Chromogenic in situ hybridization (CISH) is a reliable method for detecting HER-2 gene status in breast cancer: A multicenter study comparing three methods

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Abstract

Background: Immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) are the two assays currently used to determine HER-2 status in routine practice, with FISH considered the gold standard. Chromogenic in situ hybridization (CISH) recently emerged as a potential alternative to FISH in this study, we evaluated the accuracy of CISH and the correlation between CISH and IHC.

Design: A total of 226 breast cancer specimens were consecutively obtained from two test sites. HER-2 status was determined using IHC (Herceptest; DakoCytomation, Carpinteria, CA) and FISH (Vysis NFISH HER-2 assay; Vysis Inc., Abbott Park, IL). CISH was performed on each slide at the site where IHC was performed. HER-2 status was determined as non-amplified, low amplification, or high amplification by FISH. For CISH, positive amplification was determined by a conventional examination by regular bright-field microscopy. In this study, we evaluated the reliability of CISH by examining the concordance between CISH and IHC at three different test sites.

Results

Of the 226 breast carcinomas, 219 were primary invasive breast carcinomas and 7 were metastatic breast carcinomas. The histologic type was ductal in 171, lobular in 26 and others in 25. The successful rate of HER-2 test by IHC, FISH and CISH at each test site is shown in Table 1.

Of 221 tumors with available IHC results, 0, 1+, 2+, and 3+ scores were observed in 141 (63.8%), 19 (8.6%), 21 (9.5%), and 40 (18.1%) tumors, respectively. The corresponding FISH results were obtained in 0.71% (1/140) ≤ 2+, 23.8% (5/21) ≥ 2+ and 81.6% (31/38) ≥ 3+. For comparison purposes, IHC score of ≤ 2+ was classified as negative and 3+ was classified as positive.

For CISH (Zymed®SPOT®-Light HER-2 CISH™, Invitrogen Corporation, Camarillo, CA) at 1-5 per tumor nucleus, and amplification if the average signal was >5 or showed signal clusters. Of the 226 breast carcinomas, 219 were primary invasive breast carcinomas and 7 were metastatic breast carcinomas. The histologic type was ductal in 171, lobular in 26 and others in 25. The successful rate of HER-2 test by IHC, FISH and CISH at each test site is shown in Table 1.

The agreements among the three methods were shown in Table 3. Inter-site reproducibility of CISH and FISH results is shown in Table 4.

Conclusions

• High agreement in HER-2 status was found between the three methods, and near-perfect agreement was noted between IHC and the corresponding FISH results.

• Excellent inter-site reproducibility was found with FISH and CISH results.