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Cancer vaccine combination therapy shows survival benefit in breast cancer

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A vaccine that targets cancer cells in combination with the drug letrozole, a standard hormonal therapy against breast cancer, significantly increased survival when tested in mice, a team of UC Davis investigators has found.

The findings will be published today in the journal Clinical Cancer Research.

"We found that the vaccine and the hormonal drug letrozole were more effective when given together," said Michael DeGregorio, UC Davis professor of hematology and oncology and principal investigator of the study. "This adds critical evidence that immunotherapy with vaccines, which has traditionally been used to prevent infectious diseases, is also a promising new approach to combating cancer."

The vaccine, known as L-BLP25 (Stimuvax), specifically targets Mucin1 glycoprotein (MUC1), an antigen that is expressed in an altered form on cancer cells. When introduced into the body, the vaccine generates an immune response by T-lymphocytes, which then recognize and destroy the tumor cells. Mice in the study were injected weekly with the vaccine -- or a placebo -- for eight weeks.

In addition to the vaccine or placebo, some mice were treated with either letrozole or tamoxifen, commonly used hormonal therapies against breast cancer. Both drugs work by blocking the effects of estrogen, which can slow or stop the growth of some types of breast cancer cells

that need the hormone to grow. Although the drugs have similar actions, the benefits of the vaccine were greatest in the mice treated with letrozole; in contrast, vaccinated mice given tamoxifen actually fared worse than those given either the vaccine or tamoxifen alone.

"Hormonal drugs affect the immune system in different ways, and apparently the actions of tamoxifen prevent the vaccine from working effectively," said DeGregorio. "This highlights the importance of rigorous testing of different combinations of therapies before using them in patients."

The article, available online, is titled "L-BLP25 vaccine plus letrozole induces a TH1 immune response and has additive antitumor activity in MUC-1 expressing mammary tumors in mice."

Breast cancer is the second-leading cause of cancer death in women in the United States, following lung cancer. Most cases of breast cancer are "estrogen-dependent" and respond to hormonal therapy. For tumors that are independent of hormonal influence, treatment options are limited and would especially benefit from a new treatment strategy such as a vaccine.

The vaccine was found to work best when the tumor burden -- the amount of cancer present -- was low, indicating that the vaccine may one day be best used as a preventative measure for women at high risk of developing breast cancer or for treatment of early disease.

Vaccine therapy is a promising new cancer-fighting strategy; the first therapeutic vaccine for prostate cancer was approved by the U.S. Food and Drug Administration in 2010. Trials with L-BLP25 vaccine are currently under way for lung and pancreatic cancers, whose cells also express altered MUC1, the same tumor-associated antigen found on breast cancer cells. The current study is the first known to the authors to

demonstrate that a hormonal therapy combined with a vaccine provides additive antitumor activity and survival benefit.

"This was a true alliance between academics and industry," added DeGregorio, who noted that trials such as this one are especially expensive because of the number of mice needed and the length of time -- about three and a half years -- required to establish their findings. The study had support from the pharmaceutical company, Merck KGaA Darmstadt Germany.

DeGregorio's group will further test the vaccine with other conventional therapies and determine optimal dosing. Clinical trials in patients with breast cancer are in the planning stages.

Provided by Queen's University Belfast

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