M & I
Microbiology
and Immunology
University of North Carolina at Chapel Hill

DISSERTATION SEMINAR

Kurtis Host

"Interaction of KSHV with the Host Immune System"

Friday, April 13, 2018

3:45 p.m.

Joseph S. Pagano Conference Room (00-002)
Lineberger Comprehensive Cancer Center

Dissertation Advisor: Dr. Blossom Damania

Presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Celebration to follow at 5pm-6:30 pm in LCCC 32-001

ABSTRACT

Kurtis Matthew Host: Interaction of Kaposi's Sarcoma-associated Herpesvirus with the Host Immune System

(Under the direction of Blossom Damania)

Kaposi's sarcoma-associated herpesvirus (KSHV) is the etiological agent for three human malignancies; Kaposi's sarcoma (KS), primary effusion lymphoma (PEL), and multicentric Castleman's disease (MCD). KSHV-related diseases primarily manifest in immunocompromised hosts such as HIV positive patients, iatrogenic immune suppression, and geriatric populations. However, some subtypes of KS exist in the absence of obvious immune deficiency and remain poorly understood. KS is the leading cause of cancer in the sub-Saharan African nation of Malawi. Therefore, we sought to characterize the current clinical burden of KS in Lilongwe, Malawi, the capital city. We found that the majority of KS cases were associated with HIV. Interestingly, 9% of cases were in HIV naïve patients, suggesting a significant burden of the endemic subtype of KS. Our results suggest a needed emphasis for endemic KS research, a poorly understood subtype, as it represents a significant proportion of Malawi's leading cancer.

KSHV is recognized by the immune system, however, it encodes multiple mechanisms for thwarting effective immune responses. One mechanism implicated in escaping immune clearance is programmed death ligand 1 (PD-L1) overexpression. PD-L1 is a co-inhibitory molecule which interacts with the programmed death 1 (PD-1) receptor on T cells. PD-1:PD-L1 engagement blocks T cell receptor (TCR) signaling resulting in reduced T cell activation. Chronic PD-1:PD-L1 ligation results in T cell exhaustion. Tumor cells have been found to utilize PD-L1 to escape immune elimination. Current treatment targeting PD-L1 in certain cancer types is showing clinical efficacy. Therefore, we sought to determine if KSHV could stimulate PD-L1 expression. We found that KSHV is able to stimulate PD-L1 expression in human monocytes following infection. In addition, the cytokine profile showed a pro-inflammatory milieu. Our report is the first to show direct KSHV stimulation of PD-L1 expression and suggests that PD-L1 targeted therapeutics may have a role in KSHV mediated diseases.

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