

**James & Esther King Biomedical Research Program**

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Bridge  
(1-year project)*

**Project Title:** A New Signaling Pathway in Myocardial Ischemic Injury

**Project Summary:** The leading cause of death in the United States is heart disease and there is a clear correlation between cigarette smoking and the development and progression of cardiovascular disease. The American Heart Association estimates that 52% of heart disease deaths are directly related to cigarette smoking. Numerous studies have shown cigarette smoking can increase the incidence of myocardial infarction (MI), coronary artery disease (CAD) and atherosclerosis. Even passive smoking, environmental or second hand, increases the incidence of cardiovascular disease. Our proposed studies are focused on a recently isolated protein, the Abro1/KIAA0157 that is predominantly expressed in the heart and very little is known about its normal function. However, we have shown that the level of this protein is significantly upregulated in the heart of patients with CAD, as well as in the hearts of mice following experimentally induced MI injury. Our preliminary data suggest that Abro1 is a scaffold protein that recruits other polypeptides to form a K63-linked deubiquitinating (DUB) complex called BRISC (BRCC36-containing isopeptidase complex). Neither the role of Abro1 protein, nor the BRISC complex's function, has been characterized in the normal heart or in heart disease. We expect our studies to unravel a new pathway involved in CAD, as well as MI injury, and provide new targets for preventive and therapeutic interventions in the management and treatment of heart disease.