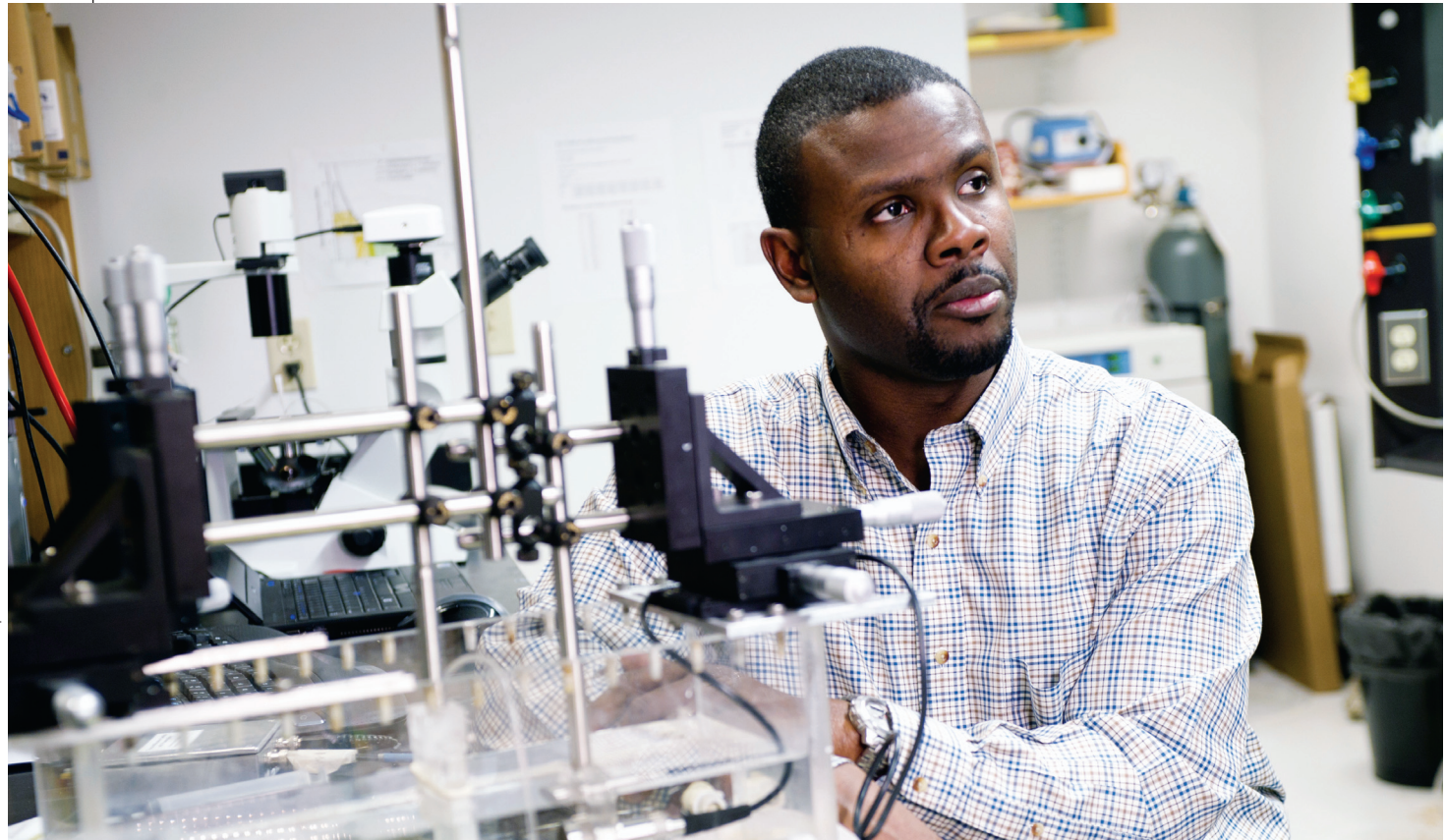


Small Wonders

**— TYRONE PORTER'S NANOPARTICLES KILL CANCER CELLS FROM THE INSIDE OUT**

BY CYNTHIA K. BUCCINI

IN THE FIGHT against cancer, chemotherapy is like birdshot, says Tyrone Porter: it attacks the tumor, but also assaults many other things, causing side effects like hair loss, nausea, and vomiting.

“You’ve got pellets flying everywhere; there’s collateral damage, innocent bystanders,” says Porter, a College of Engineering assistant professor of mechanical engineering. “There should be a better way of treating a tumor, rather than an injection that

goes to the hair follicles, your intestines; you can also get a reduction in white blood cell count, so your immune system is somewhat compromised.”

