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DNA Chip, Microarray Revolutionize Genomic Analysis

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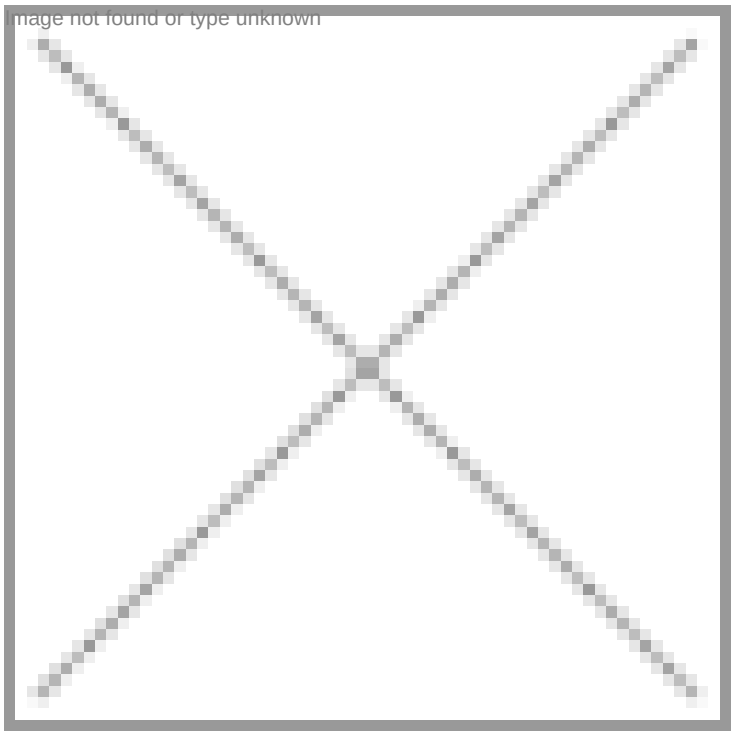

DNA Chip, Microarray Revolutionize Genomic Analysis

DNA microarray has emerged as a prime technology for the performance of gene expression analyses. Combined with bioinformatics and other advanced technology, it offers numerous applications with absolute accuracy.

Availability of whole genomic sequences of many organisms have created the need for high throughput analysis of gene expression patterns and the DNA chip and microarray technology have revolutionized functional and genomic analysis at this level. This technology uses a single chip to monitor the whole genome so that researchers can have a better picture of the interactions among thousands of genes simultaneously. In the past several years, this new technology has attracted several biologists as it generates large amount of data in little time and facilitates the quantification of thousands of genes from many samples

DNA microarrays are used to examine the gene expression changes in cancer patients. Tumor profiling, using DNA microarrays, allows the analysis of the development and the progression of complex diseases. The technology allows scientists to examine targets for drug discovery, potential diagnostic and prognostic biomarkers for many complex diseases; detect viruses and other pathogens from blood samples and thus evolved as a pathogen detection method.

DNA microarrays are recently used to identify inheritable markers, and therefore used as a genotyping tool. SNP chipsbased on DNA microarray technology allow the high throughput profiling of single nucleotide polymorphisms using a chip or array approach. This has allowed polymorphisms to be more quickly assayed and also their relevance to disease to be easily determined. Today, the technology has emerged as an indispensable research tool for gene expression profiling and mutation analysis.

The beginning

Microarray technology has evolved from southern blotting, where fragmented DNA is attached to a substrate and thenprobed

with a known gene or fragment. The use of a collection of distinct DNAs in arrays for expression profiling was first described in 1987, and the arrayed DNAs were used to identify genes whose expression is modulated by interferon. These early gene arrays were made by spotting cDNAs onto filter paper with a pin-spotting device. The use of miniaturized microarrays for gene expression profiling was first reported in 1995, and a complete eukaryotic genome (Saccharomyces cerevisiae) on a microarray was published in 1997. Affymetrix further developed DNA microarrays which were based on high-density 25-mer oligos from human cDNA sequences. Microarrays were originally designed to measure gene expression levels of a few genes.

