Mark Dewhirst  
Apex Bioscience, Celsion  
Faculty Entrepreneur

By Whitney L.J. Howell

It isn’t every day that a veterinary researcher studying the effect of plutonium exposure in dogs ends up conducting cutting-edge investigations around cancer-drug delivery systems for tumors in humans. But that’s been the exact career trajectory for Mark Dewhirst, D.V.M, Ph.D.

Now the Gustavo S. Montana Professor of Radiation Oncology at Duke University, Dewhirst opted initially for veterinary medicine because he believed it would offer research opportunities unavailable in other fields. It didn’t take long, though, for his attention to turn to medical investigations with humans.

“I started out as a veterinary radiation oncologist, taking pets with cancer and treating them. Looking to see how they would do with various therapies,” he said. “But, then, I was recruited to Duke to study tumor physiology. That led to my first foray into entrepreneurship.”

In fact, it was hemoglobin, the iron-containing protein in red-blood cells, that led Dewhirst, also the vice director for basic science in the Duke Cancer Institute, to his first company, Apex Bioscience. The venture started with an experiment into whether a single nucleotide polymorphism – a small change in one segment of DNA – in hemoglobin could increase oxygen delivery. Results showed it could.

The company, then, used its knowledge of hemoglobin function and structure to design drugs that control and change the body’s levels of nitric oxide, a molecule that can cause organ damage in high quantities.

It’s been Dewhirst’s more recent work with David Needham, Ph.D., mechanical engineering and materials science professor in the Duke Pratt School of Engineering, which has garnered the most significant attention, though. Together, he said, they’ve developed a heat-sensitive, drug-delivering liposome that’s been successful in human clinical trials with liver cancer patients.

In addition, Dewhirst used the liposomes characteristics to develop a form of the liposome that can be seen on MRI to accurately measure drug concentrations in tumors. Other investigators world-wide are using the same properties, he said with high-intensity, focused ultrasound. Doing so could allow them to actually paint a drug onto a tumor target zone in a real-time heating process. Currently, all drugs in this type of system must be water-soluble.

These discoveries led to Celsion, Dewhirst’s second company. Currently, the venture’s No. 1 product ThermoDox®, is a heat-activated form of the cancer drug doxorubicin in a liposome capsule. Through this delivery method, researchers target high drug concentrations into specific
tumor areas, turn the heat up to 39.5 degrees Celsius, and attack. The results, he said, are significant.

“It’s like a local infusion right into the tumor,” he said. “It’s massive accumulation of the drug into the tumor – 20- to 30-times higher than with free drugs. That’s an enormous difference.”

The next steps, he said, are two-pronged. His team plans to expand its work beyond using only doxorubicin, as well as testing non-water-soluble drugs.

“We’re working on cis-platinum as the next drug – it has broader applicability to be used in a variety of diseases, including cervical, head, and neck cancers,” Dewhirst said. “We’re also working to develop carriers that are lipid-soluble that are triggered by heat to use more lipid solutions.”