Myeloid HO-1 prevents kidney remote organ damage following renal IRI

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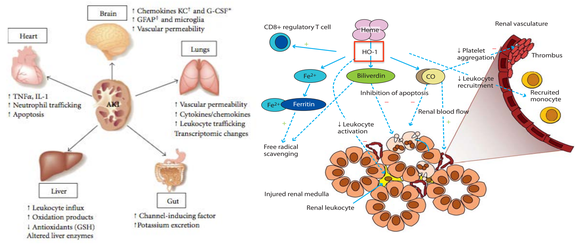
Background

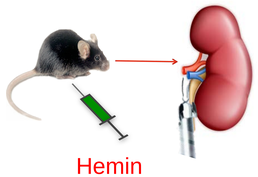


Following renal IRI, the subsequent release of pro-inflammatory cytokines (e.g., IL-1β, TNF-α, IL-6) may induce a systemic inflammatory response, resulting in pro-inflammatory cells recruitment and remote organ damage. The heme oxygenase-1 (HO-1), a stress-responsive enzyme, protects kidney from renal IRI through multiple mechanisms when pharmacology induced before ischemia. The aim of this study was to understand the role of the myeloid HO-1 in the control of kidney remote organ damage following renal IRI.

Images adapted from White LE et al. Int J Nephrol (2012) and Ferenbach DA. Nephron Exp Nephrol (2010).

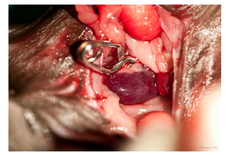
Materials & Methods

Mouse model of renal IRI



Hemin
5 mg/kg

26 min of bilateral clamping
4h/24h of reperfusion



Hemin protocol & readouts

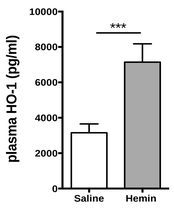
HO-1 induction: hemin 5 mg/kg 24h prior renal IRI

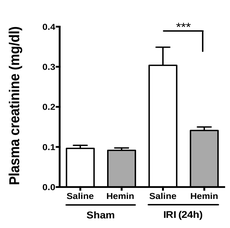
Assessment of systemic inflammation, renal IRI and, hepatic dysfunction: ELISA, plasma creatinine and, transaminases levels

Assessment of lung inflammation: ELISA and neutrophils immunostaining

Results

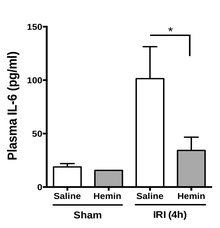
I. Preconditioning with hemin induces HO-1 and protects against renal IRI

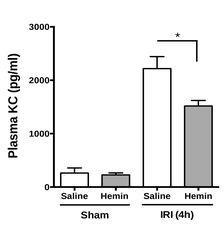




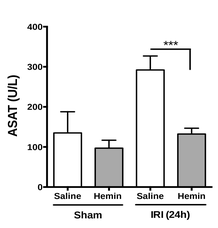
II. HO-1 mitigates systemic inflammation and subsequent remote organ damage

Systemic inflammation

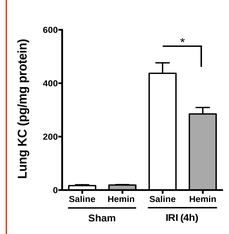


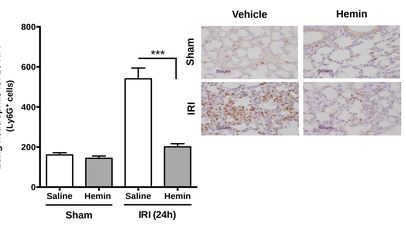


Liver



Lung





Conclusions

- **HO-1 spontaneously controls the magnitude of renal IRI and the subsequent systemic inflammation-induced remote organ damage**
- **This HO-1-mediated renoprotective pathway may be modulated by hemin administration**
- **Targeting HO-1 might represent a promising approach to prevent the impact of IRI on renal transplants and distant organs**