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:m.4983C>T

Version: 1.0

CA414778366

439962 (ClinVar)

Gene: N/A
Condition: mitochondrial disease (MONDO:0044970)
Inheritance Mode: Mitochondrial inheritance
UUID: ac4a7c00-e4d4-4089-b11e-68f9be1bd311
Approved on: 2024-10-14
Published on: 2024-12-10

HGVS expressions

NC_012920.1:m.4983C>T
J01415.2:m.4983C>T
ENST00000361453.3:c.514C>T

Uncertain Significance

Met criteria codes 2

PVS1_Strong PM2_Supporting

Not Met criteria codes 6

PS2 PS3 PS4 PP1 PP3 PM6

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.4983C>T (p.Q172Term) variant in MT-ND2 was reviewed by the Mitochondrial Disease Variant Curation Expert Panel on October 14, 2024. There are no individuals with this variant reported in the medical literature to our knowledge. There is one prior report in ClinVar for this variant, however details are not provided precluding consideration of this case for this curation. As such, there are no reported de novo occurrences or large families to consider for evidence of variant segregation. This variant is absent in the GenBank dataset, Helix dataset, and gnomAD v3.1.2 (PM2_supporting). There are no in silico predictors for this type of variant in mitochondrial DNA. This variant results in a significant truncation of the MT-ND2 protein (PVS1_strong). There are no cybrids, single fiber studies, or other functional assays reported on 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 October 14, 2024. Mitochondrial DNA-specific ACMG/AMP criteria applied (PMID: 32906214): PVS1_strong, PM2_supporting.

Met criteria codes

PVS1_Strong	✔	The transition at base position m.4983 causes a Q172Term change. This causes a significant truncation > 50% of the ND2 protein (PVS1_strong).
PM2_Supporting	✔	This variant is absent in the GenBank dataset, Helix dataset, and gnomAD v3.1.2 (PM2_supporting).

Not Met criteria codes

PS2	✖	There are no reported de novo occurrences of this variant to our knowledge.
PS3	✖	There are no cybrids, single fiber studies, or other functional assays reported on this variant.
PS4	✖	There are no individuals with this variant reported in the medical literature to our knowledge.
PP1	✖	There are no reports of large families with this variant segregating with disease.
PP3	✖	There are no in silico predictors for this type of variant in mitochondrial DNA.
PM6	✖	There are no reported de novo occurrences of this variant to our knowledge.

Curation History

Showing 1 to 2 of 2 rows