EPSTEIN-BARR VIRUS HIJACKS BRD7 TO CONTROL C-MYC-MEDIATED VIRAL LATENCY MAINTENANCE

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Abstract

The Epstein-Barr virus (EBV) switches between latent and lytic phases in hosts that are important in developing related diseases. However, the underlying mechanism of how the viral latent-lytic switch is controlled and how EBV itself mediates this regulation remains largely unknown. This study identified the upregulation of bromodomain-containing protein 7 (BRD7) during EBV latent infection. Based on ChIP-seq of endogenous BRD7 in Burkitt lymphoma cells, we found that EBV drove BRD7 to regulate both cellular and viral genomic loci, including the transcriptional activation of *c-Myc*, a recently reported regulator of EBV latency. Additionally, EBV-mediated BRD7 signals enriched around the FUSE site in chromosome 8 and the enhancer LOC108348026 in lgH locus, which might activate the *c-Myc* alleles. Thus, the exact breakpoint sequence at c-Myc translocation site between FUSE and lgH was identified in Akata cells. Mechanically, EBV-encoded nuclear antigen 1 (EBNA1) bound and recruited BRD7 to colocalize at promotor regions of the related genes, thus serving as cofactors for the maintenance of viral latency. Moreover, the disruption of BRD7 decreased the c-Myc expression, reactivated the lytic cycle by inducing BZLF1 expression. Our findings reveal the unique role of BRD7 hijacked by EBV in the maintenance of the viral latency state. The study paved a way to understand new molecular mechanism of EBV-induced chromatin remodeling and latent-lytic switch regulation, providing novel therapeutic candidate targets of EBV persistent infection.