

## James & Esther King Biomedical Research Program

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*Department of Cancer Biology  
Mayo Clinic*

*2006 Program*

*Team Science Project  
(2-year project)*

**Project Title:** Oncogenic PKC iota in Smoking-Related Lung Cancer

**Project Summary:** Lung cancer is the number one cause of cancer death in the United States and the State of Florida. According to the American Cancer Society, more than 172,000 Americans and 13,000 Floridians are diagnosed with lung cancer every year. Over 163,000 Americans and 12,000 Floridians succumb to the disease annually. Florida has the unenviable distinction of having the second highest number of deaths from lung cancer. Despite our best current treatments, lung cancer survival is only 14%. Therefore, there is a pressing need to diagnose lung cancer sooner, when the disease is more successfully treated, and to develop better drugs to treat lung cancer.

It is estimated that over 90% of lung cancer is caused by smoking, the major risk factor for this disease. Chemicals in tobacco smoke cause specific mutations in the genetic material of lung cells. These mutations lead to permanent changes that result in lung cancer. Studies by our TSP research team have shown that the two most common mutations caused by smoking, which are responsible for more than 70% of lung cancer, have a common effect on lung cells. Specifically, we have discovered that both of these mutations activate a third gene called protein kinase C iota (PKCiota). PKCiota is activated in almost all lung cancers and is required for lung cancer growth. The central theme of this proposal therefore focuses on PKCiota in smoking-related lung cancer.

The overall goals of this TSP project are to determine how PKCiota causes lung cancer and to exploit this knowledge for the improved detection and treatment of this disease. Our specific objectives are to: 1) determine how PKCiota is controlled by smoking-induced gene mutations; 2) determine how PKCiota controls lung cancer growth and spread; 3) determine if PKCiota is useful in the early detection of lung cancer; and 4) evaluate a new drug recently discovered by our group that inhibits PKCiota and shows great promise for treatment of lung cancer patients. To accomplish our goals, we have assembled a highly interactive, multi-disciplinary team of four investigators: Dr. Alan P. Fields, the team leader, is a recognized authority on the role of PKCiota in cancer; Dr. E. Aubrey Thompson is a renowned expert on cancer gene function, Dr. Derek C. Radisky has made outstanding contributions to our understanding of cancer cell biology, and Dr. Michael B. Wallace is a clinical investigator who has pioneered the use of novel techniques for lung cancer detection. This exceptional team is uniquely qualified to successfully achieve the goals of this project.