The Antimicrobial Peptide Cathelicidin protects against ischemia reperfusion-induced acute kidney injury

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Antimicrobial peptides (AMPs) expressed by epithelial and immune cells have been described for immunomodulatory effects. However, the effects and potential mechanism of resident AMPs on acute kidney injury (AKI) remain unknown. Here, we found that serum cathelicidin-related antimicrobial peptide (CRAMP) levels were reduced in patients with AKI as compared to healthy subjects. The E-cadherin-positive renal epithelial cells express CRAMP and CRAMP expression was inversely related with ischemia/reperfusion (I/R)-caused renal dysfunction in mice. Exogenous CRAMP significantly attenuated I/R-caused renal dysfunction in wildtype (WT) mice, accompanied by markedly reduced inflammatory responses and cellular apoptosis. Accordantly, worsened renal dysfunction was observed in CRAMP deficiency (Cnlp-/-) mice. CRAMP administration inhibited I/R-caused NLRP3 inflammasome and autophagy activation, which were exacerbated in Cnlp-/- mice. Furthermore, CRAMP administration decreased I/R-caused neutrophil infiltration and enhanced M2/M1 macrophage ratio. Mechanically, the immunomodulatory effect of CRAMP was dependent on the epidermal growth factor receptor (EGFR). Our results suggest that CRAMP acts as an immunomodulatory mediator of AKI and thus represents a promising therapeutic target.