

Modulation of Lung Cancer Risk by Selenium in Occupational Asbestos Exposed Male Cohort: A Mechanism-based Metabolomic Approach

Lung cancer causes more deaths from cancer worldwide than at any other site. Of the 150 million affected individuals, a large proportion remains undiagnosed during early stages because of a lack of a panel of biomarkers that detects early stages of disease. Emerging data on the potential anticarcinogenic mechanisms of selenium lend biological plausibility to its chemopreventive potential in humans. Teams of collaborators at Colorado State University and National Jewish Health conducted a randomized, double blind, placebo controlled, translational biomarker study to determine if selenium supplementation influenced markers of selenium bioactivity and biomarkers for lung tissue damage. A cohort asbestos exposed males were selected to participate (N=123) and were randomly assigned to receive either a placebo tablet or a tablet containing 200 µg high-selenium brewer's yeast for a duration of 6 months. The putative mechanisms for selenium's mode of action include protection against oxidative damage, alterations in carcinogen metabolism, stimulation of apoptosis, and inhibition of angiogenesis. The major objective of this proposal is to determine whether selenium supplementation mediates shifts in arachidonic acid and reactive oxygen species (ROS) lavage fluid (BAL), sputum and blood samples will be analyzed for small molecules implicated in inflammation and oxidative stress by mass spectrometry. These data will be integrated with gene expression profiles in lung and peripheral lymphocytes for a systems biology approach to understanding selenium's protective activity and for identification of a profile indicative of responders to selenium supplementation.