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ACCEPTED MANUSCRIPT

Assessment of the hepatocytic differentiation ability of human skin-derived ABCB5⁺ stem cells

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Abstract

The continuously decreasing willingness for liver donation aggravates treatment of end-stage liver diseases requiring organ transplantation as the only curative strategy. Cell therapy approaches using human hepatocytes or stem cell-derived hepatocyte-like cells may be a therapeutic option out of this dilemma. ABCB5-positive mesenchymal stromal cells from human skin featured promising potential to treat immune-mediated diseases. Since most of chronic liver diseases involve exaggerating immune mechanisms, it was the aim to demonstrate in this study, whether ABCB5⁺ stem cells may serve as a resource to generate hepatocytic cells for application in liver cell transplantation. Using an established single-step protocol, which had been successfully applied to differentiate mesenchymal stromal cells into the hepatocytic lineage, ABCB5⁺ skin-derived stem cells did not gain significant characteristics of hepatocytes. Yet, upon culture in hepatocytic differentiation medium, ABCB5⁺ stem cells secreted immunomodulatory and anti-fibrotic factors as well as proteins, which may prompt hepatic morphogenesis besides others. Hepatic transplantation of ABCB5⁺ stem cells, which had been prior cultured in hepatocytic differentiation medium, did not cause any obvious deterioration of liver architecture suggesting their safe application.

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