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Urine-Derived Stem Cells Alleviate Renal Fibrosis in a Mouse Model of Ischemia-Reperfusion Injury

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Objectives : After renal ischemia-reperfusion (IR) injury, the regeneration of renal tubular cells is essential for recovery. However, dysregulated repair mechanisms can result in renal fibrosis. The role of stem cells in kidney regeneration and fibrosis remains uncertain. In this study, we investigated the effects of urine-derived stem cells (UDSCs) on renal inflammation and fibrosis following IR injury.
Methods : Ten-week-old Balb/c nude male mice were divided into four groups: sham, sham with UDSC, IR, and IR with UDSC. UDSCs were administered via tail vein infusion on days 6, 7, and 8 following renal IR injury. Urine NGAL/creatinine (Cr) levels were measured, and kidney tissues were harvested on day 14 for analysis. In vitro studies included co-culturing TGF-treated HK2 cells with UDSCs, along with Klotho-siRNA silencing in UDSCs to assess their functional role.
Results : Fourteen days after IR injury, urinary NGAL/Cr levels were significantly higher in IR mice than in sham mice. However, UDSC treatment markedly reduced urinary NGAL/Cr in IR mice. H&E staining demonstrated a significant reduction in renal tubulo-interstitial injury in UDSC-treated IR mice compared to untreated IR mice. Masson's trichrome staining revealed a notable decrease in renal fibrosis in the UDSC-treated group. Furthermore, renal expression of MCP-1, osteopontin, TGF-beta, alpha-SMA, collagen IV, and F4/80-positive cells was significantly lower in UDSC-treated IR mice, while Klotho expression was elevated. In vitro, UDSCs exhibited higher Klotho protein expression than other mesenchymal stem cells and effectively suppressed fibrosis by inhibiting TGF-beta signaling in HK-2 cells. Notably, Klotho-siRNA silencing weakened the ability of UDSCs to inhibit TGF-beta-induced fibrosis.
Conclusions : UDSCs alleviate renal fibrosis following renal IR, with Klotho secretion playing a key role in their anti-fibrotic effects.