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

THESIS SEMINAR

Brent Eason

"VEGF-A inhibition as a treatment modality for Kaposi sarcoma."

Tuesday, April 16, 2019 11:00 a.m. Joseph S. Pagano Conference Room (00-002) Lineberger Comprehensive Cancer Center

Thesis Advisor: Dr. Dirk Dittmer

Presented in partial fulfillment of the requirements for the degree of Master of Science

ABSTRACT

Brent Eason: VEGF-A inhibition as a treatment modality for Kaposi sarcoma (Under the direction of Dirk Dittmer)

Kaposi sarcoma-associated herpesvirus (KSHV) is a human herpesvirus that is the etiological agent of several cancers including Kaposi sarcoma (KS), primary effusion lymphoma (PEL), and multicentric Castleman's disease (MCD). Our studies centered on the malignancy of endothelial cell origin, KS, and its predilection to both express and depend upon vascular endothelial growth factor A (VEGF-A). KS, a highly angiogenic cancer, has a heterogeneous presentation that varies with age, geography, immunocompetency, and factors that are still being explored. One approach to treatment of KS is to utilize antibody-based drugs targeting VEGF-A to prevent the angiogenesis and VEGFR signaling upon which KS is dependent. DLX1008, an anti-VEGF-A antibody single-chain variable fragment (scFv) with low picomolar affinity, was found to be highly effective in reducing tumor growth in a xenograft model of KS. This indicates that anti-VEGF-A biologics with effective biodistribution could be a useful addition to the repertoire of KS treatments.