Researchers claim to find HIV sanctuaries

The most powerful antiretrovirals may not reach virus lurking in some tissues

By Jon Cohen

For all the progress made in HIV treatment, a depressing factstands in the way of a cure. Even after powerful antiretroviral drugs (ARVs) have driven the virus down to undetectable levels in the blood, it isn’t gone. It lurks in “reservoirs,” out of reach of treatment, and if drugs are stopped it almost always rebounds. But exactly how these reservoirs stick around for a person’s entire life is contentious.

A new study supports a controversial proposal about why HIV persists in spite of aggressive treatment. The standard view is that the virus lies dormant inside of human chromosomes, out of reach of treatment because it is not replicating. The new study, published online in the 27 January issue of Nature by a prominent group of HIV/AIDS researchers, suggests instead that despite the barrage of drugs, HIV continues to replicate, sheltered in the lymph nodes, which ARVs have trouble reaching.

“The debate is over: There is ongoing replication” in people on ARVs who have no detectable virus in their blood, contends the Nature study’s lead author, virologist Steven Wolinsky of Northwestern University Feinberg School of Medicine in Chicago, Illinois. If he’s right, the current best hope of curing HIV infection—“kicking” latently infected cells to produce virus, which would lead to their destruction—will need rethinking. Instead, a cure might also have to up the dose of existing ARVs or develop others that target tissues may be far lower than in blood—not high enough to stop all viral replication (Science, 23 December 2011, p. 1614). To test that possibility, the team analyzed HIV genetic sequences in difficult-to-obtain samples of lymph nodes taken over 6 months in three patients. All had started ARVs and fully suppressed the virus on standard blood tests. HIV mutates each time it copies itself, so if the virus were replicating in the lymph nodes, the sequences should show signs of evolution. The researchers found just that: sequence changes showing that HIV had evolved in the lymph node of each patient. A slow trickle of new virus was apparently being produced.

Coffin counters that he and others have seen no signs of evolution in several studies that examined virus found in the blood of patients who take powerful ARVs for longer than a decade. He and Mellors fault the machine Wolinsky and his colleagues relied on—a Roche 454 DNA Sequencer—which is no longer used by most labs. “The reason it’s obsolete is it had unacceptably high error rates,” Mellors says.

“He’s categorically wrong,” Wolinsky counters. “As long as you know the errors introduced by the technique, you can control for it.” He points out the group analyzed each sample twice and obtained the same results.

Antiretroviral drugs reduced HIV levels in this man’s blood to minuscule levels, but his lymph node cells (purple) still produced detectable viral RNA (green).

Wolinsky and co-authors agree. They hope their study will spark clinical experiments that attempt to increase ARV concentration in lymph nodes and then assess the impact on HIV reservoirs. “It’s a spectacular debate,” Wolinsky says. “And if indeed we have ongoing replication in these drug sanctuaries, we now have a new path to a cure.”

Published by AAAS