Cellular force that drives allergy and asthma can be blocked by interferon

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A mechanism that could underlie the development of cells that drive asthma and allergies has been uncovered by immunology researchers at UT Southwestern Medical Center.

Asthma and allergies are both driven by an inappropriate activation of the immune system, primarily a subtype of white blood cells known as T helper 2 cells, or Th2 cells. These cells are normally responsible for defense against parasites, but are also the main culprits behind the symptoms of asthma and allergies.

Dr. David Farrar, Associate Professor of Immunology and Molecular Biology at UT Southwestern, and his team found that the antiviral molecules known as type I interferons (IFNs) block the development of these allergy- and asthma-driving Th2 cells.

"The fact that interferon could stop the activation of these harmful cells was of particular interest because interferons are already approved by the Food and Drug Administration for the treatment of other diseases, such as multiple sclerosis and hepatitis," said Dr. Farrar, who holds the J. Wayne Streilein, M.D. Professorship in Immunology.

The work, published in the *Journal of Immunology*, could eventually give rise to new therapies.

To demonstrate the prevalence of asthma, in the United States about 13 percent of adults – nearly 30 million people – have received a diagnosis of asthma. This frequency compares to 11 percent who have been diagnosed with heart disease and 8 percent who have had any form of cancer, according to the Centers for Disease Control and Prevention. Asthma is reported more often among women than men, among Caucasians, and in families with limited economic resources. Allergies, too, are prevalent, with more than 17.5 million people suffering from hay fever in the U.S.

The development of Th2 cells is stimulated by a particular immune molecule that triggers the production of a protein called GATA3. Frequently referred to as the master regulator of Th2 cell development, GATA3 turns on the genes that distinguish Th2 cells from other cell types, including other T cells.

Dr. Farrar's group found that type I IFNs block this process by targeting a part of the GATA3 gene known as exon 1a and turning it off, thereby inhibiting the production of the GATA3 protein and, consequently, the development of Th2 cells.

"Targeting this pathway may lead to permanent tolerance of these cells to allergens," said Dr. Farrar. "We are currently pursuing studies that may lead to clinical trials that will determine whether interferon can be used to treat allergic asthma patients."

Dr. Farrar's lab studies how a collective group of proteins called cytokines regulate immune responses. Type 1 interferon, the first immune cytokine discovered, is one of the very first lines of defense against viruses. The protein was initially identified based on its ability to inhibit influenza virus. Since then, scientists have discovered that almost any cell in the body can secrete interferon if it becomes infected with certain viruses, and that most cells can respond to interferon.

Provided by UT Southwestern Medical Center