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Urine-Derived Stem Cell attenuated renal fibrosis in ischemia-reperfusion renal injury mice.

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Objectives : Following renal ischemia-reperfusion injury (IR), renal tubular cell regeneration is crucial for recovery. However, maladaptive renal repair processes can lead to renal fibrosis. The involvement of stem cells in kidney regeneration and fibrosis remains unclear. In this study, we assessed the impact of urine-derived stem cells (UDSC) on renal inflammation and fibrosis post renal IR.
Methods : Ten-week-old Balb/c nude male mice were categorized into sham, sham with UDSC, IR, and IR with UDSC groups. UDSC were administered via tail vein infusion three times on days 6, 7, and 8 post renal IR. Urine NGAL/creatinine (Cr) levels were measured, and kidney tissues were collected on day 14. In vitro experiments involved co-culturing TGF-treated HK2 cells with UDSC, and Klotho-siRNA silencing was performed in UDSC.
Results : After 14 days of IR, urinary NGAL/Cr significantly increased in IR mice compared to sham mice. UDSC treatment significantly reduced urinary NGAL/Cr in IR mice. H&E staining revealed a significant decrease in renal tubulo-interstitial injury in UDSC-treated IR mice compared to IR mice. Masson trichrome staining showed a significant reduction in renal fibrosis area in UDSC-treated IR mice. Renal expression of MCP-1, osteopontin, TGF-beta, alpha-SMA, collagen IV, and F4/80-positive cells significantly decreased in UDSC-treated IR mice. Additionally, Klotho expression increased in UDSC-treated IR mice. In vitro, UDSCs exhibited stronger Klotho protein expression than other mesenchymal stem cells and suppressed fibrosis by inhibiting TGF-beta in HK-2 cells. Klotho-siRNA silencing attenuated the TGF-beta-inhibiting ability of UDSCs.
Conclusions : UDSCs mitigate renal fibrosis post renal IR, with Klotho secretion playing a pivotal role in these anti-fibrotic effects.