

Variant: *m.13513G>A*

Version: 1.1

[CA120632](#) 

[9702 \(ClinVar\)](#) 

Gene: MT-ND5 ([HGNC:4540](#))

Condition: mitochondrial disease ([MONDO:0044970](#))

Inheritance Mode: Mitochondrial inheritance

UUID: 7dcf79c3-61e2-40bb-bb3a-06d45c7c2c23

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HGVS expressions

NC_012920.1:m.13513G>A

J01415.2:m.13513G>A

ENST00000361567.2:c.1177G>A

Pathogenic

Met criteria codes **5**

PM6_Strong

PM5

PP1_Moderate

PS4

PP3

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.13513G>A (p. D393N) variant in MT-ND5 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 in >16 individuals with primary mitochondrial disease with onset typically in childhood with some reports of onset in adolescence who had features variably consistent with Leigh syndrome, MELAS and MELAS-like, and/or mitochondrial encephalopathy (PS4; PMID: 25681084; PMID: 27344355; PMID: 30128709; PMID: 12624137; PMID: 14520659; PMID: 17400793; PMID: 18495510). This variant has been identified as a de novo occurrence in at least 5 probands with primary mitochondrial disease (PM6_strong; PMID: 27344355; PMID: 17400793; PMID: 18495510). This variant heteroplasmy level segregated with severity in 6 families where healthy mothers were found to have the variant at low heteroplasmy levels (PP1_moderate; PMID: 25681084; PMID: 12624137; PMID: 14520659). Another variant at this amino acid position leading to a different amino acid change is classified as pathogenic by mitomap.org and ClinVar - m.13514A>G (p.D393G; PM5). The computational predictor APOGEE gives a consensus rating of pathogenic with a score of 0.97 (Min=0, Max=1), which predicts a damaging effect on gene function (PP3). In summary, this variant meets criteria to be classified as pathogenic 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: PS4, PM6_strong, PM5, PP1_moderate, PP3).

Met criteria codes

PM6_Strong	✓	This variant has been identified as a de novo occurrence in at least 5 probands with primary mitochondrial disease. Per SVI de novo guidance (Phenotype consistent with gene but not highly specific), total is 2.5 points (0.5 from Patient 1 in PMID: 18495510 + 0.5 from Patient 2 in PMID: 18495510 + 0.5 from Patient 3 in PMID: 17400793 + 0.5 from Patient 4 in PMID: 17400793 + 0.5 from case in PMID: 27344355)
PM5	✓	m.13514A>G (p.D393G) confirmed pathogenic in MITOMAP and ClinVar (one submission)
PP1_Moderate	✓	This variant heteroplasmy level segregated with severity in 6 families where healthy mothers were found to have the variant at low heteroplasmy levels (PP1_moderate; PMID: 25681084; PMID: 12624137; PMID: 14520659).
PS4	✓	This variant has been reported in >16 individuals with primary mitochondrial disease with onset typically in childhood with some reports of onset in adolescence who had features variably consistent with Leigh syndrome, MELAS and MELAS-like, and/or mitochondrial encephalopathy (PS4; PMID: 25681084; PMID: 27344355; PMID: 30128709; PMID: 12624137; PMID: 14520659; PMID: 17400793; PMID: 18495510).
PP3	✓	APOGEE: 0.97 - pathogenic

Curation History [↗](#)

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