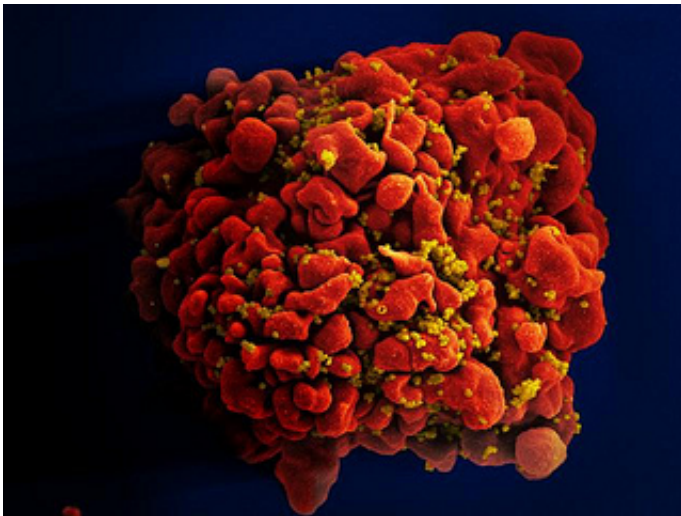


Scientists see mechanism for spontaneous HIV 'cure' (Update)

November 4 2014, by Mariette Le Roux, Brigitte Castelnau



Scanning electron micrograph of an HIV-infected H9 T cell. Credit: NIAID

French scientists claimed Tuesday to have found the genetic mechanism for a "spontaneous cure" in two HIV-infected men, proposing a new strategy for combating AIDS even as other experts urged caution.

The findings were based on a study of two men infected with the human immunodeficiency virus (HIV) who never developed AIDS symptoms.

The virus remained in their immune cells but was inactivated because its genetic code had been altered, said the scientists.

They sequenced the HIV genome in samples taken from the pair who, they said, had experienced an "apparent spontaneous cure".

The mutation may be linked to a common enzyme named APOBEC, the team said.

"The work opens up therapeutic avenues for a cure, using or stimulating this enzyme," they said in a statement.

The work, published in the journal *Clinical Microbiology and Infection*, was carried out by scientists at France's Institute of Health and Medical Research (Inserm).

Some, however, found the results unconvincing.

"If it came across my desk for review, it would get short shrift, to be honest," University of Nottingham molecular virology professor Jonathan Ball told AFP, insisting the team had provided "no evidence" of a functional cure.

HIV replicates by invading human CD4 immune cells, which it reprogrammes to become virus factories.

A rare group of people—fewer than one percent of those infected—are naturally able to rein in viral replication and keep the virus at clinically undetectable levels.

They are known as "elite controllers", but the mechanism by which they keep the virus at bay remains a mystery.

The French group looked at two such individuals, a 57-year-old man diagnosed HIV-positive in 1985, and a 23-year-old in 2011.

Though they remained infected, standard tests could not detect the virus in their blood.

In both cases, the virus was unable to replicate in immune cells due to mutations in its genetic code, the team found.

And they said this may be explained by spontaneous evolution between humans and the virus, a process called "endogenisation" that is believed to have neutralised other viruses in humans in the past.

A similar process has been witnessed in a population of koalas that has integrated an AIDS-like virus into their genes, neutralised it, and were passing resistance on to their offspring.

No evidence?

"We propose that HIV cure may occur through HIV endogenisation in humans," the team wrote.

But Ball said endogenisation can only happen by the altered virus being passed on to offspring through semen or egg cells.

"I am not aware at all of them showing the presence of the virus in any gamete," he said, referring to reproductive cells.

The team said their findings implied that persistence of HIV DNA in human cells, rather than eradication, is what may lead to a cure and protection.

The approach hitherto has been the opposite: to try and clear all traces of HIV from human cells and from cell reservoirs where they hide.

"We suggest that persistence of integrated HIV DNA is not a barrier, but

on the contrary, may be a prerequisite to HIV cure," said the study authors.

The team said they did not believe their two patients were unique or that the phenomenon was new.

And they called for "massive sequencing" of human DNA, particularly from Africans who had been exposed to HIV for longest, to find further proof.

Sharon Lewin, director of the Doherty Institute for Infection and Immunity in Melbourne, Australia, said the suggested shift in strategy "has some merit."

"But, and it is a big but, the trick will be to work out which protein is key in 'crippling' the virus," cautioned Lewin.

Daisy Ellis, policy director at the Terrence Higgins Trust AIDS charity, said "there is still quite some distance between studies like this and an eventual cure".

"For the time being, using condoms and testing regularly are our best tools against the virus."

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Citation: Scientists see mechanism for spontaneous HIV 'cure' (Update) (2014, November 4) retrieved 18 April 2024 from

<https://medicalxpress.com/news/2014-11-scientists-mechanism-spontaneous-hiv.html>

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