Allergy medicine may help treat lung cancer, research suggests

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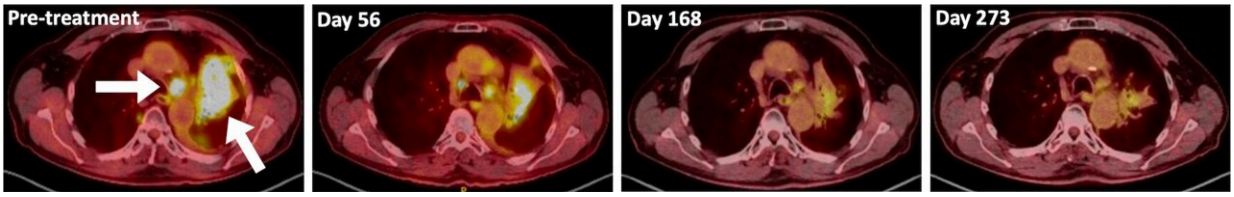

Chest scans showing lung tumors in a patient with metastatic non-small cell lung cancer prior to and after receiving dupilumab with conventional immunotherapy. Credit: LaMarche et al., Nature.

Researchers at the Icahn School of Medicine at Mount Sinai have identified an allergy pathway that, when blocked, unleashes antitumor immunity in mouse models of non-small cell lung cancer (NSCLC).

And in an early parallel study in humans, combining immunotherapy with dupilumab—an Interleukin-4 (IL-4) receptor-blocking antibody widely used for treating allergies and asthma—boosted patients' immune systems, with one out of the six experiencing significant tumor reduction.

The findings are described in a paper, titled "An IL-4 signaling axis in bone marrow drives pro-tumorigenic myelopoiesis," in the December 6 issue of *Nature* .

"Immunotherapy using checkpoint blockade has revolutionized treatment for non-small cell lung cancer, the most common form of lung cancer, but currently only about a third of patients respond to it alone, and in most patients, the benefit is temporary," says senior study author Miriam Merad, MD, Ph.D., Director of the Marc and Jennifer Lipschultz Precision Immunology Institute and Chair of the Department of Immunology and Immunotherapy at the Icahn School of Medicine at Mount Sinai.

"A big focus of our program TARGET is to use single cell technology and artificial intelligence to identify molecular immune programs that can dampen tumor immune response to checkpoint blockade."

Also known as a PD1 inhibitor, checkpoint blockade is a type of cancer immunotherapy that can unleash the cancer-killing activity of T cells.

"Using single cell technologies, we discovered that the immune cells infiltrating lung cancers, as well as other cancers we studied, exhibited characteristics of a 'type 2' immune response, which is commonly associated with allergic conditions like eczema and asthma," says first study author Nelson LaMarche, Ph.D., a postdoctoral research fellow in the lab of Dr. Merad.

"These results led us to explore whether we could repurpose a medication typically used for allergic conditions to 'rescue' or enhance tumor response to checkpoint blockade," says Thomas Marron, MD, Ph.D., Director of the Early Phase Trial Unit at Mount Sinai's Tisch Cancer Center, and co-senior author of the study.

"Strikingly, we found that IL-4 blockade enhanced lung cancer response to checkpoint blockade in mice and in six lung cancer patients with treatment-resistant disease. In fact, one patient whose lung cancer was growing despite checkpoint blockade had nearly all their cancer

disappear after receiving just three doses of the allergy medication, and his cancer remains controlled today, over 17 months later."

The researchers are encouraged by the initial results but emphasize the need for larger clinical trials to validate the drug's efficacy in treating NSCLC.

Beyond the clinical trial findings reported in the current *Nature* paper, the investigators have now expanded the clinical trial, adding dupilumab to checkpoint blockade for a larger group of lung cancer patients, and Dr. Marron recently received a grant from the Cancer Research Institute to study the effects in early-stage lung cancer as well.

Through these trials, they are searching for biomarkers that can predict which cancer patients might benefit from dupilumab treatment and which may not.

"In our relentless pursuit of progress, the Cancer Research Institute (CRI) proudly supports the visionary team at the Icahn School of Medicine at Mount Sinai. Their findings validate our commitment to funding research across the entire discovery continuum, from the lab to clinical implementation, driven by cutting-edge technology and data," says Jill O'Donnell-Tormey, Ph.D., CEO and director of scientific affairs at CRI.

"We're eager to witness our support delivering new hope by uncovering pathways to enhance checkpoint blockade responses. We champion this discovery and take pride in being part of its journey from lab to clinic, reinforcing our commitment to transforming lives."

More information: Miriam Merad, An IL-4 signalling axis in bone marrow drives pro-tumorigenic myelopoiesis, *Nature* (2023). DOI: 10.1038/s41586-023-06797-9.

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