Test Definition: MMPP

Mitochondrial Metabolites, Plasma

Overview

Useful For

Monitoring patients with mitochondrial disorders, organic acidurias, and ketone body disorders

Method Name

Gas Chromatography Mass Spectrometry (GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Plasma

Ordering Guidance

This test is **not the recommended** initial screening test for evaluating patients with suspected mitochondrial disorders, organic acidurias, and ketone body disorders. For these purposes, the preferred tests for first-tier assessment are OAU / Organic Acids Screen, Random, Urine; AAQP / Amino Acids, Quantitative, Plasma; and ACRN / Acylcarnitines, Quantitative, Plasma.

Analytes from LAPYP / Lactate Pyruvate Panel, Plasma are included in this test. If ordered together, LAPYP may be canceled.

Specimen Required

Collection Container/Tube:
Preferred: Green top (Sodium heparin)
Acceptable: Green top (Lithium heparin)
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions: Centrifuge and aliquot plasma into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.1 mL

Reject Due To

Gross	Reject

hemolysis	
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma	Frozen	7 days	

Clinical & Interpretive

Clinical Information

Mitochondrial metabolites occur as physiologic intermediates in a variety of metabolic pathways. Mitochondrial diseases, organic acidurias, and ketone disorders are groups of disorders in which one or more of these pathways are blocked, resulting in a deficiency of normal products and an abnormal accumulation of intermediate metabolites in the body. In some conditions, these excess metabolites are observed in abnormal plasma concentrations.

Mitochondrial disorders vary widely in both clinical presentation and age of onset. Patients commonly present with neurologic and myopathic features. In addition, patients may experience involvement of multiple organ systems with features such as myopathy, ophthalmoplegia, ptosis, cardiomyopathy, sensorineural hearing loss, optic atrophy, pigmentary retinopathy, diabetes mellitus, encephalomyopathy, seizures, and stroke-like episodes.

Organic acidurias typically present with either an acute life-threatening illness in early infancy or unexplained developmental delay with intercurrent episodes of metabolic decompensations in later childhood. Organic acidurias should be considered when patients present with severe and persistent metabolic acidosis of unexplained origin, elevated anion gap, and severe neurologic manifestations, such as seizures. Other findings, especially during acute episodes of metabolic decompensations, may include elevated ketones in urine or plasma, hyperammonemia, hypoglycemia, and lactic acidemia.

Ketone disorders include disorders of impaired ketone body metabolism and disorders of ketogenesis. Ketones are converted as an energy source when either carbohydrate reserves are depleted or excessive fatty acids are present. Clinical symptoms of ketone body metabolism disorders include episodes of ketoacidosis, vomiting, dehydration, and lethargy with increased risk of symptoms during periods of illness or fasting. Patients with disorders of ketogenesis experience hypoketotic hypoglycemic episodes that may result in long-term sequelae including seizure disorders, intellectual disability, and white matter changes in the brain. Treatment for ketone disorders involves avoidance of fasting and management of acute symptoms.

A diagnostic workup for mitochondrial disorders, organic acidurias, and ketone body disorders includes analysis of urine organic acids (OAU / Organic Acids Screen, Random, Urine), plasma amino acids (AAQP / Amino Acids, Quantitative, Plasma) and plasma acylcarnitines (ACRN / Acylcarnitines, Quantitative, Plasma) as recommended first-tier tests for assessment. While the mitochondrial metabolites panel complements this work up and provides additional context, this test should not be used in isolation for diagnostic purposes.

