

## 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

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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<sup>2</sup>)

-Minimum amount of tumor area: tissue 36 mm<sup>2</sup>)

-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<sup>2</sup>) and the minimum as 3 mm x 1 mm x 10 slides: approximate/equivalent to 36 mm<sup>2</sup>).

**Preferred:** Submit 3, if available, or 2 of the following specimens.

**Acceptable:** Submit **at least one** of the following specimens.

**Specimen Type:** Tissue block

**Collection Instructions:** Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

**Specimen Type:** Tissue slide

**Slides:** 1 Hematoxylin and eosin-stained and 10 unstained

**Collection Instructions:**

Submit the followings slides:

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:** Hematoxylin and eosin-stained and unstained slides will not be returned.

**Specimen Type:** Cytology slide (direct smears or ThinPrep)

**Slides:** 1 to 3 Slides

**Collection Instructions:** Submit 1 to 3 slides stained and coverslipped with a total of 5000 nucleated cells (preferred) or at least 3000 nucleated cells (minimum).

**Note:** Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.

**Additional Information:** Cytology slides will not be returned. An image of the slides will be stored per regulatory requirements.

## Specimen Minimum Volume

See Specimen Required

## Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

## 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

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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 deletion-insertion mutations (delins) 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 multi-exon deletions, duplications, larger-scale genomic copy number variants, copy neutral loss of heterozygosity, or epigenetic modifications such as promoter methylation. Delins of 1000 bp or less are detectable with at least 50 or more supporting reads.

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 alterations (ie, 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]) 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%

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(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;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**

Tissue blocks: Unused portions of blocks will be returned; Tissue slides: Hematoxylin and eosin-stained and unstained slides will not be returned. Unused slides are stored for at least 5 years; Extracted DNA: 3 months

**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
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