Certain IFITM proteins block and inhibit cell-to-cell transmission of HIV

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Shan-Lu Liu made a discovery in how specialized proteins can inhibit the virus, opening the door for progress in the fight against HIV and for the production of advanced therapeutics to combat the disease. Credit: Roger Meissen, Bond Life Sciences Center

There is little doubt that the Human Immunodeficiency Virus, or HIV, is devastating. More than 1.2 million people in the United States are living with HIV and more than 47,000 people are diagnosed annually. Now, University of Missouri researchers have made a discovery in how specialized proteins can inhibit the virus, opening the door for progress

in the fight against HIV and for the production of advanced therapeutics to combat the disease.

Human cells express Interferon Induced Transmembranes (IFITM) proteins that possess antiviral characteristics. These proteins have been shown to inhibit a number of viruses including influenza A, West Nile, Dengue fever and Ebola. In his study, Shan-Lu Liu, an associate professor in the Department of Molecular Microbiology and Immunology in the School of Medicine and an investigator in the Bond Life Sciences Center at MU, targeted IFITM proteins and their antiviral function.

"We have long understood that IFITM proteins have antiviral functions, but until now we did not know exactly how the proteins specifically inhibited the transmission of HIV" Liu said. "We've known that HIV-1, the most common HIV strain, can be transmitted from cell to cell or through a cell-free transmission in which the virus floats freely. Our research discovered that IFITM proteins can help inhibit the viral cell-to-cell infection, which is the most efficient way that HIV spreads."

Jingyou Yu, a doctoral student in MU's pathobiology graduate program, conducted experiments to show that IFITM proteins, particularly IFITM2 and IFITM3, block HIV cell-to-cell transmission. Yu then partnered with Minghua Li, who is also a graduate student in pathobiology, and discovered that IFITM proteins specifically interact with the HIV-1 envelope glycoprotein and inhibit its maturation that is required for viral infectivity and transmission. Additionally, Liu worked with research labs in Canada and New York, to reproduce and verify his findings.

"This discovery is quite surprising, given our previous finding in PLoS Pathogens where we found that this family of proteins generally affects the lipid property of cell membrane and blocks fusion of different

viruses with host cells," said Liu. "In HIV and AIDS research, scientists are constantly learning more about virus transmission and host response to viral infections. By understanding and visualizing how some IFITM proteins can inhibit and block transmission, we are getting closer to finding better therapeutic approaches in the fight against HIV."

The study, "IFITM Proteins Restrict HIV-1 Infection by Antagonizing the Envelope Glycoprotein," recently was published in *Cell Reports*.

More information: "IFITM Proteins Restrict HIV-1 Infection by Antagonizing the Envelope Glycoprotein." DOI: dx.doi.org/10.1016/j.celrep.2015.08.055

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