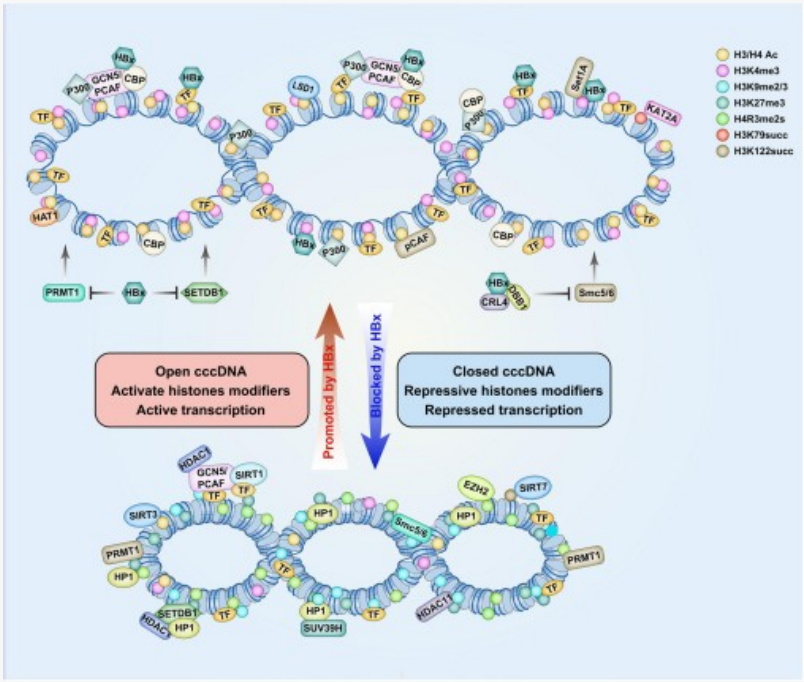
Unlocking the secrets of HBV: new hope for chronic hepatitis B cure

GA, UNITED STATES, March 24, 2025 /EINPresswire.com/ -- Chronic hepatitis B virus (HBV) infection continues to pose a major global health threat. The virus evades immune responses and antiviral therapies due to the persistence of covalently closed circular DNA (cccDNA), which serves as a viral reservoir. A recent review highlights how epigenetic regulation plays a critical role in controlling cccDNA transcription, providing a promising new therapeutic direction. Researchers are now exploring strategies to silence cccDNA, aiming for a functional cure and offering hope to millions of patients worldwide.



Schematic representation of histone-modifying factor recruitment on cccDNA minichromosomes in relation to viral protein HBx.

Hepatitis B virus infection remains one of the leading causes of liver disease, including cirrhosis and hepatocellular carcinoma. Despite widespread vaccination and antiviral treatments, millions of people still suffer from chronic hepatitis B virus (HBV) infection. The primary challenge in curing the disease lies in the persistence of covalently closed circular DNA (cccDNA), a stable viral DNA form that resides in the nucleus of infected liver cells. Current therapies, such as nucleos(t)ide analogues and interferons, fail to eliminate cccDNA, allowing the virus to rebound after treatment is stopped. These challenges underscore the need for novel therapeutic strategies that specifically target cccDNA to achieve a functional cure.

In a review (DOI: 10.1016/j.gendis.2024.101215) published in Genes & Diseases on February 3, 2024, a team of researchers from Chongqing Medical University, in collaboration with other institutions, delves into the epigenetic regulation of HBV cccDNA. The study examines the molecular mechanisms governing cccDNA activity and explores potential therapeutic approaches to silence its transcription. By focusing on chromatin-modifying enzymes, viral proteins, and noncoding RNAs, the researchers hope to uncover new pathways for a functional cure for

chronic hepatitis B.

The review highlights the complex biology of cccDNA, which forms minichromosomes in the infected liver cell nucleus. These minichromosomes bind with histone and nonhistone proteins, becoming transcriptionally active and sustaining viral replication. Key epigenetic mechanisms—such as DNA methylation, histone modifications, and the involvement of noncoding RNAs—regulate cccDNA activity. For example, DNA methylation suppresses viral transcription, while histone modifications like acetylation and succinylation can either activate or silence cccDNA transcription, providing potential targets for intervention.

One of the most compelling findings is the role of the HBV protein HBx in maintaining cccDNA transcriptional activity. HBx interacts with host factors to alter the epigenetic landscape of cccDNA, promoting an open chromatin state that facilitates viral gene expression. The study also explores emerging therapeutic strategies, including targeting HBx, utilizing epigenetic modifiers, and employing gene-editing technologies like CRISPR/Cas9 to disrupt cccDNA. These innovative approaches offer the potential to permanently silence cccDNA, paving the way for a functional cure.

Dr. Juan Chen, the corresponding author of the study, emphasized the importance of epigenetic regulation in controlling cccDNA. "Our findings underscore the critical role of epigenetic mechanisms in HBV pathogenesis. By targeting these pathways, we can develop therapies that not only suppress viral replication but also offer a functional cure for chronic hepatitis B," he said.

The implications of this review are far-reaching for the future of HBV therapies. Epigenetic modifiers, such as histone deacetylase inhibitors and DNA methyltransferase inhibitors, could be repurposed or newly designed to specifically target cccDNA. Furthermore, CRISPR/Cas9 technology offers a precise method for disrupting cccDNA, potentially leading to a permanent cure. By combining these strategies with current antiviral treatments, researchers could significantly enhance their effectiveness, bringing us closer to a functional cure for chronic hepatitis B. This research not only advances our understanding of HBV biology but also sets the stage for the next generation of therapeutic innovations in the fight against viral hepatitis.

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