

## Cancer Chemoprevention: Premise and Promise

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Cancer chemoprevention refers to inhibition, reversal or even delay of the process of carcinogenesis by use of defined nontoxic chemical substances or their mixtures. The laboratory of chemoprevention was established in US NCI in the 1970s. In 1982, the Chemoprevention Program was launched at the Division of Cancer Prevention and Control in NCI to identify a series of potential chemopreventive agents and to evaluate their efficacy. The rationale for chemoprevention intervention trials relies on results of epidemiologic and laboratory studies. Chemoprevention is now recognized as one of the most innovative and promising areas of cancer research that attempts to reduce the risk of cancer through pharmaceutical or nutritional intervention. A wide variety of substances, both synthetic and naturally occurring, have been reported to possess the ability to halt or suppress the carcinogenic processes. Recently, considerable attention has been focussed on the implications of cyclooxygenase-2 (COX-2) in human malignancies. Numerous population-based, clinical and animal studies have revealed that non-steroidal anti-inflammatory drugs (NSAIDs) with COX-2 inhibitory activity have promise as candidate chemopreventives. In this context, it is interesting to note that celecoxib, the first US FDA-approved COX-2 specific drug, has been found to reduce the polyp burden in the patients with familial adenomatous polyposis.

Besides the synthetic pharmaceuticals, a vast variety of non-nutritive components of vegetables and fruits, collectively named as phytochemicals, possess substantial cancer chemopreventive properties. Despite remarkable progress in our understanding of the carcinogenic process, the mechanisms of action of most cancer chemopreventive phytochemicals have been poorly understood. Recent studies from this laboratory have demonstrated that some ingredients of frequently used spices, such as turmeric, ginger, chili pepper, and garlic prevent conversion of normal cells to preneoplastic ones and finally malignant tumors by distinct mechanisms. Other edible phytochemicals that our research program has identified to possess substantial cancer preventive effects include EGCG in green tea, resveratrol in red wine, genistein soy, and ginseng-derived saponins. All these phytochemicals have strong anti-inflammatory as well as antioxidant effects which contribute to their remarkable cancer fighting activities.

Cancer arises when the fine-tuning of the sophisticated cellular growth signaling network is dysregulated or disrupted. One of the salient features of our research is unraveling of the common molecules and events involved in the cellular signaling network as prime molecular targets for aforementioned dietary chemopreventive phytochemicals.