The Retinoids and Cancer Prevention Mechanisms

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ABSTRACT

Carcinogenesis is a multistep process that converts normal cells into malignant cells. Once transformed, malignant cells acquire the ability to invade and metastasize, leading to clinically evident disease. During this continuum from normal to metastatic cells, carcinogenic steps can be arrested or reversed through pharmacological treatments, known as cancer chemoprevention. Chemoprevention strategies represent therapeutic interventions at early stages of carcinogenesis, before the onset of invasive cancer. Effective chemoprevention should reduce or avoid the clinical consequences of overt malignancies by treating early neoplastic lesions before development of clinically apparent signs or symptoms. Preclinical, clinical, and epidemiological data provide considerable support for cancer chemoprevention as an attractive therapeutic strategy. This clinical approach was validated in the recent tamoxifen randomized trial, demonstrating that a selective estrogen receptor modulator reduces the risk of breast cancer in women at high risk for this malignancy.

Derivatives of vitamin A, the retinoids, have reported activity in treating specific premalignant lesions and reducing incidence of second primary tumors in patients with prior head and neck, lung or liver cancers. Whether the retinoids will prevent primary cancers at these sites is not yet known. Notably, a carotenoid (β-carotene) was shown as inactive in primary prevention of lung cancers in high-risk individuals. This underscores the need for relevant in vitro models to identify pathways signaling chemopreventive effects. These models should assess the activity of candidate chemoprevention agents before the conduct of large and costly prevention trials. An improved understanding of cancer prevention mechanisms should aid in the discovery of new therapeutic targets and chemoprevention agents. Ideally, these agents should have tolerable clinical toxicities suitable for chronic administration to individuals at high risk for developing primary or second cancers. This article reviews what is now known from clinical and preclinical studies about the retinoids as cancer prevention agents.

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Mechanisms of retinoid resistance in APL RA therapy in APL has been associated with preclinical and clinical evidence of multifactorial mechanisms of resistance. Notably, decreased availability of RA in APL Conventional APL therapy combines RA with anthracyclines. Conflicting evidence exists for the involvement of Pgp in mediating retinoid resistance in APL. restoring the regulation of target genes. The Retinoids and Cancer Prevention Mechanisms. Ruthardt M. (2002). 1: Promising Cancer Chemopreventive Agents. The mechanism of action of retinoids is through modulation of cell proliferation and differentiation. Retinoids vary in their capacity to induce differentiation and to inhibit proliferation in a series of human transformed hematopoietic and epithelial cell lines. Some cytokines potentiate the retinoid-induced cell differentiation and act synergistically with retinoids to inhibit cell proliferation. The pattern of synergism is dependent upon the combination and tumor cell line tested. The rationale for the use of retinoids in cancer prevention derives from their ability to control normal differentiation in many epithelial tissues. View. Show abstract. Whether the retinoids will prevent primary cancers at these sites is not yet known. Notably, a carotenoid (beta-carotene) was shown as inactive in primary prevention of lung cancers in high-risk individuals. This underscores the need for relevant in vitro models to identify pathways signaling chemopreventive effects. An improved understanding of cancer prevention mechanisms should aid in the discovery of new therapeutic targets and chemoprevention agents. Ideally, these agents should have tolerable clinical toxicities suitable for chronic administration to individuals at high risk for developing primary or second cancers. This article reviews what is now known from clinical and preclinical studies about the retinoids as cancer prevention agents. Authors