

Conventional vaccines have cut disease deaths by 99%, but have been limited to only 13 disease targets. DNA vaccines, on the other hand, might some day prevent or cure cancer, HIV and a litany of other infectious diseases. So, what's the hold-up?

"DNA vaccines have the potential to prevent or control a host of diseases, but one of the biggest barriers has been ineffective uptake of DNA by cells. It is possible that we can overcome this barrier," says **Dr. Jeffrey B. Ulmer, Senior Director and Site Head for Vaccines Research with Novartis Corp.** (Emeryville, CA).

"Given that we have proof of principle in animals, and in some cases large animals like horses, that DNA vaccines can work, this gives us hope that they can be made to work in humans too," Dr. Ulmer says.

"Absolutely, DNA vaccines offer great hope," insists **Dr. George Pavlakis, Chief of the Human Retrovirus Section, Vaccine Branch, at the National Cancer Institute (NCI).**

"While we are still at the beginning and have a lot of work to do, we've seen very dramatic progress in the past few years with DNA vaccines," adds Dr. Pavlakis. "I believe in the near future we are going to have additional breakthroughs that will make DNA vaccines more efficient and more practical."

"One of the biggest barriers is getting DNA more effectively inside cells," explains Dr. Ulmer. "The majority of the human clinical trials that have taken place so far have simply injected a soluble solution of DNA into the muscle, very much like we do conventional vaccines. But this is a very ineffi-

What the leading DNA vaccine experts are saying:



Michael A. Egan, PhD
Senior Research Scientist
Viral Vaccine Immunology
Wyeth Pharmaceuticals

"Given the excellent activity of DNA vaccines observed in non-human primates, I believe that vaccine-elicited protective and therapeutic immunity in humans is certainly within reach."



George N. Pavlakis, MD, PhD
Chief
Human Retrovirus Section, Vaccine Branch
National Cancer Institute

"I have stated in public seminars that, in my opinion, electroporation is the gold standard for DNA vaccine delivery, giving us the best result in terms of immunogenicity of DNA vaccines."



Jeffrey B. Ulmer, PhD
Senior Director
Site Head for Vaccines Research
Novartis Corporation
Emeryville, CA

"DNA vaccines have the potential to prevent or control a host of diseases. One of the biggest barriers has been ineffective uptake of DNA by cells. It is possible we can overcome this barrier."



David P. Weiner, PhD
Professor, Pathology & Laboratory Medicine
Chair, Gene Therapy & Vaccines Program
School of Medicine
University of Pennsylvania

"Our lab's important work in the field of DNA vaccines focused on HIV therapy. We established that DNA vaccines are well-tolerated and drive immune responses in humans."

cient way of getting DNA into cells—not only just getting in, but they actually then have to go on and transfect those cells—meaning the DNA has to be taken up by the nucleus and transcribed into protein by the cells. That's a tall order. There are a lot of potential pitfalls along the way of getting the DNA from a syringe into a cell making a protein. By the time you count up how many of the plasmids you initially inject versus how many are getting to the right place doing the right thing, it's an infinitesimally small proportion of what you've injected," Dr. Ulmer says.

"Electroporation, alternatively, is a brute force way of getting DNA past one of the physical barriers and into cells," adds Dr. Ulmer. "It is conceivable this could be accomplished in humans."

Adds NCI's Dr. George Pavlakis: "I have stated in my public seminars that for us, electroporation is right now the gold standard for DNA vaccine delivery, giving us the best result in terms of immunogenicity of DNA vaccines. When this technology matures, it will be one of the most competitive for DNA vaccine delivery."