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Importance of Microarray Technology and its Applications

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ABSTRACT : DNA Microarray is one such technology which enables the researchers to investigate and address issues which were once thought to be non traceable. This technology has empowered the scientific community to understand the fundamental aspects underlining the growth and development of life as well as to explore the genetic causes of anomalies occurring in the functioning of the human body. Microarrays are significant because they possess a huge number of genes and also because of their portable size. This review addresses the potential uses of array data. We first cover the history of microarrays and the antecedent technologies that led to their development. We then discuss the methods of manufacture of microarrays and the most common biological applications.

Introduction

Molecular Biology research evolves through the development of the technologies used for carrying them out. It is not possible to research on a large number of genes using traditional methods. DNA Microarray is one such technology which enables the researchers to investigate and address issues which were once thought to be non-traceable. An array is an orderly arrangement of samples where matching of known and unknown DNA samples is done based on base pairing rules. A typical microarray experiment involves the hybridization of an mRNA molecule to the DNA template from which it is originated (Aguan et al., 2000; Berchuck et al., 2004). One can analyze the expression of many genes in a single reaction quickly and in an efficient manner. Many DNA samples are used to construct an array. The amount of mRNA bound to each site on the array indicates the expression level of the various genes. This number may run in thousands. All the data is collected and a profile is generated for gene expression in the cell. DNA Microarray technology has empowered the scientific community to understand the fundamental aspects underlining the growth and development of life as well as to explore the genetic causes of anomalies occurring in the functioning of the human body (Bumgarner, 2013).

As many important diseases can be traced down to the gene level, a long-standing research problem is to identify specific gene expression patterns linking to metabolic characteristics that contribute to disease development and progression. The microarray approach offers an expedited solution to this problem. However, it has posed a challenging issue to recognize disease-related genes expression patterns embedded in the microarray data. In selecting a small set of biologically significant genes for classifier design, the nature of high data dimensionality inherent in this problem creates substantial amount of uncertainty.

Importance of Microarray Technology

Since a microarray technology has the potential to examine the expression of several genes at a time, it promises to revolutionize the way scientists study gene expression. Microarrays are significant because they possess a huge number of genes and also because of their portable size. Microarrays are therefore, helpful when one is interested in surveying a large number of genes swiftly or when the sample of interest is small. Microarrays can also be helpful to assay gene expression within each sample or to compare gene expressions of two different cell types or tissue samples, for example, healthy and diseased tissue. DNA microarrays can be used to compare the level of gene transcription in clinical conditions in order to: 1) identify diagnostic or prognostic biomarkers; 2) classify diseases (eg, tumors with different prognosis that are indistinguishable by microscopic examination); 3) monitor the response to therapy; and 4) understand the mechanisms involved in the genesis of disease processes. For these reasons, DNA microarrays are considered important tools for discovery in clinical medicine. Microarray is being used to detect the gene expressions in prostrate cancer, oral cancer, breast cancer, ovarian cancer, and other types of cancers.

Table 1: The history of DNA arrays

Date	Advantage	Reference
1975	DNA array was created with the colony hybridization method	Grunstein and Hogness, 1975
1979	The colony hybridization adapted to create ordered arrays	Gergen et al., 1979
1991	Using robotic systems to rapidly array clones from microtiter plates onto filters	Lennon and Lehrach, 1991
1996	Create reference sets of cDNAs and cDNA filter arrays for human	Lennon et al., 1996
1996	Create a method which allowed very high-density DNA arrays to be made on glass substrates	DeRisi et al., 1996
1996	Affymetrix arrays were being used to measure variation in the human mitochondrial genome	Chee et al., 1996
1996	The Inkjet printing technology and standard oligo synthesis chemistry to produce oligo arrays	Blanchard et al., 1996
1996-1997	Affymetrix developed a wide catalogue of DNA arrays for use in expression, genotyping and sequencing analysis	Lockhart et al., 1996; Wodicka et al., 1997; Chee et al., 1996; Hacia et al., 1996
2000	DNA array technology progressed rapidly as both new methods of production and fluorescent detection were adapted to the task	Ferguson et al., 2000; Michael et al., 1998; Steemers et al., 2000; Walt, 2000; Nuwaysir et al., 2002

Types of Microarrays

Microarrays can be broadly classified according to at least three criteria: 1) length of the probes; 2) manufacturing method; and 3) number of samples that can be simultaneously profiled on one array. According to the length of the probes, arrays can be classified into "complementary DNA (cDNA) arrays," which use long probes of hundreds or thousands of base pairs (bps), and "oligonucleotide arrays," which use short probes (usually 50 bps or less). Manufacturing methods include: "deposition" of previously synthesized sequences and "in-situ synthesis." Usually, cDNA arrays are manufactured using deposition, while oligonucleotide arrays are manufactured using in-situ technologies. In-situ technologies include: "photolithography" (eg, Affymetrix, Santa Clara, CA), "ink-jet printing" (eg, Agilent, Palo Alto, CA), and "electrochemical synthesis" (eg, Combimatrix, Mukilteo, WA). The third criterion for the classification of microarrays refers to the number of samples that can be profiled on one array. "Single-channel arrays" analyze a single sample at a time, whereas "multiple-channel arrays" can analyze two or more samples simultaneously. An example of an oligonucleotide, singlechannel array is the Affymetrix GeneChip (Tarca et al., 2006; Fu and Casey, 2005).

