Test Definition: FFRWB

Friedreich Ataxia, Frataxin, Quantitative, Blood

Overview

Useful For

Diagnosing individuals with Friedreich ataxia (FA) in whole blood specimens

Monitoring frataxin levels in patients with FA

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

Genetics Test Information

Friedreich ataxia (FA) presents most commonly between 10 to 15 years 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
- Informed Consent for Genetic Testing (Spanish)

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

Collection Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Green top (sodium or lithium heparin)

Specimen Volume: 2 mL

Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**

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 1 of the following forms with the specimen:

-Neurology Specialty Testing Client Test Request (T732)

-Biochemical Genetics Test Request (T798)

Specimen Minimum Volume

1.25 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Frozen (preferred)	70 days	
	Ambient	70 days	
	Refrigerated	70 days	

Clinical & Interpretive

Clinical Information

Friedreich ataxia (FA) is an autosomal recessive disease 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.

Friedreich ataxia 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 patients with point alterations or deletions. Moreover, a molecular-based analysis cannot 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 =19 ng/mL
Adults (> or =18 years) normal frataxin: > or =21 ng/mL

Interpretation

Normal results (> or =19 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, Wednesday

Report Available
2 to 14 days

Specimen Retention Time
1 month

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
FFRWB	Frataxin, Quant, WB	80979-8

Result ID	Test Result Name	Result LOINC® Value
32253	Reason for Referral	42349-1
32254	Method	85069-3

32255	Frataxin	80979-8
32256	Interpretation	59462-2