

P026 SUMO-binding domains are involved in the regulation of tumour suppressors by the Kaposi's sarcoma-associated herpesvirus latent protein LANA2

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Kaposi's sarcoma associated-herpesvirus (KSHV) is the causal agent of Kaposi's sarcoma, primary effusion lymphoma and multicentric Castlemann's disease. LANA2 is a KSHV latent protein exclusively expressed in infected B cells that has a critical role in the pathogenesis of the virus. LANA2 is modified by SUMO and contains a SUMO interaction motif (SIM) that accounts for its interaction with other sumoylated proteins. LANA2 induces the disruption of PML-nuclear bodies (PML-NBs) and the degradation of some of its components, Sp100 and the tumor suppressor PML. PML-NBs are involved in the regulation of apoptosis, senescence and the control of viral infection, and contain other LANA2 targets such as the tumor suppressors pRb and p53, that are also sumoylated. The requirement of the SUMO-binding domains in LANA2 and in the PML-NB components on the regulation of the activity of the tumor suppressors by LANA2 is being studied. Our results show that the SIM domain as well as the lysine 160 in PML is required for its degradation by LANA2. In addition both, SIM domain and SUMO-modification domain in LANA2 are also required for PML degradation. The requirement of these LANA2 domains to inhibit PML, p53 or pRb activities will be discussed.