



Media Backgrounder – perspective and detail for journalists

AGILENT TECHNOLOGIES IN CANCER RESEARCH

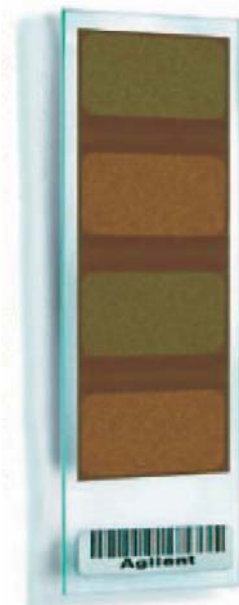


Scientists around the world use a wide range of Agilent instruments, software and reagents to study the mechanisms of cancer. As a leading provider of microarrays, sometimes referred to as “biochips,” Agilent is the source of sophisticated tools for examining the genomic aspects of cancers and other illnesses. Agilent is also a main global provider of gas chromatography (GC), liquid chromatography (LC) and mass spectrometry technology used to analyze tissue samples for proteins or metabolites in an attempt to identify markers for cancer, and detect and measure carcinogens in the environment. Agilent’s broad portfolio includes software to collect and interpret data from cancer research experiments, reagents needed to run the experiments and automation options for labs performing large volumes of work. In recent years, researchers have begun to look at cancers from multiple scientific perspectives, an approach known as “systems biology.” Agilent supports this concept by addressing multiple scientific needs.

Microarrays

Agilent is a leading provider of genomic microarrays. A microarray is a slide containing thousands of DNA segments called “probes” which can be used to examine the genomic activity within a tissue sample. Agilent uses a proprietary SurePrint platform to synthesize as many as one million high quality probes on a 1-in.x 3-in. glass slide. Because SurePrint technology is “inkjet”-based, it provides a high degree of flexibility that scientists find very useful. Probes can be designed on the customers’ computer, and Agilent can then print them on the microarray for that customers’ exact research needs.

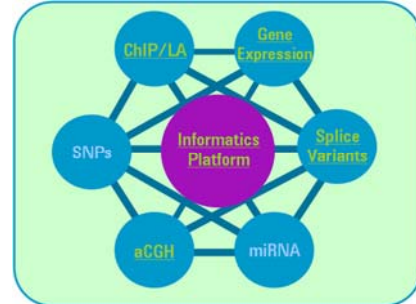
The oldest and most popular use of DNA microarrays is the study of **gene expression** –which genes in a cell are “turned on” and “off,” and how this might affect the health of the organism. About half of gene expression analyses performed worldwide is for cancer research. Other important gene expression applications include study of cardiovascular disease, immune and inflammatory diseases (such as AIDS and asthma) and central nervous system disorders.



Agilent's flexible SurePrint capability is very well-suited for emerging microarray applications which are helping researchers overcome important hurdles to discovering disease mechanisms.

Complementary microarray applications

Emerging applications complement the information obtained from gene expression studies. Increasingly, researchers are using gene expression and one or two additional applications to look at complex biological questions from more than one point of view. Informatics software is the key to triangulating these complex data sets into useful knowledge.



Oligo Comparative Genomic Hybridization Arrays (aCGH) and Copy Number Variation (CNV)

In January 2005, Agilent introduced a breakthrough platform that, for the first time, enabled researchers to use microarrays to precisely study chromosomal gains and losses associated with cancer. Previously, the only way to do this was through optical imaging of whole chromosomes, a technique with limited sensitivity, resolution, lack of quantification and throughput. "This advancement, along with the opportunity it provides to correlate genomic copy alterations with mRNA abundance and protein abundance, is going to incite a huge body of experimentation and publication among the cancer research community," said Michael Bittner of the Translational Genomics Research Institute.

