



Banana Vaccines: A Conversation with Dr. Charles Arntzen

by **Mandy Redig, University of Arizona**

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A version of this article first appeared on the [Flinn Foundation's Website](#) as part of an ongoing series of features articles profiling individuals involved with the development of the biosciences in Arizona. The following article has been modified slightly from that version.

As Archimedes could attest, inspiration can strike anywhere. Legend has it that the ancient Greek thinker discovered the mathematical laws governing buoyancy in a bathhouse while idly watching soap float. The nature of scientific research has changed since the third century B.C., but the spirit of observational inquiry that led to Archimedes's principle is still active.

When Dr. Charles Arntzen of Arizona State University visited Thailand in 1992, he was not expecting a moment of scientific "eureka" that would redirect his career. However, after observing a young Thai mother soothing her fussy infant with bits of banana, this plant molecular biologist was struck with an idea that is both startling and ingenious. What if, in addition to quieting her child, the mother could also administer a life-saving vaccine - *in the banana*?

From vision to reality

Arntzen's vision is well on its way to becoming reality, thanks to a combination of dedication and applied biotechnology. As the president emeritus of the Boyce Thompson Institute for Plant Research, founding director of the Arizona Biomedical Institute, and member of the President's Council of Advisors on Science and Technology, Arntzen is well equipped to handle the challenge



he has undertaken. His breakthrough lies in forging a link between green plants, foreign DNA, and vaccines.

Vaccination stands as one of modern medicine's greatest success stories. Early experiments by Edward Jenner and Louis Pasteur taught physicians they could prevent disease merely by exposing a patient to a weakened or inactivated pathogen. While his protocols violate today's clinical trials regulations, Dr. Jenner was able to prevent children from getting smallpox - even when he deliberately exposed them to it - after first inoculating them with the pus from cowpox.

Dr. Charles Arntzen displays some of his vaccine-carrying tomatoes. (Photo courtesy of [Arizona State University](#) and the [Flinn Foundation](#))

Today, most new vaccines contain a specific protein or set of proteins from a pathogen of interest and not the pathogen itself. A protective immune response can result from this more limited (and inherently less risky) exposure. Though materially different from those developed by Jenner and Pasteur, modern vaccines, including Arntzen's, still build upon the same fundamental principle: If the immune system is trained to recognize a pathogen prior to infection, the disease can be prevented when the actual pathogen is encountered.

Delivering to the developing world

Disease prevention via an edible vaccine is great news for people around the globe. The problem with current vaccination protocols - and the passion behind Arntzen's research - is that what works in the developed world is often much more difficult to deliver in the developing world, or simply too costly to purchase. A vaccine that requires a sterile syringe, refrigeration prior to injection, and repeated booster shots is difficult to implement in many countries. Unfortunately, this often means that the people who most need a vaccine cannot get it. In a discussion of his work, Arntzen points out that "each year diarrhea kills about two and one-half million children under the age of five." He

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persuasively uses such horrendous statistics to champion his cause. In his own words, "It's hard to be pro-infant mortality."

While Arntzen's edible vaccine is likely to win approval from children everywhere, there are actually significant medical advantages to this route of administration. An oral vaccine incorporated into a plant bypasses the need for sterile syringes, costly refrigeration, or multiple injections. Furthermore, since many of the developing world's most deadly diseases - cholera, rotavirus, and *E. coli* infection, to name a few - enter the body through the gastrointestinal tract, a vaccine that is ingested may actually provide the best protection because it mimics the natural route of infection.

Developing the edible vaccine

The trick with an edible vaccine is convincing a plant to express the genes of a foreign organism. Fortunately, Arntzen's prior work prepared him to face this challenge. As a biochemist, his career focused on unraveling the means by which photosynthetic membranes in plants capture solar energy. "What we've done for the last ten years is try to change the cellular machinery of a plant by adding a new gene, cause that gene to make a new protein, and coax the new protein into folding to the desired shape so that it accumulates. I took knowledge about plant proteins under normal circumstances and used that for something new." That something new was vaccine development.



When Arntzen started investigating the vaccine issue in the early 1990s, scientists were already using genetically engineered yeast to produce proteins for injection vaccines. Arntzen's experience with green plants led him to consider other options. He remembers thinking at the time, "Would it be possible to use a higher plant instead of a lower plant, something we already know is an agricultural crop? Can we take a potato or tomato and turn it into a green factory?"



Will these bananas one day replace vaccination with needles?

(Photos courtesy of the [Botanical Society of America](#) and [Disaster Relief](#))

Indeed, modern technology enables Arntzen to insert specific genes from a foreign organism into the genome of a green plant. Progeny plants will then produce the foreign protein. If the foreign protein happens to be an immunity-inducing pathogen protein, an edible vaccine is in the making.

Challenges beyond science

Yet the challenges of science are not the only obstacles Arntzen faces. This type of project requires a multidisciplinary approach, incorporating the skills of many types of basic and clinical scientists as well as experts in product regulation and distribution. Says Arntzen, "No biochemist can make progress in moving something forward on his own. I need linkages with people who do immunology. I need people in vaccine development. I also have increasingly found that I have to understand the regulatory environment."

