Cancer drug promises to break down barrier to HIV cure

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The reservoirs of dormant HIV have been the main barrier to a cure. Credit: anaxila/Flickr, CC BY

Researchers have found a promising way of kicking the AIDS virus out of its hiding place in infected cells, potentially removing the main

obstacle to curing HIV.

While antiretroviral treatment successfully suppresses HIV replication in an infected person, it can't completely remove the virus. This is due to the virus' ability to integrate itself into the DNA of cells, where it can lie dormant and invisible to the body's immune system for years.

These so-called "reservoirs" of what is known as "latent virus" are the primary barrier to an HIV cure. Recent research has focused on a "shock and kill" method, to shock the dormant virus out of its comfortable place in the reservoir. When the virus is active, it becomes a visible target to kill.

Previous attempts with agents called histone deacetylase (HDAC) inhibitors have shown inconsistent results. HDACs, that enable a virus to coil tightly around a cell's DNA, are the primary reason for its successful ability to hide undetected.

If an HDAC inhibitor is potent enough, it could stimulate the unravelling and activation of the virus. Research published today in *PLOS Pathogens* shows the HDAC inhibitor, romidepsin - a drug currently being used to treat cancer - to be the most potent, and thus successful, inhibitor trialled so far.

Six patients, who had been on antiretroviral treatment for around 10 years, each received three transfusions of romidepsin. The dormant HIV was activated in five of the participants, making it a detectable target for elimination.

University of Melbourne Professor and Director of the Doherty Institute, Sharon Lewin, said the results were promising.

"It is an interesting study because it shows the effects of a more potent

drug, which can activate or kick the virus out of hiding," she said.

Researchers also found romidepsin coaxed the virus out of its reservoir without suppressing the body's broader immune response.

"There's been some concern that these drugs will suppress an immune response to the virus, and they looked pretty comprehensively to show that there was no suppression of immune function, so that was encouraging as well," said Professor Lewin, who was not involved in the study.

Dr Kersten Koelsch, who was involved in the study, explained there had been concerns the HDAC inhibitors might negatively affect T cell responses, which play an important part in fighting infection.

"We know that the HIV reservoir needs to be controlled to some extent by T cell responses," said Dr Koelsch, who is a senior lecturer at UNSW Australia's Kirby Institute. "So if you had a weak T cell response after an intervention, that would be counterproductive. But it appears that this is not the case with these HDAC inhibitors."

But Dr Koelsch also stressed that although the results were positive, researchers were by no means close to a HIV cure.

"Unless a miracle happens, there's not going to be a cure for HIV for at least 10 or even 20 years," he said.

"Small studies like this can be very informative for the next study which can then build upon it, and the next study will then be another piece in the puzzle that will be important to design the study afterwards."

He said romidepsin was a "promising agent to check in future studies in combination with immunotherapies or vaccines."

This will indeed be the next phase of the two-part trial, which will use a combined therapy of romidepsin with a HIV vaccine to kill the infected cells.

"Combination studies are of highest interest now. We need to know whether the combination of activation of the virus with boosting the immune system will actually clear the infected cell. That's really what we're after now," said Professor Lewin.

Senior Research Officer at the Burnet Institute, Lachlan Gray said the latest research was extremely promising. But he added there were limitations to current HIV research as it focused only on eliminatig the viral reservoir in the blood.

"Tackling the blood reservoir has been the major focus of cure research to this point, predominantly because it is the major HIV reservoir. Importantly, this research sets the scene for efforts focused on non-blood reservoirs such as the gut, and brain" said Dr Gray, who researches HIV replication in brain cells.

"To completely eradicate HIV from the infected individual, that is, where there's a complete elimination of every HIV infected cell in the body, we need to target all reservoirs, not just the predominant blood reservoir."

"I think we're making inroads, and the more research, the more information gathered from important studies such as this, the closer we get to the end goal, which is curing HIV," he said.

Source: The Conversation