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Can a transplant drug help eliminate lingering HIV infections?

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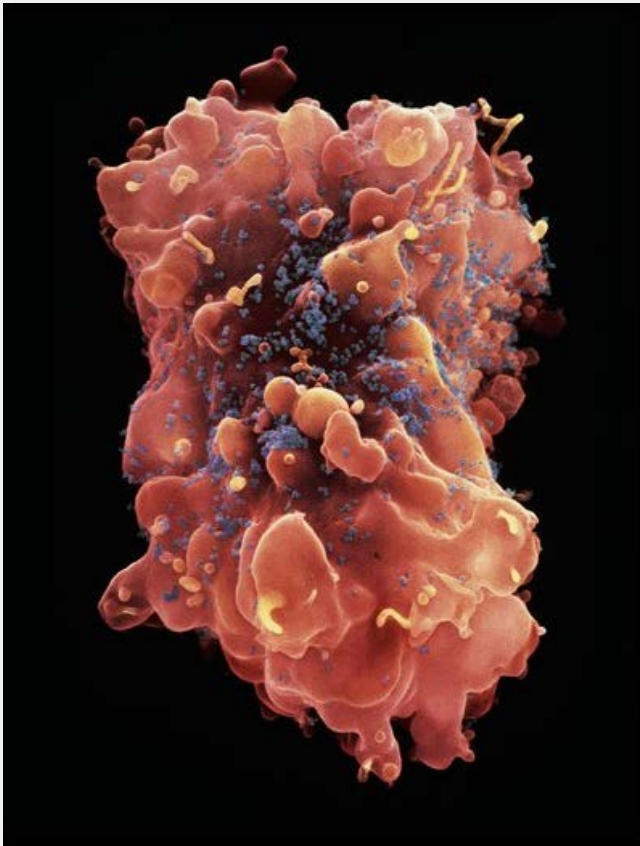
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A photographic print called "HIV Virus on the Surface of a White Blood Cell." (Fowler Museum at UCL / April 3, 2014)



HIV cure dealt a setback

By Monte Morin
April 4, 2014 | 7:00 a.m.

Researchers studying the effects of immune suppressant drugs on transplant patients with HIV have made a surprising discovery: A drug intended to hobble the body's defense system may actually help destroy dormant reservoirs of the virus that causes AIDS.

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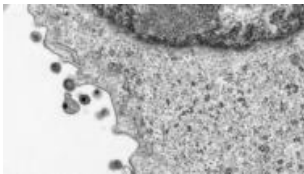
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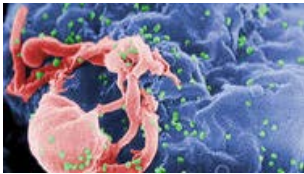
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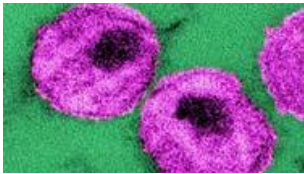
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In a [paper](#) published this week in the [American Journal of Transplantation](#), authors found that when a small group of transplant patients received the drug sirolimus, they experienced a two- to threefold drop in HIV levels, whereas patients who received other immunosuppressants did not.

"We were pleasantly surprised," said study coauthor Dr. Steven Deeks, an HIV expert and professor of medicine at University of California San Francisco. "It's difficult with any drug to affect the [HIV] reservoir."

Modern antiretroviral therapy, or ART, is able to stop the human immunodeficiency virus from replicating and destroying a patient's immune system, yet the cocktail of drugs is unable to wipe out the virus entirely.

As a result, low levels of HIV persist in the body indefinitely, and patients must continue taking costly drugs, or risk a renewed assault on their immune system.

Scientists have been pursuing a number of means of destroying these so-called reservoirs, including "[kick and kill](#)" strategies that involve activating the dormant virus and then attacking it.

Deeks and his colleagues however have proposed a different approach, one that includes reducing inflammation.

Recent research has suggested that tissue inflammation helps HIV spread, because it summons the body's immune cells, which are the preferred targets of HIV.

Sirolimus, which is also known as rapamycin, is believed to help reduce inflammation, but also has other benefits, study authors said.

Among those benefits was sirolimus' ability to prevent the immune system's T-cells from producing a protein called CCR5, which normally coats the cell's exterior.

HIV uses CCR5 as a doorway to enter the cell and once inside the host, the virus hijacks the cell's machinery and starts making copies of itself.

Nathalia Holt, a molecular biologist who was not involved in the study, said sirolimus' ability to attack HIV in several ways made it a promising treatment.

"You can see how this could work really nicely in a clinical trial," she said.

Holt, who authored the book "Cured" -- the story of two men who appear to have been cured of HIV after treatment in Berlin -- said the combination of immune suppression and HIV resistance may have played a role in at least one case.

"Multipronged approaches like this one are our best bet at finding a therapy that's curative," she said.

The recent study examined 91 kidney transplant patients with HIV -- 9% of whom received sirolimus. The data was taken from a larger, previously published trial that looked at 275 transplant patients to determine the safety and efficacy of using immunosuppressant drugs on HIV patients.

Because the study was not designed to specifically examine the effects of sirolimus, the authors said further research was needed to confirm its effects on HIV. In fact, the National Institutes of Health has agreed to sponsor a targeted study of 30 patients, according to Deeks.

"We saw a very important, statistically significant signal, but I wouldn't jump on this bandwagon that sirolimus is going to cure HIV," said coauthor Dr. Peter Stock, a transplant surgeon and professor at UCSF. "It does require a bigger study."



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VIDEO

In most transplants, the recipient's immune system responds to the new organ as it would any foreign body -- it attacks it. Because of this, most transplant patients must undergo a lifetime drug regimen that stifles their body's defense system.

For many years, transplant surgeons believed that HIV patients should not receive replacement organs because their immune systems were already compromised. To suppress it further with drugs would hasten the onset of AIDS, they reasoned.

That view began to change though with the advent of new antiretroviral drugs.

Stock said that as a transplant surgeon, he was interested to see that while sirolimus appeared to reduce HIV levels for some patients, none of the variety of immunosuppresants studied was associated with an increase in the virus.

"We didn't lose control, and that's important," Stock said.

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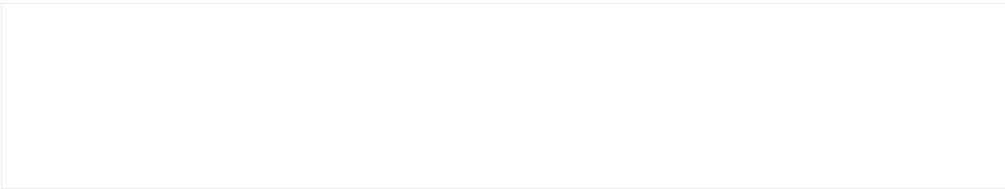
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