

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

Prenatal Detection of a known mutation - **Test 3**

- 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

- Prenatal predictive testing for individuals at risk of inheriting an already known *INI1* mutation

TESTING METHODOLOGY

We offer a **targeted detection** of a previously characterized *INI1* mutation within the family. For prenatal diagnosis, fresh or cultured CVS or amniocytes will be used for diagnostic purposes. DNA is extracted directly and the target region is amplified and analyzed for the presence or absence of the specific mutation. Maternal cell contamination is analyzed by amplification of microsatellite markers in the DNA of the maternal and fetal sample. All prenatal samples are performed in duplicate and independently by two technicians.

SPECIMEN REQUIREMENTS

(1) minimum of 15 mg of chorionic villus specimen. Send specimen in transport media in 15-mL centrifuge tube.

(2) 20 mL of amniotic fluid. Send specimen refrigerated, but not frozen.

(3) 2-T25 flasks of cultured CVS (>70% confluent), sent at ambient temperature.

(4) 2-T25 flasks of cultured amniocytes. (>70% confluent), sent at ambient temperature.

Please also send 1-5 ml of blood or buccal swab sample from mother for maternal contamination studies.

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.**
3. Please contact us (Email –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.

TURN AROUND TIME

6 business days after sample is received.

CPT CODES AND PRICES

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

\$750, - USD ([currency converter](#))

83891 (x3), 83894 (x20), 83896 (x6), 83898 (x20), 83904 (x8), 83912 (x1)

REQUIRED FORMS

[INI1 Test Requisition](#)

*Phenotypic checklist does not need to be filled out for prenatal tests.

[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 payment if being paid for by an institution

- No informed consent

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](#))