# *Variant: NC_012920.1:m.10455A>G*

Version: 1.1

## *CA913163341*

## *690123 (ClinVar)*

**Gene**: MT-TR (HGNC:4573)
**Condition**: mitochondrial disease (MONDO:0044970)
**Inheritance Mode**: Mitochondrial inheritance
**UUID:** 580cb48b-0e7f-48b8-9093-6ef8868b3734
**Approved on**: 2021-12-10
**Published on**: 2021-12-10

## *HGVS expressions*

**NC_012920.1:m.10455A>G**
J01415.2:m.10455A>G

**Uncertain Significance**

**Met criteria codes** 1

**BP4**

**Not Met criteria codes** 4

**PS3** **PS4** **PP1** **PM2**

Evidence Links 0

### Expert Panel

**Mitochondrial Diseases VCEP**

### Criteria Specification Information

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Mitochondrial Diseases VCEP***

**The m.10455A>G variant in MT-TR was reviewed by the Mitochondrial Disease Nuclear and Mitochondrial Variant Curation Expert Panel as part of the variant pilot for mitochondrial DNA variant specifications (McCormick et al., 2020; PMID: 32906214). This variant has been reported only once in the literature (PMID: 23463613; Supp Table S1B) in the homoplasmic state in an individual from H haplogroup and mother was not available for testing. This does not meet criteria for PS4_supporting which requires at least two unrelated affected individuals. There are no large families reported in the medical literature to consider for evidence of segregation. There are several occurrences of this variant in GenBank sequences queried through MITOMAP on 6/29/2020 (seen in 1-4 individuals from several haplogroups including J1c, H1b, H1j, U5a, N1a for a total of 12/51,192 frequency). The computational predictor MitoTIP suggests this variant is likely benign (10th percentile) and HmtVAR predicts it to be likely polymorphic (BP4). There are no cybrid or single fiber studies 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 U24 Mitochondrial Disease Variant Curation Expert Panel as of August 20, 2020. Mitochondrial DNA-specific ACMG/AMP criteria applied: BP4.**

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### Met criteria codes

| | | |
|---|---|---|
| **BP4** | ✓ | The computational predictor MitoTIP suggests this variant is likely benign (10th percentile) and HmtVAR predicts it to be likely polymorphic (BP4). |

### Not Met criteria codes

| | | |
|---|---|---|
| **PS3** | ✖ | There are no cybrid or single fiber studies reported on this variant. |
| **PS4** | ✖ | This variant has been reported only once in the literature (PMID: 23463613; Supp Table S1B) in homoplasmic state in individual of H haplogroup and mother was not available for testing. This does not meet criteria for PS4 which requires at least two unrelated affected individuals. |
| **PP1** | ✖ | There are no large families reported in the medical literature to consider for evidence of segregation. |
| **PM2** | ✖ | There are several occurrences of this variant in GenBank sequences queried through MITOMAP on 6/29/2020 (seen in 1-4 individuals from several haplogroups including J1c, H1b, H1j, U5a, N1a for a total of 12/51,192 frequency). |

## Curation History

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