Biology

New roles for an old-trouper vaccine?

Using a venerable bacterium that is the basis of the widely used tuberculosis vaccine, scientists at the Albert Einstein College of Medicine in New York City are hoping to develop a multipurpose vaccine effective against several major health problems, such as leprosy, malaria and parasitic diseases. Barry Bloom, William R. Jacobs and Margareta Tuckman report in the June 11 NATURE that they have designed a genetic-material-carrying "vehicle" called a shuttle phasmid that can enter bacillus Calmette-Guérin (BCG) mycobacteria. Tuberculosis vaccines made from the BCG bacteria, which are harmless relatives of those causing leprosy and tuberculosis, have been injected in an estimated 2.5 billion people.

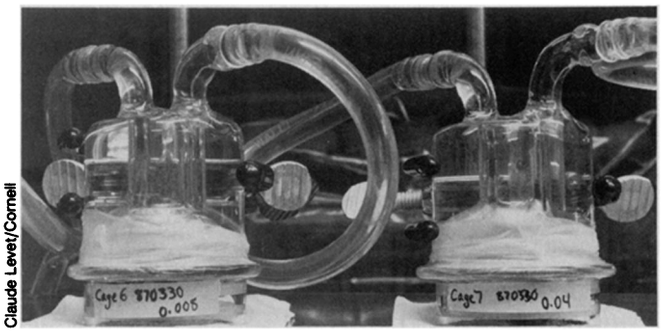
Created with DNA from a bacteriophage (a virus that infects bacteria) combined with genetic material called a cosmid from the common bacterium *Escherichia coli*, the shuttle phasmid can infect mycobacteria *and* grow in *E. coli* cultures. According to the authors, the phasmid might be used to transfer genes of disease-causing microorganisms into BCG, making a single vaccine that prevents other diseases in addition to tuberculosis. Much of the current vaccine research is concentrating on the vaccinia virus as a carrier of foreign DNA, but the BCG model may avoid rare vaccinia-associated side effects. However, the New York group has yet to show that the inserted genes remain active inside the mycobacteria.

Antifrost bacteria: So far, so good

Preliminary results from the first authorized outdoor release of genetically altered bacteria in the United States are promising, say scientists. On April 24, researchers at Advanced Genetic Sciences, Inc. (AGS) in Oakland, Calif., sprayed a test plot of strawberry plants in a nearby town with *Pseudomonas syringae*, which had been changed to retard ice crystal formation (SN: 5/2/87, p.277). Scientists say that data from the test, completed last week, show the bacteria were not found outside the test area—a possibility that has stirred controversy—which will be monitored for at least three months. Also, the *P. syringae* lowered the freezing temperature of the plants an average of 2°. Some plants had been subjected to freezing temperatures in a laboratory.

And he's housebroken

Flea farming apparently isn't as simple as it sounds, so parasitologists at Cornell University in Ithaca, N.Y., have developed an artificial dog to raise fleas in a closed environment where they can keep an eye on the pesky critters. A mongrel arrangement of tubing, sieves and glass jars, the "dog" carries its fleas near a plastic skin-like membrane, flooded on the other side by warmed blood circulating through the tubes. After feeding on the blood through the membrane, the contented fleas produce eggs, which fall through sieves and are collected. With several generations of fleas at hand, the scientists thus far have concluded that fleas actually prefer walking to hopping.



Claude Lavet/Cornell

Biomedicine

Karen Hartley reports from Washington, D.C., at the 51st annual scientific meeting of the American Rheumatism Association

Trying to unravel 'The Great Imitator'

For many allergy sufferers, the answer seems obvious—avoid the substance that causes the allergies. But for people with systemic lupus erythematosus (SLE), the answer isn't quite so simple: They are, in a sense, allergic to themselves because their immune system attacks healthy cells. Advances in treating the disease, which used to claim the lives of most of its victims, have dramatically lowered the fatality rate and paved inroads for patients to lead normal lifestyles. Last week, researchers added pinpoints to mapping the disease's cause and its treatment.

Like other inflammatory forms of arthritis, such as rheumatoid arthritis, SLE has a propensity to attack the lining of joints and other tissues. Known best for the butterfly-shaped facial rash it sometimes creates, SLE causes the body to produce excess antibodies, called autoantibodies, that target healthy cells. Production of these by B cells is either helped or suppressed by T cells; both B and T cells are immune system components that researchers believe may be part of the disease's etiology. In addition, because the body fails to clear all of these excess autoantibodies, they may lodge in and damage such vital organs as the kidneys, brain, heart and lungs.

Causing an estimated 16,000 new cases in the United States annually, SLE has a predilection for women, who are infected some nine times more than men. Symptoms include fever, appetite loss, fatigue and joint pain and swelling, although these vary in each individual by severity and frequency. The disease, often referred to as "The Great Imitator," is commonly misdiagnosed as fibrositis, skin photosensitivity and even psychosomatic illness. In addition, there are drugs that either induce SLE or exacerbate current symptoms, including hydralazine, an antihypertensive drug, and procainamide, a drug used to control irregular heartbeats.

But one group of researchers is using those drugs to try to get at the heart of what causes SLE. Bruce C. Richardson and his colleagues at the University of Michigan in Ann Arbor previously found that in a process called autoreactivity, some chemicals induce T cells to produce autoantibodies, suggesting that normal T cells may contain suppressed genes that are triggered by some mechanism to become autoreactive. The group last week presented research showing that hydralazine and procainamide produced the same effects in T cells as previously tested chemicals, including altering T cell DNA. This finding represents one more step in unraveling the complex mechanism of what activates the disease, says Gale McCarty, a rheumatologist with Georgetown University Hospital in Washington, D.C. "Once you understand the mechanism," she says, "you understand the disease."

Yet since the mechanism still is not fully understood, emphasis on treatment continues. In San Francisco, researchers at the Veterans Administration Medical Center at the University of California successfully used monoclonal antibodies to extend the life of mice with a lupus-like disease. Although David Wofsy and his colleagues previously showed they could retard progress of the disease in mice, this is the first time they actually tried to reverse advanced cases of the disease. Using the antibodies, researchers slowed the functions of helper T cells that normally aid in production of antibodies but may "overhelp" in the case of SLE. Mice more than 7 months old that were injected with the monoclonal antibodies lived 1 year past their expected death at 9 months. Untreated mice lived only about 1 more month. But because the antibodies also diminished helper T cells that might be needed for future normal immune responses, Wofsy now is looking into using just fragments of the monoclonal antibody to combat this problem.