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Vaccine Developed From Research Conducted at UCSD Offers Potential Relief to Allergy Sufferers

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An allergy vaccine developed from initial basic and pre-clinical research conducted over the past decade by faculty in the Allergy Immunology section of the Department of Medicine at the University of California, San Diego (UCSD) School of Medicine has shown promise in relieving allergy symptoms in human patients.

In a study published in the October 5, 2006 issue of *The New England Journal of Medicine* (NEJM), a research team at the Johns Hopkins Asthma and Allergy Center in Baltimore found that an investigational therapy - comprised of the major ragweed allergen protein, Amb a 1, coupled to a unique short, synthetic sequence of DNA that stimulates the immune system - significantly reduced allergy symptoms caused by ragweed in adults for at least one year when given just once a week over a six-week period.

Eyal Raz, M.D., and David Broide, MB ChB, both Professors of Medicine at the UCSD School of Medicine, led National Institute of Allergy and Infectious Diseases (NIAID)-sponsored pre-clinical studies of TLR-9 vaccines in allergy and asthma at UCSD, which contributed to the development of the novel vaccine.

"Allergies affect millions of Americans each year," said Broide. "A short course of immunotherapy that reduces allergic symptoms over an extended period of time will significantly improve the quality of life for many people."

Broide was senior author of the NEJM study, conducted by lead investigator Peter Creticos, M.D., at Johns Hopkins in Baltimore, where the ragweed pollen season lasts from mid-August to October each year. Broide is also Principal Investigator of a follow-up study sponsored by the Immune Tolerance Network and NIAID, studying the effectiveness of the TLR-9 vaccine in subjects with ragweed-induced asthma. The clinical component of these studies is being performed in collaboration with Johns Hopkins University where ragweed is endemic, and studies to identify the mechanism by which the vaccines work are being conducted at UCSD. As ragweed is not present in San Diego, no patients are being given the vaccine in San Diego.

The study initially involved 25 volunteers, ages 23 to 60 - with a history of seasonal fall allergic rhinitis (also termed hay fever or sinus allergy), positive skin test reactions to ragweed pollen, and an immediate reaction when nasally challenged with ragweed.

Prior to the start of the 2001 fall ragweed season, study participants received six injections, each a week apart, of either the investigational TLR-9 vaccine in increasingly higher doses or a placebo. They received no other injections throughout the course of the study. Fourteen volunteers received the study drug; 11 were given the placebo. The therapy was well-tolerated and caused only limited local reactions, which required neither medication nor change in treatment dose. No clinically significant, therapy-related adverse events occurred.

Throughout the 2001 and 2002 ragweed seasons, both groups of volunteers were monitored for clinical outcomes, including the number of sneezes and the degree of post-nasal drip, allergy medication use and quality-of-life scores compared with volunteers in the placebo group. The group that received the TLR-9 vaccine

experienced dramatically better outcomes which continued throughout the 2002 ragweed season, even though therapy ended one year earlier.

Currently, physicians treat patients suffering from mild and moderate ragweed allergies with antihistamines or nasal corticosteroids. However, when patients do not respond to these treatments or experience severe symptoms, the next therapeutic option is a course of subcutaneous injections of the allergen, which is called allergen immunotherapy (or allergy shots.)

Although this standard allergen immunotherapy is often effective, it has two major drawbacks. First, it can cause systemic allergic reactions, such as anaphylaxis, a hypersensitivity reaction that can lead to severe and sometimes life-threatening physical symptoms. Second, to provide lasting relief, standard immunotherapy may require frequent injections over a three-to-five-year period. The large number of injections over such an extended period of time often results in many patients not completing the treatment.

"For nearly a century, we've been following the tedious process of giving allergy sufferers one or two shots a week for up to five years to ensure its success," said Creticos. "This study is potentially an immunotherapy breakthrough in that we've shown you can induce long-lasting relief from allergic rhinitis symptoms with just a few weeks of injections."

The regimen of only six vaccine injections showed therapeutic promise when compared to the current therapy. "However, because the results are based on a small number of volunteers and the long-term safety of the therapy is unknown, additional clinical trials with longer-term follow-up are needed to adequately assess the therapy's safety and effectiveness," according to Broide.

As many as 40 million Americans suffer from seasonal allergies caused by airborne pollens produced by grasses, trees and weeds. Ragweed is one of the most common pollens in the United States and is prevalent in the Northeast, Midwest and the South.

The research was sponsored by the Immune Tolerance Network, which is funded by NIAID and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), both components of the National Institutes of Health (NIH), and the Juvenile Diabetes Research Foundation International.

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