# Test Definition: MCLBP

MayoComplete Liquid Biopsy Panel,
Next-Generation Sequencing, Cell-Free DNA

## Overview

### Useful For

As an alternative to invasive tissue biopsies to assist in tumor profiling for diagnosis, predicting prognosis, and identifying targeted therapies for the treatment and management of patients with solid tumors

As an alternative to invasive tissue biopsies for assessment of microsatellite instability status

### Genetics Test Information

This test uses targeted next-generation sequencing to determine microsatellite instability status and identify sequence variants, gene amplifications, and fusions translocation using circulating free DNA (cfDNA) in plasma. This test detects sequence variants in 33 genes, amplifications in 8 genes, and translocations in 5 genes.

Genes tested for single-nucleotide variants and deletions-insertions: *AKT1, ALK, APC, ARID1A, ATM, BRAF, BRCA1, BRCA2, BRIP1, CCND1, CD274, CDH1, CSF1R, EGFR, ERBB2, EZH2, FGFR1, FGFR2, HRAS, KIT, KRAS, MET, MYC, NRAS, NTRK1, PDGFRA, PIK3CA, POLD1, POLE, RAF1, RET, ROS1*,and *TP53*.
Genes tested for amplifications: *CCND1, CD274, EGFR, ERBB2, FGFR2, KIT, MET*, and *MYC*
Genes tested for translocations: *ALK, FGFR2, NTRK1, RET*, and *ROS1*

See Targeted Genes Interrogated by MayoComplete Liquid Biopsy 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 counseling.

### Special Instructions

- Targeted Genes Interrogated by MayoComplete Liquid Biopsy Panel

### Highlights

In addition to single nucleotide variants and small insertions/deletions sequence variants, this test also identifies gene amplifications and fusions. Microsatellite instability status is also determined as a 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

No

## Specimen

### Specimen Type
Whole blood

### Ordering Guidance
This test is **not** a prenatal screening test. For prenatal screening, consider QUAD1 / Quad Screen (Second Trimester) Maternal, Serum.

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

### Shipping Instructions
1. Specimens should be transported at ambient or refrigerated (4 degrees C) temperature.
2. Specimens are viable for 7 days when collected using the Streck Black/Tan Top Tube Kit.

### Necessary Information
**Paperwork (pathology report, oncology request form, or similar document) that indicates the cancer diagnosis must be provided.** Testing may proceed without this information; however, it aids in providing a more thorough and accurate interpretation of results. Ordering providers are strongly encouraged to provide the information and send with the specimen.

### Specimen Required
**Supplies:** Streck Black/Tan Top Tube Kit (T715)
**Container/Tube:** Streck Cell-Free DNA (cfDNA) blood collection kit
**Specimen Volume:** Two 10-mL Streck Cell-Free DNA blood collection tubes
**Additional Information:** Only blood collected in Streck Cell-Free DNA BCT tubes will be accepted for analysis. Whole blood will be processed to produce platelet-poor plasma before cfDNA isolation.

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

### Specimen Minimum Volume
One 10-mL Streck tube

### Reject Due To

| | |
|---|---|
| Whole blood collected in tubes other than Streck Cell-Free DNA tubes | Reject |

## Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole blood | Ambient (preferred) | 7 days | Streck Black/Tan top |
| | Refrigerated | 7 days | Streck Black/Tan top |

## 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 solid tumor malignancies. 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 increasingly important biomarker for determining effective immunotherapeutic treatment options for patients with solid tumors.

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 intended for the use of cell-free DNA to access genetic mutations of somatic tumors without a tissue biopsy.

### 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 by calling 800-533-1710. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Patients with a negative test result may still harbor a genomic alteration. Testing of a tissue specimen for mutations should be considered for patients who have a negative result with this test.

This test can be used to report gene amplifications but does not detect deletions.

This assay's limit of detection for detected mutations is influenced by the amount of cell-free DNA in the blood. This is a biological variable that cannot be controlled.

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 differentiate between tumor somatic alterations and CHIP (clonal hematopoiesis of indeterminate potential) mutations. Additional testing may be necessary to clarify the origin of mutations detected.

