FISH for Plasma Cell Myeloma

Background

Plasma cell myeloma is a multi-focal, bone marrow-based neoplasm of plasma cells characterized by anemia, hypercalcemia, renal dysfunction, secretion of monoclonal immunoglobulin proteins and lytic bone lesions.[1] Several cytogenetic abnormalities are known to influence the prognosis of plasma cell myeloma (See Table 1 below), and the detection of high-risk abnormalities may influence the choice of therapy.

Metaphase cytogenetic studies are frequently unsuccessful in plasma cell myeloma because the malignant cells grow poorly in culture. Fluorescence in situ hybridization (FISH) studies are capable of detecting these abnormalities in nondividing (interphase) cells, but FISH studies must be performed selectively on plasma cells because the tumor cells frequently represent only a minority of cells present in the samples submitted for analysis.[2,3] In our laboratory, plasma cells are specifically targeted for FISH analysis using sequential Giemsa staining and FISH staining with image analysis to identify and locate plasma cells and analyze FISH signals only in the plasma cell compartment.

Clinical Indications

Cleveland Clinic Laboratories offers FISH studies to detect deletions of chromosome 13q, deletions of 17p (*TP53*), and the IGH translocations t(11;14)(q13;q32) *IGH/CCND1*, t(4;14)(p13;q32) *MMSET/IGH*, and t(14;16)(q32;q32) *IGH/MAF* in bone marrow aspirates. Formalin-fixed, paraffin-embedded tissue is not acceptable.

Interpretation

FISH studies are performed using deletion probes for 13q and 17p, and an *IGH* break-apart probe in all cases with sufficient plasma cells for analysis. If an *IGH* rearrangement is detected, additional FISH studies are performed using *IGH/CCND1*, *IGH/MMSET*, and *IGH/CMAF* dual fusion probes in order to identify the translocation partner gene.

TABLE 1. PROGNOSTICALLY SIGNIFICANT MOLECULAR ABNORMALITIES IN PLASMA CELL MYELOMA

Abnormality	Genes Involved	Frequency*	Prognosis
-13/-13q	Unknown	~50%	Unfavorable
-17p	*TP53*	10%	Unfavorable
t(11;14)(q13;q32)	*CCND1/IGH*	15-20%	Neutral to Favorable
t(4;14)(p16;q32)	*MMSET/IGH*	15-20%	Unfavorable
t(14;16)(q32;q23)	*CMAF/IGH*	5-10%	Unfavorable

*Frequency defined by FISH analysis.[1,2]

Limitations of the Assay

Successful analysis depends upon the numbers of plasma cell present in the sample submitted for FISH studies and the degree of dilution by peripheral blood. Submission of a first or second draw aspirate sample is strongly recommended.

Methodology

Giemsa stained bone marrow aspirate cytospin preparations are first scanned using the BioView Duet scanner (Bioview, Rehovot, Isreal) to identify and locate plasma cells. The cytospin preparations are subsequently destained, and FISH probes applied. Slides are then re-scanned to locate plasma cells and specifically enumerate FISH signal patterns in plasma cell nuclei.

References

1. McKenna RW, Kyle RA, Kuehl WM, *et al*. Plasma Cell Neoplasms. In: Swerdlow SH, Campo ES, Harris NL, *et al*., eds. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. IARC (Lyon); 2008:200-213.
2. Ross FM, Avet-Loiseau H, Ameye G, *et al*. Report from the European Myeloma Network on interphase FISH in multiple myeloma and related disorders. *Haematologica*. 2012 Aug;97(8):1272-7.
3. Sawyer JR. The prognostic significance of cytogenetics and molecular profiling in multiple myeloma. *Cancer Genet*. 2011 Jan;204(1):3-12.

Test Overview

Test Name	FISH for Plasma Cell Myeloma
Ordering Mnemonic	FSHPCM
Methodology	Fluorescence In Situ Hybridization (FISH)
Reference Range	Normal pattern
Specimen Requirements	Volume/Size: 3 mL; Type: bone marrow; Container: EDTA (Lavender); Collection termperature: ambient: Transport temperature: refrigerated
Alternate Specimen Requirements	Volume/Size: 3 mL; Type: bone marrow; Container: Sodium heparin (Green); Collection termperature: ambient: Transport temperature: refrigerated
Billing Code	88367
CPT Codes	88367x4; additional 88367x6 added if an *IGH* translocation is identified

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