MicroRNA profiling

In April of 2007, Agilent introduced the first comprehensive microarray system for profiling human miRNAs, and a year later introduced rat and mouse miRNA microarrays. miRNAs, a class of small non-coding RNAs that are only 19-30 nucleotides long, are estimated to regulate approximately 30 percent of all human genes. Studies have shown that distinct miRNA expression patterns are associated with a number of tumor types as well as involved in regulating processes such as cell development, metabolism and viral infections. Because miRNAs are potential regulators of gene expression, scientists are increasingly interested in measuring them for research, drug discovery, other therapeutics and, eventually, diagnostic tests. Agilent's proprietary direct labeling chemistry produces excellent results from just 100 nanograms of precious sample. For quality control of miRNA samples, Agilent also offers an exclusive lab-on-a-chip based Small RNA kit for the 2100 bioanalyzer (pictured at left).



ChIP-on-chip

Chromatin immunoprecipitation (ChIP) studies, also known as Location Analysis, use microarrays to detect events that regulate gene activity. This provides insight into key pathways of illnesses such as cancer, cardiovascular disease and central nervous system disorders. ChIP-on-chip also helps scientists develop therapies. Regulatory proteins bind to genomic DNA to control DNA replication and gene expression. The proteins act as switches in the cell's regulatory circuitry. When location analysis information is combined with gene expression data, the results can be used as biomarkers. In January 2005, Agilent purchased Computational Biology Corporation

which was founded by Richard Young, Ph.D. of the Whitehead Institute at MIT. Dr. Young invented ChIP-on-chip technology and also serves as a consultant to Agilent.

Methylation

Methylation events are heritable genomic modifications that regulate gene expression without altering the DNA sequence itself. They can regulate a wide range of biological processes and genetic diseases, and irregular methylation patterns have been associated with certain cancers. Agilent offers CpG island and promoter tiling microarrays enabling genome-wide scanning of methylation events. Custom methylation arrays let researchers target specific genomic regions of interest for high-resolution analysis.

Researchers describe how they use Agilent microarrays

Agilent has compiled the Open Genomics webcast series, featuring leading researchers describing their work. You can access it at <http://www.opengenomics.com/webinars.aspx>

To access scientific publications, please visit <http://www.opengenomics.com/publications.aspx>

The Agilent Difference

Agilent's novel approach to microarray design and manufacturing offers substantial advantages over other techniques. Agilent's SurePrint manufacturing process is inkjet-based, using the same basic principal as an office inkjet printer. Instead of ink, the print head deposits nucleic acids to build spots of DNA. By contrast, Affymetrix uses photolithography, similar to methods used to fabricate semiconductors, to deposit layers of nucleic acids on their microarrays. Agilent currently prints up to 244,000 features on a 1-in.x 3-in. slide.



Inkjet microarray printing is extremely flexible and customizable, only requiring a different software file to print a different array. In addition to flexibility, the Agilent technology enables the printing of probes that are 60 nucleotide bases in length (60 mer). This provides a 5-8-fold increase in sensitivity of detection compared to the 25 mer probes dictated by photolithographic deposition.

Online design tool

Agilent also introduced the industry's first Web application for designing custom microarrays online. eArray incorporates the most up to date content from major genomic databases, including approximately 4 million validated probes. eArray also enables researchers to collaborate on array design worldwide, by sharing their designs within a collaborative environment, among far-flung consortia for example. Once an array experiment is laid out in the computer, it can be sent to the Agilent SurePrint manufacturing platform to be printed. This access to content leverages the flexibility of the printer so researchers can concentrate on their experiments more than how to produce the microarrays.

Next Generation Sequencing

The same expertise Agilent uses for custom-synthesizing oligo probes for microarrays enables the company to offer powerful tools for streamlining next generation DNA sequencing workflows. The Agilent SureSelect Target Enrichment system enables investigators to sequence just the genomic regions of interest, greatly speeding time-to-results and reducing reagent costs.

Other “omics”

Agilent provides a wide range of analytical instruments, consumables, software and services for the life sciences beyond genomics. Two important areas with cancer research implications are **proteomics** (the study of all the proteins in a biological sample) and **metabolomics** (the study of all the metabolites in a sample).



