

## Overview

### Useful For

Assisting in tumor profiling for diagnosis, predicting prognosis, and identifying targeted therapies for the treatment and management of patients with solid tumors

Identifying somatic alterations including single nucleotide variants, small deletions/insertions, gene amplifications, homozygous gene deletions, fusions, and splice variants in genes known to be associated with the tumorigenesis of solid tumors

Assessment of microsatellite instability and tumor mutational burden status

### Genetics Test Information

This test uses targeted next-generation sequencing to estimate tumor mutational burden and detect microsatellite instability, sequence variants, gene amplifications, homozygous gene deletions, fusions, and specific transcript variants in solid tumors. This panel includes a DNA subpanel for the detection of sequence alterations in 515 genes, amplification of 96 genes, homozygous deletion of 133 genes, as well as an RNA subpanel for the detection of fusions involving 55 genes and specific splice variants involving *EGFR*, *AR*, and *MET*. Sequence variants and copy number changes are concomitantly interpreted to evaluate for complete inactivation of 31 tumor suppressor genes. See [Genes Interrogated by MayoComplete Solid Tumor Panel](#) for details regarding genes interrogated by this test.

**Note:** This test is performed to evaluate for somatic (ie, tumor-specific) alterations within the genes listed. Although germline (ie, inherited) alterations may be detected, this test cannot distinguish between germline and somatic alterations with absolute certainty. Follow-up germline testing using whole blood can be performed for confirmation of suspected clinically relevant germline alterations. Germline testing should be performed along with genetic counselling.

### 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 to ensure specimen adequacy.

### Special Instructions

- [Genes Interrogated by MayoComplete Solid Tumor Panel](#)
- [MayoComplete Solid Tumor Panel DNA Panel Excluded DNA Regions](#)

### Highlights

### 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**

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
5. Pathologic diagnosis (final or preliminary)

**Specimen Required**

**This assay requires at least 20% tumor nuclei. However, 40% tumor is preferred.**

-Preferred amount of tumor area: 720 mm<sup>2</sup> tissue on up to 20 unstained slides

-Minimum amount of tumor area: 192 mm<sup>2</sup> tissue on up to 20 unstained slides

-Tissue fixation: 10% neutral buffered formalin, not decalcified

-For this test, at least 6 mm x 6 mm areas on 20 unstained slides is preferred: this is approximately equivalent to 720 mm<sup>2</sup>. The minimum acceptable area is 3.1 mm x 3.1 mm on 20 unstained slides: approximately equivalent to 192 mm<sup>2</sup>.

**Preferred:**

**Specimen Type:** Tissue block

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

**Acceptable:**

**Specimen Type:** Tissue slide

**Slides:** 1 stained and 20 unstained

**Collection Instructions:** Submit 1 hematoxylin and eosin (H and E) stained slide and 20 unstained, nonbaked 5-micron thick sections

## Test Definition: MCSTP

MayoComplete Solid Tumor Panel,  
Next-Generation Sequencing, Tumor

**Note:** The total amount of required tumor can be obtained by scraping up to 20 slides from the same block.

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

**Slides:** 2 to 6 slides

**Collection Instructions:** Submit 2 to 6 stained and coverslipped slides with a preferred total of 10,000 nucleated cells or a minimum of at least 6000 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 a [Oncology Test Request](#) (T729) with the specimen.

### Specimen Minimum Volume

See Specimen Required

### Reject Due To

|  |        |
|--|--------|
| Specimens that have been decalcified (all methods)             | Reject |
| Specimens that have not been formalin-fixed, paraffin-embedded |        |
| Bone marrow in EDTA  |        |

### 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 the treatment of solid tumor malignancies. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and

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therapy-associated risks. Tumor mutational burden and microsatellite instability status are increasingly important biomarkers for determining effective immunotherapeutic treatment options for patients with solid tumors.(1,2)

In addition to providing therapeutic insight, molecular profiling of tumors often provides prognostic and diagnostic information. Next-generation sequencing is an accurate, cost-effective method to identify variants 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 or cytology specimens to assess for Tier I and Tier II variants in 515 genes known to be associated with solid tumors.(3)

**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**

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. Treatment of tissues, such as decalcification, may cause polymerase chain reaction failure.

To ensure accuracy, this test will be performed on cases that are estimated by a pathologist to have 20% or more tumor cells, however, for optimal performance of this assay, a tumor purity of 40% is recommended.

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

This test does not detect large structural variants, large copy number changes, or deletions-insertions greater than approximately 20 base pairs in size.

Rare variants (ie, polymorphisms) may be present that could lead to false negative or false positive results.

A negative (ie, wildtype) result does not rule out the presence of an alteration that may be present but below the limits of detection of this assay.

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

A list of genomic regions in the DNA panel that have insufficient coverage to reliably detect single nucleotide variants and small deletions/insertions are listed in [MayoComplete Solid Tumor Panel DNA Panel Excluded DNA Regions](#).

**Supportive Data**

## Performance Characteristics

Verification studies demonstrated concordance between this test and the reference method for detection of single nucleotide variants (SNV) and deletions-insertions (delins) in 98.8% (503/509) and 98.6% (294/298) of variants, respectively. Detection accuracy of delins was 99.3% (277/279) in variants 1 to 10 base pairs (bp) in size, 93.3% (14/15) in variants 11 to 20 bp in size, and 75.0% (3/4) in variants greater than 20 bp in size.

