

RIT Targeting of HIV-Infected Cells

Newspapers and media outlets around the world carried news in the first weeks of November that researchers from the Albert Einstein College of Medicine of Yeshiva University (New York, NY) had developed “radioactive guided missiles” to successfully target and destroy human immune cells infected with HIV. Although some newspapers sensationalized the story almost beyond recognition, the results of the research—as described in the original article e-published on November 7 ahead of print in *PLoS Medicine*, an open access journal published by the Public Library of Science—are extraordinarily promising. Ekaterina Dadachova, PhD, lead author of the study and an associate professor in the departments of nuclear medicine and microbiology & immunology at Einstein, has been a pioneer in radioimmunotherapeutic approaches to infectious disease. She noted that applying these techniques to HIV is a logical and compelling next step. “Twenty-five years from the start of the epidemic, HIV is still an incurable disease—something completely different needs to be done to eradicate it,” she said. In previous animal studies beginning in 2001, Dadachova and colleagues successfully used RIT approaches against a variety of disease-causing microbes, including *Cryptococcus neoformans* and *streptococcus pneumoniae*.

In the HIV proof-of-principle in vitro and in vivo study, the researchers’ target was the protein gp41, one of several proteins in the HIV-1 virus that are “displayed” on the surface of HIV-1-infected cells. After obtaining antibodies that would attach specifically to gp41, the researchers labeled them with ^{213}Bi and ^{188}Re and determined their ability to selectively kill chronically HIV-1-infected human T cells and acutely HIV-1-infected human peripheral blood mononuclear cells (hPBMCs) in vitro. One group of severe combined immunodeficiency (SCID) mice harboring HIV-1-infected hPBMCs in the spleen were injected with various doses of a ^{213}Bi - or ^{188}Re -labeled monoclonal antibody (mAb), and another group of similar mice were treated with a nonradiolabeled version of the mAb. Three days after injection, the number of HIV-1-infected cells in mice receiving the radiolabeled doses was significantly (>99% in the highest dose group) reduced in a dose-

dependent manner. In addition, the number of HIV-1-infected thymocytes decreased 2.5-fold in human thymic implant grafts of SCID mice treated with the ^{188}Re -labeled antibody to gp41 compared with those treated with the control mAb. Both isotopes proved effective in eliminating the virus-infected cells from the mice, and no acute toxicities were noted.

“This study in mice supports the idea that RIT might help in treating people infected with HIV,” said Arturo Casadevall, MD, PhD, chair of the department of microbiology and immunology at Einstein and a senior author of the study. “More broadly, this work introduces a new approach for treating the many viral infections, from hepatitis C to Ebola, in which viral proteins are expressed on the surface of infected cells.”

“Today’s antiretroviral drug therapies can inhibit the multiplication of HIV and help prevent HIV from infecting additional cells,” said Harris Goldstein, MD, director of the Center for AIDS Research at Einstein and another senior author of the study. “But we currently have no way of eliminating the HIV-infected cells that make these infections chronic. The novelty of this technique is that it targets the cells infected by HIV, which act as ‘factories’ for making more of the virus. So if we could eradicate all the HIV-infected cells in a patient—which would likely require a combination of therapies—then we could start to think about curing HIV-infected patients.”

The researchers noted that RIT might be particularly useful for individuals newly exposed to HIV, such as health care workers with needlestick injuries. “Studies show that giving highly active antiretroviral therapy (HAART) to people within 24 hours of exposure to HIV can prevent infection from developing,” said Goldstein. “But if several days have passed, the virus is able to infect enough cells to cause a chronic HIV infection. By combining HAART with RIT, we may be able to prevent lifelong infection in these people by eliminating those initially infected cells.”

Planning for clinical trials using RIT approaches for treating HIV infection is now underway.

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