



## The Saga of the Potential Use of Selenium in Chemoprevention Continues

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### Editorial

Selenium, an essential nutrient whose deficiency is linked to several human diseases, was for a time considered a premier candidate as a non-toxic supplement that could reduce the risk of several different types of cancer. Enthusiasm over the potential of developing selenium as a chemopreventive supplement came from a number of independent lines of evidence. A large number of animal studies published over an extended period of time indicated that low levels of selenium were able to prevent the appearance of tumors induced by a wide variety of carcinogens. Plausible mechanisms of action were proposed based on cell culture studies showing that selenium supplementation of culture media, resulting in the inhibition of tumor cell growth, impacted several of the molecular pathways implicated in transformation and carcinogenesis. Moreover, selenium is an essential component of members of the selenoprotein family of peptides, several of which are anti-oxidants and the role of anti-oxidants in preventing cancer has also been considered a likely mechanism of chemoprevention. Human epidemiological studies have yielded a mixed bag of results, but the data on the inverse association between selenium status and cancer risk is strongest for cancers of the colon and prostate. Supported by this impressive collection of data, the largest prostate cancer prevention trial ever conducted, the Selenium and Vitamin E Cancer Prevention Trial (SELECT), was initiated by the National Cancer Institute. Involving approximately 35,000 men aged 55 or above for Caucasians and 50 and above for African Americans, individuals were randomly assigned to either a group provided 200 mg/day selenium, 400IU/day vitamin E, both or placebo. However, the study was terminated early due to lack of evidence of a benefit to those taking the supplements.

Recent papers published in the Journal of the National Cancer Institute (Volume 106, Issue 3) contribute to the ongoing confusion to the benefits and harm that can be attributed to selenium. Continuing the analysis of the SELECT data, Kristal and colleagues reported that

there was no benefit of selenium supplementation to those who began the trial with lowest baseline levels of selenium, but there was an increased risk of high grade prostate cancer among those with the highest baseline levels of selenium by almost a factor of 2. In the same issue, Geybels et al. reported the results of examining toenail selenium levels, generally taken as a long term measure of selenium status, among a large cohort of men from the Netherlands. Their data show a clear, statistically significant inverse association between selenium status and the risk of advanced prostate cancer. These results are consistent with previously conducted meta-analyses of available data that indicate a beneficial anti-cancer effect of selenium in prospective observational studies, but no benefit to selenium supplementation, as reported most recently by Vinceti et al. in the March 30th issue of the Cochrane Database Syst. Rev.

There is a general disappointment among those of us who saw great promise in the chemopreventive properties of selenium when the pre-clinical work, principally from animal data, didn't translate to human supplementation trials such as SELECT. It would have been satisfying if the results of those trials were different and we could simply recommend a pill to increase levels of selenium and so reduce cancer mortality. Instead we are faced with the complexity of biological systems and perhaps to recognize the fundamental differences that might ensue between a lifetime of selenium consumption and providing a supplement to men in their 50's, long after many of the multiple steps along the path to cancer have occurred. Conceivably, selenium may be beneficial in attenuating the accumulation of genetic errors that contribute to carcinogenesis, while the same processes affected by selenium, or completely different ones, manage to promote or protect initiated or progressing cancer cells. Only by the continued research into the consequences of selenium availability to both normal and tumor cells will this mystery be resolved and any benefits of dietary selenium intake capitalized upon.