

# SCHWANNOMATOSIS/ATYPICAL TERATOID/RHABDOID TUMOR PREDISPOSITION SYNDROME – *INI1/SMARCB1* testing

Comprehensive Test - **Test 1**

- updated 08-10-09 -

## DESCRIPTION

Mendelian Inheritance in Man number: [162091](#)

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

Schwannomatosis is a rare condition characterized by multiple schwannomas and absence of involvement of the vestibular nerve. Schwannomas can arise wherever Schwann cells occur, in the spinal cord and along peripheral and cranial nerves. The tumors manifest most commonly with pain and/or neurological deficit. Some patients with multiple non-vestibular nerve schwannomas and a negative family history are mosaic for *NF2*. In contrast, a subgroup of patients in whom schwannomas are largely confined to the peripheral nerves, do not have an underlying *NF2* mutation, but have schwannomatosis. These individuals may pass the condition on to their children.

Recently, germline mutations in the *INI1/SMARCB1* gene have been identified in families with schwannomatosis as well as in sporadic schwannomatosis patients ([Hulsebos et al, 2007](#); [Sestini et al, 2008](#); [Hadfield et al, 2008](#)). Mutations in *INI1/SMARCB1* occur in ~33% of familial schwannomatosis patients and in ~7% of sporadic schwannomatosis patients (Hadfield et al, 2008).

Constitutional *INI1/SMARCB1* mutations are also the cause of inherited predisposition to **rhabdoid tumors** ([Sevenet et al, 1999](#)).

*INI1/SMARCB1* encodes a member of the chromatin-remodelling SWI/SNF multiprotein complexes.

## INDICATIONS FOR DIRECT TESTING

- Individuals with multiple schwannomas without involvement of the vestibular nerve and no *NF2* mutation after comprehensive *NF2* mutation analysis in the blood
- predictive testing for early detection of at-risk relatives for management reasons
- Individuals with rhabdoid tumors
- Individuals who seek confirmation of a clinical diagnosis

## TESTING METHODOLOGY

We offer a **direct test** resulting in the **full characterization of the *INI1/SMARCB1* mutation**.

**RNA-based testing:**

From a fresh EDTA blood sample, a PHA-stimulated lymphocyte culture is initiated and used to extract mRNA used as the starting material for direct sequencing of the entire coding region. Mutations screened for include truncating mutations (nonsense, frameshift, splicing mutations) and missense mutations. A mutation identified at the cDNA level is thereafter characterized completely at the gDNA level. In addition, copy number alterations (multi-exon deletions or duplications) are analyzed by MLPA.

**DNA-based testing:**

Alternatively, we offer a direct test from DNA extracted from an EDTA blood sample, although RNA-based testing is the preferred method. Some splice mutations will remain undetected using this approach. Testing includes direct sequencing of all exons and flanking intronic sequence (-20 to +10 minimum) and copy number analysis by MLPA.

**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](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 within the 60-hour window. Please include the form for customs. This is especially important for samples sent from outside the US.

**TURN AROUND TIME**

Test 1: 4-5 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 RNA-based):

\$800, - USD ([currency converter](#))

83891 (x2), 83913 (x1), 83909 (x1), 83894 (x2), 83896 (x3), 83898 (x3), 83902 (x1), 83904 (x8), 83912 (x1), 88230 (x1)

OR

### Comprehensive Analysis (Test 1 DNA-based):

\$800, - USD ([currency converter](#))

83891 (x1), 83909 (x1), 83894 (x10), 83896 (x3), 83898 (x10), 83904 (x18), 83912 (x1)

### 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 *INI1* Comprehensive Analysis Test 1, but can be requested as a stand-alone test at \$300,-USD

## REQUIRED FORMS

[INI1 Test Requisition including the phenotypic data form.](#)

[Form for customs \(International shipment\)](#)

**Note:** Requests for Molecular Genetic testing for *INI1/SMARCB1* 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 if being paid for by an 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

Hadfield KD, Newman WG, Bowers NL, Wallace A, Bolger C, Colley A, McCann E, Trump D, Prescott T, Evans DG Molecular characterisation of *SMARCB1* and *NF2* in familial and sporadic schwannomatosis J Med Genet 2008 45 (6): 332-9 ([pubmed](#))

Hulsebos TJ, Plomp AS, Wolterman RA, Robanus-Maandag EC, Baas F, Wesseling P Germline mutation of *INI1/SMARCB1* in familial schwannomatosis. Am J Hum Genet. 2007 80 (4): 805-10. ([pubmed](#))

Sestini R, Bacci C, Provenzano A, Genuardi M, Papi L Evidence of a four-hit mechanism involving *SMARCB1* and *NF2* in schwannomatosis-associated schwannomas Hum Mutat 2008 29 (2): 227-31. ([pubmed](#))

Sevenet N, Lellouch-Tubiana A, Schofield D, Hoang-Xuan K, Gessler M, Birnbaum D, Jeanpierre C, Jouvret A, Delattre O Spectrum of hSNF5/INI1 somatic mutations in human cancer and genotype-phenotype correlations Hum Mol Genet 1999 8 (13): 2359-68 ([pubmed](#))