WIRED SCIENCE

HIV Evolution Outpaces Vaccines

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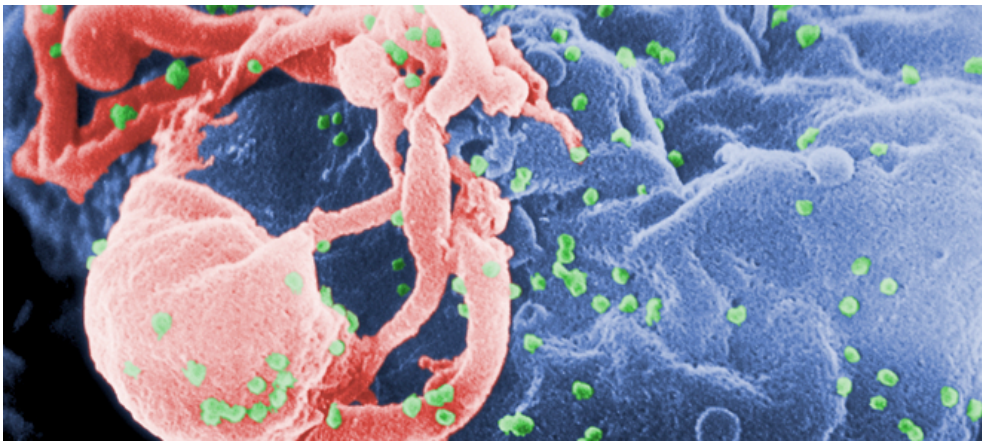

The AIDS virus is rapidly evolving to recognize and evade human immune systems, making the development of a vaccine even less likely than it already is.

Researchers already knew that HIV adapts on a person-by-person basis, but they didn't know if those changes were passed to the viral population at large. Gene sequencing of HIV samples taken from 2,800 people show that changes have spread throughout the world.

The adaptations involve genes responsible for coding proteins that are recognized by white blood cells. Troublingly, the most rapidly-evolving HIV genes appear to be those used by the human immune system to identify its enemies.

"The virus is out-running human variation," said study co-author Rodney Phillips, an Oxford University immunologist, in a press release.

The findings, published Wednesday in *Nature*, are the latest setback for the beleaguered field of AIDS vaccine development. Hundreds of millions of dollars have been spent on vaccines, none of which have worked, with the most high-profile vaccine — developed by Merck and the National Institutes of Health — appearing to increase infection risks.

However, though HIV's rapid adaptations may make vaccines — necessarily targeted at a frozen-in-time viral profile — obsolete, it's not necessarily outrunning the evolution of human immune response. That's a small consolation, but consolation nonetheless.

"It could equally be that as the virus changes, different immune responses come into play and are actually more effective," said Philip Goulder, an Oxford University pathologist and study co-author.

Citation: "Adaptation of HIV-1 to human leukocyte antigen class I." By Yuka Kawashima, Katja Pfafferott, John Frater, Philippa Matthews, Rebecca Payne, Marylyn Addo, Hiroyuki Gatanaga, Mamoru Fujiwara, Atsuko Hachiya, Hirokazu Koizumi, Nozomi Kuse, Shinichi Oka, Anna Duda, Andrew Prendergast, Hayley Crawford, Alasdair Leslie, Zabrina Brumme, Chanson Brumme, Todd Allen, Christian Brander, Richard Kaslow, James Tang, Eric Hunter, Susan Allen, Joseph Mulenga, Songee Branch, Tim Roach, Mina John, Simon Mallal, Anthony Ogwu, Roger Shapiro, Julia G. Prado, Sarah Fidler, Jonathan Weber, Oliver G. Pybus, Paul Klenerman, Thumbi Ndung'u, Rodney Phillips, David Heckerman, P. Richard Harrigan, Bruce D. Walker, Masafumi Takiguchi & Philip Goulder. Nature, Vol. 457 No. 7233, Feb. 25, 2009

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- Gene Editing Could Make Anyone Immune to AIDS
- Cellular 'Bullets' Destroy HIV, Raise Vaccine Possibilities

BBC NEWS

Rapid HIV evolution avoids attack

HIV is evolving rapidly to escape the human immune system, an international study has shown.

The Nature study highlights just how tough it could be to develop a vaccine that keeps pace with the changing nature of the virus.

