An Engineer Tackles Metastasis

By Mike Fillon

A chemical engineer at the University of Massachusetts–Amherst believes a different approach is needed for understanding breast cancer and metastasis, one based more on engineering than traditional medical research disciplines.

Shelly Peyton, Ph.D., has been awarded a three-year, $590,000 grant from the National Science Foundation to do just that: to study how various types of breast cancer interact with different human tissues—tissues she and her research team can create in the laboratory. Peyton said by studying where, how, and why breast cancer metastasizes, she hopes to develop patientspecific therapies that can attack the cancer as it tries to seek out and colonize these diverse tissues. (Peyton's grant is from a subset of the National Science Foundation, the Physical and Engineering Sciences in Oncology.)

Cancer research was not on Peyton's radar when studying for her Ph.D. “I don’t have a family history [of] cancer at all, so I’m not motivated by that,” said Peyton. Most of her graduate and postdoc work focused on cardiovascular tissue engineering.

Later, while at MIT, she worked with biological engineers who were building macroporous three-dimensional scaffolds as a model system to study adult stem cell migration. “We were interested in seeing if there was just some physical characteristics of the scaffold that we could change that would maximize stem cell migration into the middle of the scaffold. We investigated if we could predict how long the healing time for a patient with a large wound would be, based on the physical characteristics of that scaffold.” After conferring with colleagues about the tissue tropism phenomenon, which also happens in all cancers, she became interested in exploring it further.

“I decided it was a good time to change my career.”

At first glance, it may seem unusual for a chemical engineer to study cancer. Not so, said Mark E. Davis, Ph.D., professor of chemical engineering at California Institute of Technology, in Pasadena. “There are numerous engineers and other non–biological/medical scientists that have made significant contributions [to cancer research],” Davis himself is a member of the City of Hope Comprehensive Cancer Center’s Experimental Therapeutics Program.

Peyton’s approach is a variation of the Old Saw: if you’re in a hole, it might be time to stop digging. Peyton would never describe breast cancer metastasis research as being in a hole, but it is definitely in a sort of rut. “I do view a lot of cancer biology to be sort of stuck on this genetic approach,” said Peyton.

Peyton doesn’t believe it’s necessary for cancer researchers to stop digging altogether, but maybe to work in a different plot. “I’ve noticed many researchers try to find a gene or a protein that’s misregulated, and then try to focus their careers on studying how to stop that gene from causing cancer. We have been doing that for a while; I don’t think that’s going to work. I’ve wondered if the solution might be to combine what we already know about genes, protein, and cancer with my approach.”

Jacob Scott, M.D., from the Department of Radiation Oncology and Integrative Mathematical Oncology at the H. Lee Moffitt Cancer Center in Tampa, Fla., thinks Peyton may be on to something. “I think this research represents a rational next step forward that will definitely serve to advance our knowledge of metastasis,” said Scott.

“Bringing more physical science–oriented investigators to the fray in our war on cancer brings with it fresh insights that would not otherwise be represented. By using state-of-the-art techniques in tissue engineering, Peyton will be able to deconvolute the otherwise dizzying complexity inherent in the study of metastasis.” Scott is also a graduate of the Oxford University Centre for Mathematical Biology.

Peyton said the goals of her research are to unravel the questions about which type of cancer moves to each type of tissue and to find a way to stop the spread of the disease. “The critical question for me is where does it go and why. We think there are some mechanical relationships there, but we don’t know what they are yet.”

Peyton has divided her work into three broad objectives. The first one is to “quantify subtype-specific tissue tropism in breast cancer in ‘engineered metastatic microenvironments.’” To study this aspect, she and her research team will design highly controlled, reproducible biomaterial systems, which mimic the in vivo physicochemical properties of metastatic tissue.

“Using 12 human breast cancer cell lines that represent the clinically relevant disease subtypes and quantitative 3D microscopy, this proposal will systematically quantify the migration and proliferation response to these controlled physicochemical cues,” said Peyton.

Peyton is not the first researcher to investigate tissue tropism and cancer. More than 100 years ago, Stephen Paget reported on secondary breast cancer metastases occurring in specific organs. “To this day, there is no biophysical explanation for metastatic site preference,” said Peyton.

Peyton’s second objective is to quantify integrin-mediated signaling pathways.
Contrast-Enhanced Ultrasound May Aid Prostate Cancer Detection

By Mike Fillon

Clinicians who suspect their patients have prostate cancer, may soon have a better way of validating their suspicions. In a recent phase III study, researchers from Thomas Jefferson University and Hospitals in Philadelphia found that a technique, known as contrast-enhanced ultrasound (CEUS), which uses “microbubbles” to measure change in blood flow, did a much better job detecting high-grade prostate cancer than conventional biopsy methods. The study appears in the Aug. 17, 2012, online edition of the Journal of Urology.

Lead author Ethan Halpern, M.D., codirector of Jefferson’s Prostate Diagnostic Center, said as a result of the study, they found almost three times as many high-grade cancers by using half as many needle biopsies compared with systematic biopsy methods. “Today, a physician may sample 12–18 tissue cores from the prostate in order to help diagnose a patient. But with contrast-enhanced, that number drops to six or even less,” said Halpern. “As a result, we believe CEUS could prove to be more efficient for screening clinically important cancers and monitoring low-risk ones with fewer biopsies.”

CEUS has been studied before. Two smaller studies, both conducted by researchers from the Medical University in Innsbruck, Austria—one in 2007 and the second in 2010—also concluded that CEUS improved prostate cancer detection. “Our study similarly confirms an increased frequency of positive cores in CEUS-targeted biopsy compared to systematic biopsy by nearly double,” said Halpern (16.4% vs. 8.5%).