

Potential new therapeutic target for asthma, allergies and cancer

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Virginia Commonwealth University researchers have identified how a bioactive molecule involved with allergy, inflammation and cancer is transported out of mast cells, according to findings published online this week in the *Proceedings of the National Academy of Sciences*.

Mast cells are specialized cells that react to allergy-causing agents by releasing substances that trigger the body's allergic response, leading to conditions like asthma and hives. Among the molecules released by mast cells that participate in the allergic response is sphingosine-1-phosphate. This molecule is also implicated in cancer.

The work by the VCU investigators opens up a new approach to treating asthma, which affects about 15 million Americans and is increasing in incidence and mortality, especially among African-Americans. It also has implications for other allergic disorders and for cancer in terms of developing drugs that inhibit the transport of SIP out of cells.

Sarah Spiegel, Ph.D., professor and chair, VCU Department of Biochemistry, and colleagues reported how S1P, which also regulates many important physiological functions in cells, is transported out of mast cells. S1P is produced by all cells and secreted by some cells into the circulation where it can bind to specific S1P receptors. Until now, researchers have not known the mechanism by which S1P is transported out of cells.

"Our study shows that mast cells can use a special kind of transporter

that has long been known to be used by cancer cells to push anti-cancer drugs out and help them survive the treatment," said Spiegel. "Our study is the first to establish a mechanism by which S1P can be exported out of mast cells and perhaps by cancer cells as well."

In previous research, Spiegel's team found that S1P levels are significantly elevated in fluid collected from the lungs of asthmatic patients after exposure to an allergen. Those findings led Spiegel's team to believe that mast cells could be a source of S1P. Mast cells are found in all body tissues and rapidly produce and secrete a number of inflammatory substances such as histamine and S1P when activated by an inflammatory stimulus. Spiegel said that S1P in turn amplifies allergic and inflammatory responses. Therefore, S1P secreted from mast cells can orchestrate many allergic responses, including asthma, she said.

Source: Virginia Commonwealth University

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