March 26, 2012

It was around lunchtime one weekday this past fall, and Kenneth Hoyt, Ph.D., didn't have anything exciting to do.

He knew there was a biomedical engineering talk about to begin down the street from his Volker Hall office. "So, I figured what the heck," says the assistant professor of radiology and biomedical engineering. "I'll go check it out."

He watched and listened intently as Eugenia Kharlampieva, Ph.D., assistant professor of chemistry, talked about her shape-switching, hollow polymer hydrogel micro-containers with cell-mimicking shape. The capsules — with pH-triggered, shape-switching capabilities — certainly seemed to be the device Hoyt needed to continue his research on controlled drug delivery in cancer tumors using microbial contrast and targeting ultrasound agents.

"I sent Eugenia an email as soon as I got back to my office," Hoyt says. "We've been putting things together ever since."

Hoyt and Kharlampieva presented their work on innovations in drug delivery March 13 during the College of Arts & Sciences Interdisciplinary Innovation Forum. The collaboration between the College of Arts & Sciences and the School of Medicine researchers could lead to a significant breakthrough in drug delivery.

Hoyt and Kharlampieva envision using capsules as a contrast agent for ultrasound studies specially designed to target unique cancer biomarkers; those capsules, filled with a chemotherapeutic drug, also will deliver the medicine directly inside the tumor.

Hoyt will use a novel ultrasound-based technique that makes the capsules oscillate, producing temporary openings in the tumor's capillaries; he then will burst the drug-loaded microcapsules and dump the chemotherapeutic directly into the affected source.

"The potential is there for this to be a 'Holy Grail' type of drug-delivery mechanism," Kharlampieva says.

Using polymer capsules for drug delivery is a relatively novel area of research. There are only a few groups in the world taking this approach, including ones in Australia and China.

Two primary features of Kharlampieva's capsules make them unique. First, she can control their shape, making them spherical, cubicle, cylindrical or disk-like. She can also make them mimic the platelet shape of red blood cells.

The other unique feature of Kharlampieva's systems are that the polymeric shell, or walls of the capsules, are stimuli responsive. So when temperature or the body's acidity changes, the capsule swells or shrinks and can change its shape, dimensions and diffusion properties.

"Eugenia's polymer agents are a little different than what most people are trying to work with because they're both great drug-delivery vehicles and ultrasound contrast agents," Hoyt says. "Others have horse-blinders on and are convinced it has to be done a certain way. We're taking it a slightly different direction. It's a novel approach."

Model studies should begin on the drug-delivery capsules within the next six months.

Capsule shape, effectiveness

The drug-delivery system the researchers are creating is based on hydrogen-bonded interactions between water-soluble polymers. The capsule shell is very soft, elastic but robust enough to keep the shape of the object. The capsules also are non-toxic, do not kill normal

tissue and also can be modified chemically easily. They are at the submicron level in size, act like artificial cells and have a high-loading capacity.

“The main requirement for drug-delivery systems is that they should be non-toxic, biodegradable and biocompatible,” Kharlampieva says. “They also should have high-loading capacity be easily modified chemically. Our capsules are engineered that way.”

But it is the shape-changing part of the capsules that is especially unique because scientists typically can control only capsule dimension and permeability.

“There’s no question shape is important,” Kharlampieva says. “If our capsules have the shape of red blood cells they can be easily accepted at the affected site. They also can extend their lifetime in the blood stream and maybe suppress or find its way around the body’s immune response. The main idea is to extend the lifetime of the delivery mechanism.”

The researchers also want to investigate the way different cell types can accept the shaped capsules.

“We want to know the affect capsule shape has on how fast the cancer cells will uptake the chemotherapeutic,” Kharlampieva says. “If a spherical or cubical capsule approaches the affected site — how fast it can be internalized? We want to investigate that as well, and it’s why we think shape is important.”

Hoyt, who studies breast and other cancer tumors, says any disease a researcher wants to target can potentially benefit from this research. He says the capsules or contrast agents can be catered bind specifically to target proteins that tend to be overly abundant in the diseased tissue vascularity.

“You really can put anything in the capsules — even gene-therapy vectors — and presumably target any sort of disease you want,” Hoyt says. “Once this technology is developed, anything you want to get past your immune system — like through your liver, for example — we can hide inside these capsules. And the great thing is, independently, we’ve shown that the individual

building blocks making up these targeted drug-delivery vehicles works. We just need to take the next step now and get it fine tuned."

Reprinted with permission from the UAB Reporter. Original story found here.