

James & Esther King Biomedical Research Program

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*Research and Development
Bay Pines VA Medical Center*

*2007 Program
New Investigator (3-year project)*

Project Title: Role of cRaf-1/ERK Pathway on Cotinine Neurotoxicity

Project Summary: There is growing evidence that tobacco exerts toxic effects in the human brain, although the mechanisms are poorly understood. Cigarette smoke is a complex mixture of more than 4,700 chemical compounds including oxidants that stress the brain. Primary and secondary smoke is one of many potential early events promoting the development of neurodegenerative disorders for which everyone is at risk. In fact, the toxin cotinine, produced from nicotine in the body, decreases the survival of brain cells and impairs human cognitive abilities. All of our preliminary data investigating the causes of neurodegeneration for almost a decade, shows that the abnormal activity of proteins involved in memory are altered in the brain. These factors, which are activated by oxidants and other toxins, are a common theme and are also affected in stroke, epilepsy, and Alzheimer's disease. In this grant, we will use cellular and animal models to study the involvement of these factors in cotinine's effect on learning and memory and the use of potential therapies to balance the activity of these factors in the brains of people exposed to tobacco during pregnancy or adolescence.