

UAB MEDICAL GENOMICS LABORATORY

Meningiomatosis/Multiple Meningioma Panel by Next-Gen Sequencing (MEN-NG)

Ordering Information

Acceptable specimen types:

- Blood (3-6ml EDTA; no time limitations associated with receipt)
- Saliva (OGR-575 DNA Genotek; kits are provided upon request)
- DNA (extracted from lymphocyte cells, a minimum of 25µL at a concentration of 3µg, O.D. value at 260:280nm \geq 1.8)
- Flash frozen tumor sent on dry ice
- Fresh tumor or affected tissue biopsy, immersed in sterile culture media (PBS/RPMI)

Turnaround time:

25 working days for blood, saliva, or DNA; 40 working days for fresh/frozen tumor

Price, CPT codes, and Z code:

\$1,500 for blood, saliva, or DNA (USD – institutional/self-pay);

\$2,500 for fresh/frozen tumor (USD – institutional/self-pay);

CPT: 81406, 81405, and 81479 (x2)

Z code: ZB67L

Candidates for this test:

Patients with clinical features suggestive of meningiomatosis or NF2 with the inclusion of meningiomas within their phenotype.

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Specimen shipping and handling:

- Please find acceptable specimen type above.
- 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).
- To request a sample collection kit, please visit the website or email medgenomics@uabmc.edu to complete the specimen request form.
- 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

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- DNA samples must be extracted in a CLIA or equivalent certified lab

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

Disorder Background

A meningioma in childhood can be a presenting first sign of neurofibromatosis type 2 (OMIM 101000) (Smith M et al, 2011: J. Med. Genet 48:261-5).

Besides *NF2*, germline *SMARCB1* variants have been identified in patients with meningiomas (with or without schwannomas) (van den Munckhof P et al, 2012: Neurogenetics 13:1-7).

Furthermore, germline variants in *SUFU* have been found in some families with meningiomatosis (Aavikko M et al, 2012: Am. J. Hum. Genet. 91:520-6).

In addition, *SMARCE1* germline variants are associated with a tumor-predisposition syndrome with patients having an increased risk for spinal and intracranial clear cell meningiomas (Smith M et al, 2014: J. Path. 234:436-40). Clear cell meningiomas occur more frequently in young people and are defined as WHO grade 2, due to their more aggressive behavior.

As multiple meningiomas can be a sign of different tumor-predisposition syndromes that have overlapping features, a clinical diagnosis might be challenging in some individuals, making a panel-based test more cost-effective.

Test Description

The **Meningiomatosis/Multiple Meningioma Panel by NGS** involves the simultaneous sequencing of 4 genes: *NF2*, *SMARCB1*, *SMARCE1*, and *SUFU*. The test uses an extensively customized and optimized set of Agilent HaloPlex capture probes, followed by sequencing of overlapping amplicons within the regions of interest using 300bp paired-end Illumina sequencing chemistry. Each coding exon plus ~50bp of flanking intronic sequence are simultaneously sequenced. 5' and 3' untranslated sequences are not included. **The average**

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coverage is >1500x with >99% of the coding region $\geq 350x$ and 100% $\geq 200x$. This allows for **detection of very low-level mosaicism** by sequencing (as low as 3% of the alleles in 100% of the coding region with >95% confidence).

Variant and copy number calls are made using a unique bioinformatics pipeline detecting all types of variants including single nucleotide substitutions, indels, and frameshifts caused by deletion/ duplication up to 112bp. Deletion/duplication analysis for *NF2* and *SMARCB1* using MLPA is included in this test, as such variants are a part of the variant spectrum for these conditions. Deletion/duplication analysis for other genes on this panel is not offered as current empirical and biological evidence is not sufficient to allow the conclusion that an altered copy number of these genes is a mechanism critical for the phenotype associated with these conditions.

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)
- Rhabdoid Tumor Predisposition Syndrome by Next-Gen Sequencing (RT-NG)