Teasing Vaccines From Tobacco

Swine Flu Epidemic Spurs Military to Join the Hunt for Plant-Based Alternatives

By GAUTAM NAIK

The U.S. Department of Defense, caught off guard by the swift spread of the H1N1 flu virus last year and delays in producing a vaccine, is backing an unusual plan to use tobacco plants to make the vaccine.

Flu vaccines are typically grown in chicken eggs. Although the technique is slow and expensive, vaccine makers have done little to improve on this reliable method for more than 60 years. The urgent need for a better way became apparent last year.

"The response to H1N1 was a disaster," said Brett Giroir, vice chancellor for research at Texas A&M University System, part of a consortium testing plant-based vaccines for H1N1, or swine flu.

The Defense Advanced Research Projects Agency—which conducts research to protect soldiers from infectious diseases, and also is concerned about the U.S. capability to react swiftly to a bioterrorist attack, among other things—has awarded the consortium $40 million to make an initial 10 million doses of H1N1 vaccine.

Texas A&M and closely held firm G-Con will together invest a further $21 million. Details of the project, known as GreenVax, will be announced Wednesday.

For several years, vaccine companies have worked on harvesting vaccines in everything from caterpillar cells to cocker-spaniel kidney cells. Plants have certain advantages over animal parts, which may contain
pathogens harmful to humans. The tobacco plant is particularly promising: It has been extensively researched, is cheap to grow and can yield large amounts of vaccine quickly—potentially reducing production time to weeks instead of several months.

Earlier this month, Arizona State University researchers showed a plant-based drug could prevent and treat West Nile virus infection in mice. In January, Germany's Bayer AG said it was testing a plant-based vaccine for non-Hodgkins lymphoma.

In December, Medicago Inc. of Quebec City reported positive results for a tobacco-based vaccine for avian flu, or H5N1, which has killed more than 250 people world-wide. Biotechnology firm VAXX Inc. of Tucson, Ariz., says it soon plans to start a human trial of a tobacco-based vaccine for Norwalk norovirus—or "cruise ship virus"—which causes gastroenteritis in as many as 74 million Americans annually.

GreenVax is one of the more ambitious of the plant-based vaccine projects. It is partly based on research done at Fraunhofer USA Center for Molecular Biotechnology, in a partnership with the biotech firm iBio Inc., both based in Newark, Del.

**Making Vaccines from Plants**

[Diagram: Scientists isolate a protein from the flu virus that triggers a protective immune response in patients. They implant the gene for this protein into bacteria. They infect a tobacco plant with the bacteria. The gene is incorporated into the plant, directing it to produce flu proteins. The proteins are extracted from the plant and purified into a vaccine.]

As a first step, researchers at Fraunhofer isolated a protein from the H1N1 virus known to trigger a protective immune response in a patient without causing an infection. A gene for this protein was then introduced into a bacterium. Tobacco plants were placed in a special chamber and dipped into a soup of the bacteria, which caused the plants to get infected with the gene-carrying bacteria.

The infected plants then began to produce the protein from H1N1 in large quantities. The plants grew for about a week. Their leaves were then chopped up and crushed, and the protein from H1N1—the essence of the vaccine—was extracted from the slurry and purified.

Initial tests on ferrets, which can catch human flu, showed the vaccine was safe and effective. "The good news is that this vast amount of human protein isn't toxic to the plant," so it can keep producing large amounts of the vaccine's raw material, said Barry Holtz, president of G-Con. And the plants don't become "transgenic"—their seeds, for example, aren't changed, so they can't spread genetic alterations to normal plants.

The GreenVax project still has a long way to go. It needs to show that it can produce sufficient quantities of purified vaccine-ready protein quickly and safely. And such a vaccine would have to be tested in humans and get the approval of the Food and Drug Administration before it can be provided more widely.

The consortium plans to build a 145,000-square-foot vaccine production facility in Bryan, Texas, managed by G-Con. One innovation being developed: Mobile manufacturing "pods" that can be deployed swiftly in areas where the vaccine is urgently needed.
GreenVax hopes to produce the initial 10 million doses of H1N1 vaccine within 12 months. Large-scale human clinical trials are expected to begin in 2011, and could take up to 18 months to complete. The setup could be used to produce other vaccines as well.

"The science hasn't yet been unleashed to get past chicken eggs for making vaccines," says Dr. Giroir. "But now that the system is stressed, there's a reason to get past it."

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