Razavi Int J Med. 2015 May; 3(2): e29825. DOI:10.30483/rijm.2015.118325

Published online 2015 May 2. **Editorial**

Cancer Biomarkers

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Received: April 7, 2015; **Accepted:** April 20, 2015

Keywords: Cancer; Biological Markers; Guideline

In the era of personalized medicine and targeted therapies, cancer biomarker testing has an important role. Pathologists should have a good knowledge about this field and be up to date. Pathologists need well-defined guidelines for cancer biomarker testing and interpretation. Of course, these guidelines should be in concordance with oncology and other fields involved in cancer management and treatment.

What is a cancer biomarker? There is a simple definition in Wikipedia: "A cancer biomarker refers to a substance or process indicating the presence of cancer in the body". Cancer biomarkers estimate the risk, diagnostic, screening, differential diagnosis, prognostic, predictive and more important therapeutic decision role (1).

Cancer biomarker may be a serum protein or antibody, a fragment of gene, or a genetic or epigenetic alteration. The definition of National Cancer Institute (NCI) for biomarker is: "A biological molecule found in blood, other body fluids, or tissue that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. It is also called molecular maker and signature molecule (2).

Number and type of biomarkers are growing, so reference laboratories and scientific societies have an important role in standardization of these tests from sampling to reporting. In pathology labs, fixation and processing of tissues are very important, so the suitable time for fixation before processing should be determined and even included in final report. One of the oldest and well-known serum biomarkers is PSA in prostatic carcinoma. Now there are many serum tumor markers for prostatic carcinoma.

The first tissue biomarkers we know were found in breast pathology. Determination of hormonal receptors in breast cancer nowadays is a routine work in many pathology laboratories. For ER, PR, and HER2 testing and reporting, there are well-defined guidelines (3, 4). The CAP has a protocol and template for reporting breast biomarkers (5). Other biomarkers in breast field include ki-67, P 53, PTEN, PIK3CA, STAT3, BRCA-1 and BRCA-2, and molecular platform for determination of risk of recurrence and response to treatment.

In the field of gastroenterology, there are many markers in daily use. Markers for assays of MSI-H and Lynch syndrome have screening and therapeutic roles in colorectal cancer. Immunohistochemical study of MLH-1, MSH2, MSH6 and PMS2 is the first step in the evaluation of mismatch repair proteins. KRAS, NRAS, BRAF, PIk3CA, PTEN assays are now standard in colorectal cancer and are part of colorectal biomarker reporting protocols (5, 6). KRAS and NRAS mutation analysis is important for making decision about EGFR-targeted therapies.

HER2 evaluation has now therapeutic implication in gastric and esophageal cancers. Interpretation of HER2 in gastric cancer is different from breast cancer. There is also difference between endoscopic and surgical biopsies.

EGFR mutation analysis, Anaplastic Lymphoma Kinase (ALK) rearrangement, and KRAS mutational analysis are important in therapeutic decisions for non-small cell lung cancer (5, 7). Adequacy of specimen is the first step in evaluation of lung biomarkers. For EGFR, routinely 5 exons should be evaluated. Codon 12, 13 and 61 of KRAS should be considered for mutational analysis. Many techniques are acceptable for ALK rearrangement testing including In Situ Hybridization, Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), Immunohistochemistry and Next-generation (high-throughput) sequencing.

There are many well-known biomarkers in the field of hematologic malignancies. CD38, ZAP-70, IGVH mutational status, somatic mutation in Tp53 and NOTCH1, and alteration in chromosome 11, 12, 13 q and 17 are among biomarkers involved in CLL patients management. In Acute Myeloid Leukemia (AML), mutation analysis of NPM1, CEBPA and FLT3 are important. Also there are recently discovered mutations waiting to enter daily practice (8, 9).

In April and May 2015 issues of the Journal of "Archives of Pathology and Laboratory Medicine", different aspects of cancer biomarker evaluation in pathology and oncology with special attention to GI, lung and myeloid neoplasms are discussed (2, 6-14).

Cancer biomarkers are very important in management of patients from screening to treatment. They have special role in personalized and targeted therapies. The number of these markers is growing and their evaluation needs standard protocols and guidelines. The most important aspect of these assays is sampling and processing of biological samples. Coordination between oncologist, pathologist and laboratory is the mainstay of biomarker testing. Clinical problems should be clear, that is diagnosis, prognosis, or choice of therapy. It is important to select the appropriate test and the suitable tumor marker. Biomarker testing is now routine in the fields of colon cancer, breast and non-small cell carcinoma of lung. Modern pathology labs should be equipped with these tests and pathologists have an important role in selection and interpretation of these tests in harmony with oncologists.

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