

DIE-CAST: *The Dartmouth Atlas* reported that between 2003 and 2007, nearly a third of patients with advanced cancer died in hospitals and ICUs. The rate of hospital deaths ranged from 47% in Manhattan to 7% in Mason City, Iowa.



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Nanotechnology: Wee, wee work, all done at home

This past fall, the National Cancer Institute named Dartmouth a Center of Cancer Nanotechnology Excellence (CCNE)—one of only nine such centers in the nation. Along with the prestigious title came a \$12.8-million grant to fund the center for five years.

Cancer nanotechnology is a promising approach in which a magnetic field is used to heat minuscule nanoparticles that then destroy tumors. To move this concept from lab to clinic, the Dartmouth CCNE is drawing on experts from the Thayer School of Engineering, the Norris Cotton Cancer Center, and Dartmouth Medical School.

In fact, Dartmouth's grant application "had a really interesting and unique mix of clinicians, cancer biologists, and engineers," explains Jack Hoopes, D.V.M., Ph.D., who headed a nanotechnology working group for the past few years. "I think our advantage was that all of the investigators came from Dartmouth." That's unusual for big grants like the CCNEs, he says.

Cell: "We had materials scientists who understand particles who had never known much about a cell," Hoopes adds. "We had biologists who understood cancer cells and clinicians who saw the big picture of what would fit into patients. We could really do the whole thing at Dartmouth."

For now, the Dartmouth CCNE is focusing on breast

and ovarian cancers in particular. To that end, the researchers are undertaking to design new and better nanoparticles; to better understand how the nanoparticles bind to tumors and behave in the body; and, ultimately, to eliminate breast and ovarian tumors.

Patent: The first step is to design appropriate nanoparticles, says Ian Baker, Ph.D., director of the CCNE. His team is leading a project to do just that. They already have a patent pending, he says, for one new nanoparticle design.

The next challenge is to get the nanoparticles into the tumors. In cases where a tumor lies close to the surface—such as esophageal cancer, for instance—nanoparticles could be injected directly into the tumor. But for deep-seated cancers, delivering the particles will require a backdoor approach. Dartmouth CCNE researchers are designing

antibody tags to attach to the surface of the nanoparticles. Once tagged, Baker says, "The nanoparticles can be injected into the bloodstream and picked up by receptors on the surface of the tumors."

Once the nanoparticles are concentrated in the cancerous tissue, a magnetic field is applied. The field heats the minute particles, destroying or weakening the tumor. This hyperthermia technique is likely to be used in conjunction with chemotherapy or radiation therapy, Baker

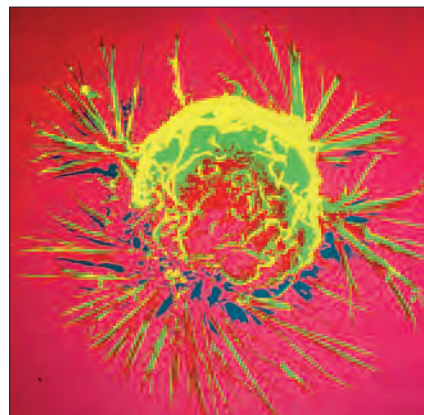
says. "The hyperthermia sensitizes a tumor to subsequent therapies," he explains.

So far, the CCNE research is all preclinical, says Keith Paulsen, Ph.D., deputy director of the center. That's by design. Under National Cancer Institute (NCI) guidelines, the CCNE grant cannot be used to fund clinical trials.

Trials: Nevertheless, the Dartmouth work is advancing quickly. Paulsen suspects clinical trials will start within the center's five-year lifetime, though they won't be funded directly by the NCI grant. "A lot of this is already occurring in animals and it's not a big stretch to push this into patients," he says.

Both Baker and Paulsen attribute the promising pace to the collaborative nature of the project. "The group challenges each other in a very positive way," says Paulsen. "I think it's going to be very productive."

KIRSTEN WEIR



This micrograph of a breast cancer cell is representative of the target of the nanotechnology group.