

Inflammation and Cancer: From Bench to Bedside?

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Commentary on “Cancer Cachexia and Targeting Chronic Inflammation: A Unified Approach to Cancer Treatment and Palliative/Supportive Care” by Neil MacDonald, CM, MD (page 157).

It was suggested in the early 19th century that cancer was linked to inflammation, but for many years, this idea was out of fashion.¹ The inflammation-cancer connection has undergone a renaissance because of compelling new information from different areas of cancer research. The connection between these two fundamental pathologies is now widely accepted and offers novel therapeutic approaches.¹⁻³

Epidemiologic studies have revealed that chronic inflammation predisposes to different forms of cancer and that usage of nonsteroidal anti-inflammatory agents provides some degree of protection against various tumors. Not only do some inflammatory conditions predispose to cancer, as exemplified by the connection between inflammatory bowel disease and colorectal cancer, but even those tumors that are epidemiologically unrelated to inflammation, such as breast cancer, are characterized by the build-up of an inflammatory microenvironment. In other words, an inflammatory component is present in the microenvironment of most neoplastic tissues, including those not causally related to an obvious inflammatory process. Manifestations of cancer-associated inflammation include the infiltration of white blood cells, the presence of polypeptide messengers of inflammation (ie, cytokines and chemokines), and the occurrence of tissue remodeling and angiogenesis.

Supported by the Italian Association for Cancer Research, Cariplo Foundation, European Commission, and the Italian Ministry of University and Health.

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J Support Oncol 2007;5:164-165 © 2007 Elsevier Inc. All rights reserved.

Inflammation and Cancer Are Inextricably Related

Strong evidence already suggests that cancer-associated inflammation promotes tumor growth and progression in what can be viewed as the extrinsic, non-cancer-cell autonomous pathway.⁴ Already in the late '70s, researchers found that a major inflammatory leukocyte population present in tumors, so-called tumor-associated macrophages, promote tumor growth.^{1,2} More recently, genetically modified mice, including some with cell-specific targeted gene inactivation, allowed dissection of the molecular pathways of inflammation leading to tumor promotion, as well as initial analysis of the role of distinct elements of the inflammatory process in different steps of tumor progression. Tumor necrosis factor, interleukin-1, the macrophage growth and attractant cytokine colony-stimulating factor 1, the prostaglandin-producing enzyme cyclooxygenase 2, the master inflammatory transcription factor NF- κ B (nuclear factor kappa B), and various enzymes involved in tissue remodeling are all essential elements for carcinogenesis and/or acquisition of a metastatic phenotype in diverse organs (eg, skin, liver, breasts, intestines).^{3,5} Moreover, over the past 5 years, a number of links between genetic events causing cancer and inflammation have emerged that, when taken together, comprise the intrinsic pathway.⁴

Targeting cancer-promoting inflammation in a therapeutic or preventive setting is in its infancy.⁶ In the article by MacDonald, the author calls for a unified approach in oncology and supportive therapy that includes anti-inflammatory strategies. For instance, he suggests that clinical trials targeting anorexia-cachexia (eg, testing anabolic steroids) should include anti-inflammatory therapy. This integrated approach should result in a comprehensive care model from time of diagnosis and represent an optimal context for future trials.

Although one cannot but concur with the general plea made in this article, a major stumbling block is represented by the heterogeneity of inflammatory reactions and cancer-promoting inflammation. Identification of molecular pathways and tailoring of anti-inflammatory strategy are likely to be essential to integrate blocking inflammation in a comprehensive cancer care program.

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