

NEUROFIBROMATOSIS Type 1

Comprehensive Test - **Test 1**

- updated 08-10-09 -

DESCRIPTION

Mendelian Inheritance in Man number: [162200](#)

Click here for [Gene Reviews](#) Clinical Summary.

Neurofibromatosis type 1 is a completely penetrant, autosomal dominant disorder with a frequency of 1/3500 births in all ethnic populations. NF1 is a progressive disorder, characterized by multiple café-au-lait spots, neurofibromas, and Lisch nodules, although additional features may develop. NF1 is notorious for its variable expression. About 50% of cases are due to new dominant mutations, where neither parent has signs of the disorder. An affected individual has a 50% risk of transmitting NF1 to each offspring, although the degree of severity can differ from person to person, even within the same family.

INDICATIONS FOR DIRECT TESTING

- Individuals suspected to have NF1 in presence of only one of the NIH diagnostic criteria
- Individuals presenting with an atypical presentation of the disease
- Individuals who seek confirmation of a clinical diagnosis
- Individuals who want to prepare for prenatal / pre-implantation diagnosis

TESTING METHODOLOGY

We offer a **direct test** based on a RNA core assay and resulting in the **full characterization of the *NF1* mutation** at the genomic DNA level. From a fresh EDTA blood sample, DNA is extracted directly and a short term phytohemagglutinin-stimulated lymphocyte culture is initiated and used as starting material to extract RNA. The complete *NF1* coding region is analyzed by a cascade of complementary mutation detection techniques, including RT-PCR, direct sequencing, microsatellite marker analysis, copy number analysis by MLPA and interphase FISH (if needed), enabling us to identify the mutation in ~95% of non-founder patients fulfilling the NIH diagnostic criteria [[Messiaen et al 2000](#), [Messiaen and Wimmer 2005](#), [Wimmer et al 2007](#), [Messiaen and Wimmer, 2008](#)].

Comprehensive NF1 testing (Test 1) as such includes direct sequencing of all coding exons, copy number analysis by MLPA plus RT-PCR and assessment of deep intronic splice mutations through RNA-studies. These splice mutations will not be detected if a DNA-based sequencing approach is used. Mutations screened for include truncating mutations (nonsense, frameshift, splicing mutations), missense mutations, multi-exon deletions and total gene deletions.

SPECIMEN REQUIREMENTS

We require 10 milliliters of whole blood. Blood samples must be collected in EDTA (purple topped) tubes. For pediatric patients or those for whom venipuncture is very difficult, please send a minimum of 3 ml in EDTA.

Segmental/ mosaic patients: We offer testing on affected tissue for patients believed to have segmental NF1 (cfr [Test 4](#)). Comprehensive testing can be performed on either neurofibromas or café-au-lait spot biopsies.

TRANSPORT

If specimen is from clinics within UAB or Kirklin Clinic, please call 934-5562 for pick-up. If specimens are being sent from some other location, please ship via UPS or Federal Express.

IMPORTANT!

Blood specimens must be kept at room temperature and received within 60 hours of collection.

1. DO NOT SHIP ON ICE.
2. Be sure that the shipping air bill is marked “**Priority**”, either Domestic or International.
3. Specimens must be packaged to prevent breakage and absorbent material must be included in the package to absorb liquids in the event that breakage occurs. Also, the package must be shipped in double watertight containers (e.g. a specimen pouch + the shipping companies Diagnostic Envelope). **You can use our collection kits, which we will send to physicians directly upon request.**
4. Please contact us (Email – mgl@genetics.uab.edu, Phone – 205-934-5562) prior to sample shipment and provide us with the **date of shipment** and the **tracking number** of the package, so that we can better ensure receipt of the samples within the 60-hour window. Please include the form for customs. This is especially important for samples sent from outside the US.

TURN AROUND TIME

Normal service: 5-6 weeks

RUSH testing: 2-3 weeks

MLPA *only*: 2-3 weeks

CPT CODES AND PRICES

Please note that prices listed correspond to institutional rates; please contact the lab for insurance rates.

Comprehensive Analysis (Test 1):

\$1200,- USD, additional \$600 for RUSH testing ([currency converter](#))

83891(x3), 83903 (x1), 83913 (x1), 83909 (x9), 83894 (x3), 83896 (x2), 83898 (x16), 83900 (x1), 83902 (x1), 83904 (x18), 88230 (x1), 83912 (x1)

For RUSH testing, please be aware that the RUSH fee is not reimbursable by insurance and in cases of private pay, patient is responsible for paying the test fee plus the RUSH fee up front. For listings of contracted insurance companies, please see our [billing information page](#)

Comprehensive Analysis (Test 1) with a *NF1* Total Gene Deletion (1.2 Mb or larger) identified as the final result will only be billed:

\$500, -USD ([currency converter](#))

83891 (x3), 83913 (x1), 88230 (x1), 83909 (x3), 83896 (x3), 83898 (x3), 83912 (x1)

For all patients where MLPA indicates presence of an *NF1* deletion or duplication, interphase FISH (200 cells) is performed.

Copy Number Analysis by MLPA only:

\$500, -USD ([currency converter](#))

83891 (x1), 83909 (x6), 83896 (x6), 83898 (x6), 83912 (x1)

*Please note that MLPA is part of the *NF1* Comprehensive Analysis Test 1, but can be requested as a stand-alone test at \$500,-USD

*If a total gene deletion has previously been identified within the family, please mark targeted mutation analysis (Test 2) on the Test Requisition instead of Copy Number Analysis only

REQUIRED FORMS

[NF1 Test Requisition including the phenotypic data form or NF1 Test Requisition- Segmental NF1 including the phenotypic data form.](#)
[Form for customs \(International shipment\)](#)

Note: Requests for Molecular Genetic testing for *NF1* will **not** be accepted for the following reasons:

- No label (patients full name and date of collection) on the specimens
- No referring physician's or genetic counselor's names and addresses
- No billing information
- No informed consent
- **No phenotypic checklist**

For more information, test requisition forms, or sample collection and mailing kits, please call: 205-934-5562.

REFERENCES

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