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DNA Microarray and its Applications in Disease Diagnosis

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Abstract: ***With the growing data on genome sequences from various species from man to bird, insect to elephant curiosity of scientific world for understanding the downstream happenings of every activity of living beings has also increased. It is not possible to study all intricate pathways by using regular PCR –techniques. DNA microarray is one of the best technique used for global gene expression analysis. By using DNA microarray we can study the basic up and down regulation of the genes involved in a certain pathways, in one single reaction. The technique has immense application in the field of disease diagnosis, cancer markers, developmental biology, metagenomics and pathway analysis.***

Keywords: microarray, gene expression, genome, transcriptome

1. Introduction

With rapid advances in the bioinformatics, computational biology, robotics and fabrication of high quality glass slides, microarray technology is increasingly being used in different laboratories all over the world. A microarray is a collection of microscopic spots arranged in an array on grid- like format and attached to a solid surface or membrane. Each individual spot is present at a precisely defined location on the substrate. In DNA microarray these spots are single stranded DNA fragments. These spots are known as *probes*. These probes hybridize with specific nucleic acid sequence called *target* which is labeled with a fluorescent dye. The extent of binding between the target and probe is quantified by measuring the signal emitted by labeling dye when scanned. Thus, utilizing the same basic principle of decades old southern blotting, microarray analysis permits the simultaneous detection and expression studies of several genes on a single chip. Two important DNA microarrays that are commonly being used are *oligonucleotide* microarray and *spotted* microarray.

Oligonucleotide microarray They have a typical probe length of 18 to 30 mers, are highly specific, hybridize with only single sample and thus give absolute expression level of the sample concerned. In this method arrays are constructed by synthesizing single stranded oligonucleotides in situ by using photolithographic technique to generate high density (> 2 80 000 features) microarray chips. In this system collection and storage of cloned DNA and PCR product is not required.

Spotted microarray These microarrays have a probe length of 500 bp to 1000 bp (c- DNA) or 25 to 100 mers (oligose) or fragments of PCR products. In this system two samples are combined on a single slide, thus give a relative expression level on each spot. They are not as specific as oligonucleotide microarray. This method is relatively low cost than oligonucleotide microarray and primary sequence information is not needed to print a DNA sequence.

Greene chip It is a panmicrobial microarray comprising a large number (about 29, 455 sixty mer) of oligonucleotide probes for vertebrate viruses, bacteria, fungi and parasites. As clinical symptoms are rarely specific for single pathogen, unbiased multiplex assays are essential for differential diagnosis. These Greene chip microarrays have the potential to allow highly multiplex and unbiased diseases surveillance. These chips are especially useful when >1 pathogenic agent is endemic in the region with outbreak caused by different agents which overlap with time and geography.

2. Applications of DNA Microarray

DNA microarray has a broad applicability that includes its usefulness in toxicology, evolution biology, drug designing and production, diseases characterization, diagnostics, forensic etc.

3. Use of DNA Microarray in Diagnostics and Theraputics

Early diagnosis of an infectious disease is always desirable to prevent its spread among livestock species and thus reduce the economic losses.

Microarray technology has been utilized in the identification of various infectious disease pathogens such as Avian influenza (H5N1), FMD, Viral Hemorrhagic Fever (Marburg virus), SARS virus etc. University of Florida and Centre of Disease Control US, have jointly developed an improved version of Flu chip that requires only matching sequences from a single gene of the influenza virus (matrix) which mutates more slowly than other 2 genes in the old version (hemagglutinin and neuraminidase genes). This chip only needs 15 sequences from a single gene to reliably identify avian influenza.

Greene chip microarrays analysis has been utilized for the investigation of samples from patients with Viral Hemorrhagic Fever like syndrome for its differential diagnosis from malarial cases. One group conduced research

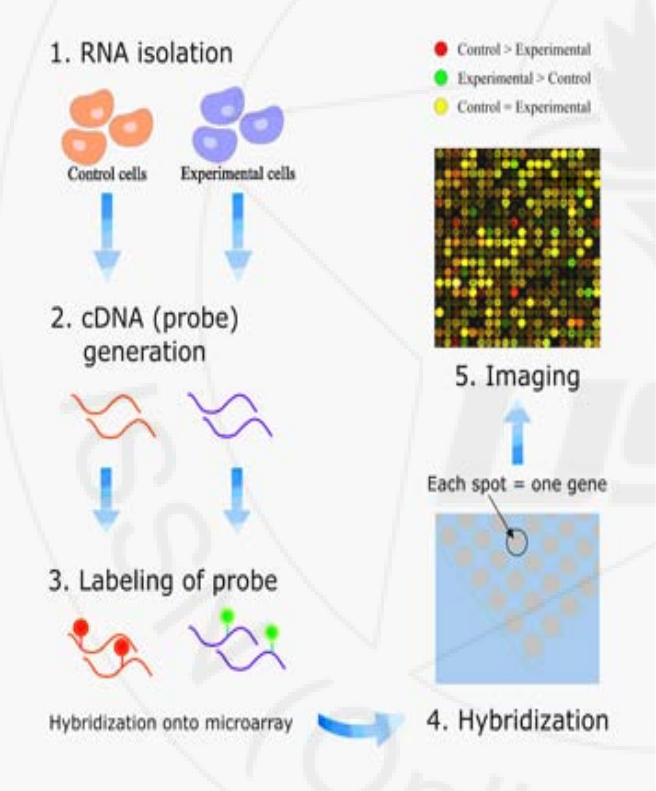
on the study of the pathogenicity of Candida albicans, a human fungal pathogen. Microanalysis revealed that Yhb1 gene was highly expressed during the fungal infection to detoxify the nitric oxide.

A large no. of microarray related studied had been carried out to characterize diseases cells in comparison to healthy cells. The pathogenicity of coxasackievirus B3 (CVB3) was examined by comparing the murine heart infected with this virus against the non infected murine hearts.

Microarray was constructed to specifically probe FMD (SNPs).

Workers also used microarrays to confirm the previous classifications of non-pathogenic, low pathogenic and highly pathogenic types of 94 different types of *Yersinia enterocolithica* strains.

Microarray technique was used by researchers to develop a pathway responsible for the regulation of expression of cyclooxygenase-2 (COX2), a pro- inflammatory protein associated with arthritis and pain.



4. DNA Microarray in Cancer Diagnosis

Microarray generated expression data can be used as a correlate of a particular cell phenotype. Such defined and specific profiles of gene expression are referred to as "*molecular signatures*". Using DNA microarray, Martin and collegues were able to identify 170 genes differentially expressed in invasive breast tumor cells. On the basis of expression profile of the marker gene, molecular signatures associated with either good or poor prognosis were generated. Same approach is being used to improve diagnosis of subtypes of tumor with different levels of malignancies. Molecular signatures have been reported to distinguish low and high grade astrocytomas which are the main type of tumor in CNS.

5. Future Perspectives

With the upcoming of microarray technology numerous genetic markers and their functions will be identified in shortest possible time. The information can be utilized in the medical research for the disease diagnosis as well as the production of the smart drugs. However, the bulky data generated by the microarray analysis is often difficult to deal with. The useful data should be properly screened as per the requirement. Further, the experiments should be confirmed independently with other techniques like northern blotting, RT-PCR and protein expression before giving the concluding remark.