Review

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Fluorescence in Situ Hybridization in Pathology

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Abstract

Fluorescence in Situ Hybridization (FISH) is a molecular cytogenetic technique that uses fluorescent probes which bind to specific chromosomal locations within the nucleus to search and detect chromosomal abnormality. In the last decade, tumor-specific chromosomal translocations, deletions, gains, amplifications, and novel oncogenes have become increasingly important in the field of diagnostic, therapeutic, and prognostic concepts in medicine. FISH technique provides a quick analysis of formalin-fixed paraffin-embedded cells which can be used in daily practice of pathology for several tumor types. Fluorescence in Situ Hybridization (FISH) technique is based on hybridization of tagged DNA probes which are fluorescent reporter molecules that affirm the presence or absence of particular genetic anomaly under fluorescence microscopy. This technique has been recently developed to screen the whole genome coexistently through multicolor whole chromosome probe techniques that multiplex-FISH or spectral-karyotyping or through an array-based method using comparative genomic hybridization. The aim of this article was to provide a theoretical survey of FISH for clinical function in surgical pathology habit.

Keywords: FISH, molecular genetics, pathology

INTRODUCTION

Fluorescence in situ hybridization technique is based on fluorescence-labeled fragments of DNA binding to interphase chromosomes of cytology materials or paraffin-embedded tissue segments. Chromosome deletions, gains, translocations, amplifications, and polisomy of certain types of tumors can be detected by FISH, which are useful in diagnostic and therapeutic purposes (1, 2).

Recently it has been found that more than 30% of soft tissue sarcomas have specific translocations and more than 30 subtypes of mesenchymal tumor can be affirmed via FISH analysis on the basis of tumor specific chimeric fusion cycles (3). These include Ewing sarcoma, myxoid liposarcomas, synovial sarcomas, solitary fibrous tumors, inflammatory myofibroblastic tumors, and alveolar rhabdomyosarcomas (4-8). Chromosomal translocations that are associated with ordinary adult epithelial tumors are as follows: adenocarcinomas of the lung, prostate, colon, kidney, breast, colorectal, thyroid, and salivary gland.

EML4-ALK Translocation

The ALK fusion oncogenes were first named in an anaplastic large-cell lymphoma, wherein a T(2;5) chromosome rearrangement activates the ALK kinase by fusion with the NPM1 on chromosome 5 ALK fusions have been announced in non-small cell lung carcinoma, breast cancers, colorectal cancers, renal cancers, and other tumor types (9). FISH test for ALK rearrangement uses dual color labeled probes of the ALK gene and 3' region of ALK. When FDA approved a new anticancer drug and its FISH detection kit (ALK FISH PROBE KIT) in 2013, EML4-ALK translocation-targeted therapy became crucial for patients with lung cancer and in surgical pathology practice (10).

ROS1 Translocation

ROS1 is a receptor tyrosine kinase of the insulin receptor group like ALK which is detected in 1.2%-1.7% of lung adenocarcinoma cases (11). ROS1 translocations have been found in young,

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nonsmoker patients with high-grade lung adenocarcinoma. A dual-probe break-apart method is used to detect ROS1 translocations similar to ALK.

TFE-3 Translocation

Renal cell carcinomas associated with Xp11.2 translocation are newly described renal tumors in the new who book (12). TFE3 break-apart FISH probe is reportedly more useful compared with immunohistochemistry for detecting TFE3 gene fusions in Xp11.2 translocation renal cell carcinoma. Rao et al. (12) proved the diagnostic value of TFE-3 in renal cell cancers by showing 17 of 24 unclassified renal cell cancers had TFE-3 rearrangement associated with Xp11.2 translocation by FISH.

TMPRSS2-ERG Gene Fusion

These fusions have been identified in approximately 50% of prostate tumors (ranging from 27% to 79%) and are also found in high-grade prostatic intraepithelial neoplasia, which may play a role in early development in prostatic carcinogenesis. The TMPRSS2-ERG gene fusion can be identified by both dual and tricolor probes (13).

HER-2/Neu Amplification

HER-2 also called c-erbB-2 is a tyrosine kinase which plays part in normal cell growth. Amplification and over-expression of the HER-2/neu gene occurs in 25%-30% of human breast cancers with a poor clinical prognosis and short survival time. Presently, HER-2 overexpression can be shown by immunohistochemistry and FISH technique. Because immunohistochemistry is a cheap and easier way than FISH, it is used when IHC results are borderline (14).

1p19q Co-Deletion

In the new who book of central nervous system 2016, it is recommended that a pathology report should contain molecular diagnosis. 1p19q co-deletion is characteristic for oligodendrogliomas that can be shown by FISH (15).

Fluorescence in Situ Hybridization (FISH) identification of chromosomal translocations has diagnostic, therapeutic, and prognostic use in lymphoma, colorectal carcinoma, thyroid carcinoma, Spitz nevi, melanoma, and salivary gland tumors (16). The most commonly used FISH methods in differential diagnosis of small B cell lyphoma are the translocation of IgH-Cyclin D1 t(11; ,14) (q13;q32) for mantle cell lymphoma; translocation of t(14;18) (q32;q21) for follicular lymphoma; translocation t(8;14) (q24;q32) for burkitt lymphoma; and translocation of BCR-ABL for chronic myeloid leukemia.

CONCLUSION

Fluorescence in Situ Hybridization (FISH) analysis of neoplasms has become one of the most interesting and improving areas in surgical pathology in the last decade. Nowadays, diagnostic and treatment choices are designated by FISH for many tumor types. The technology of FISH analyses of chromosomal alterations is rapidly evolving in the 21th century. The role of FISH in cancer diagnosis and treatment will become more significant in surgical pathology practice.

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