

Regulation of CCl₄-induced liver cirrhosis by hepatically differentiated human dental pulp stem cells

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Abstract

Liver transplantation is the most effective treatment for treating liver cirrhosis. However, a limited number of donors, graft rejection, and other complications can undermine transplant success. It is considered that cell transplantation is an alternative approach of liver transplantation. We previously developed a protocol for hepatic differentiation of cluster of differentiation 117+ stem cells isolated from human exfoliated deciduous tooth pulp (SHEDs) under hydrogen sulfide exposure. These cells showed excellent hepatic function. Here, we investigated whether hepatocyte-like cell transplantation is effective for treating carbon tetrachloride (CCl₄)-induced liver cirrhosis. SHEDs were hepatically differentiated, which was confirmed via immunological analyses and albumin concentration determination in the medium. Rats were intraperitoneally injected with CCl₄ for and the differentiated cells were injected into rat spleen. Histopathological and immunohistochemical analyses were performed. Liver functions were serologically and pathologically determined. Quantitative real-time-polymerase chain reaction was implemented to clarify the treatment procedure of liver cirrhosis. *In vitro*-differentiated hepatocyte-like cells were positive for all examined hepatic markers. SHED-derived hepatocyte transplantation eliminated liver fibrosis and restored liver structure in rats. Liver immunohistochemical analyses showed the presence of human-specific hepatic markers, *i.e.*, a large amount of human hepatic cells were very active in the liver and spleen. Serological tests revealed significant liver function recovery in the transplantation group. Expression of genes promoting fibrosis increased after cirrhosis induction but was suppressed after transplantation. Our

results suggest that xenotransplantation of hepatocyte-like cells of human origin can treat cirrhosis.

Moreover, cell-based therapy of chronic liver conditions may be an effective option.