



## Interphase FISH Analysis

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### Interphase FISH (Fluorescent In situ Hybridization) Analysis Is Useful in Determining Diagnosis and/or Prognosis in Certain B-Cell Leukemias and Lymphomas

CONVENTIONAL CYTOGENETIC ANALYSIS studies may not yield clinically useful results in certain malignant diseases due to the low proliferation rate of the neoplastic cells; this can be particularly true for B-cell disorders of all types. Improvement and availability of manufactured DNA probes for FISH have provided an alternative approach for the detection of chromosome aberrations in non-dividing cells. New probes sets are available that can detect gene fusion events, gene deletion, or chromosome aneuploidy associated with certain B-cell diseases. These probes can, therefore, be used for confirmation of diagnosis in certain clinical situations and can yield additional prognostic information.

*Mantle Cell Lymphoma* can be confused with other B-cell malignant lymphomas. However, the translocation t(11;14) is found in a high percentage of individuals with MCL. A dual color fusion translocation probe is designed and available to detect the juxtaposition of the IGH locus (14q32) sequences and the Cyclin D1 gene sequences (11q13).<sup>1</sup>

*Follicular Lymphoma* is highly associated with t(14;18).<sup>2</sup> A probe set has recently been introduced that detects the rearrangement between the IGH gene (14q32) and the BCL-2 gene (18q21) that is useful in cases in which the histology is not clear.

There is a subset of CD30-positive *Anaplastic Large Cell Lymphomas* with a NPM-ALK gene fusion (the nucleoplasmin gene and anaplastic lymphoma kinase gene) arising from the t(2;5)(p33;q35). Patients with this rearrangement comprise a distinct clinical and prognostic group who have a favorable clinical prognosis.<sup>3</sup>

The translocation t(8;14)(q24;q34) is the characteristic and most common chromosome aberration of *Burkitt-type Lymphomas and Leukemias*. On the molecular level, the t(8;14) juxtaposes the c-myc gene at 8q24 with the IgH locus on 14q32, resulting in over-expression of c-myc. Using DNA probes that detect the IgH locus and the c-myc gene, a fusion product can be detected.

Overall survival has been found to be lower in cases of *Multiple Myeloma* with monosomy 13 or deletion 13q. A multivariate analysis for overall survival showed that monosomy of chromosome 13 with nontrisomy of chromosome 6, together with S-phase plasma cell levels greater than 3% and beta-2 microglobulin serum level, were the best parameters for predicting shorter survival of patients with MM.<sup>4</sup> Probes specific to 13q can detect -13/13q-. Deletion of the p53 tumor suppressor gene on 17p13 is associated with aggressive disease with poor survival and non-response to therapy with purine analogs.<sup>5</sup> FISH provides an alternative approach for the detection of the deletion of the p53 gene in those cases where a deletion is present. (In some cases there may be DNA sequence mutation.)

In *Chronic B-cell Leukemias*, deletion of the p53 tumor suppressor gene on 17p13 is associated with a poor prognosis, and FISH will detect large deletions, if present. The presence of trisomy 12 or deletion of the

long arm of 11q23 have been shown to be associated with aggressive CLL. Deletion of 13q, on the other hand, is associated with a good prognosis in these patients. There are chromosome-specific probes which can detect these changes if they have occurred:

- Mantle Cell Lymphoma: t(11;14)-IGH/CCND1
- Follicular Lymphoma: t(14;18)-IGH/BCL2
- Non-Hodgkin's Lymphoma: t(2;5)-NPM/ALK
- Burkitt Lymphoma: t(8;14)-IGH/c-myc
- Multiple Myeloma: -13/13q-, del p53
- Chronic Lymphocytic Leukemia: +12, 13q-, del p53, del(11q)

### References

1. Katz, Ruth et al., "Detection of Chromosome 11q13 Breakpoints by Interphase Fluorescence In Situ Hybridization" American Journal of Clinical Pathology 2000, 114:248-257.
2. Vaandrager, Jan-Willem et al., "Interphase FISH detection of BCL-2 rearrangement in follicular lymphoma using breakpoint-flanking probes" Genes, Chromosomes, Cancer 2000, 27:85-94.
3. Cataldo KA, "Detection of t(2;5) in anaplastic large cell lymphoma: comparison of immunohistochemical studies, FISH, and RT-PCR in paraffin-embedded tissue" Amer Jr of Surg Path 1999, 23:1386-92.
4. Perez-Simon JA et al., "Prognostic value of numerical chromosome aberrations in multiple myeloma: A FISH analysis of 15 different chromosomes," Blood 1998, 91:3366-3371.
5. Medizinische Klinik, "p53 gene deletion predicts for poor survival and non-response to therapy with purine analogs in chronic B-cell leukemias," Blood 1995, 85:1580-9.

### Test Information

DESCRIPTION	<b>INTERPHASE FISH (FLUORESCENT IN SITU HYBRIDIZATION)</b>
CPT CODE	Please call the laboratory for specific billing information.
SPECIMEN	Blood or bone marrow in sodium heparin or transport media OR fixed, paraffin-embedded tissue. <i>Unacceptable conditions:</i> Frozen or in an additive other than sodium heparin. <i>Stability:</i> Ship to lab ASAP
SCHEDULE	As requested
TURNAROUND	5-7 days

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