

---

## 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 monitoring known patients.

### 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 cost-effective and quick 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 1 year of age or older is a fingerstick. For infants younger than 1 year, a heel stick should be used see [Dried Blood Spot Collection Tutorial](#) for how to collect blood spots via fingerstick.
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.

### Additional Information:

1. For collection instructions, see [Blood Spot Collection Instructions](#)
2. For collection instructions in Spanish, see [Blood Spot Collection Card-Spanish Instructions](#) (T777)
3. 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.

### Reject Due To

Shows serum rings Multiple layers    Reject

### Specimen Minimum Volume

1 Blood spot

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	30 days	FILTER PAPER
	Frozen	30 days	FILTER PAPER
	Refrigerated	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 98% of individuals with FA have a homozygous expansion of the GAA trinucleotide repeat in intron 1 of *FXN*. The remaining 2% 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, though 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 patients with point alterations or deletions. Moreover, a molecular-based analysis is not able to effectively monitor treatment. In contrast, a protein-based assay measuring concentration of frataxin is suitable for both diagnosis as well as treatment monitoring in individuals with FA.

**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 =21 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. Deutsch EC, Oglesbee D, Greeley NR, Lynch DR: Usefulness of frataxin immunoassays for the diagnosis of Friedreich ataxia. *J Neurol Neurosurg Psychiatry*. 2014 Sep;85(9):994-1002
2. Delaytycki MB, Bidichandani SI: Friedreich ataxia pathogenesis and implications for therapies. *Neurobiol Dis*. 2019; Dec;132:104606. doi: 10.1016/j.nbd.2019.104606
3. Boehm T, Scheiber-Mojdehkar B, Kluge B, et al: Variations of frataxin protein levels in normal individuals. *Neurol Sci*. 2011 Apr;32(2):327-30 doi: 10.1007/s10072-010-0326-1
4. Hanson E, Sheldon M, Pacheco B, et al: Heart disease in Friedreich's ataxia. *World J Cardiol*. 2019 Jan;11(1):1-12

**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.(Deutsch EC, Santani AB, Perlman SL, et al: A rapid, noninvasive immunoassay for frataxin: utility in assessment of Friedreich ataxia. Mol Genet Metab. 2010 Oct-Nov;101(2-3):238-245 doi:10.1016/j.ymgme.2010.07.001; 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

**Specimen Retention Time**

1 year

**Performing Laboratory Location**

Rochester

**Fees & Codes**
**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 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	Reporting Name	LOINC®
32249	Reason for Referral	42349-1
32250	Method	85069-3
32251	Frataxin	80980-6
32252	Interpretation	59462-2