

PREPARATION OF MICROARRAY FOR DISEASE DETECTION - A SURVEY ON DIFFERENT METHODS

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Abstract- Microarray is a pattern of ssDNA probes which are immobilized on a surface called a chip or a slide. It is used to detect the expression of thousands of gene at the same time. Microarrays (biochip) plays an important role in the drug discovery. The biochip is used to monitor changes in gene expression in response to drug treatments and also used to examine the response of the host against pathogen. The oligonucleotide microarrays provides a rapid, specific and high throughput means for the detection and identification of the food-borne pathogens. In this paper we have described microarray-based tests or methods for detecting the various kinds of diseases. By using several methods and tools like allergen microarray one can screen the serum IgE reactivity. cDNA microarrays has been developed for analysing estrogen responsive genes and in detecting anti hormone therapy. Evaluation of the potential of pathogenicity is determined by detection of a range of virulence factors and serotype determination. Micro RNA identifier array used for the detection of various type of micro RNA in human or for simultaneous detection and genotyping of different virus types in a single reaction.

Keywords- Microarray, DNA, RNA, Gene

1. INTRODUCTION

Microarray is multiplex lab on a chip. It is a pattern of ssDNA probes which are immobilized on a surface called chip or a slide. A microarray is 2D array on a solid substrate that assays large amounts of biomolecules, using high throughput screening miniaturized, multiplexed and parallel processing and detection methods. A glass slide or a silicon thin film cell is used as a substrate. This substrate have a collection of microscopic DNA spots attached to a solid surface. The concept of microarrays was first introduced in antibody microarray by Tse Wen Chang in 1983. To detect specific DNA or RNA in sample, microarray chip is arranged as check board of 10^5 or 10^6 spots of features. Different types of microarrays has been created such as antibody microarray, DNA microarray, Protein microarray, and Sandwich ELISA microarray. A microarray is a laboratory tool which is used to detect the expression of thousands of gene at the same time. Microarrays (biochip) plays an important role in the drug discovery. The biochip is used to monitor changes in gene expression in response to drug treatments and also used to examine the response of the host against pathogen. DNA microarrays rapidly generates the information necessary for the identification and validation of the novel therapeutic targets. The expression levels of large numbers of genes simultaneously or genotype multiple regions of a genome is carried out using DNA microarrays. Each DNA spot contains picomoles of a specific DNA sequence, known as probes. These can be a short section of a gene or other DNA element that are used to hybridize target. cDNA are the clones derived from the genomic library that was constructed for the determination of the complete genome sequence used as target. To determine relative abundance of nucleic acid sequences in the target Probe, target hybridization is detected and quantified by detection of fluorophore, silver, or chemiluminescent labelled targets. Detection of contamination in animals and foodstuffs could be traced quickly using this tool. Micro RNA identifier array used for the detection of various type of micro RNA in human or for simultaneous detection and genotyping of different virus types in a single reaction, is commercially available. Greiner Bioone PapilloCheck DNA chip micro array assay is used. It is clear that macrophages are versatile cells and in fishes they play a host defence of innate immune. Macrophage transcriptome in sweet fish can be studied using RNA sequencing, and using the sequences the microarray then developed. Screening of special tissue or cell response to a stimulus can be assayed using microarrays. Serum IgE reactivity can be screened by using a tool called allergen microarrays. The cross reactivity patterns and dominating binding allergens were identified by using allergen microarray. IgE mediated cross reactivity among various allergenic sources and dominating allergenic sources can be identified by using allergen microarray. Sometimes food borne pathogenic microorganisms are responsible for the health problems and also life threatening for people throughout the world. Several agents like bacteria, fungi, parasites, and other chemical toxins are also responsible for food borne diseases. E.coli, Salmonella, Shigella, Bacillus, Listeria monocytogenes, Vibrio cholera are the most important food borne bacterial pathogens. PCR is an important tool for pathogen detection, but at the same time it is not possible to accurately identify PCR products without downstream sequencing, southern blotting or dot blotting. Hence microarray technology is developed and the advantage of this technology is high performance, miniaturization, ease of automation, ability to process samples in parallel.

