Test Definition: MCLNG

MayoComplete Lung Cancer-Targeted Gene Panel with Rearrangement, Tumor

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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, and activating exon 14 skipping mutations in *MET*.

This test also uses multiplex reverse transcription polymerase chain reaction to detect gene fusions by identifying specific rearrangements (fusions) within the *ALK, ROS1* and *RET* genes and expression imbalance for *ALK, ROS1, RET, NTRK1, NTRK2,* and *NTRK3* genes. See Targeted Genes and Methodology Details for MayoComplete Lung 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 Lung Cancer Panel
- Targeted Genes Fusions Interrogated by MayoComplete Lung Cancer Panel

Highlights

This test evaluates formalin-fixed paraffin-embedded tumor or cytology slides from patients with lung cancer for gene mutations and fusions 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)/Polymerase Chain Reaction (PCR)

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 360 mm(2)
-Minimum amount of tumor area: tissue 72 mm(2)
-These amounts are cumulative over up to 15 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 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 15 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 15 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 15 slides from the same block.

Additional Information: Unused unstained slides will not be returned.

Specimen Type: Cytology slides (direct smears or ThinPrep)
Slides: 2 to 4 Slides
Collection Instructions: Submit 2 to 4 slides stained and coverslipped with a preferred total of 10,000 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 (FDA) 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.

This test uses formalin-fixed paraffin-embedded tissue or cytology slides to assess for somatic mutations within the *ALK, BRAF, EGFR, ERBB2, HRAS, KRAS, MDM2, MET, NRAS, RET, ROS1,* and *STK11* genes; identifies gene fusions involving *ALK, ROS1, RET, NTRK1, NTRK2,* and *NTRK3* genes by specific rearrangements (fusions) within the *ALK, ROS1*, and *RET* genes; and expression imbalance for the *ALK, ROS1, RET, NTRK1, NTRK2,* and *NTRK3* genes, as well as *MET* exon 14 skipping alterations. The results of this test can be useful for assessing prognosis and guiding treatment of individuals with lung tumors. These data can also be used to help determine clinical trial eligibility for patients with alterations in genes not amenable to current FDA-approved targeted therapies.

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
-Lung carcinomas with *ALK* rearrangements may be sensitive to ALK inhibitors
-Lung carcinomas with *ROS1* rearrangements may be sensitive to ROS1 inhibitors
-Lung carcinomas with *RET* rearrangements may be sensitive to RET inhibitors
-Solid tumors with *NTRK* rearrangements may be sensitive to multikinase 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 or fusion 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 insertion/deletion mutations will be detected in the *ALK*, *BRAF*, *EGFR*, *ERBB2*, *HRAS*, *KRAS*, *MDM1*, *MET*, *NRAS*, *RET*, *ROS1*, and *STK11* genes only. This test may detect single exon deletions but does not detect multi-exon deletions, duplications, or genomic copy number variants. This test does not detect point mutations, insertion/deletion mutations, large single or multi-exon deletions or duplications, or genomic copy number variants for the *NTRK1*, *NTRK2*, and *NTRK3* genes.

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)

Gene fusions (rearrangements) and expression imbalance will be detected when involving the *ALK*, *ROS1*, *RET*, *NTRK1*, *NTRK2*, and *NTRK3* genes only.

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 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 status was observed between this test and the reference method.

Clinical Reference

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Performance

Method Description

Next-generation sequencing is performed to determine microsatellite instability (MSI) status and evaluate the presence of a mutation in all coding regions of the *ALK, BRAF, EGFR, ERBB2, HRAS, KRAS, MDM2, MET, NRAS, RET, ROS1* and *STK11* genes.

Qualitative detection using the Idylla GeneFusion Assay is performed to detect rearrangements (fusions) within the *ALK, ROS1* and *RET* genes, *MET* exon 14 skipping, and expression imbalance for *ALK, ROS1, RET, NTRK1, NTRK2* and *NTRK3* genes.

See Targeted Genes and Methodology Details for MayoComplete Lung 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 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
MCLNG	MayoComplete Lung Cancer Panel	101378-8

Result ID	Test Result Name	Result LOINC® Value
617833	Result	82939-0
617834	Interpretation	69047-9
617835	Additional Information	48767-8
617836	Specimen	31208-2
617837	Tissue ID	80398-1
617838	Method	85069-3
617839	Disclaimer	62364-5
617840	Released By	18771-6