Depending upon the kind of immobilized sample used construct arrays and the information fetched, the Microarray experiments can be categorized in three ways:

Microarray Expression Analysis

The study of gene expression profiling of cells and tissue has become a major tool for discovery in medicine. Microarray experiments allow description of genome-wide expression changes in health and disease. The results of such experiments are expected to change the methods employed in the diagnosis and prognosis of disease in obstetrics and gynecology. In this experimental setup, the cDNA derived from the mRNA of known genes is immobilized. The sample has genes from both the normal as well as the diseased tissues. Spots with more intensity are obtained for diseased tissue gene if the gene is over expressed in the diseased condition. This expression pattern is then compared to the expression pattern of a gene responsible for a disease (Fu and Casey, 2005; Tarca, et al., 2006).

Microarray for Mutation Analysis

One of the many application areas of the microarray format is to genotype or detect disease-causing or disease-predisposing mutations in the human genome for diagnostics, carrier identification and pharmacogenetic profiling. For this analysis, the researchers use gDNA. The genes might differ from each other by as less as a single nucleotide base.

A single base difference between two sequences is known as Single Nucleotide Polymorphism (SNP) and detecting them is known as SNP detection. The recently developed single nucleotide polymorphism (SNP) array can be used to measure both DNA polymorphism and dosage changes. The development of single nucleotide polymorphism (SNP) arrays enables simultaneous detection of a large number of DNA polymorphic loci in a simple way. Further technical developments make SNP arrays capable of analyzing both signal intensity variations and changes in allelic composition in parallel. SNP arrays can

also detect both copy number changes and copy-neutral LOH (loss-of-heterozygosity) events. Fan et al. have provided a detailed review of the mechanism of different SNP genotyping methods (Xueying, et al., 2007; Cinoo, et al., 2012).

Comparative Genomic Hybridization

In recent years, however, researchers have increasingly turned to newer cytogenetic techniques. One such method is comparative genomic hybridization (CGH), which provides an alternative means of genome-wide screening for copy number variations. First developed to detect copy number changes in solid tumors, CGH uses two genomes, a test and a control, which are differentially labeled and competitively hybridized to metaphase chromosomes. In an attempt to overcome some of the aforementioned limitations associated with traditional CGH, investigators have developed a newer method that combines the principles of CGH with the use of microarrays (Theisen, 2008). Instead of using metaphase chromosomes, this method—which is known as array CGH, or simply aCGH—uses slides arrayed with small segments of DNA as the targets for analysis (Lucito et al., 2003).

Applications of DNA Microarray Technology

Disease diagnosis

Microarray technology will help researchers to learn more about many different diseases, including heart disease, mental illness and infectious diseases, to name only a few. In the past, scientists have classified different types of cancers based on the organs in which the tumors develop. With the help of microarray technology, however, they will be able to further classify these types of cancers based on the patterns of gene activity in the tumor cells. Researchers will then be able to design treatment strategies targeted directly to each specific type of cancer (Bumgarner, 2013; Cinoo, et al., 2012).

Drug discovery

Medicinal chemistry has increasingly employed microarrays to identify both key target genes and gene networks that can regulate the effectiveness of drugs. One important application of DNA microarray technology, within the context of drugs effectiveness and safety evaluation studies, is its use as a screening tool for the identification of biochemical pathways, potential targets for novel molecular therapeutics, for the identification of molecular mechanisms of toxicity and to understand and predict individual drug sensitivity and resistance (Bumgarner, 2013; Roman, 2008).

Toxicological Research

One important application of microarray technology, within the context of neurotoxicological studies, is its use as a screening tool for the identification of molecular mechanisms of toxicity. Such approaches enable researchers to identify those genes and their products (either single or whole pathways) that are involved in conferring resistance or sensitivity to toxic substances (Bumgarner, 2013; Vrana, et al., 2003).

Immunology

DNA microarray technology has been applied in immunological researches such as the development, maturation, activation and differentiation of immune cells, the regulation of immune responses, the molecular mechanism of allergy, the relation between phenotype and gene expression, and immunological pharmacology, etc. It has deepened our perception of the immune system. It will as well be helpful in the research of the regulative mechanism of traditional Chinese medicine (TCM) toward immune cells and immune responses, the therapeutic mechanisms of TCM toward allergy, the standardization of differentiation of syndrome and herbal pharmacology, etc (Ma and Zhang, 2004; Fu and Casey, 2005; Bumgarner, 2013).

Conclusion

Microarrays are able to simultaneously monitor the expression levels of thousands of genes. Such gene expression information can be used in medicine for comparing clinically relevant groups (eg, healthy vs diseased), uncovering new subclasses of diseases, and predicting clinically important outcomes, such as the response to therapy and survival. However, the improved understanding that can be gained with this technology is critically dependent on the quality of the analytical tools employed. This article was written to provide the obstetrician and gynecologist with an introduction to the subject, as well as alert the readership about some of the potential pitfalls associated with the analysis of these large datasets. The literature cited provides additional sources to improve the understanding of this complex subject.

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