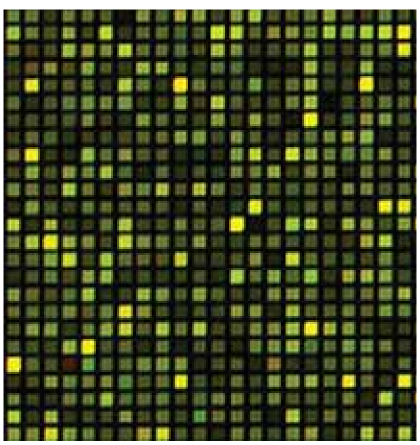
DNA Microarray

Studying the activity of genes

"The ability of an organism to live and function depends upon the activity of thousands of genes and the complex interaction between those genes and the proteins they produce. A powerful laboratory tool, a ***DNA microarray****, provides a glimpse into this world of genetic interactions by distinguishing cells based on the activity of their genes."*



Want more information:

learn.genetics.utah.edu/units/biotech/microarray/

a step-by-step detailed overview of the microarray experiment. Developed at the University of Utah as part of their Virtual Biotechniques Laboratory

www.ncbi.nlm.nih.gov/About/primer/microarrays.html

Microarrays: Chipping Away at the Mysteries of Science and Medicine, a Science Primer from the National Center for Biotechnology Information (NCBI).

Microarray –
What you need to know:

- *Proteins are the building blocks of our cells.*
- *Genes are specific segments of DNA that contain the instructions for creating proteins.*
- *Genes use a messenger molecule called mRNA to direct protein production.*
- *Generally, the more mRNA made by a gene, the greater amount of protein produced.*
- *Microarrays measure the amounts of mRNA produced by a set of genes. They can be used to compare patterns of gene activity between different cell types or the same cell type under different conditions.*
- *Microarrays have enabled researchers to make great strides in distinguishing between specific types of cancers and their response to treatments.*

Although most cells in an organism contain genetic material, not all sets of genes are active in every cell. For example, a subset of cells in the pancreas produces the protein insulin, regulating the breakdown of carbohydrates while specialized cells in the adrenal gland produce a group of proteins that regulate fluid balance in the body. While the cells in both the pancreas and adrenal gland posses identical genetic information, the specific genes which actively direct protein production are different. Studying patterns of gene expression – which genes are active and which are inactive – allows scientists to understand how cells function normally and when they are diseased.

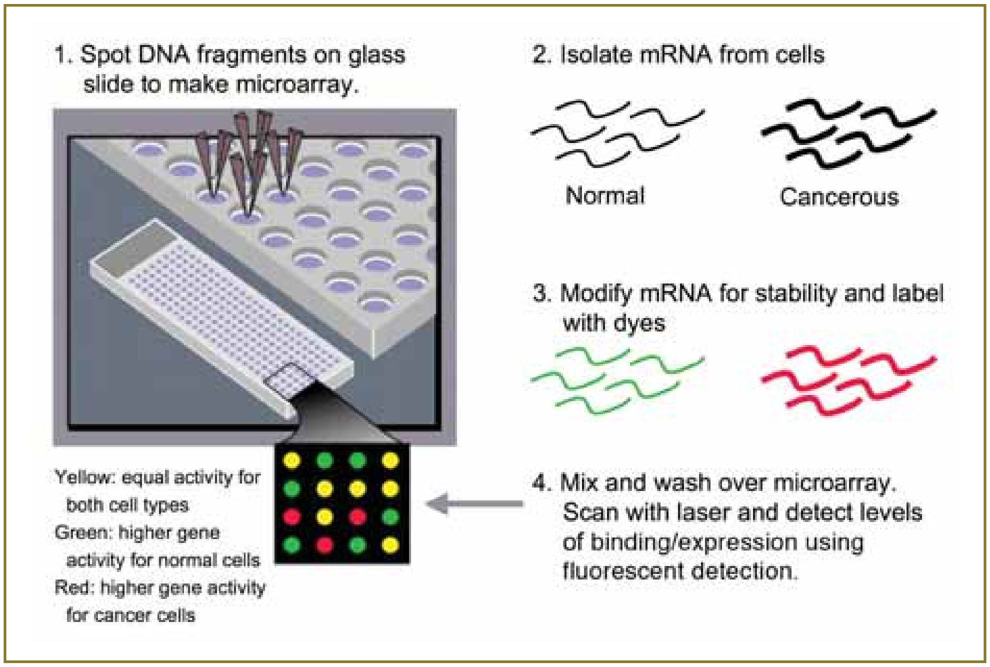
Examined until recently on a "gene-by-gene" basis, this research offered only a limited understanding of the relationships between various genes - rather like trying to understand how an automobile works by looking at each individual part rather than observing how they function within an assembled vehicle. DNA microarray technology now provides scientists a "big picture" view of these cellular players, capturing an organism's gene expression patterns in a single snapshot. Useful for surveying a large number of genes quickly, DNA microarrays measure gene expression within a single sample or compare activity in different cell samples, such as healthy and diseased.

