Variant: NC_012920.1:m.9055G>A

Version: 1.1

CA337098169

693067 (ClinVar)

Gene: MT-TV (HGNC:4577)
Condition: mitochondrial disease (MONDO:0044970)
Inheritance Mode: Mitochondrial inheritance
UUID: deb388e1-396f-49b1-a9d2-1eec588b172c
Approved on: 2021-12-10
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HGVS expressions

NC_012920.1:m.9055G>A
J01415.2:m.9055G>A
ENST00000361899.2:c.529G>A

Benign

Met criteria codes 2

BP4 **BA1**

Evidence Links 3

Expert Panel

Mitochondrial Diseases VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Mitochondrial Diseases VCEP

The m.9055G>A (p.A177T) variant in MT-ATP6 is a missense variant that reaches benign stand-alone criteria (BA1). The highest population minor allele frequency in GenBank (51,863 GenBank sequences) is 4.24%; in gnomad v3.1.2 is 5.393% (homoplasmic occurrences); and in Helix (196,554 sequences, 91% lineage N bias) is 8.05%. These are all higher than the ClinGen Mitochondrial Disease Nuclear and Mitochondrial Variant Curation Expert Panel - mtDNA specifications - threshold (>0.01 or 1%). Furthermore, m.9055G>A is a haplogroup-defining variant for K at 99.7%. It is also found in Z3b (100%) and U8b (100%). Therefore, this meets this criterion (BA1). As a note, the K haplogroup is common in the Ashkenazi Jewish population. m.9055 G>A is a haplogroup-defining variant for K at 99.7%. Subgroup frequencies are K1 (99.3%) and K2 (99.7%). Additionally, the computational predictor APOGEE gives a consensus rating of neutral with an extremely low pathogenicity predictor score, 0.2 (Min=0, Max=1), evidence that does not predict a damaging effect on gene function (BP4). In summary, this variant meets criteria to be classified as benign for primary mitochondrial disease inherited in a mitochondrial manner. However, if this variant is identified in an individual who is a member of a different haplogroup than described above, consider further evaluation of this variant. This classification was approved by the NICHD U24 Mitochondrial Disease Variant Curation Expert Panel on May 20, 2021. Mitochondrial DNA-specific ACMG/AMP criteria applied: BA1, BP4.

Met criteria codes

BP4	✓	The computational predictor APOGEE gives a consensus rating of neutral with an extremely low pathogenicity predictor score, 0.2 (Min=0, Max=1), evidence that does not predict a damaging effect on gene function (BP4).
BA1	✓	The highest population minor allele frequency in GenBank (51,863 GenBank sequences) is 4.24%; in gnomad v3.1.2 is 5.393% (homoplasmic occurrences); and in Helix (196,554 sequences, 91% lineage N bias) is 8.05%. These are all higher than the ClinGen Mitochondrial Disease Nuclear and Mitochondrial Variant Curation Expert Panel - mtDNA specifications - threshold (>0.01 or 1%). Furthermore, m.9055G>A is a haplogroup-defining variant for K at 99.7%. It is also found in Z3b (100%), U8b (100%). Therefore, this meets this criterion (BA1). As a note, the K haplogroup is common in the Ashkenazi Jewish population. m.9055 G>A is a haplogroup-defining variant for K at 99.7%. Subgroup frequencies are K1 (99.3%), K2 (99.7%). However, if an individual with this variant is a member of a different haplogroup than those where the variant is a marker, consider further evaluation. gnomAD v3.1 has a homoplasmic AF of 5.393% in 56368 mt sequences **PubMed:32461654** Establishes haplogroup K as common in Ashkenazi Jews **PubMed:24104924** Using Allele Search at mitomap.org for 9055 G>A shows qualifying allele frequencies for BA1 in both the Mitomap (4.24%) and Helix (8.05%) databases. **PubMed:25489354**

Curation History

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