Test Definition: FFRBS

Friedreich Ataxia, Frataxin, Quantitative, Blood Spot

Overview

Useful For

Diagnosing individuals with Friedreich ataxia in blood spot specimens

Monitoring frataxin levels in patients with Friedreich ataxia

This test is **not useful** for carrier detection.

Genetics Test Information

Friedreich ataxia (FA) presents most commonly between 10 to 15 years of age with progressive neurologic changes including spasticity and ataxia.

Decreased frataxin protein levels are diagnostic of FA and can also be utilized for ongoing medical monitoring.

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Highlights

Frataxin protein analysis is a quick, cost-effective test method for establishing a diagnosis of Friedreich ataxia (FA) and will detect rare variants otherwise missed by common molecular-based trinucleotide repeat analysis.

This assay is available for the diagnosis of individuals with FA and monitoring frataxin levels in known patients, regardless of the individual's age.

Method Name

Immunoassay

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Necessary Information

Provide a reason for testing with each specimen.

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood spot collection card
Acceptable: PerkinElmer 226 (formerly Ahlstrom 226) Filter Paper and Whatman Protein Saver 903 Paper
Specimen Volume: 2 blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect Dried Blood Spot Samples.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 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. Due to lower concentrations of DNA yielded from blood spots, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be needed to complete testing.
2. For collection instructions, see Blood Spot Collection Instructions
3. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
4. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

1 Blood spot

Reject Due To

Shows serum rings Multiple layers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	30 days	FILTER PAPER
	Refrigerated	30 days	FILTER PAPER
	Frozen	30 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Friedreich ataxia (FA) is an autosomal recessive disease affecting approximately 1:50,000 individuals in the white population. The disease is clinically characterized by progressive spasticity, ataxia, dysarthria, absent lower limb reflexes, sensory loss, and scoliosis. Cardiac involvement occurs with the development of myocardial fibrosis due to mitochondrial proliferation and loss of contractile proteins. It tends to be correlated with the clinical neurologic age of onset and the GAA triplet repeat length, but not the duration of disease or the severity of neurologic symptoms. Although most individuals begin experiencing initial symptoms between 10 and 15 years of age, atypical late-onset forms with initial symptoms presenting after age 25 do occur.

FA is caused by variants in the *FXN* gene encoding a mitochondrial protein, frataxin. Variants in this gene lead to a reduced expression of frataxin, which causes the clinical manifestations of the disease. Approximately 96% of individuals with FA have a homozygous expansion of the GAA trinucleotide repeat in intron 1 of *FXN*. The remaining 4% of FA patients have the trinucleotide expansion on 1 allele and a point alteration or deletion on the second allele. Normal alleles contain between 5 to 33 GAA repeats. Disease-causing alleles typically range from 66 to 1700 repeats, although the majority of individuals with FA have repeats ranging from 600 to 1200.

Historically, FA has been diagnosed by use of a DNA-based molecular test to detect the presence of the GAA expansion. Unfortunately, testing for the triplet repeat expansion will miss those with point alterations or deletions. Moreover, a molecular-based analysis is not able to effectively monitor treatment. In contrast, this protein-based assay measuring concentration of frataxin is suitable for both diagnosis as well as treatment monitoring in individuals with FA.

For patients with a low frataxin level, molecular repeat expansion analysis of the *FXN* gene (AFXN / Friedreich Ataxia, Repeat Expansion Analysis, Varies) allows for detection of disease-causing expansion alleles.

Reference Values

Pediatric (<18 years) normal frataxin: > or =15 ng/mL
Adults (> or =18 years) normal frataxin: > or =21 ng/mL

Interpretation

Normal results (> or =15 ng/mL for pediatric and > or =23 ng/mL for adult patients) in properly submitted specimens are not consistent with Friedreich ataxia.

For results outside the normal reference range an interpretative comment will be provided.

Cautions

No significant cautionary statements

Clinical Reference

1. Oglesbee D, Kroll C, Gakh O, et al. High-throughput immunoassay for the biochemical diagnosis of Friedreich ataxia in dried blood spots and whole blood. Clin Chem. 2013;59(10):1461-1469. doi:10.1373/clinchem.2013.207472
2. Deutsch EC, Oglesbee D, Greeley NR, Lynch DR. Usefulness of frataxin immunoassays for the diagnosis of Friedreich ataxia. J Neurol Neurosurg Psychiatry. 2014;85(9):994-1002
3. Delatycki MB, Bidichandani SI. Friedreich ataxia- pathogenesis and implications for therapies. Neurobiol Dis. 2019;132:104606. doi:10.1016/j.nbd.2019.104606
4. Boehm T, Scheiber-Mojdehkar B, Kluge B, Goldenberg H, Laccone F, Sturm B. Variations of frataxin protein levels in normal individuals. Neurol Sci. 2011;32(2):327-330. doi:10.1007/s10072-010-0326-1
5. Hanson E, Sheldon M, Pacheco B, Alkubeysi M, Raizada V. Heart disease in Friedreich's ataxia. World J Cardiol. 2019;11(1):1-12. doi:10.4330/wjc.v11.i1.1

Performance

Method Description

The immunoassay utilizes frataxin-specific monoclonal antibodies bound to Luminex microspheres as capture antibodies and biotinylated frataxin-specific polyclonal antibodies as detection antibodies. Streptavidin-phycoerythrin attaches to the biotin and when exposed to light at 352 nM emits a photon that is measured and that signal is used to determine the amount of frataxin in the sample.(Oglesbee D, Kroll C, Gakh O, et al. High-throughput immunoassay for the biochemical diagnosis of Friedreich ataxia in dried blood spots and whole blood. Clin Chem. 2013;59(10):1461-1469. doi:10.1373/clinchem.2013.207472; 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. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed

Twice per month, Thursday

Report Available

14 to 30 days

Specimen Retention Time

1 year

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
FFRBS	Frataxin, Quant, BS	80980-6

Result ID	Test Result Name	Result LOINC® Value
32249	Reason for Referral	42349-1
32250	Method	85069-3
32251	Frataxin	80980-6
32252	Interpretation	59462-2