Disruption of CD40 Results in Significantly Attenuated Renal Inflammation Following Glycerol-Induced Acute Kidney Injury

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Introduction: We have shown that disruption of the prominent pro-inflammatory receptor CD40 attenuates renal tubular atrophy and tubular cell death following high salt diet in our CD40 knockout (KO) model in addition to significantly reduced renal fibrosis following experimentally induced ischemic renal injury. We have also demonstrated significantly reduced pro-inflammatory and pro-fibrotic signaling in human CD40 KO renal proximal tubule epithelial cells. We performed the following study to test the hypothesis that disruption of CD40 significantly attenuates acute kidney injury (AKI).

Methods: Age matched (8-week-old) C57/BL6 wild-type and C57/BL6 CD40 KO male mice (n=8) were administered glycerol (7.5 ml/kg in 50% glycerol) to induce AKI. After 24h, animals were euthanized and kidneys were assessed for evidence of renal injury.

Results: Renal expression of CD40 was increased in the proximal tubules of wild-type mice in response to AKI. CD40 KO mice demonstrated reduced renal inflammation compared with wild-type mice following AKI. In addition, CD40 KO mice demonstrated significantly attenuated renal cortex gene expression of inflammatory markers IL1β, TGFβ1, and the fibrosis marker Col3a1 following AKI compared to wild-type (all $p<0.05$).

Conclusion: Disruption of CD40 results in significant attenuation of renal inflammation following experimentally induced AKI. Our results indicate that disruption of CD40 signaling may be a promising therapeutic target for the treatment of AKI.

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