The researchers showed HIV was able to adapt rapidly to counter human genes controlling immune system molecules that can target it for destruction.

However, they stressed this would not effect the impact of anti-HIV drugs.

> " **The implication is that once we have found an effective vaccine, it would need to be changed on a frequent basis to catch up with the evolving virus** "
> Professor Philip Goulder
> University of Oxford

HIV has already killed 25 million people, and an estimated 33 million are currently infected.

However, HIV does not kill all people at the same rate. On average, without treatment it takes 10 years for the infection to progress to Aids, but some people develop the disease within 12 months, while others do not do so for more than 20 years.

The rate of progress is tied to genes which control production of key immune system molecules called human leucocyte antigens (HLAs).

Humans differ in the exact HLA genes they have, and even small differences can have a big impact on how quickly Aids develops.

The researchers examined HIV genetic sequences and HLA genes in over 2,800 people in countries, including the UK, Australia, South Africa, Canada and Japan.

'Escape' mutations

They found mutations that enabled HIV effectively to neutralise the effect of a particular HLA gene were more frequent in populations with a high prevalence of that specific gene.

For example, a HLA gene called B*51 is particularly effective at controlling HIV - unless the virus is carrying an "escape" mutation in its genetic make-up.

The researchers found that in Japan, where the B*51 gene is common, two-thirds HIV-positive people without the gene carry HIV armed with the "escape" mutation.

In contrast, in the UK, where the gene is much less common, just 15%-25% of this group of patients are infected with HIV which carries the same key mutation.

Lead researcher Professor Philip Goulder, of the University of Oxford, said similar effects were seen for every HLA gene examined.

He said: "This shows that HIV is extremely adept at adapting to the immune responses in human populations that are most effective at containing the virus.

"This is high-speed evolution that we're seeing in the space of just a couple of decades."

"The temptation is to see this as bad news, that these results mean the virus is winning the battle.

"That's not necessarily the case. It could equally be that as the virus changes, different immune responses come into play and are actually more effective.

"The implication is that once we have found an effective vaccine, it would need to be changed on a frequent basis to catch up with the evolving virus, much like we do today with the flu vaccine."

Big challenge

Jo Robinson, of the HIV charity Terrence Higgins Trust, said: "HIV is a complex virus which is constantly changing.

"This kind of research suggests that if we're able to create a vaccine that works against HIV, the virus will always be one step ahead.

"In that case we'd be in a situation where we need to constantly update the HIV vaccine, a bit like we see with a different flu vaccine each year."

Keith Alcorn, of the HIV information service NAM, said: "These findings indicate the enormous challenge involved in developing a vaccine against HIV.

"People need to be aware that the research required to develop a successful vaccine may take decades, during which the virus will continue to evolve, as this research shows."

Story from BBC NEWS:
http://news.bbc.co.uk/go/pr/fr/-/1/hi/health/7907774.stm

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PRESS ASSOCIATION

Rapid evolution of Aids virus could hamper HIV vaccine treatment, experts warned

Aids virus 'evading immune system'

15 hours ago

Rapid evolution of the Aids virus could make it more difficult to fight HIV with a vaccine, experts have warned.

A new study led by researchers at Oxford University shows that the virus is changing to evade the human immune system.

The scientists looked at the genetic codes of HIV viruses from more than 2,800 people around the world. They compared them with human leucocyte antigen (HLA) genes from the same group.

HLA enables the immune system to recognise and kill infected cells, including those invaded by the Aids virus. Everyone has his or her own unique set of HLA genes.

HIV mutations that allow the virus to evade certain versions of HLA were found more often in populations with those HLA genes. This was strong evidence that HIV was adapting to the human immune system at population level.

One of the HLA genes most successful at controlling HIV is known as HLA-B*51. But in people with this gene, HIV tends to change into a mutant form that is immune to it.

Around 96% of HIV positive people with the HLA-B*51 gene were found to have the mutation.

"We saw similar effects in every mutation that we looked at," said Professor Philip Goulder, who led the Oxford scientists. "This shows that HIV is extremely adept at adapting to the immune responses in human populations that are most effective at containing the virus."

Co-author Professor Rodney Phillips, also from Oxford University, said: "Where a favourable HLA gene is present at high levels in a given population, we see high levels of the mutations that enable HIV to resist this particular gene effect. The virus is out-running human variation, you might say."

The findings are published in the journal Nature.