

Fungal infections can trigger and exacerbate asthma

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(Medical Xpress)—A common fungal infection can trigger asthma and make it much worse by way of a route not targeted by existing asthma drugs, report researchers at Boston Children's Hospital. Their findings, published online by *Nature Medicine* on September 1, have implications for some patients with severe asthma who may be chronically exposed to fungi and can become highly sensitized.

The findings from this mouse study explain why existing [asthma drugs](#) don't work well in fungal-associated asthma. "As we understand the different pathways to asthma, we can develop better therapies," says senior investigator Dale Umetsu, MD, PhD, of Boston Children's Division of Immunology and also a professor at Harvard Medical School. "Most existing therapies are good for [allergic asthma](#), but they're not effective in many patients, whose asthma may involve non-classical pathways."

When Umetsu and colleagues exposed the mice to the fungus *Aspergillus fumigatus*, a mold common in the indoor and outdoor environment, they developed airway hyperreactivity, the cardinal feature of asthma, within just a few days. Since allergic responses in mice typically take 10 to 14 days to develop, this finding suggested that the fungus triggers an immediate, [innate immune response](#).

Traditional asthma-control drugs, such as [inhaled corticosteroids](#), act on pathways involving Th2 cells, a type of T cell in the [adaptive immune system](#) that is important in allergy. However, the new study shows, in

mice and in human cell cultures, that *Aspergillus* directly activates a recently discovered group of T cells, known as natural killer T cells (NKT cells), via a lipid molecule on its surface, asperamide B. In live mice, asperamide B alone was enough to induce airway hyperreactivity.

Umetsu and colleagues first showed in 2006 that NKT cells can trigger asthma in people in the absence of Th2 cells. The cells have been shown to be activated by various bacteria, but this is the first demonstration of their activation by a fungus.

Although *Aspergillus* and NKT cells initiate asthma through non-allergic means, patients can become sensitized to the fungus and develop chronic allergic reactions that make their respiratory disease more severe. Previous studies indicate that 28 percent of patients with asthma and 45 percent of patients with severe asthma become sensitized to *Aspergillus*.

Umetsu's investigations support the growing idea that asthma is a collection of different disease processes that all cause airways to become twitchy and constricted. In 2011, for example, his lab showed that influenza infection—which often requires asthmatic children to be hospitalized—exacerbates asthma by activating not Th2 cells or NKT cells, but yet another group of immune cells called natural helper cells or innate lymphoid cells.

"We need to understand the specific asthma pathways present in each individual with asthma and when they are triggered, so we can give the right treatment at the right time," Umetsu says.

Some academic research groups are using antifungal agents in asthma, with some success, Umetsu notes. In the future, he would like to target NKT cells in patients with severe asthma if a successful targeting method could be found.

More information: [dx.doi.org/10.1038/nm.3321](https://doi.org/10.1038/nm.3321)

Provided by Children's Hospital Boston

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