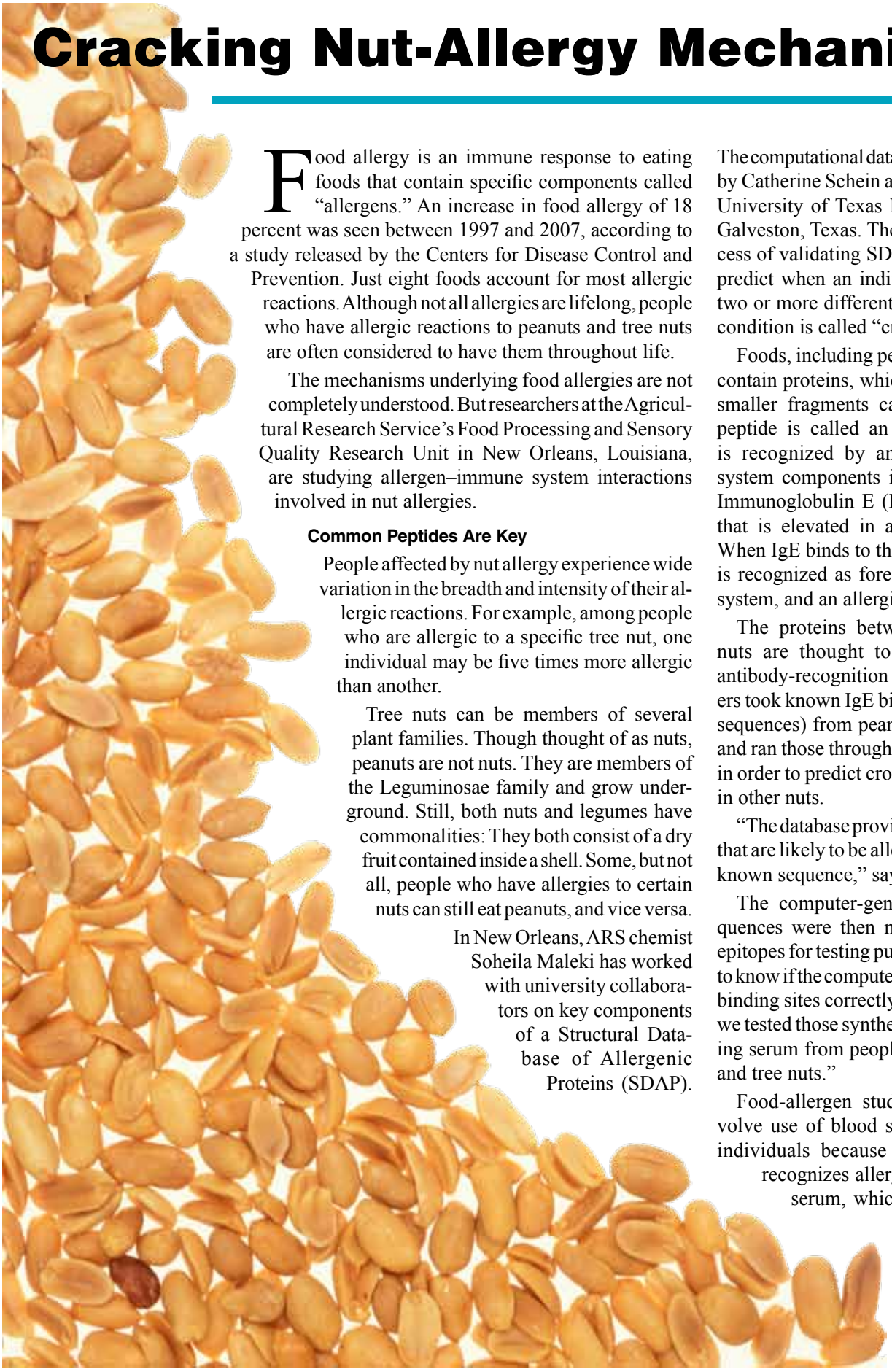
Cracking Nut-Allergy Mechanisms



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Food allergy is an immune response to eating foods that contain specific components called "allergens." An increase in food allergy of 18 percent was seen between 1997 and 2007, according to a study released by the Centers for Disease Control and Prevention. Just eight foods account for most allergic reactions. Although not all allergies are lifelong, people who have allergic reactions to peanuts and tree nuts are often considered to have them throughout life.

The mechanisms underlying food allergies are not completely understood. But researchers at the Agricultural Research Service's Food Processing and Sensory Quality Research Unit in New Orleans, Louisiana, are studying allergen–immune system interactions involved in nut allergies.

Common Peptides Are Key

People affected by nut allergy experience wide variation in the breadth and intensity of their allergic reactions. For example, among people who are allergic to a specific tree nut, one individual may be five times more allergic than another.