Terminologies that have been used in the literature to describe this technology include biochip, DNA chip, DNA microarray, and gene array. Affymetrix, Inc. owns a registered trademark, GeneChip, which refers to its high density, oligonucleotide-based DNA arrays.

Today, there are more than 1,000 microarray core facilities are available and over 100 service companies are offering microarray processing services worldwide. India is a late entrant to the microarray world. However, rapid progress in the last few years has resulted in establishment of over 50 microarray facilities and five commercial microarray service providers in India.

Application advances

As more information accumulates, scientists could able to use microarrays to ask increasingly complex questions to perform more intricate experiments. With new advances, researchers are able to better understand the functions of new genes based on similarities in expression patterns with those of known genes. Ultimately, these studies promise to expand the size of existing gene families, reveal new patterns of coordinated gene expression across gene families, and uncover entirely new categories of genes. Furthermore, because the product of any one gene usually interacts with those of many others, our understanding of how these genes coordinate will become clearer through such analyses, and precise knowledge of these inter-relationships will emerge. The use of microarrays may also speed up the identification of genes involved in the development of various diseases as it enables scientists to examine a much larger number of genes. This technology will also help in the examination of integration of gene expression and function at the cellular level, reveals how multiple gene products work together to produce physical and chemical responses for both static and changing cellular needs.

Developing new protein arrays and constructing miniaturized flow-through systems, which can potentially take thistechnology from the research bench into industrial, clinical and other routine applications, exemplify the intense developments that are now ongoing in this field. Recent growth in the field of protein microarray shows the potential applications of enzyme–substrate, DNA–protein and different types of protein–protein interactions. The technology is now more heavily regulated in terms of the bioinformatics, which has led to the generation of more credible results.

Rini Mukherjee Saxena, senior product manager, Agilent Technologies said, ''Many studies have focused on the methylation state of specific genomic sites that are thought to play important roles in cellular processes. Conventional methods of analyzing this event are labor intensive, low-throughput and expensive. Microarray-based methods have evolved as powerful high-throughput analysis tools capable of detecting and mapping DNA methylation changes on a previously unachievable genome-wide scale."

Other researchers in the field expect that DNA chips will enable clinicians and in some cases even patients to quickly and inexpensively detect the presence of a whole array of genetically based diseases and conditions, including AIDS, Alzheimer's disease, cystic fibrosis, and some forms of cancer. Moreover, the technology could make it possible to conduct widespread disease screening

cost-effectively, and to monitor the therapies more effectively. So far, only a few companies have commercialized DNA-chip products, and the barriers to market entry remain great.

Challenges

Microarray technology is an expensive technology in terms of cost of required equipment, reagents and trained manpower. The technology is rapidly advancing; frequent upgradation of machines and methods becomes a major bottle neck in maintaining a microarray lab.

The major hurdle in the efficient utilization of microarray technology is the lack of trained manpower to analyze themicroarray data. Expertise in spread sheet and database operations and analysis packages are essential for efficient statistical analysis of data and to find significant patterns.

As DNA-chip companies prepare to bring their products to market, they have to face major technological, manufacturing and regulatory challenges. The technology trade-offs involve finding ways to increase the number of arrays on a single chip, as well as increasing the rate of production to meet expected demand.

The main challenge involves achieving all these market-oriented parameters at a cost that supports a commercially acceptable price. In a tight managed-care marketplace that places a premium on technologies that can either show quick savings or more-efficient results, some analysts say that such unit prices will limit the growth of the DNA-chip market.

Future

Microarray technology offers a ray of hope to personalized drugs and molecular diagnostics as it enables global views of biological processes. With technical development that offers increased sensitivity, microarray technology is expected to

become an indispensable tool in the fields of biology, biotechnology, drug discovery, and other application areas. If DNA microarray is used for the development of pharmaceutical products, it can considerably reduce the cost and time for the entire process of drug discovery and development, and can also contribute in developing personal drugs. Although this marketplace is in its infancy, with considerable challenges remaining to be overcome, the speed with which manufacturers are progressing toward commercialization will soon make DNA chips a viable alternatives to traditional chemical assays. Indeed, manufacturers hope that within a decade they will usher in a new era in diagnosis and treatment for diseases and conditions that have genetic origins.

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