Resistance

Neutrophils promote tumour resistance to radiation therapy

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Proc Natl Acad Sci USA. 2019 Sep 10;116(37):18584-18589. doi: 10.1073/pnas.1901562116. Epub 2019 Aug 28.

Abstract

Nearly two-thirds of cancer patients are treated with radiation therapy (RT), often with the intent to achieve complete and permanent tumour regression (local control). Radiotherapy is the primary treatment modality used to achieve local control for many malignancies, including locally advanced cervical cancer, head and neck cancer, and lung cancer. The addition of concurrent platinum-based radiosensitising chemotherapy improves local control and patient survival. Enhanced outcomes with concurrent chemoradiotherapy may result from increased direct killing of tumour cells and effects on non-tumour cell populations. Many patients treated with concurrent chemoradiotherapy exhibit a decline in neutrophil count, but the effects of neutrophils on radiation therapy are controversial.

To investigate the clinical significance of neutrophils in the response to radiotherapy, we examined patient outcomes and circulating neutrophil counts in cervical cancer patients treated with definitive chemoradiation. Although pretreatment neutrophil count did not correlate with outcome, lower absolute neutrophil count after starting concurrent chemoradiotherapy was associated with higher rates of local control, metastasis-free survival, and overall survival. To define the role of neutrophils in tumour response to radiation therapy, we used genetic and pharmacological approaches to deplete neutrophils in an autochthonous mouse model of soft tissue sarcoma. Neutrophil depletion prior to image-guided focal irradiation improved tumour response to radiotherapy.

Our results indicate that neutrophils promote resistance to radiation therapy. The efficacy of chemoradiotherapy may depend on the impact of treatment on peripheral neutrophil count, which has the potential to serve as an inexpensive and widely available biomarker.