

Mouse model shows potential efficacy of HIV prevention strategy

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A new kind of laboratory mouse can be used to test the efficacy of much-needed methods to prevent transmission of HIV, the virus that causes AIDS, according to research by J. Victor Garcia and colleagues at the University of Texas Southwestern Medical Center in Dallas.

The findings, published in *PLoS Medicine*, demonstrate the utility of such mice for animal testing of pre-exposure antiviral drugs to protect against HIV infection. Such mice also provide a new way of evaluating microbicides and other prevention approaches that have generally required testing in macaques, using viruses that are related, but not identical, to HIV.

Unmodified mice cannot be infected with HIV. Earlier laboratory-modified mice, such as the SCID-hu mouse, contain human thymic tissue that can only become infected after direct injection, but not through any of the natural routes of HIV transmission in humans including the genital route. However, of the 2.5 million newly acquired HIV infections estimated to have occurred in 2007, more than half were in women, mostly through unprotected vaginal sex with an infected male partner.

The new development involves “BLT” mice, which have been transplanted with human blood cells, liver, and thymus tissue. The researchers found that human cells necessary for HIV infection distributed themselves in the female reproductive tract of BLT mice, rendering them susceptible to vaginal infection with HIV. They also

found that infection spread to other organs in a way that resembles the course of HIV infection in humans. Finally, they showed that vaginal infection could be blocked by treating the mice with antiretroviral drugs that are currently being evaluated as pre-exposure prophylaxis (PrEP) -- a possible means of HIV prevention in humans at risk for sexual exposure to HIV.

These findings support the promising results of PrEP studies from established, but costly, macaque models. Whether the BLT mouse – or any animal model -- provides a reliable predictor of HIV prevention in humans can only be determined by comparison of animal experiments to actual human trials.

The paper is discussed in a related perspective article by Barbara Shacklett (University of California Davis), entitled “Can the New Humanized Mouse Model Give HIV Research a Boost?” At this stage, says Dr Shacklett, “the most prudent approach is to consider the new humanized rodents and the more established, nonhuman primate models as complementary systems, both of which can yield useful information but neither of which is infallible.”

Citation: Denton PW, Estes JD, Sun Z, Othieno FA, Wei BL, et al. (2008) Antiretroviral pre-exposure prophylaxis prevents vaginal transmission of HIV-1 in humanized BLT mice. PLoS Med 5(1) e16.

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