MAYO CLINIC LABORATORIES

Test Definition: LUNGP

Lung Cancer Panel, Tumor

Overview

Useful For

Identifying lung tumors that may respond to targeted therapies by assessing multiple gene targets within the *EGFR, BRAF, KRAS, HRAS, NRAS, ALK, ERBB2*, and *MET* genes simultaneously

Diagnosis and management of patients with lung cancer

This test is **not intended for** use for hematological malignancies.

Genetics Test Information

This test uses targeted next-generation sequencing to evaluate for somatic mutations within the *EGFR, BRAF, KRAS, HRAS, NRAS, ALK, ERBB2*, and *MET* genes. See Targeted Gene Regions Interrogated by Lung Panel in Special Instructions for details regarding the targeted gene regions evaluated by this test.

Of note, this test is performed to evaluate for somatic mutations within solid tumor samples. This test is not intended for use for hematological malignancies. Additionally, this test 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

- Targeted Gene Regions Interrogated by Lung Panel
- Tissue Requirements for Solid Tumor Next-Generation Sequencing

Highlights

Evaluates formalin-fixed, paraffin-embedded tumor or cytology slides from patients with lung cancer for gene mutations to identify candidates for targeted therapy.

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.

Method Name
Polymerase Chain Reaction (PCR)-Based Next-Generation Sequencing

NY State Available
Yes

Specimen

Specimen Type
Varies

Necessary Information
Pathology report (final or preliminary) at minimum containing the following information must accompany specimen in order 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 180 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 Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm 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 slide

Slides: 1 stained and 10 unstained

Collection Instructions: Submit 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.

Specimen Type: Cytology slide (direct smears or ThinPrep)

Slides: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and cover slipped 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.

Forms

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

Reject Due To

Other	Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded

Specimen Minimum Volume

See Specimen Required

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		

	Frozen		
	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 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.

Next-generation sequencing has recently emerged as an accurate, cost-effective method to identify alterations across numerous genes known to be associated with response or resistance to specific targeted therapies. This test uses formalin-fixed paraffin-embedded tissue or cytology slides to assess for common somatic mutations in 8 genes known to be associated with lung cancer. 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.

See Targeted Gene Regions Interrogated by Lung Panel in Special Instructions for details regarding the targeted gene regions evaluated by this test.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided.

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 (wild-type) result does not rule out the presence of a mutation that may be present but below the limits of detection of this assay.

Point mutations and small insertion/deletion mutations will be detected in the *EGFR, BRAF, KRAS, HRAS, NRAS, ERBB2*, *ALK,* and *MET* genes only. This test does not detect large single or multiexon deletions or duplications or genomic copy number variants in any of the genes tested.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for updated interpretation. 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 PCR failure.

Supportive Data

We have developed a next-generation sequencing assay to detect somatic mutations that can be used to assist in predicting prognosis and identifying targeted therapies for the management of patients with lung cancer. This assay has been shown to be very reproducible, having a 100% concordance for intra- and interassay reproducibility experiments.

We observed 96.2% concordance, detecting 75 of 78 somatic mutations that had previously been detected by various other molecular methods. These mutations included 61 SNPs and 17 Indels across *ALK* (n=3), *BRAF* (n=15), *EGFR* (n=17), *ERBB2* (n=7), *HRAS* (n=2), *KRAS* (n=17), *MET* (n=5), and *NRAS* (n=12) genes in 70 known unique samples. No pathogenic variants were detected in the 29 unique, known mutation negative samples.

Clinical Reference

1. Beadling C, Neff TL, Heinrich MC, et al: Combining highly multiplexed PCR with semiconductor-based sequencing for rapid cancer genotyping. J Mol Diagn 2013;15:171-176

2. Sharma SV, Bell DW, Settleman J, Haber DA: Epidermal growth factor receptor mutations in lung cancer. Nat Rev Cancer 2007;7(3):169-181

3. Mok TS: Personalized medicine in lung cancer: What we need to know. Nat Rev Clin Oncol 2011;8:661-668

4. Cheng L, Alexander RE, Maclennan GT, et al: Molecular pathology of lung cancer: key to personalized medicine. Mod Path 2012;25(3):346-369

5. Shigematsu H, Gazdar AF: Somatic mutations of epidermal growth factor receptor signaling pathway in lung cancers. 2006 Jan 15;118(2):257-262

6. Gao G, Ren S, Li A, et al: Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) therapy is effective as first-line treatment of advanced non-small-cell lung cancer with mutated EGFR: a meta-analysis from 6 phase III randomized controlled trials. Int J Cancer 2012 Sep 1;131(5):E822-829

7. Eberhard DA, Johnson BE, Amler LC, et al: Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non-small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. J Clin Oncol 2005;23(25):5900-5909

8. Frampton GM, Ali SM, Rosenzweig M, et al: Activation of MET via Diverse Exon 14 Splicing Alterations Occurs in Multiple Tumor Types and Confers Clinical Sensitivity to MET Inhibitors. Cancer Discov 2015 Aug 5(8):850-859

Performance

Method Description

Next-generation sequencing is performed to test for the presence of a mutation in targeted regions of the *EGFR, BRAF, KRAS, HRAS, NRAS, ALK, ERBB2*, and *MET* genes. See Targeted Gene Regions Interrogated by Lung Panel in Special Instructions for details regarding the targeted gene regions identified by this test.(Unpublished Mayo method)

PDF Report

No

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81445-Targeted genomic sequence analysis panel, solid organ neoplasm

Slide Review

88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
LUNGP	Lung Cancer Panel, Tumor	In Process

Result ID	Reporting Name	LOINC®
44150	Result Summary	50397-9
44151	Result	82939-0
44152	Interpretation	69047-9
44153	Additional Information	48767-8
44154	Specimen	31208-2
44155	Source	31208-2
46913	Tissue ID	80398-1
44156	Released By	18771-6