The limit of detection for calling a somatic variant (SNV and small delins) is 2% variant allele frequency (VAF) for regions having at least 150X median exon coverage depth. Gene amplification and homozygous gene deletion detection are most accurate at 40% or more tumor purity. For gene amplifications, the overall sensitivity was 100% (79/79), specificity was 100% (11,249/11,249), and accuracy was 100% (11,328/11,328). For homozygous gene deletion the overall sensitivity was 95.1% (116/122), specificity was 99.99% (15,570/15,572), and accuracy was 99.9% (15,686/15,696). For bi-allelic inactivation, the overall sensitivity was 100% (140/140), specificity was 100% (3,518/3,518), and accuracy was 100% (3,658/3,658).

Of the 130 microsatellite sites available for evaluation in this assay, at least 20% of sites are required to be unstable to classify the case as MSI-High. Microsatellite instability (MSI) evaluation is most accurate at a tumor purity of 40% or more, although, highly unstable tumors may be detectable at 20% tumor. During verification studies, 100% concordance was observed between this test and orthogonal methods used to detect MSI status.

Tumor mutational burden (TMB) was measured as mutations per megabase (Mb) for regions with greater than 50X coverage. When TMB scores were classified as TMB-Low (<10 mut/Mb) or TMB-High (> or =10 mut/Mb), 83.3% (50/60) concordance was achieved between this test and orthogonal assays detecting TMB status. TMB values are most accurate at greater than or equal to 40% tumor purity.

Fusions are detected with the presence of 3 or more supporting reads passing pipeline filters and splice variants with 10 or more supporting reads. For fusions and splice variants, the overall sensitivity was 98.0% (151/154), specificity was 94.8% (91/96), and accuracy was 96.8% (242/250). Fusion and splice variant detection are most accurate at greater than or equal to 20% tumor purity.

Table 1. Analytical Sensitivity

| Variant type              | Threshold for positivity                     | Recommended tumor purity |
|---------------------------|--|--------------------------|
| SNV                       | > or =2% VAF with >150X median exon coverage | > or =20%                |
| DELIN                     | > or =2% VAF, < or =20 bp                    | > or =20%                |
| Gene amplification*       | N/A  | > or =40%                |
| Homozygous gene deletion* | N/A  | > or =40%                |
| MSI status                | > or =20% sites unstable= MSI-H              | > or =40%                |
| TMB status                | > or =10 variants per megabase= TMB-High     | > or =40%                |

|                |                           |           |
|----------------|---------------------------|-----------|
| Fusion         | > or =3 supporting reads  | > or =20% |
| Splice variant | > or =10 supporting reads | > or =20% |

\*Gene amplifications and homozygous deletions will be called by the bioinformatic pipeline and subjected to expert manual review to optimize sensitivity and specificity.

### Clinical Reference

1. Subbiah V, Solit DB, Chan TA, Kurzrock R. The FDA approval of pembrolizumab for adult and pediatric patients with tumor mutational burden (TMB) > or =10: a decision centered on empowering patients and their physicians. *Ann Oncol.* 2020;31(9):1115-1118. doi:10.1016/j.annonc.2020.07.002
2. 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
3. Li MM, Datto M, Duncavage EJ, et al. Standards and guidelines for the interpretation and reporting of sequence variants in cancer: A joint consensus recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. *J Mol Diag.* 2017;19(1):4-23. doi:10.1016/j.jmoldx.2016.10.002
4. Mikhail FM, Biegel JA, Cooley LD, et al. Technical laboratory standards for interpretation and reporting of acquired copy-number abnormalities and copy-neutral loss of heterozygosity in neoplastic disorders: a joint consensus recommendation from the American College of Medical Genetics and Genomics (ACMG) and the Cancer Genomics Consortium (CGC). *Genet Med.* 2019;21(9):1903-1916. doi:10.1038/s41436-019-0545-7

## Performance

### Method Description

Next-generation sequencing is performed to estimate tumor mutational burden and microsatellite instability status, somatic sequence variants, gene amplifications, homozygous gene deletions, gene fusions, and specific transcript variants in solid tumors. This test detects single nucleotide variants and small insertions and deletion within 515 genes, amplification of 96 genes, homozygous deletions in 133 genes, fusions involving 55 genes, and splice variants involving *EGFR*, *AR*, and *MET*. (Instruction manual: TruSight Oncology 500 High-Throughput. Illumina; 11/2020)

See [Genes Interrogated by MayoComplete Solid Tumor Panel](#) for details regarding genes interrogated by this test.

### PDF Report

Supplemental

### Day(s) Performed

Varies

### Report Available

14 to 21 days

### Specimen Retention Time

FPPE tissue: Unused portions of FPPE blocks will be returned. Unused, unstained slides: 5 years; Stained slides:

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

### CPT Code Information

81459

88381-Microdissection, manual

### LOINC® Information

| Test ID | Test Order Name                | Order LOINC® Value |
|---------|--------------------------------|--------------------|
| MCSTP   | MayoComplete Solid Tumor Panel | 73977-1            |

| Result ID | Test Result Name                   | Result LOINC® Value |
|-----------|------------------------------------|---------------------|
| 610425    | Result                             | 82939-0             |
| 610426    | Interpretation                     | 69047-9             |
| 610427    | Additional Information             | 48767-8             |
| 610428    | Clinical Trials                    | 82786-5             |
| 610429    | Variants of Uncertain Significance | 93367-1             |
| 610430    | Specimen                           | 31208-2             |
| 610431    | Tissue ID                          | 80398-1             |
| 610432    | Method                             | 85069-3             |
| 610433    | Disclaimer                         | 62364-5             |
| 610434    | Released By                        | 18771-6             |