World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:9, No:09, 2015

Implementation of Cord- Blood Derived Stem Cells in the Regeneration of Two Experimental Models: Carbon Tetrachloride and S. Mansoni Induced Liver Fibrosis

Authors : Manal M. Kame, Zeinab A. Demerdash, Hanan G. El-Baz, Salwa M. Hassan, Faten M. Salah, Wafaa Mansour, Olfat Hammam

Abstract : Cord blood (CB) derived Unrestricted Somatic Stem Cells (USSCs) with their multipotentiality hold great promise in liver regeneration. This work aims at evaluation of the therapeutic potentiality of USSCs in two experimental models of chronic liver injury induced either by S. mansoni infection in balb/c mice or CCL4 injection in hamsters. Isolation, propagation, and characterization of USSCs from CB samples were performed. USSCs were induced to differentiate into osteoblasts, adipocytes and hepatocyte-like cells. Cells of the third passage were transplanted in two models of liver fibrosis: (1) Twenty hamsters were induced to liver fibrosis by repeated i. p. injection of 100 µl CCl4 /hamster for 8 weeks. This model was designed as; 10 hamsters with liver fibrosis and treated with i.h. injection of 3x106 USSCs (USSCs transplanted group), 10 hamsters with liver fibrosis (pathological control group), and 10 hamsters with healthy livers (normal control group). (2) Murine chronics S.mansoni model: twenty mice were induced to liver fibrosis with S. mansoni ceracariae (60 cercariae/ mouse) using the tail immersion method and left for 12 weeks. This model was designed as; 10 mice with liver fibrosis were transplanted with i. v. injection of 1×106 USCCs (USSCs transplanted group). Other 2 groups were designed as in hamsters model. Animals were sacrificed 12 weeks after USSCs transplantation, and their liver sections were examined for detection of human hepatocyte-like cells by immunohistochemistry staining. Moreover, liver sections were examined for fibrosis level, and fibrotic indices were calculated. Sera of sacrificed animals were tested for liver functions. CB USSCs, with fibroblast-like morphology, expressed high levels of CD44, CD90, CD73 and CD105 and were negative for CD34, CD45, and HLA-DR. USSCs showed high expression of transcripts for Oct4 and Sox2 and were in vitro differentiated into osteoblasts, adipocytes. In both animal models, in vitro induced hepatocyte-like cells were confirmed by cytoplasmic expression of glycogen, alpha-fetoprotein, and cytokeratin18. Livers of USSCs transplanted group showed engraftment with human hepatocyte-like cells as proved by cytoplasmic expression of human alpha-fetoprotein, cytokeratin18, and OV6. In addition, livers of this group showed less fibrosis than the pathological control group. Liver functions in the form of serum AST & ALT level and serum total bilirubin level were significantly lowered in USSCs transplanted group than pathological control group ($p < 0.001$). Moreover, the fibrotic index was significantly lower ($p< 0.001$) in USSCs transplanted group than pathological control group. In addition liver sections, of i. v. injection of 1×106 USCCs of mice, stained with either H&E or sirius red showed diminished granuloma size and a relative decrease in hepatic fibrosis. Our experimental liver fibrosis models transplanted with CB-USSCs showed liver engraftment with human hepatocyte-like cells as well as signs of liver regeneration in the form of improvement in liver function assays and fibrosis level. These data provide hope that human CB- derived USSCs are introduced as multipotent stem cells with great potentiality in regenerative medicine & strengthens the concept of cellular therapy for the treatment of liver fibrosis.

Keywords : cord blood, liver fibrosis, stem cells, transplantation
Conference Title : ICCSCE 2015 : International Conference on Cell and Stem Cell Engineering
Conference Location : Rome, Italy
Conference Dates : September 17-18, 2015