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Commentary

Role of Liver Regeneration in Hepatocellular Carcinoma

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DESCRIPTION

The liver is a vital organ that plays a crucial role in many physiological processes, such as detoxification, metabolism, and bile production. The liver has a remarkable regenerative capacity, allowing it to recover from various insults, including drug-induced liver injury, viral hepatitis, and surgical resection. However, this regenerative capacity is also a double-edged sword, as it can lead to the development of Hepatocellular Carcinoma (HCC), the most common type of liver cancer. In this article, we will discuss the cellular origins of regenerating liver and HCC.

Cellular origins of regenerating liver

The liver has two sources of cells that can regenerate the organ: hepatocytes and cholangiocytes. Hepatocytes are the primary functional cells of the liver, responsible for the majority of its metabolic functions, such as protein synthesis, lipid metabolism, and detoxification. Cholangiocytes, on the other hand, are epithelial cells that line the bile ducts, which are responsible for transporting bile from the liver to the intestine. Cholangiocytes also play a crucial role in liver regeneration.

The cellular origins of liver regeneration have been extensively studied in animal models, primarily in mice. In response to liver injury, hepatocytes undergo a process called compensatory hyperplasia, in which they increase in size and number to compensate for the loss of damaged cells. This process is regulated by several signaling pathways, including the Wnt/β-catenin, Notch, and Hippo pathways, among others. Recent studies have also identified a population of liver-resident stem cells, known as Hepatic Progenitor Cells (HPCs), which can differentiate into both hepatocytes and cholangiocytes, contributing to liver regeneration.

Cholangiocytes, on the other hand, play a critical role in liver regeneration when hepatocyte proliferation is compromised, such as in chronic liver disease or extensive liver resection. Cholangiocytes can undergo a process called ductular reaction, in which they proliferate and differentiate into hepatocyte-like cells, contributing to liver regeneration. The molecular mechanisms underlying ductular reaction are not yet fully understood, but recent studies suggest that several signaling pathways, including the Notch and Hedgehog pathways, among others, may be involved.

Cellular origins of hepatocellular carcinoma

HCC is the most common type of liver cancer, accounting for 75%-85% of all cases. HCC typically develops in the setting of chronic liver disease, such as viral hepatitis B or C, alcoholic liver disease, or non-alcoholic fatty liver disease. HCC can also develop in patients with genetic liver diseases, such as hemochromatosis or alpha-1 antitrypsin deficiency.

The cellular origins of HCC are still a matter of debate, but several hypotheses have been proposed. One hypothesis suggests that HCC develops from a population of hepatic progenitor cells, which can differentiate into both hepatocytes and cholangiocytes. This hypothesis is supported by several studies showing that HCC tumors can contain cells with both hepatocyte and cholangiocyte markers, suggesting a hybrid hepatocyte-cholangiocyte origin. However, other studies have challenged this hypothesis, showing that HCC tumors can also arise from mature hepatocytes or cholangiocytes.

Another hypothesis suggests that HCC develops from a population of liver stem cells, known as oval cells, which are activated in response to chronic liver injury. Oval cells are bipotent cells that can differentiate into both hepatocytes and cholangiocytes, and they have been implicated in liver regeneration and HCC development.

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