

Overview

Useful For

Primarily for identifying mutations that help in the diagnosis of specific soft tissue and bone tumors (sarcoma)

Secondarily for identifying mutations that have therapeutic or prognostic significance

Assessing microsatellite instability for immunotherapy decisions

Genetics Test Information

This test uses targeted next-generation sequencing to evaluate for somatic mutations within the *ALK*, *APC*, *BAP1*, *BCOR*, *BRAF*, *CDKN2A*, *CTNNB1*, *DICER1*, *EED*, *EGFR*, *FGFR4*, *GNA11*, *GNA14*, *GNAQ*, *GNAS*, *H3-3A*, *H3-3B*, *KIT*, *MDM2*, *MED12*, *MYOD1*, *NF1*, *PDGFRA*, *PDGFRB*, *PTPRD*, *ROS1*, *SMARCB1*, *SUZ12*, *TERT*-promoter, *TP53*, and *TSC2* genes. This test also assesses for microsatellite instability status and *BCOR* internal tandem duplications. See [Targeted Genes and Methodology Details for MayoComplete Sarcoma Panels](#) for details regarding the targeted gene regions evaluated by this test.

This test is performed to evaluate for somatic mutations within solid tumor samples. It **does not assess** for germline alterations within the genes listed.

Additional Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---------|--------------------|----------------------|------------------|
| SLIRV | Slide Review in MG | No | Yes |

Testing Algorithm

When this test is ordered, slide review will always be performed at an additional charge.

Special Instructions

- [Tissue Requirements for Solid Tumor Next-Generation Sequencing](#)
- [Targeted Genes and Methodology Details for MayoComplete Sarcoma Panels](#)

Highlights

This test evaluates formalin-fixed, paraffin-embedded tumor or cytology slides to assist in the diagnosis and management of patients with sarcoma.

This test detects *BCOR* internal tandem duplications of exon 15.

Microsatellite instability (MSI) status is also determined (microsatellite stable, MSI-High) as part of this test and is often clinically actionable for determining the efficacy of immunotherapy in solid tumors.

Method Name

Sequence Capture and Targeted Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Multiple oncology (cancer) gene panels are available. For more information see [Hematology, Oncology, and Hereditary Test Selection Guide](#).

Necessary Information

A pathology report (final or preliminary), at minimum containing the following information, **must accompany specimen 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 20% tumor nuclei.

- Preferred amount of tumor area with sufficient percent tumor nuclei: tissue 216 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 this document, the sizes are given as 4 mm x 4 mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3 mm x 1 mm x 10 slides: approximate/equivalent to 36 mm(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 slides

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.
Additional Information: Unused unstained slides will not be returned.

Specimen Type: Cytology slides (direct smears or ThinPrep)
Slides: 1 to 3 Slides
Collection Instructions: Submit 1 to 3 slides stained and coverslipped with a preferred total of 5000 nucleated cells, or a minimum of at least 3000 nucleated cells.
Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.
Additional Information: Cytology slides will not be returned.

Specimen Minimum Volume
See Specimen Required

Reject Due To

| | |
|---|--------|
| Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded, except for cytology slide Extracted nucleic acid (DNA/RNA) | Reject |
|---|--------|

Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---------------|---------------------|------|-------------------|
| Varies | Ambient (preferred) | | |
| | Refrigerated | | |

Clinical & Interpretive

Clinical Information

Molecular analysis of biomarkers is increasingly being utilized in oncology practices to support and guide diagnosis, prognosis, and therapeutic management of patients. For example, the identification of *MYOD1* mutations can be helpful in establishing a diagnosis of sclerosing rhabdomyosarcoma. In addition, microsatellite instability status is an important biomarker for determining effective immunotherapeutic treatment options for patients with solid tumors.

This next-generation sequencing assay interrogates targeted regions to assess for the presence of somatic mutations across 31 genes associated with soft tissue tumors: *ALK*, *APC*, *BAP1*, *BCOR*, *BRAF*, *CDKN2A*, *CTNNB1*, *DICER1*, *EED*, *EGFR*, *FGFR4*, *GNA11*, *GNA14*, *GNAQ*, *GNAS*, *H3-3A*, *H3-3B*, *KIT*, *MDM2*, *MED12*, *MYOD1*, *NF1*, *PDGFRA*, *PDGFRB*, *PTPRD*, *ROS1*, *SMARCB1*, *SUZ12*, *TERT*-promoter, *TP53*, and *TSC2* genes. This test also assesses for *BCOR* internal tandem duplications.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretation of molecular biomarker analysis includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions

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

DNA variants of uncertain significance may be identified.

A negative result does not rule out the presence of a variant that may be present but below the limits of detection of this assay. The analytical sensitivity of this assay for sequence reportable alterations is 5% mutant allele frequency with a minimum coverage of 500X in a sample with 20% or more tumor content.

Point mutations and small insertion/deletion mutations will be detected in the *ALK*, *APC*, *BAP1*, *BCOR*, *BRAF*, *CDKN2A*, *CTNNB1*, *DICER1*, *EED*, *EGFR*, *FGFR4*, *GNA11*, *GNA14*, *GNAQ*, *GNAS*, *H3-3A*, *H3-3B*, *KIT*, *MDM2*, *MED12*, *MYOD1*, *NF1*, *PDGFRA*, *PDGFRB*, *PTPRD*, *ROS1*, *SMARCB1*, *SUZ12*, *TERT*-promoter, *TP53*, and *TSC2* genes only. This test may detect single exon deletions but does not detect multiexon deletions, duplications, or genomic copy number variants.

