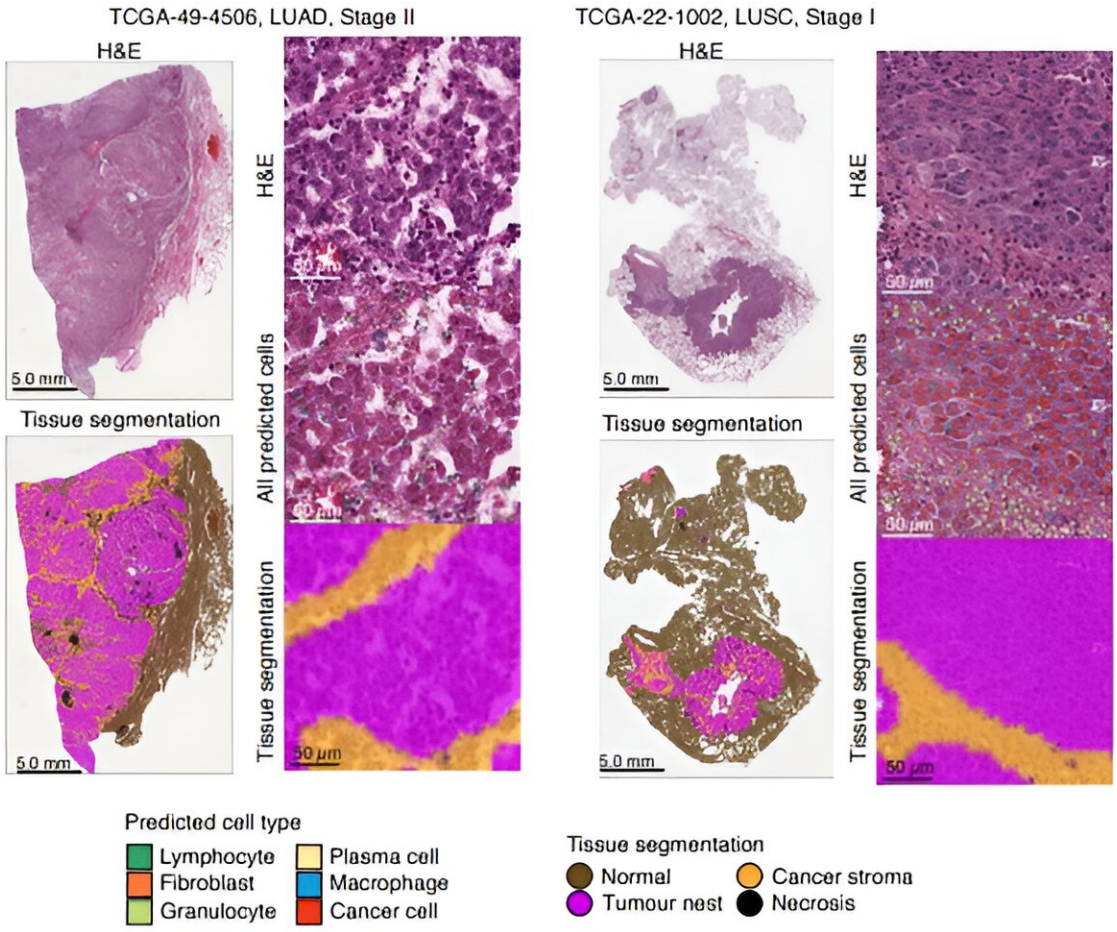
Looking at the environment around tumors could help predict how cancer spreads

April 10 2024



Representative images of high granulocyte infiltration in the tumor nest and stroma for LUAD (left) and LUSC (right). Credit: *Cancer Discovery* (2024). DOI: 10.1158/2159-8290.CD-23-1380

Examining the immune cells in the environment around a tumor could help to predict how a person's cancer might progress and respond to treatment, according to new research led by UCL and the Francis Crick Institute.

The study, published in *Cancer Discovery* and reported at the American Association for Cancer Research Annual Meeting 2024, is part of the Rubicon project, which aims to create a detailed map of lung cancer immunology to speed up the development of new treatments.

The team classified four different environment subtypes found around lung tumors, each associated with different patterns of cancer progression. Cancers identified as having low levels of immune infiltration by T and B cells, but high levels of neutrophils, were more likely to spread to other parts of the body.

The tumor microenvironment is a mixture of cancer cells, immune cells, structural proteins and blood vessels. Because the makeup of the microenvironment can vary throughout and around the tumor, looking at multiple sites of the tumor and its surroundings is helpful to get a more accurate picture of what is happening during disease progression.

The researchers used advanced imaging techniques to map single cells and outline four different microenvironments in lung cancer, by investigating samples of tumors and normal tissue from 81 patients with non-small cell lung cancer (NSCLC) taking part in the TRACERx study.

They looked at T and B cells, macrophages and neutrophils, which are all types of white blood cell involved in immune response. Each class of microenvironment is composed of varying numbers of immune cells in different areas of the tumor:

- 28% of tumors had a very active immune environment, with high

numbers of T and B cells and macrophages in the inner and outer parts of the tumor. These were described as "immune hot."
- 24% of tumors had a low infiltration of T cells and macrophages in the inner part of the tumor, but many B and T cells in the outer part of the tumor, without many macrophages.
- 17% of tumors had a less active immune environment, with low numbers of T and B cells and macrophages throughout the tumor.
- 19% of tumors had a low infiltration of T and B cells and macrophages throughout the tumor, but a large number of neutrophils.

In the fourth subtype, identified as having high levels of neutrophils, the researchers observed that tumors were also further away from a reliable blood supply. Subsequent evolutionary changes in these tumors enabled evasion from the T and B immune cells that are able to attack the cancer.

By comparing tumors likely and unlikely to spread, the researchers saw that the number of neutrophils was higher in tumors that were more likely to spread. They then used statistical and machine learning methods to confirm this association.

The results suggest that measuring the number of neutrophils could be an effective clinical test, helping clinicians to determine who might need additional treatment to prevent cancer spread.

Mihaela Angelova, a postdoctoral fellow in the Cancer Evolution Laboratory at the Crick and co-senior author of the study, said, "We've shown that high infiltration of neutrophils could be a marker for cancer evolution and spread. These tumors were genetically altered, separated from the blood supply and managed to evade the immune system, making them better able to spread."

Professor Charlie Swanton, co-senior author of the study from UCL

Cancer Institute, Head of the Cancer Evolution Laboratory at the Crick and Chief Clinician at Cancer Research UK, said, "Lung cancer, particularly if caught at a later stage, is hard to treat, and mapping the environment around the tumor can help us to categorize cancers and work out personalized treatment strategies for patients.

"This research highlights the importance of pairing the evolutionary history of a tumor with information on how the tumor microenvironment organizes in 3D to build the most accurate picture of an individual's cancer."

The researchers are now investigating what happens to the tumor microenvironment as the cancer metastasizes—spreads and becomes genetically varied throughout the body.

More information: Katey S. S. Enfield et al, Spatial Architecture of Myeloid and T Cells Orchestrates Immune Evasion and Clinical Outcome in Lung Cancer, *Cancer Discovery* (2024). DOI: 10.1158/2159-8290.CD-23-1380

Provided by University College London