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Hybrid immune cells in early-stage lung cancer spur anti-tumor T cells to action

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The microenvironment of tumors is a mix of cell types, mostly comprised of inflammatory cells. White blood cells, recruited from the blood and bone marrow, represent a significant portion of these inflammatory cells and influence nearly all steps of tumor progression. One type, called tumor associated neutrophils (TANs), predominates; however, the role of TANs in tumor development remains largely unexplored in humans.

Researchers from the Perelman School of Medicine at the University of Pennsylvania have now identified a unique subset of these cells that exhibit hybrid characteristics of two immune cell types—neutrophils and antigen-presenting cells—in samples from early-stage human lung cancers. This is the first study to describe this phenomenon in a human tumor. Senior author Evgeniy B. Eruslanov, PhD, a research assistant professor from the Department of Surgery, and colleagues published their findings this month in *Cancer Cell*.

The goal of this research was to characterize TANs and determine their specific roles in the regulation of T cell responses in patients with early-stage lung cancer. Understanding the role of TANs in regulating T cell responses in cancer patients is particularly important because cytotoxic T lymphocytes are the chief effector cells mediating antitumor immunity.

"We tried to ascertain the function of this hybrid subset of TANs," Eruslanov said. "Are they there to help the tumor grow or to fight its existence? We show that small size, early-stage lung tumors can induce

the formation of a unique type of tumor-associated cells that can trigger and support anti-tumor T cell responses, thus potentially limiting the growth of the cancer" Eruslanov said.

To figure out how to harness natural anti-tumor capabilities of immune cells, they needed to know what happens in human tumor tissue. This was made possible by coauthor Sunil Singhal, MD, an associate professor of Surgery, who provided fresh tumor tissue from lung-cancer patients and participated in research.

"Our findings demonstrate that the early-stage lung tumor microenvironment can drive neutrophils to differentiate into a cell subset with enhanced anti-tumor capabilities. Interestingly, this hybrid population disappears as tumors enlarge," Singhal said.

These findings demonstrate the potential anti-tumor role of these cells in early-stage cancer and may provide opportunities to boost the anti-tumor efficacy of cytotoxic T cells. An understanding of the cellular and molecular processes in early stage tumors will allow researchers to identify which immune forces need to be augmented to facilitate natural protection against tumor development.

"We want to take advantage of these unique early tumor neutrophils to help them better stimulate the anti-tumor cytotoxic T cells," Eruslanov said. "Perhaps if we can expand the hybrid neutrophils in patients early on, we can augment anti-tumor T cell activity."

Provided by University of Pennsylvania School of Medicine