Variant allele frequency (VAF) is the percentage of sequencing reads supporting a specific variant divided by the total sequencing reads at that position. In somatic testing, VAF should be interpreted in the context of several factors including, but not limited to, tumor purity/heterogeneity/copy number status (ploidy, gains/losses, loss of heterozygosity) and sequencing artifact/misalignment.(1,2)

Rare polymorphisms may be present that could lead to false-negative or false-positive results.

The presence or absence of a variant may not be predictive of response to therapy in all patients.

Test results should be interpreted in the context of clinical, tumor sampling, histopathological, and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for discussion. 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 cytology slides and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause polymerase chain reaction failure.

Supportive Data**Performance Characteristics:**

The limit of detection for calling a somatic variant (single nucleotide variants [SNV] and deletions-insertions [delins, formerly indels]) is 5% variant allele frequency if there is at least 500x deduplicated coverage.

Verification studies demonstrated concordance between this test and the reference method for detection of SNV and delins is 99.7% (699/701) and 96.6% (226/231), respectively. Concordance for the detection of delins was 98.9% (186/188) in variants 1 to 10 base pairs (bp) in size, 95.8% (23/24) in variants 11 to 50 bp in size, and 88.9% (8/9) in variants 51 to 200 bp in size.

Microsatellite instability (MSI) evaluation is accurate at a tumor purity of at least 10% for colorectal tumors and 20% for other tumor types. During verification studies, 98% (200/204) concordance for MSI status was observed between this test and the reference method.

Clinical Reference

1. Strom SP. Current practices and guidelines for clinical next-generation sequencing oncology testing. *Cancer Biol Med*. 2016;13(1):3-11. doi:10.28092/j.issn.2095-3941.2016.0004
2. Spurr L, Li M, Alomran N, et al. Systematic pan-cancer analysis of somatic allele frequency. *Sci Rep*. 2018;8(1):7735. Published 2018 May 16. doi:10.1038/s41598-018-25462-0
3. Apellaniz-Ruiz M, McCluggage WG, Foulkes WD. DICER1-associated embryonal rhabdomyosarcoma and adenosarcoma of the gynecologic tract: Pathology, molecular genetics, and indications for molecular testing. *Genes Chromosomes Cancer*. 2021;60(3):217-233
4. Agaram NP, LaQuaglia MP, Alaggio R, et al. MYOD1-mutant spindle cell and sclerosing rhabdomyosarcoma: an aggressive subtype irrespective of age. A reappraisal for molecular classification and risk stratification. *Mod Pathol*. 2019 Jan;32(1):27-36. doi:10.1038/s41379-018-0120-9
5. WHO Classification of Tumours Editorial Board: Soft tissue and bone tumours. 5th ed. World Health Organization; 2022. WHO Classification of Tumours. Vol 3.
6. Gao P, Seebacher NA, Hornicek F, et al. Advances in sarcoma gene mutations and therapeutic targets. *Cancer Treat Rev*. 2018;62:98-109
7. Marino-Enriquez A, Lauria A, Przybyl J, et al. BCOR Internal tandem duplication in high-grade uterine sarcomas. *Am J Surg Pathol*. 2018;42(3):335-341. doi: 10.1097/PAS.0000000000000993
8. Marcus L, Lemery SJ, Keegan P, Pazdur R. FDA approval summary: Pembrolizumab for the treatment of microsatellite instability-high solid tumors. *Clin Cancer Res*. 2019;25(13):3753-3758. doi:10.1158/1078-0432.CCR-18-4070

Performance**Method Description**

Next-generation sequencing is performed to determine microsatellite instability status and evaluate the presence of a mutation in targeted regions of the *ALK*, *APC*, *BAP1*, *BCOR*, *BRAF*, *CDKN2A*, *CTNNB1*, *DICER1*, *EED*, *EGFR*, *FGFR4*, *GNA11*, *GNA14*, *GNAQ*, *GNAS*, *H3-3A*, *H3-3B*, *KIT*, *MDM2*, *MED12*, *MYOD1*, *NF1*, *PDGFRA*, *PDGFRB*, *PTPRD*, *ROS1*, *SMARCB1*, *SUZ12*, *TERT*-promoter, *TP53*, and *TSC2* genes. See [Targeted Genes and Methodology Details for MayoComplete Sarcoma Panels](#) for details regarding the targeted gene regions evaluated by this test. (Unpublished Mayo method)

A pathology review and macro dissection to enrich for tumor cells are performed prior to slide scraping.

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

12 to 20 days

Specimen Retention Time

FFPE tissue block: Unused portions of blocks will be returned within 10-14 days after testing is complete; FFPE tissue/cytology slides: Unused slides are stored indefinitely; Digital images are obtained and stored for all slides used in testing

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81457

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|-------------------------------------|--------------------|
| MCSMP | MayoComplete Sarcoma Mutation Panel | 73977-1 |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|------------------|---------------------|
| 617857 | Result | 82939-0 |
| 617858 | Interpretation | 69047-9 |

Test Definition: MCSMP

MayoComplete Sarcoma Mutation Panel,
Next-Generation Sequencing, Tumor

| | | |
|--------|------------------------|---------|
| 617859 | Additional Information | 48767-8 |
| 617860 | Specimen | 31208-2 |
| 617861 | Tissue ID | 80398-1 |
| 617862 | Method | 85069-3 |
| 617863 | Disclaimer | 62364-5 |
| 617864 | Released By | 18771-6 |