



Role of Microarray in Cancer Biology

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ABSTRACT

Miroarrays offer a powerful approach for the analysis of gene expression that can be used for a wide variety of experimental purposes. However there are several types of microarray platforms that are available. Microarray represents a potentially powerful tool for better understanding of the role of the microenvironment on tumour biology. The present study is done to explore the various approaches of microarray, importance of biomarkers in microarray, and its significance in treatment of different types of cancer. The aim of this paper was to explore the various applications of microarray and its role in cancer biology.

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INTRODUCTION

Microarray technology is a potent platform for biological research [1]. Microarrays allow simultaneous analysis of thousands of DNA sequences for genomic research as well as diagnostic applications. This technology exhibits the most recent and exciting advance in the application of hybridization-based methods to analysis in the biological sciences [1]. Gene expression profiling of cancers represents the major research category by the use of microarrays and emerges to be the most robust approach for molecular characterization of cancers [2]. Depending on the type of probes used, microarray systems are categorised into either oligonucleotide or cDNA. Oligonucleotide microarrays generally comprise a hybridization slide spotted with oligonucleotides ranging in length from 16-70-mer. It can be used for gene expression, mutation, SNP (single nucleotide polymorphism) and genotyping analyses. Oligonucleotide microarrays have been

developed as an approach for rapid mutation analysis of selected gene sequences, and are efficient in sequence analysis, diagnosing genetic diseases and gene polymorphism studies [3]. A typical DNA microarray-based method is less time-consuming and is affordable when compared to conventional sequencing, and has an important role in high throughput sequence analysis [4]. cDNA microarrays are commonly used in analyzing gene expression. Furthermore, expression of thousands of genes can be analyzed at a time. Using cDNA microarrays is comparatively easy and are used in several research groups. A cDNA microarray usually comprises a slide spotted with cDNA probes ranging in size from a few hundred to 1,000 bp [5]. Biomarkers can be used clinically to predict the potency and toxicity of anticancer drugs and hence help to achieve individualized treatment. Ryu *et al.* identified seven overexpressed proteins and seven underexpressed proteins in GC by using a proteomics method [5,6]. Jang *et al.* Iso tried to

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identify biomarker candidates by analyzing proteome profiles [7]. Yasui *et al.* performed serial analysis of gene expression in order to search for other new biomarkers [8]. Therefore, only a few potential biomarkers have been documented, such as regenerating gene family members 4 [9], olfactomedin [10], resistin and visfatin [11]. Cancer can occur due to various factors [12][13][14]. There are several methods to treat cancer Siberian ginseng, perennial herb belonging to the Araliaceae family used in traditional medicines to treat hypertension, thrombus, inflammation and cancer [15][16][17]. Several studies have revealed that naturally occurring medicinal plants inhibit the growth of various cancers [18][19][20]. There are studies that show the treatment of cancer using nanotechnology [21][22]. There were several studies done related to developing effective drugs against cancer and diabetes in our department [23][24][25][26].

DNA microarray analysis is one among the latest technologies in the field of cancer genetics research and can measure the expression levels of large numbers of genes simultaneously. It is represented by a collection of microscopic DNA spots attached to a solid surface [27]. Microarrays contribute a means of measuring changes in expression of all the genes or alternatively spliced mRNAs at the same time. Previously we have focused our research on various invitro and invivo studies. [28–47] We have currently shifted our focus to this retrospective analysis. This ability provides researchers with immense potential to conduct experiments that were impossible just a few years ago, and also allows unique challenges in experiment design and data analysis [48].

