

Innate Immune System Can Kill HIV When a Viral Gene Is Deactivated



Human cells have an intrinsic capacity to destroy HIV. However, the virus has evolved to contain a gene that blocks this ability. When this gene is removed from the virus, the innate human immune system destroys HIV by mutating it to the point where it can no longer survive.

This phenomenon has been shown in test tube laboratory experiments, but now researchers at the University of North Carolina School of Medicine have demonstrated that the same phenomenon occurs in a humanized mouse model, suggesting a promising new target for tackling the virus, which has killed nearly 30 million people worldwide since it first appeared three decades ago.

A family of human proteins called APOBEC3 effectively restrict the growth of HIV and other viruses, but this action is fully counteracted by the viral infectivity factor gene (*vif*) in HIV. In the study, researchers intravenously infected humanized mice with HIV. They found that the most commonly transmitted strains of HIV are completely neutralized by APOBEC3 proteins when *vif* is removed from the virus.

“Without the *vif* gene, HIV can be completely destroyed by the body's own immune system,” said J. Victor Garcia, PhD, professor of medicine at the UNC School of Medicine and senior author on the study. “These results suggest a new target for developing drugs fully capable of killing the virus.”

Garcia and his colleagues pioneered the humanized mouse model used for these studies. The aptly named “BLT” mouse is created by introducing human bone marrow, liver and thymus tissues into animals without an immune system of their own. The mice have a fully functioning human immune system and can be infected with HIV in the same manner as humans. In previous research, Garcia and his team have effectively prevented intravenous, rectal, vaginal and oral transmission of HIV in the mice with pre-exposure prophylaxis (PrEP).

For the current study, Garcia and his colleagues also infected BLT mice with another, highly harmful strain of the virus. The results show that this strain of HIV does continue to replicate, even without *vif*, but at a much slower rate and without harming the human immune system. Further, the researchers found that virus replication in this case was limited to one tissue—the thymus—in the entire body.

“These findings demonstrate a fundamental weakness in HIV,” said John F. Krisko, PhD, lead author on the study. “If this weakness can be exploited, it might eventually lead to a cure for HIV/AIDS,” Krisko said.

The study appears March 28 in the online journal *PLoS Pathogens*.

In addition to Garcia and Krisko, other study authors are Francisco Martinez-Torres, PhD, and John L. Foster, PhD, all of the Center for AIDS Research at the University of North Carolina School of Medicine.

University of North Carolina School of Medicine via newswise

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