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Microarray technology to the fore

06 November 2007 | News

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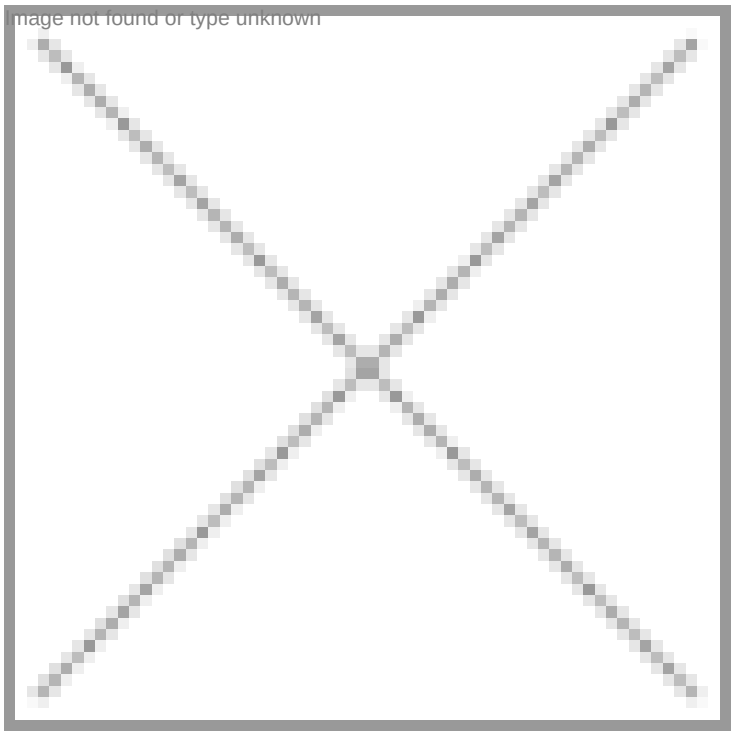

Microarray technology to the fore

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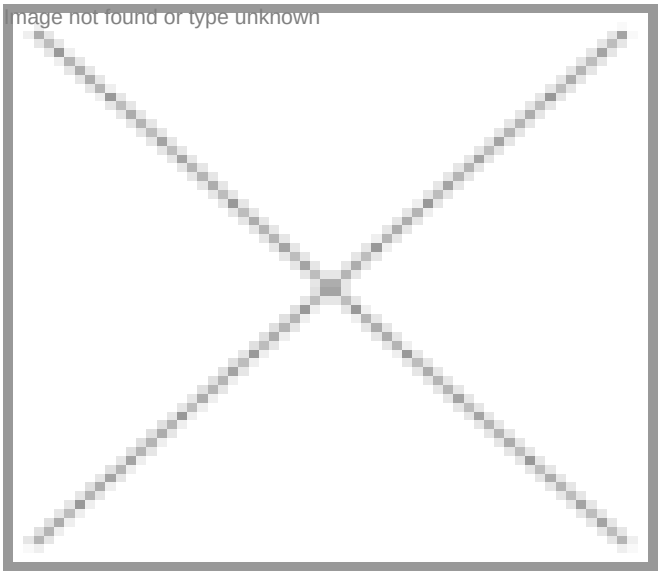

The microarray industry has evolved very rapidly from providing highly specialized techniques for a few genetic researchers to becoming a laboratory standard in molecular biology and clinical research. Because of the phenomenal growth, several research groups have started producing nanoarrays, in which thousands of binding sites can be printed into the area of a single conventional microarray spot. Novel, high-throughput methods for expressing and purifying proteins can also help companies build vast libraries of recombinant proteins to place on chips.

Microarrays

Microarrays are small pieces of glass dotted with thousands of strands of DNA, each of which corresponds to a specific gene in the genome. They are also known as DNA chips or biochips. In a single experiment, microarrays can measure genome-wide differences between diseased and healthy cells.

It is a fast, new tool for acquiring information. The advent of microarray has allowed toxicologists to analyze the differential expression of thousand of genes in a single experiment quickly and efficiently that were not possible with the conventional methods used in toxicology.

