

# Wright State's Gene Expression Laboratory Brings an Innovative Technology to the Miami Valley

By Mark Willis

A gene array or "DNA chip" looks as unassuming as a 3.5-inch computer diskette, but it represents a revolutionary new technology that is changing how biomedical scientists study gene expression. The pharmaceutical industry has begun to use the technology now to develop new drugs, and in a few years pathologists and other physicians are likely to use DNA chips for diagnosing diseases and selecting treatments most appropriate for individual patients.

The Gene Expression Laboratory (GEL) at Wright State University School of Medicine is the first facility in the Miami Valley region to acquire gene array technology. The GEL was established last year in collaboration with the Air Force Research Laboratory at Wright-Patterson Air Force Base. Since then GEL researchers have launched studies of gene expression in Gulf War Syndrome (funded by the Department of Defense) and cancer (funded by the National Cancer Institute). Soon the GEL's technology and expertise will be shared with a wider range of Wright State faculty, including clinical collaborators, through a seed grant program supported by the Kettering Fund.

"Using gene arrays to determine global changes in gene expression for cells or tissue

samples represents a new paradigm in scientific research," explains Steven Berberich, Ph.D., associate professor of biochemistry and molecular biology at Wright State. "Basic and clinical researchers no longer need to limit their investigations to individual or a small number of genes previously shown to correlate with a given disease state. Gene array technology provides a wealth of data about thousands of genes that may be active or inactive at any given point in time."

DNA chips are available now for a host of species. The typical human DNA chip used in the GEL contains 8,000 different genes, each identified as a spot or "feature" arranged on a grid. Each feature is approximately 24 microns wide.

The DNA chip provides a fixed reference in an assay that begins with isolating messenger RNA from cell or tissue samples. The RNA is converted to a probe which is tagged with a fluorescent marker, then applied to the chip. Probe from RNA expressed by specific genes in the sample binds to corresponding genes on the chip. Excess probe for RNA that hasn't matched with genes on the chip is washed off, then the chip is placed in a laser scanner that measures the fluorescent intensity of the features. Each feature's fluorescence is proportional to the

amount of probe present, which is proportional to the amount of RNA present in the sample.

The resulting gene expression profile indicates which genes were active and inactive in the sample. According to Dr. Berberich, the profile is a "snapshot" in time documenting gene expression at the moment when the RNA was isolated. When examining cells stimulated with a toxin, for example, the snapshot could be completely different 30 minutes later. While many of the cells genes are expressed in a constant manner, others may fluctuate in response to extracellular stimuli or inappropriate growth signals.

"As a basic scientist, I now can understand new pathways in gene expression that would have taken years to study using more traditional methods such as Northern blotting, because I would have had to systematically examine each of the genes. This is like doing 8,000 Northern blots at the same time," Dr. Berberich says.

"Now I can get an instant picture or profile of gene expression, and use that information to better understand genes that might be encoding proteins in different pathways. It opens up new avenues for researchers by letting us look at patterns of change in how genes are turned on and off."

Air Force toxicologists are exploring the technology to determine whether it can predict the toxicity of new chemical compounds. Comparing gene expression profiles of known toxins with those produced by cells exposed to new compounds may reveal patterns of change that are reliable predictors of toxicity. This application of toxico-genomics may eliminate or reduce the need for animal studies.

A number of laboratories around the country have used gene array technology to evaluate the types and stages of different cancers. Researchers have sampled the RNA from human tumors to determine whether gene expression profiles can be used to classify them. In certain cases, they have been able to identify subsets as small as 50 genes that serve as good predictors. Some of the tumor subgroups classified this way are known to respond better than others to specific cancer treatments. In the not-to-distant future, gene expression profiling promises to assist pathologists in diagnosing cancers and oncologists in selecting treatments. The technology may be valuable also in designing new medications.

“Clinicians will use the profiles as indicators,” Dr. Berberich says. “The first benefit is likely to be better diagnoses, followed by improved matching of patients to treatments.”

Another GEL study supported by the Kettering Fund will investigate patterns of gene expression in ovarian and endometrial tumors. The research collaboration includes Dr. Berberich; Madhavi Kadakia, Ph.D., assistant professor of biochemistry and molecular biology; and William Nahhas, M.D., professor of obstetrics and gynecology and medical director of the Gynecologic Oncology Center at Miami Valley Hospital. The study’s goal is determining the effectiveness of gene expression profiles in diagnosing these cancers.

*For more information about Wright State’s Gene Expression Laboratory, contact:  
Dr. Berberich at (937) 775-4494  
email: [steven.berberich@wright.edu](mailto:steven.berberich@wright.edu)*