In fact, satisfying regulatory policies has been one of the most painstaking elements of Arntzen's work. He is determined to demonstrate that his vaccine passes the rigorous requirements of the Food and Drug Administration, thereby silencing any critics who would accuse him of "dumping" experimental technology on the world's poor. Indeed, an interview with Arntzen reveals him to be passionate and articulate in explaining the rationale behind his work. His ideas involve sophisticated science and technology, but his

motives are grounded in a genuine concern and humanitarian interest.

Questions concerning genetically modified organisms

Not everyone agrees with him, though. In an interview with Nova and PBS in October 2000, Dr. Jane Rissler, a senior scientist with the Union of Concerned Scientists, expressed the opinion that in the context of genetically modified foods, "It's a ploy to convince relatively well-to-do people in the industrialized world to approve of this technology. It's playing on the guilt of relatively well-off people, that somehow if they don't approve of this technology by agreeing to buy the products, the result will be people dying of starvation in the developing world."

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While directed at genetically modified foods in general and not specifically edible vaccines, her comments do strike at the heart of the debate over genetically modified organisms (GMOs) that has also stirred up controversy between the United States and Europe. Some scientists feel GMOs are safe while others do not. In a 2000 interview with PBS, Jeremy Rifkin, president of the Foundation on Economic Trends, recalls the time in 1983 when the United States government approved the release of the first GMO, a bacteria that prevents frost from forming on agricultural crops: "All of our regulations had been set up in an era in which physics and chemistry ruled. It seemed to me that we needed to have a thorough and thoughtful global discussion on the potential environmental implications of reseeded the earth with genetically modified organisms."

Critics of GMO technology argue that not enough testing has been done (or is even possible) to ensure that genetically altered organisms will not have negative environmental consequences. Arntzen recognizes these concerns and much of his time is spent working to first ensure that his work meets rigorous standards of integrity and then to translate that information to the public. He says, "To a large extent I rely on the regulatory side [agencies] to help in the education and acceptance. I have to be constantly alert to those issues because it's always something that can always rise up." In fact, Arntzen's protocols take such concerns into consideration. As a result, the genetically altered vaccine-producing plants are not grown freely, thereby minimizing the risk that such genes would be unintentionally incorporated into other species.

Exciting results from recent clinical trials

From an efficacy perspective, Arntzen's most recent clinical trials are particularly exciting. Human volunteers who enrolled in a study at the University of Maryland at Baltimore started producing antibodies against Norwalk virus (which causes acute bouts of diarrhea) after eating Arntzen's creations - genetically engineered potatoes. Negotiations are in progress to start clinical trials abroad with the [International Vaccine Institute in Korea](#), a new center funded in large part by the Bill and Melinda Gates Foundation. Clinical trials of cholera vaccines are also planned to take place there as well as in Vietnam and Cambodia, regions where cholera is still a serious medical concern.

In addition, during a recent scientific conference held at the Flinn Foundation's Phoenix office, tentative connections were made with company representatives from Egypt and

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or tomatoes. Both products can be easily freeze-dried, transported, and reconstituted. Since many target countries have a long history of herbal medicine, Arntzen is interested in working within already-existing ideas. "Our goal is not to make the decision for how we want (the freeze-dried dose) introduced," he said. "We want to work with them."

In the meantime, Arntzen is still working on the banana vaccine. His original, utopian vision was of a communal banana tree where villagers could dose themselves. Unfortunately, this scenario does not adequately address the concerns related to any vaccination protocol - efficacy, quality control, and dosage regulation. As a result, Arntzen's current efforts focus on tomatoes and potatoes, which have shorter growing seasons, are easier to manipulate in an experimental setting, and can be freeze-dried in controlled doses. Practicality hasn't inhibited his idealism, however. To this day he keeps a jar of Gerber's baby food - banana, of course - on the corner of his desk for inspiration.

Arizona's sunny skies and warm weather are known to attract people from all over the world - who can resist playing golf in short sleeves in December? Arizonans are fortunate that warm weather is also good for growing plants. A combination of ASU's offer of the Florence Ely Nelson Presidential Endowed Chair and greenhouse opportunities brought Arntzen to Phoenix. He sounds remarkably like a winter tourist when he exclaims, "The weather is perfect!" Yet unlike the tourists, Arntzen is excited about greenhouse horticulture, not golf. In its own way, a functional edible vaccine would indeed be a hole-in-one.

India. This meeting, organized by Arizona Biodesign Institute on behalf of the Production of Vaccines from Applied Crop Sciences (ProVACS) Center, highlighted technical advances in plant-based vaccines. Arntzen, the keynote speaker at the meeting, said, "We intend to visit India. They're willing to fund clinical trials there - we could send vaccine materials to them and they're interested in developing the product."

Setting the stage for the banana vaccine

For now, all such clinical trials will involve modified potatoes



Arntzen at work in the greenhouse (Photo courtesy of [Arizona State University](#) and the [Flinn Foundation](#))

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