Test Definition: FAO

Fatty Acid Oxidation Probe Assay, Fibroblast Culture

Overview

Useful For

In vitro confirmation of biochemical diagnoses of the following fatty acid oxidation disorders:
-Short-chain acyl-CoA dehydrogenase deficiency
-Medium-chain acyl-CoA dehydrogenase deficiency
-Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency
-Trifunctional protein deficiency
-Very long-chain acyl-CoA dehydrogenase deficiency
-Carnitine palmitoyl transferase deficiency type II
-Carnitine-acylcarnitine translocase deficiency

Confirmation of the following organic acid disorders:
-2-Methylbutyryl-CoA dehydrogenase deficiency
-Isobutyryl-CoA dehydrogenase deficiency

This test is **not useful for** prenatal testing**.**

This assay is **not informative** if the deficient enzyme is not physiologically expressed in skin fibroblasts.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	Yes

Testing Algorithm

When this test is ordered, a fibroblast culture will always be performed at an additional charge. If viable cells are not obtained, the client will be notified.

For more information see Newborn Screen Follow-up for Elevated C14:1 +/- Other Long-Chain Acylcarnitine

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)
- Newborn Screen Follow-up for Elevated C14:1 +/- Other Long-Chain Acylcarnitine

Method Name

Tandem Mass Spectrometry (MS/MS)

NY State Available

Yes

Specimen

Specimen Type
Tissue

Ordering Guidance
This test is recommended only after appropriate analyte testing, including acylcarnitines, organic acids, acylglycines, and/or fatty acids has been performed.

For more information see:
-ACRN / Acylcarnitines, Quantitative, Plasma
-OAU / Organic Acids Screen, Random, Urine
-AGU20 / Acylglycines, Quantitative, Random, Urine
-FAPCP / Fatty Acid Profile, Comprehensive (C8-C26), Serum

Necessary Information
Provide clinical information

Specimen Required
Submit only 1 of the following specimens:

Specimen Type: Cultured fibroblasts
Container/Tube: T-75 or T-25 flask
Specimen Volume: 1 Full T-75 flask or 2 full T-25 flasks
Specimen Stability Information: Ambient (preferred)/Refrigerated

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. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin).
Specimen Volume: 4-mm Punch
Specimen Stability Information: Refrigerated (preferred)/Ambient

Forms
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)

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

Reject Due To

Specimen in formalin or fixative preservative	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Varies		

Clinical & Interpretive

Clinical Information

Mitochondrial fatty acid beta-oxidation plays an important role in energy production during periods of fasting. When the body's supply of glucose is depleted, fatty acids are mobilized from adipose tissue, taken up by the liver and muscles, and oxidized to acetyl-CoA (acetyl coenzyme A). In the liver, acetyl-CoA is the building block for the synthesis of ketone bodies, which enter the blood stream and provide an alternative substrate for production of energy in other tissues when the supply of glucose is insufficient to maintain a normal level of energy. Disorders of fatty acid oxidation (FAO) are characterized by hypoglycemia, hepatic dysfunction, encephalopathy, skeletal myopathy, and cardiomyopathy. Most FAO disorders have a similar presentation, and their biochemical diagnosis can, at times, be difficult. Commonly used metabolite screens, such as urine organic acids, plasma acylcarnitines, and fatty acids, are influenced by dietary factors and the clinical status of the patient. This can lead to incomplete diagnostic information or even false-negative results. The purpose of the in vitro probe assay is to offer screening for several defects of FAO and organic acid metabolism under controlled laboratory conditions using fibroblast cultures.

Reference Values

An interpretive report will be provided.

Interpretation

Abnormal results will include a description of the abnormal profile in comparison to normal and abnormal controls. In addition, the concentration of the acylcarnitine species that abnormally accumulated in the cell medium are provided and compared to the continuously updated reference range based on analysis of normal controls.

Interpretations of abnormal acylcarnitine profiles also include information about the results' significance, a correlation to available clinical information, possible differential diagnoses, recommendations for additional biochemical testing and confirmatory studies if indicated, name and phone number of contacts who may provide these studies, and a phone number to reach one of the laboratory directors in case the referring provider has additional questions.

Cautions

Sometimes, an abnormal acylcarnitine profile cannot differentiate between 2 disorders. In such instances, independent biochemical (eg, specific enzyme assay when available) or molecular genetic analyses are required. Recommendations for such testing will be included in the report.

In addition, electron transfer flavoprotein (ETF) deficiency and ETF-dehydrogenase deficiency (multiple acyl-CoA dehydrogenase deficiency; glutaric acidemia type II) may be, but are not always, detected by this method.

Clinical Reference

1. Ensenauer R, Vockley J, Willard JM, et al. A common mutation is associated with a mild, potentially asymptomatic phenotype in patients with isovaleric acidemia diagnosed by newborn screening. Am J Hum Genet. 2004;75(6):1136-1142. doi:10.1086/426318
2. Rinaldo P, Matern D, Bennet MJ. Fatty acid oxidation disorders. Ann Rev Physiol. 2002;64:477-502
3. Shen JJ, Matern D, Millington DS, et al: Acylcarnitines in fibroblasts of patients with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency and other fatty acid oxidation disorders. J Inherit Metab Dis. 2000;23:27-44. doi:10.1023/a:1005694712583
4. Matern D, Huey JC, Gregersen N, et al. In vitro diagnosis of short-chain acyl-CoA dehydrogenase (SCAD) deficiency. J Inherit Metab Dis. 2001;24(Suppl.1):66
5. Merritt JL, Norris M, Kanungo S. Fatty acid oxidation disorders. Ann. Transl. Med. 2018;6(24):473. doi:10.21037/atm.2018.10.57

Performance

Method Description

Skin fibroblasts are incubated with cell medium enriched with palmitic acid (C16:0 fatty acid), L-carnitine, and isotopically labeled L-valine ([13]C-Val) and L-isoleucine ([13]C-Ile). Cell lines deficient of one of the enzymes involved in fatty acid oxidation and branched chain amino acid metabolism fail to metabolize acyl-CoA species, which accumulate in the cell medium as acylcarnitines. The medium is separated from the cells following the incubation. The cell pellet is used for protein determination and the medium will be spotted and dried on filter paper. An acylcarnitine analysis is performed by tandem mass spectrometry using a 1/4" filter paper punch, following the addition of isotopically labeled acylcarnitines as internal standards, extraction and derivatization to methyl esters. The assay is performed in triplicate.(Matern D. Acylcarnitines, including in vitro loading tests. In: Blau N, Duran M, Gibson KM, eds. Laboratory Guide to the Methods in Biochemical Genetics. Springer-Verlag; 2008; Cowan T, Pasquali M. Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed

Varies

Report Available

15 to 71 days depending on rapidity of growth

Specimen Retention Time

6 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

82017

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
FAO	Fatty Acid Ox Probe Assay, Fibro	74533-1

Result ID	Test Result Name	Result LOINC® Value
23487	Interpretation	59462-2
23489	Reviewed By	18771-6