A DNA chip is made of many different DNA sequences stuck to a flat surface. Each spot on the surface contains a different sequence. A DNA microarray allows to probe a solution for thousands of different sequences all at once. For a particular experiment, a researcher would place a sample of diseased tissue, tagged with fluorescent dye onto a gene-laden chip, which is subsequently read by the scanner. Should any DNA in the sample match any of the genes on the chip, that part of the chip would light up, providing clues about the role of that specific gene in a particular disease. This means they can look for millions of DNA sequences in one go.

Emergence of microarray technology or biochips has revolutionized and added a new dimension to diagnostics technology and there has been a great excitement amongst the medical fraternity regarding its implications on human health.

Microarray technologies are likely to find significant scope in genomics and proteomics, with miniaturization enabling high-throughput processing. The applications they cover include genotyping, mutation screening, gene expression, and protein-interaction studies. DNA microarray studies promise to expand the size of existing gene families, reveal new patterns of coordinated expression across gene families, and uncover entirely new categories of genes.

The potential of microarrays extends beyond peptides and nucleotides. Another segment that could receive a boost from the developments in microarray technology is disease diagnosis. Promising results from the use of DNA microarrays to classify subtypes of cancer may help determine the most appropriate treatment strategy. Microarrays' portability, rapid assay times, and smaller sample requirements could be major factors in encouraging their uptake in the healthcare sector despite their current high costs. Conversely, increased use should bring costs down.

Market for microarrays

Over the past few years, the markets for DNA based microarrays have exploded. These microarrays are used in both academic research, medical diagnosis and drug discovery. From a market that could be measured in the tens of millions five years ago, DNA microarrays have undergone a period of explosive growth to become a several hundred million dollar industry today. Not only has microarray production become a significant industry with sales in the several hundreds of millions of dollars, but goods like substrates, probes and marker molecules needed to supply microarray production have become its own industry as well.

Demand for microarrays, microfluidic devices, and other biochips bears out that optimism. World BioChip Market, a report by Frost & Sullivan, forecasts that the market will grow at an annual rate of over 50 percent in the next few years. Because of the growing demand Affymetrix, the technology's current market leader, faces increasing competition. Affymetrix currently controls 82 percent of the DNA microarray market in terms of sales. There is definitely a race between Affymetrix, Agilent Technologies and other players to increase the number of data sets generated, to drive the trend toward miniaturization, and to make the promise of high-throughput screening. Overall, DNA microarray use will continue to increase over the next few years.

Major global players

Global market participants

The major players in the DNA Microarray business include Affymetrix, Illumina, GE Healthcare, Ocimum Biosolutions, Applied Biosystems, Beckman Coulter, Eppendorf Biochip Systems, and Agilent Technologies.

- Affymax
- Affymetrix
- Agilent Technologies
- Applera Corp
- BioTrove
- Celera Genomics
- Eppendorf
- Excelln Life Sciences
- Genomic Solutions
- Hitachi
- Illumina
- Lucent Technologies
- Luminex
- Micronics
- Motorola
- Quantum Dot Corp
- Roche Diagnostics

Affymetrix based in Santa Clara, California offers a variety of gene chips, including human DNA arrays and chips for identifying HIV strains or detecting mutations in cancer genes. These chips are sold under the trademarked name "GeneChip". Spinco Biotech promotes Affymetrix for GeneChip system-the Gold Standard for Microarray. GeneChip, the most advanced platform reduces the time and cost of discovery research. Affymetrix holds over 140 important patents for expression profiling, mutation analysis, genotyping and SNP analysis. Any company which wants to enter this market, be it for basic research, for the development of new medications, or for disease diagnostics, needs to acquire a licence from Affymetrix. They have several collaboration relationships with other companies that utilize their patented GeneChip technology.

Roche Diagnostics, another important player in the segment passed a milestone on the road to personalized medicine with the introduction of its first DNA chip-the AmpliChip CYP450 which caused a stir in Europe and the US. As the first DNA chip test in the world to receive regulatory approval, it represents a pioneering new discovery. The AmpliChip CYP450 Test can help physicians adjust dosing and select drugs by predicting a phenotype based on a genotype so that patient treatment can be individualized to get the best therapeutic results possible. Estimates indicate that systematic use of the AmpliChip test before treatment could improve overall efficacy by 10-20 percent and avoid 10-15 percent of all serious side effects.

