

# Research Brief 173: Are There Links Between Selenium Intake and Bladder Cancer?

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## Background

Funded by SBRP for more than 13 years, Dr. Margaret Karagas has led a series of large scale epidemiologic studies in New England to characterize the risk of cancer associated with exposures to environmentally relevant levels of arsenic. Her interdisciplinary research group, which includes epidemiologists, molecular biologists, biostatisticians, pathologists, clinical investigators, chemists, and geologists, has:

- Developed and tested ultra-trace analytic methods to measure and speciate multiple metals in environmental and biological samples.
- Determined that measurement of arsenic in toenail samples can serve as a biomarker of low dose arsenic exposures.
- Established a database of over 6,000 New Hampshire residents (controls, bladder cancer cases, and squamous and basal cell skin carcinoma cases) with extensive individual data, drinking water samples, biological samples, and tumor tissue samples.
- Conducted GIS analyses of drinking water arsenic concentrations, identifying four distinct “clusters” of high household water arsenic levels, one near the Coakley Landfill Superfund site. Follow-on studies led to a geologically-based model of arsenic distribution in groundwater.

Using these tools, Dr. Karagas’ research group was the first to provide information regarding individual biomarker exposure to arsenic and risk of cancers in a geographically defined US population. Their work established an association between arsenic in drinking water and an increased risk of bladder cancer.

## Advances

Recent studies suggest that selenium intake may help prevent several types of cancer, including bladder cancer. To investigate the selenium-bladder cancer link and the mechanism by which selenium might act, Dr. Karagas’ group investigated the association of toenail selenium concentration with bladder cancer incidence in a large population-based case-control study from New Hampshire. In a publication led by postdoctoral fellow, Dr. Kristin Wallace, they compared data from 857 bladder cancer cases and 1,191 general population controls, evaluating age, gender, smoking status (never, moderate, and heavy), pack-years of smoking, and histopathology including tumor stage and grade.

There may be several molecular pathways by which bladder cancer evolves. One hypothesis involves alterations in the p53 gene. In response to DNA damage, p53 normally mediates cell cycle arrest or apoptosis. To investigate this, Dr. Karagas’ study, in collaboration with urothologist Dr. Alan Schned and investigators Drs. Karl Kelsey and Angeline Andrew, included classification of tumors according to the presence or absence of p53 alterations.

SBRP-funded research has identified other links between dietary intake and disease:

- Dr. Mary Gamble, Columbia University SBRP, found that folic acid supplementation may reduce body stores of arsenic and contribute to the prevention of arsenic-induced illnesses
- Dr. Bernhard Hennig, University of Kentucky SBRP, determined that antioxidant nutrients can protect against endothelial cell damage mediated by PCBs, and that some dietary fats can increase endothelial dysfunction induced by PCBs
- Dr. Howard Hu, Harvard School of Public Health SBRP, found that calcium supplements can significantly reduce fetal lead exposure and toxicity by suppressing bone resorption in the pregnant mother
- Dr. Habibul Ahsan, Columbia University SBRP, is investigating selenium and vitamin E as chemopreventive agents against arsenic-induced diseases in Bangladesh

Overall, the researchers found that higher toenail selenium levels were *not* significantly associated with a lower risk of bladder cancer. However, they did find inverse associations (higher toenail selenium levels associated with lower risk of bladder cancer) in three subgroups:

- Cases with p53 altered cancers
- Moderate smokers
- Women, although the association was not statistically significant

### Significance:

Several epidemiologic studies have observed inverse associations between selenium and the risk of bladder cancer. However, these were relatively small, often with less than 100 cases. With a much larger sample size, and unique histopathology data, this study raises the possibility that selenium may be preventive in certain molecular phenotypes of tumors (e.g., p53 altered) or within certain subsets of a population (e.g., women or moderate smokers).

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### To learn more about this research, please refer to the following sources:

Wallace, K., K.T. Kelsey, A. Schned, J.S. Morris, A.S. Andrew, and M.R. Karagas. 2009. Selenium and risk of bladder cancer: a population-based case-control study. *Cancer Prevention Research* 2(1):70-73.  
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