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Center News

MSKCC Opens Genomics Laboratory

Until recently, scientists have only been able to study one gene at a time, a laborious process that severely limited their ability to see the big picture of genetic changes in cells. But a new technology is promising to monitor thousands of genes simultaneously, a feat that will improve the way doctors diagnose tumors and allow them to better predict the course of disease.

This new technology is the thrust behind the creation of MSK's new Genomics Core Laboratory, which opened in January. The lab employs the use of DNA chips, also called microarrays, to allow researchers to compare the molecular differences between healthy cells and different types of tumor cells, giving clues about which tumors may be more aggressive and which may be more slow growing, or which may be more likely to respond to one therapy over another. This information will help doctors diagnose tumors with amazing precision and help predict how a patient will respond to a particular therapy. It also could lead to the development of new therapies that exclusively target cancer cells, sparing damage to normal, healthy cells.

Agnès Viale heads MSK's new Genomics Core Laboratory, which is shedding new light on the genetic differences of cancer.

"The new facility is being used by both clinical and basic-science researchers," said Agnès Viale, head of the new laboratory. "The microarrays don't give you all the answers about the causes of cancer, but they give researchers a lot of clues about the direction for further studies."

Microarrays measure levels of messenger RNA, the written instructions made by DNA that tell the cell which proteins to make. By studying genes that are "turned on" inside a cell,

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Genetic Aspects of Disease

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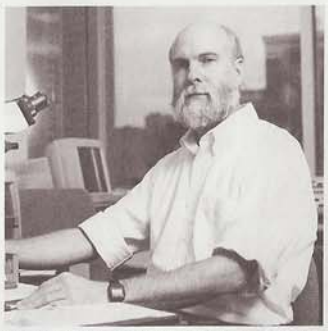
so-called gene expression, researchers can find out which genes are expressed in higher levels than they should be and which genes may be missing altogether. Some chips allow the analysis of up to 12,000 genes at the same time, providing an overall snapshot of gene expression.

"Many of the studies we are doing with these microarrays are designed to ask clinically relevant questions," said William L. Gerald of the Department of Pathology, who was involved in setting up the laboratory. "Why do some tumors metastasize and others don't? Why are some more aggressive than others? Why do some tumors respond to a particular drug and others don't? What changes in tumors when they become resistant to therapy?" All of these questions can be explored with microarrays.



William L. Gerald uses DNA chips to study the genetic aspects of several tumor types, including prostate cancer and neuroblastoma, a pediatric tumor.

One of Dr. Gerald's interests is studying the gene expression of prostate tumors. He and his colleagues plan to use microarrays to identify the molecular differences between slow-growing prostate tumors and those that grow aggressively. Patients with aggressive tumors could then receive the most potent therapies, while those with slow-growing tumors could opt for a less-invasive treatment.

"In the past, tumor diagnosis was based on what we could detect based on physical examination of the patient and microscopic analysis of the tumor tissue," said Carlos Cordon-Cardo, Head of MSK's Division of Molecular Pathology. "Now we can incorporate the information provided by new tools like microarrays to classify tumors based upon the comprehensive analysis of gene expression. Integrating this information will help cancer patients and their doctors in identifying those tumors with an aggressive behavior and selecting the most appropriate therapy based on the molecular makeup of their disease."

Microarrays also help researchers ask questions about the fundamental differences between cancer cells and normal cells. By figuring out which genes are missing or overexpressed in a particular tumor type, researchers can begin to figure out which genes or proteins might be good targets for developing new therapies. The Genomics Core Laboratory is also using microarrays to study RNA from mice and rats, enabling development of better animal models for studying disease and testing therapies.

Despite the promise of microarrays, they are still a new technology, and there are some limitations. One is the overwhelming amount of data that are generated from these chips. Another hurdle is making the leap from studying gene expression to understanding proteins, which are responsible for actually carrying out cell functions. "Looking at gene expression is only the first step in showing us what goes wrong in cancer cells," said Paul Tempst, head of the Targeted Proteomics Laboratory. "Gene expression alone does not show us all of the changes and interactions that can occur in proteins after they are made. But expression levels show us which proteins are worth looking at."

Researchers predict that microarrays will start yielding clinically useful information soon. "MSK is in a very special position to take advantage of the knowledge that can be gained from this new technology," said Dr. Cordon-Cardo. "Just as important as access to technology is access to the clinically relevant questions that will really influence patient care. We need to utilize the incredible resources we have at our institution to bring light to the disease in people who are sick today, as well as those who will be sick tomorrow."