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Landscape of the Epstein-Barr virus-host chromatin interactome and gene regulation

The three-dimensional (3D) chromatin structure of Epstein–Barr virus (EBV) within host cells and the underlying mechanisms of chromatin interaction and gene regulation, particularly those involving EBV's noncoding RNAs (ncRNAs), have remained incompletely characterized. In this study, we employed state-of-the-art techniques of 3D genome mapping, including protein-associated chromatin interaction analysis with paired-end tag sequencing (ChIA-PET), RNA-associated chromatin interaction technique (RDD), and super-resolution microscopy, to delineate the spatial architecture of EBV in human lymphoblastoid cells. We systematically analyzed EBV-to-EBV (E–E), EBV-to-host (E–H), and host-to-host (H–H) interactions linked to host proteins and EBV RNAs. Our findings reveal that EBV utilizes host CCCTC-binding factor (CTCF) and RNA polymerase II (RNAPII) to form distinct chromatin contact domains (CCDs) and RNAPII-associated interaction domains (RAIDs). The anchors of these chromatin domains serve as platforms for extensive interactions with host chromatin, thus modulating host gene expression. Notably, EBV ncRNAs, especially Epstein–Barr-encoded RNAs (EBERs), target and interact with less accessible regions of host chromatin to repress a subset of genes via the inhibition of RNAPII-associated chromatin loops. This process involves the cofactor nucleolin (NCL) and its RNA recognition motifs, and depletion of either NCL or EBERs alters expression of genes crucial for host infection control, immune response, and cell cycle regulation. These findings unveil a sophisticated interplay between viral and host genomes that underlies EBV's ability to orchestrate gene regulation and pathogenesis in infected cells.

Keywords

Epstein-Barr virus, chromatin, 3D genome, gene regulation, noncoding RNA, host-virus interaction

Biography

Dr. Meizhen Zheng is an Assistant Professor and Principal Investigator at SUSTech. Her research focuses on innovative 3D genome mapping and multi-omics technologies for understanding chromatin interactions. She is first or corresponding author in Nature, Science Advances, The EMBO Journal, and Briefings in Bioinformatics. Dr. Zheng has secured major research funding, holds multiple patents, serves as a reviewer for scientific journals, mentors graduate students, and actively promotes international collaboration in genomics.

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