

Could allergic reactions be prevented? Team identifies key protein that triggers symptoms

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Spring is in the air, and that means allergic reaction-causing pollen is, too.

It's [reported](#) that 20 percent of the Canadian population lives with hay fever and [nearly 10 percent have food allergies](#). And the problem is only getting worse.

"Allergies are absolutely an epidemic," says Brock University Associate Professor of Health Sciences Adam MacNeil.

Antihistamines and decongestants can bring some temporary relief to the annoyance, pain and in some cases, danger arising from [allergic reactions](#), but what if a reaction could be stopped before symptoms start to appear?

A Brock research team has discovered that blocking a particular protein early in the process leading to an allergic reaction could essentially eliminate allergic symptoms.

"A major novelty of the finding is that this protein, which is pretty well-known and has been looked at in a number of other [cells](#) and contexts, happens to affect both the early and late phase of an allergic reaction," says Colton Watson, a Ph.D. student supervised by MacNeil.

The protein, called TAK1, is in [mast cells](#), which can be found in tissues such as the skin, respiratory tract, digestive tract and other areas that are in contact with the external environment.

Like other immune cells, mast cells protect the body from infections caused by pathogens such as parasites, bacteria and viruses, maintaining healthy tissue in the process. But strangely, mast cells can also react to allergens such as pollen, animal dander and certain foods that should pose no real threat.

This sets off a process in which TAK1 is activated and sends out a signal that splits into two.

The Brock team found one signal leads to degranulation, where cellular 'packages' called granules release molecules that lead to the hives, itchiness, swelling and other immediate 'early phase' symptoms of an allergic reaction.

The other signal sets off pathways that produce proteins called cytokines and chemokines, designed to promote inflammation and recruit additional immune cells to fight off infection.

But what if there is no infection?

Because the allergen itself is not a dangerous pathogen, the proteins end up causing further unnecessary inflammation and tissue damage several hours later in the 'late phase.'

"Mast cells are not evolutionarily programmed to do this," says MacNeil, who has received funding from the Canada Foundation for Innovation's John R. Evans Leaders Fund (JELF) and NSERC's Discovery Grant program to pursue this research.

"Allergens like peanuts or shellfish pose no real threat and as such, the aggressive immune response is misguided and harmful," he says. "It's an inappropriate manifestation of the immune system; an overreaction to something that is innocuous and not dangerous."

Watson says that although previous research has focused on TAK1's role in other immune cells responding to actual infections, it's never been looked at in the context of allergically-activated mast cells.

"We wanted to determine if the role of TAK1 in other [immune cells](#) is conserved in allergically-activated mast cells, and to see if we could therefore target TAK1 to stabilize these mast cells by preventing its activation," he says.

What's unique about the team's research compared to earlier studies is that they showed TAK1 plays a profound role in bringing about allergic reactions through processes in mast cells and that inhibiting TAK1 stops the allergic events in their tracks preventing them from proceeding to the early and late stages of allergic reactions.

The researchers verified that a chemical generated by fungus—5Z-7-oxozeaenol—widely referred to as "OZ" potently inhibits TAK1.

"The results generated provide a strong pool of evidence to support additional investigation into the potential of targeting TAK1 in the treatment of allergic inflammation," says the study, "TAK1 signaling activity links the [mast](#) cell cytokine response and degranulation in allergic inflammation," published in the *Journal of Leukocyte Biology*.

Watson and MacNeil stress that it's too early to determine if drugs modelled from OZ can mitigate allergic reactions, saying that they and other researchers can build upon what they found in this study.

"The next step is to use the knowledge gained from this study to take rational and targeted strategies for novel therapeutic design," says MacNeil.

More information: Colton J.F. Watson et al. TAK1 signaling activity links the mast cell cytokine response and degranulation in allergic inflammation, *Journal of Leukocyte Biology* (2020). [DOI: 10.1002/JLB.2A0220-401RRR](https://doi.org/10.1002/JLB.2A0220-401RRR)

Provided by Brock University

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