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: NC_012920.1(MT-ND4L):m.10644G>A

Version: 1.1

CA414806210

618217 (ClinVar)

Gene: MT-ND4L (HGNC:4539)
Condition: mitochondrial disease (MONDO:0044970)
Inheritance Mode: Mitochondrial inheritance
UUID: c47e43b9-f1c3-4747-a060-ebd287ff9802
Approved on: 2023-04-25
Published on: 2025-06-03

HGVS expressions

NC_012920.1:m.10644G>A
J01415.2:m.10644G>A
ENST00000361335.1:c.175G>A

Uncertain Significance

Met criteria codes 1

BP4

Not Met criteria codes 3

PS3 PS4 PM2

Evidence Links 0

Expert Panel

Mitochondrial Diseases VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Mitochondrial Disease Nuclear and Mitochondrial Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1_mtDNA*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Mitochondrial Diseases VCEP

The m.10644G>A (p.V59M) variant in MT-ND4L was reviewed by the Mitochondrial Disease Nuclear and Mitochondrial Variant Curation Expert Panel on April 25, 2023. There are no individuals or families with primary mitochondrial disease with this variant reported in the medical literature to our knowledge. This variant is present in population databases and is seen in individuals from several different haplogroups (MITOMAP: 0.013%, 8/61,883; gnomAD v3.1.2: 0.025%, 114/56,428 homoplasmic occurrences, one heteroplasmic occurrence; Helix: 0.029%, 56/195,893 homoplasmic occurrences). The computational predictor APOGEE gives a consensus rating of neutral with a score of 0.3 (Min=0, Max=1), which predicts a neutral effect on protein function (BP4). There are no cybrids, single fiber studies, or other functional assays reported for this variant. In summary, this variant meets criteria to be classified as uncertain significance for primary mitochondrial disease inherited in a mitochondrial manner. This classification was approved by the NICHD/NINDS U24 ClinGen Mitochondrial Disease Variant Curation Expert Panel on April 25, 2023. Mitochondrial DNA-specific ACMG/AMP criteria applied (PMID: 32906214): BP4.

Met criteria codes

BP4	✔	The computational predictor APOGEE gives a consensus rating of neutral with a score of 0.3 (Min=0, Max=1), which predicts a neutral effect on protein function (BP4).

Not Met criteria codes

PS3	✖	There are no cybrids, single fiber studies, or other functional assays reported for this variant.
PS4	✖	There are no individuals or families with primary mitochondrial disease with this variant reported in the medical literature to our knowledge.
PM2	✖	This variant is present in population databases and is seen in individuals from several different haplogroups (MITOMAP: 0.013%, 8/61,883; gnomAD v3.1.2: 0.025%, 114/56,428 homoplasmic occurrences, one heteroplasmic occurrence; Helix: 0.029%, 56/195,893 homoplasmic occurrences).

Curation History

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