Is nanochemoprevention the future of chemoprevention?

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In this presentation I will introduce the concept of cancer chemoprevention as originally coined and defined by M. Sporn et al. in 1976. Proof of concept, that chemoprevention is a valid approach for preventing and controlling cancer incidence and progression, was obtained in 1998 with the landmark study of tamoxifen, a synthetic Selective Estrogen Receptor Modulator (SIRM) that was evaluated in high risk women for breast cancer. In the following years, additional SIRMs and other drug-based or vaccine-based chemopreventive approaches have been attempted and several were stemmed with success in phase III clinical trials and consequently obtained FDA approval for the prevention of various types of cancer. Surprisingly, diet-based chemopreventive agents, despite promising results in preclinical settings and epidemiolaogical studies, failed to show efficacy in phase III clinical trials. Alternative experimental approaches have been introduced, and are currently being used in preclinical studies, with both drug-derived and diet-derived chemopareventive components. These include: (1) Identifying cancer preventive agents that have specific molecular or cellular targets, (2) extensive preclinical mechanistic evaluation of agents before clinical trials are instituted, (3) defining biomarkers that can be used as early predictors of efficacy, and (4) since genetic heterogeneity exists between individuals and tumor types, prescribing personalized drug- or diet- derived chemopreventive agents. Emphasis will be given to the concept of nanochemoprevention as introduced by Siddiqui et al. in the landmark study with the green tea bioactive component EGCT. Finally, I will introduce d-α-Tocopheryl polyethylene glycol 1000 succinate (TPGS), a water-soluble form of vitamin E, which I consider as the most promising amphipathic nano-carrier and a powerful tool in the formulation of lipophilic and poorly soluble compounds. The lack of TPGS toxicity in physiological cells, the targeted induction of apoptosis only in certain cancer cell types and its reported ability to overcome multi drug resistance, make TPGS ideal for nanoformulations. Besides improving the compound's bioavailability, TPGS could produce additive or synergistic chemopreventive effects with the encapsulated component.