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Structural and Functional Polymorphism in Hepatitis B Virus Oncogene, HBx

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Abstract

Background: HBV is now firmly associated with the incidence of Hepatocellular Carcinoma. This oncogenic potential of HBV is primarily due to an oncogene referred to as HBx. The present study deals with the sequential and structural variations found in the HBx protein encoded by the genomes of different HBV genotypes.

Methods: In total 5991 sequences of HBx belonging to different genotypes of HBV were aligned to procure consensus sequences of each genotype. The sequence was than used to construct molecular structure of HBx employing iterative threading alignment. The models were optimized and refined for the structural and thermodynamic parameters. The selected models were used to develop structures of HBx of each genotype which were in turn compared for their structural attributes, dimer formation and molecular interactions with p53.

Results: The sequence alignment reveals considerable conservation in the HBx sequences of different genotypes. The strongly conserved C-terminal region is a component of p53 interaction region of HBx. The most diverged region was found to be dimerization region spanning 25 to 50 aa. Structurally, HBx molecule has found to be nearly disordered except the C-terminal p53 binding region that adopts helical conformation. This in turn may explain in part the promiscuous nature of HBx in terms of binding with multiple binding partners. These observations have been further verified by GlobPlot analysis. The disordered region potentially rendered variations in the intra and inter molecular complexes of HBx as observed by molecular docking analysis.

Conclusion: The data highlights the variations in the structural characteristics of HBx that underscores the variations in the pathological and oncogenic consequences of HBV infections rendered by different HBV genotypes.

Keywords

HBV, HBx, Hepatocellular carcinoma, oncogene, p53

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References