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Mesenchymal stem cells ameliorate renal fibrosis by galectin-3/Akt/GSK3β/Snail signaling pathway in adenine-induced nephropathy rat

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Background: Tubulointerstitial fibrosis (TIF) is one of the main pathological features of various progressive renal damages and chronic kidney diseases. Mesenchymal stromal cells (MSCs) have been verified with significant improvement in the therapy of fibrosis diseases, but the mechanism is still unclear. We attempted to explore the new mechanism and therapeutic target of MSCs against renal fibrosis based on renal proteomics.

Methods: TIF model was induced by adenine gavage. Bone marrow-derived MSCs was injected by tail vein after modeling. Renal function and fibrosis related parameters were assessed by Masson, Sirius red, immunohistochemistry, and western blot. Renal proteomics was analyzed using iTRAQ-based mass spectrometry. Further possible mechanism was explored by transfected galectin-3 gene for knockdown (Gal-3 KD) and overexpression (Gal-3 OE) in HK-2 cells with lentiviral vector.

Results: MSCs treatment clearly decreased the expression of α-SMA, collagen type I, II, III, TGF-β1, Kim-1, p-Smad2/3, IL-6, IL-1β, and TNFα compared with model rats, while p38 MAPK increased. Proteomics showed that only 40 proteins exhibited significant differences (30 upregulated, 10 downregulated) compared MSCs group with the model group. Galectin-3 was downregulated significantly in renal tissues and TGF-β1-induced rat tubular epithelial cells and interstitial fibroblasts, consistent with the iTRAQ results. Gal-3 KD notably inhibited the expression of p-Akt, p-GSK3β and snail in TGF-β1-induced HK-2 cells fibrosis. On the contrary, Gal-3 OE obviously increased the expression of p-Akt, p-GSK3β and snail.

Conclusion: The mechanism of MSCs anti-renal fibrosis was probably mediated by galectin-3/Akt/GSK3β/Snail signaling pathway. Galectin-3 may be a valuable target for treating renal fibrosis.

Keywords: Adenine, Mesenchymal stem cells, Interstitial fibrosis, Galectin-3, Proteomics

Biography

Bo Chen, deputy director of Department of Human Anatomy and Embryology, comes from School of Basic Medical Sciences, Southwest Medical University, Luzhou city, Sichuan Province, China. He has his expertise in stem cells treatment for acute or chronic kidney diseases. He devotes to exploring the new mechanism of renal fibrosis in MSCs against renal fibrosis, and looking for the effective anti-fibrotic targets and drugs.