Effective inducing systems of hepatic differentiation from bone marrow mesenchymal stem cells

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Mesenchymal stem cells (MSCs) are multipotent non-hematopoietic cells capable of differentiating into hepatocytes. Valproic acid (VPA), a histone deacetylase inhibitor, has recently exhibited profound therapeutic activity in preclinical tumor test. A research group in China investigated the induction of hepatic differentiation of mouse bone marrow MSCs (mBM-MSCs) by VPA. Direct evidences have been shown that the usefulness of VPA in the trans-differentiation of mBM-MSCs into hepatocytes both in vitro and in vivo.

Recent studies suggest that MSCs possess a greater differentiation potential than once thought and several hepatic differentiation protocols from bone marrow cells have been established. However, the incidence of bone marrow-derived hepatocytes was low. Moreover, a long culture period is needed in most cases.

A research article to be published on July 14, 2010 in World Journal of Gastroenterology addresses this question. The research team led by Professor Shao JZ from College of Life Sciences of Zhejiang University used mouse to investigate the role of VPA on hepatic differentiation of mBM-MSCs. The article indicates that additional exposure of mBM-MSCs to VPA considerably increased the hepatic differentiation in vitro and improved the liver injury by increased homing efficiency of cells to the damaged site in vivo.

The MSCs were successfully isolated from mouse bone marrow and demonstrated that they could differentiate into hepatocytes induced by VPA and well-defined cytokines in a sequential way. The present study demonstrated that VPA-mediated facilitation of hepatic differentiation was regulated by the selective expression of fibroblast growth factor (FGF) and hepatocyte growth factor (HGF) receptors, the increased amounts of acetylated H3 and H4 as well as the structural de-condensation of chromatin. These results provide new insights into the relationships between the epigenetic modification mediated by VPA and the hepatic differentiation from mBM-MSCs.

These findings may also be applicable to study endoderm differentiation and offers an unlimited source of functional hepatocyte-like cells applicable for pharmaco-toxicological research and testing, also this induced system has numerous potential advantages in clinical application.

More information: Dong XJ, Zhang H, Pan RL, Xiang LX, Shao JZ. Identification of cytokines involved in hepatic differentiation of mBM-MSCs under liver-injury conditions. World J Gastroenterol 2010; 16(26): 3267-3278 www.wjgnet.com/1007-9327/full/v16/i26/3267.htm

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