Lymphology 56 (2023) 1-2

EDITORIAL

ONCOLYMPHOLOGY: IMMUNE INTERACTIONS AND CANCER

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ABSTRACT

The proposed term "oncolymphology" encompasses the intimate relationship between cancer growth and the immune responses.

Keywords: Cancer, Immune Responses, Oncolymphology

Cancer is a heterogeneous disease arising from genomic mutations (1,2) or epigenetic changes (3). Within a cancer cell population, heterogeneous clones may develop resulting in cancer heterogeneity within a tumor, between different metastatic deposits, and between patients. The cancer microenvironment exerts a selective force akin to Darwinian "natural selection" (4) that promotes the development of invasive clones to metastasize from the primary site to the distant sites, in accordance with Paget's seed and soil hypothesis for cancer spread (5). Cancer metastasis may occur through the lymphatic vessels to the sentinel lymph nodes or through blood vessels, or via both pathways (6). The molecular mechanisms of cancer evolution and spread are under intense study (7).

In the literature, while the genetics and proteinomics of cancer have been emphasized, the cancer microenvironment especially the immune responses to cancer and the T cell repertoire of the host have not been highlighted. Recent elucidation of molecular mechanisms of immune responses to cancer and the application of immune checkpoint blockade (8) in the successful treatment of cancer (9) have established firmly the significance of immune interactions and cancer.

The relationship between T cells and cancer neoantigens (10) is being investigated to delineate the extent of such a relationship and the potential exploitation for cancer immunotherapy. The dynamic interactions bet-ween cancer metastasis and T cell repertoire (11), may change during different stages of cancer evolution from a single cell to a clonal population and the development of invasive clones to metastatic sites. Thus, it is appropriate to coin this intimate relationship between cancer growth and immune responses as a new field, ***oncolymphology***: immune interactions with cancer. This relationship is perhaps best illustrated in the conundrum of sentinel lymph node (SLN) with respect to cancer metastasis and invasion. The SLN is the sentinel guard against cancer invasion and yet it may act as a gateway or incubator for cancer to proliferate and metastasis to systemic sites (12).

Recent findings have explained this conundrum in that in early cancer evolution within the primary site, chemokines from the cancer cells may be transported to the SLN (13) to condition the SLN microenvironment

with the acquisition of certain cells within the SLN to produce growth factors or cytokines being associated with the restructuring of the extracellular matrix (14) to form the pre-metastatic niche, which allows cancer cells from the primary site to invade the lymphatic vessels and take hold in the SLN to survive and proliferate. Once the residence of cancer cells is firmly secured, they may proliferate and invade the high venular endothelial vessels within the SLN for systemic metastasis (15). Recent promising study using single cell analysis of melanoma SLNs has shown that immunologic changes compromise antimelanoma immunity and contribute to a high relapse rate in SLN positive patients (16). The challenge is to delineate all these steps of cancer metastasis on a molecular basis with development of therapeutic maneuvers to block these steps, which were further discussed at the 9th International Cancer Metastasis Congress held in May 2023 in San Francisco, CA (www.cancermetastasis.org) (17).

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