

MRTG-2/15/2009-Houseman (Benjamin)

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“Pharmacologic Dissection of the Phosphoinositide-3-Kinase Pathway in Cardiac Preconditioning and Postconditioning”

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Summary: Brief periods of mild cardiac injury that occur prior to or shortly after prolonged injury, referred to as cardiac pre-conditioning and post-conditioning, have been shown to reduce myocardial infarct size and improve recovery of cardiac function. The phosphoinositide-3-kinase (PI3K) pathway is upregulated during both pre-conditioning and post-conditioning, but we lack a detailed understanding of cardiac PI3K in these processes because the enzyme family comprises three different isoforms with overlapping cellular functions. This grant proposal utilizes a panel of selective inhibitors of PI3K to determine which isoforms of the enzyme regulate cardiac pre-conditioning and post-conditioning in both cell culture and animal models of cardiac ischemia. These experiments will provide valuable insight into the roles of cardiac PI3K isoforms and will guide the development of selective therapeutics for reducing cardiac morbidity and mortality in both operative and non-operative settings.