

Of Mice and Peanuts: A new mouse model for peanut allergy

January 12 2009

Chicago researchers report the development of a new mouse model for food allergy that mimics symptoms generated during a human allergic reaction to peanuts. The animal model provides a new research tool that will be invaluable in furthering the understanding of the causes of peanut and other food allergies and in finding new ways to treat and prevent their occurrence, according to experts at the National Institute of Allergy and Infectious Diseases (NIAID), the component of the National Institutes of Health (NIH) that funded the research. Peanut allergy is of great public health interest because this food allergy is the one most often associated with life-threatening allergic reactions, resulting in up to 100 deaths in the United States each year.

The findings of the research team, led by Paul Bryce, Ph.D., of the Feinberg School of Medicine at Northwestern University, appear in the January issue of the *Journal of Allergy and Clinical Immunology*. The development of new animal models for food allergy was identified as a critical need by the 2006 NIH Expert Panel on Food Allergy Research.

"Food allergies affect the health and quality of life of many Americans, particularly young children," says NIAID Director Anthony S. Fauci, M.D. "Finding an animal model that mimics a severe human allergic reaction to peanuts will help us better understand peanut allergy and develop new and improved treatment and prevention strategies."

Allergic reactions to food can range from mild hives to vomiting to difficulty breathing to anaphylaxis, the most severe reaction.

Anaphylaxis may result from a whole-body allergic reaction to the release of the chemical histamine, causing muscles to contract, blood vessels to dilate and fluid to leak from the bloodstream into the tissues. These effects can result in narrowing of the upper or lower airways, low blood pressure, shock or a combination of these symptoms, and also can lead to a loss of consciousness and even death.

The most significant obstacle to developing an animal model of food allergy is that animals are not normally allergic to food. Scientists must add a strong immune stimulant to foods to elicit a reaction in animals that resembles food allergy in humans. Because of this requirement, useful animal models have been developed only in the last few years, and such animal models have until now used cholera toxin as the immune stimulant.

Dr. Bryce's team took the novel approach of feeding mice a mixture of whole peanut extract (WPE) and a toxin from the bacteria *Staphylococcus aureus*, called staphylococcal enterotoxin B (SEB) to simulate the human anaphylactic reaction to peanuts in mice.

"Persistent *S. aureus* colonization is commonly found on the skin of people with eczema and in the nasal cavities of people with sinusitis," says Dr. Bryce. "The history between *S. aureus* and allergic diseases led us to use staphylococcal toxins to stimulate food allergy in animals."

According to Dr. Bryce, the results using the SEB/WPE mixture were considerably better than those seen with previous animal models, which failed to mimic many features of food allergy. They showed that the SEB/WPE mixture stimulated severe symptoms in mice that closely resemble those found in human anaphylaxis, including swelling around the eyes and mouth, reduced movement and significant problems breathing. Additionally, mice given the SEB/WPE mixture had high blood levels of histamine, which indicates a severe allergic reaction.

The researchers also observed that the blood and tissues of mice in the SEB/WPE group had higher-than-normal numbers of eosinophils, which are white blood cells often associated with allergy-related inflammation. Future studies will be needed to determine if eosinophils play an important role in human food allergy.

These results, say Dr. Bryce, suggest that this animal model of food allergy will be useful for many types of future research studies.

Approximately 4 percent of Americans have food allergies. For reasons that are not well understood, the prevalence in children increased by 18 percent between 1997 and 2007. The most common causes of food allergies are milk, eggs, shellfish, peanuts, tree nuts, wheat and soy.

Each year there are between 15,000 and 30,000 episodes of food-induced anaphylaxis, which are associated with 100 to 200 deaths in the United States.

Reference: K Ganeshan et al. Impairing oral tolerance promotes allergy and anaphylaxis: a new murine food allergy model. *Journal of Allergy and Clinical Immunology*. DOI: 10.1016/j.jaci.2008.10.011 (2008).

Source: NIH/National Institute of Allergy and Infectious Diseases

Citation: Of Mice and Peanuts: A new mouse model for peanut allergy (2009, January 12) retrieved 19 November 2023 from

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