Early lung cancer coopts immune cell into helping tumors invade the lungs

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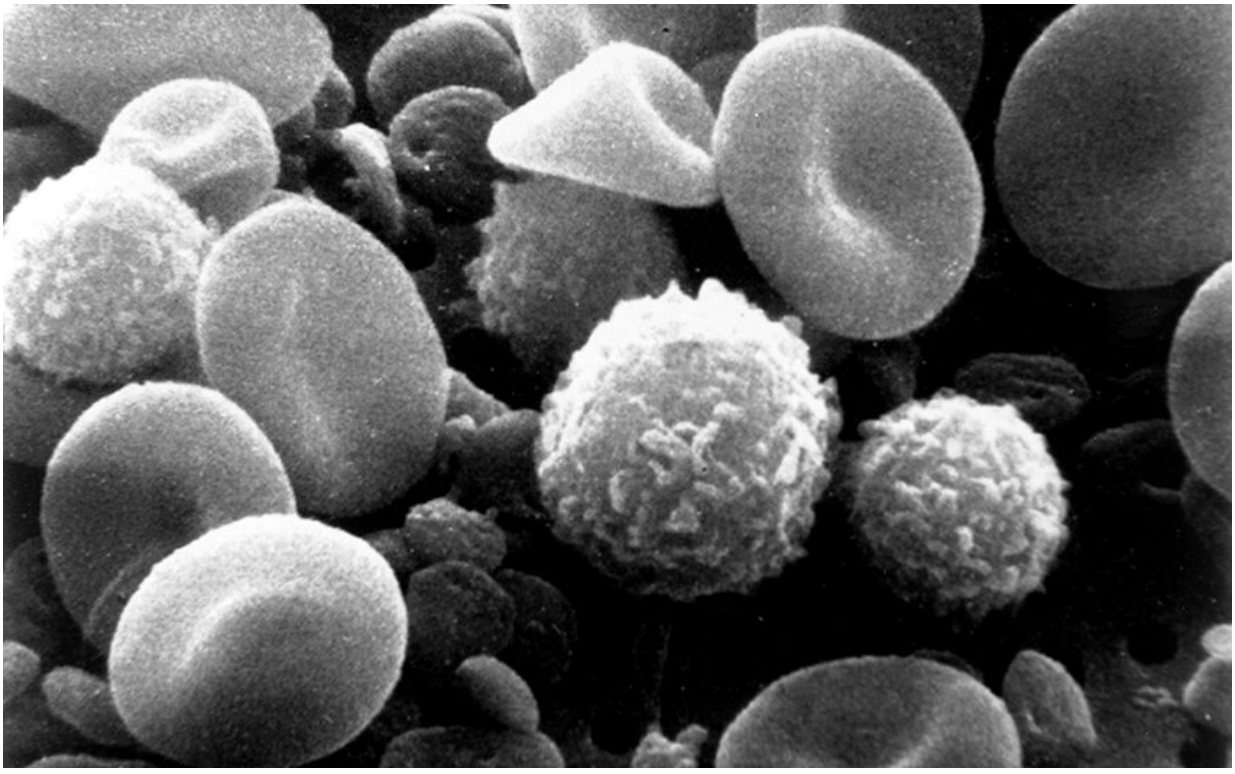

Myeloid immune cells alongside red blood cells in an electron micrograph of human blood. Credit: National Cancer Institute

Immune cells that normally repair tissues in the body can be fooled by tumors when cancer starts forming in the lungs and instead help the tumor become invasive, according to a surprising discovery reported by

Mount Sinai scientists in *Nature* in June.

The researchers found that early-stage lung cancer tumors coopt the immune cells, known as tissue-resident macrophages, to help invade lung tissue. They also mapped out the process, or program, of how the macrophages allows a tumor to hurt the tissues the macrophage normally repairs. This process allows the tumor to hide from the immune system and proliferate into later, deadly stages of cancer.

Macrophages play a key role in shaping the tumor microenvironment, the ecosystem that surrounds tumors in the body. By investigating this microenvironment, researchers can find key players that drive tumor growth that can be tested as targets for immunotherapy. But modifying macrophages therapeutically has proven difficult.

In this study, scientists studied tissue samples from lung cancer tumors and surrounding lung tissue in 35 patients to see the role of macrophages in the development of the tumors.

The study's lead author, Miriam Merad, MD, Ph.D., Director of the Precision Immunology Institute at the Icahn School of Medicine at Mount Sinai, and a multidisciplinary team of thoracic surgeons, pathologists, and medical oncologists within the Institute of Thoracic Oncology devised a comprehensive study that began when patients went into surgery to have cancerous lesions removed. The patients' lung tumor samples, samples of surrounding healthy lung tissue, and blood samples were immediately analyzed on a cellular level at Mount Sinai's Human Immune Monitoring Center to map out the immune system components they contained.

Researchers identified the macrophages at play in the early development of lung cancer, identifying a potential target for future drug development. They also found that the process that allows the

macrophages to help tumors invade lung tissues is present in mice as well, which will allow them to manipulate the macrophages in future mouse models knowing that the manipulation is relevant to humans.

Half of all early-stage lung cancers relapse, and once they do and reach later stages, it is deadly and irreversible. Knowing how to attack the cancer at an early stage could have huge impacts on the number of patients relapsing and their overall survival.

"These findings are very important for Mount Sinai in the future as we have a very strong lung cancer screening program that identifies patients with early lung cancer lesions before they become fully invasive," said Dr. Merad, who is also the Director of the Human Immune Monitoring Center and a member of the Institute of Thoracic Oncology and The Tisch Cancer Institute at Mount Sinai. "These findings will help devise immunoprevention strategies to prevent tumor progression in patients at risk by reprogramming macrophages and killing the tumor without surgery."

More information: Tissue-resident macrophages provide a pro-tumorigenic niche to early NSCLC cells, *Nature* (2021). DOI: 10.1038/s41586-021-03651-8 , www.nature.com/articles/s41586-021-03651-8

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