Discovery suggests a new way to prevent HIV from infecting human cells

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Researchers at the University of Minnesota have discovered how HIV binds to and destroys a specific human antiviral protein called APOBEC3F. The results suggest that a simple chemical change can convert APOBEC3F to a more effective antiviral agent and that shielding of a common feature shared by related proteins may yield a similar outcome.

This discovery highlights the potential for a novel approach to combating HIV/AIDS that would seek to stabilize and harness the innate antiviral activity of certain human proteins, according to lead author John Albin, a researcher in the laboratory of Reuben Harris, associate professor of biochemistry, molecular biology and biophysics in the College of Biological Sciences.

The finding was published in the Journal of Biological Chemistry. For a copy of the abstract and/or full article, contact Preston Smith or John Albin.

Human cells produce a family of antiviral proteins (called APOBECs) that have the unique and natural ability to destroy HIV. But HIV has evolved a way to overcome restriction using an accessory protein called Vif (virion infectivity factor) to degrade the APOBEC proteins and allow the virus to spread. Albin and colleagues learned where Vif interacts with one antiviral protein, APOBEC3F, and showed how the connection can be interrupted by a simple chemical change on the surface of APOBEC3F. They also noted that similar interaction sites are

found on the same surface in other members of this antiviral protein family.

"This suggests that the interaction between Vif and these antiviral APOBEC proteins could be blocked with a drug that would shield the Vif interaction region," Albin says. "Such an intervention has the potential to allow as many as seven natural antiviral drugs to spring into action and prevent HIV from spreading."

The Harris lab is focuses on understanding every level of the vital interaction between these human cellular proteins and HIV Vif. They envision that future studies will involve a more refined mapping of the physical interactions between Vif and APOBEC3 proteins, investigation of the potential for HIV to resist stabilizing changes in APOBEC3 proteins, and screens for drug-like compounds that help the cellular APOBECs destroy HIV.

John Albin, a student in the Combined MD-PhD Training Program at the University of Minnesota Medical School, and is completing a thesis under the guidance of his advisor, Reuben Harris, through the Microbiology, Immunology & Cancer Biology PhD program. His studies in the Harris lab focus on the potential of APOBEC proteins to impact HIV evolution and pathogenesis.

This latest finding builds on a body of research from Harris's lab about the relationship between HIV and APOBEC proteins. In 2003 and 2004, Harris helped discover that the APOBEC proteins have the ability to counteract HIV infection.

Harris, who won a 2009 challenge grant from the Bill & Melinda Gates Foundation to explore ways to block HIV and APOBEC3 interaction, has been studying mechanisms of mutation for nearly 20 years, first as a doctoral student at the University of Alberta, then as a post-doctoral

fellow at the Laboratory of Molecular Biology in Cambridge, England, and for the past seven years as an NIH supported principal investigator at the University of Minnesota. His laboratory focuses on how mutations can be harnessed to destroy pathogens.

Provided by University of Minnesota