Tree nuts can be members of several plant families. Though thought of as nuts, peanuts are not nuts. They are members of the Leguminosae family and grow underground. Still, both nuts and legumes have commonalities: They both consist of a dry fruit contained inside a shell. Some, but not all, people who have allergies to certain nuts can still eat peanuts, and vice versa.

In New Orleans, ARS chemist Soheila Maleki has worked with university collaborators on key components of a Structural Database of Allergenic Proteins (SDAP). The computational database was developed by Catherine Schein and colleagues at the University of Texas Medical Branch, in Galveston, Texas. The team is in the process of validating SDAP's ability to help predict when an individual will react to two or more different types of nuts. This condition is called "cross-reactivity."

Foods, including peanuts and tree nuts, contain proteins, which are digested into smaller fragments called "peptides." A peptide is called an "epitope" when it is recognized by antibodies—immune system components in the bloodstream. Immunoglobulin E (IgE) is an antibody that is elevated in allergic individuals. When IgE binds to the epitopes, the food is recognized as foreign by the immune system, and an allergic reaction occurs.

The proteins between cross-reactive nuts are thought to have similar IgE antibody-recognition sites. The researchers took known IgE binding sites (epitope sequences) from peanut and nut proteins and ran those through the SDAP database in order to predict cross-reactive epitopes in other nuts.

"The database provides other sequences that are likely to be allergenic based on the known sequence," says Maleki.

The computer-generated binding sequences were then made into synthetic epitopes for testing purposes. "We needed to know if the computer predicted the novel binding sites correctly," says Maleki. "So we tested those synthesized sequences using serum from people allergic to peanut and tree nuts."

Food-allergen studies commonly involve use of blood serum from allergic individuals because their serum's IgE recognizes allergenic epitopes. The serum, which was provided by

cooperators at the University of California Davis, allowed the team to match previously unknown epitopes within the major allergenic proteins known to be common to a variety of nut and peanut allergies.

The authors found that similar immunoglobulin epitopes on allergenic proteins, as defined by SDAP, could account for some of the cross-reactivity between peanuts and tree nuts. The finding indicates that SDAP can be useful for predicting previously unidentified cross-reactive epitopes, based on their similarity to known IgE epitopes.

"The novel sequences we found and validated using the database are similar, but not identical, to the sequences we fed into the software," says Maleki. "We were able to confirm sites that the immune system sees and binds but that we could not have predicted otherwise."

The study was funded by the U.S. Environmental Protection Agency and the National Institutes of Health and was published in *Allergy* in 2011.

Increasing Diagnostic Reliability

Previously, Maleki had assessed the diagnostic reliability of standard peanut-allergy tests. She found that while people generally eat peanuts that have been heat treated (via roasting or boiling), the extracts that are commonly used to diagnose peanut allergies are from *raw* peanuts. She and colleagues hypothesized that raw peanut proteins undergo specific changes during roasting that may contribute to increases in allergenic properties. (See story on page 16).

Since then, Maleki and colleagues have published a series of studies that shed light on the molecular differences between raw and heat-treated nuts in terms of their inherent peptides that trigger human allergic reactions.

The major allergenic proteins (or allergens) of peanut are known as "Ara h 1," "Ara h 2," and "Ara h 3." For one study, Maleki looked into how the peanut-roasting process alters how well an allergic individual's immunoglobulins bind to peanut allergens. The team compared the reaction by human IgE antibody to the heated and unheated forms of Ara h 1. The study showed that roasting-induced side reactions, such as browning, increased the amount of IgE that recognizes and binds to Ara h 1—when compared to the amount that binds to Ara h 1 from raw peanuts.

"This result partly accounts for the increased allergenic properties observed in processed, roasted peanuts," says Maleki. The study was published in 2012 in *Molecular Nutrition and Food Research*.

In another study, Maleki and colleagues in Spain showed that a combination treatment of heat and high pressure (autoclaving) applied to peanuts significantly reduced allergic reaction. Autoclaving involves a higher moisture environment, similar to steaming or boiling, than roasting. As result, autoclaving does not initiate the browning effect that comes with roasting. The less allergenic reaction to the combination-treated peanuts was confirmed by skin-prick tests applied to volunteers known to have peanut allergies.

"Proteins become unfolded with autoclaving," says Maleki. "If you unfold the protein, you may reduce allergenicity." The study was published in 2012 in *Food Chemistry*.

Insights into allergen-immune system interactions will help with preventing and diagnosing serious food allergy.—By **Rosalie Marion Bliss,** ARS.

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People tend to eat peanuts that have been roasted or boiled, while the extracts commonly used to diagnose peanut allergies are from raw nuts. An ARS chemist has studied raw and cooked peanuts and revealed peptide differences that may be responsible for allergic reactions.

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