

Preface

Although cancer may be experienced by any age group, incidence increases with time, suggesting in many cases there is a prolonged period from the time of initiation to the time of invasive and metastatic cancer. Accordingly, numerous opportunities for intervention are apparent, either through primary prevention at early stages or through therapeutic interventions during later stages of carcinogenesis. In general, cancer chemoprevention is considered as the use of drugs, vitamins, or other agents to reduce the risk of (or delay the development or recurrence of) cancer. The concept of implementing cancer chemoprevention through the use of nontoxic agents, dietary and natural sources, has emerged as an appropriate strategy for controlling disease progression.

Research in the area of cancer chemoprevention has grown over the past few decades, and this has become a rather specialized field of study. Phytochemicals from natural products are recognized as promising agents that play a role in cancer prevention as well as in cancer therapy. Dietary constituents as well as natural products have been demonstrated to modulate common signaling pathways in cancer development. These naturally occurring compounds could become important agents for the prevention of various types of cancer.

In the field of natural products in cancer prevention and therapy, there is the need to review the progress that has been made during the last 50 years and to identify the challenges ahead.

This volume of *Topics in Current Chemistry* addresses the hurdles and challenges in the practice of human cancer prevention in the general population. The process of slowing the progression of cancer is applicable to many cancers with long latency. Although cancer chemoprevention has proven to be a successful strategy in animals, its application to humans has met with limited success.

In this volume, Hasan Mukhtar and his colleague discuss various challenges associated with chemoprevention of cancer with focus on studies with green tea. Allan Conney and his colleague discuss the inhibition of ultraviolet B radiation (UVB)-induced nonmelanoma skin cancer by discovery of a path from tea to caffeine to exercise to decreased tissue fat. From the inhibitory effects of tea and caffeine in UVB-induced skin carcinogenesis, his group further demonstrated the role of increased locomotor activity and decreased tissue fat in skin cancer.

Gary Stoner summarizes the beneficial effects of berries in the prevention of esophageal squamous cell carcinoma in rodents as well as recent data from a human clinical trial in China. He concludes that the use of berry preparations might be a

practical approach for the prevention of esophageal squamous cell carcinoma in China and, potentially, other high-risk regions for this disease. Young-Joon Surh demonstrates that cancer chemopreventive and therapeutic potential of guggulsterone, a phytosterol derived from the gum resin of guggul plants. With anti-inflammatory, antioxidative properties, and cancer chemopreventive and therapeutic potential, the underlying molecular mechanisms and chemopreventive/therapeutic targets of guggulsterone were discussed.

In the context of cancer prevention approaches, the importance of chemoprotection against cancer by isothiocyanates is discussed by several investigators. Albenia Dinkova-Kostova notes that the isothiocyanates are among the most extensively studied chemoprotective agents, and the Cruciferae family represents a rich source of glucosinolates. There have been numerous examples of the chemoprotective effects of isothiocyanates in a number of animal models of experimental carcinogenesis at various organ sites and against carcinogens of several different types. She indicates that the efficient protection in tumorigenesis and metastasis might be due to multiple mechanisms, involving the Keap1/Nrf2/ARE and NF- κ B pathways. The Keap1-Nrf2 signaling pathway is further discussed as a key target for cancer prevention by Thomas Kensler. He reports the ongoing clinical evaluation of broccoli or broccoli sprouts rich in either sulforaphane or its precursor form in plants for cancer prevention in Qidong, China. He indicates that interventions with well-characterized preparations of broccoli sprouts may enhance the detoxication of aflatoxins and air-borne toxins, which may in turn attenuate cancer in targeted populations.

Tony Kong also discusses dietary phytochemicals and cancer chemoprevention focusing on the oxidative stress, Nrf2 and epigenomics. His recent studies show that dietary phytochemicals possess cancer chemopreventive potential through the induction of Nrf2-mediated antioxidant/detoxification enzymes and anti-inflammatory signaling pathways to protect organisms against cellular damage caused by oxidative stress. He concludes that the advancement and development of dietary phytochemicals in cancer chemoprevention research requires the better understanding of the Nrf2-mediated antioxidant, detoxification, and anti-inflammatory systems and corresponding in vitro and in vivo epigenetic mechanisms. Clarissa Gerhäuser summarizes important epigenetic approaches in her extensive review of in vitro and in vivo data on natural products and cancer prevention. A role of epigenetic regulation in cancer chemoprevention and new challenges in future nutri-epigenetic research are also discussed.

CS Yang and his colleagues argue the importance of understanding of differential effects of specific forms of tocopherols in cancer prevention. Many epidemiological studies have suggested that a low vitamin E nutritional status is associated with increased cancer risk. However, several recent large-scale human trials have produced negative results in cancer prevention and therapy with α -tocopherol. He notes that a better understanding of the biological activities of different forms of tocopherols is needed. For safe and inexpensive cancer prevention with tocopherols, use of a naturally occurring tocopherol mixture is suggested for broad anticancer activity of various types of cancer.

Scott Lippman discusses the evolution of chemoprevention research in exciting new directions. Since large chemoprevention trials in unselected patients have often been negative, this trend promises to be reversed by more-focused and novel trial designs emphasizing the identification of molecular targets and predictive biomarkers. He points out the importance of clinical study designs, relevant biomarkers, and surrogate endpoints in new prevention trials. His review in this issue highlights several promising natural agents and how early clinical development may elucidate their role in personalized cancer chemoprevention. Kathryn Gold emphasizes the need for personalizing cancer prevention through a reverse migration strategy. She proposes a new approach to drug development, drawing on the experience in the treatment of advanced cancer to bring agents, biomarkers, and study designs into the prevention setting. She concludes that personalized therapy may develop more effective, tolerable chemoprevention by identifying molecular drivers of cancer and using matched targeted agents.

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