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Mathematical modeling uncovers mysteries of HIV infection in the brain

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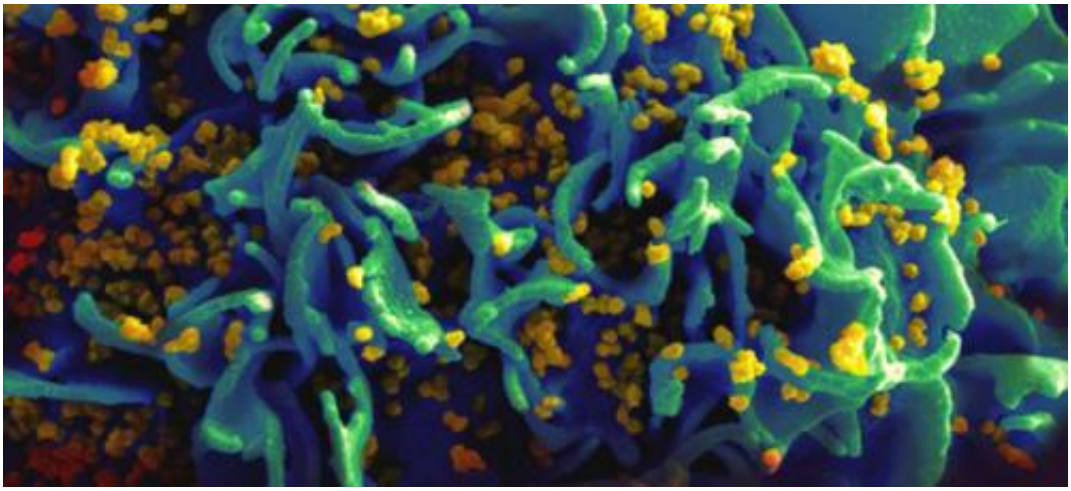

An HIV-infected cell. Credit: NIAID

After uncovering the progression of HIV infection in the brain thanks to a new mathematical model developed by a UAlberta research team, clinicians and researchers are developing a nasal spray to administer drugs more effectively.

The group that developed the model—led by PhD student Weston Roda and Michael Li, a professor in the Department of Mathematical and Statistical Sciences—used data from patients who died five to 15 years after they were infected, as well as known biological processes for the HIV virus to build the model that predicts the growth and progression of HIV in the brain, from the moment of infection onward. It is the first

model of an infectious disease in the brain.

HIV infection in the brain has been a proverbial black box for scientists since the development of antiretroviral therapy in the 1990s.

"The nature of the HIV virus allows it to travel across the blood-brain barrier in infected macrophage—or white blood cell—as early as two weeks after infection. Antiretroviral drugs, the therapy of choice for HIV, cannot enter the brain so easily," said Roda.

This creates what is known as a viral reservoir, a place in the body where the virus can lay dormant and is relatively inaccessible to drugs. Prior to this study, scientists could only study brain infection at autopsy. The new model allows scientists to backtrack, seeing the progression and development of HIV infection in the brain. Using this information, researchers can determine what level of effectiveness is needed for antiretroviral therapy in the brain to decrease active infection.

"The more we understand and can target treatment toward viral reservoirs, the closer we get to developing total suppression strategies for HIV infection," said Roda. In fact, his results are already being put to use in a University of Alberta lab.

A research team led by Chris Power, Roda's co-supervisor who is a professor in the Division of Neurology, is planning clinical trials for a nasal spray that would get the drugs into the brain faster—with critical information on dosage and improvement rate provided by Roda's model.

"Our next steps are to understand other viral reservoirs, like the gut, and develop models similar to this one, as well as understand latently infected cell populations in the brain," said Roda. "With the antiretroviral therapy, infected cells can go into a latent stage. The idea is to determine the size of the latently infected population so that clinicians

can develop treatment strategies"

The paper, "Modeling brain lentiviral infections during antiretroviral therapy in AIDS," was published in the *Journal of Neurovirology*.

Provided by University of Alberta