DNA vaccines for rabies, rotavirus advance

The newest vaccine technology has moved a step closer to benefiting some of the world's poorest people. Two studies of animals show that inexpensive and durable DNA vaccines work well against rabies and viral diarrhea—diseases that hit developing countries hardest.

"This shows us that a new generation of vaccine technology is working its way forward," says Bruce G. Gellin, an epidemiologist at Vanderbilt University in Nashville, Tenn. DNA vaccines deliver genetic material encoding compounds designed to alert the immune system to an invading virus.

Although a preventive human vaccine against rabies exists, it is expensive and so is usually given only to veterinarians and researchers working with animals.

Scientists at Rocky Mountain Laboratories in Hamilton, Mont., which is part of the National Institute of Allergy and Infectious Diseases, have now developed a DNA vaccine at a fraction of the current vaccine's cost. The DNA encodes a glycoprotein found on the rabies virus. In a test on 12 cynomolgus monkeys, the DNA vaccine proved as effective as the commercial one.

Eight monkeys received the new vaccine, two were given the standard vaccine, and two remained unvaccinated. After initial vaccination, the two with the standard vaccination showed higher antibody levels than the DNA vaccine group. After a booster shot 6 months later, all those receiving either of the vaccines showed stronger immunity, the researchers report in the August Nature Medicine.

Seven months after the booster, the monkeys were infected with rabies. All 10 of those that had been vaccinated survived; the two controls died.

Six of the eight monkeys getting the DNA vaccine produced more antibodies than the two getting the commercial vaccine, study coauthor Donald L. Lodmell, a virologist at Rocky Mountain Laboratories says.

"This immune response is telling us that the animals were very well primed," Lodmell says. "When challenged with the virus, there was a tremendous response."

Although only a handful of people have died of rabies in recent years in the United States, the disease kills more than 40,000 worldwide annually. Uncontrolled outbreaks of rabies still occur in Asia and Africa, where the virus is endemic in places.

"We're primarily looking at [the DNA vaccine] as a prophylaxis—getting the vaccine into a large population," particularly people who don't have access to any treatment, Lodmell says.

A person exposed to the virus by an animal bite now gets a series of injections of vaccine and often several doses of antibody-creating immunoglobulin. This treatment doesn't work after symptoms have appeared. By that time, the disease is nearly always fatal.

Life-saving treatment for rabies in the United States can cost $1,000 per person, says study coauthor Charles E. Rupprecht, a microbiologist at the Centers for Disease Control and Prevention in Atlanta. Even pre-exposure vaccination costs as much as $400.

By contrast, the DNA vaccine could be provided for as little as 5 to 10 cents a shot, Lodmell says. Even if the commercial cost were 10 times greater, "that would still be orders of magnitude cheaper than the currently available vaccine," Rupprecht says. Moreover, the DNA vaccine "is very stable . . . and doesn't get denatured by heat," he says.

That attribute of DNA vaccines is also valuable in the fight against rotavirus. This virus causes diarrhea that kills almost 900,000 children every year, most in developing countries. While an injectible, traditional vaccine against the virus exists, the new rotavirus DNA vaccine is both edible and durable, making it the first oral DNA vaccine, the researchers contend.

When tested in mice, the encapsulated vaccine survived a trip through the animal's stomach and unleashed its DNA in the intestines or bloodstream, researchers report in the July Journal of Virology. Absorbed into cells, the DNA directs production of proteins that spur an immune response to rotavirus.

"Next, we'll try to do this in veterinary animals, such as pigs and cows," says study coauthor John E. Herrmann, a virologist at the University of Massachusetts Medical School in Worcester.

Both vaccines are inexpensive and resistant to tropical weather, attributes that "can greatly simplify vaccine delivery to the hardest parts of the planet to reach," Gellin says. Having an edible vaccine further simplifies logistics.

"As more people work with [the DNA vaccine technology], increasing its efficiency, it's really going to be a primary method of vaccination for the future," says Harriet L. Robinson of the Yerkes Primate Research Center at Emory University in Atlanta. *—N. Seppa*

Tiles of DNA assemble with a designer fit

A handy homeowner might take pride in designing a pattern of tiles to beautify a kitchen floor. Now, chemists at New York University have assembled some tiles of their own. Neither linoleum nor ceramic, these miniature plates are made of DNA.

Nadrian C. Seeman and his colleagues have designed rectangular, DNA blocks that readily assemble themselves into predictable, two-dimensional patterns. The team reports its findings in the Aug. 6 Nature.

Extended into three dimensions, these DNA arrays could act as scaffolding for building more complex materials with intricate, nanoscale structures, Seeman says. One of the group's collaborators, Erik Winfree of the California Institute of Technology in Pasadena is exploring the use of such crystals in DNA-based computers (SN: 7/13/96, p. 26).

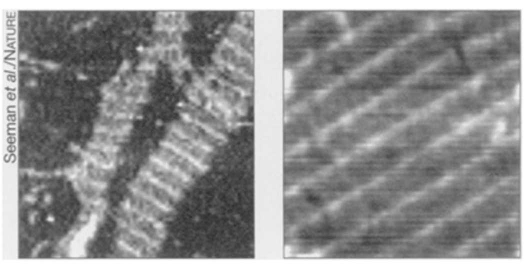
By connecting two short, parallel strands of double-helix DNA at two places, the researchers created rigid tiles about 4 nanometers across and 13 or 16 nm long. They constructed the tiles to have different sticky ends—short stretches of unpaired bases that can match up with complementary bases on other tiles—enabling tiles to fit together in a precise way.

By assembling these tiles into a flat layout, the team created two distinct patterns of stripes, differently spaced. One arrangement used two types of tile and the other used four types

"We can generate predictable patterns on the [intermediate] scale by making specific alterations of sticky ends on the molecular scale," Seeman says. The tiles, mixed in a solution, come together to form crystals. Removed from the solution, dried, and examined with an atomic force microscope, the crystals look like striped sheets.

In order to view the pattern, the researchers attached a short loop of DNA to one type of tile in each set. The microscope, which works "basically like a phonograph needle," then detects the loop as a bulge on the face of the tile, Seeman explains. The images show stripes whose spacing corresponds to that expected for the tile size and pattern.

In an analogous way, researchers could attach other molecules to the tiles, perhaps a different molecule to each type differentiated by its particular sticky ends. Seeman and his colleagues are now working to create three-dimensional DNA crystals that could assemble materials having precisely controlled microstructures. *—C. Wu*



Seeman et al./NATURE

DNA crystals: A set of two tile types forms ripply sheets with stripes about 33 nm apart (left), and tiles of four types produce stripes about 66 nm apart (right), shown in images from an atomic force microscope.