High-Mobility Group Box 1 Preconditioning Protects Against Liver Ischemia-Reperfusion Injury

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Technology description

High mobility group box 1 (HMGB1) is a nuclear factor released extracellularly as a late mediator of lethality in sepsis as well as following necrotic but not apoptotic death. Here we demonstrate that in contrast to the proinflammatory role of HMGB1, preconditioning with HMGB1 results in protection from inflammation and organ injury following hepatic ischemia and reperfusion (I/R). Pretreatment of mice with HMGB1 significantly decreased liver damage after I/R in association with markedly lower serum TNF and IL-6 compared to controls. The protection observed in mice pretreated with HMGB1 was associated with a higher expression of IL-1R-associated kinase-M (IRAK-M), a negative regulator of toll-like receptor (TLR)-4 signaling compared to controls. We thus explored the possibility that HMGB1 preconditioning was mediated through TLR4 activation. HMGB1 preconditioning failed to provide protection in TLR4 mutant (C3H/HeJ) mice, but successfully reduced damage in TLR4 wild-type (C3H/HeOuj) mice. Use of HMGB1 as a preconditioning agent may be a potential strategy in settings of ischemic injury to decrease organ damage.Use of HMGB1 as a preconditioning agent may be a potential strategy in settings of ischemic injury to decrease organ damage. Non Provisional and PCT Patent Applications Filed

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