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Editorial

Biomarkers in cancer diagnosis – Status and challenges

Ashutosh Chauhan

Department of Biotechnology, Faculty of Biomedical Sciences, Uttarakhand Ayurved University, Dehradun-248001, Uttarakhand, India.

E-mail: ashutosh_biotech2006@yahoo.com; Tel: +91-9675598199.

Cancer is the second largest disease throughout the world with an increasing mortality over the past few years. This is mainly because of highly heterogeneous in nature and a few effective therapeutic strategies for the treatment. This also represents challenges amongst healthcare professionals and governments. Although a significant advance has been made in cancer treatment, the morbidity and mortality are still enormous. The possibility of detecting cancer at early stages, before it spreads to distant tissues, has been a matter of great interest amongst physicians and scientists because early diagnosis is a key factor for the successful treatment of cancer (Borrebaeck, 2017). To achieve this, we still need of a potential biomarker with significant diagnostic accuracy for cancer.

As per the National Cancer Institute, a biomarker is a biological molecule found in blood, other body fluids, or tissues that are the sign of a normal or abnormal process, or of a condition or disease, such as cancer. More recently, the definition has been broadened to include biological characteristics that can be objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention (Naylor, 2003). A biomarker may be a molecule secreted by a tumour or a response of the body toward cancer. A biomarker can be tumour specific and tumour associated. Tumor-specific biomarkers are considered as a direct result of oncogenesis, while tumour-associated markers are various proteins, enzymes, hormones and immunoglobulins which occur in the blood and are mediated by the tumour itself or by the influence of the tumour on the involved tissues. These biomarkers can be used in early diagnosis, primary treatment selection, post-treatment risk stratification, prognosis and treatment response. The diagnostic value of any biomarker is usually performed with sensitivity and specificity. Specificity means that ability of the marker to detect non-diseased subjects whereas sensitivity refers to the ability to identify diseased subjects. Consequently, sensitivity and specificity could be computed across all possible cutoff or threshold values and both are inversely related to each other. Receiver operating characteristic curve is a performance indicator of a biomarker depends on specificity and sensitivity. Definitive cutoff value for a biomarker is to achieve the highest sensitivity and specificity. Before practising in clinical setup a potential biomarker must surpass analytic validity, clinical validity, and clinical utility. Classically, a biomarker is synthesised by the tumour and released into circulation or expressed at the cell surface in large quantity by malignant cells. In most of the cases, cancer can only be diagnosed by tissue biopsy and biomarkers are usually not used to diagnose cancer. The tissue is generally considered unsuitable as a possible screening tool. Serum/blood biomarkers are defined as substances changing quantitatively in the blood during tumour development. Urine is one of the most interesting and useful biofluids for routine testing and provides an excellent resource for the discovery of novel biomarkers due to the ease and less invasive nature of the collection. Unlike blood, urine is not subject to homeostatic mechanisms. Therefore, greater fluctuations could occur in urine than in blood, which better reflects the changes in the human body. Saliva is another source of diagnosis with great potential to be used in the early detection and prevention of many cancerous diseases. Saliva, as a non-invasive and safe source, could be a substitute for blood in the diagnosis of diseases. Human faecal also provide an opportunity to diagnosis as a faecal occult blood test and faecal immunochemical test with high specificity and low sensitivity. So far discovered biomarkers are from genomics, epigenomics, noncoding RNA, metabolomics, a liquid biopsy (CTC, CtDNA, mtDNA and exosome) and microbiome.

Till now, early diagnosis remains difficult and

mainly depends on imaging modalities not on biomarkers. The major problem in the identification of cancer biomarkers is their very low concentration in the tissue or fluid in small and early-stage cancer lesions. Even when tumour marker levels are high, they are not specific enough to confirm the presence of cancer. Sometimes proteins and/or modified proteins may vary among individuals, between cell types, and even within the same cell under different stimuli or different disease states. Hence, it is difficult to know which value obtained from an individual is accurate and what value in different patients indicates a problem. In some cases, normal cells, as well as cancer cells, can produce similar markers. Biomarkers are not always present in early-stage of cancers. Differences in sample collection, handling or storage, and profiling techniques among various research sites may change the protein profile obtained from a given sample (Span et al., 2004). Therefore, standardisation issues regarding biological variation, pre-analytical variables, and analytical variability must be tackled before standard values can be proven. So far chromatography, mass spectrometry, gel electrophoresis, microarrays and polymerase chain reaction-based quantification are the key methods used in biomarker development.

During the few decades, there has been a tremendous rise in a number of research studies dedicated toward the development of biomarker. Only a few have stood the test of time and can be used clinically. Among commonly utilised biomarkers in clinical practice are PSA, AFP, CA125, and CEA. Notably, most of the well-established biomarkers for screening could be used as a diagnostic marker is PSA is a well-recognized example. PSA, in combination with a digital rectal examination (DRE), is the most commonly used diagnostic tool for prostate cancer. Traditionally single biomarkers were used but these have come under scrutiny due to their low sensitivity and specificity screening setting. So for superior performance, a combination of multiple biomarkers as a panel for assessment, or as part of validated algorithms that also incorporate other clinical factors can be done. The challenge and future perspective of biomarkers, by facilitating the combination of therapeutics with diagnostics, promise to play an important role in the development of personalised medicine. Before using in clinical practice a potential biomarker must need to be validated and standardised for unnecessary failure in the later stage of development. Further interdisciplinary research in genetics, biotechnology and electronic and nanotechnology cab be exploited to develop a biomarker to improve sensitivity and specificity. Such as, use of biosensor is a good example of this approach to detect the biomarker. Hence, such modern approaches are needed to diagnose cancer in the early stage to decrease the morbidity and mortality.

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