

The effect of environmental chemicals on the tumor microenvironment

ABSTRACT

Potentially carcinogenic compounds may cause cancer through direct DNA damage or through indirect cellular or physiological effects. To study possible carcinogens, the fields of endocrinology, genetics, epigenetics, medicine, environmental health, toxicology, pharmacology and oncology must be considered. Disruptive chemicals may also contribute to multiple stages of tumor development through effects on the tumor microenvironment. In turn, the tumor microenvironment consists of a complex interaction among blood vessels that feed the tumor, the extracellular matrix that provides structural and biochemical support, signaling molecules that send messages and soluble factors such as cytokines. The tumor microenvironment also consists of many host cellular effectors including multipotent stromal cells/mesenchymal stem cells, fibroblasts, endothelial cell precursors, antigen-presenting cells, lymphocytes and innate immune cells. Carcinogens can influence the tumor microenvironment through effects on epithelial cells, the most common origin of cancer, as well as on stromal cells, extracellular matrix components and immune cells. Here, we review how environmental exposures can perturb the tumor microenvironment. We suggest a role for disrupting chemicals such as nickel chloride, Bisphenol A, butyltins, methylmercury and paraquat as well as more traditional carcinogens, such as radiation, and pharmaceuticals, such as diabetes medications, in the disruption of the tumor microenvironment. Further studies interrogating the role of chemicals and their mixtures in dose-dependent effects on the tumor microenvironment could have important general mechanistic implications for the etiology and prevention of tumorigenesis.

Keyword: Environmental chemicals; Tumor microenvironment; Carcinogens