

Isolation of Hepatocytes with High Regenerative Capacity for Repair of Liver Injuries

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Technology description

Researchers at UC San Diego have developed a method whereby hepatocytes can be derived from iPSCs, however, this procedure does not generate fully functioning hepatocytes. Other approaches use ductal cells, which also does not generate fully functional hepatocytes. The inventors have overcome these issues by utilizing these newly discovered cells. Hybrid hepatocytes (HybHP) are morphologically similar to conventional hepatocytes but also express the bile duct gene expression program and low amounts of Sox9, undergo extensive proliferation and do not give rise to HCC. The cells can be used to treat liver injury or disease via transplantation.

The liver is one of the body's most multifunctional organs, controlling glycolytic and urea metabolism, cholesterol levels, blood detoxification, and the biosynthesis of pivotal hormones and proteins. The most intriguing and amazing character of the liver is its ability to quickly self-regenerate or repair in response to acute liver mass loss or chemical-induced injury. However, the regenerative capacity of the mature hepatocytes is continually and severely compromised during the development of diverse chronic liver diseases, such as non-alcoholic fatty liver disease and chronic viral hepatitis. In this scenario, hepatic progenitor cells (HPCs) become activated and spontaneously copy themselves. Due to the expansion of the hepatocellular carcinoma (HCCs), there is a risk of carcinogenesis and thus raises concerns about the therapeutic use of these cells in the clinic.

Related Materials

[Font-Burgada J, Shalapour S, Ramaswamy S, Hsueh B, Rossell D, Umemura A, Taniguchi K, Nakagawa H, Valasek MA, Ye L, Kopp JL, Sander M, Carter H, Deisseroth K, Verma IM, Karin M. Hybrid Periportal Hepatocytes Regenerate the Injured Liver without Giving Rise to Cancer. Cell, August 13, 2015](#)

Advantages

Unlike conventional hepatocytes, the HybHP can be efficiently grown in vitro with a ductal phenotype and expanded indefinitely. Later, these cells can be reverted to the hepatocyte phenotype for transplantation. Unresectable HCC and end-stage liver disease require can only be treated by liver transplantation, but the availability of appropriate donor livers is limited; this overcomes this obstacle.

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