Experimental treatment regimen effective against HIV

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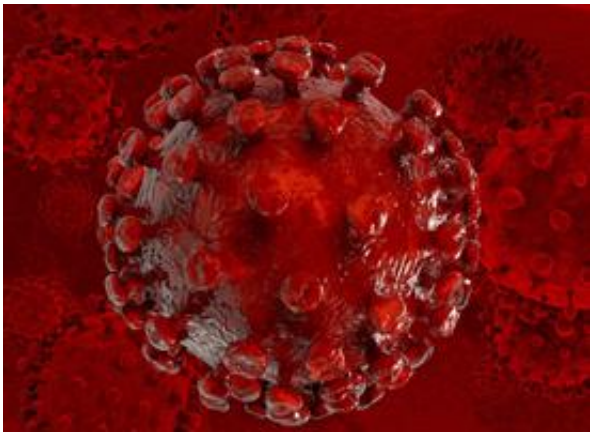

HIV virus

Protease inhibitors are a class of antiviral drugs that are commonly used to treat HIV, the virus that causes AIDS. Scientists at the University of Nebraska Medical Center designed a new delivery system for these drugs that, when coupled with a drug developed at the University of Rochester School of Medicine and Dentistry, rid immune cells of HIV and kept the virus in check for long periods. The results appear in the journal *Nanomedicine: Nanotechnology, Biology and Medicine*.

While current HIV treatments involve pills that are taken daily, the new regimens' long-lasting effects suggest that HIV treatment could be administered perhaps once or twice per year.

Nebraska researcher Howard E. Gendelman designed the investigational drug delivery system–a so-called "nanoformulated" protease inhibitor. The nanoformulation process takes a drug and makes it into a crystal, like an ice cube does to water. Next, the crystal drug is placed into a fat and protein coat, similar to what is done in making a coated ice-cream bar. The coating protects the drug from being degraded by the liver and removed by the kidney.

When tested together with URMC-099, a new drug discovered in the laboratory of UR scientist Harris A. ("Handy") Gelbard M.D., Ph.D., the nanoformulated protease inhibitor completely eliminated measurable quantities of HIV. URMC-099 boosted the concentration of the nanoformulated drug in immune cells and slowed the rate at which it was eliminated, thereby prolonging its therapeutic effect.

"The chemical marriage between URMC-099 and antiretroviral drug nanoformulations could increase drug longevity, improve patient compliance, and reduce general toxicities," said Gendelman, lead study author and professor and chair of the Department of Pharmacology and Experimental Neuroscience at Nebraska, who has collaborated with Gelbard for 24 years. "We are excited about pursing this research for the treatment and eradication of HIV infections."

The two therapies were tested together in laboratory experiments using human immune cells and in mice that were engineered to have a human immune system. Gendelman and Gelbard believe that the nanoformulation technology helps keep the protease inhibitor in white blood cells longer and that URMC-099 extends its lifespan even more.

Gelbard, director of UR's Center for Neural Development and Disease, developed URMC-099 to treat HIV-associated neurocognitive disorders or HAND, the memory loss and overall mental fog that affects half of all patients living with HIV. He tested it with several protease inhibitors,

including the nanoformulated version developed by Gendelman, as any patient prescribed URMC-099 would also be taking antiretroviral therapy. The goal was to determine whether the drugs could be safely administered together. Much to Gelbard and Gendelman's surprise, URMC-099 increased the effectiveness of the nanoformulated drug.

"Our ultimate hope is that we're able to create a therapy that could be given much less frequently than the daily therapy that is required today," said Gelbard. "If a drug could be given once every six months or longer that would greatly increase compliance, reduce side effects and help people manage the disease, because they won't have to think about taking medication every day."

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