

## James & Esther King Biomedical Research Program

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*Chemistry and Biochemistry  
Florida State University*

*2009 Program  
New Investigator (3-year project)*

**Project Title:** Mechanism of Kinetic Cooperativity in Monomeric Human Glucokinase

**Project Summary:** Diabetes is a vastly understated consequence of tobacco use. Indeed, smoking more than doubles the risk of developing type 2 diabetes. Unlike other diabetes risk factors, the diabetes-promoting effects of tobacco act independently of an individual's weight or fitness level. Nicotine appears to provide the key link between tobacco use and diabetes. Progressive and persistent exposure to nicotine results in a slow deterioration in the body's ability to process glucose. When normal glucose processing is abolished, diabetes can result. The objective of this grant is to understand how glucose is processed within the body and how nicotine acts to disrupt this process. In particular, our work focuses on the mechanism of action of a single human protein called glucokinase. Glucokinase is a key regulator of glucose homeostasis, yet much is unknown about how this protein responds to changing glucose levels. Importantly, glucokinase has emerged as an attractive therapeutic target for diabetes. In the last five years, several drugs have been developed that target glucokinase, and several have been shown to be effective at modulating blood glucose levels in animal models. The successful completion of this grant will provide critical new information about the role of glucokinase in tobacco-associated diabetes. This information has the potential to significantly impact future efforts to design glucokinase-targeted therapeutics for diabetes and hyperinsulinemia.