UK-based robotics manufacturer Genetix offers the latest linear drive technology robotics for micro arraying, protein excision, cell screening and selection, liquid dispensing and a host of related reagents and consumables. Genetix last year appointed Labmate (Asia) its marketing partner for microarrayers and microarray scanners in India.

In 2005, Agilent Technologies introduced for the first time its DNA microarray-based genomics solutions into India's growing life sciences market. Agilent's life science technologies address demand from government-funded research institutions and pharmaceutical companies which improve the productivity of gene-expression and genomics research. The key applications of Agilent's microarray-based solutions include: gene expression, toxicogenomics, comparative genomic hybridization and agro-biotech.

Eppendorf Biochip Systems (EBS), the microarray division of Eppendorf, Germany has introduced a new pathway specific Dualchip microarray series. Two identical arrays on the slide with each gene spotted in triplicates along with unique hybridization frames prove to be a special advantage while comparing samples for differential gene expression. Well defined controls and internal standards guarantee the highest quality in terms of sensitivity and data reproducibility. The colorimetric Silverquant Microarray Detection and Scanning System along with the software from EBS has revolutionized the technology to a greater extent with a heavy cost cutting on the capital investment for such facilities. The new technology is directed to address the exact need of the researcher with a major focus on the cost of microarray experiments in life science research. Dualchip portfolio continues not only with gene expression analysis but also to transcription factor (TF) chips for MAPK and stem cell kits.

Therefore it is clear that the DNA chip and microarray market in India is dominated by the MNCs. But where does India stand in this whole scenario? Though there are very few players in India but there has been many interesting developments taking place since the last two years.

The global microarray sales amount to
$600 million, a market that is currently growing at about 10 percent annually.

Applications

The microarrays are being put to a variety of applications including- DNA sequencing/resequencing, single nucleotide polymorphisms (SNPs), functional genomics, studies involving reverse genetics, diagnostics and genetic mapping, genomic mismatch scanning (GMS), agricultural biotechnology and proteomics.

DNA microarrays now play a key role in product development in the pharmaceutical industry. Biochip manufacturers have found their major customers to be largely pharma firms, with scientists employing the technology to search for new molecular targets for drugs. This is a very important area because drug companies need to analyze large quantities of different chemical compounds.

The DNA microarray industry is comprised of companies which supply microarray slides, microarrayers (eg. robotic spotters and photolithographic equipment), scanners, software for designing and analyzing microarrays and pre-spotted slides.

What gives DNA chips their power is their flexibility, compact size, speed, and low cost. Scientists can put hundreds of thousands of distinct DNA sequences on a microscopic grid. DNA chips can gather an incredible variety of data very quickly. And because chips can be mass-produced, they are likely to be very inexpensive in the near future. That will allow easy collection of genetic information from many, many individuals, opening up all kinds of opportunities to help doctors diagnose and treat their patients.

DNA chips and microarrays are used in testing for infectious diseases and metabolic disorders. Additionally, they are used for pregnancy testing, drug abuse, heavy metal toxicity testing, genetic testing, and elated health complications. There are various products and technologies available in the market today and those on the verge of commercialization.

Innovations in the development of simple-to-use and minimally invasive chips and array kits aid in increasing their patient usage and advances in bio-diagnostics such as the DNA diagnostics, are driving the market for rapid tests. However, developing these products requires huge amounts of time and experimentation, especially to identify the disease marker before developing and commercializing a suitable diagnostic platform. This necessitates commitment and huge investments for R&D, as it usually takes several years to commercialize.

Indian players

Genotypic, a genomics and bioinformatics company in India, provides end-to-end microarray-based genomics solutions, gene expression analysis and consulting services in the Indian life sciences market. Genotypic have recently announced that it has achieved Agilent Certified Microarray Service Provider status. Genotypic is the first Indian company to be provided the Agilent Certified Service Provider status and the first in the world to be certified for all three Agilent solutions in gene expression, aCGH and location analysis. Agilent's DNA microarray platform is available for analysis and consultation at the Genotypic laboratory in Bangalore and pharmaceutical and biotech companies leverage Agilent's DNA microarray platform by sending their samples to the Genotypic laboratory for analysis and consultation.

