

## Friedreich Ataxia DNA Screen

### Background

Friedreich ataxia is an autosomal recessive neurodegenerative disorder that, in 94% of cases, is caused by an abnormal expansion of a GAA trinucleotide repeat in both alleles of the *FXN* gene. In these cases, the DNA test provides a definitive diagnosis by measuring the number of GAA repeats in both *FXN* alleles. The remaining 6% of affected individuals are compound heterozygotes; one allele has an abnormally expanded GAA repeat and the other allele is nonfunctional due to a single nucleotide mutation outside of the GAA repeat region.

### Indications for Testing

- Confirm a clinical diagnosis
- Diagnostic testing for patients with cerebellar, motor neuron, or sensory dysfunction with echocardiographically-proven hypertrophic cardiomyopathy
- Differential diagnosis of a patient with complicated ataxia, especially when neither parent is affected with ataxia
- Differential diagnosis of combined motor neuron disease and sensory loss, especially when cerebellar dysfunction is present
- Carrier testing of subjects from families with a Friedreich ataxia patient, with appropriate genetic counseling
- Prenatal diagnosis of at-risk pregnancies, with appropriate genetic counseling
- **Notes:** Vitamin E deficiency may mimic Friedreich ataxia. If more than one generation is affected with ataxia, consider the dominant spinocerebellar ataxia tests.
- 

### Genetic Counseling

Genetic counseling can be useful to patients and families considering genetic testing. The laboratory can provide referrals to genetics clinics in the patient's locale or a listing can be found at [www.genetests.org](http://www.genetests.org)

### Ordering

1. Obtain blood sample.
  - For prenatal testing, call the Genetics Lab; blood samples of carrier parents may also be required.
2. Fill out a Clinical Lab Request - Genetics for each patient.  
(available at <http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm>).  
Request: "Friedreich Ataxia"
3. Provide information needed for test interpretation:
  - Reason for ordering test
  - Clinical history of patient
  - Family history / pedigree
4. Call Laboratory Medicine Community Services (206) 598-6066 to arrange the best method of shipment.

### Sample Requirements and Specimen Handling

Whole blood - EDTA (purple top) - 5 mL. (Note: Heparin (green top) tubes are not acceptable.)  
Samples should be received within 72 hours of collection. Samples may be refrigerated until shipped.  
For prenatal diagnosis specimens, consult Genetics Laboratory.

### **Test Frequency and Reporting**

Test results usually within two weeks of specimen receipt. Prenatal samples are expedited.  
A written interpretative report is provided.

### **References**

1. Lynch DF, Farmer JM, Balcer LJ, Wilson RB. Friedreich ataxia: Effects of genetic understanding on clinical evaluation and therapy. *Arch Neurol* 59:743-747, 2002.
2. Alper G, Narayanan V. Friedreich's ataxia. *Pediatr neurol* 28:335-341, 2003.
3. Bit-Avragim N, et al. The GAA repeat expansion in intron 1 of the frataxin gene is related to the severity of cardiac manifestations in patients with Friedreich's ataxia. *J Mol Med* 78:626-632, 2001.
4. Bidichandani SI, Ashizawa T. Friedreich Ataxia. In: *GeneReviews at GeneTests: Medical Genetics Information Resource (database online)*. Copyright, University of Washington, Seattle. 1997-2003. Available at <http://www.genetests.org>
5. Bradley JL, Blake JC, Chamberlain S, et al. Clinical, biochemical and molecular genetic correlations in Friedreich's ataxia. *Hum Mol Genet* 9:275-82, 2000.
6. De Castro M, Garcia-Planells J, Monros E, et al. Genotype and phenotype analysis of Friedreich's ataxia compound heterozygous patients. *Hum Genet* 106:86-92, 2000.