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 for 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 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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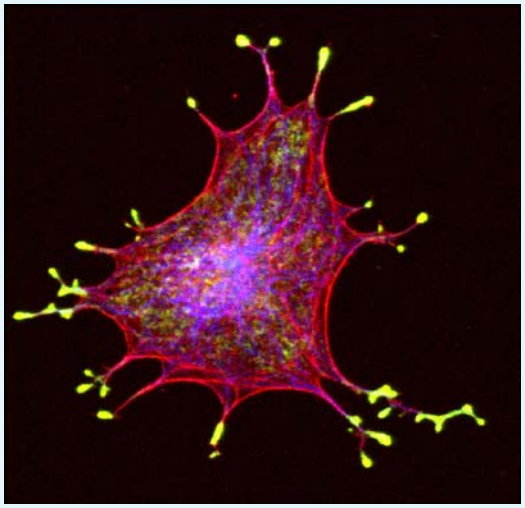
Neurofibromatosis Type 1 (NF1) & Neurofibromatosis-like syndrome (NFLS)



Melanocyte showing melanosomes - Alistair Hume/Wellcome

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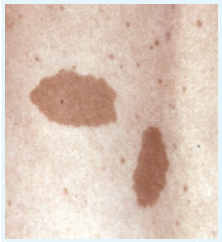
Neurofibromatosis Type 1 (NF1) and Neurofibromatosis-like syndrome (NFLS)

NF1 is a fully penetrant, progressive, autosomal dominant disorder with a frequency of 1 in 3500 births worldwide. NF1 is characterized by multiple CAL-spots, skinfold freckling, Lisch nodules, and tumors of the nervous system such as neurofibromas, gliomas, and malignant peripheral nerve sheath tumors. Other frequently observed features are specific bone abnormalities, vascular complications, short stature, macrocephaly and learning problems. NF1 is notorious for its variable expression. Neurofibromatosis Type 1 is caused by mutations in the ***NF1*** gene, encoding neurofibromin, on chromosome 17q11.2. An affected individual has a 50% risk of transmitting the disorder to each child, although the degree of severity can differ from person to person, even within the family. About 50% of cases are due to new dominant mutations, where neither parent has signs of the disorder. Some sporadic patients develop signs due to a mutation that arose after conception and may carry the mutation only in a portion of their cells.

Recently, a new autosomal dominant condition, the Neurofibromatosis-like Syndrome (NFLS) was identified, consisting of CAL-spots, skinfold freckling and macrocephaly. NFLS is not associated with the high incidence of peripheral and central nervous system tumors seen in individuals with NF1. NFLS is caused by loss-of-function mutations in the ***SPRED1*** gene on chromosome 15.



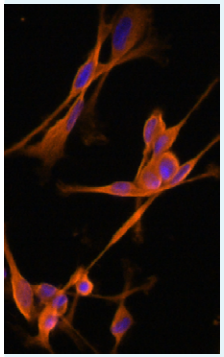
Typical CAL-spots

The Medical Genomics Laboratory offers comprehensive genetic testing for both disorders.

Neurofibromatosis Type 1

We offer comprehensive, expeditious and cost-effective *NF1* mutation analysis using a cascade of complementary mutation detection techniques, including direct sequencing of the entire coding region, transcript analysis detecting all possible splice mutations, analysis of copy number changes such as one-to-multiple exon deletions or duplications and microdeletions encompassing the *NF1* gene as well as flanking genes by FISH and MLPA. These techniques allow identification of an NF1 mutation in >95% of non-founder patients fulfilling NIH criteria. A fresh EDTA blood sample (minimum 3 cc) is needed for this comprehensive analysis and takes 5 weeks.

Segmental NF & mosaic NF



***In vitro* cultured Schwann cells**

Patients suspected to have segmental NF or mosaic NF may not have a mutation in blood lymphocytes. In these patients, testing can now be performed starting from a fresh biopsy of a neurofibroma or café-au-lait spot and culture of Schwann cells or melanocytes. Direct contact with the laboratory is necessary to implement thls approach.

Neurofibromatosis-like syndrome

We offer comprehensive, expeditious and cost-effective *SPRED1* mutation analysis, using sequencing of the entire coding region and MLPA analysis detecting dosage alterations.

Indications for NF1 testing

- Individuals suspected to have NF1 in presence of only one NIH diagnostic criterion
- Individuals who seek genetic confirmation of a clinical diagnosis
- Individuals who want to prepare for prenatal/ pre-implantation diagnosis

Indications for SPRED1 testing

- Individuals with CAL-spots and no *NF1* mutation after comprehensive *NF1* mutation analysis

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