MAYO CLINIC LABORATORIES

Test Definition: MCCRC

MayoComplete Colorectal Cancer Panel, Next-Generation Sequencing, Tumor

Overview

Useful For

Primarily for determining will respond to various targeted therapies/immunotherapy

Predicting prognosis from microsatellite instability status

Genetics Test Information

This test uses targeted next-generation sequencing to determine microsatellite instability status and to evaluate for somatic mutations within the *APC, BRAF, HRAS, KRAS, MLH1, MSH2, MSH6, NRAS,* and *PMS2* genes. See Targeted Genes and Methodology Details for MayoComplete Colorectal Cancer Panel 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, (Bill Only)	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 Colorectal Cancer Panel

Highlights

This test evaluates formalin-fixed, paraffin-embedded tumor or cytology slides from patients with colorectal cancer for gene mutations to identify candidates for targeted therapy.

Microsatellite instability (MSI) status is 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 Oncology Somatic NGS Testing 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 216mm(2)
-Minimum amount of tumor area: tissue 36mm(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 Requirements for Solid Tumor Next-Generation Sequencing. 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 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 cover slipped 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.

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

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 slides Extracted nucleic acid (DNA/RNA)	Reject

Specimen Stability Information

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

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 US Food and Drug Administration 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. Microsatellite instability status is an important biomarker for determining effective immunotherapeutic treatment options for patients with solid tumors.

Next-generation sequencing is an accurate, cost-effective method to identify mutations across numerous genes known

to be associated with response or resistance to specific targeted therapies.

This test is a single assay that uses formalin-fixed paraffin-embedded tissue to assess for common mutations in the following genes known to be associated with colorectal cancer: *APC, BRAF, HRAS, KRAS, MLH1, MSH2, MSH6, NRAS,* and *PMS2.* The results of this test can be useful for assessing prognosis and guiding treatment of individuals with colorectal cancer.

See Targeted Genes and Methodology Details for MayoComplete Colorectal Cancer Panel for details regarding the targeted gene regions evaluated by this test.

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 *APC, BRAF, HRAS, KRAS, MLH1, MSH2, MSH6, NRAS,* and *PMS2* genes. This test may detect single exon deletions but does not detect multi-exon deletions, duplications, or genomic copy number variants in any of the genes tested.

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 and/or incomplete.

This test cannot reliably determine if a variant identified in *PMS2* exons 11-15 originated from *PMS2* or the highly homologous pseudogene *PMS2CL*. In the instance that a reportable variant is detected in *PMS2* exons 11-15, additional testing will be recommended in the patient report.

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% (226/234), respectively. Concordance for the detection of delins was 98.9% (186/188) in variants 1-10 base pairs (bp) in size, 95.8% (23/24) in variants 11-50 bp in size, and 88.9% (8/9) in variants 51-200 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 assessment was observed between this test and the reference method.

Clinical Reference

1. U.S. Food and Drug Administration (FDA): Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA; Updated March 29, 2022, Accessed August 3, 2022. Available at www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling2. 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 Jul 1;25(13):3753-3758. doi: 10.1158/1078-0432.CCR-18-4070
3. Vogelstein B, Papadopoulos N, Velculescu VE, et al: Cancer genome landscapes. Science. 2013 Mar 29;339:1546-1558
4. Di Nicolantonio F, Martini M, Molinari F, et al: Wild-type BRAF is required for response to Panitumumab or Cetuximab in metastatic colorectal cancer. J Clin Oncol. 2008 Dec 10;26(35):5705-5712
5. Lievre A, Bachet JB, Le Corre D, et al: KRAS mutation status is predictive of response to Cetuximab therapy in colorectal cancer. Cancer Res. 2006 Apr 15;66(8):3992-3995
6. Jones JC, Renfro LA, Kipp BR, et al: Non-V600BRAF mutations define a clinically distinct molecular subtype of metastatic colorectal cancer. J Clin Oncol. 2017 Aug 10;35(23):2624-2630

Performance

Method Description

Next-generation sequencing is performed to determine microsatellite instability status and evaluate the presence of a mutation in all coding regions of the *APC, BRAF, HRAS, KRAS, MLH1, MSH2, MSH6, NRAS,* and *PMS2* genes. See Targeted Genes and Methodology Details for MayoComplete Colorectal Cancer Panel 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 tissue slides are stored indefinitely; Digital images are obtained and stored for all slides used in testing

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 Regional Manager. 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
88381 - Microdissection, manual
81445

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MCCRC	MayoComplete CRC Panel	73977-1

Result ID	Test Result Name	Result LOINC® Value
617865	Result	82939-0
617866	Result Summary	69047-9
617867	Additional Info	48767-8
617868	Specimen	31208-2
617869	Tissue ID	80398-1
617870	Method	85069-3
617871	Disclaimer	62364-5

617872	Released By	18771-6