

Isolation of epithelial cells with hepatobiliary phenotype

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Key words: liver regeneration; hepatic progenitor cells; hepatocytes; biliary epithelium; pluripotent differentiation.

SUMMARY

The regenerative capacity of the liver after partial hepatectomy or chemical injury is well known. In human liver, the resident progenitor cells are called "hepatic progenitor cells" (HPCs) while the term "oval cells" should be discouraged in order to indicate the stem cell compartment. The aim of our study was first to analyse the cellular aspects of liver regeneration through differentiation in cholangiocytes and hepatocytes, and then to characterise resident progenitor cells, using "primary cultured hepatocytes" derived from healthy adult human livers. Human hepatocytes were isolated from fresh surgical specimens of patients who underwent hepatic resections in our Clinical Centre surgery operating room. Hepatic differentiation and function were analysed by immunocytochemistry techniques and the presence of liver epithelial cell populations within normal adult human liver, was demonstrated by immunohistochemistry analysis. These cells expanded *in vitro* and showed the capacity for self-renewal and multipotent differentiation. Human liver stem cells expressed several mesenchymal markers, such as CD44, but not haematopoietic stem cell markers. In addition, these cells expressed alpha-fetoprotein, albumin, CK7 and CK19, indicating a partial commitment to hepatic and biliary cells. Interestingly the expression of both hepatocytes and biliary markers in HPCs reflects the bipotential nature of the hepatic stem cells toward both the hepatic and biliary lineage.

According to their immature and bipotential phenotype, hepatic epithelial cells might represent a pool of precursors in the healthy human adult liver.

INTRODUCTION

Evidence from several studies indicates the presence of resident stem cells in the adult liver (Fausto, 2004). The cell types involved in hepatic regeneration are still undefined, and the contribution of both mature hepatocytes and resident stem cells has been suggested (Crosby, 2002). **Studies on liver regeneration after experi-**