Porter is closing in on that better way. He and his team are making tiny particles that when loaded with chemotherapy drugs and injected intravenously will accumulate only in the tumor, where they can be stimulated to release the drugs. “The ultimate goal,” he says, “is to localize the therapy. I want to

specifically treat the tumor.”

Porter’s targeted approach takes advantage of structural weaknesses in the blood vessels that feed cancerous tumors. A tumor, basically a collection of cells dividing uncontrollably, can continue to grow only if it increases its blood supply.

“Because a tumor is growing faster than healthy cells, the blood vessels have to grow at an accelerated rate,” he says. That results in tiny imperfections or openings in the lining of the blood vessels, making them

prone to leaks. The particles that Porter is designing are small enough to slip through those gaps and collect in the tumor. At less than 800 nanometers each, about 1/20th the size of red blood cells, the particles are invisible to the human eye, and even to some microscopes.

“You can design a particle of the right size and with the right sort of structural components that you can inject systemically,” he says, “and they will circulate and pass from the vasculature

◀ **THE CHALLENGE** Tyrone Porter is creating particles that remain stable for up to 48 hours while circulating in the bloodstream. The longer they circulate, the greater the likelihood of success.

and collect in the tumors.”

Porter and his team are creating two kinds of particles, or nanocarriers, to package a wide variety of chemotherapy drugs. Liposomes can carry drugs that are soluble in water-based solutions like

blood and are made up of naturally occurring cellular components called phospholipids, which can be purchased in a dried form and mixed together in the proper ratios.

The other type of nanocarrier, synthetic polymers, are compounds that can encapsulate drugs not soluble in fluids. “Polymers allow for a great deal of creativity and control,” says Porter. “You can synthesize a polymer to have a particular chemistry, structure, and behavior in the body.”

For Porter’s strategy to work, he must overcome a few challenges. The particles must remain stable while circulating in the bloodstream for 24 to 48 hours. The longer they circulate, he says, the greater the likelihood they will collect in the tumor.

And because not all tumors are alike—some

have a “dead” core, with fewer blood vessels growing at their center—Porter has to design particles that can distribute the drugs throughout the entire tumor by binding to certain receptors on the membranes of the cancer cells. While cells will internalize these bound particles in sac-like structures called endosomes, they will treat the particles as foreign invaders. Cells will increase

▶ **WEB EXTRA**
Tyrone Porter explains how to treat tumors with nanomedicine in a video at bu.edu/bostonia.

the acidity within the endosome, which ultimately destroys the particle and its drug payload.

Porter is making nanocarriers that can turn the tables

on those cancer cells by breaking the endosomal walls as the pH falls, releasing the chemotherapeutic agents. The trick is to create a particle that releases the drug before the sac gets too acidic. “We don’t want to run the risk of breaking down the drug,” he says. “An endosome’s pH will get as low as four or five. The liposome we’re working on will release the drugs when the pH drops to about 6.5.”

Such a drug delivery method may be effective on cancers where receptors have already been identified, such as certain cancers of the breast, prostate, and cervix.

For tumors whose cores are not dead, Porter is building nanocarriers that



↑ **HEAT SOURCE** Porter is building nanocarriers that will release their drugs when an external heat source, such as a focused ultrasound transducer (bottom), raises the temperature inside the tumor. He must also monitor the temperature in real time.

are stimulated to release the drug with an external heat source once they accumulate inside the tumor. Using a device that resembles a magnifying glass—called a focused ultrasound transducer—he heats the particles four or five degrees above body temperature for about five minutes. “We can heat a diameter of anywhere from one to two millimeters and a length of five to ten milliliters,” he says. It’s very small—roughly a grain of rice.”

The challenge with temperature-sensitive particles, Porter says, is controlling the heat. “You have to come up with a way to monitor the temperature in real time over the duration of heating. The approach people are working on

now is using magnetic resonance thermometry. You can measure temperature changes within a tenth of a degree Celsius.”

Porter, who is now testing both kinds of nanocarriers in rats, says that it could be 5 or 10 years before the treatment is ready for clinical use.

“You can still administer the drug through an intravenous injection,” he says. “But now that you’ve packaged the drug, you’re protecting your organs, your skin, your hair follicles, your white blood cells from the toxic effects of the drug while still delivering a high dose to the cancer cells. As a result, you can effectively kill the cancer cells while minimizing collateral damage to the healthy tissue.”

» Cells respond to invaders by increasing acidity, which destroys the particle and its payload.