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

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BACKGROUND

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 (HPCs), there is a risk of carcinogenesis and thus raises concerns about the therapeutic use of these cells in the clinic.

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 uses 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.

STATE OF DEVELOPMENT

Demonstrated in a mouse model of liver disease. These cells can repopulate a diseased mouse liver more efficiently than conventional hepatocytes.

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.

INTELLECTUAL PROPERTY INFO

This technology is available for licensing

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 - 08/13/2015

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	2018-0369291-A1	12/27/2018	2015-246
Patent Cooperation Treaty	Published Application	2016179148	11/10/2016	2015-246

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OTHER INFORMATION

KEYWORDS

iPSCs, liver transplantation, hepatocellular carcinoma, liver injuries

CATEGORIZED AS

- **Medical**
  - Disease: Metabolic/Endocrinology

RELATED CASES

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