Medical Xpress

Study uses the patient's tumor to form vaccine

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A new process for creating a personalized vaccine may become a crucial tool in helping patients with colorectal cancer develop an immune response against their own tumors. This dendritic cell (DC) vaccine, developed at Dartmouth and described in a research paper published this week in the journal *Clinical Cancer Research*, was used after surgical resection of metastatic tumors to try to prevent the growth of additional metastases.

"The results of the study suggest a new way to approach cancer treatment," said Richard Barth Jr., MD, Chief of General Surgery at Dartmouth-Hitchcock Medical Center and a member of the Gastrointestinal Clinical Oncology Group at Dartmouth-Hitchcock Norris Cotton Cancer Center, who is the study's principal investigator. "Basically, we've worked out a way to use dendritic cells, which initiate immune responses, to induce an antitumor response."

Dendritic cells are critical to the human body's immune system, helping identify targets, or antigens, and then stimulating the immune system to react against those antigens. The new research grew dendritic cells from a sample of a patient's blood, mixed them with proteins from the patient's tumor, and then injected the mixture into the patient as a vaccine. The vaccine then stimulated an anti-tumor response from T-cells, a kind of white blood cell that protects the body from disease.

In the study, Barth first operated on 26 patients to remove tumors that had spread from the colon to the liver. While some of these patients

would be expected to be cured with surgery alone, most of them would eventually die from tiny metastases that were undetectable at the time the tumors were removed from the liver. The DC vaccine treatment was given one month after surgery. The results were that T-cell immune responses were induced against the patient's own tumor in more than 60% of the patients. The patients were followed for a minimum of 5.5 years. Five years after their vaccine treatment, 63% of the patients who developed an immune response against their own tumor were alive and tumor-free. In contrast, just 18% of the patients who did not develop an immune response against their own tumor were alive and tumor-free.

"We showed that a tumor lysate-pulsed DC vaccine can induce immune responses against the patient's own tumor in a high proportion of patients," stated Dr. Barth, who has been investigating DC-based vaccines in mice and patients for more than 10 years. "There were two basic questions we wanted to answer: one, can we generate an antitumor response, and two, does it matter? From our research, the answer to both questions is yes."

He said DC vaccines have been a research interest at many institutions, and previous studies showed that DC vaccines could not reduce or eliminate measurable metastatic tumor deposits. "It turned out we were asking the T-cells to do too much," he commented. "The small number of T-cells that are generated by a vaccine can't destroy a large tumor. However, what they may be able to do is search out and destroy tumor cells that exist as only microscopic tumor deposits. Once we brought patients into a measurable tumor-free condition with surgery, the anti-tumor T-cells induced by the DC vaccine may help keep them that way."

Follow-up studies are necessary to more fully understand the mechanisms of the DC vaccine and its impact on long-term survival rates, Dr. Barth said. He believes this study may open the door to a significant change in cancer treatment in the future. The DC vaccine is

non-toxic, while traditional chemotherapies are highly toxic. "It's your own immune system doing the fighting," he commented. "I'm optimistic that this really will have an impact."

Provided by Dartmouth-Hitchcock Medical Center