

## **HBV: In Search of a Cure**

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Chronic viral hepatitis caused by HBV and HCV infection afflicts over 325 million individuals worldwide and is the major cause of liver cancer and liver transplants. Chronic HBV infection also leads to over 1 million deaths every year. The discovery and development of highly effective and safe curative direct-acting antiviral therapies has transformed the lives of HCV patients. However, no such cure exists for those suffering from HBV infection. HBV presents a particularly difficult challenge for the development of curative therapies. It has a complex lifecycle that is not only responsible for producing new infectious virus, but also generates viral proteins that are effective at enabling viral evasion of the host immune response. In addition, it deposits a reservoir of stable genetic material in the nucleus of a liver cell, and key pieces of its genetic material integrate into the host genome. Consequently, a therapeutic strategy to achieve an HBV cure must suppress the ability of the virus to replicate itself, eliminate viral proteins that suppress the host immune response and enable the reawakening of HBV specific immune function. In order to achieve this, a combination of agents with different mechanisms of action will be required. Progress toward the development of direct-acting antivirals that in combination have the potential to achieve an HBV functional cure will be discussed.