Test Definition: FECHZ

FECH Gene, Full Gene Analysis

Overview

Useful For

Confirmation of a diagnosis of erythropoietic protoporphyria (EPP) following positive biochemical genetic test results obtained through PEE / Porphyrins Evaluation, Whole Blood

Carrier testing for individuals with a family history of EPP in the absence of known mutations in the family

Testing Algorithm

See Porphyria (Cutaneous) Testing Algorithm in Special Instructions.

Special Instructions

- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Porphyria (Cutaneous) Testing Algorithm
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

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

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

Acceptable:

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, see Blood Spot Collection Instructions in Special Instructions.

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

3. 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: Biochemical Disorders Patient Information(T527) in Special Instructions

3. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-Benign Hematology Test Request (T755)

-Inborn Errors of Metabolism Test Request (T798)

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

Erythropoietic protoporphyria (EPP) is an inherited disorder of porphyrin metabolism whose clinical manifestations include painful photodermatosis without blisters and liver disease. The disorder results from decreased activity of the enzyme ferrochelatase (FECH). FECH is the last of 8 enzymes acting sequentially in the heme biosynthetic pathway and is encoded by the *FECH* gene located on chromosome 18.

The skin symptoms in EPP include immediate painful photosensitivity, usually beginning in early infancy upon sun exposure. Repeated photosensitivity episodes result in skin thickening and areas of hyperkeratosis. This is typically noted on areas where sun exposure is most common, such as the dorsa of the hands and on the face. A small number of patients with EPP develop liver complications. Hepatic disease in EPP may include cholelithiasis and chronic liver disease progressing to rapid acute liver failure.

Biochemically, EPP is characterized by elevated protoporphyrin levels in red blood cells, which fluorescence under Wood's light due to the accumulation of free protoporphyrin IX. Protoporphyrin elevations may also be found in plasma and stool, but not in all patients. Urine protoporphyrin levels are usually normal unless there is liver involvement. Studies have also suggested that a reduction in activity of ferrochelatase to <50% of normal levels can induce clinical manifestations. The gold standard test for the diagnosis of EPP is biochemical analysis (PEE / Porphyrins Evaluation, Whole Blood), interpreted in the context of clinical features.

In most patients with EPP, a pathogenic *FECH* mutation that reduces enzyme activity by 50% can be identified on only 1 allele. Clinical expression of EPP typically requires a hypomorphic (low expression) FECH allele (IVS3-48T->C) in trans (on a different chromosome) with the mutation. IVS3-48T->C is a variant of the FECH gene associated with reduced gene expression. This variant is found in approximately 10% of the general Caucasian population. Autosomal recessive inheritance (2 pathogenic mutations in trans) is infrequent, accounting for <4% of EPP cases. In contrast to patients with 1 pathogenic mutation and the low-expression allele, missense mutations are far more common than null mutations.

It is uncertain whether protoporphyric liver failure is more common among individuals with a single null (splicing defect, nonsense, or frameshift) mutation than those with 2 pathogenic mutations as some literature has suggested. In any case, it is certain that all EPP patients should be monitored for hepatic disease and actively manage their photosensitivity.

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 erythropoietic protoporphyria (EPP) disease may have mutations that are 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 EPP disease. For carrier testing, it is important to first document the presence of a ferrochelatase (*FECH*) gene mutation in an affected family member.

This test does not exclude the presence of mutations within other genes, such as *ALAS2* (aminolevulinate, delta-, synthase 2), that are associated with EPP, X-linked or otherwise.

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. Lecha M, Puy H, Deybach JC: Erythropoietic protoporphyria. Orphanet J Rare Dis 2009;4:19

3. Schneider-Yin X, Gouya L, Meier-Weinand A, et al: New insights into the pathogenesis of erythropoietic protoporphyria and their impact on patient care. Eur J Pediatr 2000;159:719-725

4. Rufenacht UB, Gouya L, Schneider-Yin X, et al: Systematic analysis of molecular defects in the ferrochelatase gene from patients with erythropoietic protoporphyria. Am J Hum Genet 1998;62:1341-1352

5. Whatley SD, Mason NG, Holme SA, et al: Molecular epidemiology of erythropoietic protoporphyria in the U.K.. Br J Dermatol 2010;162:642-646

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 ferrochelatase (*FECH*) 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

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
FECHZ	FECH Gene, Full Gene Analysis	94233-4

Result ID	Test Result Name	Result LOINC Value
53901	Result Summary	50397-9
53902	Result	82939-0
53903	Interpretation	69047-9
53904	Additional Information	48767-8
53905	Specimen	31208-2
53906	Source	31208-2
53907	Released By	18771-6

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