Researchers make progress toward treatment for dangerous allergies

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New research published in the journal *Nature Chemical Biology* shows that a group of scientists, led by faculty at the University of Notre Dame, has made concrete progress toward the development of the first-ever inhibitory therapeutic for Type I hypersensitive allergic reactions.

"Our allergy inhibition project is innovative and significant because we brought a novel molecular design approach to selectively inhibit mast cell degranulation—the key event in triggering a food allergic response—which has the potential to improve the quality of life for affected patients," said Basar Bilgicer, assistant professor of chemical and biomolecular engineering at Notre Dame and an investigator in the University's Advanced Diagnostics & Therapeutics initiative.

Allergic reactions are caused when a person's immune system reacts to normally harmless substances in the environment. An allergic reaction can be the source of a simple itch or sneezing; however, Type I hypersensitive allergic reactions can go as far as a life-threatening anaphylactic shock. Mast cells, which are a type of white blood cell, function to protect the body from harmful pathogens such as parasites. In Type I hypersensitive allergic conditions, mast cells show a response to otherwise harmless substances (allergens) and result in severe, even potentially lethal, symptoms. The most common examples to Type I hypersensitivity are food allergies, such as to peanuts or shellfish, which affect 15 million Americans and approximately 8 percent of children.

Through the new research, Bilgicer and his group designed a special

molecule, called a heterobivalent inhibitor (HBI), which when introduced into a person's bloodstream can, in essence, out-compete allergens like egg or peanut proteins in their race to attach to mast cell receptors.

"Unlike current treatments, such as epinephrine, which help a body endure through an allergic reaction, our HBIs, if introduced into the bloodstream, would actually stop further progression of the allergic reaction from taking place," said Bilgicer.

"We are figuring out the optimum binding sites on the mast cell receptors to attach to, in order to prevent allergens from interacting with them and to prevent the allergic reaction before it even starts in the first place."

The team has demonstrated the effectiveness of their inhibitor molecule on allergic reaction using animal models of allergy. Their next set of targets are a variety of allergens that affect humans—including peanuts, penicillin and dust mites—and they will design HBIs that would be successful inhibitors for each.

More information: Inhibition of weak-affinity epitope-IgE interactions prevents mast cell degranulation, DOI: 10.1038/nchembio.1358

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