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

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIBR</td>
<td>Fibroblast Culture</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CRYOB</td>
<td>Cryopreserve for Biochem Studies</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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
- Informed Consent for Genetic Testing
- Newborn Screening Follow-up for Isolated C5 Acylcarnitines Elevations (also applies to any plasma or serum
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 Type: Skin biopsy

Supplies: Fibroblast Biopsy Transport Media (T115)

Container/Tube: Sterile container with any standard cell culture media (e.g., minimal essential medium, 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**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Tissue</td>
<td>Varies</td>
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**Specimen Stability Information**

**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**


**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, Pasqualli 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

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<td>FAO</td>
<td>Fatty Acid Ox Probe Assay, Fibro</td>
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