Medical Xpress

HIV uses several strategies to escape immune pressure

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A study of how HIV mutates in response to immune system pressure by Emory Vaccine Center researchers shows that the virus can take several escape routes, not one preferred route.

The results are online and scheduled for publication in the September issue of the journal *Public Library of Science Pathogens*.

The human immune system has the ability to temporarily overpower HIV in early infection. Recent research has shown that most newly infected patients develop neutralizing antibodies. These are blood proteins that glob onto the virus and would allow patients to defend themselves - if they were facing only one target.

The problem: HIV's ability to mutate, disguising itself enough to get away from the antibodies. HIV eventually wears down the immune system into exhaustion.

The Emory team's results suggest that if researchers succeed in identifying a vaccine component that can stimulate neutralizing antibodies, HIV's capacity for rapid mutation could still be a confounding factor.

A single type of neutralizing antibody may not be enough to contain HIV, says senior author Cynthia Derdeyn, PhD, associate professor of pathology at Emory University School of Medicine, Emory Vaccine Center and Yerkes National Primate Research Center.

"These neutralizing antibodies work really well - they hit the virus fast and hard," she says. "But so far, every time we look, the virus escapes."

Derdeyn and her colleagues collaborated with a public health program directed by Susan Allen, PhD, professor of global health at Emory's Rollins School of Public Health, that enrolls heterosexual couples with one HIV-positive partner in Zambia. The program provides thousands of couples counseling and condom supplies every three months. Despite these measures, a low level of HIV transmission still occurs.

The collaboration allowed the team to take blood samples a few weeks after infection occurred and then later as two participants' immune responses continued. Senior researchers Rong Rong and Bing Li isolated individual viruses over the first two years of HIV infection and tested how well the patients' own antibodies could neutralize them.

"In one patient where we had very early samples, there was evidence that neutralizing antibody came up within weeks, and that's earlier than what was previously thought," Derdeyn says.

The initially infecting virus starts off homogenous because of a "genetic bottleneck" effect.

In both patients, some viruses mutated part of their outer proteins so that after the mutation, an enzyme would be likely to attach a sugar molecule to it. The sugar interferes with antibody attack. However this tactic, known as the "glycan shield," was not observed in all cases. Other viruses mutated the part of the outer protein that the neutralizing antibodies stick to directly. In both patients, many changes in the virus' genetic code were necessary for escape.

"We need to understand early events in the immune response if we are going to figure out what a potential vaccine should have in it," Derdeyn

says. "What we can show is that even in one patient, several escape strategies are going on."

That means that in order to be immune to HIV infection, someone may need to have several types of neutralizing antibodies ready to go. Seeing how the virus mutates will allow researchers to choose the best parts to put in a vaccine, she says.

A companion paper in the same issue of *PLOS Pathogens* from South African researchers demonstrates similar cycles of neutralizing antibody attack and escape.

More information: R. Rong et al. Escape from Autologous Neutralizing Antibodies in Acute/Early Subtype C HIV-1 Infection Requires Multiple Pathways. *PLOS Pathogens* (2009).

Source: Emory University (news : web)