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

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

**Disclaimer**: The MayoComplete Liquid Biopsy Panel (MCLBP) assay uses next-generation sequencing (NGS) to identify somatic mutations (ie, single nucleotide variants [SNV], deletions-inserts [delins]), gene amplifications, gene fusions, and assess microsatellite instability (MSI) status in patients with solid tumors. The MCLBP assay's performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. However, gene fusions and MSI status have not been fully validated with clinical samples due to the rarity of such positive samples. Any fusion or MSI-H status detected by MCLBP will be orthogonally confirmed until enough clinical samples are obtained. Confirmational testing will be performed using the TruSight Oncology 500 (TSO 500) ctDNA assay, which includes 523 genes and detects somatic mutations (ie, SNV/delins), gene amplifications, gene fusions, and assess MSI status as well as tumor mutation burden.

## Supportive Data

Performance Characteristics:
Limit of detection (LOD) for single nucleotide variants (SNV) is 0.5% for hotspot mutations, 1% for other SNV; 2.5% for deletion-insertions (delins), and 2 supporting reads for fusions. LOD for amplification is between 1.2- and 1.6-fold changes (2.4-3.2 copies) depending on specific genes and presence of sufficient single nucleotide polymorphisms (SNP) for allelic imbalance assessment. LOD for microsatellite instability (MSI) is 2% tumor DNA. MSI status is classified as MSI-High (MSI-H) detected (> or =2 sites unstable), and MSI-H not detected (<2 sites unstable).
Concordance for the detection of SNV and delins was 99%, gene amplifications 95%, fusions 100%, and MSI-H status 88% (with non-endometrial cases at 100%).

## Clinical Reference

1. Schwaederle M, Husain H, Fanta PT, et al. Use of liquid biopsies in clinical oncology: Pilot experience in 168 patients. Clin Cancer Res. 2016;22(22):5497-5505
2. Kilgour E, Rothwell DG, Brady G, Dive C. Liquid biopsy-based biomarkers of treatment response and resistance. Cancer Cell. 2020;37(4):485-495
3. Leighl NB, Page RD, Raymond VM, et al. Clinical utility of comprehensive cell-free DNA analysis to identify genomic biomarkers in patients with newly diagnosed metastatic non-small cell lung cancer. Clin Cancer Res. 2019;25(15):4691-4700
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
5. Wan JCM, Massie C, Garcia-Corbacho J, et al. Liquid biopsies come of age: towards implementation of circulating tumour DNA. Nat Rev Cancer. 2017;17(4):223-238
6. Aggarwal C, Thompson JC, Black TA, et al. Clinical implications of plasma-based genotyping with the delivery of personalized therapy in metastatic non-small cell lung cancer. JAMA Oncol. 2019;5(2):173-180

## Performance

### Method Description
Blood samples are collected in Streck Cell-Free DNA blood collection tubes, and cell-free DNA (cfDNA) is isolated from double-spun plasma. Next-generation sequencing is performed on the cfDNA using the PGDx Elio Plasma Resolve chemistry.(Package insert: PGDx Elio Plasma Resolve. Person Genome Diagnostics Inc; 2020)

See Targeted Genes Interrogated by MayoComplete Liquid Biopsy Panel for details regarding genes interrogated by this test.

### PDF Report
No

### Day(s) Performed
Monday through Friday

### Report Available
7 to 10 days

### Specimen Retention Time
Whole blood: 2 weeks (if available); 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
81463

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|

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|---|---|---|
| MCLBP | MayoComplete Liquid Biopsy Panel | 73977-1 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 614940 | Result Summary | 50397-9 |
| 614465 | Result | 82939-0 |
| 614466 | Interpretation | 69047-9 |
| 614467 | Additional Information | 48767-8 |
| 614468 | Specimen | 31208-2 |
| 614469 | Source | 31208-2 |
| 614470 | Method | 85069-3 |
| 614471 | Disclaimer | 62364-5 |
| 614472 | Released By | 18771-6 |
| MG143 | Reason for Referral - Cancer Type | 42349-1 |