

NEUROFIBROMATOSIS Type 1

Comprehensive Testing in **Affected Tissues - Test 4**

- updated 08-10-09 -

DESCRIPTION

Online 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.

Segmental patients may only have NF1 symptoms over a defined area of their body, and the symptoms may be due to a postzygotic mutation, creating a mosaic individual.

In patients with **mild non-localized NF1 symptoms**, disease can also be due to a postzygotic mutation, present in the affected tissues, but not in the blood lymphocytes ([Maertens et al, 2007](#)). Comprehensive testing in affected tissues can confirm somatic mosaicism for NF1.

INDICATIONS FOR DIRECT TESTING

- Individuals suspected to have **segmental NF1** and in whom no mutation was found in the blood lymphocytes by comprehensive *NF1* mutation analysis
- Sporadic patients who have symptoms of NF1 but in whom no *NF1* mutation was identified in the blood lymphocytes. **Mosaic NF1** can be diagnosed starting from biopsies from either CAL-spots or neurofibromas.

TESTING METHODOLOGY

We offer a **comprehensive test** in cultured cells from the affected region (**Schwann cells** or **melanocytes**) resulting in the full characterization of the *NF1* mutation at the genomic DNA level ([Maertens et al, 2007](#), [De Schepper et al, 2007](#)). The complete *NF1* coding region is analyzed by a cascade of complementary mutation detection techniques, 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](#)]. Mutations screened for include truncating mutations (nonsense, frameshift, splicing mutations including deep-intronic splice mutations), missense mutations, multi-exon deletions and total gene deletions. We always fully characterize the mutation at the genomic DNA level.

SPECIMEN REQUIREMENTS

Segmental testing requires analysis of an affected region. Either a skin biopsy of a café-au-lait spot or fresh tumor tissue can be used to perform the comprehensive testing. Please contact us at mgl@genetics.uab.edu or 205-934-5562 to set up a time **prior** to taking biopsy/biopsies in your patient, so we can provide individualized advice and ship out appropriate collection/transport media and forms prior to surgery.

- **Testing from café-au-lait spots**

Comprehensive *NF1* testing from café-au-lait spots requires selective culturing of **melanocytes** from a skin biopsy. We require **2-3 3mm punch biopsies** for testing. Biopsies must be collected in **special transport media** that will be shipped to your facility prior to surgery. Please allow 2-3 days for delivery.

[Instructions for collecting and shipping skin biopsies \(CAL-spots\) for NF1 testing](#)

- **Testing from fresh neurofibroma tissue**

Comprehensive *NF1* testing from a tumor specimen requires selective culturing of the **Schwann cells**. We require a **minimum of 2 biopsies of separate fresh neurofibromas** (size of an eraserhead), collected in **special transport media** that will be shipped to your facility prior to surgery. Please allow 2-3 days for delivery.

[Instructions for collecting and shipping neurofibromas for NF1 testing](#)

TRANSPORT

Specimens for segmental *NF1* testing must be shipped in the appropriate transport media. **Please contact our lab at 205-934-5562 in order to obtain the transport media and shipping instructions.** Please allow 2-3 days for delivery. Specimens must be immediately placed in the transport media, and then sealed and shipped to our lab via overnight delivery service or international priority service.

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.

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).
4. **Always** 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.

TURN AROUND TIME

Turn-around time is dependent on the **size and quality of the tissue specimen** we receive and the time it takes until sufficient cultured melanocytes or Schwann cells are obtained, however the following general turn-around times can be estimated:

Testing from skin biopsies: 4-5 months
Testing from neurofibromas: 3-4 months

CPT CODES AND PRICES

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

\$2600, - USD ([currency converter](#))
83891 (x6), 83903 (x2), 83913 (x2), 83909 (x18), 83894 (x6), 83896 (x4), 83898 (x32), 83902 (x2), 83904 (x36), 88230 (x2), 83912 (x2)

REQUIRED FORMS

[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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Wimmer K, Roca X, Beiglbock H, Callens T, Etzler J, Rao A, Krainer A, Fonatsch C, Messiaen L (2007) Extensive in silico analysis of NF1 splicing defects uncovers determinants for splicing outcome upon 5' splice-site disruption. Hum Mutat. 28(6): 599-612. [\(pubmed\)](#)