Reference Values

LACTIC ACID
< or = 4000.0 nmol/mL

2-HYDROXYBUTYRIC ACID
< or = 124.0 nmol/mL

3-HYDROXYBUTYRIC ACID
< or = 700.0 nmol/mL

PYRUVIC ACID
< or = 350.0 nmol/mL

cis-ACONITIC ACID
< or = 9.0 nmol/mL

CITRIC ACID
< or = 250.0 nmol/mL

3-HYDROXYPROPIONIC ACID
< or = 12.4 nmol/mL

3-HYDROXY-2-METHYLBUTYRIC ACID
< or = 2.5 nmol/mL

3-HYDROXYISOVALERIC ACID
< or = 15.4 nmol/mL

SUCCINIC ACID
< or = 10.0 nmol/mL

FUMARIC ACID
< or = 5.0 nmol/mL

3-METHYLGLUTACONIC ACID
< or = 1.6 nmol/mL

MALIC ACID
< or = 20.0 nmol/mL

2-KETOBUTYRIC ACID
< or = 16.0 nmol/mL

2-KETOISOVALERIC ACID
< or = 35.0 nmol/mL

ACETOACETIC ACID
< or = 350.0 nmol/mL

3-METHYL-2-KETOVALERIC ACID
< or = 70.0 nmol/mL

2-KETOISOCAPROIC ACID
< or = 70.0 nmol/mL

2-METHYLCITRIC ACID
< or = 1.0 nmol/mL

2-KETOGLUTARIC ACID
< or = 40.0 nmol/mL

Interpretation

An interpretive report based on pattern recognition is provided. The individual quantitative results support the interpretation of the mitochondrial metabolite profile but are not diagnostic by themselves.

The elevation of 3-hydroxyisovaleric acid can be explained by several differential diagnoses that cannot always be distinguished by the mitochondrial metabolite profile. Differential diagnoses will be noted in the interpretative comment.

For patients without a prior known diagnosis, abnormal results are typically not sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on a mitochondrial metabolite profile, independent biochemical or molecular genetic analyses are required.

Cautions

3-Hydroxyisobutyric acid can cause a false elevation in the quantitation of 3-hydroxybutyric acid. Patients affected by 3-hydroxyisobutyric aciduria may have falsely elevated 3-hydroxybutyric acid.

Gross elevations of methylmalonic acid may interfere with the quantitation of 3-hydroxyisovaleric and succinic acid. When observed, the report will include a comment indicating presence of interference.

Gross elevations of acetoacetic acid may interfere with the quantification of 3-methyl-2-ketovaleric acid. When observed, the report will include a comment indicating presence of interference.

Clinical Reference

1. Munnich A, Rotig A, Cormier-Daire V, Rustin P. Clinical presentation of respiratory chain deficiency. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed July 5, 2024. Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225086827
2. Robinson BH. Lactic acidemia: Disorders of pyruvate carboxylase and pyruvate dehydrogenase. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed July 5, 2024. Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225087140

3. Shoffner JM. Oxidative phosphorylation diseases. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019 Accessed July 5, 2024. Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225088339
4. Mitchell GA, Fukao T. Inborn errors of ketone body metabolism. In: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease McGraw-Hill Education; 2019. Accessed July 5, 2024. Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225087757

Performance

Method Description
Plasma specimen is spiked with a mixture of labeled internal standards following oximation of keto acids. The samples are acidified and extracted. After evaporation, the dry residue is silylated and analyzed by capillary gas chromatography/mass spectrometry using selected ion monitoring with positive electron impact ionization and stable isotope dilution.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Wednesday

Report Available
3 to 9 days

Specimen Retention Time
2 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

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

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MMPP	Mitochondrial Metabolites, P	101455-4

Result ID	Test Result Name	Result LOINC® Value
616819	Interpretation	59462-2
616798	Lactic acid	2524-7
616799	2-Hydroxybutyric acid	69843-1
616800	3-Hydroxybutyric acid	6873-4
616801	Pyruvic acid	32338-6
616802	cis-Aconitic acid	75083-6
616803	Citric acid	15038-3
616804	3-Hydroxypropionic acid	47536-8
616805	3-Hydroxy-2-methylbutyric acid	69789-6
616806	3-Hydroxyisovaleric acid	72450-0
616807	Succinic acid	35871-3
616808	Fumaric acid	75081-0
616809	3-Methylglutaconic acid	33273-4
616810	Malic acid	75068-7
616811	2-Ketobutyric acid	In Process
616812	2-Ketoisovaleric acid	35868-9
616813	Acetoacetic acid	35867-1
616814	3-Methyl-2-ketovaleric acid	35869-7
616815	2-Ketoisocaproic acid	35870-5
616816	2-Methylcitric acid	26904-3
616817	2-Ketoglutaric acid	69803-5
616818	Reviewed by	18771-6