MAYO CLINIC LABORATORIES

Test Definition: MCLNM

MayoComplete Lung Cancer Mutations, Next-Generation Sequencing, Tumor

Overview

Useful For

Diagnosis and management of patients with lung cancer

Assessing microsatellite instability

Genetics Test Information

This test uses targeted next-generation sequencing to determine microsatellite instability status and to evaluate for somatic mutations within the *ALK, BRAF, EGFR, ERBB2, HRAS, KRAS, MDM2, MET, NRAS, RET, ROS1,* and *STK11* genes. See Targeted Genes and Methodology Details for MayoComplete Lung Cancer Mutations 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.
This test identifies activating exon 14 skipping mutations in *MET*

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 Lung Cancer Mutations

Highlights

This test evaluates formalin-fixed, paraffin-embedded tumor or cytology slides from patients with lung 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 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(2) and the minimum as 3 mm x 1 mm x 10 slides: approximate/equivalent to 36 mm(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 wit 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 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.

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

Next-generation sequencing has recently emerged as 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 lung cancer: *ALK, BRAF, EGFR, ERBB2, HRAS, KRAS, MDM2, MET, NRAS, RET, ROS1,* and *STK11*. The results of this test can be useful for assessing prognosis and guiding treatment of individuals with lung cancer.

Current data suggests that:
-The efficacy of EGFR-targeted therapies in patients with non-small cell lung cancer is limited to tumors with mutations in the *EGFR* gene
-Metastatic non-small cell lung cancer with *BRAF V600E* mutations may be sensitive to targeted therapy
-Metastatic non-small cell lung cancer with *KRAS G12C* mutations may be sensitive to targeted therapy
-Advanced or metastatic non-small cell lung cancer with *MET* exon 14 skipping mutations may be sensitive to MET inhibitors

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 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 will be detected in the *ALK, BRAF, EGFR, ERBB2, HRAS, KRAS, MDM2, MET, NRAS, RET, ROS1,* and *STK11* genes only. This test may detect single exon deletions but does not detect multiexon deletions, duplications, or genomic copy number variants.

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 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, formerly indels]) is 5% variant allele frequency and having 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) of variants, respectively. Concordance for the detection of delins was 98.9% (186/188) in variants 1 to10 base pair (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

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12. Clay R, Kipp BR, Jenkins S, et al. Computer-aided nodule assessment and risk yield (CANARY) may facilitate non-invasive prediction of EGFR mutation status in lung adenocarcinomas. Sci Rep. 2017;7(1):17620. doi:10.1038/s41598-017-17659-6

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 *ALK, BRAF, EGFR, ERBB2, HRAS, KRAS, MDM2, MET* (including exon 14 skipping), *NRAS, RET, ROS1*, and *STK11* genes. See Targeted Genes and Methodology Details for MayoComplete Lung Cancer Mutations 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 is 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

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
MCLNM	MayoComplete Lung Cancer Mutations	102042-9

Result ID	Test Result Name	Result LOINC® Value
617841	Result	82939-0
617842	Interpretation	69047-9
617843	Additional Information	48767-8
617844	Specimen	31208-2
617845	Tissue ID	80398-1
617846	Method	85069-3
617847	Disclaimer	62364-5
617848	Released By	18771-6