Public Abstract
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Title:ANTECEDENT HYDROGEN SULFIDE ELICITS AN ANTI-INFLAMMATORY PHENOTYPE IN POSTISCHEMIC MURINE SMALL INTESTINE

Ischemia followed by reperfusion (I/R) is now well-recognized as one form of acute inflammation in which leukocytes play a key role. Recognition of the importance of the inflammatory process to the pathogenesis of I/R injury has led to an intensive research effort directed at identifying strategies to prevent leukocyte infiltration into post-ischemic tissues. Preconditioning is a phenomenon through which antecedent exposure to a particular stimulus confers protection against a subsequent prolonged ischemic event. The development of a protected phenotype occurs in response to a diverse array of preconditioning stimuli; each of these preconditioning stimuli appears to promote the production of the gaseous monoxide, nitric oxide (NO), as an initial triggering event in the acquisition of tolerance to I/R. Recent work has shown that NO acts as an endogenous regulator of a second gaseous signaling molecule with vasorelaxant properties, hydrogen sulfide (H2S). While it had been assumed that H2S acts solely as a toxic, environmental pollutant with minimal physiological and pathophysiological significance, it is now apparent that H2S is also synthesized endogenously in mammalian tissue. These observations suggest that, like NO, H2S has the ability to fulfill a physiologic role in regulating cardiovascular function, distinct from its toxicologic effect. In light of these observations, we postulated that H2S inhibits inflammation after I/R injury, through four separate, yet not necessarily distinct, mechanisms. The aims of this dissertation addressed the hypothesis that H2S elicits a preconditioning stimulus and protects against ischemia/reperfusion (I/R) injury through an eNOS-/p38 MAPK-/K channel-/HO-1 dependent mechanism.