

Tumor-associated neutrophils stimulate T cell responses in early-stage human lung cancer



Studies suggest that tumor initiation and progression are commonly accompanied by a low grade underlying inflammation. Tumor-infiltrating myeloid cells represent a significant proportion of the inflammatory cell population in the tumor microenvironment, and they influence nearly every step in tumor progression. Among these different types of myeloid cells are tumor-associated macrophages (TAMs). TAMs have been the best characterized and are generally considered protumoral. While the role of tumor-associated neutrophils (TANs) in cancer progression remains unclear and has been investigated only recently in murine models. Characterization of human TANs is even less well developed. TANs are generally considered to have dichotomous protumor and antitumor effects in murine tumor models but it is not known if this happens in humans too. Human correlative studies using immunohistochemistry have shown that TAN infiltrates are associated with a poor prognosis for patients with certain cancers such as head and neck, renal cell carcinoma, melanoma, hepatocellular cancer and colon cancer. In contrast, the high tumor neutrophil counts have been associated with a favorable outcome for patients with gastric cancer while the results in

lung cancer have been divergent. The goal of this study therefore was to provide a phenotypic and functional characterization of TANs in surgically resected lung cancer patients. The researchers found that TANs constituted 5%–25% of cells isolated from the lung tumors. They also displayed a specific set of chemokine receptors that included CCR5, CCR7, CXCR3, and CXCR4 and proinflammatory factors MCP-1, IL-8, MIP-1 α , and IL-6. They also showed that both TANs and regular blood neutrophils isolated from distant nonmalignant lung tissue were able to stimulate T cell proliferation and IFN- γ release. Thus demonstrating that cross-talk between TANs and activated T cells brought about substantial upregulation of costimulatory molecules on the neutrophil surface, stimulating T cell proliferation in a positive-feedback loop. The study was therefore able to show that in the earliest stages of lung cancer, TANs are not immunosuppressive, but rather stimulate T cell responses.

[Eruslanov, E. et al. 2014. Tumor-associated neutrophils stimulate T cell responses in early-stage human lung cancer. *The Journal of Clinical Investigation*.](#)