Medical Genomics Laboratory

The Medical Genomics Laboratory at UAB is a CLIA– and CAP-certified laboratory working within the Department of Genetics. We provide molecular genetic testing in common and rare hereditary disorders, with an emphasis on comprehensive testing for large and complex genes.

We are the only laboratory in the country offering a comprehensive testing approach to all variant forms of the neurofibromatoses: NF1, NFLS, segmental NF, NF2, schwannomatosis.

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We work closely with the UAB Neurofibromatosis Clinic led by neurologists and geneticists Dr. Bruce Korf, Chair of the Department of Genetics, and Dr. Lane Rutledge, Director of Clinical Services.

The clinic serves patients and their families dealing with the lifelong medical, psychological and social implications of any of the various forms of neurofibromatosis.

Full information on the Medical Genomics Laboratory test menu, specimen requirements and instructions for shipping can be found at

www.genetics.uab.edu/medgenomics

Medical Genomics Laboratory

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Neurofibromatosis Type 2 (NF2)
&
Schwannomatosis (INI1/SMARCB1)

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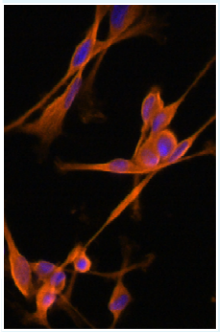
Neurofibromatosis Type 2 (NF2) and Schwannomatosis (INI1/SMARCB1)

Neurofibromatosis Type 2 (NF2)

Mendelian Inheritance in Man number: 101000.

Neurofibromatosis Type 2, an autosomal dominant disorder with a frequency of one in 33,000-40,000 births in all populations, is caused by mutations in the *NF2* gene on chromosome 22. NF2 is characterized by bilateral vestibular schwannomas with associated symptoms of tinnitus, hearing loss, and balance dysfunction. Other signs associated with this disorder are meningiomas, schwannomas of cranial nerves or of the dorsal roots, ependymomas, and juvenile posterior cataract. About 50% of patients are sporadic and have the disorder due to a *de novo* dominant mutation. These are "founder" patients, and up to 30% of founder patients are mosaic for a NF2 mutation. All children of an affected individual have a 50% risk of inheriting the altered NF2 gene copy.



***In vitro* cultured Schwann cells**

We offer comprehensive, expeditious, cost-effective *NF2* mutation analysis, using a cascade of complementary mutation detection techniques, including direct sequencing of the entire coding region, transcript analysis detecting all splice mutations, MLPA analysis for copy number changes such as exon deletions or duplications and microdeletions encompassing the *NF2* gene. These techniques allow identification of a mutation in >90% of non-founder NF2 patients. A fresh EDTA blood sample (minimum 3 cc) is needed for this analysis.

Mosaic NF2

Up to 30% of founder patients may be mosaic for a NF2 mutation; this means that the mutation may only be present in certain cell types, and testing of blood lymphocytes may not yield identification of a mutation. In patients with clinical features of NF2 and a negative result by testing blood lymphocytes, comprehensive testing by direct sequencing of the entire *NF2* coding region, copy number analysis by MLPA, and Loss of Heterozygosity (LOH) analysis using microsatellite markers is available starting from fresh, snap-frozen, or paraffin-embedded **tumor** tissue.

Schwannomatosis

Mendelian Inheritance in Man number: 162091.

Constitutional *INI1/SMARCB1* mutations can cause the inherited predisposition to atypical teratoid/rhabdoid tumor syndrome (AT/RT).

Schwannomatosis is a rare condition characterized by multiple schwannomas and absence of involvement of the vestibular nerve. Schwannomas can arise along peripheral and cranial nerves (but not the eighth nerve) and most commonly manifest with pain and/or neurological deficit. Germline mutations in the *INI1/SMARCB1* gene have been identified in families with schwannomatosis as well as in some sporadic schwannomatosis patients. In addition, the schwannomas in these patients show inactivation of both *INI1/SMARCB1* and *NF2*. We offer comprehensive *INI1/SMARCB1* mutation analysis starting from a fresh EDTA blood sample or starting from schwannoma tumor tissue, using direct sequencing of the entire coding region (tumor or blood), transcript analysis detecting all splice mutations (blood only) and MLPA analysis for copy number changes (tumor or blood).

Indications for NF2 testing

- Individuals who seek genetic confirmation of a clinical or suspected diagnosis
- Individuals who want to prepare for predictive testing of at-risk relatives for management reasons
- Individuals who want to prepare for prenatal/pre-implantation diagnosis

Indications for INI1/SMARCB1 testing

- Individuals with multiple schwannomas without involvement of the vestibular nerve **and** no NF2 mutation after comprehensive NF2 mutation analysis in the blood
- Individuals with atypical teratoid/rhabdoid tumors
- Individuals who seek confirmation of a clinical diagnosis

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