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Variant: m.12706T>C

Version: 1.1

CA120628

9698 (ClinVar)

Gene: MT-ND5 (HGNC:4540)
Condition: mitochondrial disease (MONDO:0044970)
Inheritance Mode: Mitochondrial inheritance
UUID: 65f6d23f-1a7e-4870-b49e-ca0a9fb875d3
Approved on: 2022/6/30
Published on: 2022/6/30

HGVS expressions

NC_012920.1:m.12706T>C
J01415.2:m.12706T>C
ENST00000361567.2:c.370T>C

Likely Pathogenic

Met criteria codes 4

PS2_Moderate PS4_Moderate PM2_Supporting PP3

Not Met criteria codes 1

PS3

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.12706T>C (p.F124L) variant in MT-ND5 has been reported in at least seven unrelated individuals with primary mitochondrial disease and features including Leigh syndrome, MELAS and MELAS-like, and ophthalmoplegia (PS4_moderate; PMIDs: 34200828, 17317336, 21364701, 23847141, 14684687, 11938446). There is one report of a de novo occurrence of this variant (PS2_moderate, PMID: 17317336). This variant is absent in the GenBank dataset, Helix dataset, and gnomAD v3.1.2 (PM2_supporting). The computational predictor APOGEE gives a consensus rating of pathogenic with a score of 0.9 (Min=0, Max=1), which predicts a damaging effect on gene function (PP3). There are no cybrid studies, single fiber studies, or other functional assays reported. In summary, this variant meets criteria to be classified as likely pathogenic for primary mitochondrial disease inherited in a mitochondrial manner. This classification was approved by the NICHD/NINDS U24 Mitochondrial Disease Variant Curation Expert Panel on April 11, 2022. Mitochondrial DNA-specific ACMG/AMP criteria applied (PMID: 32906214): PS4_moderate, PS2_moderate, PM2_supporting, PP3.

Met criteria codes

PS2_Moderate	✔	There is one report of a de novo occurrence of this variant (PS2_moderate, PMID: 17317336).
PS4_Moderate	✔	The m.12706T>C (p.F124L) variant in MT-ND5 has been reported in at least seven unrelated individuals with primary mitochondrial disease and features including Leigh syndrome, MELAS and MELAS-like, and ophthalmoplegia (PS4_moderate; PMIDs: 34200828, 17317336, 21364701, 23847141, 14684687, 11938446).
PM2_Supporting	✔	This variant is absent in the GenBank dataset, Helix dataset, and gnomAD v3.1.2 (PM2_supporting).
PP3	✔	The computational predictor APOGEE gives a consensus rating of pathogenic with a score of 0.9 (Min=0, Max=1), which predicts a damaging effect on gene function (PP3).

Not Met criteria codes

PS3	✖	There are no cybrid studies, single fiber studies, or other functional assays reported.

Curation History

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