

## James & Esther King Biomedical Research Program

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*2010 Program  
New Investigator Research  
(3-year project)*

**Project Title:** Understanding the Mechanisms of Smoking on Complex Diseases from NOS2A-Smoking Interaction

**Project Summary:** Cigarette smoking (CS) is a strong environmental factor for many complex diseases, including Parkinson's disease (PD) and age-related macular degeneration (AMD). Prevention and treatment of CS-related diseases requires knowledge of the underlying molecular mechanisms of CS, which remain elusive. The genetic revolutions of the past decade have provided substantial insights into the etiology of complex diseases. Statistical evidence for interaction between CS and genes has been reported in many cases. For example, genetic variants in the inducible nitric oxide synthase (NOS2A) gene have been associated with increased disease risk and significantly interacted with CS in PD and AMD. Understanding the mechanisms for these statistical interactions has great potential to make novel findings on CS's biological effects as the genetic approach tackles the question from an unconventional angle. As the first step to illustrate the CS-NOS2A interaction, this study will map all CS-interacting variants in NOS2A using cutting-edge genomic technologies and evaluate them in well-powered datasets using PD and AMD as primary disease models. NOS2A has been associated with other CS-related diseases, such as cancer and stroke. Therefore, knowledge gained from this study will be a valuable resource for studies focusing on other CS-related diseases.