

Laying the Groundwork for a New Cancer Preventive Vaccine

Fred Hutch scientists aim to uncover secrets of immune response to the virus behind Kaposi sarcoma, a cancer that affects people with advanced HIV.

December 11, 2024 By Fred Hutch News Service

Behind one fifth of cancer cases around the world lurks a pathogen. The connective-tissue cancer Kaposi sarcoma even gave its name to the herpesvirus that causes it: Kaposi sarcoma-associated herpesvirus, or KSHV. Though uncommon in the U.S., KS is a problem in regions where HIV still exacts a major public health toll.

“KS is among the most common cancers among people with HIV, and is a leading cancer in several African countries,” said Fred Hutch KS specialist [Warren Phipps, MD, MPH](#).

To rectify gaps in treatment and prevention, Phipps and Fred Hutch colleagues [Jim Boonyaratanakornkit, MD, PhD](#), and [Andrew McGuire, PhD](#) have teamed up to lay the groundwork for a KSHV vaccine. An effective KSHV vaccine would revolutionize how providers approach KSHV-related diseases, Phipps said.

The collaborators secured a five-year, \$3.84 million grant from the National Cancer Institute to [characterize the immune response to KSHV infection](#). These insights will inform design of an immune system-stimulating vaccine and could aid scientists working to develop other therapeutics.

To Phipps’ clinical expertise in KS and KSHV, Boonyaratanakornkit and McGuire bring expertise in identifying and characterizing the immune cells and proteins that respond to viral infection. McGuire has done similar work on Epstein-Barr virus, another herpesvirus that can promote cancer.

“There are a lot of potential synergies,” Boonyaratanakornkit said. “Right now, KSHV is kind of a black box. We can really move the needle if we focus resources and labs on the problem.”

A need for new approaches

KSHV, also known as human herpesvirus 8, or HHV-8, is not as widespread as other herpesviruses, like HSV-1 and -2 and chickenpox. Most initial KSHV infections produce no symptoms, and the virus has a [varied geographic distribution](#). While over 50% of people in Africa have KSHV,

prevalence drops to 20-30% around the Mediterranean, and less than 10% in Europe and the U.S.

KSHV infects a range of cells, including certain immune cells and cells that line the skin and blood vessels. Once inside, KSHV sets up permanent residence, slumbering but rousable. If an infected person's immune function weakens, as in the later stages of HIV infection, the virus can reawaken and promote tumor development. Widespread antiretroviral treatment has made KS rare in the U.S., but in areas like sub-Saharan Africa where HIV is prevalent but therapeutics are less accessible, KS remains a problem.

KS shows up as characteristic dark purple patches on the skin. KSHV can also cause other cancers, including a type of lymphoma, as well as a lymphoproliferative disorder called multi-centric Castleman's disease.

Kaposi sarcoma has a high rate of complications and death, but the limited effectiveness of current treatments leaves patients in urgent need of new preventive and therapeutic approaches, Phipps said.

"The project is a good example of how Fred Hutch investigators can leverage the tremendous investment that the Fred Hutch [Global Oncology program](#) and the [Uganda Cancer Institute-Fred Hutch Collaboration](#) have made over many years to address questions of critical importance to improve the care of cancer worldwide," he said.

Outlining the immune response against KSHV

Understanding how our bodies build protection against KSHV, and what areas of the virus are most important to target, will be key to building a vaccine that elicits a protective immune response.

The new project capitalizes on each investigator's area of proficiency, as well as a biobank compiled as part of the [longstanding collaboration](#) between Fred Hutch and the UCI in Kampala, Uganda.

"These clinical cohorts are quite unique and represent a wide range of participant characteristics," Phipps said. "Multiple samples were collected longitudinally which will allow us to evaluate changes in antibody responses to KSHV over time."

Collected during three longitudinal clinical studies, samples were donated by adults and children, by participants with and without KS, and by people infected with KSHV as well as those who were not infected.

Herpesviruses are notoriously difficult to vaccinate against, but the team is taking advantage of technological advances that will give them unprecedented insight into the virus and how to neutralize it, Boonyaratanakornkit said.

He brings experience in culturing viruses and running the assays that test how well immune proteins called antibodies block or "neutralize" a microbe, as well as identifying regions of the virus that are key to that neutralization. McGuire has developed strategies to isolate and

characterize the immune cells that make antibodies.

“No one really knows, is it possible to prevent KSHV infection and disease?” McGuire said. “We’re trying to develop tools to dissect what is really happening in infected people, and then trying to leverage that information to address this unmet need for vaccination.”

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