# Is hepatic differentiation of embryonic stem cells induced by valproic acid and cytokines?

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Embryonic stem (ES) cells, known for their capacity to proliferate indefinitely and differentiate into almost all types of cells including hepatocytes, have raised the hope of cellular replacement therapy for liver failure. There have been several protocols available for hepatic fate specification from ES cells, however, most of the protocols currently used result in low yield or purity of functional hepatocytes. Valproic acid (VPA), a histone deacetylase inhibitor, has been demonstrated to facilitate the hepatic differentiation of mesenchymal stem cells. However, little is know about whether VPA could induce the hepatic differentiation of ES cells.

A research team from China reported such research and the development of a protocol for direct hepatic lineage differentiation, from early developmental progenitors to a population of mature hepatocytes, based on sequential induction with VPA and cytokines. Results showed that VPA can direct the hepatic specification of ES cells and largely participates in the differentiation of ES cells into hepatic progenitors. Further differentiation of hepatic progenitors into mature hepatocytes requires supplementation with cytokines. Their study will be published on November 7, 2009 in the *World Journal of Gastroenterology*.

Their research may not only be helpful for the clinical application of hepatocyte transplantation, but also provide an in vitro research model for the better investigation and understanding of the entire developmental process of hepatocytes, from ES cells to hepatic

progenitors, and then to mature hepatocytes. Furthermore, as VPA is an epigenetic modulator, their results may also be of benefit to the research of mechanisms of epigenetic modifications during liver development.

More information: Dong XJ, Zhang GR, Zhou QJ, Pan RL, Chen Y, Xiang LX, Shao JZ. Direct hepatic differentiation of mouse embryonic stem cells induced by valproic acid and cytokines. World J Gastroenterol 2009; 15(41): 5165-5175, www.wjgnet.com/1007-9327/15/5165.asp

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