MAYO CLINIC LABORATORIES

# Test Definition: MCCRC

MayoComplete Colorectal Cancer Panel, Next-Generation Sequencing, Tumor

## Overview

### Useful For

Primarily for determining patient response to various targeted therapies or 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 somatic mutations within the *APC, BRAF, HRAS, KRAS, MLH1, MSH2, MSH6, NRAS, PIK3CA*, *PIK3R1*, *PMS2*, *POLE* and *PTEN* 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 test** 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 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 Requirements 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:** 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 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. An image of the slides will be stored per regulatory requirements.

### 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
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
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, PIK3CA*, *PIK3R1*, *PMS2*, *POLE* and *PTEN.* The results of this test can be useful for assessing prognosis and guiding treatment of individuals with colorectal cancer.

### 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 mutations 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 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 *APC, BRAF, HRAS, KRAS, MLH1, MSH2, MSH6, NRAS, PIK3CA*, *PIK3R1*, *PMS2*, *POLE* and *PTEN* genes. 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 base pairs or less are detectable with at least 50 or more supporting reads.

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

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 genetic 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% (226/234), 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 assessment 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. U.S. Food and Drug Administration (FDA). Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA; Updated September 23, 2024, Accessed November 24, 2025. Available at www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
4. 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
5. Vogelstein B, Papadopoulos N, Velculescu VE, et al. Cancer genome landscapes. Science. 2013;339:1546-1558
6. 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;26(35):5705-5712
7. 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;66(8):3992-3995
8. 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;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, PIK3CA*, *PIK3R1*, *PMS2*, *POLE* and *PTEN* 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 macrodissection to enrich 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
88381 - Microdissection, manual
81457

### 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 | Interpretation | 69047-9 |
| 617867 | Additional Information | 48767-8 |
| 617868 | Specimen | 31208-2 |
| 617869 | Tissue ID | 80398-1 |
| 617870 | Method | 85069-3 |
| 617871 | Disclaimer | 62364-5 |
| 617872 | Released By | 18771-6 |