Biomedicine

Lisa Seachrist reports from the Ninth International Congress of Immunology in San Francisco

Using peptides to block the flu. . .

Every year, scientists scramble to predict which version of the influenza virus will predominate so they can produce that year's flu vaccine. And every year, people need to get the new vaccine to ward off the flu. These complications arise because influenza strains constantly mutate parts of themselves, presenting new targets to the immune system. Now, Japanese researchers are examining small, unchanging parts of the virus to find ways of protecting against many different flu strains.

Kazumasa Ogasawara and his colleagues at Hokkaido University in Sapporo, Japan, created a vaccine by inserting a peptide consisting of seven amino acids from the unchanged hemagglutinin protein of the flu virus into a protein capable of binding to immune cells that fight infection. The researchers then treated mice with either the seven-amino-acid peptide or the peptide vaccine and exposed them to strains of influenza from the past 10 years.

Mice that received the peptide-only treatment got influenza symptoms. But the mice that got the peptide vaccine produced antibodies that neutralized all varieties of influenza. The animals "were 100 percent protected from the disease," says Ogasawara.

However, the mice remained immune for only 2 weeks; after that, they needed a vaccine booster. Ogasawara notes that the effects of the vaccine will need to be longer-lived before it can provide practical protection for humans.

. . .and using bacteria to stymie viruses

When a virus infects a cell, the immune system calls in killer T cells to prevent the virus from spreading throughout the body. But killer T cells can attack only those cells that the virus has already infected—a response known as cell-mediated immunity. Now, Los Angeles researchers are using a ubiquitous bacterium to produce viral peptides inside cells in order to provoke a response from killer T cells.

The bacterium, *Listeria monocytogenes* (LM), is found everywhere, especially in soil and soil-grown food products. When LM infects, it invades cells of the body and lives inside them—much as a virus does. The immune system mounts an attack, including the cell-mediated response, against the bacterium.

Because LM has no ill effects on most people, Jeff F. Miller and his team from the University of California, Los Angeles, wondered if it could serve as a vehicle for protection against other infections. They inserted peptides from a number of viruses into the single chromosome of LM to see if infection with altered bacteria would generate a protective response.

Miller's colleague Hao Shen inserted the genetic sequence for an eight-amino-acid peptide from the lymphocytic meningitis virus (LCMV) into the chromosome of LM. Mice that he infected with the altered LM bacteria didn't get LCMV when exposed to the virus.

And colleague Eric R. Jensen used the technique to arrest the cottontail rabbit papilloma virus in rabbits—a model for viruses that induce human tumors, such as cervical cancers. Jensen, however, needed to include an entire viral protein in the LM chromosome, not just a small peptide. The rabbits first became infected with the papilloma virus and developed wartlike growths. But after 5 weeks, the papillomas in the rabbits that had been infected with the altered LM had shrunk or completely disappeared. The papillomas on the control animals continued to grow.

The researchers are a long way from using LM to vaccinate humans against viral disease. While protection from the viruses continued for a long time, LM has some serious risks. People with compromised immune systems can become quite ill with LM. "Clearly, an attenuated form of the bacteria would need to be developed before it could be used in humans," says Jensen.

Environment

Breast effects of hormonal pollutants

Breast tissue is exquisitely sensitive to its hormonal milieu, especially the body's rhythmic ebbs and flows of estrogen and other sex hormones. Might the developing ubiquity of pollutants that mimic these hormones (SN: 1/8/94, p.24) be affecting breast cancer rates in women (SN: 7/3/93, p.10)?

That question spurred Nadine M. Brown and Coral A. Lamartiniere of the University of Alabama at Birmingham to study such agents in female rats approaching puberty. In the July-August ENVIRONMENTAL HEALTH PERSPECTIVES, they report that these compounds indeed alter the maturation rate of mammary tissue, which can change vulnerability to cancer.

Breast tissue begins its gradual maturation early in a rodent's life. As in humans, immature breast tissue in rats consists of bulb-shaped terminal end buds that, under the direction of female sex hormones, branch out and differentiate into a tree of lobules. These lobules, which secrete milk when stimulated by the hormonal changes of pregnancy, face a far lower risk than end buds of turning cancerous. So the researchers assayed end-bud-to-lobule transformation rates following week-long exposures to hormonelike chemicals.

Compared to untreated rats, those given DDT, the drug diethylstilbestrol (a synthetic estrogen), or genistein (a plant estrogen found in soybeans) all exhibited a host of mammary changes characterized by cellular proliferation, a decreased proportion of end buds, and an increased share of lobules. By hastening mammary development, these changes might be interpreted as reducing the tissue's window of vulnerability to carcinogens, Brown says. Indeed, she points out, the genistein data may explain why women in Japan—with its soy-rich cuisines—face such a low incidence of breast cancer.

By contrast, TCDD—the most potent dioxin—retarded mammary maturation. Says Brown, this "potentially detrimental" change certainly raises a question about whether TCDD might indirectly contribute to cancer risk by lengthening the window of vulnerability to breast carcinogens.

A better way to manage smog

Although the numerous volatile organic chemicals (VOCs) that generate smog ozone don't all operate with the same efficiency, current federal regulations aimed at controlling smog provide no incentives for polluters to eliminate the most potent VOCs first, notes a team of researchers in the July 28 SCIENCE. Indeed, their new analysis indicates, ozone problems could actually worsen if, in the process of cutting total VOCs, polluters substituted highly reactive ones for barely reactive alternatives. In contrast, they argue, regulating VOCs on the basis of reactivity could as much as double the ozone reduction achieved per dollar spent to control them.

California already ranks—and regulates—VOCs this way as part of two vehicle-emissions programs. And while the federal government should too, says analysis coauthor Armistead Russell of Carnegie Mellon University in Pittsburgh, it should not stop there. Russell would reward all polluters for reducing the overall reactivity of the VOCs they emit—from industrial plants and consumer products such as paints to any companies that signed onto the smog-emissions trading program proposed by EPA last week. The latter would allow a VOC emitter to buy a "credit" to pollute from a company that had already reduced its emitted VOCs more than regulations required.

Some critics have argued against such a policy, on the grounds that an individual VOC's reactivity can vary with climate, typical cloud cover, even prevailing, coincident pollutants. But Russell says his team's new analysis found that these factors don't matter much: Whatever alters the reactivity of one VOC does much the same thing to most of the rest. So volatility differences between VOCs change little.