Scientists discover molecule that does double duty in stopping asthma attacks

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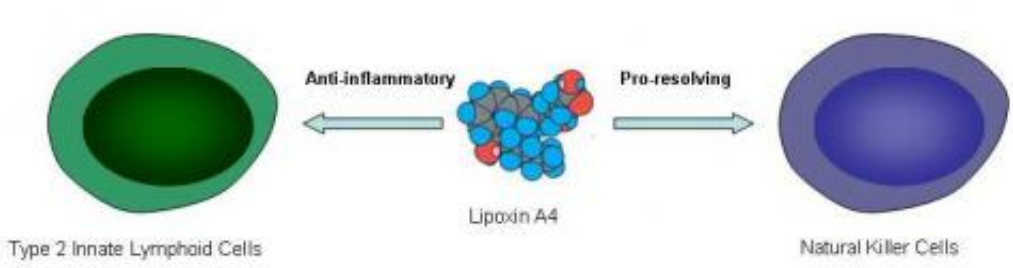

Lipoxin A4's process of quelling airway inflammation is similar to putting out a forest fire, according to Bruce Levy, M.D., Pulmonary and Critical Care Medicine Division, BWH Department of Internal Medicine. Molecular image courtesy of Levy Lab. Credit: Levy Lab

Scientists from Brigham and Women's Hospital are on the brink of the next treatment advancement that may spell relief for the nearly nineteen million adults and seven million children in the United States suffering from asthma. The scientists discovered two new drug targets in the inflammatory response pathway responsible for asthma attacks.

The study will be published on February 27, 2013 in *Science Translational Medicine*.

Researchers studied the lungs and blood of 22 people with mild and severe asthma. They saw that immune cells called natural killer cells and

type 2 innate lymphoid cells played significant roles in airway inflammation in study participants with severe asthma.

Natural killer cells decreased airway inflammation by encouraging programmed cell death in immune cells called eosinophils, whereas type 2 innate lymphoid cells promoted airway inflammation by secreting cell-signaling molecules called interleukin-13.

Both mechanisms were controlled by a molecule called lipoxin A4 which is responsible for resolving inflammation. To achieve this, lipoxin A4 acted in both pro-resolving and anti-inflammatory ways. The researchers saw that lipoxin A4 encouraged natural killer cells to decrease inflammation by facilitating eosinophil cell death. Lipoxin A4 also discouraged type 2 innate lymphoid cells from promoting inflammation by blocking interleukin-13 secretion.

"Stopping airway inflammation is similar to putting out a forest fire," said Bruce Levy, MD, Pulmonary and Critical Care Medicine Division, BWH Department of Internal Medicine, senior study author. "Firefighters tackle forest fires in two ways—dousing the fire with water and clearing away dry brush that could fuel the fire. Lipoxin A4 does just that to resolve inflammation. It is an airway inflammation fighter that performs the double duty of dampening pathways that ignite inflammation while at the same time clearing away cells that fuel inflammation."

In previous studies, Levy and his team discovered that lipoxin A4 production was defective in patients with severe asthma. Together with their new findings, this observation provides researchers and drug manufacturers with a new direction toward boosting lipoxin A4 in severe asthmatics when designing next-generation asthma therapies.

"Most patients with severe asthma have chronic airway inflammation

that never fully resolves. This can lead to daily and often disabling symptoms despite available therapies. Our study provides new information on cellular targets that regulate inflammation and will enable the development of lipoxin-based therapeutics to decrease chronic inflammation in asthma and other diseases." said Levy.

Provided by Brigham and Women's Hospital