Hepatocellular carcinoma (HCC) ranks as the third leading cause of cancer-related death worldwide with currently limited treatment options. Chronic hepatitis B virus (HBV) infection accounts for HCC development in more than 50% of cases. The lifetime risk of HBV carriers to develop cirrhosis, liver failure or HCC is estimated to be as high as 15-40%. Although several pathways and triggers contributing to HCC development have been described, many features of hepatocellular carcinogenesis and the attributed direct role of viral factors remain elusive. Host genetic factors, the geographic area and epidemiologic factors, as well as the direct risk related to chronic HBV and hepatitis C virus (HCV) infections, account for geographical and gender differences of HCC prevalence. There is growing evidence that hepatocarcinogenesis is a multistep process. Human HCC is typically preceded by chronic inflammation and apoptotic and nonapoptotic cell death with compensatory liver proliferation. However, we still lack a thorough understanding of the common underlying molecular mechanisms. High levels of HBV replication and chronicity of inflammation are known to independently increase the risk for HCC. A direct carcinogenic role of viral factors is very likely to contribute to liver cancer since HCC is known to also occur in noncirrhotic livers of individuals with an inactive chronic or even with occult HBV infection with no significant histological signs of
inflammation or cytopathic effects. Furthermore, synergistic or independent viral risk factors for primary liver cancer development have been described, such as HBV genotype, integration of viral DNA into the host genome and direct effects of viral proteins. A broader understanding of these viral factors in hepatocarcinogenesis might give rise to new diagnostic and therapeutic means in the future. We review the current state of research in liver cancer development and focus on the role of direct viral factors in HBV infection.

Stichworte: Hepatocarcinogenesis; Direct viral factors in hepatocarcinogenesis; Liver cancer; Hepatocellular carcinoma; Chronic hepatitis B infection; Direct role of viral proteins

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