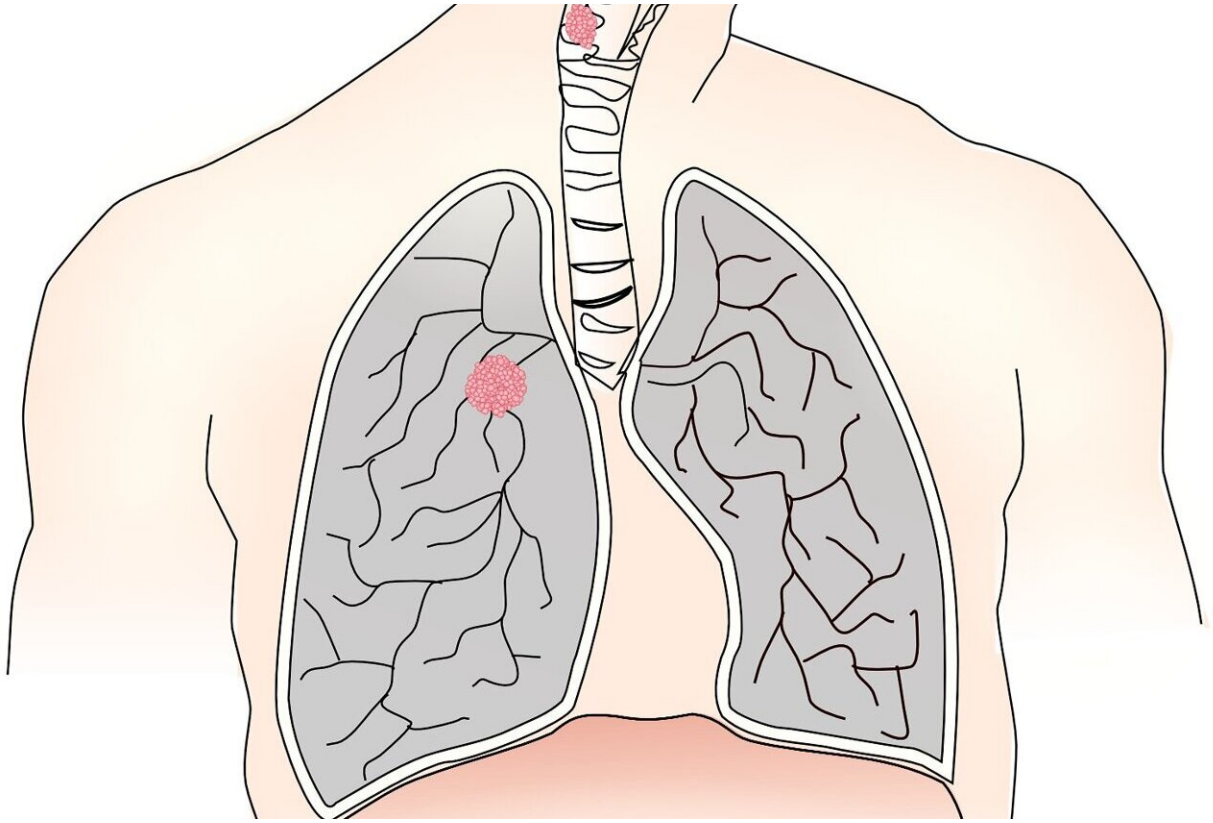
Genetics of nearby healthy tissue may help catch lung cancer's return

November 8 2023



Credit: Pixabay/CC0 Public Domain

Genetic information collected from seemingly healthy tissue near lung tumors may be a better predictor of whether cancer will come back after treatment than analysis of the tumors themselves, according to new

research led by NYU Langone Health and its Perlmutter Cancer Center.

The new study focuses on lung adenocarcinoma, a cancer that forms in alveolar epithelial cells and accounts for about a third of all lung cancers in the United States, according to the U.S. Centers for Disease Control and Prevention. Most patients are cured if tumors are surgically removed early in the disease's progression, but residual cancer cells regrow in about 30% of cases and can lead to death. Consequently, experts have long searched for biomarkers, or predictors of recurrence, that might prompt more aggressive initial treatment.

The study included 147 men and women treated for early-stage lung cancer. It explored the utility value of the transcriptome, the complete set of RNA molecules that tell cells what proteins to make. Analysis of RNA collected from apparently healthy tissue adjacent to tumor cells accurately predicted that cancer would recur 83% of the time, while RNA from tumors themselves was only informative 63% of the time.

"Our findings suggest that the pattern of gene expression in apparently healthy tissue might serve as an effective and until now elusive biomarker to help predict lung cancer recurrence in the earliest stages of the disease," said study co-lead author Igor Dolgalev, Ph.D.

Published online Nov. 8 in the journal *Nature Communications*, the investigation is the largest to date comparing genetic material from tumors and adjacent tissue and for their ability to predict recurrence, says Dolgalev, an assistant professor in the Department of Medicine at NYU Grossman School of Medicine and a member of Perlmutter Cancer Center.

For the study, the research team collected almost 300 tumor and healthy tissue samples from lung cancer patients. The study investigators then sequenced the RNA from each sample and fed these data, along with

whether or not recurrence occurred within five years of surgery, into an artificial intelligence algorithm. This program used machine learning to build mathematical models that estimated recurrence risk.

The findings revealed that the expression of genes associated with inflammation, or heightened immune system activity, in adjacent and apparently normal lung tissue, was especially useful for making predictions. This defensive reaction, the study authors say, should not be present in tissue that is truly healthy and may be an early warning sign of disease.

"Our results suggest that seemingly normal tissue that sits close to a tumor may not be healthy after all," said study co-lead author Hua Zhou, Ph.D., a bioinformatician at NYU Grossman and a member of Perlmutter Cancer Center. "Instead, escaped tumor cells might be triggering this unexpected immune response in their neighbors."

"Immunotherapy, which bolsters the body's immune defenses, might therefore help combat tumor growth before it becomes visible to traditional methods of detection," added study co-senior author and cancer biologist Aristotelis Tsirigos, Ph.D.

Tsirigos, a professor in the Department of Pathology at NYU Grossman and a member of Perlmutter Cancer Center, cautions that the investigation worked backwards, training the computer program using cases already known to have had disease return.

As a result, the study team next plans to use the program to prospectively assess recurrence risk in patients newly treated for early-stage lung cancer, says Tsirigos, who is also director of NYU Langone's Applied Bioinformatics Laboratories.

More information: Inflammation in the tumor-adjacent lung as a

predictor of clinical outcome in lung adenocarcinoma, *Nature Communications* (2023). DOI: 10.1038/s41467-023-42327-x