

# NEUROFIBROMATOSIS Type 2

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

- 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 in a founder patient in whom no mutation was identified by comprehensive testing in the blood lymphocytes
- Sporadic patients with multiple schwannomas
- Testing in an affected patient to prepare for predictive testing for early detection of at-risk relatives for management reasons
- Testing in an affected patient to prepare for prenatal diagnosis and/or pre implantation diagnosis

### **TESTING METHODOLOGY**

We offer a **comprehensive test** using gDNA-based direct sequencing of all NF2 exons (and flanking acceptor/donor intronic sequences) and MLPA analysis to detect copy number changes. Copy number changes are confirmed by quantitative PCR or aCGH.

Using this approach, mutation detection rate in leukocytes is >90% in **non-founder** NF2 patients. Mutations detected include truncating mutations (nonsense, frameshift, splicing 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). As RNA is most often degraded in available tumor material, a **DNA-based comprehensive analysis** is applied.

### **SPECIMEN REQUIREMENTS**

We require **snap-frozen tumor tissue (preferred), a fresh tumor specimen immersed in PBS or culture medium (preferred), OR a tumor block.**

In cases where surgery is scheduled, the MGL prefers that the tumor that is removed be cleaned of normal surrounding tissue, snap-frozen and shipped overnight to the MGL on dry ice.

**If a tumor block is the only available material, we request that the whole tumor block be sent to us for processing. After the analysis, the tumor block will be sent back to the referring site.** If the entire tumor block cannot be sent, we request that a part of the tumor is carved out from the block, avoiding the surrounding normal tissue and paraffin. To ensure that only the tumor will be excised, cut from the middle of the block where the tumor is positioned. To prevent contamination, first cut off some slices from the block using a clean knife. The minimum diameter of the tumor sample should be 0.5 cm. Place the tumor sample in a sterile container. We cannot accept samples that are not processed in this manner.

For sporadic patients with multiple schwannomas but without vestibular nerve involvement and in whom *NF2* mutations are found in the tumor, we will only be able to differentiate between mosaic NF2 and schwannomatosis if material from **2 separate tumors** is available and provided. There will be no additional cost associated with the analysis of more than one tumor.

## 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.

1. Be sure that the shipping air bill is marked “**Priority**”, either Domestic or International.
2. 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).
3. Please contact us (Email – [mgl@genetics.uab.edu](mailto: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

4-5 weeks

## CPT CODES AND PRICES

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

\$1400, - USD ([currency converter](#))

83891 (x2), 83907 (x2), 83909 (x9), 83894 (x14), 83896 (x1), 83898 (x16), 83904 (x14), 83912 (x1)

## 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 institution
- 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](#))