Ocimum Biosolutions, a life sciences R&D enabling company, is working mainly on three focus areas-BioIT, BioMolecules, and BioResearch. The BioMolecules division produces microarrays and oligonucleotides. The Microarray Division has been acquired from MWG Biotech (Germany) and produces catalog OciChip arrays, Custom OciChip arrays and offers microarray hybridization services. Ocimum took over MWG's portfolio of DNA chips on the completed genomes of a multitude of model organisms including rat, mouse and zebra fish as well as DNA chips representing the complete human genome. Ocimum handles the business of custom arrays, chips made to customer specification, and the oligo sets for clients who want to produce their own chips.

Bangalore-based XCyton Diagnostics has developed the DNA Chip for simultaneous identification of 15 different pathogens causing eye infections.

Xcytoscreen Keratoconjuctivitus, Uveitis, Retinitis and Endophthalmitis, the specific and sensitive dignostic kits for the

detection of 15 microrganisms responsible for infection to both eyes and brain have been developed for the first time in the country and is based on Nucleic Acid Amplification technology and Macro-chip. "About 200,000 people suffer from eye infections in India every year and a million globally. The Xcyto-Screen kit has the advantage of being able to detect a series of the eye infecting microorganisms" said Dr. Ravikumar, managing director, XCyton Diagnostics at the product launch event. In addition, the Xcyto-Screen HPV kit-the DNA chip for genotyping Human Papilloma viruses responsible for cervical cancer and the diagnostic kit for meningitis and encephalitis was also launched. "Infection with HPV is the main cause of cervical cancer, the second most common cancer in women," remarked Dr Ravikumar.

Polyclone Bioservices provides DNA Array services including spotting, hybridization and data analysis. Polyclone is evaluating some of the leading microarray platforms to enhance its target screening platform to apply for its clinical genomics projects. It is embarking on a pilot project with its partners to study the drug response of specific families of genes in various types of cancer by using its proprietary microarray screening platform.

Mumbai-based Biotron Healthcare India is engaged in the distribution of products from the leading manufacturers. "We have been offering microarray equipments, prespotted slides and microarray scanner from overseas companies like K Biosciences, UK; Takara, Japan and Vidar, US to the Indian customers" said Venkatesh Voleti, director, sales, Biotron Healthcare.

Expanding applicability

The dynamic nature of the growing number of infective agents and the absence of specific and efficient treatments for several viral, bacterial and genetic diseases has created the need for rapid identification and diagnosis. The ability of rapid test methods to give real-time results within minutes, as compared to hours of lab testing increases their acceptance and usage by the medical community as it saves time for both patient and physician.

DNA chips and microarrays represent a broad class of technologies rather than a single technique. Thus their applicability is expanding beyond their present use in gene expression profiling and the recognition of diseases based on the profiles of genes. Beyond that, expression studies will lead into proteomic studies. Development of chips at different levels for different purposes, including tissue chips addressing issues such as the functions of genes.

The precision of microarray assays has been a significant concern among end users. This can be a debilitating problem in the diagnostics industry, which traditionally requires a high degree of precision. Standardization is also receiving a lot of attention from researchers, especially with the current need to compare data obtained from different platforms now available. Since there is a major market for microarray technologies ahead, scientists are working on remedial measures.

DNA and protein and small molecule chips have moved rapidly from concept to reality. Soon other biochips are likely to appear in the laboratory. Such microdevices will give life science researchers significant benefits including higher throughput, more automation, cost savings, and ideally ease of use. Increasingly, biochips and microarrays will find their way out of the research laboratory and into medical offices and hospitals. The use of microarrays for diagnostic purposes would enable simultaneous testing of different markers, point of care diagnostics, and reduced time as well as reagent consumption with a reduction in overall cost.

These applications of DNA chips will be realized and will expand in future for the benefit of mankind, in the fields of health care and agricultural biotechnology. With the maturing of technology and falling costs, biochips can revolutionize drug discovery.

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