KSHV and Viral Epigenomics

Hsing-Jien Kung[1], Amy Pei-Ching Chang [2]

[1] National Health Research Institutes, Taiwan
[2] National Yang Ming University, Taiwan

Kaposi's sarcoma-associated herpesvirus (KSHV), also designated human herpesvirus type 8 (HHV-8), has been linked to Kaposi's sarcoma (KS) as well as primary effusion lymphoma (PEL or body-cavity B-lymphoma [BCBL]), and a subset of multicentric Castleman's disease. KS is the most common HIV/AIDS-associated malignancy. In KSHV associated malignancies, persistent infection of virus and regulation of latent to lytic state appear to play critical roles. Chromatin remodeling is tightly linked to the transcriptional states of herpesvirus genomes and is considered to be a key step in the transition from latent to lytic state and vice versa. SUMOylation of chromatin proteins has been shown to have profound effect on the condensation of viral episomes. In this presentation, I will summarize our labs' discoveries that KSHV encodes a SUMO E3 ligase, K-bZIP and a SUMO-targeting Ubiquitin ligase, K-Rta, which function to modulate histone demethylases and PML-bodies to affect viral reactivation. By removing SUMO, K-Rta potently initiates the viral early gene transcription and lytic replication. K-bZIP on the other hand, decorates viral chromatin with SUMO2/3 marks in euchromatin region to control the level of viral reactivation and possibly entry of latency. KSHV viral latency to lytic replication switch thus represents a suitable model for studying epigenomic control of global gene expressions.