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-CYB):m.12241del

Version: 1.1

CA915952144

690169 (ClinVar)

Gene: MT-TS2 (HGNC:4575)
Condition: mitochondrial disease (MONDO:0044970)
Inheritance Mode: Mitochondrial inheritance
UUID: 2a4ee240-e4a1-419d-bbfd-d0e83b796214
Approved on: 2023-08-22
Published on: 2024-03-19

HGVS expressions

NC_012920.1:m.12241del
J01415.2:m.12241del

Uncertain Significance

Met criteria codes 1

BP4

Not Met criteria codes 8

BS1 PP1 PS2 PS3 PS4 BA1 PM6 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.12241del variant in MT-TS2 was reviewed by the Mitochondrial Disease Variant Curation Expert Panel on August 22, 2023. This variant has not been reported in the medical literature as causative in affected individuals or families with primary mitochondrial disease to our knowledge. There are several occurrences in population databases. The frequency in the MITOMAP GenBank sequences is 16/61,168 (0.026%). The frequency in the Helix dataset is 81/195,983 (0.041%) homoplasmic occurrences in addition to 22 heteroplasmic occurrences. The frequency in gnomAD v3.1.2 is 53/56,425 (0.094%) and these occurrences are homoplasmic in individuals from various backgrounds. In all three population databases, this variant is seen across individuals from different haplogroups. MitoTIP suggests this variant is benign (37th percentile; BP4). 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 August 22, 2023. Mitochondrial DNA-specific ACMG/AMP criteria applied (PMID: 32906214): BP4.

Met criteria codes

BP4	✔	MitoTIP suggests this variant is benign (37th percentile; BP4).

Not Met criteria codes

BS1	✖	There are several occurrences in population databases.The frequency in the MITOMAP GenBank sequences is 16/61,168 (0.026%). The frequency in the Helix dataset is 81/195,983 (0.041%) homoplasmic occurrences in addition to 22 heteroplasmic occurrences. The frequency in gnomAD v3.1.2 is 53/56,425 (0.094%) and these occurrences are homoplasmic in individuals from various backgrounds. In all three population databases, this variant is seen across individuals from different haplogroups.
PP1	✖	This variant has not been reported in the medical literature as causative in affected individuals or families with primary mitochondrial disease to our knowledge.
PS2	✖	This variant has not been reported in the medical literature as causative in affected individuals or families with primary mitochondrial disease to our knowledge.
PS3	✖	There are no cybrids, single fiber studies, or other functional assays reported on this variant.
PS4	✖	This variant has not been reported in the medical literature as causative in affected individuals or families with primary mitochondrial disease to our knowledge.
BA1	✖	There are several occurrences in population databases.The frequency in the MITOMAP GenBank sequences is 16/61,168 (0.026%). The frequency in the Helix dataset is 81/195,983 (0.041%) homoplasmic occurrences in addition to 22 heteroplasmic occurrences. The frequency in gnomAD v3.1.2 is 53/56,425 (0.094%) and these occurrences are homoplasmic in individuals from various backgrounds. In all three population databases, this variant is seen across individuals from different haplogroups.
PM6	✖	This variant has not been reported in the medical literature as causative in affected individuals or families with primary mitochondrial disease to our knowledge.
PM2	✖	There are several occurrences in population databases.The frequency in the MITOMAP GenBank sequences is 16/61,168 (0.026%). The frequency in the Helix dataset is 81/195,983 (0.041%) homoplasmic occurrences in addition to 22 heteroplasmic occurrences. The frequency in gnomAD v3.1.2 is 53/56,425 (0.094%) and these occurrences are homoplasmic in individuals from various backgrounds. In all three population databases, this variant is seen across individuals from different haplogroups.

Curation History

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