Help from herpes? Coinfection induces acyclovir to inhibit HIV

September 10 2008

A surprising interaction may enable development of new HIV treatment strategies by exploiting infection with multiple pathogens. The research, published by Cell Press in the September 11th issue of the journal *Cell Host and Microbe,* demonstrates that a drug commonly used to treat herpes directly suppresses HIV in coinfected tissues and thus may be beneficial for patients infected with both viruses.

Commonly, individuals infected with HIV are infected also with other microbes. Infection with human herpesvirus (HHV), especially with herpes simplex virus-2 (HSV-2), is often associated with HIV. These HHV infections may be either active or dormant, but HIV infection makes HHV reactivation more likely.

For many years, acyclovir (ACV), a well-studied drug, has been used safely to treat HHV in humans. "HHV has a unique ability to phosphorylate ACV to activate it, making the drug quite specific for HHV and, for the same reason, relatively non-active against other viruses, including HIV," offers senior study author Dr. Leonid Margolis from the National Institute of Health. Nevertheless, some patients coinfected with HIV and HSV-2 exhibit lower HIV levels after ACV treatment.

"We decided to investigate this phenomenon experimentally using small blocks of human tissues" says Dr. Margolis. "Drs. Andrea Lisco and Christophe Vanpouille who performed this work in my laboratory found that although ACV doesn't inhibit HIV in 'sterile' cell lines, it does,

surprisingly, suppress HIV in tissues that carry no HSV-2 but various other HHVs." In collaboration with a prominent AIDS researcher Dr. Raymond Schinazi from Emory University and Dr. Matthias Gotte from McGill University, the researchers found that phosphorylated ACV that is formed in HHV-infected cells directly inhibits the HIV-1 reverse transcriptase (RT), thus preventing HIV from copying itself.

These results not only help to explain the response to ACV seen in patients coinfected with HSV-2 and HIV, but also suggest that ACV may be used against HIV in patients infected with various other HHVs, including the low-pathogenic and ubiquitous HHV-6 and HHV-7. Moreover, in collaboration with Drs. Balzarini from Catholic University of Leuven and McGuigan from Cardiff University, Dr. Margolis and his team demonstrated that new strategies for development of novel HIV inhibitors based on ACV structure can now be developed. "We provide definitive experimental evidence of inhibition of HIV-1 RT activity by phosphorylated ACV and demonstrate that ACV phosphorylation occurring in human tissues infected by various HHVs transforms this widely-used inexpensive anti-herpes drug into a direct HIV inhibitor," concludes Dr. Margolis.

Source: Cell Press