Using 'the language of cells' to find new treatments for asthma, allergies

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Yale researchers have discovered that microRNAs, small ribonucleic acids that drive communication between cells, present a new potential pathway for treating allergies and asthma. The study was published in the latest issue of the *Journal of Allergy and Clinical Immunology*.

The scientists—led by Shervin Takyar, M.D., associate professor and specialist in pulmonary disease at Yale—found that a specific microRNA known as miR-1 has a direct impact on allergic airway inflammation and that altering the levels of miR-1 can help relieve the symptoms of asthma and allergies.

It's approaching allergy and asthma treatment from an entirely new paradigm, Takyar said, one that focuses on "the language of cells."

About 10 years ago, he and other Yale researchers began looking at the endothelial cells that line blood vessels within the nose and lung tissues where asthma and allergy symptoms arise. In patients with asthma and rhinosinusitis (inflammation of the sinuses common to allergy sufferers), these blood vessels let in high numbers of eosinophils, the white blood cells that cause inflammation in the lungs and nasal passages

"We asked: 'What if we could stop these blood cells at the gate?'" Takyar said.

The researchers zeroed in on one of these "gatekeepers," miR-1, which directly impacted whether the blood vessel gateways were open or shut.

"There's a difference in the cellular language between people who naturally let eosinophils into their lungs and people who naturally don't," Takyar said. "We wanted to understand the language of the cells of these healthier people."

Takyar and Geoffrey Chupp, M.D., professor of medicine and director of the Yale Center for Asthma and Airway Disease, studied both human lung samples and sinonasal tissues and found that patients whose tissue had low miR-1 levels had greater inflammation, poorer asthma control, and increased hospitalizations.

They showed that by delivering miR-1 intranasally and altering miR-1 levels in the blood vessels of mouse models, they were able to reverse the lung inflammation and reduce the white blood cells that cause allergy and asthma symptoms by more than 50%, as well as reducing airway inflammation, mucus levels, and asthma symptoms. In their current study, the researchers also show that by administering miR-1 to human blood vessels directly they can reduce the entry of human eosinophils into tissues.

Asthma rates are increasing, said Takyar, and new

forms of asthma are on the rise that are not well controlled by existing medications. Some 300 million people worldwide suffer from allergic asthma. At the same time, more people are being diagnosed with chronic rhinosinusitis, which affects more than 10% of the U.S. adult population. Like those with asthma, said Takyar, many of these sufferers find no relief for their persistent congestion, runny noses, and headaches, even after surgery.

Takyar says delivering miR-1 to patients suffering from asthma and chronic rhinosinusitis who are not finding relief from current medications shows promise. "Here is a new language," he says. "We're getting in line with how cells talk and using their language to close gateways, and we expect to see real improvements in severe asthma and allergy patients."

More information: Asawari Korde et al. An endothelial microRNA-1–regulated network controls eosinophil trafficking in asthma and chronic rhinosinusitis, *Journal of Allergy and Clinical Immunology* (2020). DOI: 10.1016/j.jaci.2019.10.031

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