Tumor microenvironment of hepatitis B virus-associated hepatocellular carcinoma

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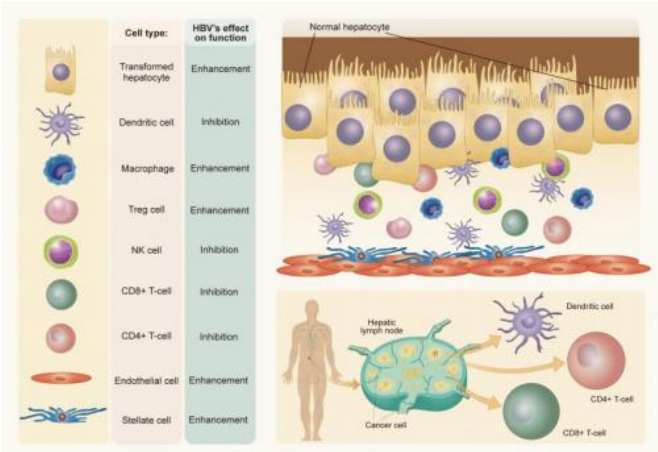

HBV modulates the activity of cellular components of the tumor microenvironment, having the potential to both enhance and inhibit activity. Credit: ©Science China Press

Hepatocellular carcinoma (HCC) is one of the few cancers in which a continued increase in incidence has been observed over recent years. Globally, there are approximately 750,000 new cases of liver cancer reported each year. Importantly, population-based studies show that HCC ranks as the third leading cause of cancer-related deaths worldwide. Also, a large proportion of HCC patients display symptoms of intrahepatic metastases or postsurgical recurrence, with a five-year survival rate of around only 30-40%.

Among the various pathogenic factors, HBV infection accounts for about 60% of the total liver cancer in developing countries and around 23% of cases in developed countries. The persistent presence of HBV DNA in the serum of infected individuals has been found to be a strong indicator for the development of HCC.

In contrast to a majority of cancer types, such as breast, lung, and prostate cancer in which a tumor emerges within a relatively healthy tissue, the initiation of HCC, especially HBV-associated HCC, is intimately associated with a chronically diseased liver tissue. The HBV-initiated tumorigenic process often goes with or occurs secondary to long-term symptoms of chronic hepatitis, inflammation and cirrhosis. The HBV-associated tumor microenvironment forms a complex system in which both cellular and subcellular components with reciprocal signaling contribute critically to the carcinogenic progression.

Scientists based in the US and in China review these critical issues of tumor microenvironment in an article entitled "The hepatitis B virus-associated tumor microenvironment in hepatocellular carcinoma," published in the Beijing-headquartered journal *National Science Review*. Their review summarizes the components and mechanisms to demonstrate both underlying themes and the inherent complexity of these interacting systems in the initiation, progression, and metastasis of HBV-positive HCC.

Xiao-Fan Wang, the corresponding author of the article, is professor of pharmacology and cancer biology at Duke University Medical School, Durham, North Carolina. Co-author Geoffrey Markowitz is a graduate student in Xiao-Fan Wang's lab. Co-author Pengyuan Yang, an alumnus from Xiao-Fan's lab, is now a professor at Institute of Biophysics, Chinese Academy of Sciences in Beijing, China.

The three scientists outline some of the cellular and non-cellular components in the microenvironment and explore these components and mechanisms in the initiation, progression, and metastasis of HBV-positive HCC. In the HBV-associated HCC microenvironment, the cellular components include tumor-infiltrating lymphocytes, dendritic cells, macrophages and Kupffer cells, natural Killer cells, carcinoma-associated fibroblasts, hepatic stellate

cells, endothelial cells, and so on. The non-cellular factors consist of cytokines and chemokines, growth factors and other soluble proteins, miRNAs and the physical microenvironment. All of these components lead to the complicated tumor microenvironment.

With an intricate background, the microenvironment for HCC initiation, progression, and metastasis is deemed to be highly dynamic and interactive with the involvement of many stromal cell types and soluble factors. Therapies that target the microenvironment are a promising new angle for treating this disease and helping alleviate the burden of this monstrous malignance.

More information: Pengyuan Yang, Geoffrey J. Markowitz, Xiao-Fan Wang. "The hepatitis B virus-associated tumor microenvironment in hepatocellular carcinoma". *National Science Review* (September 2014) 1 (3): 396-412 , nsr.oxfordjournals.org/content/1/3/396.full

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