Study identifies trigger for alternate reproduction of HIV-related cancer virus

April 17 2012

A research team led by Children's National Medical Center has identified a trigger that causes latent Kaposi's sarcoma-associated herpesvirus (KSHV) to rapidly replicate itself. KSHV causes Kaposi's sarcoma, primary effusion lymphoma, and other cancers that commonly affect immunocompromised patients, including those with AIDS. Appearing in the online edition of the *Journal of Virology*, the study identifies apoptosis, or the programmed death of a virus' host cell, as the trigger for high-level viral replication.

"Finding that the programmed death of a host cell triggered rapid production of Kaposi's sarcoma-associated herpesvirus, means that KSHV has the ability to sense and respond to critical changes in the cells that it grows in, something we didn't know before," stated lead author Alka Prasad, PhD, who is a member of the Center for Cancer and Immunology Research at Children's National Medical Center. "We previously thought that the virus was more of an inanimate entity. This newly discovered pathway is clearly helpful to the virus and clues researchers in on how we might target treatments. If the host cell died quickly, before the virus could reproduce, then the virus could not infect any new cells. Having the ability to sense when the host cell is about to die and reproduce quickly in response gives the virus an evolutionary advantage. In addition, cancers caused by KSHV and other herpesviruses are commonly treated with drugs that kill cells, so the results could have a significant effect on the treatment of KSHV-related cancers, which we will need to explore."

KSHV and the cancers it causes most commonly afflict patients with AIDS and other disorders that impact the immune system. KSHV attaches to white blood cells and either actively replicates through a controlled gene expression program or remains latent. A specific genetic protein in the virus, called an ORF50 gene product, is thought to control the transition from latency to replication. Using a derivative of this specific protein that blocks gene expression and replication, the scientists found that when apoptosis was induced, KSHV replicated itself. They also discovered that whether this derivative was present or not, apoptopsis induced the virus' replication.

"In addition to looking at the clinical implications of these research findings, we now need to focus in on the pathway that links apoptosis to this particular replication pathway and perhaps expand our research from KSHV to include another example of herpesvirus," commented Steven Zeichner, MD, PhD, the senior author on the paper, who is a principal investigator for the Center for Cancer and Immunology Research at Children's National and a professor at the George Washington University School of Medicine. The study was supported in part by the new NIH-funded District of Columbia Center for AIDS Research, of which Children's National is a key member.

Provided by Children's National Medical Center