Targeted irradiation: A new weapon against HIV?

November 7 2006

Antiretroviral therapy can keep HIV infection in check and delay and ameliorate the symptoms of HIV/AIDS. However, the drugs do not manage to eradicate the virus completely; individuals have to stay on the drugs permanently. Preclinical studies in mice by Ekatarina Dadachova and colleagues (Albert Einstein College of Medicine) published in the international open-access journal PLoS Medicine now suggest a new strategy to locate and kill many if not all HIV-infected cells in the body.

Radioimmunotherapy refers to an approach pioneered by cancer researchers in which patients are injected with antibodies against specific molecules characteristic of cancer cells (or in this case, HIV-infected cells) which carry a radioactive isotope. The approach takes advantage of the antibody's ability to rapidly hone in on its target cells and deliver the radioactive payload which then selectively kills the target cells and any HIV particles within it.

The study included some test-tube experiments on HIV infected human white blood cells as well as experiments on HIV infected mice that were injected with the radioactive antibodies. The researchers found that HIV infected white blood cells were successfully killed by radioactive antibodies that had been developed against specific proteins in the HIV particle that are routinely displayed at the surface of infected cells.

Two different types of antibodies and two different types of radioactive payload were tried. Both antibodies were very effective in targeting HIV infected cells, but one type of radioactive tag (213-Bismuth) was more

efficient in killing the HIV-infected target cells than the other (188-Rhenium).

Then, mice were infected with HIV and treated with the radioactive antibodies (these particular mice had a deficient immune system, which means that they can be infected with the HIV virus that normally does not infect mice). The number of HIV infected cells was reduced in the treated mice compared with control animals, which were treated with antibodies not joined to a radioactive tag. The greater the antibody dose, the greater the proportion of HIV infected cells that were killed.

To assess 'collateral damage' the researchers examined whether the treatment with the radioactive antibodies damaged the red blood cells in the infected mice. They saw a drop in red blood cell numbers only for the mice receiving the highest dose of antibodies, suggesting that there is dose at which the antibodies are efficient and selective at killing their specific target cells.

These results provide initial support for the idea that radioimmunotherapy could work against HIV/AIDS and are encouraging for two reasons: First, because HIV is a formidable opponent and patients and doctors need as many different strategies as possible to help patients control the disease. And second, because they hint at the possibility of eradicating HIV completely, something that Dadachova and colleagues speculate would have the best chance of working at the early stage of infection right after someone is exposed to the virus.

Citation: Dadachova E, Patel MC, Toussi S, Apostolidis C, Morgenstern A, et al. (2006) Targeted killing of virally infected cells by radiolabeled antibodies to viral proteins. *PLoS Med* 3(11): e427.

dx.doi.org/10.1371/journal.pmed.0030427