

**Self, William**

Department of Molecular Biology and Microbiology  
University of Central Florida

2005 Program  
New Investigator (3-year project)

**Project Title:** Inhibition of Selenoprotein Synthesis by Arsenic Leading to Lung Cancer

**Project Summary:** Selenium is a required micronutrient in mammals. Selenium is required for the activity of several enzymes that act to prevent oxidative damage in cells. An increase in oxidative stress, caused by a decrease in the ability to produce selenoproteins, can result in damage to DNA, lipids and protein. DNA damage results in mutations that can ultimately lead to increased incidence of cancer. Thus, one's ability to produce active selenoproteins is tied directly to the occurrence of cancer in the organism as a whole. For this reason selenium has been touted as an antioxidant that can reduce one's risk for many types of cancer by preventing oxidative stress.

Arsenic is known to cause lung cancer, however the molecular mechanisms behind arsenic-induced carcinogenesis are poorly understood. Many recent studies have determined that treating human cells with certain chemical forms of arsenic lead to an increase in oxidative stress and reactive oxygen species (ROS). The mechanism behind this increase is not understood. However the consensus of many scientists studying the cancer-causing effects of arsenicals is that these compounds cause an increase of ROS leading to mutations and subsequently increased rates of cancer.

Our laboratory has preliminary data demonstrating that certain arsenic compounds interfere with the cell's ability to synthesize selenoproteins. We also have shown that one form of arsenic can inhibit the first step in selenoprotein synthesis in vitro. Based on this data, we believe that the reason that certain arsenicals cause cancer is due to a decrease in synthesis of active selenoproteins. We are testing whether this is the mechanism by which arsenic compounds cause cancer.

A recent study in the Journal of the American Medical Association (December 2004) showed that the risk for lung cancer increased dramatically in smokers who had a higher intake of arsenic. This study also demonstrated that arsenic intake alone could lead to higher rates of lung cancer in non-smokers. Arsenic is found in ubiquitously in the environment and most often as a contaminant in the water supply. Based on this strong association between increased rates of lung cancer and smoking, we aim to test whether arsenical compounds can block selenoprotein synthesis in human lung cells. We also aim to find nutritional sources of selenium that can bypass the effect(s) of arsenic on selenium metabolism. Thus we hope not only to demonstrate why arsenic contributes to development of cancer, but to identify a source of selenium that can be used as a nutritional supplement to reduce lung cancer rates, especially in smokers. Since many active smokers have trouble quitting, this may lead to a decrease rates or delayed onset of lung cancer in those who can not fight their addiction to cigarettes.