MAYO CLINIC LABORATORIES

Test Definition: METF

MET (7q31), FISH, Ts

Overview

Useful For

Providing prognostic information and guiding treatment primarily for patients with lung, gastric, and renal tumors as well as other tumor types

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
_PBCT	Probe, +2	No	No
_PADD	Probe, +1	No	No
_PB02	Probe, +2	No	No
_PB03	Probe, +3	No	No
_IL25	Interphases, <25	No	No
_I099	Interphases, 25-99	No	No
_I300	Interphases, >=100	No	No

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

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
Collection Instructions: 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
MET is a proto-oncogene and its overexpression is associated with disease progression. Recent studies have shown *MET* amplification to be a major mechanism of acquired resistance to epidermal growth factor receptor tyrosine kinase domain inhibitor (EGFR-TKI). *MET* amplification has been reported in approximately 5% of patients not treated with EGFR-TKI and up to 20% of patients with acquired resistance to gefitinib or erlotinib.

Reference Values
An interpretive report will be provided.

Interpretation
A positive result is detected when the *MET*:D7Z1 ratio is > or =2.0.
The *MET* locus is reported as amplified when the *MET*:D7Z1 ratio of 2.0 or greater.
Patients with 5 or more copies of *MET* have a poor prognosis.
The absence of an abnormal clone does not rule out the presence of a neoplastic disorder.

Cautions
This test is not approved by the US Food and Drug Administration and 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 29 paraffin-embedded tissue samples from patients with various tumors. A series of normal control samples were used to generate the normal cutoffs. The probe performed as intended and abnormalities including aneusomy, duplication and deletion of *MET* were identified, and may be observed in addition to *MET* amplification in tumor samples.

Clinical Reference

1. Cappuzzo F, Marchetti A, Skokan M, et al: Increased *MET* gene copy number negatively affects survival of surgically resected non-small-cell lung cancer patients. J Clin Oncol 2009;27(10):1667-1674

2. Go H, Jeon YK, Park HJ, et al: High MET gene copy number leads to shorter survival in patients with non-small cell lung cancer. J Thorac Oncol 2010;5(3):305-313

3. Okuda K, Sasaki H, Yukiue H, et al: MET gene copy number predicts the prognosis for completely resected non-small cell lung cancer. Cancer Sci 2008;99(11):2280-2285

4. Karamouzis MV, Konstantinopoulos PA, Papavassiliou AG: Targeting MET as a strategy to overcome crosstalk-related resistance to EGFR inhibitors. Lancet Oncol 2009;10:709-717

5. Engelman JA, Zejnullahu K, Mistudomi T, et al: MET amplification leads to gefitinib resistance in lung cancer by activating ERBB3 signaling. Science 2007;316:1039-1043

Performance

Method Description

The test is performed using a commercially available probe set for *MET* and the centromere region of chromosome 7 (D7Z1). 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 probes are hybridized to the appropriate target areas and 2 technologists each analyze 30 interphase nuclei (60 total) with the results expressed as a ratio of *MET*:D7Z1 signals.(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 using an analyte specific reagent. Its performance characteristics were 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)