

Obesity Promotes Lung Cancer by Suppressing Immune Response

Roswell Park team finds evidence that excess abdominal fat undermines the immune system's attack on developing tumors.

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Highlights

- Research pinpoints dysfunctional immune cells in the airway.
- Findings refute earlier studies suggesting high BMI is protective.
- Results appear in the *Journal of Thoracic Oncology*.

Buffalo, N.Y. — A research team led by experts at Roswell Park Comprehensive Cancer Center has documented new evidence that excess abdominal fat increases the risk of developing non-small cell lung cancer. Published in the [Journal of Thoracic Oncology](#), the findings show that the immune system's attack on developing tumors is undermined in obese patients, contradicting earlier studies suggesting that patients with a high body mass index (BMI) are at lower risk for the disease.

The study was led by senior authors [Sai Yendamuri, MD, MBA, FACS](#), Chair of Thoracic Surgery, and [Joseph Barbi, PhD](#), Assistant Professor of Oncology in the Department of Immunology.

“Our results provide strong evidence that obesity is a risk factor driving lung cancer development and that strategies to correct the effects of obesity on airway immune cells may help us to prevent or intercept early-stage lung cancers in people at high risk of developing lung cancer,” says Dr. Yendamuri, who is also a Senior Vice President and Chief Strategy Officer at Roswell Park.

“Now we know that obesity impairs the lung's immune defenses before and during the early stages of tumor development,” says Dr. Barbi.

Focusing on people at elevated risk of developing lung cancer because of their smoking history, the researchers analyzed data for 1,170 current or former smokers through an observational case-control study, including 576 people diagnosed with Stage I or II non-small cell lung cancer (NSCLC) who were treated with surgery at Roswell Park between 2009 and 2020, and another 576 people

who underwent lung cancer screening at Roswell Park between 2015 and 2022. Those in the control group were tracked for at least a year to determine whether they later developed cancer.

Both those with a cancer diagnosis and the people in the control group underwent CT scans that captured the total fat area (TFA) in the abdominal region—a more accurate and physiologically meaningful definer of overweight or obesity than BMI. Records showed that those in the healthy but high-risk control group who had relatively high TFA were more likely than those with lower TFA to develop lung cancer.

But why? Examining the airway immune environment in human patients and in laboratory studies, the researchers found that the lungs of obese subjects contained higher numbers of regulatory T cells, or tregs, which appeared to play a key role in allowing the lung cancer to grow unchecked, while other immune cells that ordinarily would be capable of killing tumor cells appeared defective. As a result, preclinical models with excess fat developed lung tumors faster.

While obesity has been shown to increase the risk of developing at least 13 types of cancer and lead to poor outcomes after diagnosis, its role has been less clear in lung cancer. Shedding light on the link between cancer and overweight/obesity is especially critical because the percentage of the U.S. population with a BMI over 25 has increased to 66% over the last 40 years, with more than half that population falling into the obese category (BMI 30+).

The team is now focused on identifying other ways in which obesity compromises the immune system's cancer-fighting defenses in the lung and the underlying mechanisms.

Randall Smith Jr., PhD, of the Department of Thoracic Surgery, and Yeshwanth Vedire, MD, former postdoctoral researcher at Roswell Park, are co-first authors of the study.

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