Scientists identify immunological profiles of people who make powerful HIV antibodies

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Barton F. Haynes in a screen shot from the video. Credit: Shawn Rocco/Duke Health

One of the main mysteries confounding development of an HIV vaccine is why some people infected with the virus make the desired antibodies after several years, but a vaccine can't seem to induce the same response.

A research team led by scientists at the Duke Human Vaccine Institute has been unraveling that mystery, detailing new insights in a study published July 29 in the journal *Science Immunology*.

Studying 100 HIV-infected people—half whose immune systems eventually made antibodies capable of broadly neutralizing the virus and half whose immune systems did not—the researchers found several key immune differences that should help in the development of a how-to manual for an effective vaccine.

"This work gives us the beginning of an understanding of the immune mechanisms that control development of broadly neutralizing antibodies, which is a major goal of a successful HIV vaccine," said Barton F. Haynes, M.D., director of the Duke Human Vaccine Institute and senior author of the study. "This moves forward important concepts for vaccine design to overcome a roadblock that has been present since we began this work 30 years ago."

In earlier work, Haynes and colleagues studied a person with both HIV and a form of lupus erythematosus, which is an autoimmune disease. The person's immune system both controlled the virus and developed broadly neutralizing antibodies.

The researchers have hypothesized that the same immune disruptions that caused the person to develop lupus were somehow enabling the broadly neutralizing antibodies to fulfill their potential and fight the virus.

Now, by directly studying large numbers of HIV-infected people whose immune systems made broadly neutralizing antibodies, the researchers found that they have similar immune alterations, or perturbations, as found in individuals with autoimmune disease.

"In essence, HIV cloaks its vulnerable sites that the immune system wants to see by making them resemble our own tissues, thereby creating an environment in which the virus is protected and the beneficial antibodies are treated as a threat to the body", said lead author Anthony Moody, M.D., chief medical officer of the Duke Human Vaccine Institute.

"These findings suggest that for a broadly neutralizing antibody-inducing HIV vaccine to be successful, we will need to mimic with vaccination the immune perturbations that occur in the setting of HIV infection," Haynes said.

"The important point here is that the first step to finding a way around a roadblock, is to be able to understand the biology behind the problem," Haynes said. "We now know what we need to do. The next step is to figure out how to safely mimic what happens in infection when the right antibodies are induced."

More information: M Moody et al. Immune perturbations in HIV-1-infected individuals who make broadly reactive neutralizing antibodies. *Science Immunology* DOI: 10.1126/sciimmunol.aag0851 (2016).

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