MAYO CLINIC LABORATORIES

Test Definition: METF

MET (7q31), FISH, Tissue

Overview

Useful For

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

Reflex Tests

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

Testing Algorithm

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

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test does not include a pathology consultation. If a pathology consultation is requested, order PATHC / Pathology Consultation, and appropriate testing will be added at the discretion of the pathologist and performed at an additional charge.

Multiple oncology (cancer) gene panels are also available. For more information see Hematology and Oncology Test Selection Guide.

Additional Testing Requirements

Confirmation testing by Microarray testing to resolve atypical fluorescence in situ hybridization results is available, order CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A pathology report is required for testing to be performed. If not provided, appropriate testing and/or interpretation may be compromised or delayed. Acceptable pathology reports include working drafts, preliminary pathology, or surgical pathology reports.

2. The following information must be included in the report provided:

-Patient name

-Block number-must be on all blocks, slides, and paperwork

-Date of collection

-Tissue source

3. 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:

Preferred

Specimen Type: Tissue block (fresh tissue is **not acceptable**)

Collection Instructions:

1. Submit a formalin-fixed, paraffin-embedded tumor tissue block.

2. Blocks prepared with alternative fixation methods (eg, Prefer, Bouin's) will be attempted but are less favorable for successful results. Provide fixation method used.

Additional Information:

1. Paraffin-embedded specimens can be from any anatomic location (skin, soft tissue, lymph node, etc).

2. Decalcified paraffin-embedded specimens will have testing attempted; however, the success rate is approximately 50%.Testing **may be** canceled if sufficient tumor tissue is not present.

3. **Submitted fresh tissue specimens will be canceled upon receipt**. If only fresh tissue is available, embed in paraffin prior to sending.

Acceptable

Specimen Type: Tissue slides

Slides: 1 Hematoxylin and eosin stained and 3 unstained

Collection Instructions: Submit 3 consecutive unstained, positively charged, unbaked slides with 5 micron-thick sections of the tumor tissue and 1 slide stained with hematoxylin and eosin.

Additional Information: Broken or cracked unstained slides will be rejected. Stained slides that were broken and repaired (ie, double mounted) at the client site will not be rejected, as, in most cases, they can still be reviewed under the microscope. However, due to the double mounting, digital scanning cannot be performed.

Forms

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

Specimen Minimum Volume

Slides: 1 Hematoxylin and eosin stained and 2 unstained

Reject Due To

Broken or cracked unstained slides	Reject
Broken or cracked stained slides that cannot be repaired	Reject

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. *MET* amplification has also been identified in several other cancers including colorectal adenocarcinoma, gastric adenocarcinoma, and gastroesophageal adenocarcinoma.

Reference Values

An interpretive report will be provided.

Interpretation

MET will be clinically interpreted as positive, negative or equivocal.

Establishment of a clear definition of *MET* amplification has been challenging with the evolution of criteria, as the need to differentiate between true MET amplification and chromosome 7 polysomy has become clear.

For this assay, *MET* will be reported as amplified (positive) when there is a MET:D7Z1 ratio greater than 2.0 and an average of greater or equal to 5 MET signals/nucleus based on current scientific literature.

Because various other definitions have been proposed, results indicating a greater or equal to 5 MET signals/nucleus with a MET:D7Z1 ratio less than 2.0 will be reported as an equivocal result as this finding likely reflects chromosome 7 polysomy but may represent an unusual mechanism of *MET* amplification. Similarly, results indicating a MET:D7Z1 ratio greater than 2.0 and less than 5 MET signals/nucleus will be reported as equivocal. Chromosomal microarray studies (CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded) may be considered in these instances to clarify the FISH results.

A result with a MET:D7Z1 ratio less than or equal to 2.0 and an average of less than 5 MET signals/nucleus will be considered negative for amplification of *MET*.

Patients with 5 or more copies of *MET* have a poor prognosis.

A negative result suggests a *MET* gene amplification is not present.

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.

This fluorescence in situ hybridization (FISH) assay does not rule out other chromosome abnormalities.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for FISH assays. Non-formalin fixed specimens will not be rejected.

Paraffin-embedded tissues that have been decalcified may not be successful for FISH analysis. The success rate of FISH studies on decalcified tissue is approximately 50%, but FISH will be attempted if sufficient tumor is present for analysis.

FISH studies will be attempted if sufficient tumor is present for analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing if insufficient tissue/tumor is available for testing.

If no FISH signals or a lack of sufficient tumor tissue are observed post-hybridization, the case will be released indicating a lack of FISH results.

Broken or cracked unstained slides are not compatible with the instrumentation used in our performing laboratories and will be rejected. Additional material may be requested.

Attempts will be made to repair broken or cracked stained slides; however, if they are unable to be repaired (ie, shattered in transit), they will be rejected and discarded due to safety concerns.

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. Karamouzis MV, Konstantinopoulos PA, Papavassiliou AG. Targeting MET as a strategy to overcome crosstalk-related resistance to EGFR inhibitors. Lancet Oncol. 2009;10(7):709-717

3. Engelman JA, Zejnullahu K, Mitsudomi T, et al. MET amplification leads to gefitinib resistance in lung cancer by activating ERBB3 signaling. Science. 2007;316(5827):1039-1043
4. Zhang M, Li G, Sun X, et al. MET amplification, expression, and exon 14 mutations in colorectal adenocarcinoma. Hum Pathol. 2018;77:108-115
5. An X, Wang F, Shao Q, et al. MET amplification is not rare and predicts unfavorable clinical outcomes in patients with recurrent/metastatic gastric cancer after chemotherapy. Cancer. 2014;120(5):675-682
6. Lai GGY, Lim TH, Lim J, et al. Clonal MET amplification as a determinant of tyrosine kinase Inhibitor resistance in epidermal growth factor receptor–mutant non–small-cell lung cancer. J Clin Oncol. 2019;37(11):876-884
7. Recondo G, Che J, Janne PA, Awad MM. Targeting MET dysregulation in cancer. Cancer Discov. 2020;10(7):922-934

Performance

Method Description
This test is performed using a commercially available MET probe set with an MET probe and a chromosome 7 centromere probe (D7Z1). Paraffin-embedded tissue samples 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 engraving tool on the back of the unstained slide to be assayed. Each probe set is hybridized to the appropriate target areas, as indicated on the H and E, and 60 interphase nuclei are scored within the targeted areas. The results are expressed as a ratio of MET:D7Z1 signals.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
7 to 10 days

Specimen Retention Time
Slides used for analysis are retained by the laboratory in accordance with regulatory requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

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

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
METF	MET (7q31), FISH, Ts	90926-7

Result ID	Test Result Name	Result LOINC® Value
55203	Result Summary	50397-9
55204	Interpretation	69965-2
55206	Result	62356-1
CG938	Reason for Referral	42349-1
55207	Specimen	31208-2
55208	Source	31208-2
55209	Tissue ID	80398-1
55210	Method	85069-3
55211	Additional Information	48767-8
55212	Disclaimer	62364-5
55224	Released By	18771-6