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Plants make vaccine for treating type of cancer

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Plants could act as safe, speedy factories for growing antibodies for personalized treatments against a common form of cancer, according to new findings from the Stanford University School of Medicine. The findings came in the first human tests of an injectable vaccine grown in genetically engineered plants.

The treatments, which would vaccinate cancer patients against their malignant cells, could lead to earlier personalized therapy to tackle follicular B-cell lymphoma, an immune-system malignancy diagnosed in about 16,000 people each year.

Doctors regard follicular B-cell lymphoma as a chronic, incurable disease. The standard treatment, chemotherapy, has such severe side effects that patients often opt for watchful waiting in the early stages of illness. However, plant-grown vaccines, which lack side effects, could allow earlier, more aggressive management of the cancer.

"This would be a way to treat cancer without side effects," said Ronald Levy, MD, professor of oncology and the Robert K. and Helen K. Summy Professor in the School of Medicine, who is the study's senior author. "The idea is to marshal the body's own immune system to fight cancer."

The findings will appear July 21 in the advance online issue of the *Proceedings of the National Academy of Sciences*. The study was a phase-1 trial that showed plant-grown cancer vaccines were safe for

patients and could be produced quickly and cheaply. Sixteen newly diagnosed lymphoma patients received the treatment; none experienced any side effects from plant-grown vaccines.

Future studies will test the vaccine's effectiveness.

The cancer vaccines rely on a biological quirk of follicular B-cell lymphoma, which is a type of non-Hodgkin's lymphoma. The cancer starts when a single immune cell multiplies uncontrollably, producing many identical clones of itself. The clones all carry the same antibody on their exterior, a marker that is unique to the cancer and is not found on any of the body's healthy cells. Levy's vaccination strategy is to inject many copies of the cancer-specific antibody into a newly diagnosed lymphoma patient, stimulating the patient's immune system to seek and destroy malignant cells.

Previous trials of this kind of vaccine, produced in animal cells and tested in mice and humans, have had mixed success, and the vaccines are not yet commercially available. Growing cancer vaccines in plants could circumvent some of the hurdles to turning the concept into a real treatment, Levy said.

Because each person's cancer antibody is unique, every patient needs a personalized vaccine. Growing personalized vaccines in animal cells takes months, costs thousands of dollars per patient and comes with the theoretical risk that a patient might inadvertently be infected with an animal virus that contaminated the cells used to grow the vaccine. Personalized vaccines could also be produced with genetically engineered bacteria, but bacteria-grown vaccines aren't ideal, either.

"The plant system has some advantages," said Levy, who is also a member of the Stanford Cancer Center and a Howard Hughes Medical Institute investigator.

The researchers chose tobacco plants that were genetically engineered to reproduce quantities of the vaccine. To make a tobacco plant churn out a human antibody, scientists isolate the antibody from the patient's tumor and put the antibody gene into a modified version of the tobacco mosaic virus. They infect a tobacco plant with the gene-carrying virus by scratching the virus on its leaves. The virus takes the gene into the plant's cells, which then churn out lots of antibody. After a few days, technicians snip off the plant's leaves, grind them up and purify the antibody. Only a few plants are needed to make enough vaccine for each patient.

"The new manufacturing system allows very rapid production of a vaccine," said Charles Arntzen, PhD, a professor of plant biology at the Arizona Biodesign Institute at Arizona State University, who was not involved in the research. "I think without the speed, it would be hard to convince a cancer patient to wait for a vaccine to be developed, rather than going on some other therapy."

"It's pretty cool technology," Levy said. "And it's really ironic that you would make a treatment for cancer out of tobacco. That appealed to me." None of the harmful chemicals found in cigarettes end up in the purified vaccines.

Not only is the technology fast, cheap and safe, but Levy said there's reason to expect that the plant-grown antibodies will generate a stronger immune response than those made in animal cells. Both plant and animal cells attach sugars to antibodies and other proteins during biochemical processing, but the plant and animal sugars are different. The difference might prompt a more robust immune response to plant-grown antibodies, Levy said.

The next research step is a phase-2 clinical trial to test the effectiveness of plant-grown vaccines in a larger group of lymphoma patients, Levy

said. He's optimistic, adding, "We know that if you get the immune system revved up, it can attack and kill cancer."

Source: Stanford University