Overview

Useful For

In vitro confirmation of biochemical diagnoses of the following fatty acid oxidation disorders:

-Short-chain acyl-CoA dehydrogenase (SCAD) deficiency

-Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency

-Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency

-Trifunctional protein deficiency

-Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency

-Carnitine palmitoyl transferase deficiency type II (CPT-II)

-Carnitine-acylcarnitine translocase (CACT) deficiency

Confirmation of the following organic acid disorders:

-2-Methylbutyryl-CoA dehydrogenase (SBCAD) deficiency

-Isobutyryl-CoA dehydrogenase (IBD) deficiency

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

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

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
FIBR	Fibroblast Culture	Yes	Yes
CRYOB	Cryopreserve for Biochem Studies	No	Yes

Testing Algorithm

When this test is ordered, a fibroblast culture and cryopreservation for biochemical studies will always be performed at an additional charge. However, for multiple assays on a patient utilizing fibroblast culture, only 1 culture is required regardless of the number of assays ordered. If viable cells are not obtained within 30 days, client will be notified.

See Newborn Screening Follow-up for Isolated C5 Acylcarnitines Elevations (also applies to any plasma or serum C5 acylcarnitine elevations) in Special Instructions.

Special Instructions

C5 acylcarnitine elevations)
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

FAO: Fibroblasts Incubated with Enriched Medium followed by Tandem Mass Spectrometry (MS/MS)

CRYOB: Fibroblast Subculture followed by Cryopreservation and Storage

NY State Available

Yes

Specimen

Specimen Type

Tissue

Advisory Information

This test is recommended only after appropriate analyte testing, including acylcarnitines, organic acids, acylglycines, and/or fatty acids (ACRN / Acylcarnitines, Quantitative, Plasma; OAU / Organic Acids Screen, Urine; ACYLG / Acylglycines, Quantitative, Urine; FAPCP / Fatty Acid Profile, Comprehensive [C8-C26], Serum), has been performed.

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 24 hours

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 in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Biochemical Genetics Patient Information (T602) in Special Instructions.

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism 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 and Interpretive

Clinical Information

Mitochondrial fatty acid beta-oxidation plays an important role in energy production, particularly in skeletal and heart muscle, and in hepatic ketone body formation. 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 often leads to incomplete diagnostic information or even false-negative results. Enzyme assays are limited to one enzyme per assay, and molecular assays for common genetic variants are limited by the frequent occurrence of compound heterozygous patients with uncommon, private alterations, which must be distinguished from unaffected carriers. Furthermore, neither specific enzyme assays nor molecular genetic testing are available for all of the known defects. 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 those 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) or molecular genetic analyses are required. Recommendations for such testing will be included in the report.

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 Dec;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 (MS/MS) 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, incl. 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. 2017:1139-1158)

PDF Report

No

Day(s) and Time(s) Test Performed

Varies

Analytic Time

15 to 71 days depending on rapidity of growth

Maximum Laboratory Time

71 days

Specimen Retention Time

3 years-Check with the lab for availability

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

82017-Acylcarnitines; quantitative, each specimen

88233-Fibroblast culture

88240-Cryopreservation for biochemical studies

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
FAO	Fatty Acid Ox Probe Assay, Fibro	35574-3

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