

NEUROFIBROMATOSIS Type 2

Comprehensive Test - **Test 1**

- updated 08-10-09 -

DESCRIPTION

Mendelian Inheritance in Man number: [101000](#)

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

Bilateral Acoustic Neurofibromatosis, Central Neurofibromatosis

Neurofibromatosis type 2 is characterized by bilateral vestibular schwannomas with associated symptoms of tinnitus, hearing loss and balance dysfunction. Other findings include meningiomas of the brain, schwannomas of other cranial nerves or of the dorsal roots of the spinal cord and juvenile posterior subcapsular cataract. NF2 is an autosomal dominant disorder with a frequency of 1:33-40,000 births in all populations. About 50% of patients are due to a de novo mutation, where neither parent has signs of the disorder. The offspring of an affected individual have a 50% risk of inheriting the altered *NF2* gene.

INDICATIONS FOR TESTING

- Confirmatory diagnostic testing
- Testing in an affected patient to prepare for predictive testing and early detection of at-risk relatives for management reasons
- Predictive testing for early detection of at-risk individuals for management reasons
- Testing in an affected patient to prepare for prenatal diagnosis and/or pre implantation diagnosis

TESTING METHODOLOGY

We offer a **direct test** using cDNA-based direct sequencing of the entire coding region and MLPA analysis to detect copy number changes. Copy number changes are confirmed by long range RT-PCR, quantitative PCR and/or aCGH.

Using this approach, mutation detection rate in leukocytes is 93% in **non-founder** NF2 patients. Mutations detected include truncating mutations (nonsense, frameshift, splicing mutations including deep intronic splice mutations), missense mutations, multi-exon deletions or duplications and total gene deletions.

In about 25-30% of **founders** (simplex cases, patients with unaffected parents), mutations are not detected in blood lymphocytes as a result of somatic mosaicism. Only mutations with mosaicism levels greater than 10% can be detected in lymphocyte DNA ([Evans et al, 2007](#)). Identification of the majority of mosaic mutation requires testing of tumor tissue ([Evans et al, 2007](#)); more information can be found under [NF2 Test 4](#), testing from tumor tissue.

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.

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.

TURN AROUND TIME

Normal service: 4-5 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):

\$1250,- USD, additional 600 for RUSH testing ([currency converter](#))

83891 (x2), 83913 (x1), 83909 (x9), 83894 (x11), 83896 (x7), 83898 (x15), 83902 (x1), 83904(x7), 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](#)

Copy Number Analysis by MLPA only:

\$300, - USD ([currency converter](#))

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

*Please note that MLPA is part of the NF2 Comprehensive Analysis Test 1, but can be requested as a stand-alone test at \$300,-USD

REQUIRED FORMS

[NF2 Test Requisition including the phenotypic data form.](#)
[Form for customs \(International shipment\)](#)

Note: Requests for Molecular Genetic testing for NF2 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

Baser M, Friedman J, Aeschliman D, Joe H, Wallace A, Ramsden R, Evans DG - Predictors of the risk of mortality in neurofibromatosis 2. Am J Hum Genet 71:715. 2002 ([pubmed](#))

Evans DG, Ramsden RT, Gokhale C, Bowers N, Huson SM, Wallace A Should NF2 mutation screening be undertaken in patients with an apparently isolated vestibular schwannoma? Clin Genet. 71 (4): 354-8, 2007 ([pubmed](#))

Kluwe L, Nygren A, Errami A, Heinrich B, Matthies C, Tatagiba M, Mautner V Screening for large mutations of the NF2 gene. Genes Chromosomes Cancer 42:384, 2005 ([pubmed](#))