

Overview

Useful For

Confirmation of diagnosis of malonyl-CoA decarboxylase deficiency

Carrier screening in cases where there is a family history of malonyl-CoA decarboxylase deficiency, but disease-causing mutations have not been identified in an affected individual

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Testing Algorithm

If skin biopsy is received, fibroblast culture for genetic test will be added and charged separately.

Special Instructions

- [Molecular Genetics: Biochemical Disorders Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

Method Name

Polymerase Chain Reaction (PCR) Followed by DNA Sequence Analysis and Gene Dosage Analysis by Multiplex Ligation-Dependent Probe Amplification (MLPA)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send specimen in original tube.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Cultured fibroblasts

Container/Tube: T-75 or T-25 flask

Specimen Volume: 1 Full T-75 or 2 full T-25 flasks

Specimen Stability Information: Ambient (preferred)/Refrigerated <24 hours

Specimen Type: Skin biopsy

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 [T115]).

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. [Molecular Genetics: Biochemical Disorders Patient Information](#)(T527) in Special Instructions

3. If not ordering electronically, complete, print, and send an [Inborn Errors of Metabolism Test Request](#) (T798) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

[Malonyl-coenzyme A decarboxylase \(MCD\)](#) deficiency is a rare autosomal recessive inborn error of fatty acid metabolism characterized by reduced activity of mitochondrial malonyl-CoA decarboxylase. This enzyme is responsible for conversion of intramitochondrial malonyl-CoA to acetyl-CoA and carbon dioxide. This leads to an accumulation of malonyl-CoA, which is a strong inhibitor of carnitine palmitoyltransferase-I (CPT-I), an enzyme active in beta-oxidation of fatty acids. The resulting effect is impairment of the breakdown of fatty acids. Isoforms of CPT-I have been found in skeletal and heart muscle, liver, and brain, and symptoms seem to correlate with the localization of these isoforms. The phenotype associated with MCD deficiency is variable, but may include developmental delay, seizures, hypotonia, metabolic acidosis, hypoglycemia, ketosis, and cardiomyopathy.

The diagnosis of MCD deficiency is based on the findings of high urinary excretion of malonic acid and a mild increase in dicarboxylic acid. Acylcarnitine analysis by tandem mass spectrometry shows high blood levels of malonylcarnitine (C3DC), which can be detected by neonatal screening before the appearance of symptoms. Determination of MCD activity in cultured fibroblasts can confirm the diagnosis, although this testing is not currently clinically available in the United States.

Mutations in the *MLYCD* gene are responsible for MCD deficiency. The *MLYCD* gene is located on chromosome 16 and has 5 coding exons. Several different mutations have been described including missense, nonsense, small insertions and deletions, as well as large genomic deletions.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of malonyl-CoA decarboxylase (MCD) deficiency may have a mutation that is not identified by this method (eg, promoter and deep intronic mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of MCD deficiency. For carrier testing, it is important to first document the presence of a *MLYCD* gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical and biochemical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

In addition to disease-related probes, the multiplex ligation-dependent probe amplification technique utilizes probes localized to other chromosomal regions as internal controls. In certain circumstances, these control probes may detect other diseases or conditions for which this test was not specifically intended. Results of the control probes are not normally reported. However, in cases where clinically relevant information is identified, the ordering physician will be informed of the result and provided with recommendations for any appropriate follow-up testing.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med* 2015 May;17(5):405-424
2. Salomons GS, Jakobs C, Landegge Pope L, et al: Clinical, enzymatic and molecular characterization of nine new patients with malonyl-coenzyme A decarboxylase deficiency. *J Inher Metab Dis* 2007;30:23-28
3. Wightman PJ, Santer R, Ribes A, et al: *MLYCD* mutation analysis: evidence for protein mistargeting as a cause of *MLYCD* deficiency. *Hum Mutat* 2003;22:288-300

Performance

Method Description

Bidirectional sequence analysis is used to test for the presence of a mutation in all coding regions and intron/exon boundaries of the *MLYCD* gene. Additionally, gene dosage analysis (multiplex ligation-dependent probe amplification) is used to test for the presence of large deletions and duplications in this gene. (Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly, varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

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

81479 - Unlisted molecular pathology procedure

Fibroblast Culture for Genetic Test

88233-Tissue culture, skin or solid tissue biopsy (if appropriate)

88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MLYCZ	MLYCD Gene, Full Gene Analysis	94208-6

Result ID	Test Result Name	Result LOINC Value
53519	Result Summary	50397-9
53520	Result	82939-0
53521	Interpretation	69047-9
53522	Additional Information	48767-8
53523	Specimen	31208-2
53524	Source	31208-2
53525	Released By	18771-6