

Abstract Submission No.: A-1330

TREM2 Macrophage Regulates the Process of AKI-CKD Transition by Suppressing Inflammation via a PI3K/Akt Signaling Pathway.

yating zhang, yiming zhou

Department of Sun Yat-sen University Medical Research Center, Sun Yat-sen Memorial Hospital, Guangzhou, China

Objectives : The purpose of this study is to investigate the role of TREM2 macrophages in AKI-CKD transition, and to uncover TREM2 as a potential new target for the development of novel cell therapies for the treatment of AKI-CKD transition.

Methods : For in vivo experiments, we first generated a unilateral ischemia-reperfusion (UIRI) AKI-CKD transition model using WT and Trem2^{-/-} mice. The serum and kidney tissues were collected after UIRI. The levels of serum creatinine, urea nitrogen and urinal proteins were measured in two groups. Kidney inflammation and fibrosis levels were determined by qPCR and WB. Macrophages in the kidney of were sorted out using magnetic bead, and the population of TREM2 macrophages was detected by flow cytometry. For in vitro experiments, we collected bone marrow-derived macrophages from mice and cultured under hypoxia condition to mimic the state of ischemia-reperfusion. Flow cytometry, qPCR, and WB were used to detect the level of macrophage activation and inflammation. RNA-seq analysis was used to explore the molecular mechanism of Trem2 regulation of macrophage activation.

Results : Here, we demonstrated that Trem2^{-/-} mice exhibited higher level of serum creatinine, BUN and urinal proteins compared with that of WT mice after UIRI. Renal morphological results showed an increased level of fibrosis in Trem2^{-/-} mice after UIRI. qPCR and WB results indicated that knock out Trem2 increased the levels of pro-inflammatory cytokines both in vitro and in vivo, which may increase the transition of AKI-CKD. Mechanistically we discovered that knock out Trem2 decreased the activation of PI3K-AKT pathway, which reduced macrophage phagocytosis and increased cytokine production. In addition, administration of macrophages with overexpressed Trem2 protected mice from UIRI-induced AKI-CKD transition.

Conclusions : Our study elucidated that Trem2 is a protective molecule in macrophages for AKI-CKD transition. In addition, we demonstrated a translational potential of Trem2 over-expressed macrophages as a cell therapy for kidney diseases.

Fig1.png

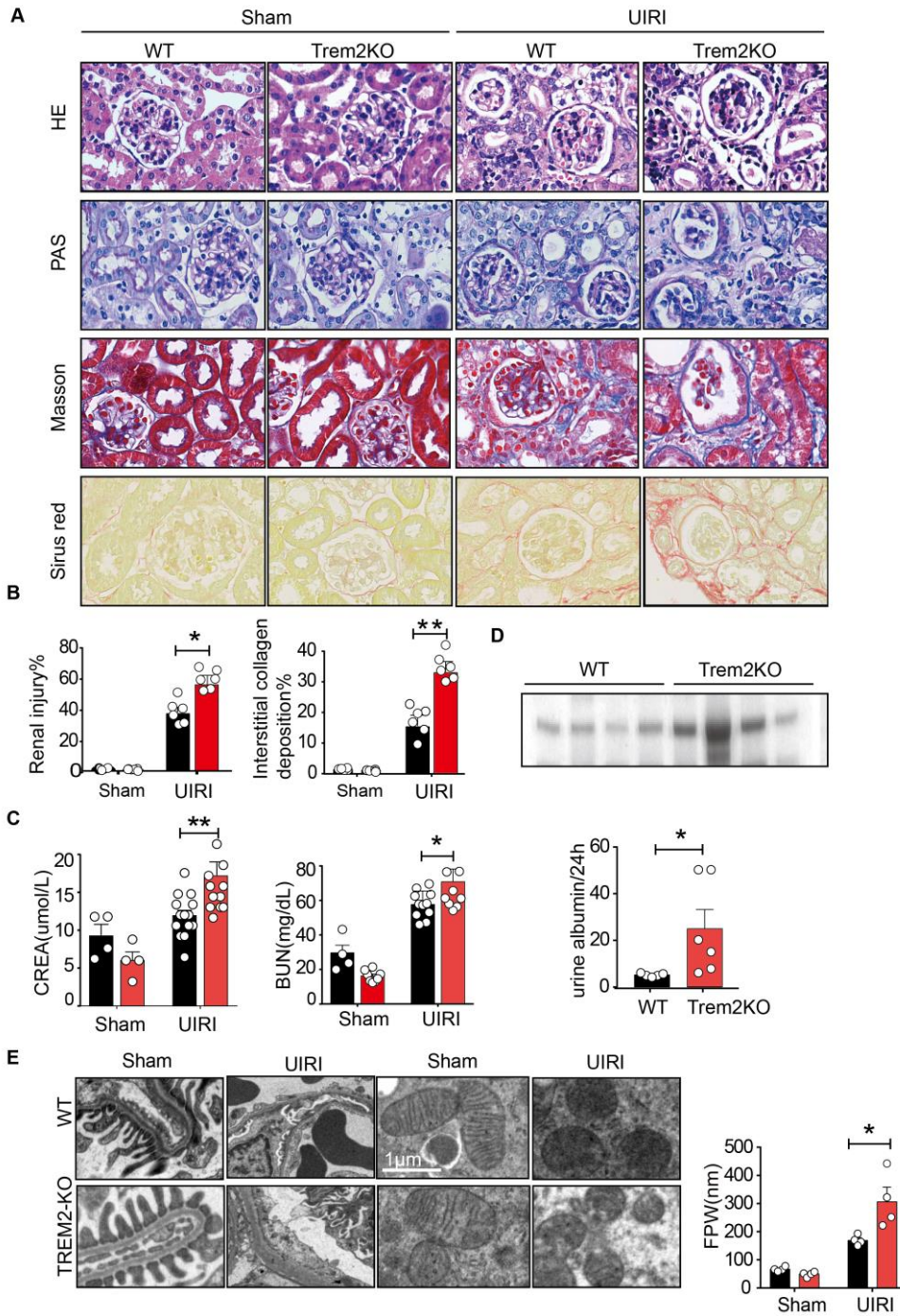


Fig1.png