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2. REVIEW OF LITERATURE

Zheng Yi-wuet.al., in their paper have described that Allergen micro-arrays are powerful tools for screening of serum IgE-reactivity [1]. In their study allergen micro-arrays were used to identify dominating IgE-binding allergens and cross-reactivity patterns among selected Chinese allergy patients. They concluded in their paper that the first allergen micro-array analysis of sera from Chinese allergy patients clearly confirmed that group 1 and group 2 are the major allergens for house dust mites. Darrell P. Chandler et.al., in their paper described microarray-based tests that combine solution-phase amplification chemistry and microarray hybridization within a single microfluidic chamber [2]. In their paper they have demonstrated that single-step, integrated, closed-amplicon gel element microarrays that are as simple and uncomplicated as many real-time PCR tests can address microarray work flow challenges and clinically relevant infectious disease diagnostic problems. A Inoue et.al., in their paper described that estrogen plays an important role in many physiological events including carcinogenesis and the development of human breast cancer [3]. They first carried out estrogen-responsive expression profiling of approximately 9000 genes in estrogen receptor-positive human MCF-7 breast cancer based on the results, estrogen-responsive genes were selected for production of a custom-made cDNA microarray. They finally in their paper concluded that some genes were suggested to be induced or repressed by estrogen in one cell line or several cell lines. Further analysis will be needed to clarify the functions of these genes. Xin-Jiang Lu et.al., in their paper have described that macrophages play an important role in first-line host defense of innate immune in fishes[4]. In their paper they concluded that their results contribute to understanding the specific regulation mechanism of LECT2 in macrophage activation, and the combination of transcriptome analysis and microarray assay is a good method for screening a special tissue or cell response to a stimulus or pathogen in non-model fish species. Bugarelet al., in their research paper discussed about micro-array development, based on the GeneDisc array for the genetic identification of 12 O-types and 7 H-types of Shiga toxin producing *Escherichia coli* including the most clinically relevant Enterohemorrhagic *E. coli* serotypes [5]. O antigens and H-types genes selected for genetic identification showed a high specificity and concordance with serology. The micro-array also had a high specificity for enterohemorrhagic *E. coli* associated virulence factors, including Shiga toxins 1 and 2, intimin, enterohemolysin, serine protease, catalase peroxidase the type II secretion system, subtilase cytotoxin, autoagglutinating adhesin and type III secreted effectors encoded in the genomic islands OI-122 and OI-71. The *eae* gene was detected in all typical enterohemorrhagic *E. coli* strains. The common virulence plasmid associated genes in Shiga toxin-producing *Escherichia coli* strains were *katP*, *espP*, and *etpD*. This supports their association with virulence. This array constitutes a valuable approach for the identification of Shiga toxin-producing *Escherichia coli* strains with a high potential for human virulence. This report demonstrated that the GeneDisc array can be used for the fast and simultaneous detection of several serotypes and virulence factors of Shiga toxin producing *Escherichia coli*. This facilitates molecular risk assessment of the potential virulence of Shiga toxin-producing *Escherichia coli* isolates.

Sun, Y., Koo, S., et al., in their research paper discussed about MicroRNA expression using microarray [6]. MicroRNAs are believed to play important roles in developmental and other cellular processes by hybridizing to complementary target mRNA transcripts. Determining the pattern of global miRNA expression levels in mammals and other higher eukaryotes is essential to understand both the mechanism of miRNA transcriptional regulation as well as to help identify miRNA regulated gene expression. The microarray used here is a novel, selective and sensitive approach to monitor miRNA expression in mammalian cells and tissues. They have identified miRNAs that are selectively expressed in skeletal muscle, heart and kidney. The results have been validated by subsequent confirmation of mir expression using northern blot analysis. Major differences in the expression of mir have been detected in samples from diverse sources, suggesting highly regulated mir expression, and specific gene regulatory functions for individual miRNA transcripts. Five different miRNAs were found to be preferentially expressed in human kidney compared with other human tissues. By performing comparative sequence analysis, they have proposed the presence of a putative transcriptional regulatory mediator for miRNAs in kidney. Use of this array based approach will lead to a greater understanding of recently identified class of gene regulating RNA molecules in future.