The Microarray Experiment:

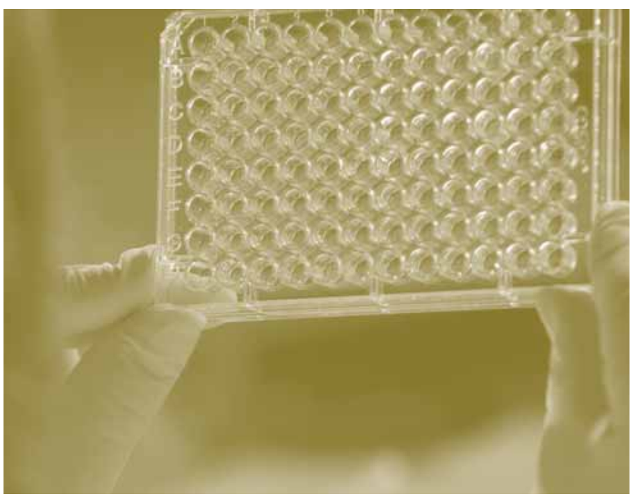
There are several approaches to constructing and analyzing a DNA microarray. One approach assembles the DNA microarray using robotic machines to affix small pieces of a gene to a single spot on a glass, plastic or silicon microscope slide. By arranging other genes elsewhere on the slide in a grid-like pattern, thousands of individual spots are organized in a space about the size of a human thumbnail. A specific set of genes or the entire collection from an organism can be included. After assembling the microarray, scientists collect the sample to be studied, and isolate and modify the cell's mRNA, linking it to a small fluorescent dye. The mRNA is washed over the microarray. The mRNA from a specific gene will bind to its corresponding DNA spot on the slide. If the gene was very active, producing many mRNA copies, a high level of binding occurs. Conversely, low gene activity results in only a small number of bound mRNA copies.

Scanning the microarray slide with a laser activates the fluorescent dye attached to the bound mRNA. Measuring the amount of fluorescence at each spot correlates with the activity of the genes represented at each position on the microarray.

Microarray technology has become an excellent method to classify types of cells. For example, if the mRNA from two cell



types is linked to different dyes, variation in expression can be identified on the basis of intensity differences in fluorescence. This ability to differentiate expression patterns has been especially useful in cancer research. Historically, scientists grouped cancers based on the organs in which the tumors develop and the appearance of the cancer cells. With microarray technology, patterns of gene expression clearly define cancer subtypes. Initial studies suggest these expression-based groupings may be more accurate at predicting which tumors are most likely to metastasize or respond to a specific form of treatment. Researchers can then design treatment strategies targeted directly to each specific type of cancer, based on which genes exhibit unusually high or low levels of gene expression. In addition, by examining the differences in gene activity between untreated and treated tumor cells, scientists can better understand how different therapies affect tumors and in turn, develop more effective treatments. ■



EGEN Announces Successful Completion of Phase I Trial

Expression Genetics (EGEN) has announced the completion of a Phase I clinical study evaluating the company's lead drug candidate, EGEN-001. The study, conducted at The University of Alabama at Birmingham and Baylor College of Medicine, evaluated the safety, tolerance, preliminary efficacy and biological activity of the EGEN-001 in 13 patients with advanced recurrent epithelial ovarian cancer. The product, utilizing the company's proprietary TheraPlas® delivery technology, is composed of interleukin-12 (IL-12) gene expression plasmid formulated with a biocompatible delivery polymer and is designed to increase local concentration of IL-12 protein. IL-12 is a potent anti-cancer cytokine which works by enhancing the body's immune system against cancer and inhibiting tumor blood supply. EGEN-001 for treatment of ovarian cancer has been granted Orphan Drug Status by the FDA.

"We are quite pleased with the safety profile of EGEN-001 observed in this initial clinical trial and are encouraged by some of the preliminary efficacy and activity results we have seen resulting from the administration of EGEN- 001 monotherapy in advanced ovarian cancer patients," said Dr. Danny H. Lewis, CEO of EGEN. "We have completed the necessary regulatory process and expect to immediately begin enrollment of patients in our next study which will combine EGEN-001 administration with conventional chemotherapy in platinum-sensitive recurrent ovarian cancer patients."

For more info: **www.egen.com**. EGEN is a proud Associate of the Hudson-Alpha Institute for Biotechnology.