Humanized mouse infected with HIV vaginally and rectally allows testing

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The "humanized mouse" developed by Dr. J. Victor Garcia-Martinez has allowed the University of Texas Southwestern physician-scientist to conduct HIV/AIDS studies that would have been impossible without such a small animal model of HIV infection. The virus only infects humans and chimpanzees, which are protected as endangered species.

But because the new mouse model is a chimera, with a human immune system, it can be infected. Last year, using these humanized mice, a team of scientists led by Dr. Garcia-Martinez demonstrated that antiretroviral drugs given before and after exposure to HIV could prevent vaginal transmission of the virus. That suggests the possibility that women at high risk of HIV infection might one day be able to take a pill on a regular basis. And, since the drugs tested are already available, having gone through the long and complex approval process, that day might be sooner rather than later.

On Sunday, April 19, Dr. Garcia-Martinez tells fellow scientists attending Experimental Biology 2009 in New Orleans that the team is now using the mouse model to obtain evidence that these same approaches apply to protecting men.

Dr. Garcia-Martinez's presentation, updating improvements in the humanized mouse and in the progress of this and other work using the mouse model of human HIV/AIDS infection, is part of the scientific program of the American Society for Biochemistry and Molecular Biology.

First created in 2006, by Dr. Garcia and colleagues at UT Southwestern and the University of Minnesota, the humanized mouse used in these studies represented a new frontier in the preclinical testing of experimental drugs. Early mice models of disease were created by breeding mice that were immunodeficient in order that they would not reject grafts of human tissue. The big advance in the mouse created by Dr. Garcia-Martinez's group is that the mouse develops a human immune system, thanks to transfer of fetal human liver and thymic tissue cells that repopulate the bone marrow, which produces more cells.

The problem with using animals other than humans and chimpanzees for HIV/AIDS studies had been that the other animals, including ordinary mice, never become infected even when exposed to massive amounts of the virus. But the Garcia-Martinez mouse model (called BLT for bone marrow-liver-thymus) can easily be infected with HIV by both rectal and vaginal transmission, since both areas of the mouse body contain human cells.

With a long term-goal to investigate novel approaches to prevent HIV transmission, the team began with male to female infection. Women are at higher risk of infection during heterosexual sex with an infected partner, and women worldwide account for more than half of the estimated 11,000 newly acquired infections every day, with a majority of those transmissions occurring via the vaginal route. However, says Dr. Garcia-Martinez, male to male sexual contact accounts for a high proportion of the HIV/AIDS cases in the United States and rates of such transmission continue to rise, despite extensive educational campaigns.

Dr. Garcia-Martinez believes these statistics clearly reflect an urgent need to devise and implement potential interventions that could prevent both vaginal and rectal HIV-1 transmission especially among high-risk populations. The humanized mouse model provides an increasingly effective tool to move in that direction.

Source: Federation of American Societies for Experimental Biology (news : web)