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UAMS Receives \$2.9 Million NIH Grant to Study Virus that Can Trigger Cancers

LITTLE ROCK — A discovery at the University of Arkansas for Medical Sciences (UAMS) that a viral protein helps a cancer-associated herpesvirus evade the immune system has led to a five-year, \$2.9 million research grant from the National Institutes of Health (NIH).

Craig Forrest, Ph.D., will use the grant to help reveal functions of the viral protein known as latency-associated nuclear antigen (LANA). The research is focused on LANA's roles during infection by the gamma herpesvirus known as Kaposi sarcoma-associated herpesvirus (KSHV).

Ultimately, Forrest, a professor in the College of Medicine Department of Microbiology and Immunology, hopes the work will someday lead to a vaccine for Kaposi sarcoma and other cancers caused by gamma herpesviruses.

Kaposi sarcoma is a rare cancer that affects the skin, lymph nodes and internal organs, and is caused by KSHV, a member of the gamma herpesvirus family. Gamma herpesviruses, including KSHV and the Epstein-Barr virus (EBV), are known for establishing lifelong infections in their hosts. For most people, the viruses remain latent, only reactivating under certain conditions.

KSHV is of particular concern because it is associated with several types of cancer, especially in people with compromised immune systems, such as those living with human immunodeficiency virus (HIV).

Forrest said he became excited when a Ph.D. student in his lab, Steven Murdock Jr., found that the presence of LANA correlated with an almost nonexistent immune response against the virus.

"First of all, it was great preliminary data to support the rationale for the NIH grant proposal," said Forrest, who has been studying gamma herpesviruses since 2003. "But second of all, I thought, 'That's amazing, and now what can we do to figure out how the virus is preventing immune recognition?""

At the end of the five-year grant, he hopes to have figured out what the mechanism is that LANA uses for preventing immune detection by the body.

LANA plays a crucial role in maintaining gamma herpesviruses in a latent state, allowing the infection to remain in the body without any symptoms. By understanding how LANA helps KSHV evade immune detection, Forrest hopes to uncover new ways to prevent or treat KSHV-associated cancers.

"We're excited about what we might discover," he said. "It would be amazing to figure out how this virus can persist in the body for so long and what we can do to prevent it from causing cancer."

The research involves creating genetically modified "chimeric" viruses that incorporate KSHV genes to simulate human infection and test potential treatments.

"When we placed the human KSHV LANA gene into our gamma herpesvirus model, it worked just fine for latency but also introduced unique characteristics, such as suppressing viral replication," Forrest said. "This suggests the virus may be using LANA as an immune evasion tactic, preventing the immune system from recognizing and eliminating the infection."

The study will also explore how the immune suppression influences disease development.

"Our new chimeric viruses will help us understand how KSHV genes affect infection and disease in different settings," Forrest said. "Our hypothesis is that the virus' stealthy behavior could give it more opportunity to cause cell transformation and drive tumor development."

UAMS is the state's only health sciences university, with colleges of Medicine, Nursing, Pharmacy, Health Professions and Public Health; a graduate school; a hospital; a main campus in Little Rock; a Northwest Arkansas regional campus in Fayetteville; a statewide network of regional campuses; and eight institutes: the Winthrop P. Rockefeller Cancer Institute, Jackson T. Stephens Spine & Neurosciences Institute, Harvey & Bernice Jones Eye Institute, Psychiatric Research Institute, Donald W. Reynolds Institute on Aging, Translational Research Institute, Institute for Digital Health & Innovation and the Institute for Community Health Innovation. UAMS includes UAMS Health, a statewide health system that encompasses all of UAMS' clinical enterprise. UAMS is the only adult Level 1 trauma center in the state. UAMS has 3,485 students, 915 medical residents and fellows, and seven dental residents. It is the state's largest public employer with more than 11,000 employees, including 1,200 physicians who provide care to patients at UAMS, its regional campuses, Arkansas Children's, the VA Medical Center and Baptist Health. Visit <u>www.uams.edu</u> or <u>www.uamshealth.com</u>. Find us on <u>Facebook</u>, <u>X</u> (formerly Twitter), <u>YouTube</u> or <u>Instagram</u>.

