Medical Xpress

Research identifies a protein group that may kick-start allergic reactions

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(Medical Xpress) -- Allergies, or hypersensitivities of the immune system, are more common than ever before. According to the Asthma and Allergies Foundation of America, one in five Americans suffers from an allergy — from milder forms like hay fever to more severe instances, like peanut allergies which can lead to anaphylactic shock.

While medications like antihistamines can treat the symptoms of an allergic reaction, the treatment is too limited, says Prof. Ronit Sagi-Eisenberg, a cell biologist at Tel Aviv University's Sackler Faculty of Medicine. Cells release dozens of molecules during an allergic reaction, and available medications address only a small subset. Now she and her

fellow researchers are working to identify what triggers allergic reactions in the body, with the goal of stopping an allergic reaction before it starts.

The answer may lie within the Rab family, a group of 60 proteins that are known to regulate the distribution of proteins throughout the body. Along with her Ph.D. student Nurit Pereg-Azouz, Prof. Sagi-Eisenberg found that 30 of these proteins determined how cells react to an allergen, and two of these have been identified for further research as instruments of preventative medication. When the chain of events leading up to an allergic reaction can be understood, drugs can be developed to inhibit the initial reaction, explains Prof. Sagi-Eisenberg.

This research has been published in *The Journal of Immunology*.

Getting to the root

Allergic reactions can appear as rashes, respiratory difficulties, or swelling, but they're all caused by the same mechanism. When exposed to an allergen, the body activates the immune system. But mast cells, located throughout the body, sense that the immune system has mistakenly been activated against something that is not bacterial or viral, and they release biologically active molecules to create an inflammatory response.

So what causes mast cells to react? Prof. Sagi-Eisenberg and her team work to identify the exact chain of events in an allergic reaction. They looked to the Rab family of proteins as a potential source for answers, screening for the proteins' involvement in initiating allergic reaction.

"We genetically manipulated mast cells so that they contained mutated versions of these proteins, which were already active without an allergen," explains Prof. Sagi-Eisenberg. If a protein was relevant, it would cause an allergic reaction. "This new methodology allowed us to

screen for the functional impact of each member of this family, determining if they either inhibited or activated the allergic process."

In the end, the researchers flagged 30 proteins that were relevant to the process of creating an allergic reaction in the body, and have identified two that appear to be the most involved. Further research will use these two proteins as tools to gain more understanding of allergic reactions.

Targeted drugs could prevent allergic reaction

An allergic reaction is not only a function of two proteins interacting — it's the result of a chain of events. By identifying crucial links in such a chain, researchers can create targeted drugs that break the chain. New medications that target tumor cells, for example, are directed at halting the tumor's ability to function and grow, starving it of crucial blood and oxygen supplies. Prof. Sagi-Eisenberg envisions similar medications for allergies, with medications that address the source of the allergic reaction instead of the symptoms.

The need for such medications is pressing. Steroids, the only available type of drug that effectively prevents mast cells from secreting biologically active agents, also cause harm to kidneys, bones, and the immune system. Patients may suffer more from the treatment than they do from the allergy itself. Alternative medications that are as effective as steroids but will be devoid of their adverse side effects are desperately needed. Prof. Sagi-Eisenberg's work will help to identify proteins that can be targeted by medications without impacting the function of other cells, she hopes.

Provided by Tel Aviv University

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