

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

Target Mutation Analysis - **Test 2**

- 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

- Predictive testing for early detection of at-risk relatives for management reasons

TESTING METHODOLOGY

We offer a **targeted detection** of a previously characterized *INI1* mutation within the family. From a fresh EDTA blood sample, DNA is extracted directly and the target region is amplified and analyzed for presence or absence of the specific mutation.

Test 2 is provided **free of charge** to all relevant relatives of a proband in whom a novel **missense** alteration was found that needs further clarification to come to a final conclusion. As the final conclusion on the pathogenicity of a missense alteration relies on accurate phenotypic data, the testing in relevant relatives is provided free of charge only if a phenotypic checklist is filled out by a healthcare professional that made the

clinical assessment of the relatives. The correct interpretation of the results also relies on the correct disclosure of the biological relationships.

SPECIMEN REQUIREMENTS

We require 1 milliliter of whole blood. Blood samples must be collected in EDTA (purple topped) tubes.

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). **You can use our collection kits, which we will send to physicians directly upon request.**

TURN AROUND TIME

2-3 weeks

CPT CODES AND PRICES

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

\$250,- USD ([currency converter](#))
83891 (x1), 83894 (x4), 83898 (x4), 83904 (x3), 83912 (x1)

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:** we offer **free of charge** targeted testing to all relevant relatives of a proband in whom a **novel missense variant** was identified. Testing of these relatives may allow us to make a final conclusion on the pathogenicity of the novel missense variant and allow us to provide better counseling now and in

the future. Free of charge targeted testing will only be provided if the necessary **phenotypic information on the proband and relatives filled out by a healthcare professional** accompanies the samples. If no phenotypic information is provided, we will charge the institution for the test.

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](#))