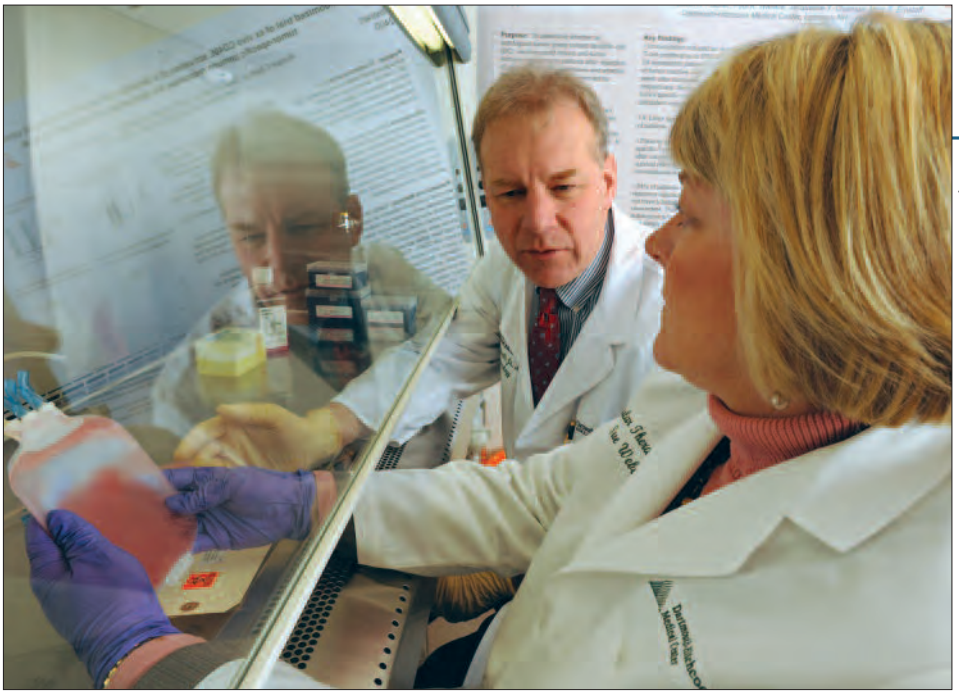

JON GILBERT FOX

Barth observes as lab technician Susan Webber processes a dendritic cell culture like those used in the trial.

Trial tests cancer vaccine made from tumor cells

It sounds like a case of asking the fox to guard the henhouse: To create a vaccine against metastatic colorectal cancer, DMS researchers enlisted the help of tumor cells.

Colorectal cancer can often be treated by removing the tumor surgically. But if the cancer has spread to other organs, such as the liver, the outlook is grim. These metastatic tumors can also be treated with surgery, but the cancer usually returns anyway. Most such patients eventually die of the disease—about 50,000 people each year in the U.S.

Trial: DMS cancer surgeon Richard Barth, M.D., having seen many cases of metastatic colorectal cancer over the course of his career, does research aimed at giving physicians better tools to use against the disease. Years of effort developing a vaccine in mice led recently to a clinical trial in which patients were treated with a mixture made up of immune cells and bits of tumors, both taken from each individual patient to create personalized vaccines.

All of the 26 patients in the study had colorectal cancer that had spread to the liver. The initial tumors in the colon or rectum had been removed some time earlier, but the cancer had returned. About three weeks after surgeons removed the metastatic tumors from the liver, the research team—which included Barth, research assistant Dawn Fisher, and other physicians and scientists—created the vaccines. They took blood samples from each patient and kept them in conditions that fostered the growth of dendritic cells, a type of immune cell that activates the immune system by alerting other cells to the presence of a threat. They then added bits of proteins from each patient's tumor, which the dendritic cells engulfed and displayed on their surfaces. The proteins presented on the dendritic cells are the immune system's version of a "Wanted" poster, alerting the immune system that cells with those specific proteins are a threat. Those dendritic cells were then injected back into the patient's lymph nodes, where they activated T cells to find and destroy tumor cells with those antigens.

But 11 of the other 22 patients developed an immune response.

"The idea is that the T cells that are activated by the dendritic cells can . . . find these little tumor cells and kill them before they have a chance to grow," Barth says.

The first milestone for the study was to measure how many of the patients had an immune response. Two of the 26 already had metastases before the vaccine was given; both died within a year of vaccination. And the blood samples taken from two other patients did not have enough cells to conduct all the analyses of the immune response.

Survived: But 11 of the other 22 patients developed an immune response to the vaccine within one week of treatment. Of those 11, seven (64%) survived without a recurrence of cancer for at least five years. And of the 11 patients who did *not* develop an immune response within one week, only two (18%) survived five years without a recurrence. The vaccine seemed to have made a difference in those patients who responded to it. The researchers published the results in the journal *Clinical Cancer Research*.

Barth was excited by the outcome. "We couldn't find any other characteristics that would account for why people had a better survival other than the fact that they had this immune response," he says. It will take a randomized trial in which some patients receive the vaccine and others do not to provide definitive evidence. But, he says, "this is certainly suggestive."

One aspect of the study proved disappointing. The vaccine given to 12 of the patients included another molecule, called CD40 ligand, in addition to the dendritic cells and pieces from the patients' tumors. This molecule has been shown in mice to improve the ability of dendritic cells to signal an alarm to the immune system. But in this trial it had no effect on the strength of the immune response.

Effect: Eventually, Barth hopes to test the vaccine in a randomized trial. First he plans to create a stronger vaccine to have the best chance for success in a trial. He's not sure why some patients responded and others did not, but it's possible that a stronger vaccine could have an effect on more patients.

"This is a big clinical need," Barth says. "Over half the patients are dying of the cancer. We need better treatments." AMOS ESTY