

BIOLOGY BECOMES ELECTRIC

## Detecting Lung Cancer Early

The electronic circuit board analogy not only describes biological processes, but also some experimental equipment used to investigate those processes. Using a DNA microarray whose wafer-like platform resembles that of a computer chip and an electric laser scanning microscope to “read” genetic patterns on the platform, two NIH-funded biomedical researchers in BU’s Pulmonary Center, Jerome Brody and Avrum Spira, have devised a promising method to detect lung cancer in its early stages.

And not a moment too soon. Lung cancer remains the most lethal form of cancer in both men and women. The disease has a mortality rate of about 85 percent, in large part because it is often diagnosed at a late stage. No effective diagnostic test yet exists to indicate its presence at an early stage.

The sensitivity of bronchoscopy, the standard noninvasive lung cancer diagnostic currently in use, is about 30-60 percent—too low to determine the presence of early stage lung cancer and avoid potentially unnecessary biopsy and surgery. In the last year Brody and Spira have developed a new test that examines a pattern of gene expression in epithelial cells that line the large airway, which they believe react the same way to inhaled substances as those deeper in the lung. This test—coupled with bronchoscopy, which draws samples from deeper tissues—could detect lung cancer at an early stage with 95 percent accuracy.

“Our hypothesis was that if we could sample relatively easily accessible epithelial, or surface, cells from the conducting airways of individuals and measure the expression of thousands of genes in those cells, we could learn something about the presence and type of cancer inside the lung,” says Brody.

To zero in on a biomarker for cancer in airway cells, Brody and Spira gathered epithelial samples from 200 smokers with and without cancer via bronchoscopy of the large airways. They then dumped messenger RNA from the airway epithelial cells onto a DNA microarray—a glass slide with millions of short DNA sequence fragments representing the entire human genome, each with fluorescent dye attached. Using an electric laser scanning microscope that causes the fluorescent dye at all the fragments to light up, the researchers next determined the level of RNA-binding activity at each DNA fragment based on the intensity of the light produced. Applying bioinformatics techniques, Spira converted those fluorescent intensities to data and identified patterns of activity in 80 genes that could distinguish smokers with and without lung cancer. This study is described in the March 2007 edition of *Nature Medicine*.

In a subsequent experiment this year, Brody and Spira applied the same procedure to sample epithelial cells obtained non-invasively from the noses and mouths of smokers and nonsmokers. “We have generated preliminary data to suggest that the epithelial cells lining the nose and mouth respond in a very similar way to cigarette smoke at a gene expression level as bronchial epithelia,” says Spira. “This allows the nose and mouth cells to be used as a surrogate for cells deeper within the airway inside the chest.”

Brody and Spira next plan to conduct a 600- to 800-patient clinical trial to validate that their



Jerome Brody, shown inspecting an airway specimen with research coordinator Martine Dumas.

The Conversation:  
Hearing and Speaking

Engaging with Islam

**Biology Becomes  
Electric**

Tapping the Power of Microbes

**Detecting Lung Cancer Early**

Gauging Muscle Dysfunction

Preventing Premature Labor

Upgrading Kidney Stone  
Treatment

Bringing Research to the  
Community

Sights and Sounds:  
Explorations in the Arts

Answering The Biggest  
Questions About The  
Smallest Matter

Defending Innovation:  
Intellectual Property in  
the 21st Century

Talking about Religion  
and Culture

Raising the Game: FIRST  
Robotics

Graphene: Particle  
Physics at Your  
Fingertips?

---

### RELATED LINKS

Pulmonomics Lab