MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: October 3, 2023
Effective Date: October 12, 2023

Mitochondrial DNA Deletion Heteroplasmy, ddPCR, Varies

Test ID: DMITO

Useful for:

- Assessing the heteroplasmy level of previously detected large mitochondrial DNA (mtDNA) deletions
- Screening family members for previously detected large mtDNA deletions
- This test **is not recommended for** first tier diagnostic testing for mitochondrial disorders.
- This test **does not assess** mtDNA depletion.

Genetics Information:

- This test utilizes droplet digital polymerase chain reaction (ddPCR) for confirmation and determination of heteroplasmy levels of previously detected large mitochondrial DNA (mtDNA) deletions.
- Identification of heteroplasmy for large mtDNA deletions may assist with the diagnosis, prognosis, clinical management, recurrence risk assessment, familial screening, and genetic counseling for mtDNA deletion syndromes.

Reflex Tests:

Test ID	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	No	No

Testing Algorithm:

For skin biopsy or cultured fibroblast specimens, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Methods:

Droplet Digital Polymerase Chain Reaction (ddPCR)

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Specimen Type:	**Whole blood**
Preferred:	Lavender top (EDTA)
Acceptable:	Any anticoagulant
Specimen Volume:	3 mL
Collection Instructions:	1. Invert several times to mix blood 2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information:	Ambient (preferred) 4 days/Refrigerated
Minimum Volume:	1 mL

Specimen Type:	**Cultured fibroblasts**
Container/Tube:	T-25 flask
Specimen Volume:	2 Flasks
Collection Instructions:	Submit confluent cultured fibroblast cells from a skin biopsy. Cultured cells from a prenatal specimen will not be accepted.
Specimen Stability Information:	Ambient (preferred)/Refrigerated (<24 hours)
Additional Information:	A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type:	**Skin biopsy**
Supplies:	Fibroblast Biopsy Transport Media (T115)
Container/Tube:	Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.
Specimen Volume:	4-mm punch
Specimen Stability Information:	Refrigerated (preferred)/Ambient
Additional Information:	A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type:	**Muscle tissue biopsy**
Supplies:	Muscle Biopsy Kit (T541)
Collection Instructions:	Prepare and transport specimen per instructions in Muscle Biopsy Specimen Preparation Sheet.
Specimen Volume:	10-80 mg
Specimen Stability Information:	Frozen (preferred)/Ambient/Refrigerated

Specimen Type:	**Snap frozen nerve tissue biopsy**
Collection Instructions:	Prepare snap frozen tissue biopsy per surgical procedure
Specimen Volume:	0.25-0.5 cm
Specimen Stability Information:	Frozen

Specimen Type:	**Blood spot**
Supplies:	Card-Blood Spot Collection (Filter Paper) (T493)
Preferred:	Collection card (Whatman Protein Saver 903 Paper)
Acceptable:	PerkinElmer 226 (formerly Ahlstrom 226) filter paper, or blood spot collection card
Specimen Volume:	2 to 5 Blood spots
Collection Instructions:	1. An alternative blood collection option for a patient 1 year of age or older is a fingerstick. For infants younger than 1 year, a heel stick should be used. See How to Collect Dried Blood Spot Samples via fingerstick. 2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours. 3. Do not expose specimen to heat or direct sunlight. 4. Do not stack wet specimens. 5. Keep specimen dry.
Specimen Stability Information:	Ambient (preferred)/Refrigerated
Additional Information:	1. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing. 2. For collection instructions, see Blood Spot Collection Instructions. 3. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777). 4. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800).
Minimum Volume:	2 spots

Shipping Instructions:

Specimen preferred to arrive within 96 hours of collection.

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Ordering Guidance:

For diagnosis of a mitochondrial DNA deletion syndrome, the recommended first tier test is MITOP/ Mitochondrial Full Genome Analysis, Next-Generation Sequencing (NGS), Varies.

Interpretation:

The interpretation of molecular biomarker analysis includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions:

Clinical Correlations:

- Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.
- If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

Technical Limitations:

- This assay will not detect the breakpoints for large mitochondrial deletions or single nucleotide variants that cause mitochondrial disease. Therefore, the absence of a detectable variant does not rule out the possibility that an individual is affected with mitochondrial disease. This test can only detect mitochondrial DNA (mtDNA) deletions that include the *mt-ND4* or *mt-ND2* genes.
- Some individuals who have a mitochondrial deletion syndrome may have a deletion that is not identified by this assay. The absence of a deletion, therefore, does not eliminate the possibility of a mitochondrial DNA deletion syndrome. For predictive testing of asymptomatic individuals, it is important to first document the presence of a deletion in an affected family member.
- Of note, absence of a mitochondrial deletion does not rule out the presence of a deletion below the limits of detection of this assay (<10% heteroplasmy).
- Rare variants exist that could lead to false-negative or false-positive results. If results obtained do not match clinical findings, additional testing should be considered.

CPT Code:

81479

Day(s) Performed: Monday through Friday **Report Available:** 7 to 10 days

Questions

Contact Michelle Raths, Laboratory Resource Coordinator at 800-533-1710.