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HIGHLIGHT

Regulation of latency to lytic life cycle: multiple tricks by KSHV RTA

Jiemin Wong

The Institute of Biomedical Sciences and School of Life Sciences, East China Normal University, Shanghai 200241, China

The herpesviruses are large enveloped DNA viruses that infect a wide spectrum hosts including human being. A key characteristic of all herpesviruses is their ability to establish life-time latency within the infected host and to periodically reactivate and enter the lytic replication to produce infectious virus progeny. During latency the 120–300 kb double-stranded DNA genomes of these viruses are maintained as multiple copies of circular episomes within the nuclei of the host cells. Lytic replication is marked by an increase in viral gene expression and the production of infectious virus progeny. How the viruses switch from latency to lytic replication has been a central question for study. In this issue of *Frontiers in Biology*, a review by Yang and Wood entitled "The replication and transcription activator (RTA) of Kaposi's sarcoma-associated herpesvirus/human herpesvirus-8" focuses on the viral RTA, the key protein for triggering KSHV from latency to lytic replication (Fig. 1). As a member of the herpesviruses, Kaposi's sarcoma-associated herpesvirus or human herpesvirus 8 (KSHV or HHV8, respectively) is the cause of Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease. In this comprehensive review, we can learn not only the gene expression programs of KSHV in the latency and lytic phases, the regulation of RTA itself, but also the multiple mechanisms that RTA utilizes to transactivate its target genes, including selective DNA-binding, utilizing cellular coactivators and promoting repressor degradation.

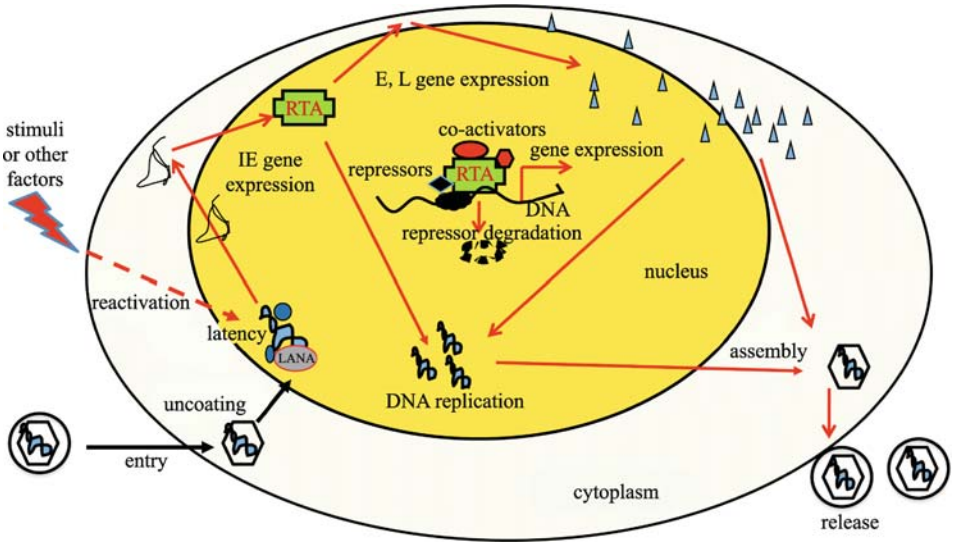

Fig. 1 KSHV life cycle. KSHV enters the cell, releases DNA into cellular nucleus and usually establishes latency (black arrows). Upon stimulation or spontaneous reactivation KSHV undergoes lytic replication (red arrows). RTA is an immediate early (IE) gene product, which is sufficient and necessary to drive KSHV lytic replication by activating KSHV early (E) and late (L) expression cascade and KSHV DNA replication. The viral particles are then assembled and released from the cell subsequently. The diagram in the middle indicates the mechanisms RTA used to activate gene expression by: 1. DNA binding; 2. coactivator usage; 3. promoting repressor degradation.

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E-mail: jmweng@bio.ecnu.edu.cn