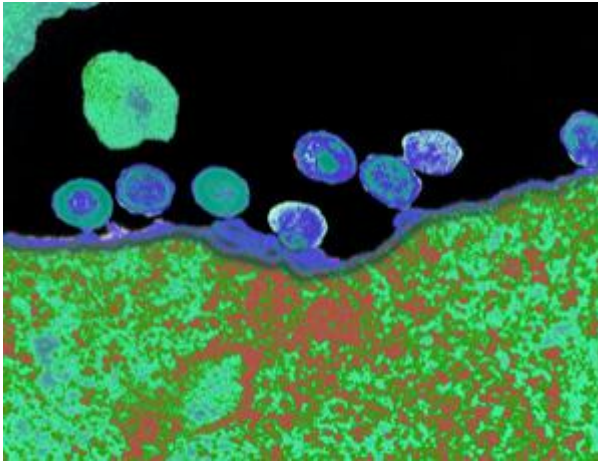


New Scientist

By Andy Coghlan

February 19, 2010



HIV is the cure (Image: Voisin/Phanie/Rex Features)

A company is planning to inject people with an HIV vaccine made of the deadly virus itself, albeit a deactivated version.

Vaccines against many viruses, including flu, are made from deactivated versions of those viruses, but [such an approach](#) was previously dismissed as too risky in the case of HIV.

Now [Virxsys](#) of Gaithersburg, Maryland, is resurrecting the controversial approach, thanks to successful tests of a similar vaccine against SIV – also known as simian HIV – in monkeys.

"We said 'let's use HIV against itself', and that's what we're doing," says Gary McGarrity, Virxsys's vice president of scientific and clinical affairs.

High-profile flop

The idea of turning to the virus itself follows years of frustration with prospective vaccines based on viruses other than HIV, such as adenoviruses that cause colds.

Adenoviruses have been modified to carry parts of the HIV virus. Although there were hints of [modest success](#) with one such vaccine last year, the [previous best bet proved to be a high-profile flop in 2007, during a trial dubbed "STEP"](#).

Crucially, the new tests in monkeys suggest a vaccine based on HIV itself might be more effective than these attempts. The company is planning to apply for approval to perform human trials.

Virxsys says such trials would initially be only in people who already carry the virus, rather than in healthy people at risk of infection. This will certainly make for a less controversial trial, as it would avoid any chance of the vaccine going "live" and infecting people who didn't have HIV to start with.

Virus slashed

For now, though, the company's latest results, presented on Thursday at the 2010 annual [Conference on Retroviruses and Opportunistic Infections](#) in San Francisco, are limited to a vaccine based on a deactivated version of simian HIV called SIV.

Virxsys researchers described how they vaccinated monkeys, and then six months later injected them with SIV. Within weeks of receiving the injection of SIV, concentrations of the virus had fallen by at least 95 per cent in those treated.

After a year, when the trial ended, these concentrations remained low, whereas untreated monkeys became progressively sicker as their immune systems were depleted by the virus. "We expect them to die in the next few weeks," says McGarrity.

What's more, in vaccinated animals, concentrations of CD4+ cells – the immune cells that both HIV and SIV attack and kill - remained the same, suggesting their immune systems were able to withstand SIV infection.

"These results give us the green light to proceed," says Franck Lemiale of Virxsys, who led the two-year trial and presented the results. "We cannot be sure that this will work as well in humans, but this is the point of performing clinical trials.

Entry only

Virxsys is convinced that the HIV vaccine it is planning would be safe because, as in their SIV vaccine, all the genes that would usually make it infectious and able to multiply itself would be removed. "It can't replicate," says Lemiale.

All that would be left of the dozen or so genes that HIV normally has would be the three – called *gag*, *pol* and *rev* – that enable it to infiltrate cells and embed itself into their DNA. This means the vaccine's version of the virus only undergoes one cycle of protein production, which enables it to get inside a few cells, but then can't spread further.

The hope is that the vaccine version of HIV would invade sentinel cells, known as dendritic cells - as the SIV-based vaccine did in the monkeys. These would then prime the immune system's T-cells to attack the real virus, should it turn up in the body.

Dodge this

The monkey trials also suggested that a vaccine based on HIV itself might be more effective than previous vaccines based on cold viruses.

The "STEP" HIV-vaccine trial had to be halted prematurely in 2007 when it emerged that antibodies produced by the body against the vaccine may have [provided HIV with more target cells to infect](#), speeding its spread.

But Virxsys's tests in monkeys revealed that the animals did not produce antibodies against the SIV-based vaccine itself. This suggests that an HIV-based vaccine might dodge the problems that dogged the STEP trial.

Potent mix?

Virxsys is not the first company to successfully test SIV-based vaccines in monkeys. A team led by [David Evans](#) of Harvard Medical School in Southborough, Massachusetts, reported successfully protecting monkeys a year ago with a similar "single-cycle" vaccine, this time containing all but one of the SIV genes, but he had no intention of transferring the work to people.

There is still the possibility, however, that in people that already have HIV, the vaccine version of the virus could recombine with the incumbent full-strength strain, and evolve into an even more potent adversary.

Evans thinks Virxsys has made this less likely by limiting the vaccine virus to a single cycle of infection. "That certainly makes it safer than a replication-competent live attenuated virus," he says.