Retrovirology

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Oral presentation

Kaposi Sarcoma Herpesvirus: Update

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The incidence of HIV-related cancer before and during the ART era indicates that oncogenic viruses continue to contribute to the majority of these cancers and they are therefore considered opportunistic malignancies. ART has lead to a definitive decline in the incidence of certain AIDS-defining cancers including Kaposi sarcoma (KS) and non-Hodgkin's lymphoma. Before ART, non-AIDS-related malignancies accounted for 1% of all causes of death in this population, this has now raised to over 25% because of the sharp decline of competitive risks, the relative frequent co-infection in this population with the oncogenic viruses Hepatitis B or C, the aging of the HIV-infected population and the possible direct contribution to oncogenesis by HIV-1 or ART.

Due to the HIV-pandemic, KS is now one of the most common tumors overall in sub-Saharan Africa. Kaposi sarcoma-associated herpesvirus (KSHV or HHV8) is essential in the etiopathogenesis of KS. The global seroprevalence of KSHV largely reflects the incidence of KS. In the vast majority of infected individuals KSHV persists without harm to its host. When the balance between pathogen and host immunity is disturbed, KSHV reactivation and outgrowth of KSHV infected cells occur.

The transcriptome of KS tumor cells is closest to that of lymphatic endothelial cells (LEC). We determined the global effect of KSHV infection of LEC on genes involved in immunity. We compiled a group of 834 genes, classified into six functional clusters, including antigen presentation, inflammation (cytokines and chemokines), apoptosis, interferon response, cell adhesion, and cell signaling. Over 30% of genes were significantly deregulated after infection of LEC ($q < 0.005$). The inflammation, antigen presentation, and interferon response profiles of infected LEC correlated to that seen in KS. We determined the expression levels of surface proteins involved in antigen presentation by FACS, and cytokines by protein arrays. Infection led to the downregulation of key proteins involved in antigen presentation. We also observed an expression pattern of chemokines associated with T cell, monocyte, and dendritic cell migration and conducted chemotaxis assays to assess the functional relevance of these data. Overall, we characterise the immune profile of LEC and show its profound regulation by KSHV, resulting in multiple immune evasion pathways.