"Tumor development and treatment of EBV-associated lymphomas in immune competent humanized mice"

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Abstract: Tumorigenesis and treatment of EBV-associated lymphomas in immune competent humanized mice will be studied in four aims.

1. Analyze viral gene expression pattern and differentiation stages of in vivo EBV infected B cells. Expression of the transformation-associated EBV latent antigens is tightly connected to the differentiation stage of the infected B cells in humans. We are interested if these infection programs also exist in our infected humanized mice, and if they can give rise to different types of EBV-associated lymphomas.

2. Characterize the components and development of the in vivo primed EBV specific immune control. Dendritic cells, natural killer cells and T cells have been implicated in EBV specific immune control, and will be analyzed during primary EBV infection in vivo.

3. Investigate the influence of co-infection with the oncogenic Kaposi's sarcoma-associated herpesvirus on B cell transformation by EBV and on EBV specific immune control in vivo. Primary effusion lymphoma is always associated with KSHV infection and often with co-infection by EBV. Therefore, changes in B cell transformation and immune control of EBV after coinfection with KSHV will be analyzed.

4. Identify inhibitors of the main EBV oncogene product, latent membrane protein 1 (LMP1). LMP1 is the main EBV oncogene and required for EBV transformed B cell survival. Therefore, we will screen for LMP1 inhibitors, and if promising compounds are identified, test them for efficacy against EBV-associated lymphomas in vivo.

Beyond oncogenic herpesvirus infections, this model might prove useful to study pharmacological and immunological treatments of human tumors in vivo.