

The Aga Khan University Hospital

Clinical Laboratories Update

FISH Based Detection of MYC, BCL2 and BCL6 Gene Rearrangements in Mature Aggressive B-Cell Lymphoma

Introduction

B-cell lymphoma is a large group of heterogeneous disorders that encompass a majority of non-Hodgkin lymphomas. Included in this group are follicular lymphoma (FL), Burkitt Lymphoma (BL), and diffuse large B-cell lymphoma (DLBCL). The characteristic chromosome abnormality $t(14;18)$ results in IGH/BCL2 fusion is seen in about 80% of FL and about 20-30% of DLBCL, while most patients with BL harbor the characteristic $t(8;14)$ producing cMYC/IGH fusion.

In the 2016 revision of the WHO classification of lymphomas, the term high-grade B-cell lymphoma has been repurposed. Most cases in this category include so-called double and triple-hit lymphomas falling into the sub-group designated high-grade B-cell lymphoma with MYC and BCL2 and BCL6 rearrangements. Double and triple-hit lymphomas can show a morphological spectrum of findings but are united by the presence of rearrangements involving MYC, with either BCL2 or BCL6 or both. BCL6 gene rearrangements are also associated with B-cell lymphoma, whereas cyclin D1 gene rearrangement, especially the $t(11;14)$, distinguishes mantle cell lymphoma (ML) from other lymphoproliferative disorders and hence is diagnostic for ML.

Principle of the Assay

For Fluorescent *in situ* hybridization assay, formalin fixed paraffin embedded tissue sections are hybridized to fluorescently labeled dual color break apart probes specific for BCL6, BCL2 and MYC genes (Abbott, Illinois, USA). After several washes' slides are examined for gene rearrangement under a fluorescent microscope equipped with appropriate filters. Fluorescent signals are recorded and interpreted according to the published guidelines.

Specimen Collection

Formalin Fixed Paraffin Embedded Tissue (FFPET)

Test order

This test can be ordered as piecemeal (MYC, BCL2 and BCL6 in combination) or independently based on clinical and immune-histopathological diagnosis.

Limitations

- Fixatives other than formalin or paraffin-embedded tissues that have been decalcified are not suitable for FISH analysis
- Samples will not be reported in which the tumor content is around or below the diagnostic threshold of the assay.

Reporting Schedule:

Performed Daily, Test will be reported after 7 days