Schwannomatosis/Multiple Schwannoma Panel on Tumor Block (SCHP)

Ordering Information

Acceptable specimen types:

- A minimum of 2 anatomically distinct tumor samples is suggested, however, a single tumor can be provided.
- A blood (3-6ml whole blood in EDTA) specimen may be provided for free of charge targeted testing of any suspected germline variants identified during tumor testing.
- Tumor block should have a surface area $\geq$ 5mm squared or the specimen contains at least 3-6 loose paraffin curls (no slides) that are 30-50 microns thick.
- Specimen should contain at least 70% pure tumor content and $>80\%$ nucleated cells.

Turnaround time:

30 working days

Price, CPT codes, and Z code:

$2,500 (USD – institutional/self-pay);
CPT: 81404, 81405 (x3), and 81406 (x2)
Z code: ZB68A

Candidates for this test:

Patients with multiple schwannomas with or without vestibular schwannomas and/or no variant identified by blood based testing.
For sporadic patients with multiple schwannomas but without vestibular nerve involvement and in whom NF2 variants are found in the tumor, we will only be able to differentiate between mosaic NF2 and schwannomatosis if material from 2 separate tumors is available and provided. There will be no additional cost associated with the analysis of more than one tumor.

Specimen shipping and handling:

- Please find acceptable specimen type above.
- Please see website or contact us for instructions for collecting and shipping tumor blocks for testing.
- All submitted specimens must be sent at room temperature. DO NOT ship on ice.
- 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 company’s diagnostic envelope).
- Please contact the MGL (via email at medgenomics@uabmc.edu, or via phone at 205-934-5562) prior to sample shipment and provide us with the date of shipment and tracking number of the package so that we can better ensure receipt of the samples.

Required forms:

- Test Requisition Form
- Form for Customs (for international shipments)

Note: Detailed and accurate completion of this document is necessary for reporting purposes. The Medical Genomics Laboratory issues its clinical reports based on the demographic data provided by the referring institution on the lab requisition form. It is the responsibility of the referring institution to provide accurate information. If an amended report is necessary due to inaccurate or illegible documentation, additional reports will be drafted with charge.
Requests for testing may 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

For more information, test requisition forms, or sample collection and mailing kits, please call: 205-934-5562.

Disorder Background

Schwannomas are nerve sheath tumors which are nearly always benign but can cause significant pain. Isolated schwannomas are common in the general population, but the development of multiple non-intradermal schwannomas (in the absence of bilateral vestibular schwannomas, congenital cataracts or ependymomas, typically associated with constitutional NF2) as typically seen in schwannomatosis patients, is rare. Presence of multiple non-intradermal schwannomas, in the absence of a family history of NF2, can be found in individuals with mosaic Neurofibromatosis type 2, or in individuals carrying germline variants in either \textit{SMARCB1} or \textit{LZTR1}.

Individuals with schwannomatosis do not typically develop bilateral vestibular schwannomas, ependymomas, meningiomas (typically associated with NF2), nor neurofibromas or astrocytomas (associated with NF1). However, clinical overlap with neurofibromatosis type 2 exists: some \textit{SMARCB1}-positive patients have developed meningiomas or a unilateral vestibular schwannoma; and some \textit{LZTR1}-positive patients have been reported with a unilateral/bilateral vestibular schwannoma. Whereas both NF2 and schwannomatosis present with variable expressivity, penetrance for NF2 is close to 100%, whereas non-penetration is well documented in schwannomatosis, although the exact frequency is not known.

Test Description
We offer a comprehensive test using DNA-based direct sequencing and copy number analysis by MLPA of the NF2, SMARCB1, and LZTR1 genes. Using this approach, variant detection rate in leukocytes is >90% in non-founder NF2 patients. Variants detected include truncating variants (nonsense, frameshift, splicing variants), missense variants, multi-exon deletions or duplications and total gene deletions.

In about 25-30% of founders (simplex cases, patients with unaffected parents), variants are not detected in blood lymphocytes as a result of somatic mosaicism. Only variants with mosaicism levels greater than 10% can be detected in lymphocyte DNA (Evans et al, 2007). Identification of the majority of mosaic variant requires testing of tumor tissue (Evans et al, 2007). As RNA is most often degraded in available tumor material, a DNA-based comprehensive analysis is applied.

REFERENCES available on website.

Other related testing options:

- Next-Gen Sequencing and Deletion/Duplication analysis of NF2 only (NF2-NG)
- Schwannomatosis/Multiple Schwannoma Panel by Next-Gen Sequencing (SCH-NG)
- NF2 gDNA Sequencing and Deletion/Duplication Analysis on Tumor Block (NF24)