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### **“Kaposi Sarcoma-Associated Herpesvirus Tissue Reservoirs”**

#### **Abstract**

Kaposi sarcoma-associated herpesvirus (KSHV), also known as Human Herpesvirus 8 (HHV-8), is the causative agent of cutaneous cancer known as Kaposi's Sarcoma (KS). KSHV is similar to other herpesviruses which can establish a latent lifelong infection and could be reactivated to lead to disease such as KS. KSHV infection is found to be prevalent in sub-Saharan African (SSA) countries like Zambia and Tanzania, and KS is still one of the most common cancers in these countries where HIV-1 infection is also epidemic. The co-infection of KSHV and HIV-1 leads to the development of an aggressive form of KS, known as Epidemic KS (EpKS). Currently little is known about how latent KSHV infection leads to KS, and there are no effective KS treatments with high cancer recurrence rates even after chemo or radiotherapies. Thus, there is a need to develop strategies to prevent KS and to develop more effective treatment regimens. A crucial step for prevention is to identify where the virus lays dormant in the body so that future therapeutics can be designed to specifically target and eliminate KSHV-infected cells in the infected tissues.

In collaboration with the University of Zambia Teaching Hospital, we obtained serum and tissue samples from 10 autopsy subjects for this pilot study to investigate the tissue distribution of these reservoirs and the cell types that are infected by the KSHV. All subjects died of various causes, but not KS. Each subject has 27 different tissue samples including different parts of the brain (a known KSHV reservoir), lymph nodes from different sites, and all the major organs such as the spleen and lung. To determine which subjects were exposed to KSHV and/or HIV-1, serum from each individual was subjected to an in-house KSHV serology immunofluorescence assay. The HIV-1 infection status was also determined using a commercially available HIV serology kit. Subjects that were confirmed to have KSHV-specific antibodies were selected for further analysis of KSHV distribution among various tissues. To detect the presence of KSHV viral DNA in tissues DNA was extracted from several 6µm thick sections of FFPE blocks of each tissue from the selected subjects using a commercially available FFPE DNA extraction kit. The concentration of extracted DNA was measured using a Qubit fluorometer. Nested PCR against a KSHV viral gene (Latency Associated Nucleus Antigen, LANA) was performed to detect which tissue has KSHV DNA. The KSHV DNA positive tissues are further analyzed by histology, immunohistochemistry, and immunofluorescence to identify the cell type of the KSHV infected cell. Findings from this pilot study will provide insights into identifying the dominant cell type that KSHV preferentially infects and the tissues that harbor the virus.