Conclusions: miRNA let-7e is involved in renal differentiation via the modulation of GSK3β phosphorylation and β-catenin production. The inhibitory effect of miRNA let-7e on PKCβ reduces GSK3β phosphorylation and β-catenin production during the differentiation process in mouse embryonic stem cells (mESCs).

HUMAN LIVER STEM CELLS CONTRIBUTE TO RENAL REGENERATION AFTER ACUTE INJURY

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Introduction and Aims: We recently identified and characterized a mesenchymal stromal cell like population resident in the human liver. This human liver stem cell (HLSC) population expresses specific mesenchymal stem cell markers (CD29, CD73, CD44, CD105 and CD166), specific hepatic cell markers (albumin, cytokeratin 8 and 18) and embryonic markers (Oct4, Nanog, Musashi). Moreover, HLSC are able to differentiate into osteocytes, condrocytes, hepatocytes and beta-like cells. When injected in an experimental model of fulminant liver failure, HLSCs protect from death and improve liver function and morphology by a paracrine mechanism. The aim of this study was to test whether the action of this unique cell population is limited to the liver or has a broad regenerative potential as a tool for cell therapy of acute kidney injury (AKI).

Methods: In vivo experimental AKI was induced by intramuscular injection of glycercol in SCID mice and different concentration of HLSCs (75,000, 350,000 and 1x10^6) or vehicle were intravenously injected at day 3 after injury. Mice were sacrificed 2 days after HLSC injection (day 5 after injury). Renal morphology and function were evaluated by histology and by blood urea nitrogen (BUN) and creatinine plasma levels. Tubular cell proliferation was evaluated by 5-bromo-2-deoxy-uridine (BrdU) incorporation and by staining with antibody against proliferating cell nuclear antigen (PCNA). Apoptosis was evaluated by Tnuel. The engraftment capacity of CFSE-labelled HLSCs in the kidney and the possible mechanism of protection were investigated.

Results: The lesions observed in mice with AKI injected with vehicle alone at day 5 after glycercol injection, included tubular hyper trophy, casts, vacuolization, and necrosis of proximal and distal tubular epithelium. In AKI mice injected with different doses of HLSCs the tubular lesions were less severe in comparison to those of mice treated with vehicle alone. The morphological recovery was associated with a significant reduction of plasma levels of creatinine and BUN. At 48 hours after HLSC administration, we observed a significant increase in tubular cell proliferation. The best results were obtained with the injection of 350,000 HLSCs.

Conclusions: The regenerative potential of HLSCs, a mesenchymal stromal cell population resident in human liver, is not limited to liver injury but they are able to accelerate in vivo the recovery of glycercol-induced AKI in SCID mice.

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