Meet the Researcher

Zsolt Toth , PhD

"I am honored to receive funding from the American Cancer Society, which will help our research to better understand how an oncogenic herpesvirus establishes life-long infection in humans. This grant will enable our systematic efforts to identify the key viral and host factors in tumor herpesvirus infection, which can serve as novel therapeutic targets in the future. Our ultimate goal is to eliminate the spreading of cancer-causing herpesviruses in the human population."

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Controlling the Establishment of Oncogenic Herpesvirus Infection

It is estimated that viral infections are involved in 15-20% of human cancers. Currently, there are seven human tumor viruses known. Of them Kaposi"s sarcoma-associated herpesvirus (KSHV) is responsible for the development of Kaposi"s sarcoma, primary effusion lymphoma (PEL), and aggressive forms of multicentric Castleman"s disease. Aggressive forms of the KSHV-associated malignancies can be more frequently developed in elderly, immunosuppressed people undergoing organ transplantation or malnourished children in Africa. There are still no KSHV specific drugs or vaccines to halt KSHV infection or KSHV-associated cancers.

After initial infection, KSHV establishes a persistent, latent infection in the human body. Latency is a dormant state of KSHV when only a few viral genes (called latent genes) are expressed while the expression of lytic viral genes responsible for viral replication and virus production are repressed in the infected cells. Importantly, the vast majority of cancer cells in KSHV-associated tumors carry the virus in latency. The latent viral genes expressed in the cancer cells ensure the survival and growth of cancer cells. Thus, establishment and maintenance of viral latency following infection is a prerequisite for KSHV infection-associated tumorigenesis. However, despite the importance of viral latency in KSHV pathogenesis, the molecular mechanism of the establishment and maintenance of KSHV latency is still poorly understood. Thus, the goal of our proposal is to explore the mechanism underlying the establishment of KSHV latency, which can facilitate the development of antiviral approaches to inhibit persistent KSHV infection and viral tumorigenesis.

Our effort led to the identification of several new cellular factors that can play a role in the inhibition of viral gene expression, which is critical for the establishment of KSHV latency following infection of cells. Our proposal focuses on the role of the latent KSHV protein LANA and our recently discovered essential function of LANA as facilitator of stepwise coating of the virus with repressive protein complexes and a region within the KSHV DNA as recruiter of LANA during the establishment and maintenance of KSHV latency. Our findings will help better understand how a human oncogenic virus can hijack and repurpose human factors in order to hide in the infected cells, which is the initial step for the life-long infection and toward virus-induced oncogenesis. Our results can facilitate new therapeutic intervention for inhibition of persistent KSHV infection and KSHV-associated cancers.

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