Study reveals 3-D landscape of how hepatitis B virus interacts with human chromatins

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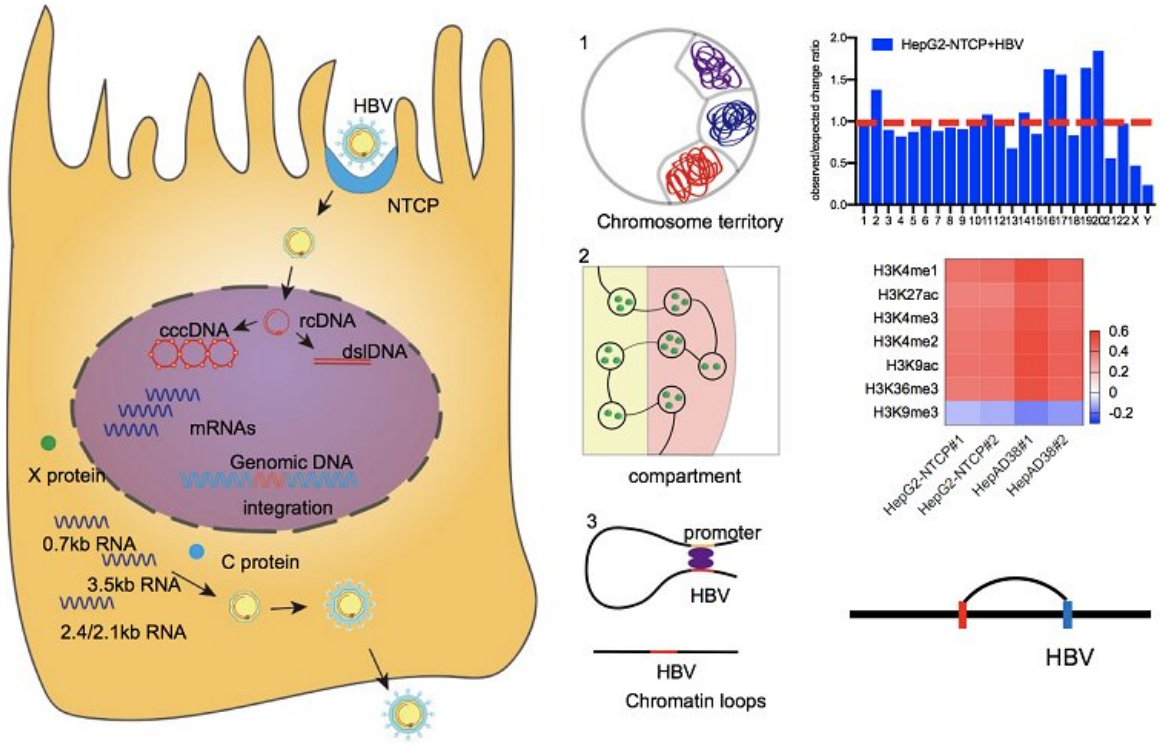

The model of the spatial organization of HBV DNAs in human nuclear. Credit: Dr. YANG Pengyuan's group

Hepatitis B virus (HBV), a small enveloped DNA virus belonging to the Hepadnaviride family, remains a serious global health problem. Uncontrolled chronic HBV infection can lead to life-threatening end-

stage chronic liver diseases, such as cirrhosis and Hepatocellular carcinoma.

The human nuclear HBV DNAs, including both covalently closed circular DNA (cccDNA) and integrated HBV DNA forms, are considered primary contributors to the development and progression of HBV-associated liver diseases.

Prof. Yang Pengyuan from the Institute of Biophysics (IBP) of the Chinese Academy of Sciences (CAS) and Prof. Ji Xiong from School of Life Sciences in Beijing University emphasized the key roles of nuclear HBV DNAs in human cells and investigated how HBV DNAs interact with human chromatins. Their study was published in *Cell Discovery* online on Dec. 29.

The researchers firstly employed a highly sensitive technology, 3C-high-throughput genome-wide translocation sequencing (3C-HTGTS), to globally identify HBV DNA-host DNA contacts in cellular models of HBV infection.

Interestingly, HBV DNA did not randomly position in host genome, but instead preferentially establish contacts with the host DNA at active chromatin regions. Importantly, the data from 3C-HTGTS revealed another kind of HBV DNA, integrated HBV DNA, could form chromatin loop with host genomic DNA at transcriptionally active region of human genome.

Based on the identification on the HBV DNA-host DNA contacts, the researchers revealed H3K4me1-marked regions modified by KMT2C/D were also observed in the HBV cccDNA mini-chromosome and strongly influenced HBV transcription.

Furthermore, HBV infection influenced host gene expression

accompanied with HBV DNA-host DNA contacts.

These findings provided a high throughput 3-D landscape for the spatial organizations of cccDNA and integrated HBV DNA within the human genome, and a foundation to further understand the mechanisms of HBV modulation of liver disease development and progression in the future.

More information: Bo Yang et al. 3D landscape of Hepatitis B virus interactions with human chromatins, *Cell Discovery* (2020). DOI: 10.1038/s41421-020-00218-1

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