MedicalXpress

Study finds that apoptosis triggers replication of common viruses

August 27 2013

Researchers from Children's National Medical Center have found that an alternate, "escape" replication process triggered by apoptosis—the process of cell death or "cell suicide"—appears to be common in human herpesviruses (HHV). The findings have implications for better understanding of viruses and of disease conditions and treatments, like chemotherapy, that stimulate apoptosis. The study was published online, ahead of print, in the *Journal of Virology*.

HHV are linked to a range of childhood and adult diseases, including chickenpox, mononucleosis, roseola, cold sores, and genital sores, and can be particularly troublesome for patients who are immunosuppressed because they have cancer or AIDS. Some HHV types are so common as to be nearly universal in humans. A central feature is their ability to remain latent for long periods of time, and then reactivate after the latent phase. Previously, reactivation was attributed largely to waning immunity, immunosuppression, or exposure to certain inducing agents.

In this study, Children's National researchers examined cell lines latently infected with several herpesviruses: HHV-4 or Epstein Barr Virus, the causative agent of mononucleosis; HHV-6A; HHV-6B, which causes the disease roseola in infants and infects almost all children in the first few years of life; HHV-7; and HHV-8 (or Kapsosi's Sarcoma-associated Herpesvirus), to explore whether an alternate, apoptosis-induced replication program is a common feature of HHV biology. They found that apoptosis triggers an alternate replication pathway in each HHV type studied.

"Our findings suggest that most if not all HHV types can sense that the host cell is dying, which prompts them to launch an emergency replication process," said lead author Alka Prasad, PhD, a post-doctoral fellow in the Center for Cancer and Immunology Research of the Children's Research Institute at Children's National. "Herpesviruses have genes that try to prevent apoptosis, but when the viruses cannot block the host cell from undergoing apoptosis, they apparently launch this alternate process to reproduce before the cell dies—suggesting that these herpesviruses are not simply destructive 'cell-bombs' but more nuanced organisms that engage in a dialogue with the host cell."

The study also found that commonly used chemotherapy agents activate this replication process, indicating that these and other treatments that promote apoptosis may activate latent HHV.

"Our findings make great sense from an evolutionary point of view. If the viruses didn't have this emergency alternative way of reproducing then, if the cell they were living in died, they would have no chance of making additional viruses. With this alternative process, the viruses have a chance of reproducing. This study also helps explain some observations that previously did not quite fit, like why HHV seemed to be activated in conditions associated with apoptosis," said senior author Steven Zeichner, MD, PhD, Senior Investigator for Children's Research Institute at Children's National and Professor of Pediatrics and Microbiology at George Washington University. "Clinically, these results suggest it may be beneficial to treat patients with antivirals against HHV when we expect apoptosis to be induced, such as in chemotherapy for cancer patients."

These new findings build on earlier research led by Children's National that showed HHV-8 to have an alternate replication path triggered when the host cell undergoes apoptosis and that this process generates a high volume of virus but with a lower infectivity rate.

More information: jvi.asm.org/content/early/2013 … 78-13.abstract#aff-2

Provided by Children's National Medical Center