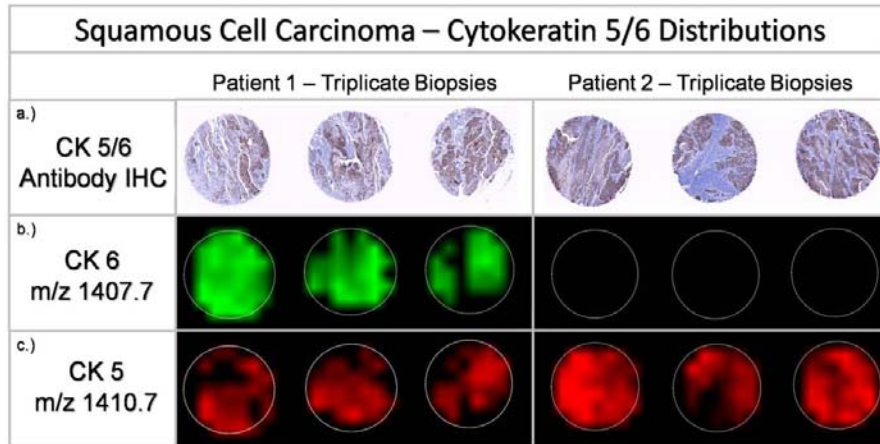


**TATRC Highlighted Research News Article:  
“Advanced Proteomics Program for Assessment of Disease Progression and  
Therapeutic and Clinical Outcomes”**

November 5, 2009

**Will That Cancer Spread?**

**New Technology Can Tell Early On**



a) **Standard histology:** CK5/6 antibody commonly used shows reactivity with both CK5 and CK6, with distribution assumed to be approximately the same.

b, c) **Imaging Mass Spectrometry:** directly identifies both CK5 and CK6 independently *in situ* through trypsin generated peptides, revealing different phenotypes in the two patients studied.

*Two patient samples that look the same when using a standard antibody stain to diagnose squamous cell carcinoma are actually different when using imaging mass spectrometry to directly identify two proteins (CK 6 and CK 5) in the samples. This new diagnostic technology developed by Dr. Richard Caprioli is faster and more accurate than current methods.*

Image courtesy of Vanderbilt Mass Spectrometry Research Center

Not all cancers are created equal.

The debates currently raging as to when to screen for cancer revolve around a central issue: current diagnostic methods can determine whether an individual has breast cancer—or ovarian cancer or prostate cancer or colon cancer—but they cannot tell at an early stage whether it is a highly aggressive type of tumor that is likely to spread or not.

New technology pioneered by Dr. Richard Caprioli of Vanderbilt University can analyze the protein molecules within cells to identify these differences—in minutes. Caprioli’s approach could be in regular use within two to three years.

A molecule is the smallest particle of a substance that still contains all the properties of that substance. Two cells may look the same under a microscope—but when one examines the protein molecules within them, differences become apparent.

Proteins are the building blocks of the body and carry out all bodily functions, from digestion to the working of our brains. Discovering what has gone wrong with a certain protein or the way it is working is the key to treating disease.

“The scientific community has discovered that disease is molecularly specific; it could be that it’s even molecularly different in each person,” explains Caprioli, director of the Vanderbilt Mass Spectrometry Research Center. “We have the ability now to work at the molecular level, to personalize medicine. This is a revolution in health as momentous as the discovery of bacteria and viruses.”

Caprioli has played a key role in developing a technique called imaging mass spectrometry that can produce images of biological molecules in tissue samples. This technique can provide a physician with “molecular fingerprints” of a patient’s tissue, which could help diagnose disease, individualize treatment and follow the patient’s response to therapy.

“The way we have applied mass spectrometry to biology will profoundly enhance our ability to treat diseases earlier and in a more effective manner,” says Caprioli. “While we’re initially focusing on cancer to prove the technology, we can see applying it to rapidly detect public health threats from external biological and chemical agents.”

The technology developed by Caprioli’s team uses the molecular weight of proteins (or drugs or other compounds) to map their location in a tissue sample. It involves applying a dot matrix to the sample and then “zapping” it with a laser that places each protein molecule in a specific spot in the matrix. It is a highly sensitive method for directly identifying not only a particular chemical or protein in a piece of tissue but exactly how it is distributed.

Caprioli explains, “The key to our project is that the technology is very fast. We’re using supercomputers and specialized programs that can analyze the protein structure of a sample in minutes, instead of days. This has enabled us to examine the large quantities of samples required to determine trends.”

What Caprioli has done, in effect, is “train” a computer to recognize normal versus cancerous tissue, and even different subtypes of cancer.

His lab is analyzing thousands of biopsies and tissues that have been banked by physicians and researchers throughout the country. The team is correlating the mass spectral data with clinical data to validate the results.

So far, Caprioli has proved the technology can tell the difference between aggressive and nonaggressive lung and breast cancers—adding even greater detail to the existing pathology reports. And this is just the beginning.

The Vanderbilt-based Advanced Proteomics Program that Caprioli leads serves as a national resource for medical researchers. It is supported by federal agencies such as the U.S. Army Medical Research and Materiel Command's Telemedicine and Advanced Technology Research Center.

TATRC Director Col. Karl Friedl notes, "Dr. Caprioli is a world-class researcher and leader in this technology so vital to personalized medical care. These efforts advance the care of our warfighters and our citizens."

Says Caprioli, "Rapidly scanning a patient's very molecules sounds like 'Star Trek.' But it's happening now!"