS2). Furthermore, splicing predictors (SPLICE AI) do not predict a deleterious effect (BP7). In summary, this synonymous variant meets criteria to be classified as benign for PDHA1- related pyruvate dehydrogenase deficiency in an X-linked manner. PDHA1-specific ACMG/AMP criteria applied: (BA1, BS2, BP7). This was reviewed with the PDHA1 expert panel on 4/6/2021 and approved on 4/6/2021.

Met criteria codes

BP7			SPLICE AI scoring- 0.2 is minimum cut off, 0.5 recommended, 0.8 high precision Acceptor and Donor Loss splice AI score = 0.00 Acceptor and Donog Gain Splice AI score = 0.01
BA1			Allele frequency is gnomAD 13% as of 4/5/2021, including in >9,000 males and >5,000 female homozygotes
BS2			More than 9000 hemizygotes in gnomAD

Curation History [↗](#)

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