A dose of DNA to fight influenza virus

Nearly every year, the influenza virus reinvents itself in order to outwit our immune systems and cause the familiar fevers, sniffles, and muscle aches of the flu. And nearly every year, in response, virus detectives around the world pool their sleuthing skills to predict which three influenza strains will predominate during the upcoming flu season.

For the past 30 years, manufacturers have used this epidemiological knowledge to fashion vaccines that produce antibodies against the virus' ever-changing outer coat. Unfortunately, these vaccines may remain effective for only one flu season.

Now, a vaccine made from DNA could change all that.

Using a piece of DNA that carries instructions for the manufacture of a protein on the virus' outer coat, as well as one from its inner depths, researchers from Merck Research Laboratories in West Point, Pa., have created a vaccine that "offers better protection against a new variant of influenza," says senior scientist Margaret A. Liu. The finding could lead to longer-lasting, more protective vaccines.

Normally, influenza vaccines work by stimulating an immune response to the proteins on the outer coat of the virus. The prospect of creating a vaccine solely from a piece of DNA first arose in 1990, when researchers inserted circular pieces of DNA, known as plasmids, into the muscles of mice. The genes in the plasmids turned on, directing the muscle cells to create the proteins encoded by the genes.

In 1993, the Merck researchers showed that a plasmid containing the gene for the internal nucleoprotein (NP) of influenza evoked an immune response to a different strain of the influenza virus in mice.

"The internal nucleoprotein is an attractive target for a vaccine because it is a very conserved [common] portion of the virus," says Liu. Influenza must adapt itself in order to infect mice. The Merck team chose to test the procedure in ferrets because these animals fall victim to the same influenza strains as humans. The researchers created a DNA vaccine that included genes for the outer hemagglutinin (HA) protein as well as the inner NP of the Hawaiian and Beijing strains.

By using ferrets, the researchers could test their DNA vaccine directly against the standard vaccine used during the 1992–93 flu season.

But the influenza of 1992–93 presented an unusual twist. Late in the season, a new strain of virus—one to which sufferers of the first version had no immunity—arrived in the United States from Asia. The new strain, known as Georgia, was "very virulent and resulted in a fair number of deaths," says Liu. The researchers exposed the ferrets to the Georgia strain. As they report in the June NATURE MEDICINE, the DNA vaccine protected the animals against infection, whereas the standard vaccine did not.

Liu says scientists don't know how the DNA vaccine gets into an animal's cells, but once there, the plasmid instructs cells to produce the viral proteins. By reacting to the external protein produced, the immune system creates antibodies capable of blocking the virus from infecting other cells. However, by manufacturing internal proteins common to many different strains, the cells recruit a different portion of the immune system to destroy already infected cells. Using the common proteins, the researchers hope to protect against most strains. "This way, if we guess wrong, people may still be protected," says Liu.

Dominick Iacuzio of the National Institute of Allergy and Infectious Diseases in Bethesda, Md., finds the vaccine's ability to recognize many strains of influenza important to its success. "This is a very promising new way of vaccination," he says, despite the preliminary nature of Liu's work.

Liu agrees that DNA vaccines are still a long way from general use. Before clinical trials can begin, the Food and Drug Administration must approve DNA for use as a vaccine. Until then, researchers must rely on detective work and luck.

— L. Seachrist

Novel dyes alter the frequency of light

In their efforts to use laser light for communications and computing, scientists are constantly conjuring up new materials capable of modulating and controlling the properties of those laser signals. Among the most intriguing—and perhaps most useful—materials of this sort are those exhibiting nonlinear optical behavior that increases the frequency of light passing through them.

This effect gives optical signals a boost; they pack a more powerful punch going out than they do coming in.

In the June 1 NATURE, Geoffrey J. Ashwell, a materials scientist at Cranfield University in England, and his colleagues describe a "most unusual" result. They have found a new kind of dye—a specialized, nonlinear material used in lasers and optical communication—that appears to violate the traditional rules of optical physics.

The new dye doubles the frequency of light penetrating it, an established phenomenon known as second-harmonic generation. However, it does so in a completely unfamiliar way.

Ordinarily, researchers working with these special dyes emphasize the "noncentrosymmetry" of the molecules involved. In other words, dye molecules that consist of two mirror-image halves shouldn't produce the desired frequency-doubling effect.

Yet Ashwell's results show that this well-accepted rule does not always hold. His team synthesized a set of dyes, containing a central "squaraine" core, that have entirely centrosymmetric structures. According to current theoretical understanding, these molecules should not double a laser light's frequency. Yet they do.

"Heresy," says J.L. Brédas, a materials scientist at the University of Mons-Hainaut in Belgium, referring lightheartedly to the scientists' departure from conventional wisdom in the field of nonlinear optics.

"Whether or not the results of Ashwell and colleagues bring any direct benefits to nonlinear optical applications," Brédas adds, "it is clear that they are most exciting from a conceptual standpoint."

The unexpected properties of the new dyes not only make them potentially useful for optical signaling, but also stand accepted thinking in the field of optical communication on its head, says Brédas.

The finding points to the possibility of other mechanisms at work in the frequency-doubling process, suggesting that there may be alternative approaches to the control of laser light for signaling purposes.

Ashwell says that he finds these results more interesting than useful at the moment, though he agrees that the new dyes may have future applications in optical switching or laser modulation.

"Nonlinear optical phenomena are at the heart of modern communications systems in which optical signals need to be transmitted, processed, and stored," Brédas says.

Almost any research review or lecture dealing with nonlinear optical effects, he adds, "starts by emphasizing the overall noncentrosymmetry required for such processes to take place in any significant way."

In view of such molecular symmetry requirements, says Brédas, the approach of Ashwell and his colleagues "does indeed seem heretical."

Moreover, Ashwell's team tested the nonlinear optical effect with a very thin film of the dye, called a Langmuir-Blodgett monolayer, yet nevertheless obtained one of the strongest frequency-doubling signals ever reported.

Consequently, "the new results," Brédas observes, "open up an entirely new line of thinking in this technologically important field."

— R. Lipkin