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$_2$S). Similar to NO, H$_2$S has the ability to fulfill a
physiologic role in regulating cardiovascular function, distinct from its toxicologic
effect. This dissertation shows that H$_2$S inhibits inflammation after I/R injury,
through four separate, yet not necessarily distinct, mechanisms. The aims of this
dissertation addressed the hypothesis that H$_2$S elicits a preconditioning stimulus
and protects against I/R injury through an eNOS-/p38 MAPK-/K channel-/HO-1
dependent mechanism.