MAYO CLINIC LABORATORIES

Test Definition: H2MT

HER2, Misc. Tumor, FISH, Tissue

Overview

Useful For

Guiding cancer therapy, as patients with *HER2* amplification may be candidates for therapies that target the human epidermal growth factor receptor 2 (HER2) protein (eg, trastuzumab [Herceptin], pertuzumab)

Confirming the presence of *HER2* amplification in cases with 2+ (low level) or 3+ (high level) HER2 protein overexpression by immunohistochemistry

Testing Algorithm

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

A charge and CPT code is applied for each probe set hybridized, analyzed, and reported.

NOTE: in accordance to criteria set forth in the 2013 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guideline for breast cancer, reflex testing will not be performed using the alternative chromosome 17 probe when the FISH result is equivocal.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test is only for primary or metastatic tumors other than breast, urothelial, or gastroesophageal.

-For breast tumors, order H2BR / *HER2* Amplification Associated with Breast Cancer, FISH, Tissue.

-For urothelial tumors, order H2UR / *HER2* Amplification Associated with Urothelial Carcinoma, FISH, Tissue.

-For gastroesophageal tumors, order H2GE / *HER2* Amplification Associated with Gastroesophageal Cancer, FISH, 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.

3. The pathology report must include type of fixation used as well as the time of fixation (recommended: >6 hours and <72 hours).

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 a 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 slide.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Amplification of the *HER2* oncogene and overexpression of the human epidermal growth factor receptor 2 (HER2) protein have been associated with a shorter disease-free survival and shorter overall survival and poorer overall survival in some cancers. Patients whose breast or gastroesophageal cancers demonstrate *HER2* amplification or overexpression may be candidates for treatment with the drugs that target the HER2 protein or its downstream pathways (eg, trastuzumab [Herceptin], pertuzumab, lapatinib).

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided. Results are interpreted utilizing the 2013 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines for breast tumors.

Specimens with equivocal (Group 4) results as defined by 2013 ASCO/CAP guidelines will not have reflex testing performed using an alternative FISH probe set. The report will include a complete interpretation including the *HER2*:D17Z1 results.

The degree of *HER2* amplification varies in tumors. Some exhibit a high level of amplification (*HER2*:D17Z1 ratio >4.0), whereas others exhibit low-level amplification (*HER2*:D17Z1 ratio of 2.0-4.0). It is not currently known if patients with different levels of amplification have a similar prognosis or response to therapy.

Reports also interpret the *HER2* copy number changes relative to chromosome 17 copy number (aneusomy) or potential structural genomic abnormalities that increase *HER2* copy number.

Rare cases may not show *HER2* amplification but have human epidermal growth factor receptor 2 (HER2) protein overexpression demonstrated by immunohistochemistry. The clinical significance of HER2 protein overexpression in the absence of *HER2* gene amplification is unclear. However, these patients may have a worse prognosis and may be candidates for treatments that target the HER2 protein or its downstream pathways.

Cautions

This test is not approved by the FDA and should be used as an adjunct to existing clinical and pathologic information.

The prognostic information provided by the *HER2* status of a patient's tumor should not be interpreted in isolation because other prognostic features (eg, lymph node status, tumor size) may be of equal or greater importance in determining the patient's prognosis.

Supportive Data

Retrospective data was reviewed on miscellaneous (not breast or gastroesophageal) tumors using the PathVysion HER2 probe set. The FISH results were compared to immunohistochemistry (IHC) testing. The correlation of FISH and IHC results are similar to those observed in validation studies for breast tumor specimens, so the same interpretative guidelines will be followed.

Clinical Reference

Wolff AC, Hammond ME, Hicks DG, et al: Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society for Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Onc 2013 Nov 1;31(31):3997-4013

Performance

Method Description

The test is performed using the PathVysion HER2 DNA probe set (Abbott Molecular) with a *HER2* probe and a chromosome 17 centromere probe (D17Z1). 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 is 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 set is hybridized to the appropriate target areas and 2 technologists each analyze 30 interphase nuclei (60 total) with the results expressed as a ratio of *HER2:*D17Z1 signals. The results are interpreted based on the 2013 guidelines established by the American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP), available at www.cap.org/apps/docs/committees/immunohistochemistry/validated_dual_probe_ish_assay.pdf.(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

88377

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
H2MT	HER2, Misc. Tumor, FISH, Tissue	96893-3

Result ID	Reporting Name	LOINC®
603096	Result Summary	50397-9
603097	Interpretation	69965-2
603098	Result	62356-1
GC032	Reason for Referral	42349-1
603099	Specimen	31208-2
603100	Source	85298-8
603101	Tissue ID	80398-1
603102	Fixative	8100-0
603103	Method	85069-3
603104	Additional Information	48767-8
603105	Disclaimer	62364-5
603106	Released By	18771-6