

Ubiquitination of Epstein-Barr Virus Lytic Proteins

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Epstein-Barr virus (EBV) is a human herpesvirus that infects lymphoid and epithelial cells. During the switch from latency to lytic cycle, the virus expresses proteins that are required for viral lytic replication, capsid assembly and viral maturation. The virus expresses two transcription factors, Rta and Zta, which are critical to the transcriptional activation of lytic genes. Rta is known to be modified by SUMO. We find that RNF4, an SUMO-targeted ubiquitin E3 ligase, promotes ubiquitination of Rta and Zta and knockdown of RNF4 expression enhances viral replication and virion production, showing how ubiquitination influences EBV lytic progression. Additionally, TRIM5 α that possesses the ubiquitin E3 ligase activity can recognize retroviral capsid and restrict retrovirus. We also find that TRIM5 α promotes ubiquitination of two EBV capsid proteins, VCA and BORF1. These two capsid proteins bind to the C-terminal B30.2 domain in TRIM5 α . Knockdown of TRIM5 α expression increases the production of virions. Our study shows that ubiquitination critically influences EBV lytic development.