

Study uncovers details of allergic response in asthma patients

By Robin Arnette

According to research performed by NIEHS scientists, an enzyme normally produced in the body to help fight inflammation, also suppresses allergic responses in asthma patients. The study, which appeared online Feb. 28 in the *American Journal of Respiratory and Critical Care Medicine*, may help researchers understand the development and exacerbation of asthma.

The research team found that knocking out the enzyme cyclooxygenase-2 (COX-2) in mice, or treating normal mice with COX-2 inhibitors, led to elevated levels of a special type of helper immune cell. These immune cells, called T helper type 9 (Th9), are associated with asthma.

Hong Li, Ph.D., is a research fellow in the NIEHS Laboratory of Respiratory Biology and first author on the report. He and his colleagues tested three groups of mice — normal mice with functional COX-2 as a control, normal mice that were given COX-2 inhibitors, and mutant mice that lacked the COX-2 gene. They allowed the mice to become allergic to ovalbumin, the main protein in egg whites, by exposing them to the protein. The researchers then measured how many Th9 cells each group made and their levels of COX-2 metabolites.

“The control mice had very few Th9 cells, while the COX-2 inhibited mice and the mice without the COX-2 gene made double the number of Th9 cells,” Li said. “Our results show that COX-2 is responsible for suppressing Th9 cell formation.”

As a reinforcement of their findings, the researchers also tested healthy human adults and asthmatics, and found that the asthma patients had significantly more Th9 cells.

Li explained that although Th9 cells are associated with asthma, they normally help fight infections. This dichotomy arises because Th9 cells secrete a chemical messenger, or cytokine, known as interleukin 9 (IL-9), which increases inflammation in the body and leads to the exacerbation of asthma symptoms.

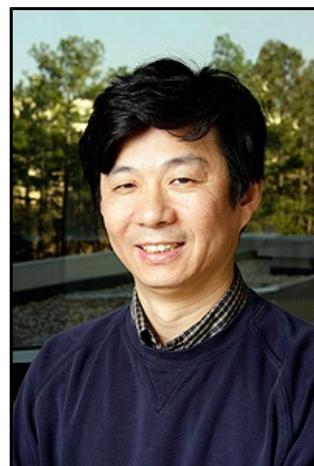
According to NIEHS Scientific Director Darryl Zeldin, M.D., corresponding author of the study, the research team was able to pinpoint the key players in the asthma COX-2 mechanism.

“We determined that two of the metabolites of COX-2, prostaglandins E2 and D2, suppress Th9 cell generation and function,” he said. “Although this information doesn’t provide a cure for asthma, we hope to use what we’ve learned to help asthma sufferers lessen their symptoms in the future.”

Citation: Li H, Edin ML, Bradbury JA, Graves JP, DeGraff LM, Gruzdev A, Cheng J, Dackor RT, Wang PM, Bortner CD, Garantziotis S, Jetten AM, Zeldin DC. (<http://www.ncbi.nlm.nih.gov/pubmed/23449692>) 2013. COX-2 inhibits Th9 differentiation during allergic lung inflammation via downregulation of IL-17RB. *Am J Respir Crit Care Med*; doi:10.1164/rccm.201211-2073OC [Online 28 February 2013].



In addition to his duties as NIEHS Scientific Director, Zeldin also heads the Environmental Cardiopulmonary Disease Group in the Laboratory of Respiratory Biology. (Photo courtesy of Steve McCaw)



Li said the research team is currently investigating whether gene differences, also known as polymorphisms, in COX-2 are associated with asthma (Photo courtesy of Steve McCaw)

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