Blood cell insights offer potential boost to lung cancer therapies

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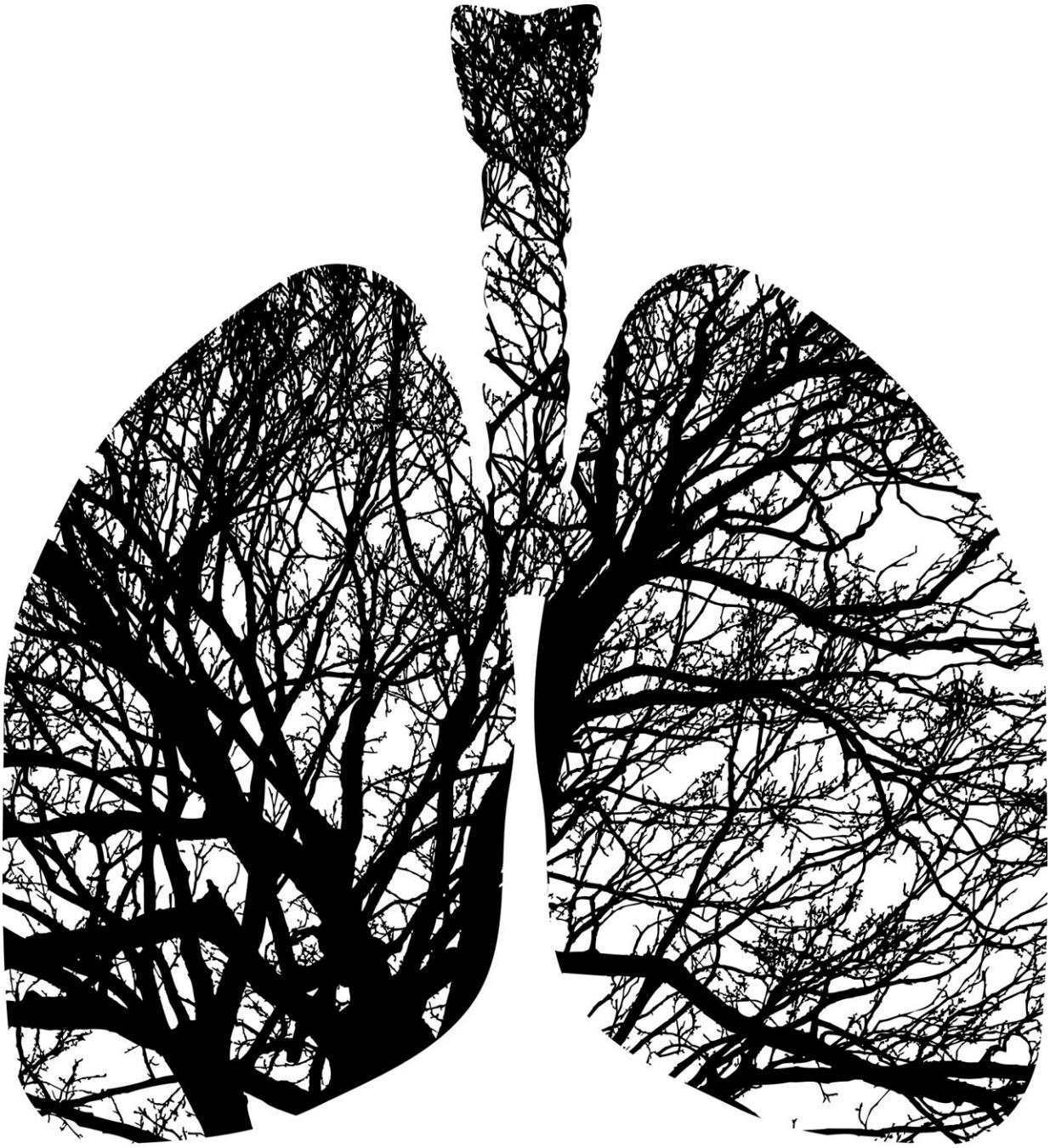

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Fresh discoveries about a certain type of immune cell could give lung cancer patients a more accurate prognosis and better identify who will

benefit from immunotherapies.

Researchers have found that the location in and around tumors of cytotoxic T cells, which play a key role in fighting cancer, may help predict patient survival and indicate whether or not treatments will work. The findings could help to pave the way for improved immunotherapies—powerful but expensive life-extending treatments that currently fail in 80% of cases—allowing them to work more effectively in more patients, researchers say.

Experts caution, however, that further research and tests are needed alongside the integration of new technologies before any application in clinical practice is possible.

The work is published in the *Journal for ImmunoTherapy of Cancer*.

Lung cancer is one of the most common cancers worldwide and is the leading cause of cancer-related deaths. It is often diagnosed at an advanced stage when conventional treatments are less effective.

For this study, University of Edinburgh researchers investigated why immunotherapy fails so often against the disease by examining molecules that can interfere with the activity of T cells, a type of white blood cell that fights disease.

Immunotherapies work by boosting the activity of cytotoxic T cells, which play a key role in patrolling the body to detect and kill cancer cells, but often become "exhausted" when battling tumors. As tumors grow, they use complex mechanisms to escape destruction, including interfering with the activity of immune cells, such as T cells.

The team examined tumor tissue from 162 patients undergoing surgery for non-small cell lung cancer (NSCLC), the most common type, which

accounts for more than 80% of lung cancer cases. The results revealed that high levels of two enzymes (CD39 and CD73), found on the surface of many different types of immune cells, were associated with reduced patient survival if found in tissue near the tumors.

T cells have an in-built safety mechanism designed to stop them from becoming overactive when fighting an infection. By raising the levels of these enzymes, tumors exploit this and escape destruction.

The team also found that both the location and types of T cells that express these enzymes could also play an important role in helping to predict a patient's prognosis and the success of immunotherapy. High levels of CD39 on the surface of cytotoxic T cells located inside tumor nests—clusters of cancer cells—were associated with increased patient survival and a better response to immunotherapy.

In contrast, when the same CD39 cytotoxic T cells were found outside of these tumor nests, in a region called the stroma, they did not affect patient survival.

High levels of CD39 on the surface of another type of T cell, known as regulatory T cells, which normally prevent the immune system from becoming overactive, were associated with reduced survival.

The findings were consistent even when other factors were taken into consideration—such as a patient's age, tumor size and whether they received chemotherapy in addition to surgery.

Understanding the mechanisms that suppress T cells and control their location could improve immunotherapy outcomes and better predict which patients will benefit from them, researchers say.

Dr. Ahsan Akram, Cancer Research UK Clinician Scientist Fellow at the

University of Edinburgh's Centre for Inflammation Research, said, "This study helps us to understand that we need to know the types of T cells in the cancer and their location within the tumors to begin to appreciate the complexity we are dealing with. We hope these results will lead to more research in this area, and in the future could help to identify patients who will do well with immunotherapies, as well as identifying earlier those that may not, so alternative treatments can be tried."

Dr. Catherine Elliot, Cancer Research UK Director of Research Funding Communications, noted, "Immunotherapy is an exciting and growing focus of cancer research. We are delighted to see the findings of this research, which helps us to better understand why these treatments work better in some people than others. We hope that this can lead to more effective treatments for cancer patients."

More information: Location of CD39+ T cell subpopulations within tumors predict differential outcomes in non-small cell lung cancer, *Journal for ImmunoTherapy of Cancer* (2023). DOI: 10.1136/jitc-2023-006770

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