Bronet al., in their research paper discussed about determining the global transcriptional response in a food-associated lactic acid bacterium during bile stress using a microarray [7]. Clone based DNA micro arrays were used to describe the global transcriptional response of *Lactobacillus plantarum* towards porcine bile. Comparison of differential transcript profiles obtained during growth of *L. plantarum* on plates with and without bile revealed 28 and 62 putative genes, of which the expression was at least 2 to 5 fold up or down regulated by bile, respectively. Approximately, 50% of these genes appeared genetically linked, and 12 bile responsive gene clusters were identified. Typical stress related functions, including glutathione reductase and glutamate decarboxylase, involved in oxidative and acid stress encoded by seven of the identified bile responsive genes and gene clusters respectively. 14 bile-responsive genes and gene clusters were identified that encode proteins and are located in the cell envelope, including the *dlt* operon and the *F1F0* ATPase. The identification of a relatively high number of genes encoding cell envelope functions indicates a major impact of bile acids on the integrity and functionality of the cytoplasmic membrane and cell wall. The data presented here provide valuable clues towards the defence mechanisms that play a role during bile stress in *L. plantarum*.

Jones, J et al., in their study evaluated the Greiner Bio one PapilloCheck micro array assay for detection of Human Papillomavirus in comparison with Hybrid Capture II (hc2) and PCR-enzyme immunoassay (PCR-EIA) using the GP5/6+ primers [8]. Total 878 Samples from a cytologically defined population were analysed and 187 samples also had histology information. On all three platforms 674 out of 878 samples gave a consistent result. The obtained genotype results by

PapilloCheck and PCR-EIA were compared and 94% were consistent. The poor Kappa agreement for detection of high risk type 35 with all inconsistent results being HR positive by PCR-EIA assay but negative on the PapilloCheck platform was the main difference. When HR HPV positive samples were linked with clinical result there was no statistically significant difference between the performance of each assay. PapilloCheck detected the highest number of HR Human Papillomavirus infections in samples with histology confirmed as CIN1, CIN2 and CIN.

Debouck, C. and Goodfellow, P.N., in their paper have worked on the several gene expression patterns in normal cells and tissues, pathogens, diseases, gene expression in response to drug treatments, model systems [9]. As per their study the expression pattern of the gene provides indirect information about the function. They revealed that the expression data have their own limitations, and mRNA may not reflect the protein levels and the expression of protein always may not have the physiological consequences.

Cheung, S.Wet al., have developed microarray for the clinical diagnosis of chromosomal disorders using the large insert genomic DNA clones as the targets for CGH [10]. The purpose of their study was to develop and validate the CGH biochip that would have been provided an alternative to the telomere FISH (fluorescence in-situ hybridization) as well as the disease specific FISH.

Keramaset al., according to their study, have developed DNA microarray for the rapid detection of *Campylobacter* to the subspecies level, mainly *C.jejuni* and *C.coli* [11]. They have described a new approach for the detection of bacteria in some of the specific *Campylobacter* spp. They have clearly indicated that this method has high potential to be basis of automated mass screening system.

Wang et al., in their paper, have developed the oligonucleotide microarray which is a powerful tool for the detection and identification of food-borne bacterial pathogens [12]. They have described that the specific target spectra produced by the gene-chip may be eventually expanded through the addition of purely designed oligonucleotide probes into a microarray. They also have revealed that the accuracy may also be improved by increasing as well as readjusting the oligonucleotide probes in the array.

3. CONCLUSION

In summary, we have concluded that the microarrays are mainly used biosensors for the disease detection. In our survey, every methods and analysis in which the biochips are used in disease detection gives the best output. DNA microarrays rapidly generates the information necessary for the identification and validation of the novel therapeutic targets. Microarray technology is developed and the advantage of this technology is high performance, miniaturization, ease of automation, ability to process samples in parallel. In every methods which is used in analysis and detection the microarray based test shows good results. Combination of solution-phase amplification chemistry and microarray hybridization within a single microfluidic chamber can be described by microarray based tests. For reducing the number of steps and minimizing the potential for a sample or amplicon cross contamination, the biochemical approach improves microarray workflow. Use of array based approach will lead to a greater understanding of gene regulating RNA molecules in future.

4. REFERENCES

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