

Overview

Useful For

A circulating biomarker in myopathy-related mitochondrial disease as well as other conditions
Investigation of patients suspected of having a mitochondrial myopathy
This assay is **not suitable** for carrier detection.

Testing Algorithm

[Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#)

Special Instructions

- [Biochemical Genetics Patient Information](#)
- [Epilepsy: Unexplained Refractory and/or Familial Testing Algorithm](#)

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Plasma

Specimen Required

Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Green top (sodium heparin)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Collection Instructions:

1. Draw blood and centrifuge immediately.
2. Aliquot plasma into plastic vial.
3. Do not expose specimen to heat or direct sunlight.

Forms

1. [Biochemical Genetics Patient Information](#) (T602)
2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
[-Neurology Specialty Testing Client Test Request](#) (T732)
[-Biochemical Genetics Test Request](#) (T798)

Reject Due To

Gross hemolysis OK

Gross lipemia OK

Gross icterus OK

Specimen Minimum Volume

0.2 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Refrigerated (preferred)	90 days	
	Frozen	90 days	
	Ambient	28 days	

Clinical & Interpretive
Clinical Information

Mitochondria perform many important metabolic functions, the most vital being the production of energy in the form of adenosine triphosphate (ATP) through the electron-transport chain and the oxidative phosphorylation system, which consists of 5 complexes (complex I-V). Each of these complexes consists of 4 to 46 subunits encoded by both nuclear and mitochondrial DNA. Mitochondrial diseases are caused by defects in any of the relevant metabolic pathways and have an estimated prevalence of 1:8500. Mitochondrial diseases are varied and include mitochondrial DNA deletion syndromes such as Kearns-Sayre syndrome (KSS), mitochondrial depletion syndromes such as those caused by alterations in the *TK2* and *SUCLA2* or *POLG* and *C10orf2* genes, and mitochondrial point mutation syndromes such as mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS), as well as others.

The clinical features of mitochondrial diseases vary widely and include lactic acidosis, myopathy, ophthalmoplegia, ptosis, cardiomyopathy, sensorineural hearing loss, optic atrophy, pigmentary retinopathy, diabetes mellitus, encephalomyopathy, seizures, and stroke-like episodes.

A diagnostic workup for a mitochondrial disorder may demonstrate elevations of the lactate-to-pyruvate ratio (LAA / Lactate, Plasma and PYR / Pyruvic Acid, Blood) and an elevated growth differentiation factor 15 (GDF15) level. GDF15 is a protein of the transforming growth factor beta superfamily. GDF15 is overexpressed in muscle and serum in patients with various types of mitochondrial diseases, including those with mitochondrial deletion, depletion, and point mutation syndromes. Therefore, increased levels of GDF15 can indicate the need for further investigations including molecular studies and muscle biopsy to confirm the presence of a possible neuromuscular mitochondrial disease.

Reference Values

3 months* and older: < or =750 pg/mL

*This test is not recommended for infants younger than 3 months of age due to the high levels of growth differentiation factor 15 contributed from the placenta during pregnancy.

Interpretation

Abnormal results along with clinical findings may be suggestive of mitochondrial disease. Additional workup is indicated.

Cautions

This is a screening test for neuromuscular mitochondrial disease. Results can be elevated for other reasons including in individuals with cancer, cardiovascular disease, diabetes, and pregnancy.

Results are normally elevated in children younger than 3 months of age due to the high levels found in the placenta

during pregnancy.

Clinical Reference

1. Poulsen NS, Madsen KL, Hornsyld TM, et al: Growth and differentiation factor 15 as a biomarker for mitochondrial myopathy. *Mitochondrion*. 2020 Jan;50:35-41
2. Kalko SG, Paco S, Jou C, et al: Transcriptomic profiling of TK2 deficient human skeletal muscle suggests a role for the p53 signalling pathway and identifies growth and differentiation factor-15 as a potential novel biomarker for mitochondrial myopathies. *BMC Genomics*. 2014 Feb 1;15:91
3. Sugulle M, Dechend R, Herse F, et al: Circulating and placental growth-differentiation factor 15 in preeclampsia and in pregnancy complicated by diabetes mellitus. *Hypertension*. 2009 Jul;54(1):106-112
4. Yatsuga S, Fujita Y, Ishii A, et al: Growth differentiation factor 15 as a useful biomarker for mitochondrial disorders. *Ann Neurol*. 2015 Nov;78(5):814-823

Performance**Method Description**

Growth differentiation factor 15 (GDF15) ELISA is a quantitative sandwich enzyme immunoassay technique. Specimen is incubated in wells that have been coated with anti-GDF15 antibody. After incubation and washing, the wells are incubated with an enzyme-linked polyclonal antibody specific for human GDF15. After a second incubation and washing step, the wells are incubated with a substrate solution producing a blue color. A stop solution is added turning the blue color to yellow, which is then read at 450 and 570 nm on a microplate reader. The absorbance at 570 is subtracted from the absorbance at 450 to correct for optical imperfections and the resulting absorbance is directly proportional to the level of GDF15 in the specimen. (Package insert: Human GDF15 Immunoassay. R and D Systems, Inc; 2014)

PDF Report

No

Specimen Retention Time

1 month

Performing Laboratory Location

Rochester

Fees & Codes**Test Classification**

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

83520