PrEP treatment prevented HIV transmission in humanized mice

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Systemic pre-exposure administration of antiretroviral drugs provides protection against intravenous and rectal transmission of HIV in mice with human immune systems, according to a new study published January 21, 2010 in the online journal *PLoS ONE.*

"These results provide evidence that a universal approach to prevent all forms of HIV transmission in all settings might be possible," said J. Victor Garcia-Martinez, Ph.D., professor in the department of medicine at the University of North Carolina at Chapel Hill School of Medicine and senior author of the study. "This could greatly facilitate the implementation of a single program capable of targeting virtually all groups of people at high risk of HIV infection."

According to data from the national Centers for Disease Control and Prevention, HIV diagnoses increased by a staggering 15 percent between 2004 and 2007. Rectal exposure is the leading cause of HIV transmission among men who have sex with men, and since the beginning of the epidemic, more than 500,000 have been diagnosed with HIV in the United States alone and more than 300,000 have died.

These latest findings are welcome news after the recent announcements that an AIDS vaccine trial in Thailand showed only marginal success and a large international trial of a vaginal microbicide found no evidence that it reduces the risk of HIV infection.

The research, using pre-exposure prophylaxis (PrEP) with

antiretrovirals, was conducted using a humanized mouse model developed by Garcia-Martinez and colleagues at the University of Texas Southwestern Medical Center. The animals are known as "BLT" mice, because they are transplanted with human bone marrow, liver and thymus cells, which results in a fully functioning human immune system.

"Although results from humanized mice cannot be extrapolated directly to humans, our data indicate that one intervention approach could potentially block multiple routes of HIV transmission in people," said the paper's lead author, Paul Denton, Ph.D., who is a research instructor in the department of medicine at the UNC School of Medicine.

The humanized mice were either control mice and received no drugs or were administered the commonly prescribed antiretroviral drug therapy Truvada and then exposed to HIV - either rectally or intravenously - at a level much higher than would occur in typical human exposure. None of the nine treated BLT mice that were exposed rectally showed any sign of the virus after exposure; they were completely protected. However, 12 of the 19 control BLT mice became HIV positive following rectal exposure.

Among humanized mice exposed intravenously, a transmission route which is more difficult to block, all six of the control BLT mice became infected, but seven of the eight treated BLT mice - 90 percent - were protected against the virus.

Garcia-Martinez's team previously demonstrated that PrEP is also highly effective against vaginal HIV transmission and with this study their research shows that PrEP can prevent HIV spread by the three modes that account for over 90 percent of all HIV infections worldwide.

Results of this study not only have important human clinical

implications, but also could significantly improve drug studies. There are already PrEP trials in humans, but their continuation is threatened due in part to ethical concerns over administering drugs to healthy people with no hard evidence that they will work.

"Now the head of a clinical trial can take this research to a ministry of health or review board and say, 'Look, we have positive experimental evidence that if we do this right it has a chance to work,'" Denton said.

Mark Wainberg, Ph.D., who is professor of microbiology and virology at McGill University in Montréal and director of the McGill AIDS Centre, said, "This is outstanding work that helps to advance the field of HIV prevention science. This research provides excellent rationale for the continuation of PrEP clinical trials."

"It is painfully clear that treatment alone will not put a dent in the progression of the AIDS epidemic," said Garcia-Martinez, also an investigator in the UNC Center for AIDS Research. "There is a strong need for interventions like PrEP that could prevent new infections and slow the epidemic."

Provided by University of North Carolina