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Radioactive tracers map spread of HIV analogue

Monkey study uses labelled antibodies and routine imaging to track infection and lingering reservoirs of virus.

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Scientists have imaged an analogue of HIV as it spread through the bodies of live macaque monkeys using radioactive markers and routine radiology techniques. The researchers hope to use the method to follow lurking human infections that could otherwise evade detection.

Monkey Business Images/REX

Macaque bodies can harbour the simian version of HIV even when their blood counts of the virus are virtually undetectable.

Francois Villinger, a virologist at Emory University School of Medicine in Atlanta, Georgia, and his team worked with rhesus macaques (*Macaca mulatta*) that had been infected with simian immunodeficiency virus (SIV), the non-human-primate equivalent of HIV, for between two and six years.

The scientists tagged SIV antibodies, which bind to the outer envelope of the virus, with copper-64, a radioactive isotope used in experimental radiotherapy against cancer. The isotopes emit signals that can be captured using scanning techniques called positron-emission tomography (PET) and computed tomography (CT) — both widely used in modern hospitals.

At the International Science Symposium on HIV and Infectious Diseases in Chennai, India, in late January, Villinger reported that after he and his collaborators injected the macaques with the tagged antibodies, they were able to map the presence of the virus as it replicated extensively in the large intestines, lymph nodes, spleen and nasal areas of chronically infected monkeys. The team verified the finding by checking cells from tissue samples for SIV.

Hidden virus

Some monkeys controlled the infection, either naturally or after treatment with antiretroviral drugs, and had undetectable levels of virus in their blood plasma. But the scanning images showed a residual signal in the small intestines, lymph tissues and male reproductive tract, although none was present in the large intestines.

When the scientists monitored macaques that had been infected with SIV for only two weeks, they found abundant viral signals in the upper body, including the lungs and nose, which gradually cleared. As the infection became chronic, the signals amplified in the lower gut.

Villinger said that in humans infected with HIV, the technique could help to detect hidden reservoirs of virus that are not eliminated through treatment with anti-HIV drugs.

"The model presented provides very important insights about where to look," virologist Asier Sáez-Cirión of the Pasteur Institute in Paris, told *Nature* after attending Villinger's talk. His team is trying to establish if there are hidden reservoirs in people who are infected with HIV but seem to be able to control its multiplication.

Ramesh Paranjape, director of India's National AIDS Research Institute in Pune, says the studies indicate that the virus persists in the mucus lining of the nose, and that it remains in multiple tissues in the body even after six months of antiretroviral treatment. "A longer follow-up will help in understanding the dynamics of the virus reservoir and sites of multiplication in animals successfully treated," says Paranjape, who also was on hand at the meeting.

However, some of the scientists interviewed by Nature at the meeting pointed to several challenges that need to be addressed before the tool can be used in disease management. In particular, they said, the method is not yet very good at quantifying the amounts of viral particles present in any particular region of the body.