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Perspective

A Prospective: Hepatitis B Virus X Protein could be a Therapeutic Target for the Cure of Hepatitis B Virus Infection

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ABSTRACT

Cirrhosis and hepatocellular cancer are linked to chronic hepatitis B infection. Virus replication necessitates the HBx (Hepatitis B Viral protein). Therapeutic targeting of Hepatitis B Virus (HBV) infection *via* its protein X (HBx) has emerged as a promising strategy for combating HBV. This article examines the prospective benefits and difficulties of targeting HBV infection with HBx, highlighting its implications for future therapeutic interventions. HBx-targeted therapies have the potential to revolutionise the treatment landscape for chronic HBV infection by interfering with viral replication and reducing HBx-induced pathogenesis. To completely realise the potential of HBx-targeted therapies, challenges such as HBx variability, off-target effects, and successful clinical translation must be addressed. Collaboration among researchers, clinicians, and policymakers is essential for realising the potential of HBx-targeted therapies and enhancing the health outcomes of individuals with HBV infection.

Keywords: Hepatitis; Infection; Hepatitis B Viral protein

DESCRIPTION

HBV, which remains to be a significant global health burden, continues to impact millions of people worldwide. Although modern treatments, such as antiviral drugs and interferon therapies, have demonstrated efficacy in suppressing viral replication, they are unable to eliminate completely the virus from those who are infected. Persistence of covalently closed circular DNA of in recent years, therapeutic targeting of the HBx has gained appeal as a promising approach to treating HBV infection.

Several therapeutic strategies under trails such as proteasomal degradation of HBx by dicoumarol, which is NADPH Quinone Oxidoreductase (NQO1) inhibitor [1], Thiourea derivatives, which block the transactivation function of HBx and reduced HBV replication, nitazoxanide, block the HBx binding to Host Factor like DDB1 [2], antibodies against HBx [3], vaccine against HBx [4], and small interfering RNA mediated degradation of HBx [5]. These all approaches have the potential to neutralize HBx activity, reduced viral load and prevent its pathogenic effects. Importantly, HBx plays an important role in HBV replication and pathogenesis, making it a suitable therapeutic target (Figure 1). The potential benefits and drawbacks of utilising HBx to treat HBV infection are discussed in this opinion article, with an emphasis on the implications for prospective therapeutic strategies.

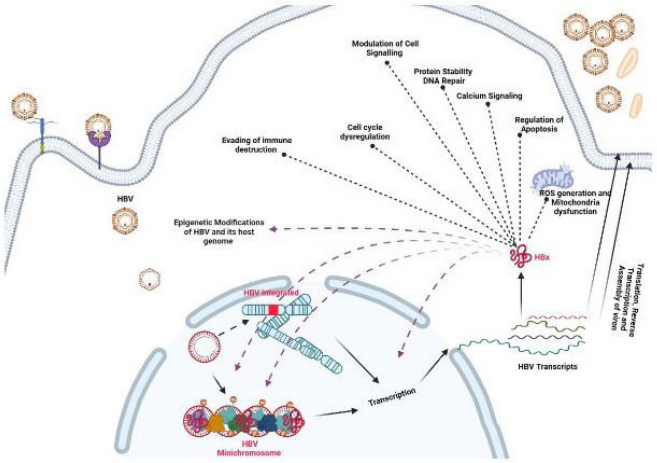

Figure 1: Illustrates how important Hepatitis B viral protein X (HBx) is for maintaining Chronic Hepatitis B infection (CHB), which in turn promotes host factors to be disrupted and subsequently leads to Hepatocellular Carcinoma (HCC).

Benefits of using HBx to target HBV infection

HBV replication: HBx is essential for the persistence, maintenance

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and viral replication. It might be able to stop important stages of the viral life cycle, such as transcription, translation, and encapsulation, by targeting HBx [6,7]. By reducing viral load through the inhibition of HBx-mediated mechanisms, chronic HBV patients may benefit from viral clearance and functional cure.

HBx-induced pathogenesis: Hepatocellular Carcinoma (HCC), one of the liver conditions associated with HBV, has been linked to HBx [8]. The risk of developing HCC may be decreased by precisely targeting HBx and weakening its transactivation function. For those who have persistent HBV infections, this strategy may have a major impact on long-term results

Combination therapy: Combining current antiviral treatments with HBx targeting may have beneficial synergistic effects. Enhancing viral suppression, preventing the development of drug resistance, and even cutting the length of treatment are all possible with complementary modes of action. Combination therapies with HBx-targeted treatments could be an effective way to achieve long-term viral control and enhance patient outcomes.

Challenges and way forward

HBx variation: Various HBV genotypes and subtypes show significant genetic and functional heterogeneity in the HBx protein [9]. The development of universal HBx-targeted treatments that are effective against all strains of HBV may face difficulties due to HBV genome diversity. For successful implementation of targeted therapies, a thorough understanding of HBx diversity and its effect on viral replication and pathogenesis is required.

Off-target effects: It is essential to develop selective inhibitors that target HBx selectively without disrupting cellular proteins or processes. Off-target effects could have unforeseen consequences and endanger the safety of patients. To reduce off-target effects and ensure their therapeutic specificity, HBx-targeting should be carefully designed and optimised.

Clinical translation and accessibility: It takes rigorous preclinical and clinical evaluations to bring HBx-targeted treatments from the bench to the bedside. To determine the therapeutic potential of these therapies, thorough research is required, including safety, effectiveness, and pharmacokinetic investigations. To guarantee that HBx-targeted therapies are widely accessible, it is also important to take into account issues like cost, scalability, and accessibility, especially in areas with little resources where HBV prevalence is highest.

CONCLUSION

A practical strategy to address this global health issue is therapeutic targeting of HBV infection *via* HBx. HBx-targeted treatments have the potential to completely alter the way chronic HBV infection is treated by interfering with viral replication and lessening HBx-induced pathogenesis. To successfully translate research findings into clinical applications, however, a number of obstacles must be overcome, including HBx variability, off-target effects, and other factors. Realising the full potential of HBx-targeted therapies and enhancing outcomes for people with HBV infection depend on addressing these issues through cooperative efforts among researchers, physicians, and representatives.

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