

## The Scientist: NewsBlog:

"Pharmed" vaccine passes early test

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A team of researchers has completed human tests of the first plant-produced vaccine for non-Hodgkin's lymphoma. The successful [results](#) of a phase I clinical trial suggest that plants could provide a safe, inexpensive reservoir to "grow" vaccines for the common human cancer, according to a study published tomorrow (July 22) in the *Proceedings of the National Academy of Sciences*.

The trial "builds upon all the advances in immunology that have come out in the last half-dozen years," said [Charles Arntzen](#), co-director of the Center for Infectious Diseases and Vaccinology at Arizona State University and editor of the paper. The vaccine has a "real opportunity for commercial success," he said.

Follicular B-cell lymphoma is a cancer of malignant B-cells in the immune system affecting more than 16,000 people each year. "Every tumor starts from one cell," said [Ronald Levy](#), a Stanford University oncologist and senior author on the paper. That cell, a malignant B-cell, has a unique immunoglobulin (Ig) molecule on its surface which is cloned into each new tumor cell. The cell-surface Ig provides an ideal target for therapies, but the difficulty in designing a vaccine, noted Levy, is that every tumor is different, so the therapy must be personalized for each individual.

Custom producing a vaccine through animal cell cultures is time-consuming and expensive, so Levy began searching for [new methods of production](#). When plant technicians from [Large Scale Biology Corporation](#) in California approached him and said they could produce the vaccine proteins in tobacco plants, he said, "Oh yeah? I'll give you a gene for a mouse tumor, and you show me that it works," recalled Levy. "They came back in a month, I checked [the vaccine] in mice, and it worked. I said, 'Okay, let's move it into people.'"

To produce the vaccine, a biopsy is taken from a lymphoma patient. The gene for the B-cell surface Ig is isolated and then patched into a tobacco mosaic virus expression vector. The virus is scratched onto the leaves of a tobacco plant, where it begins to replicate. After a week, the plant is harvested, the protein quickly purified, and the vaccine injected into the patient. Total time from biopsy to treatment averages three to four months, according to the paper. Animal-based vaccine production for B-cell lymphoma takes double that time, said Levy.

The [plant-based vaccine](#) produced no side effects aside from mild injection-site reactions and some flu-like symptoms. The researchers did not evaluate efficacy, although they observed cellular immune responses in most of the sixteen patients who completed the study. In [previous animal studies](#), mice with transplanted B-cell tumors given two vaccinations of plant-derived antigens had an 80-percent survival rate after 60 days. Those who did not receive the vaccine died within 21 days.

Levy's vaccine is not the first human vaccine to be produced from plants. In 1992, Arntzen and colleagues produced one for hepatitis B, also from tobacco plants. But today, 16 years later, Arntzen laments, there is still little commercial interest in the field, although plant-produced vaccines for hepatitis B and Norwalk virus have also undergone early testing in humans. Virtually any protein produced in yeast or Chinese hamster ovary cells (a common host for industrial production of recombinant proteins) can be produced in plants, he said, yet no plant-based vaccine is on the market. He speculates the slow development is a result of uncertainty on behalf of pharmaceutical companies. "Uncertainty is the kiss of death," said Arntzen. Still, he hopes plant biotech "will be the next revolution in protein manufacturing." Levy agreed. "I'm pretty amazed" by the technology, he said. "It should be advanced further."