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Delivering a Virus Imposter Quicker

With H1N1 vaccine supplies delayed, attention turns to faster-to-make "virus-like particles."

By David Dobbs

As the current race between H1N1 and vaccine deliveries makes painfully clear, it's [hard to produce](#) a flu vaccine fast enough to outrun a pandemic. But, with two new flu vaccine candidates beginning clinical trials this month, the "virus-like particle," or VLP, vaccine may be about to fulfill a long-heralded potential as a flu vaccine that arrives more quickly.

The key biomedical distinction of a VLP vaccine is its antigen--the component that provokes an immune response in the person vaccinated. VLP vaccines don't use dead or weakened flu viruses as antigens, as conventional approaches do. Instead, VLP vaccines use little protein shells, grown in either plants or insect cells, that look just like real viruses to the body's immune system but that contain no influenza genetic material.

"The particle exactly replicates the virus, but because there's none of the genetic material that makes a virus active, it presents no danger," says [Polly Roy](#), a professor of virology at the UK's London School of Hygiene and Tropical Medicine who was one of the first VLP researchers. The lack of genetic material also spares the need for the formalin and detergent treatments that conventional antigens undergo to render them noninfectious but that also compromise their power.

Most significant, VLP vaccines can be made quickly. "From the time you identify an outbreak and publish the genetic sequence online, you can have a vaccine in full production within three or four months," says [Ted Ross](#), a microbiologist and geneticist who researches VLPs at the University of Pittsburgh's Center for Vaccine Research. This offers a huge improvement over the present approach, which has struggled to produce a vaccine for H1N1 in seven months. It's also fast enough to check a flu pandemic before it switches hemispheres--as the swine flu did when it followed the winter from the north to the south this past May and June.

VLPs have been an around-the-corner promise for over 20 years. But they've now reached a stage at which even disinterested observers believe, as Columbia University virologist [Vincent Racaniello](#) put it, that VLP vaccines "really seem to be coming into their own." Over the past decade, researchers solved many small but crucial technical and manufacturing problems, ranging from how to design effective antigens to how to produce them reliably in quantity. A crucial step came in 2006 when the U.S. Food and

Drug Administration approved the first VLP-based vaccine, Gardasil, the first vaccine proven effective against the human papillomavirus, which can cause genital warts and cervical cancer. This was "a huge breakthrough," says the University of Pittsburgh's Ross, because it suggested that the FDA, generally conservative about vaccines, was convinced of the safety of VLP-based vaccines.

Since then, VLP flu vaccines have moved onto the fast track, and VLP vaccines have done well in animal trials against [avian](#), swine, and seasonal flu, and against Ebola as well. Now two of the leading developers, [Novavax](#), of Maryland, and [Medicago](#), of Quebec City, have taken VLP flu vaccines all the way through preclinical animal testing and into human clinical trials, two of which are beginning this month.

The companies use different manufacturing processes. Medicago grows its VLPs in transgenic tobacco plants, which are simple to manipulate, fast to grow, and easily raised in high-tech greenhouses that can be built almost anywhere. The company injects full-grown tobacco plants with genetic information from a target virus, and the plants produce VLPs in their biomass that can be extracted a few weeks later. Novavax uses an insect cell-culture approach, growing its VLPs in a line of identical "immortalized" cells taken 20 years ago from a caterpillar called a fall armyworm. The armyworm cells are injected with a recombinant baculovirus--a virus that only infects insects--that is tweaked to resemble a targeted flu virus. The cell responds by producing and secreting VLPs that have a shell identical to that of the flu virus but contain no flu RNA.

Both processes are relatively cheap and fast. To illustrate, the 400-person phase I clinical trial of Novavax's swine flu vaccine candidate that began in Mexico this week was developed from the [genetic information](#) released on the H1N1 virus in early May and has already been through the design, small-scale production, and animal testing phases. Over this same time span, conventional makers have just barely started making the first deliveries of a vaccine that required no fresh design, no animal testing, and only minimal human testing.

The VLP effort, of course, may trip on any number of obstacles. Yet unless this trial by Novavax and a parallel avian-flu trial by Medicago reveal a fundamental flaw in the VLP approach--in contradiction of the successful animal trials of these vaccines and a successful phase I human trial of Novavax's seasonal flu vaccine--VLP vaccines seem within reach of becoming the sort of effective, safe, and quickly produced flu vaccine the world lacks.

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