ANTECEDENT HYDROGEN SULFIDE ELICITS AN ANTI-INFLAMMATORY PHENOTYPE IN POSTISCHEMIC MURINE SMALL INTESTINE

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ABSTRACT

Ischemia followed by reperfusion (I/R) is now well-recognized as one form of acute inflammation in which leukocytes play a key role. 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 (H_2S). Similar to NO, H_2S has the ability to fulfill a physiologic role in regulating cardiovascular function, distinct from its toxicologic effect. This dissertation shows that H_2S inhibits inflammation after I/R injury, through four separate, yet not necessarily distinct, mechanisms. The aims of this dissertation addressed the hypothesis that H_2S elicits a preconditioning stimulus and protects against I/R injury through an eNOS-/p38 MAPK-/K channel-/HO-1 dependent mechanism.