

**PI Name:** LE, DAI-TRANG ELIZABETH.  
**Project Title:** The Role of Adenosine in Chronic Ischemic Cardiomyopathy  
**Project Start:** 30-SEP-2003  
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**ICD:** NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**Abstract:** *DESCRIPTION (provided by applicant): The candidate received superb training in myocardial contrast echocardiography (MCE) and coronary physiology research in Dr. Sanjiv Kaul's experimental laboratory and is committed to the development of an academic career in cardiovascular medicine. The K08 grant would allow her to achieve her immediate career goals, which are to continue to develop expertise in the field of MCE as new ultrasound equipment and microbubbles are developed, to gain an understanding of the pathogenesis of chronic ischemic cardiomyopathy, to learn histopathologic, immunohistochemical, ELISA, EIA, RIA, and SPA techniques, and to become familiar with cardiac MRI as a research tool. Her long-term career goals include development into an independent investigator in the experimental laboratory in the subject of chronic LV dysfunction and MCE, participation in translational research protocols with a focus on chronic ischemia and therapeutics for ischemic congestive heart failure (CHF), and practicing clinical cardiology with an emphasis on coronary artery disease and echocardiography. In sum, she is committed to developing a successful academic career in cardiovascular medicine. CHF is a major health problem in industrialized countries and its prevalence, morbidity, and mortality are rapidly rising. The pathophysiology of ischemic CHF is not well understood. The overall aim of this research proposal is to investigate the role of adenosine in chronic ischemic cardiomyopathy in a canine model of ameroid-induced left ventricular (LV) dysfunction. An A1 allosteric enhancer, a selective A2A agonist and antagonist, and a selective A3 agonist will be given to study their effects on angiogenesis, apoptosis, inflammation, vasodilation, and cardioprotection. At baseline, maximal LV dysfunction, and 1 month, 3 months, and 6 months after administration of the adenosine agonist or antagonist, we will perform MCE to examine myocardial perfusion and angiogenesis, contrast echo imaging of inflammation, MRI to examine myocardial mass, LV volume, and regional and global LV function, microspheres injection to assess myocardial blood flow, and interstitial fluid collection from the myocardium to examine the presence of cytokines and white blood cells. After the 6-month evaluation, histopathology and immunohistochemistry will be performed to correlate functional changes with histologic evidence of inflammatory changes, apoptosis, and angiogenesis. The research environment involves close mentoring by Drs. Kaul and Siragy, use of their lab space, and enthusiastic support from the division chief and consultants, including Dr. Joel Linden who is an authority on the role of adenosine in cardiovascular physiology and pharmacology.*