Agilent 1200 Series Liquid Chromatography systems (l.) used to separate proteins from sample mixtures and Agilent mass spectrometers (r.) used to detect, identify and measure protein molecules.

Proteomics tools

Agilent has developed a unique suite of tools enabling scientists to isolate, identify and compare complex sets of proteins in the search for disease markers. It includes:



Agilent 1200 Series liquid chromatography (LC) system, one of the world's best selling systems in life sciences, environmental analysis, food testing, pharmaceutical analysis and other applications. The Rapid Resolution version provides up to 20 times faster analysis and 60% higher resolution than conventional HPLC without sacrificing precision or sensitivity. The 1290 UHPLC can run any method developed for any other LC. These are used by themselves or coupled to mass spectrometers.



Agilent's Multiple Affinity Removal System (MARS) used to remove the 14 most abundant proteins from human serum, enabling scientists to study low abundance proteins of interest.

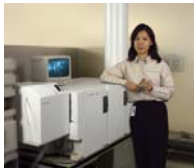


The innovative Agilent 3100 OFFGEL Fractionator which can dramatically increase the number of proteins identified through prefractionation of proteins and peptides prior to LC/MS analysis. The resulting fractions are in-solution, making recovery for LC/MS analysis much easier than with old fashioned slab gels.



Agilent's exclusive microfluidic chip-based **HPLC-Chip/MS**, which integrates columns, connection capillaries and nanospray ion source for superior robustness, reliability and ease-of-use when plugged into an Agilent mass spectrometer.

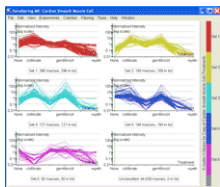
Tools used for Proteomics and Metabolomics



Agilent's extensive portfolio of mass spectrometers, including the **6250 Accurate-Mass Quadrupole Time-of-Flight** instrument (pictured) which delivers the ultimate in versatility and analytical performance for profiling, identifying, and characterizing biomarkers. The instrument is pictured with an **HPLC-Chip Cube**, which is the interface between the HPLC-Chip and the mass spectrometer.



The **Agilent 6410 Triple Quadrupole mass spectrometer**, shown equipped with an HPLC-Chip Cube, is a popular platform for validating biomarkers.



Informatics software plays a crucial role in enabling scientists to derive knowledge from the mountains of data generated by gene expression, proteomics or metabolomics experiments. Agilent has developed **GeneSpring GX** for gene expression and **GeneSpring MS** for mass spectrometry-based experiments that let researchers import, analyze and visualize these large, complex data sets. For simpler proteomics experiments, Agilent also offers **mass profiling** software. **Spectrum Mill** reduces bottlenecks in large scale proteomic analysis by quickly identifying proteins and peptides via fast database searches.

More information is available at www.proteomics-lab.com

Metabolomics tools.

Metabolomics is rapidly emerging as a logical complement to large-scale expression profiling and proteomics studies—offering valuable insight into the biochemistry of organisms. But given the vast chemical diversity of metabolites, metabolomics also presents significant analytical challenges. Agilent Technologies offers the industry's most complete range of products for metabolomic investigation. In addition to LC and LC/MS, Agilent offers the following tools which are well-suited for metabolomics experiments:



The Agilent 5975C is the latest generation of the most popular gas chromatograph/mass spectrometer (GC/MS) of all time. It's extremely high MS resolution, low mass deviation, superior sensitivity and excellent spectral integrity make it well suited for the rigors of metabolomics analysis. The GC section of the system delivers rock-steady performance, high productivity and innovative in-oven flow controls enabling useful new applications.



Agilent is the exclusive provider of the **METLIN Personal Metabolite Database**, which can greatly improve metabolite identification by significantly narrowing the list of possible identities. It is one of the most comprehensive metabolite databases in the world today.

Please visit <http://www.chem.agilent.com/Scripts/IDS.asp?IPage=42052> for more information.