Overview

Useful For
Identifying solid tumors that may respond to targeted therapies by simultaneously assessing for rearrangements involving targeted regions of the *NTRK1*, *NTRK2*, and *NTRK3* genes resulting in fusion transcripts

This test is not useful for hematologic malignancies.

Genetics Test Information
This test uses next-generation sequencing to identify rearrangements (fusions) involving targeted regions of the *NTRK1*, *NTRK2*, and *NTRK3* genes.

The assay was designed to detect the most common *NTRK* gene fusions and novel gene fusion partners in the targeted gene regions. See [NTRK RNA Targeted Gene Fusions](#) table in Special Instructions for details.

Of note, this test is performed to evaluate rearrangements (fusions) within solid tumor samples. This test is not intended for use for hematological malignancies.

Additional Tests

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<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
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<td>Slide Review in MG</td>
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Testing Algorithm
When this test is ordered, slide review will always be performed at an additional charge.

Special Instructions
- [NTRK RNA Targeted Gene Fusions](#)
- [Tissue Requirements for Solid Tumor Next-Generation Sequencing](#)

Highlights
This test evaluates formalin-fixed, paraffin-embedded tumor slides from patients with advanced solid tumors for rearrangements (fusions) involving targeted regions of the *NTRK1*, *NTRK2*, and *NTRK3* genes to identify candidates for targeted therapy. Current data suggests that solid tumors with *NTRK* rearrangements may be sensitive to multikinase inhibitors.

Method Name
Polymerase Chain Reaction (PCR)-Based Next-Generation Sequencing (NGS)

NY State Available
Yes
Specimen

Specimen Type
Varies

Necessary Information
Pathology report (final or preliminary) at minimum containing the following information must accompany specimen in order for testing to be performed:

1. Patient name
2. Block number—must be on all blocks, slides and paperwork (can be handwritten on the paperwork)
3. Tissue collection date
4. Source of the tissue

Specimen Required
This assay requires at least 10% tumor nuclei.
- Preferred amount of tumor area with sufficient percent tumor nuclei: tissue 144 mm(2)
- Minimum amount of tumor area: tissue 36 mm(2).
- These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.
- Tissue fixation: 10% neutral buffered formalin, not decalcified
- For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing in Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm x 10 slides: approximate/equivalent to 36mm(2).

Preferred:
Specimen Type: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

Acceptable:
Specimen Type: Tissue slide
Slides: 1 stained and 10 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 10 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.

Note: The total amount of required tumor nuclei can be obtained by scraping up to 10 slides from the same block.

Forms
If not ordering electronically, complete, print, and send a Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume
See Specimen Required

Reject Due To

| Other | Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, |
Clinical & Interpretive

Clinical Information
Targeted cancer therapies are defined as antibody or small molecule drugs that block the growth and spread of cancer by interfering with specific cell molecules involved in tumor growth and progression. Multiple targeted therapies have been approved by the FDA for treatment of specific cancers. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and therapy-associated risks.

Fusions involving the \textit{NTRK1}, \textit{NTRK2}, or \textit{NTRK3} genes (i.e., NTRK gene fusions) form through intra- and interchromosomal rearrangements. \textit{NTRK} gene fusions lead to activation of downstream MAPK, PIK, and STAT3 signaling pathways and act as oncogenic drivers of multiple types of pediatric and adult solid tumors. In solid tumors, the presence of an \textit{NTRK} gene fusion is a biomarker for response to tropomyosin receptor kinase (TRK) inhibitor therapy.

This test assesses for fusions involving the \textit{NTRK1}, \textit{NTRK2}, and \textit{NTRK3} genes. The results of this test can be useful in guiding treatment of individuals with advanced solid tumors.

See the \textit{NTRK RNA Targeted Gene Fusions} table in Special Instructions for details regarding the targeted gene regions evaluated by this test.

Reference Values
An interpretive report will be provided.

Interpretation
An interpretive report will be provided.

Cautions
This test is not designed to differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

A negative (wild-type) result does not rule out the presence of a rearrangement (fusion) that may be present but below the limits of detection of this assay. The analytical sensitivity of this assay is a minimum coverage of 10 targeted fusion reads with 5 unique fusion molecules in a sample with 10% or greater tumor content.

Only gene rearrangements (fusions) involving targeted breakpoints in \textit{NTRK1}, \textit{NTRK2}, and \textit{NTRK3} genes will be detected. This test does not detect point mutations, insertion/deletion mutations, large single or multiexon deletions or
duplications, or genomic copy number variants in any of the genes tested.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling, and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for updated interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause PCR failure.

**Clinical Reference**

**Performance**

**Method Description**
Next-generation sequencing (NGS) is performed to test for the presence of rearrangements involving targeted breakpoints in the NTRK1, NTRK2, and NTRK3 genes. Rearrangement nomenclature is based on a custom reference sequence using genome build GRCh37 (hg19). See [NTRK RNA Targeted Gene Fusions](#) for details regarding the targeted gene regions identified by this test. (Unpublished Mayo method)

**PDF Report**
No

**Day(s) Performed**
Monday through Friday

**Report Available**
14 to 21 days

**Specimen Retention Time**
Unused portions of blocks will be returned. Unused slides are stored indefinitely.

**Performing Laboratory Location**
Rochester

**Fees & Codes**
Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81194
Slide Review
88381-Microdissection, manual

LOINC® Information

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