DNA vaccine to fight allergies created by UCSD medical researchers

May 14, 1996

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The symptoms are all too familiar: the itching, congestion, sneezing, those watery eyes...it's no surprise. For millions, these are the telltale signs of an allergy.

From merely annoying to potentially deadly, allergies have thwarted the best attempts at long-lasting relief.

But now, medical scientists at the University of California, San Diego have developed an anti-allergy vaccine made from a snippet of DNA that not only shows promise of preventing allergies from launching an attack, it also may wipe them out for good.

"What this offers is not just a way to prevent and treat allergies," said Dennis Carson, M.D., director of The Sam and Rose Stein Institute for Research on Aging at the UCSD School of Medicine. "Although we have only performed animal studies, we believe we have something that is a potentially curative."

In an article published in the May 14 issue of the Proceedings of the National Academy of Sciences, Carson and a team of UCSD researchers describe a potential new vaccine that, when injected into the skin, blocks an allergic reaction at its source.

"We're not dealing with the periphery of the disease," said Eyal Raz, M.D., assistant professor of medicine with the Stein Institute and principal investigator of the study. "We're attacking it at its roots."

The vaccine, which could be applied merely by scratching the skin with a device similar to that used for an allergy sensitization test, would be cost-effective, safer and specific to the allergy protein or allergen causing the symptoms.

Pending approval from the Food and Drug Administration, it's expected that patient studies with the new vaccine could begin in 24 months for hay fever, bee stings and asthma. Besides allergies, the vaccine also might help combat certain parasitic disorders.

Till now, allergies generally have been treated with a host of anti-histamine drugs that block the allergic reaction and steroids that quell inflammation. Some sufferers have turned to shots that expose their bodies to increasing doses of allergen. But the needle may not work against all irritants, may need to be repeated over time, and sometimes triggers serious, and potentially fatal, reactions.

"We've solved the problem of having to be injected all the time," said Raz. "Plus, we don't expect severe adverse reactions." Also participating in the study were Helen Tighe, Yukio Sato, Maripat Con, Jean A. Dudler, all of the Stein Institute; Susan L. Swain, with the UCSD Cancer Center; and Hans L. Spiegelberg, with the UCSD Department of Pediatrics.

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.

Since then, potential DNA vaccines have been created to treat a variety of other ailments, including influenza and HIV.

In their PNAS paper, the UCSD researchers describe a vaccine built from a DNA plasmid that carries instructions for an antigen combination that mimics a potential allergen.

When the antigen combination alone is injected in laboratory mice, a cascade of chemical reactions commonly seen among allergic patients--known as a Th2 (T-helper type 2) response-- was initiated. Typically, once the Th2 switch is turned on, certain immune proteins called interleukin 4 (I1-4) are created which, in turn, triggers the production of immunoglobulin E (IgE), the master switch of allergic reactions. When exposed to an allergen, IgE causes allergic cells called mast cells to burst open, releasing histamines and other chemicals that cause the sneezing, sniffling, and congestion commonly experienced by allergy sufferers.

By contrast, when the DNA vaccine encoding the antigen was injected into the mice, the result was what is known as a Thl (T-helper type 1) reaction. In this response, the mice generated gamma interferon rather than 11-4, with little--if any--IgE production.

In a second set of experiments, the researchers exposed these seemingly immune mice to a strong antigen to see if they were protected. They were.

In a third experiment, the researchers wanted to see if the DNA vaccine would switch Th2 mice to the Thl condition, in effect, reversing their condition. They could.

"Combined, these experiments verified that the vaccine could offer protection against allergens in addition to switching off an existing allergenic condition, pointing out the importance of this approach for clinical situations," said Raz.

The reasons why DNA immunization leads to a Thl response and protein immunization leads to a Th2 response are not understood, the researchers said. Further studies are under way to find an explanation.

However, Raz suggested the vaccine works better when injected into the skin rather than the muscle because the skin contains a relatively high percentage of cellular components called antigen preventing cells (apc) that help form a protective barrier against outside invaders.

"If you deliver DNA into this apc-enriched environment, you would initiate by far a more protective and more efficient immune response to a gene product, either by transecting skin cells or by transecting directing the apcs," said Raz.

The research was supported by grants from the National Institutes of Health and the CIBA-Geigy Corporation.

(May 14, 1996)