Test Definition: GFDZ

FTCD Gene, Full Gene Analysis

Overview

Useful For

Second-tier test for confirming glutamate formiminotransferase deficiency (indicated by biochemical testing or newborn screening)

Ruling out other diseases associated with high levels of urine formiminoglutamate

Carrier screening in cases where there is a family history of glutamate formiminotransferase 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: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)

Method Name

Polymerase Chain Reaction (PCR) Followed by DNA Sequence Analysis

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:

Preferred:

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 flask 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

Specimen Type: Blood spot

Supplies: Card - Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Ahlstrom 226 filter paper, or Blood Spot Collection Card (T493)

Specimen Volume:2 to 5 Blood Spots on collection card (Whatman Protein Saver 903 Paper; Ahlstrom 226 filter paper; or Blood Spot Collection Card, T493)

Collection Instructions:

1. An alternative blood collection option for a patient >1 year of age is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

3. Do not expose specimen to heat or direct sunlight.

4. Do not stack wet specimens.

5. Keep specimen dry

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information:

1. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

2. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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: Congenital Inherited Diseases Patient Information (T521) 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

Blood: 1 mL
Blood Spots: 5 punches-3 mm diameter

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

Glutamate formiminotransferase deficiency is an autosomal recessive inborn error of folate and histidine metabolism caused by a deficiency of the enzyme, glutamate formiminotransferase-cyclodeaminase, which is encoded at the *FTCD* loci on chromosome 21q22.3. Glutamate formiminotransferase deficiency presents as a clinical spectrum that ranges from asymptomatic to severe. Individuals with the severe form of disease are reported to have mental and physical retardation and anemia, whereas the mild form is associated with a lesser degree of developmental delay. Of note, the association of the enzyme deficiency with mental retardation has been disputed in the literature.

An elevated amount of urine formiminoglutamate (FIGLU) is a cardinal sign of glutamate formiminotransferase deficiency for both the severe and mild clinical phenotypes. However, higher levels of urine FIGLU are observed in patients with milder forms of the disease and these levels occur in the absence of histidine loading; whereas the presence of FIGLU in the urine is typically only observed in severe cases after L-histidine administration. In addition, the severe form of disease is associated with elevated serum folate levels, whereas the milder form of disease is not.

As there are discrepancies in FIGLU and serum folate levels among affected individuals, confirmation of suspected cases of glutamate formiminotransferase deficiency may require a liver biopsy for enzymology or the identification of 2 disease-causing mutations in the *FTCD* gene. Identification of 2 *FTCD* mutations establishes a molecular diagnosis of glutamate formiminotransferase deficiency, and rules out other diseases associated with high levels of urine FIGLU, such as folate or methylcobalamin deficiencies. Evaluation of the *FTCD* gene by molecular genetic testing is recommended as a second-tier test subsequent to a positive newborn screen or biochemical test.

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 glutamate formiminotransferase deficiency may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation(s), therefore, does not eliminate the possibility of positive carrier status or the diagnosis of glutamate formiminotransferase deficiency. For carrier testing, it is important to first document the presence of a *FTCD* 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 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.

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. Hilton JF, Christensen KE, Watkins D, et al: The molecular basis of glutamate formiminotransferase deficiency. Hum Mutat 2003;22:67-73

3. Solans A, Estivill X, de la Luna S: Cloning and characterization of human FTCD on 21q22.3, a candidate gene for glutamate formiminotransferase deficiency. Cytogenet Cell Genet 2000;88:43-49

Performance

Method Description

Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the *FTCD* 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

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

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
GFDZ	FTCD Gene, Full Gene Analysis	94200-3

Result ID	Test Result Name	Result LOINC Value
53929	Result Summary	50397-9
53930	Result	82939-0
53931	Interpretation	69047-9
53932	Additional Information	48767-8
53933	Specimen	31208-2
53934	Source	31208-2
53935	Released By	18771-6