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-ND6):m.14633A>G

Version: 1.1

CA414823366

618219 (ClinVar)

Gene: MT-TN (HGNC:4570)
Condition: mitochondrial disease (MONDO:0044970)
Inheritance Mode: Mitochondrial inheritance
UUID: e0804895-ec82-4adb-89f4-3974966b66c5
Approved on: 2023-03-28
Published on: 2023-03-29

HGVS expressions

NC_012920.1:m.14633A>G
J01415.2:m.14633A>G
ENST00000361681.2:c.41T>C

Uncertain Significance

Met criteria codes 1

BP4

Not Met criteria codes 10

PS2 PS3 PS4 PP1 PP3 PM6 PM2 BA1 BS1 BS3

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.14633A>G (p.M14T) variant in MT-ND6 was reviewed by the Mitochondrial Disease Nuclear and Mitochondrial Variant Curation Expert Panel on March 28, 2023. There are no individuals or families with this variant reported in the medical literature to our knowledge. There are several occurrences in population databases. This variant is absent in GenBank MITOMAP sequences. It is present in 0.005% of individuals in gnomAD v3.1.2 (two homoplasmic occurrences in individuals of European background and haplogroup HV; one homoplasmic occurrence in an individual of African/African American background and haplogroup L3) and in 0.005% of individuals in the Helix dataset (10 homoplasmic occurrences and two heteroplasmic occurrences). In silico tools (APOGEE) predict this variant to be neutral (score of 0.4, BP4). There are no cybrid, single fiber, or other studies 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 March 28, 2023. Mitochondrial DNA-specific ACMG/AMP criteria applied (PMID: 32906214): BP4.

Met criteria codes

BP4	✔	In silico tools (APOGEE) predict this variant to be neutral (score of 0.4, BP4).

Not Met criteria codes

PS2	✖	There are no individuals or families with this variant reported in the medical literature to our knowledge.
PS3	✖	There are no cybrid, single fiber, or other studies reported for this variant.
PS4	✖	There are no individuals or families with this variant reported in the medical literature to our knowledge.
PP1	✖	There are no individuals or families with this variant reported in the medical literature to our knowledge.
PP3	✖	In silico tools (APOGEE) predict this variant to be neutral (score of 0.4, BP4).
PM6	✖	There are no individuals or families with this variant reported in the medical literature to our knowledge.
PM2	✖	There are several occurrences in population databases. This variant is absent in GenBank MITOMAP sequences. It is present in 0.005% of individuals in gnomAD v3.1.2 (two homoplasmic occurrences in individuals of European background and haplogroup HV; one homoplasmic occurrence in an individual of African/African American background and haplogroup L3) and in 0.005% of individuals in the Helix dataset (10 homoplasmic occurrences and two heteroplasmic occurrences).
BA1	✖	There are several occurrences in population databases. This variant is absent in GenBank MITOMAP sequences. It is present in 0.005% of individuals in gnomAD v3.1.2 (two homoplasmic occurrences in individuals of European background and haplogroup HV; one homoplasmic occurrence in an individual of African/African American background and haplogroup L3) and in 0.005% of individuals in the Helix dataset (10 homoplasmic occurrences and two heteroplasmic occurrences).
BS1	✖	There are several occurrences in population databases. This variant is absent in GenBank MITOMAP sequences. It is present in 0.005% of individuals in gnomAD v3.1.2 (two homoplasmic occurrences in individuals of European background and haplogroup HV; one homoplasmic occurrence in an individual of African/African American background and haplogroup L3) and in 0.005% of individuals in the Helix dataset (10 homoplasmic occurrences and two heteroplasmic occurrences).
BS3	✖	There are no cybrid, single fiber, or other studies reported for this variant.

Curation History

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