Classification of microarray systems

Microarray technology is generally used for gene expression profiling. In addition to gene expression analysis, the microarray technique has been improved for mutation or SNP detection using allele-specific hybridization comprising oligonucleotides. This category of microarray is called an 'oligonucleotide microarray' [49]. Oligonucleotide microarrays can detect mutations or SNP by differentiating between perfectly matched and mismatched signals. Commercially available oligonucleotide microarrays consist of the *p53* GeneChip and HuSNP arrays from Affymetrix, that were manufactured using photolithographic techniques [50]. Numerous oligonucleotide microarrays have been developed for detecting *K-ras* mutations, methylation and *RET* mutations in MEN2 (Multiple Endocrine Neoplasia type 2) syndromes [51]. Oligonucleotide microarrays exhibit a high sensitivity in terms of point mutation detection and can function as fast as reliable genetic devices, which simplifies detecting mutations [52].

cDNA microarrays are efficient in profiling gene expression patterns of tens of thousands of genes in one experiment. DNA targets, in the form of 3 expressed sequence tags (ESTs), are arrayed onto glass slides (or membranes) after which they are probed using fluorescent or radioactively labelled cDNAs. Although both cDNA and oligonucleotide arrays are capable of analysing patterns of gene expression, fundamental differences exist between the two ways of approach [53].

Importance of Biomarker

A biomarker is described as a "characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" [54]. Therefore, a biomarker can be a blood test, a response to a validated questionnaire, or radiographic measurements, and its objective is to guide patient management. Biomarkers may be prognostic, predictive, or surrogate in nature, or they can provide different roles. A prognostic biomarker contributes evidence about a patient's eventual outcomes from a disease independent of a given therapy, whereas a predictive biomarker evaluates the possibility of response/benefit to a particular therapy in a specific context [55]. Protein biomarkers in the serum guarantees for noninvasive disease detection and classification. The discovery of new and clinically productive protein biomarkers would be supported by highly efficient protein detection methods [56]. As biomarkers are used in diagnosing and treating cancer, some other methods in treating cancer

Applications of Microarray

The use of microarrays can be extremely effective both in understanding the fundamental biology and in the treatment of cancer. Important applications comprise of: (a) development of a more global understanding of the gene expression changes that result in malignant progression; (b) exploring diagnostic and prognostic indicators and biomarkers of response; (c) discover and validation of new molecular targets; (d) provision of a better understanding of the molecular mode of action during lead identification and optimisation; (e) prediction of potential side-effects in the course of preclinical development and toxicology studies; (f) verification of the molecular mode of action during hypothesis-testing early clinical trials; (g) recognising genes involved in conferring drug sensitivity and resistance; and (h) prediction of patients more likely to benefit from the drug and use in general pharmacogenomic studies [57].

Role of Microarray in Cancer

The use of gene expression microarrays is especially important in cancer. This is because the

accumulation and combinatorial effects of abnormalities that drive the initiation and malignant development of cancer result from the altered sequence or expression level of cancer-causing genes. These genetic abnormalities, which could be inherited or acquired, result in the 'big six' hallmark characteristics of cancer, namely: (a) self-sufficiency in proliferative growth signals; (b) insensitivity to growth inhibitory signals; (c) evasion of apoptosis; (d) acquisition of limitless replicative potential; (e) induction of angiogenesis; and (f) induction of invasion and metastasis [58][59]. A study showed that using microarray techniques which allowed the analysis of gene expression on a large scale it was shown that the genetic profile of metastasis in a person is similar to the corresponding primary tumor. Thus, it was possible to define the gene expression profile of the tumor at diagnosis which was shown to correlate with prognosis and metastasis formation [27]

DNA micro-array-based tumor gene expression profiles have been developed and are used in the tumor diagnosis and classification. Many studies have indicated that a subset of genes is characteristically expressed in ovarian cancers [60], oral cancers [61], melanomas [62], colorectal carcinomas [63] and prostate carcinomas [64][65]. Molecular classifications using DNA micro-array is very useful for the determination of primary sites in metastatic carcinomas [66] as well as the classification of soft tissue sarcomas [67]. Gene expression profiles by DNA microarray analysis exhibit significant intertumoral variations in the same histologic type of tumors. It has been documented that DNA micro-array analysis can be a new approach for the classification of soft tissue tumors [67].

CONCLUSION

The current review focuses on DNA microarray-cDNA and oligonucleotide microarray. There are other different types of microarray- tissue microarray, protein microarray etc. The present study focuses on applications of microarray related to cancer, applications other fields were not covered. In future, further review can be done in detail including other types of microarray as well as applications. Microarray technologies are becoming more important in cancer research hence microarrays are more important for diagnostic classification of cancer.

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