MAYO CLINIC LABORATORIES

Test Definition: RETF

RET (10q11), FISH, Ts

Overview

Useful For

Identifying *RET* gene rearrangements in patients with late-stage, lung adenocarcinomas that are negative for *EGFR* mutations and *ALK* rearrangements

Testing Algorithm

This test does not include a pathology consult. If a pathology consultation is requested, PATHC / Pathology Consultation should be ordered and the appropriate FISH test will be ordered and performed at an additional charge.

This test includes a charge for application of the first probe set (2 FISH probes) and professional interpretation of results.

Additional charges will be incurred for all reflex probes performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No
_IL25	Interphases, <25	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_PBCT	Probe, +2	No, (Bill Only)	No

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A pathology report is required in order for testing to be performed. Acceptable pathology reports include working drafts, preliminary pathology or surgical pathology reports.

2. A reason for testing must be provided. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Tissue

Preferred: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block. Blocks prepared with alternative fixation methods may be acceptable; provide fixation method used.

Acceptable: Slides

Slides: Four consecutive, unstained, 5 micron-thick sections placed on positively charged slides, and 1 hematoxylin and eosin-stained slide.

Forms

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

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Minimum Volume

Two consecutive, unstained, 5 micron-thick sections placed on positively charged slides, and 1 hematoxylin and eosin-stained slide.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container

Tissue	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Lung cancer is the leading cause of cancer mortality in developed countries. The discovery of a variety of genetic alterations in non-small-cell lung cancer (NSCLC) has enabled the use of targeted therapy such as the anaplastic lymphoma kinase (ALK) inhibitor, crizotinib, and the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, erlotinib, for NSCLC with *ALK* rearrangements and *EGFR* mutations, respectively.

Abnormalities of the *RET* proto-oncogene at chromosome 10q11 have been identified as the causative genetic abnormality in the neoplasia predisposition syndrome multiple endocrine neoplasia type II (MEN2), as well as in thyroid carcinomas. Recently, chromosomal rearrangements of *RET* have been identified in a subset of lung adenocarcinomas. Patients with tumors harboring *RET* rearrangements may benefit from RET kinase inhibitors, but the clinical benefits of the inhibitor has not yet been clarified.

Reference Values

An interpretive report will be provided.

Interpretation

A positive result is detected when the percent of cells with an abnormality exceeds the normal cutoff for the probe set.

A positive result suggests rearrangement of the *RET* locus and a tumor that may be responsive to RET kinase inhibitor therapy.

A negative result suggests no rearrangement of the *RET* gene region at 10q11.

Cautions

This test is not approved by the U.S. Food and Drug Administration, and it is best used as an adjunct to existing clinical and pathologic information.

Fixatives other than formalin (eg, Prefer, Bouin) may not be successful for FISH assays however nonformalin-fixed samples will not be rejected.

Paraffin-embedded tissues that have been decalcified are generally unsuccessful for FISH analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing.

Supportive Data

The probe set was independently validated in a blinded study on 20 paraffin-embedded lung adenocarcinoma tissue samples and 25 noncancerous control samples. Rearrangements of *RET* were verified in samples previously identified with a *RET* rearrangement using reverse-transcriptase-PCR testing methods. The normal controls were used to generate a normal cutoff for this assay.

Clinical Reference

1. Suehara Y, Arcila M, Wang L, et al: Identification of *KIF5B-RET* and *GOPC-ROS1* fusions in lung adenocarcinomas through a comprehensive mRNA-based screen for tyrosine kinase fusions. Clin Cancer Res 2012;18(24):6599-6608

2. Matsubara D, Kanai Y, Ishikawa S, et al: Identification of *CCDC6-RET* fusion in the human lung adenocarcinoma cell line, LD-2/ad. J Thorac Oncol 2012;7(12):1872-1876

3. Kohno T, Ichikawa H, Totoki Y, et al: *KIF5B-RET* fusions in lung adenocarcinoma. Nat Med 2012;18(3):375-377

4. Lipson D, Capelleti M, Yelensky R, et al: Identification of new *ALK* and *RET* gene fusions from colorectal and lung cancer biopsies. Nat Med 2012;18(3):382-384

Performance

Method Description

This test is performed using a laboratory-developed *RET* dual-color break-apart strategy probe (BAP).
Paraffin-embedded tissues are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin (H and E)-stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped etcher on the back of the unstained slide to be assayed. The probe is hybridized to the appropriate target areas and 2 technologists each analyze 50 interphase nuclei (100 total) per probe set with the results expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

Slides and H&E used for analysis are retained by the laboratory in accordance to CAP and NYS requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

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

88271x2, 88291-DNA probe, each (first probe set), Interpretation and report

88271x2-DNA probe, each; each additional probe set (if appropriate)

88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)

88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)

88271x3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)

88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)

88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
RETF	RET (10q11), FISH, Ts	90927-5

Result ID	Reporting Name	LOINC®
52243	Result Summary	50397-9
52245	Interpretation	69965-2
54596	Result	62356-1
CG756	Reason for Referral	42349-1
52246	Specimen	31208-2
52247	Source	31208-2
52248	Tissue ID	80398-1
52249	Method	85069-3
52250	Released By	18771-6
55124	Additional Information	48767-8
53820	Disclaimer	62364-5